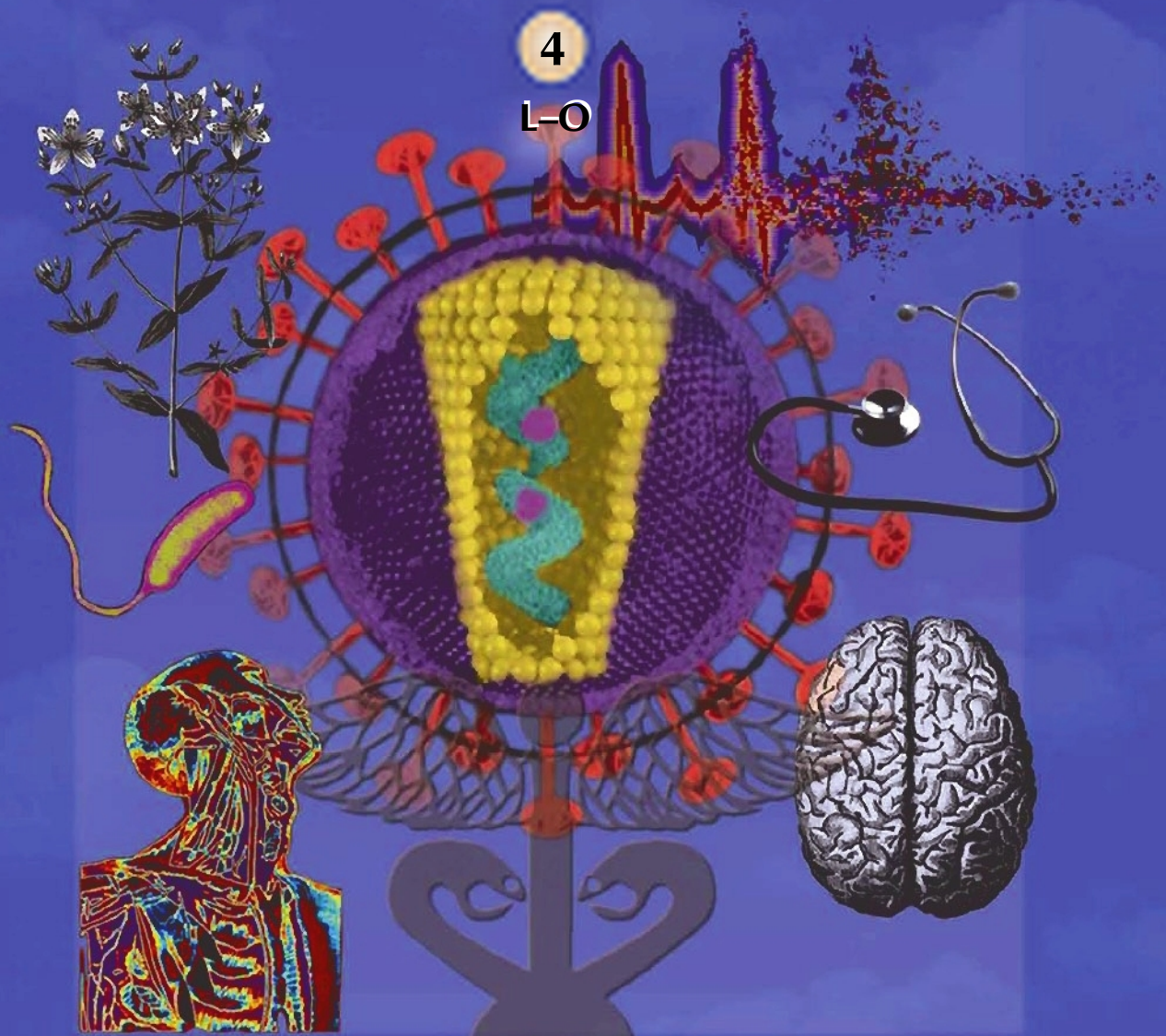
The GALE ENCYCLOPEDIA of Medicine

FOURTH EDITION

VOLUME

4

L–O



The GALE ENCYCLOPEDIA *of* MEDICINE

FOURTH EDITION

The GALE ENCYCLOPEDIA of MEDICINE

FOURTH EDITION

VOLUME

4

L–O

LAURIE J. FUNDUKIAN, EDITOR

GALE
CENGAGE Learning

Detroit • New York • San Francisco • New Haven, Conn • Waterville, Maine • London

GALE
CENGAGE Learning

Gale Encyclopedia of Medicine, Fourth Edition

Project Editor: Laurie J. Fundukian

Image Editors: Donna Batten and Kristin Key

Editorial: Donna Batten, Kristin Key, Jacqueline Longe, Kristin Mallegg, Brigham Narins, Jeffrey Wilson, Alejandro Valtierra

Product Manager: Kate Hanley

Editorial Support Services: Andrea Lopeman

Indexing Services: Factiva, a Dow Jones Company

Rights Acquisition and Management: Robyn Young

Composition: Evi Abou-El-Seoud

Manufacturing: Wendy Blurton

Imaging: John Watkins

Library of Congress Cataloging-in-Publication Data

Gale encyclopedia of medicine—4th ed. Laurie J. Fundukian, editor.
p. ; cm.
Other title: Encyclopedia of medicine
Includes bibliographical references and index.
ISBN 978-1-4144-8646-8 (set : alk. paper) ISBN 978-1-4144-8647-5 (volume 1 : alk. paper)-- ISBN 978-1-4144-8648-2 (volume 2 : alk. paper)--
ISBN 978-1-4144-8649-9 (volume 3 : alk. paper)-- ISBN 978-1-4144-8650-5 (volume 4 : alk. paper)-- ISBN 978-1-4144-8651-2 (volume 5 : alk. paper)--
ISBN 978-1-4144-8633-8 (volume 6 : alk. paper)--
1. Internal medicine--Encyclopedias. I. Fundukian, Laurie J. II. Title: Gale Group III. Title: Encyclopedia of medicine.
[DNLM: 1. Internal Medicine--Encyclopedias--English. 2. Complementary Therapies--Encyclopedias--English. WB 13]

RC41.G35 2011
616.003–dc22 2010053605

Gale
27500 Drake Rd.
Farmington Hills, MI, 48331-3535

ISBN-13: 978-1-4144-8646-8 (set)
ISBN-13: 978-1-4144-8647-5 (vol. 1)
ISBN-13: 978-1-4144-8648-2 (vol. 2)
ISBN-13: 978-1-4144-8649-9 (vol. 3)
ISBN-13: 978-1-4144-8650-5 (vol. 4)
ISBN-13: 978-1-4144-8651-2 (vol. 5)
ISBN-13: 978-1-4144-8633-8 (vol. 6)

ISBN-10: 1-4144-8646-4 (set)
ISBN-10: 1-4144-8647-2 (vol. 1)
ISBN-10: 1-4144-8648-0 (vol. 2)
ISBN-10: 1-4144-8649-9 (vol. 3)
ISBN-10: 1-4144-8650-2 (vol. 4)
ISBN-10: 1-4144-8651-0 (vol. 5)
ISBN-10: 1-4144-8633-2 (vol. 6)

This title is also available as an e-book.
978-1-4144-8691-8
Contact your Gale, a part of Cengage Learning sales representative for ordering information.

Printed in China
1 2 3 4 5 6 7 15 14 13 12 11

CONTENTS

LIST OF ENTRIES

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W

X

Y

Z

PLEASE READ—IMPORTANT INFORMATION

The *Gale Encyclopedia of Medicine, Fourth Edition* is a health reference product designed to inform and educate readers about a wide variety of health topics such as diseases, disorders and conditions, treatments and diagnostic tests, diets, alternative treatments, and prevention. Gale, Cengage Learning believes the product to be comprehensive, but not necessarily definitive. It is intended to supplement, not replace, consultation with a physician or other healthcare practitioners. While Gale, Cengage Learning has made substantial efforts to provide information that is accurate, comprehensive, and up-to-date, Gale, Cengage Learning makes no representations or warranties of any kind, including without limitation, warranties of merchantability or fitness for a particular purpose, nor does it guarantee the accuracy, comprehensiveness, or timeliness of the information contained in this product. Readers should be aware that the universe of medical knowledge is constantly growing and changing, and that differences of opinion exist among authorities. Readers are also advised to seek professional diagnosis and treatment for any medical condition, and to discuss information obtained from this book with their healthcare provider.

INTRODUCTION

The *Gale Encyclopedia of Medicine 4 (GEM4)* is a one-stop source for medical information on common medical disorders, conditions, tests, treatments, drugs, and other health-related topics, including high-profile diseases such as AIDS, Alzheimer's disease, cancer, and heart disease. This encyclopedia avoids medical jargon and uses language that laypersons can understand, while still providing thorough coverage of each topic. The *Gale Encyclopedia of Medicine 4* fills a gap between basic consumer health resources, such as single-volume family medical guides, and highly technical professional materials.

Scope

More than 1,800 full-length articles are included in the *Gale Encyclopedia of Medicine 4*, including disorders/conditions, tests/procedures, and treatments/therapies. Many common drugs are also covered, with generic drug names appearing first and brand names following in parentheses—e.g., acetaminophen (Tylenol). Prominent individuals in medicine are highlighted as sidebar biographies that accompany the main topical essays. Articles follow a standardized format that provides information at a glance. Rubrics include:

Disorders/Conditions	Tests/Treatments
Definition	Definition
Demographics	Purpose
Description	Precautions
Causes and symptoms	Description
Diagnosis	Preparation
Treatment	Aftercare
Prognosis	Risks
Prevention	Normal/abnormal results
Resources	Resources
Key terms	Key terms

In recent years, there has been a resurgence of interest in holistic medicine that emphasizes the connection between mind and body. Aimed at achieving and maintaining good health rather than just eliminating disease, this approach has come to be known as alternative medicine. The *Gale Encyclopedia of Medicine 4* includes a number of essays on alternative therapies, ranging from traditional Chinese medicine to homeopathy and from meditation to aromatherapy. In addition to full essays on alternative therapies, the encyclopedia features specific **Alternative treatment** sections for diseases and conditions that may be helped by complementary therapies. The *Gale Encyclopedia of Medicine 4* also includes entries on diets, nutrition, and general wellness.

Inclusion Criteria

A preliminary list of diseases, disorders, tests, and treatments was compiled from a wide variety of sources, including professional medical guides and textbooks as well as consumer guides and encyclopedias. The general advisory board, made up of public librarians, medical librarians, and consumer health experts, evaluated the topics and made suggestions for inclusion. The list was sorted by category and sent to *GEM4* medical advisors, certified physicians with various medical specialities, for review. Final selection of topics to include was made by the medical advisors in conjunction with the Gale, Cengage Learning editor.

About the Contributors

The essays were compiled by experienced medical writers, including physicians, pharmacists, nurses, and other health care professionals. *GEM4* medical advisors reviewed the completed essays to ensure that they are appropriate, up to date, and medically accurate.

How to Use this Book

The *Gale Encyclopedia of Medicine 4* has been designed with ready reference in mind.

- Straight **alphabetical arrangement** allows users to locate information quickly.
- Bold-faced terms function as **print hyperlinks** that point the reader to related entries in the encyclopedia.
- **Cross-references** placed throughout the encyclopedia direct readers to where information on subjects without entries can be found. Synonyms and acronyms are also cross-referenced.
- Lists of **key terms** are provided where appropriate to define unfamiliar terms or concepts. A **glossary** of key terms is also included at the back of Volume 6.
- Valuable **contact information** for organizations and support groups is included with each entry. The appendix contains an extensive list of organizations arranged in alphabetical order.
- The **resources section** directs users to additional sources of medical information on a topic.
- A comprehensive **general index** allows users to easily target detailed aspects of any topic, including Latin names.

Graphics

The *Gale Encyclopedia of Medicine 4* is enhanced with 765 images, including photos, charts, tables, and detailed illustrations.

ADVISORY BOARD

An advisory board comprised of medical specialists from a variety of backgrounds provided invaluable assistance in the formulation of this encyclopedia. This advisory board performed a myriad of duties, from defining the scope of coverage to reviewing individual entries for accuracy and accessibility. We would therefore like to express our sincere thanks and appreciation for all of their contributions.

CONTRIBUTORS

Margaret Alic, Ph.D.
Science Writer
Eastsound, WA

Janet Byron Anderson
Linguist/Language Consultant
Rocky River, OH

Lisa Andres, M.S., C.G.C.
Certified Genetic Counselor and Medical Writer
San Jose, CA

Greg Annussek
Medical Writer/Editor
New York, NY

Bill Asenjo, Ph.D.
Science Writer
Iowa City, IA

William Atkins
Medical Writer
Pekin, IL

Sharon A. Aufox, M.S., C.G.C.
Genetic Counselor
Rockford Memorial Hospital
Rockford, IL

Sandra Bain Cushman
Massage Therapist, Alexander Technique Practitioner
Charlottesville, VA

Howard Baker
Medical Writer
North York, Ontario

Laurie Barclay, M.D.
Neurological Consulting Services
Tampa, FL

Jeanine Barone
Nutritionist, Exercise Physiologist
New York, NY

Julia R. Barrett
Science Writer
Madison, WI

Donald G. Barstow, R.N.
Clincal Nurse Specialist
Oklahoma City, OK

Carin Lea Beltz, M.S.
Genetic Counselor and Program Director
The Center for Genetic Counseling
Indianapolis, IN

Linda K. Bennington, C.N.S.
Science Writer
Virginia Beach, VA

Issac R. Berniker
Medical Writer
Vallejo, CA

Kathleen Berrisford, M.S.V.
Science Writer

Bethanne Black
Medical Writer
Atlanta, GA

Jennifer Bowjanowski, M.S., C.G.C.
Genetic Counselor
Children's Hospital Oakland
Oakland, CA

Michelle Q. Bosworth, M.S., C.G.C.
Genetic Counselor
Eugene, OR

Barbara Boughton
Health and Medical Writer
El Cerrito, CA

Cheryl Branche, M.D.
Retired General Practitioner
Jackson, MS

Michelle Lee Brandt
Medical Writer
San Francisco, CA

Maury M. Breecher, Ph.D.
Health Communicator/Journalist
Northport, AL

Ruthan Brodsky
Medical Writer
Bloomfield Hills, MI

Tom Brody, Ph.D.
Science Writer
Berkeley, CA

Leonard C. Bruno, Ph.D.
Medical Writer
Chevy Chase, MD

Diane Calbrese
Medical Sciences and Technology Writer
Silver Spring, MD

Richard H. Camer
Editor
International Medical News Group
Silver Spring, MD

Rosalyn Carson-DeWitt, M.D.
Medical Writer
Durham, NC

Laura Jean Cataldo, RN, Ed.D.
Medical Writer
Myersville, MD

Lata Cherath, Ph.D.
Science Writing Intern
Cancer Research Institute
New York, NY

Linda Chrisman
Massage Therapist and Educator
Oakland, CA

Lisa Christenson, Ph.D.
Science Writer
Hamden, CT

Geoffrey N. Clark, D.V.M.
Editor
Canine Sports Medicine Update
Newmarket, NH

Rhonda Cloos, R.N.
Medical Writer
Austin, TX

Gloria Cooksey, C.N.E
Medical Writer
Sacramento, CA

Amy Cooper, M.A., M.S.I.
Medical Writer
Vermillion, SD

David A. Cramer, M.D.
Medical Writer
Chicago, IL

Esther Csapo Rastega, R.N., B.S.N.
Medical Writer
Holbrook, MA

Arnold Cua, M.D.
Physician
Brooklyn, NY

Tish Davidson, A.M.
Medical Writer
Fremont, CA

Dominic De Bellis, Ph.D.
Medical Writer/Editor
Mahopac, NY

Lori De Milto
Medical Writer
Sicklerville, NJ

Robert S. Dinsmoor
Medical Writer
South Hamilton, MA

Stephanie Dionne, B.S.
Medical Writer
Ann Arbor, MI

Martin W. Dodge, Ph.D.
Technical Writer/Editor
Centinela Hospital and Medical Center
Inglewood, CA

David Doermann
Medical Writer
Salt Lake City, UT

Stefanie B. N. Dugan, M.S.
Genetic Counselor
Milwaukee, WI

Doug Dupler, M.A.
Science Writer
Boulder, CO

Thomas Scott Eagan
Student Researcher
University of Arizona
Tucson, AZ

Altha Roberts Edgren
Medical Writer
Medical Ink
St. Paul, MN

Karen Ericson, R.N.
Medical Writer
Estes Park, CO

L. Fleming Fallon Jr., M.D., Dr.PH
Associate Professor of Public Health
Bowling Green State University
Bowling Green, OH

Karl Finley
Medical Writer
West Bloomfield, MI

Faye Fishman, D.O.
Physician
Randolph, NJ

Janis Flores
Medical Writer
Lexikon Communications
Sebastopol, CA

Risa Flynn
Medical Writer
Culver City, CA

Paula Ford-Martin
Medical Writer
Chaplin, MN

Janie F. Franz
Writer
Grand Forks, ND

Sallie Freeman, Ph.D., B.S.N.
Medical Writer
Atlanta, GA

Rebecca J. Frey, Ph.D.
Research and Administrative Associate
East Rock Institute
New Haven, CT

Cynthia L. Frozena, R.N.
Nurse, Medical Writer
Manitowoc, WI

Jason Fryer
Medical Writer
San Antonio, TX

Ron Gasbarro, Pharm.D.
Medical Writer
New Milford, PA

Julie A. Gelderloos
Biomedical Writer
Playa del Rey, CA

Gary Gilles, M.A.
Medical Writer
Wauconda, IL

Harry W. Golden
Medical Writer
Shoreline Medical Writers
Old Lyme, CT

Debra Gordon
Medical Writer
Nazareth, PA

Megan Gourley
Writer
Germantown, MD

Jill Granger, M.S.
Senior Research Associate
University of Michigan
Ann Arbor, MI

Melinda Granger Oberleitner, RN, DNS
Acting Department Head and Associate Professor
Department of Nursing
University of Louisiana at Lafayette
Lafayette, LA

Alison Grant
Medical Writer
Averill Park, NY

Elliot Greene, M.A.
Former president, American Massage Therapy Association

Massage Therapist
Silver Spring, MD

Peter Gregutt
Writer
Asheville, NC

Laith F. Gulli, M.D.
Consultant Psychotherapist in Private Practice
Lathrup Village, MI

Kapil Gupta, M.D.
Medical Writer
Winston-Salem, NC

Maureen Haggerty
Medical Writer
Ambler, PA

Clare Hanrahan
Medical Writer
Asheville, NC

Ann M. Haren
Science Writer
Madison, CT

Judy C. Hawkins, M.S.
Genetic Counselor
The University of Texas Medical Branch
Galveston, TX

Caroline Helwick
Medical Writer
New Orleans, LA

David Helwig
Medical Writer
London, Ontario

Lisette Hilton
Medical Writer
Boca Raton, FL

Katherine S. Hunt, M.S.
Genetic Counselor
University of New Mexico Health Sciences Center
Albuquerque, NM

Kevin Hwang, M.D.
Medical Writer
Morristown, NJ

Holly Ann Ishmael, M.S., C.G.C.
Genetic Counselor
The Children's Mercy Hospital
Kansas City, MO

Dawn A. Jacob, M.S.
Genetic Counselor
Obstetrix Medical Group of Texas
Fort Worth, TX

Sally J. Jacobs, Ed.D.
Medical Writer
Los Angeles, CA

Michelle L. Johnson, M.S., J.D.
Patent Attorney and Medical Writer
Portland, OR

Paul A. Johnson, Ed.M.
Medical Writer
San Diego, CA

Cindy L. A. Jones, Ph.D.
Biomedical Writer
Sagescript Communications
Lakewood, CO

David Kaminstein, M.D.
Medical Writer
West Chester, PA

Beth A. Kapes
Medical Writer
Bay Village, OH

Janet M. Kearney
Freelance Writer
Orlando, FL

Christine Kuehn Kelly
Medical Writer
Havertown, PA

Bob Kirsch
Medical Writer
Ossining, NY

Joseph Knight, P.A.
Medical Writer
Winton, CA

Melissa Knopper
Medical Writer
Chicago, IL

Karen Krajewski, M.S., C.G.C.
Genetic Counselor
Assistant Professor of Neurology
Wayne State University
Detroit, MI

Jeanne Krob, M.D., F.A.C.S.
Physician, Writer
Pittsburgh, PA

Jennifer Lamb
Medical Writer
Spokane, WA

Richard H. Lampert
Senior Medical Editor
W.B. Saunders Co.
Philadelphia, PA

Jeffrey P. Larson, R.P.T.
Physical Therapist
Sabin, MN

Jill Lasker
Medical Writer
Midlothian, VA

Kristy Layman
Music Therapist
East Lansing, MI

Victor Leipzig, Ph.D.
Biological Consultant
Huntington Beach, CA

Brenda Wilmoth Lerner, RN
Medical Editor and Writer
Montrose, AL

Lorraine Lica, Ph.D.
Medical Writer
San Diego, CA

John T. Lohr, Ph.D.
Assistant Director, Biotechnology Center
Utah State University
Logan, UT

Larry Lutwick, M.D., F.A.C.P.
Director, Infectious Diseases
VA Medical Center
Brooklyn, NY

Suzanne M. Lutwick
Medical Writer
Brooklyn, NY

Nicole Mallory, M.S.
Medical Student
Wayne State University
Detroit, MI

Warren Maltzman, Ph.D.
Consultant, Molecular Pathology
Demarest, NJ

Adrienne Massel, R.N.
Medical Writer
Beloit, WI

Ruth E. Mawyer, R.N.
Medical Writer
Charlottesville, VA

Richard A. McCartney M.D.
Fellow, American College of Surgeons
Diplomat American Board of Surgery
Richland, WA

Bonny McClain, Ph.D.
Medical Writer
Greensboro, NC

Sally C. McFarlane-Parrott
Medical Writer
Ann Arbor, MI

Mercedes McLaughlin
Medical Writer
Phoenixville, CA

Alison McTavish, M. Sc.
Medical Writer and Editor
Montreal, Quebec

Liz Meszaros
Medical Writer
Lakewood, OH

Betty Mishkin
Medical Writer
Skokie, IL

Barbara J. Mitchell
Medical Writer
Hallstead, PA

Mark A. Mitchell, M.D.
Medical Writer
Seattle, WA

Susan J. Montgomery
Medical Writer
Milwaukee, WI

Louann W. Murray, PhD
Medical Writer
Huntington Beach, CA

Bilal Nasser, M. Sc.
Senior Medical Student
Universidad Iberoamericana
Santo Domingo, Domincan Republic

Laura Ninger
Medical Writer
Weehawken, NJ

Nancy J. Nordenson
Medical Writer
Minneapolis, MN

Teresa Odle
Medical Writer
Albuquerque, NM

Lisa Papp, R.N.
Medical Writer
Cherry Hill, NJ

Lee Ann Paradise
Medical Writer
San Antonio, TX

Patience Paradox
Medical Writer
Bainbridge Island, WA

Barbara J. Pettersen
Genetic Counselor
Genetic Counseling of Central Oregon
Bend, OR

Genevieve Pham-Kanter, M.S.
Medical Writer
Chicago, IL

Collette Placek
Medical Writer
Wheaton, IL

J. Ricker Polsdorfer, M.D.
Medical Writer
Phoenix, AZ

Scott Polzin, M.S., C.G.C.
Medical Writer
Buffalo Grove, IL

Elizabeth J. Pulcini, M.S.
Medical Writer
Phoenix, AZ

Nada Quercia, M.S., C.C.G.C.
Genetic Counselor
Division of Clinical and Metabolic Genetics
The Hospital for Sick Children
Toronto, ON, Canada

Ann Quigley
Medical Writer
New York, NY

Robert Ramirez, B.S.
Medical Student
University of Medicine & Dentistry of New Jersey
Stratford, NJ

Kulbir Rangi, D.O.
Medical Doctor and Writer
New York, NY

Esther Csapo Rastegari, Ed.M., R.N./B.S.N.
Registered Nurse, Medical Writer
Holbrook, MA

Toni Rizzo
Medical Writer
Salt Lake City, UT

Martha Robbins
Medical Writer
Evanston, IL

Richard Robinson
Medical Writer
Tucson, AZ

Nancy Ross-Flanigan
Science Writer
Belleville, MI

Anna Rovid Spickler, D.V.M., Ph.D.
Medical Writer
Moorehead, KY

Belinda Rowland, Ph.D.
Medical Writer
Voorheesville, NY

Andrea Ruskin, M.D.
Whittingham Cancer Center
Norwalk, CT

Laura Ruth, Ph.D.
Medical, Science, & Technology Writer
Los Angeles, CA

Karen Sandrick
Medical Writer
Chicago, IL

Kausalya Santhanam, Ph.D.
Technical Writer
Branford, CT

Jason S. Schliesser, D.C.
Chiropractor
Holland Chiropractic, Inc.
Holland, OH

Joan Schonbeck
Medical Writer

Massachusetts Department of Mental Health
Marlborough, MA

Laurie Heron Seaver, M.D.
Clinical Geneticist
Greenwood Genetic Center
Greenwood, SC

Catherine Seeley
Medical Writer

Kristen Mahoney Shannon, M.S., C.G.C.
Genetic Counselor
Center for Cancer Risk Analysis
Massachusetts General Hospital
Boston, MA

Kim A. Sharp, M.Ln.
Writer
Richmond, TX

Judith Sims, M.S.
Medical Writer
Logan, UT

Joyce S. Siok, R.N.
Medical Writer
South Windsor, CT

Jennifer Sisk
Medical Writer
Havertown, PA

Patricia Skinner
Medical Writer
Amman, Jordan

Genevieve Slomski, Ph.D.
Medical Writer
New Britain, CT

Stephanie Slon
Medical Writer
Portland, OR

Linda Wasmer Smith
Medical Writer
Albuquerque, NM

Java O. Solis, M.S.
Medical Writer
Decatur, GA

Elaine Souder, PhD
Medical Writer
Little Rock, AR

Jane E. Spehar
Medical Writer
Canton, OH

Lorraine Steefel, R.N.
Medical Writer
Morganville, NJ

Kurt Sternlof
Science Writer
New Rochelle, NY

Roger E. Stevenson, M.D.
Director
Greenwood Genetic Center
Greenwood, SC

Dorothy Stonely
Medical Writer
Los Gatos, CA

Liz Swain
Medical Writer
San Diego, CA

Deanna M. Swartout-Corbeil, R.N.
Medical Writer
Thompsons Station, TN

Keith Tatarelli, J.D.
Medical Writer

Mary Jane Tenerelli, M.S.
Medical Writer
East Northport, NY

Catherine L. Tesla, M.S., C.G.C.
Senior Associate, Faculty
Dept. of Pediatrics, Division of Medical Genetics
Emory University School of Medicine
Atlanta, GA

Bethany Thivierge
Biotechnical Writer/Editor
Technicality Resources
Rockland, ME

Mai Tran, Pharm.D.
Medical Writer
Troy, MI

Carol Turkington
Medical Writer
Lancaster, PA

Judith Turner, B.S.
Medical Writer
Sandy, UT

Amy B. Tuteur, M.D.
Medical Advisor
Sharon, MA

Samuel Uretsky, Pharm.D.
Medical Writer
Wantagh, NY

Amy Vance, M.S., C.G.C.
Genetic Counselor
GeneSage, Inc.
San Francisco, CA

Michael Sherwin Walston
Student Researcher
University of Arizona
Tucson, AZ

Ronald Watson, Ph.D.
Science Writer
Tucson, AZ

James E. Waun, MD, MA, RPh
Adjunct Assistant Professor of Clinical Pharmacy
Ferris State University
East Lansing, MI

Ellen S. Weber, M.S.N.
Medical Writer
Fort Wayne, IN

Ken R. Wells
Freelance Writer
Laguna Hills, CA

Jennifer F. Wilson, M.S.
Science Writer
Haddonfield, NJ

Kathleen D. Wright, R.N.
Medical Writer
Delmar, DE

Jennifer Wurges
Medical Writer
Rochester Hills, MI

Mary Zoll, Ph.D.
Science Writer
Newton Center, MA

Jon Zonderman
Medical Writer
Orange, CA

Michael V. Zuck, Ph.D.
Medical Writer
Boulder, CO

L

Labor and delivery *see* **Childbirth**
Labor induction *see* **Induction of labor**

Labyrinthitis

Definition

Labyrinthitis is an inflammatory disorder of the inner ear, or the system of passages called the bony labyrinth that contains the vestibular system, which senses changes of position to the head. The disorder is often a complication of **otitis media**. Derived from the Latin word labyrinthus, the medical condition called labyrinthitis is produced by the spread of bacterial or viral infections from the head or respiratory tract into the inner ear. A person with labyrinthitis will have irritation and swelling of the inner ear, along with a reduced ability to maintain their balance and a diminished ability to hear in one or both ears.

Demographics

Anyone can contract the various forms of labyrinthitis. Viral labyrinthitis is the most common form of the disorder. It is usually reported in adults from 30 to 60 years of age. The viral condition is rarely seen in children.

Description

Labyrinthitis is characterized by **dizziness** or feelings of **motion sickness** caused by disturbance of the sense of balance. Along with a balance disorder, people with labyrinthitis may also experience **hearing loss** and **tinnitus**. People who are getting over an upper respiratory tract infection (URI) often get labyrinthitis.

People at increased risk from labyrinthitis include those with previous **ear surgery**, frequent infections, alcohol **abuse**, tobacco use, **fatigue**, **stress**, dizziness or hearing loss, diabetes, **stroke**, migraine headaches, use of certain drugs (especially **aspirin**), trauma of the head or spine, ear disease, or high blood pressure.

Causes and symptoms

Causes

The disease agents that cause labyrinthitis may reach the inner ear by one of three routes:

- Bacteria may be carried from the middle ear or the membranes that cover the brain.
- Viruses that cause mumps, measles, influenza, and colds may reach the inner ear following an upper respiratory infection.
- Rubella virus can cause labyrinthitis in infants prior to birth.

The major cause of labyrinthitis is viral. Some of the viruses that can cause labyrinthitis are the cytomegalovirus, **mumps** virus, **rubella** virus, **influenza** virus, herpes simplex virus 1, and adenovirus. Other causes of labyrinthitis include severe stress, head injuries, **allergies**, medicine reactions, or toxic drugs.

Symptoms

The primary symptoms of labyrinthitis are vertigo (dizziness, abnormal sense of movements), accompanied by hearing loss (in one ear) and a sensation of ringing in one or both ears (called tinnitus). Vertigo occurs because the inner ear, part of the vestibular system that coordinates sensory inputs, controls the sense of balance as well as hearing. Difficulty focusing of the eyes is another symptom. Oftentimes patients have trouble sensing both linear and rotational motion. Some patients also experience **nausea**, **fever**, **anxiety**, **vomiting**, general sickness, and spontaneous eye movements (**nystagmus**) in the direction of the unaffected ear. Other symptoms include earache, weakness in the face (possibly on one side more than the other side), decreases in eyesight, and stiffness or **pain** in the neck. Inflammation in the middle

KEY TERMS

Labyrinth—The bony cavity of the inner ear.

Meniere's syndrome—A disease of the inner ear marked by recurrent episodes of vertigo and roaring in the ears lasting several hours. Its cause is unknown.

Otitis media—Inflammation of the middle ear. It can lead to labyrinthitis.

Vertigo—A sensation of dizziness marked by the feeling that one's self or surroundings are spinning or whirling.

ear (otitis media) can also occur. Bacterial labyrinthitis may produce a discharge from the infected ear.

A common side effect of labyrinthitis is anxiety. Such a problem can produce panic attacks, heart **palpitations**, and **tremors**. In serious cases, depression can happen.

Diagnosis

The diagnosis of labyrinthitis is based on a combination of the patient's symptoms and history—especially a history of a recent upper respiratory infection. The doctor will test the patient's hearing, and order a laboratory culture to identify the organism if the patient has a discharge. A complete physical and neurological examination will include the head and neck, especially in the areas of the otologic, ocular, and cranial nerves. The otologic examination will consist of looking for signs of **mastoiditis** (an infection of the temporal bone of the skull behind the ear), **cellulitis** (inflammation of connective tissue), or previous ear surgery, along with an inspection of the ear canal, the tympanic membrane, and the middle ear. The ocular exam should include an inspection of the eyes with respect to general motion and eyelid response, along with other abnormalities of vision. The neurologic exam will consist of an inspection in and about the cranial nerve.

If there is not a history of a recent infection, the doctor will order extra tests in order to exclude injuries to the brain or Meniere's disease. Possible tests include an electronystagmography (ENG), **electroencephalography** (EEG), head computed tomography (CT) scan, hearing test, and head **magnetic resonance imaging** (MRI) scan.

Treatment

Medication

Patients with minor labyrinthitis are initially given bed rest and plenty of fluids at home. They are asked to avoid sudden changes in position, not to read, avoid bright lights, and to gradually resume normal activities as symptoms decrease. They are prescribed **antibiotics**, either by mouth or intravenously to clear up the infection.

More pronounced symptoms of labyrinthitis may require care in a hospital or other health care facility. Intravenous fluids and medicines to control **vomiting**, dizziness, and nausea are also given. Patients may be given meclizine (Antivert, Bonine), scopolamine (Maldemar, Scopace, Transderm-Scop), or prochlorperazine (Compazine, Buccastem, Phenotil) for vertigo and nausea. For anxiety and depression, antidepressants or sedative-hypnotics (Valium) are given.

To treat labyrinthitis itself, selective serotonin-reuptake inhibitors have been found to be effective. They work by stimulating neural growth within the inner ear, along with relieving some of the symptoms like dizziness. **Corticosteroids**, such as prednisone, have also been shown to be an effective way to treat labyrinthitis during its early stages. When a virus causes labyrinthitis, antiviral medicines such as valacyclovir are used as early as possible so as not to permanently damage the inner ear. Vestibular **rehabilitation** therapy (VRT) is also provided to treat dizziness.

Surgery

Some patients require surgery to drain the inner and middle ear.

Supportive care

Patients with labyrinthitis should rest in bed for three to five days until the acute dizziness subsides. Patients who are dehydrated by repeated vomiting may need intravenous fluid replacement. In addition, patients are advised to avoid driving or similar activities for four to six weeks after the acute symptoms subside, because they may have occasional dizzy spells during that period.

Prognosis

Most patients with labyrinthitis recover completely within two to three weeks, although it often takes five to six weeks for the vertigo to disappear completely and the patient's hearing to return to normal. To return

completely back to normal conditions (without dizziness and balance problems) a recovery time of months or even a year or so is sometimes the case. Hearing usually returns to normal. In a few cases, the hearing loss is permanent, and other symptoms may never return to normal. Dizziness may continue with older patients.

Prevention

The most effective preventive strategy includes prompt treatment of ear and respiratory infections by medical professionals, as well as the monitoring of patients with mumps, **measles**, influenza, or colds for signs of dizziness or hearing problems.

Resources

BOOKS

McPhee, Stephen, and Maxine A. Papadakis, editors. *Current Medical Diagnosis and Treatment*. New York: McGraw-Hill Medical, 2008.

Oxford Handbook of Auditory Science. Oxford, UK: Oxford University Press, 2010.

Polensek, S. H. *Ferri's Clinical Advisor: Instant Diagnosis and Treatment*. Philadelphia: Mosby Elsevier, 2008.

OTHER

"Inner Ear, Labyrinthitis." eMedicine, WebMD. (January 14, 2010), http://emedicine.medscape.com/article/856215-overview. (accessed July 22, 2010).

"Labyrinthitis." Medline Plus, National Library of Medicine and National Institutes of Health. (September 27, 2008), http://www.nlm.nih.gov/medlineplus/ency/article/001054.htm. (accessed July 22, 2010).

Rebecca J. Frey, PhD

Laceration repair

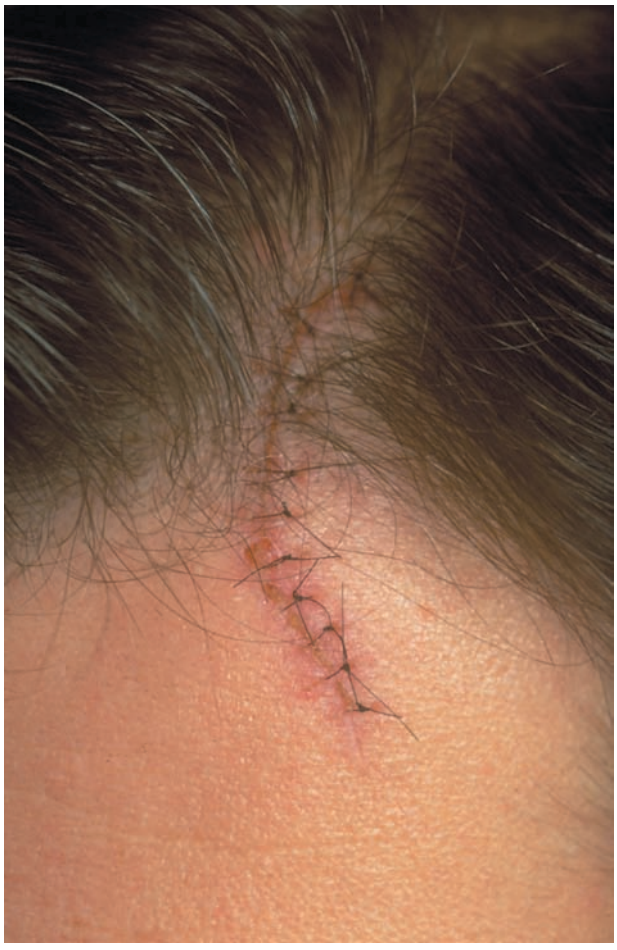
Definition

A laceration is a wound caused by a sharp object producing edges that may be jagged, dirty, or bleeding. Lacerations most often affect the skin, but any tissue may be lacerated, including subcutaneous fat, tendon, muscle, or bone.

Purpose

A laceration should be repaired if it:

- continues to bleed after application of pressure for ten to fifteen minutes
- is more than one-eighth to one-fourth inch deep
- exposes fat, muscle, tendon, or bone
- causes a change in function surrounding the area of the laceration
- is dirty or has visible debris in it
- is located in an area where an unsightly scar is undesirable.



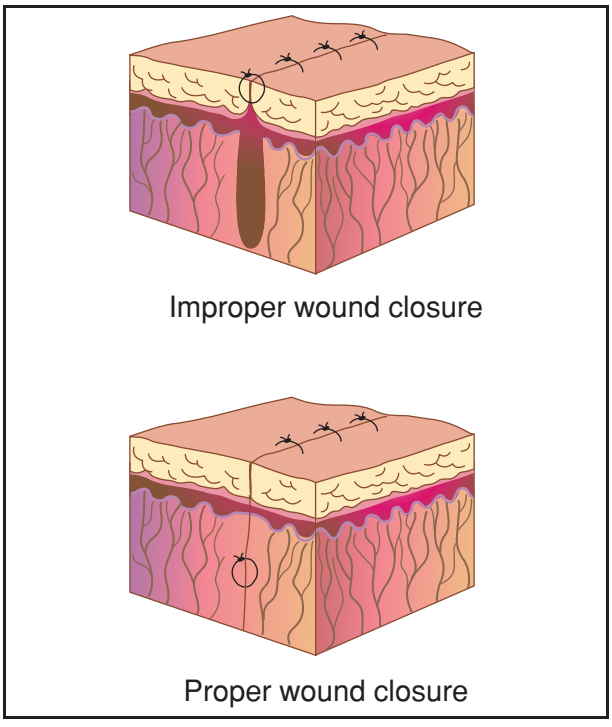
Eleven sutures are necessary to close up the laceration on this person's forehead. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Precautions

Lacerations are less likely to become infected if they are repaired soon after they occur. Many physicians will not repair a laceration that is more than eight hours old because the risk of infection is too great.

Description

Laceration repair mends a tear in the skin or other tissue. The procedure is similar to repairing a tear in clothing. Primary care physicians, emergency room



A laceration is a traumatic break in the skin caused by a sharp object producing edges that may be jagged, dirty, or bleeding. The underlying tissue may also be severed. In such instances, the physician may place absorbable sutures in the tissue to help bring the edges together before the skin is sutured close. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

physicians, and surgeons usually repair lacerations. The four goals of laceration repair are to stop bleeding, prevent infection, preserve function, and restore appearance. Insurance companies do pay for the procedure. Cost depends upon the severity and size of the laceration.

Before repairing the laceration, the physician thoroughly examines the wound and the underlying tendons or nerves. If nerves or tendons have been injured, a surgeon may be needed to complete the repair. The laceration is cleaned by removing any foreign material or debris. Removing **foreign objects** from penetrating **wounds** can sometimes cause bleeding, so this type of wound must be cleaned very carefully. The wound is then irrigated with saline solution and a disinfectant. The disinfecting agent may be mild soap or a commercial preparation. An antibacterial agent may be applied.

Once the wound has been cleansed, the physician anesthetizes the area of the repair by injecting a local anesthetic. The physician may trim edges that are jagged or extremely uneven. Tissue that is too damaged to heal must be removed (**debridement**) to prevent infection. If the laceration is deep, several absorbable stitches

KEY TERMS

Debridement—The act of removing any foreign material and damaged or contaminated tissue from a wound to expose surrounding healthy tissue.

(sutures) are placed in the tissue under the skin to help bring the tissue layers together. Suturing also helps eliminate any pockets where tissue fluid or blood can accumulate. The skin wound is closed with sutures. Suture material used on the surface of a wound is usually non-absorbable and will have to be removed later. A light dressing or an adhesive bandage is applied for 24–48 hours. In areas where a dressing is not feasible, an antibiotic ointment can be applied. If the laceration is the result of a human or animal bite, if it is very dirty, or if the patient has a medical condition that alters wound healing, oral **antibiotics** may be prescribed.

Aftercare

The laceration is kept clean and dry for at least 24 hours after the repair. Light bathing is generally permitted after 24 hours if the wound is not soaked. The physician will provide directions for any special wound care. Sutures are removed 3–14 days after the repair is completed. Timing of suture removal depends on the location of the laceration and physician preference.

The repair should be observed frequently for signs of infection, which include redness, swelling, tenderness, drainage from the wound, red streaks in the skin surrounding the repair, chills, or **fever**. If any of these occur, the physician should be contacted immediately.

Risks

The most common complication of any laceration repair is infection. Risk of infection can be minimized by cleansing the wound thoroughly. Wounds from **bites** or dirty objects or wounds that have a large amount of dirt in them are most likely to become infected.

All lacerations will heal with a scar. Wounds that are repaired with sutures are less likely to develop **scars** that are unsightly, but no one can predict how wounds will heal and who will develop unsightly scars. **Plastic surgery** can improve the appearance of many scars.

Resources

OTHER

"Caring for Cuts and Scrapes at Home." *Mayo Clinic Online*. http://www.mayohealth.org/mayo/9611/htm/cuts_sb.htm.

"Laceration Repair." *ThriveOnline*. http://thriveonline.oxygen.com.

Mary Jeanne Krob, MD, FACS

Lacerations *see* **Wounds**

Lacrimal duct obstruction

Definition

A lacrimal duct obstruction is a condition caused by a partial or complete blockage of the tear duct, the thin channel (small tube) that normally drains tears from the surface of the eye and into the nose. A blocked tear duct occurs usually when the drainage system between the inside corner of the eye and the inside of the nose is obstructed by something or does not properly open. When either case happens, tears on the surface of the eyes are not allowed to move into the nose so that they can be reabsorbed into the body or evaporated into the air. Consequently, the tear duct sac fills with tears. If not treated promptly, such a situation can lead to a watery, irritated eye that first becomes swollen and inflamed and, later, possibly infected.

Demographics

An obstruction of the tear duct is rarely found in healthy adults. When it does appear in an adult it usually results from an injury suffered in or around the eyes. However, tear duct blockage has been verified to be more prominent in older adults, being an age-related condition. The condition can also be present at birth, with about 6 to 20 out of 100 newborn babies having lacrimal duct obstruction. When this case arises, it is congenital and is called nasolacrimal duct obstruction.

Description

The lacrimal glands, located above each eyeball, produce tears. The tears flow over the eye, and then drain through the nasolacrimal ducts. A tiny hole at the inner edge of each eyelid marks the opening of the ducts, which lead to the lacrimal sacs located on the side of the nose. The tears pass from the sacs into the nasolacrimal ducts and then into the nose. Once in the nose, they are either reabsorbed by the body or evaporated into the air.

When a tear duct becomes obstructed, tears may spill over the eyelids and run down the face. Stagnant tears within the system can become infected, leading to recurrent red eyes and infections. Excessive tearing can also produce secondary skin changes on the lower eyelids.

Increased risks for acquiring lacrimal duct obstruction include:

- premature birth
- age and gender (females are more at risk than males; as are older people over younger ones)
- chronic eye infections (dacrosystitis)
- family history of blocked tear ducts
- previous cancer treatments (chemotherapy or radiation), especially of the face or head
- abnormal bone growth or tumors around the eyes
- chronic eye inflammation (conjunctivitis)
- previous surgeries of the eye or eyelid, along with nasal or sinus surgery
- use of glaucoma medications

Causes and symptoms

An obstructed lacrimal tear duct can result in inflammation and infection of the lacrimal sac. The area beneath the eyes next to the nose can become red, inflamed, and sensitive to the touch. The area usually is swollen, painful, and there may be a mucous discharge from the opening of the nasal corner of the eye. Blurred vision may also occur, along with bloody tears. Common complaints include **itching**, irritation, burning, redness, foreign body sensation, and tearing. Symptoms are worsened by cold weather, high winds, bright sunlight, and exposure to upper respiratory infections.

The first symptom to appear is usually excessive tearing. It may occur as the appearance of wet-looking eyes or grow as large as excessive amounts of tears running down the cheeks. Newborns have symptoms starting from a few days to a few weeks after being born. In all ages, symptoms include redness and inflammation around the eye or nose. Yellow mucus may appear from the corners of the eye. Eventually, eyelids may stick together. Infection is usually a latter-stage symptom, especially in the eyelids.

Children frequently have a congenital lacrimal duct obstruction. Six to ten percent of all children are born before their tear ducts are open. The unopened tear duct is caused by immature tissue at the end of the tear duct, which causes it not to open normally. Children may also acquire lacrimal duct obstruction due to infections, abnormal growth of the nasal bone, and undeveloped openings in the corners of the eyes.

In adults, a common cause of lacrimal duct obstruction is involution, which is progressive degeneration occurring naturally with advancing age,

resulting in shriveling of organs or tissues. Other causes include:

- eyelid disorders
- infections by bacteria, viruses, fungi, and parasites
- inflammation
- regular use of eye drops or excessive use of nasal spray
- topical medications that treat eye problems
- systemic chemotherapy
- trauma from previous surgeries to the bone at the side of the nose
- injuries to the face
- abnormal development of the skull and face
- foreign bodies
- sinus disease
- nasal polyps
- cysts and stones
- malignant or benign tumors

Smoking tobacco products can also increase the likelihood of tear blockages.

Diagnosis

The medical professional will rely initially on the patient's medical history and a **physical examination**. If the primary symptom is excessive tearing, the first step is for the health care professional to determine if the overflow of tears is due to an increase in tear production or a decrease in tear drainage. Tests will establish the amount of tears being produced and whether the tears are draining normally. Such tests include the fluorescein dye disappearance (test for ability of tears to drain), irrigation and probing (test for ability to drain and presence of blockage), and dacryocystography or dacryoscintigraphy (test to indicate cause of blockage with use of medical scans).

Causes of increased tear production may include trichiasis, a disease in which the eyelashes produce constant irritation, and eyelid malpositions and diseases. If abnormal tear production is ruled out, then obstructions in tear drainage is the most likely cause of the excessive tearing. Additional observations of swollen lacrimal sac area and purulent eye discharge indicate that there may be a lacrimal duct infection present. To define the diagnosis, the lacrimal discharge may be cultured to determine possible infective agents, while various imaging techniques may be used to detect the type of obstruction. Dye tracer tests are also used to test for blockages.

Treatment

Lacrimal duct obstructions in children often resolve spontaneously, with 95% showing resolution before the child is one year old. Daily massaging (two to four times each day) of the lacrimal sac may help open the blockage. A topical antibiotic ointment may be applied if infection is present. If the blockage is not resolved after several weeks to months of this therapy, a physician may attempt forceful irrigation. Dilation, probing, and irrigation to open up the duct under **general anesthesia** or under a restraint is a last resort, after six months to one year or so of less invasive treatments. The dilation, probing, and irrigation technique is usually successful in the vast majority of the cases with children.

In adults, the condition is generally correctable, with conservative treatments usually recommended. The cause of the blockage and a person's age may make treatment more difficult. The infected or inflamed area may be massaged, with warm compresses applied to provide relief and speed the healing process. The health care provider may also irrigate the infected area. Topical antibiotic ointments and oral **antibiotics** are often applied to reduce infection. The use of **analgesics** such as **aspirin** may be recommended to control discomfort and reduce swelling.

The eyes can be kept clean by wiping drainage away from them. Moisten a cotton call or clean washcloth with warn water. Wipe carefully and gently once from the inner to the outer part of the eye. Repeat multiple times, if necessary; with a new cotton ball or washcloth. To clean eyelashes, use a gentle downward motion onto the eyelash with a moist cotton ball. If the eyelash contains dried substances, apply a warm, moistened cotton ball over the eye lash for a few minutes.

Minimally invasive treatments or surgeries may also be necessary if conservative measures fail to help. One such treatment is stenting or intubation. Tiny polyurethane- or silicone-based tubes are used to clear blockages or to widen narrowing of the tear ducts. The most frequent surgery is called an external dacryocystorhinostomy. An incision is made on the side of the nose so the surgeon can insert a stent.

In another treatment, balloon catheter dilation helps to resolve problems with passages narrowed by inflammation, scarring, or other related problems. In one such surgery, a complete reconstruction of the drainage system is performed. Called conjunctivodacryocystorhinostomy, it creates to new passageway (an artificial duct) for the tears to drain.

Procedures called endoscopic or endonasal are also sometimes used. Without making an incision, the

KEY TERMS

Lacrimal duct—A short canal leading from a small orifice at the medial angle of each eyelid to the lacrimal sac.

Lacrimal gland—An almond-shaped gland that secretes tears.

Lacrimal sac—The dilated upper end of the nasolacrimal duct in which the lacrimal ducts empty.

Nasolacrimal duct—A channel that transmits tears from the lacrimal sac to the nose.

Purulent—Consisting of or containing pus.

Tear—A drop of the clear, salty fluid secreted by the lachrimal gland.

Trichiasis—A disease of the eye, in which the eyelashes, being turned in upon the eyeball, produce constant irritation by the motion of the lids.

surgeon inserts tiny instruments attached to cameras through the nasal opening to correct the problem.

As with children, the procedure called dilation, probing, and irrigation can also be effectively applied to adults.

Prognosis

Most adults respond positively to conservative treatments. If such approaches fail to clear the obstruction, surgical procedures are available, with success rates greater than 90%. The vast majority of children out grow the condition, and treatments are usually unnecessary. However, when treatments are necessary, they usually solve the problem.

Prevention

Lacrimal duct obstruction is not preventable. In many cases, the cause of a lacrimal duct obstruction is not known. Most of the cases are congenital (present at birth). However, there are several effective ways to minimize the chances of having a blockage of the tear ducts. For parents, if your child has blockage of the tear ducts, keep the baby away from winds, sunlight, and coldness.

For adults, always treat sinus or eye infections promptly. When engaging in strenuous **exercise** and activities (such as bicycling) or contact sports (such as hockey)—when injuries to the face are likely—always wear a helmet or protective eye gear. In addition, do not smoke tobacco products and do not abuse nasal sprays.

Resources

BOOKS

Fekrat, Sharon, and Jennifer S. Weizer, editors. *All About Your Eyes*. Durham, NC: Dike University Press, 2006.

McPhee, Stephen, and Maxine A. Papadakis, editors. *Current Medical Diagnosis and Treatment*. New York: McGraw-Hill Medical, 2008.

Reinhard, Thomas, and Frank Larkin, editors. *Cornea and External Eye Disease*. Berlin, Germany: Springer, 2008.

Yanoff, Myron, et al., editors. *Ophthalmology*. Edinburgh, Scotland: Mosby Elsevier, 2009.

OTHER

"Blocked Tear Ducts." Mayo Clinic. (October 16, 2008), http://www.mayoclinic.com/health/blocked-tear-duct/DS01096. (accessed July 23, 2010).

"Blocked Tear Ducts." WebMD. (April 11, 2008), http://www.webmd.com/eye-health/tc/blocked-tear-ducts-topic-overview. (accessed July 23, 2010).

"Nasolacrimal Duct Obstruction." eMedicine. (January 6, 2010), http://emedicine.medscape.com/article/1210141-overview. (accessed July 23, 2010).

ORGANIZATIONS

American Academy of Ophthalmology, P.O. Box 7424, San Francisco, CA, 94120-7424, (415) 561-8500, (415) 561-8533, http://www.aao.org/.

American Optometric Association, 243 North Lindbergh Boulevard, St. Louis, MO, 63141, (314) 991-4100, (800) 365-2219, http://www.aoanet.org.

National Eye Institute, 2020 Vision Place, Bethesda, MD, 20892-3655, (301) 496-5248, http://www.nei.nih.gov/.

Judith Sims

Lacrimal sac infection *see* **Dacryocystitis**

Lactate dehydrogenase isoenzymes test

Definition

The enzyme lactate dehydrogenase (also known as lactic dehydrogenase, or LDH) is found in the cells of almost all body tissues. The enzyme is especially concentrated in the heart, liver, red blood cells, kidneys, muscles, brain, and lungs. The total LDH can be further separated into five components or fractions labeled by number: LDH-1, LDH-2, LDH-3, LDH-4, and LDH-5. Each of these fractions, called isoenzymes, is used mainly by a different set of cells or tissues in the body. For this reason, the relative amounts of a particular isoenzyme of LDH in the blood can provide valuable diagnostic information.

Purpose

The LDH isoenzymes test assists in differentiating **heart attack**, anemia, lung injury, or **liver disease** from other conditions that may cause the same symptoms (differential diagnosis).

Precautions

Strenuous **exercise** may raise levels of total LDH, specifically the isoenzymes LDH-1, LDH-2, and LDH-5. Alcohol, anesthetics, **aspirin**, **narcotics**, procainamide, fluorides, and mithramycin may also raise levels of LDH. Ascorbic acid (vitamin C) can lower levels of LDH.

KEY TERMS

Differential diagnosis—Comparing and contrasting the signs, symptoms, and laboratory findings of two or more diseases to determine which is causing the patient's condition.

Enzyme—A protein that regulates the rate of a chemical reaction in the body, increasing the speed at which the change occurs.

Isoenzyme—One of a group of enzymes that bring about the same reaction but are vary in their physical properties.

Description

LDH is found in the cells of almost all body tissues. When certain conditions injure cells in tissues containing LDH, it is released into the bloodstream. Because LDH is so widely distributed throughout the body, analysis of total LDH will not help make a diagnosis of a particular disease. Because this enzyme is actually composed of five different isoenzymes, however, analysis of the different LDH isoenzyme levels in the blood can help in the diagnosis of some diseases.

The five LDH isoenzymes are: LDH-1, LDH-2, LDH-3, LDH-4, and LDH-5. In general, each isoenzyme is used mostly by the cells in a specific tissue. LDH-1 is found mainly in the heart. LDH-2 is primarily associated with the system in the body that defends against infection (reticuloendothelial system). LDH-3 is found in the lungs and other tissues, LDH-4 in the kidney, placenta, and pancreas, and LDH-5 in liver and striated (skeletal) muscle. Normally, levels of LDH-2 are higher than those of the other isoenzymes.

Certain diseases have classic patterns of elevated LDH isoenzyme levels. For example, an LDH-1 level higher than that of LDH-2 is indicative of a heart attack or injury; elevations of LDH-2 and LDH-3 indicate lung injury or disease; elevations of LDH-4 and LDH-5 indicate liver or muscle disease or both. A rise of all LDH isoenzymes at the same time is diagnostic of injury to multiple organs. For example, a heart attack with congestive **heart failure** may cause symptoms of lung and liver congestion. Advanced **cancer** and autoimmune diseases such as lupus can also cause this pattern.

One of the most important diagnostic uses for the LDH isoenzymes test is in the differential diagnosis of myocardial infarction or heart attack. The total LDH level rises within 24–48 hours after a heart attack, peaks in two to three days, and returns to normal in approximately five to ten days. This pattern is a useful tool for a delayed diagnosis of heart attack. The LDH-1 isoenzyme level, however, is more sensitive and specific than the total LDH. Normally, the level of LDH-2 is higher than the level of LDH-1. An LDH-1 level higher than that of LDH-2, a phenomenon known as "flipped LDH," is strongly indicative of a heart attack. The flipped LDH usually appears within 12–24 hours after a heart attack. In about 80% of cases, flipped LDH is present within 48 hours of the incident. A normal LDH-1/LDH-2 ratio is considered reliable evidence that a heart attack has not occurred.

It should be noted that two conditions might cause elevated LDH isoenzymes at the same time and that one may confuse the other. For example, a patient with **pneumonia** may also be having an acute heart attack. In this instance, the LDH-1 level would rise with the LDH-2 and LDH-3. Because of this complication, some laboratories measure only the LDH-1 and consider an elevated LDH level with LDH-1 higher than 40% to be diagnostic of heart damage. LDH isoenzymes test is not used much anymore for diagnosis of heart attack. Tests for the protein troponin, which is found in myocardial cells, have been found to be more accurate.

Preparation

This test requires a blood sample. The patient need not fast (nothing to eat or drink) before the test unless requested to do so by the physician.

Risks

Risks for this test are minimal. The patient may experience slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after the vein is punctured (venipuncture), or an accumulation of blood under the puncture site (hematoma).

Results

Reference values for normal levels of LDH isoenzymes vary from laboratory to laboratory but can generally be found within the following ranges:

- LDH-1: 17–27%
- LDH-2: 27–37%
- LDH-3: 18–25%
- LDH-4: 8–16%
- LDH-5: 6–16%

Increased levels of LDH-1 are seen in myocardial infarction, red blood cell diseases like **hemolytic anemia**, **kidney disease** including **kidney transplantation** rejection, and testicular tumors. Increased levels of LDH-2 are found in lung diseases such as pneumonia and congestive heart failure, as well as in lymphomas and other tumors. Elevations of LDH-3 are significant in lung disease and certain tumors. Elevations of LDH-4 are greatly increased in **pancreatitis**. High levels of LDH-5 are found in liver disease, intestinal problems, and skeletal muscle disease and injury, such as **muscular dystrophy** and recent muscular trauma.

Diffuse disease or injury (for example, collagen disease, **shock**, low blood pressure) and advanced solid-tumor cancers cause significant elevations of all LDH isoenzymes at the same time.

Resources

BOOKS

Pagana, Kathleen Deska, and Timothy J. Pagana. *Mosby's Manual of Diagnostic and Laboratory Tests*. 4th ed. St. Louis: Mosby, 2009.

Janis O. Flores

Lactate dehydrogenase test

Definition

Lactate dehydrogenase, also called lactic dehydrogenase, or LDH, is an enzyme found in the cells of many body tissues, including the heart, liver, kidneys, skeletal muscle, brain, red blood cells, and lungs. It is responsible for converting muscle lactic acid into pyruvic acid, an essential step in producing cellular energy.

Purpose

Lactic dehydrogenase is present in almost all body tissues, so the LDH test is used to detect tissue alterations and as an aid in the diagnosis of **heart attack**, anemia, and **liver disease**. Newer injury markers are becoming more useful than LDH for heart attack diagnosis.

Precautions

Because the LDH enzyme is so widely distributed throughout the body, cellular damage causes an elevation of the total serum LDH. As a result, the diagnostic usefulness of this enzyme by itself is not as valuable as determination of the five fractions that comprise the LDH. These fractions are called isoenzymes and are better indicators of disease than is the total LDH. The fractions are LDH-1, LDH-2, LDH-3, LDH-4, and LDH-5. A normal total LDH level does not mean that individual isoenzyme levels should not be measured. Individual isoenzyme ranges can help differentiate a diagnosis.

Description

When disease or injury affects tissues containing LDH, the cells release LDH into the bloodstream, where it is identified in higher than normal levels. For example, when a person has a heart attack, the LDH level begins to rise about 12 hours after the attack and usually returns to normal within 5–10 days. The LDH is also elevated in diseases of the liver, in certain types of anemia, and in cases of excessive destruction of cells, as in **fractures**, trauma, muscle damage, and shock.

Cancers can also elevate LDH level. Additionally, some patients have chronically elevated LDH with no identifiable cause and no apparent consequence.

Preparation

This test requires a blood sample. It is not necessary for the patient to fast (nothing to eat or drink) before the test unless the physician requests it.

Risks

Risks for this test are minimal, but may include slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after venipuncture, or hematoma (blood accumulating under the puncture site).

Results

Reference ranges for total LDH vary from laboratory to laboratory. Normal values are also higher in childhood. For adults, in most laboratories, the range

KEY TERMS

Enzyme—A protein that regulates the rate of a chemical reaction in the body, increasing the speed at which the change occurs.

Isoenzyme—One of a group of enzymes that catalyze the same reaction but are differentiated by variations in physical properties.

can be up to approximately 200 units/L, but is usually found within 45-90 U/L.

Abnormal results

Due to the fact that many common disease processes cause elevations in the total LDH level, a breakdown of the five different isoenzymes that make up the total LDH is often helpful for diagnosis. In certain disorders, the total LDH may be within normal limits, but individual isoenzyme elevations can indicate specific organ or tissue damage. For example, the LDH-2 fraction is normally greater than LDH-1 in the blood. After an acute heart attack, however, the LDH-1 rises over the LDH-2 in what is known as a "flipped LDH."

Certain diagnoses can be assisted by determination of the total LDH. One example is **infectious mononucleosis**, in which the LDH is usually more elevated than a liver enzyme called AST. Conversely, in cases of viral hepatitis, the liver enzymes AST and ALT are greatly increased over the LDH.

Resources

BOOKS

Pagana, Kathleen Deska, and Timothy J. Pagana. *Mosby's Manual of Diagnostic and Laboratory Tests*. 4th ed. St. Louis: Mosby, 2009.

Janis O. Flores

Lactation

Definition

Lactation is the medical term used for **breastfeeding**. It also specifically refers to the synthesis and secretion of milk.

Purpose

Breastfeeding provides a baby with **nutrition** in the form of breast milk. Not only does breast milk contain all the nutrients needed by a rapidly developing newborn, but it also contains antibodies that provide the baby with additional protection from common early childhood diseases.

Precautions

Most common illnesses cannot be transmitted via breast milk. However, some viruses, including HIV (the virus that causes **AIDS**) can be passed in breast milk; for this reason, women who are HIV-positive should not breastfeed. Vitamin D supplements are often recommended for babies who are breastfed because breast milk is low in vitamin D, a vitamin that promotes strong bones.

Many medications have not been tested in nursing women, so it is not known if these drugs can affect a breast-fed child. A nursing woman should always check with her doctor before taking any medications, including over-the-counter drugs.

In addition, these drugs are not safe to take while nursing:

- radioactive drugs for some diagnostic tests
- chemotherapy drugs for cancer
- bromocriptine
- ergotamine
- lithium
- methotrexate
- street drugs (including marijuana, heroin, amphetamines)
- tobacco

Breastfeeding women should not drink alcohol for at least two hours before breastfeeding, and should not smoke.

Description

Early in a woman's **pregnancy** her milk-producing glands, called mammary glands, begin to prepare for the baby's arrival and by the sixteenth week of pregnancy the breasts are ready to produce milk. Shortly after the baby is born, the expulsion of the placenta triggers hormone shifts in the woman's body to activate lactation. The levels of the hormones estrogen and progesterone fall abruptly while the level of the hormone prolactin—the main hormone involved in the biosynthesis of milk—increases. The anterior pituitary gland secretes prolactin during lactation in very large quantities so that by 36–96 hours after the baby's birth the woman's milk volume has dramatically increased. After this time, the volume of

milk the mother produces levels off and the removal of milk becomes the predominant factor in regulating the volume of milk production.

Another hormone called oxytocin controls the release of milk from the breasts. The baby's sucking stimulates nerve endings in the nipple, which signal the mother's pituitary gland to release the oxytocin. This is called the "let–down reflex." While the baby's sucking is the primary stimulus for the reflex, a baby's cry, thoughts of the baby, or the sound of running water also may trigger the response.

Breast milk cannot be duplicated by artificial milk, although both contain protein, fat, and carbohydrates. Breast milk changes to meet the specific needs of a baby. In particular, the mother produces milk called colostrum at the end of pregnancy and in the initial postpartum period. Colostrum is called "first milk" and is thicker than mature milk. It is yellowish in color and is rich in proteins, many of which are immunoglobulins that can protect the child against illness and **allergies**. Immunoglobulins are part of the body's natural defense system against infections and other agents that can cause disease. Breast milk also helps a baby's own immune system mature faster. As a result, breast-fed babies have fewer ear infections, bouts of **diarrhea**, **rashes**, allergies, and other medical problems than bottle-fed babies do.

Benefits

In addition to providing some protection against infection, breast milk has other benefits. Because it is easily digested, babies are less likely to get constipated.

Breastfeeding is also good for the mother. It releases hormones that stimulate the uterus to contract, helping the uterus to return to normal size after delivery and reducing the risk of bleeding. The act of producing milk burns calories, which helps the mother to lose excess weight gained during pregnancy. Breastfeeding also may be related to a lower risk of **breast cancer**, **ovarian cancer**, and **cervical cancer**.

Breast milk is free, and saves money by eliminating the need to buy artificial milk (formula), bottles, and nipples. It also eliminates the need to sterilize feeding equipment and mix formula with clean, pathogen-free water, a critical consideration in many developing countries. Because breast-fed babies overall have fewer illnesses, their health care costs may be lower.

Breastfeeding should begin as soon as possible after birth and should continue every two to three hours. However, all babies are different; some need to nurse very frequently at first, while others can go much longer between feedings. A baby should be fed at least eight to 12 times in 24 hours. Because breast milk is easily digested, a baby may be hungry again as soon as one and one-half hours after the last meal. Frequent nursing will also help in increasing milk production.

Some babies have no trouble breastfeeding, while others may need some assistance. Once the baby begins to suck, the mother should make sure that most of the areola (the colored part of the nipple) is in the baby's mouth. Proper latching-on will help stimulate milk flow and will prevent nipple soreness.

Breastfeeding mothers should offer the baby both breasts at each feeding. Breastfeeding takes about 15–20 minutes on each side. After stopping the feeding on one side, the mother should burp the baby before offering the other breast. If the baby does not continue feeding, the next feeding should begin with the second breast.

Mothers can tell if the baby is getting enough milk by checking diapers; a baby who is wetting between four to six disposable diapers or six to eight cloth diapers and who has three or four bowel movements in 24 hours is probably getting enough milk.

Preparation

Loose, front-opening clothes and a good nursing bra are recommended. Mothers should find a comfortable chair with lots of pillows, supporting the arm and back, in which to nurse. Feet should rest on a low footstool with knees raised slightly. The baby should be level with the breast. The new mother may have to experiment with different ways of holding the baby before finding one that is comfortable for both the mother and baby.

Several members of the health care team, including obstetricians, nurses, midwives, and lactation consultants, are equipped to provide guidance and support to mothers who wish to breastfeed their babies. By meeting specific eligibility requirements and passing an independent examination, lactation consultants may be certified by the International Board of Lactation Consultants. Such certification demonstrates that these consultants possess the necessary skills, knowledge, and attitudes to provide quality breastfeeding assistance. It is important for new mothers to understand that breastfeeding is something that mothers and babies must learn to do together. The development of a satisfying breastfeeding relationship requires patience on the mother's part and the mother may benefit from the support and guidance of a lactation consultant or other qualified member of her health care team.

KEY TERMS

Areola—The pigmented, circular area surrounding the nipple of each breast.

Bromocriptine—A drug used to treat Parkinson's disease that can decrease a woman's milk supply.

Ergotamine—A drug used to prevent or treat migraine headaches. This can cause vomiting, diarrhea, and convulsions in infants.

Immunoglobulin—A protein produced by plasma cells; a component of the immune system. Transferred in utero and through breast milk, immunoglobulins provide passive immunity to the baby.

Lactation—Secretion of milk from the breasts; the act of breastfeeding.

Latch-on—The process whereby the baby opens the mouth widely and first exerts negative pressure on the mother's nipple and then positive pressure. Good latch-on will result in adequate transfer of milk into the baby's mouth and prevent sore nipples from occurring.

Lithium—A drug used to treat manic depression (bipolar disorder) that can be transmitted in breast milk.

Methotrexate—An anticancer drug also used to treat arthritis that can suppress an infant's immune system when taken by a nursing mother.

Postpartum—Refers to the six-week period after childbirth.

Complications

New mothers may experience breastfeeding problems, including:

- Engorged breasts. Breasts that are too full can prevent the baby from sucking. Expressing milk manually or with a breast pump can help, as can warm showers and compresses.
- Sore nipples. In the early weeks nipples may become sore and even cracked. Treatments include changing the position that the baby nurses in, ensuring that the baby has latched on to most of the areola, and using lanolin-based lotion on the nipples. Nipple shields are sometimes effective as a short-term remedy, but their use may reduce milk supply, further irritate the breast, and change the baby's sucking pattern.
- Inverted nipples: A mother with inverted nipples may still breastfeed in most instances. The baby should be enticed to open the mouth widely before latching on. The mother can use various techniques to evert the nipple such as wearing a breast shell between feedings, rolling the nipple, pulling the nipple out, and applying a breast pump on the breast for a few seconds before starting the breastfeeding session.
- Infection. Soreness and inflammation on the breast surface or a fever in the mother, may be an indication of a breast infection called mastitis. Antibiotics and continued nursing on the affected side may solve the problem.

Results

There are no rules about when to stop breastfeeding. A baby needs breast milk or artificial milk for at least the first year of life. As long as a baby eats age-appropriate solid food, the mother may nurse for several years.

Health care team roles

Several members of the health care team, including obstetricians, nurses, midwives, and lactation consultants, are equipped to provide guidance and support to mothers who wish to breastfeed their babies. By meeting specific eligibility requirements and passing an independent examination, lactation consultants may be certified by the International Board of Lactation Consultants. Such certification demonstrates that these consultants possess the necessary skills, knowledge, and attitudes to provide quality breastfeeding assistance. It is important for new mothers to understand that breastfeeding is something that mothers and babies must learn to do together. The development of a satisfying breastfeeding relationship requires patience on the mother's part and the mother may benefit from the support and guidance of a lactation consultant or other qualified member of her health care team.

Resources

BOOKS

Lauwers, Judith, and Anna Swisher. *Counseling the Nursing Mother: A Lactations Consultant's Guide,* 5th ed. Sudbury, MA: Jones & Bartlett Learning, 2011.

Lauwers, Judith. *Quick Reference for the Lactation Professional.* Sudbury, MA: Jones & Bartlett Publishers, 2009.

Walker, Marsha. *The Nipple in Breastfeeding and Lactation.* Amarillo, TX: Hale, 2010.

PERIODICALS

Chamblin, Carol. "Guidelines for Preterm and Late Preterm Infants." *Journal of Human Lactation*. 25(4) (November 2009): 401–403.

Champ, Martine, and Christine Hoebler. "Functional Food for Pregnant, Lactating Women and in Perinatal Nutrition: a Role for Dietary Fibers?" *Current Opinion in Clinical Nutrition & Metabolic Care*. 12(6) (November 2009): 565–74.

Dowling, Alexander A., and Donna L. Furman. "What do Low-Income Women Say About Breastfeeding?" *Breastfeeding Medicine*. 5 (February 2010): 17–23.

ORGANIZATIONS

International Board of Lactation Consultant Examiners (IBLCE), 6402 Arlington Blvd., Suite 350, Falls Church, VA, 22042, (703) 560-7330, (703) 560-7332, iblce@ibcle.org, www.iblce.org.

La Leche League International, PO Box 4079, Schaumburg, IL, 60168–4079, (800) 525-3243, (847) 519-9585, http://www.llli.org.

Nadine M. Jacobson
Tish Davidson, A.M.

Lactic acid test

Definition

Lactic acid is an acid produced by cells during chemical processes in the body that do not require oxygen (anaerobic metabolism). Anaerobic metabolism occurs only when too little oxygen is present for the more usual aerobic metabolism (oxygen requiring). Lactic acid is a contributing factor in **muscle cramps**. It is also produced in tissues when conditions such as **heart attack** or **shock** reduce the blood supply responsible for carrying oxygen. Normally, lactic acid is removed from the blood by the liver. When an excess of lactic acid accumulates for any reason, the result is a condition called lactic acidosis.

Purpose

The lactic acid test is used as an indirect assessment of the oxygen level in tissues and to determine the cause and course of lactic acidosis.

Precautions

During blood collection, the patient should be instructed to relax the hand. Clenching and unclenching the fist will cause a build-up of potassium and lactic acid from the hand muscles that will falsely elevate the levels.

Description

The degree of acidity is an important chemical property of blood and other body fluids. Acidity is expressed on a pH scale where 7.0 is neutral, above 7.0 is basic (alkaline), and below 7.0 is acidic. A strong acid has a very low pH (near 1.0). A strong base has a very high pH (near 14.0). Blood is normally slightly alkaline or basic. It has a pH range of 7.35–7.45. The balance of acid to base in blood is precisely controlled. Even a minor deviation from the normal range can severely affect many organs.

Lactic acid (present in the blood as lactate ion) is a product of the breakdown of glucose to generate energy. It is found primarily in muscle cells and red blood cells. The lactate ion concentration in the blood depends on the rates of energy production and metabolism. Levels may increase significantly during **exercise**.

Together, lactic acid and another chemical (pyruvate) form a reversible reaction regulated by the oxygen supply to the blood and tissues. When oxygen levels are low, pyruvate converts to lactic acid; when oxygen levels are adequate, lactic acid converts to pyruvate. When the liver fails to metabolize lactose sufficiently or when too much pyruvate converts to lactate, lactic acidosis occurs. Measurement of blood lactate levels is recommended for all patients with symptoms of lactic acidosis. Testing is generally indicated if the blood pH level falls below 7.25–7.35.

Because of the close relationship between pyruvate and lactic acid, comparison of blood levels of the two substances can provide reliable information about tissue oxidation. However, pyruvate measurement is technically difficult and seldom performed. Lactic acid is measured more often, in either venous or arterial blood samples.

Preparation

This test requires a blood sample. The patient should have nothing to eat or drink (**fasting**) from midnight the night before the test. Because lactic acid is produced by exertion, the patient should rest for at least one hour before the test.

Risks

Risks for this test are minimal. The patient may experience slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after puncture of the vein (venipuncture), or an accumulation of blood under the puncture site (hematoma).

KEY TERMS

Acidosis—A disturbance of the balance of acid to base in the body causing an accumulation of acid or loss of alkali (base). There are two types of acidosis: metabolic and respiratory. One of the most common causes of metabolic acidosis is an overdose of aspirin. Respiratory acidosis is caused by impaired breathing caused by conditions such as severe chronic bronchitis, bronchial asthma, or airway obstruction.

Results

Reference values vary from laboratory to laboratory but can be found within the following ranges:

- Venous blood: 4.5–19.8 mg/dL
- Arterial blood: 4.5–14.4 mg/dL

High blood lactate levels, together with decreased oxygen in tissues, may be caused by strenuous muscle exercise, shock, hemorrhage, severe infection in the blood stream, heart attack, or cardiac arrest. When tissue oxygenation is low for no apparent reason, increased lactate levels may be caused by systemic disorders like diabetes, leukemia, **liver disease**, or kidney failure. Defects in enzymes may also be responsible, as in glycogen storage disease (von Gierke's disease). Lactate is also increased in certain instances of intestinal obstruction.

Lactic acidosis can be caused by taking large doses of **acetaminophen** and alcohol and by intravenous infusion of epinephrine, glucagon, fructose, or sorbitol. Antifreeze **poisoning** can also cause lactic acidosis. In rare instances, a diabetic medication, metformin (Glucophage), causes lactic acidosis. People with weak kidneys should not take metformin.

Resources

BOOKS

Pagana, Kathleen Deska, and Timothy J. Pagana. *Mosby's Manual of Diagnostic and Laboratory Tests*. 4th ed. St. Louis: Mosby, 2009.

Paul A. Johnson, Ed.M.

Lactic acidosis *see* **Metabolic acidosis**

Lactogen test *see* **Prolactin test**

Lactogenic hormone test *see* **Prolactin test**

Lactose intolerance

Definition

Lactose intolerance refers to the inability of the body to fully digest lactose, which is a type of sugar found in milk. It is also sometimes called lactose deficiency. Although the condition is neither serious nor fatal, it can cause much discomfort in the form of gastrointestinal distress. Many people have low levels of the enzyme lactase in their bodies (which break down lactose) but do not show any symptoms of lactose intolerance. Thus, people with lactose intolerance have both low lactase levels and the associated symptoms. The condition can be regulated by reducing or eliminating the consumption of products containing milk.

Demographics

The condition of being lactose intolerant is common in adults around the world. However, it is more common in such ethnic groups as Africans, African Americans, South Americans, Asians, Native Americans, and people from Mediterranean descent. It is less common in people descended from, or living in, northern and western parts of Europe and North America. The age at which lactose intolerance first begins can vary. In Caucasians, the first signs of lactose intolerance can begin as early as the age of five years. In African Americans, the age is even earlier, at two years. An estimated 30 million American adults (out of about 220 million adults, in 2010, about 14%) have some degree of lactose intolerance by the age of 20 years.

Description

Lactose is the form of sugar present in milk and other dairy products, and some non-dairy products, too. Human milk is considered the product with the highest concentration of lactose, with about 9%. Unprocessed cow milk has about 4.7% of lactose. The enzyme lactase, which is normally produced by cells lining the small intestine, breaks down lactose into substances that can be absorbed into the bloodstream. When dairy products are ingested, the lactose reaches the digestive system and is broken down by lactase into the simpler sugars of glucose and galactose. The liver changes the galactose into glucose, which then enters the bloodstream and raises the blood glucose level. Lactose intolerance occurs when, due to a deficiency of lactase, lactose is not completely broken down, unprocessed lactose proceeds into the colon (large intestine), and the glucose level does not rise. While not

usually dangerous, lactose intolerance can cause severe discomfort in the form of bloating, **diarrhea**, and gas.

It is estimated that from 30 to 50 million Americans, young and old, suffer from the symptoms of lactose intolerance, but not everyone who is deficient in lactase experiences symptoms. Experts contend that approximately 75% of the adult population worldwide does not produce enough lactase and is at risk for some or all of the symptoms of lactose intolerance.

Risk factors

Many factors may cause increasing risk of contracting lactose intolerance. Some of these major factors include:

- Ethnicity (certain ethnic groups are more predisposed to it)
- Age (as one ages the condition becomes more common)
- Diseases (especially relating to the small intestines, such as Celiac disease and Crohn's disease)
- Premature babies (reduced levels of lactase are common in infants born prematurely)
- Radiation (directed toward the abdominal area).

Causes and symptoms

Lactose intolerance can be caused by some diseases of the digestive system and by injuries to the small intestine that result in a decreased production of lactase. This type of the condition is called secondary lactose intolerance. While rare, some children are also born unable to produce the enzyme. This type is called congenital lactose intolerance, being passed down from both parents to the child through autosomal recessive inheritance. For many, however, lactase deficiency develops naturally because, after about two years of age, the body produces less lactase. When age is a factor in acquiring the condition, it is called primary lactose intolerance.

Overall, symptoms include **nausea**, cramps, diarrhea, abdominal bloating, gas (flatulence), floating and foul-smelling stools, **malnutrition**, and weight loss. In children, an additional symptom is slow growth. The symptoms, which may be mild to severe, usually occur between 30 minutes to two hours after eating or drinking lactose-containing foods.

Diagnosis

Usually health care professionals measure the absorption of lactose in the digestive system by using the lactose tolerance test, lactose-hydrogen breath test, or stool acidity test. Each of these can be performed outpatient, through a hospital, clinic or doctor's office.

People taking the lactose tolerance test must fast before being tested. They then drink a lactose-containing liquid for the test and medical personnel take blood samples during the next two hours to measure the patient's blood glucose level. The blood glucose level, or blood sugar level, indicates how well the body is digesting the lactose. A diagnosis of lactose intolerance is confirmed when blood glucose level does not rise. This test is not administered to infants and very young children because they are more prone to **dehydration**, which can result from diarrhea from the liquid.

Health care professionals measure the amount of hydrogen in the breath using the lactose-hydrogen breath test. Hydrogen is usually detected only in small amounts in the breath. However, when bacteria ferment undigested lactose, which is found in the colon, hydrogen in the breath is produced in greater quantities. The hydrogen is exhaled after being absorbed from the intestines and carried through the bloodstream to the lungs. The hydrogen breath test involves having the patient drink a lactose-containing beverage. Health care professionals monitor the breath at regular intervals to see if the hydrogen levels rise, which indicates improper lactose digestion. People taking the test who have had certain foods, medications, or cigarettes before the test may get inaccurate results. While the test is available to children and adults, newborns and young children should not have it because of the risk of dehydration from drinking the beverage that can cause diarrhea in those who are lactose intolerant.

A stool acidity test measures the amount of acid in the stool. This is a safe test for newborns and young children. The test detects lactic acid and other short-chain fatty acids from undigested lactose fermented by bacteria in the colon. Glucose might also be in the stool sample, resulting form unabsorbed lactose in the colon.

Medical professionals may also examine the small intestines with a procedure called an enteroscopy. A thin, flexible tube, which is called an endoscope, is inserted through the mouth or nose and down into the upper gastrointestinal tract. Balloons, attached to the endoscope, allow the physician the ability to observe the small intestine. A procedure called a **colonoscopy** may also be used. A tube is inserted into the rectum and up into the small intestine. In both cases, tissue samples may be removed and examined by trained laboratory technicians.

Treatment

Pediatricians might recommend that parents of newborns and very young children who are suspected

of having lactose intolerance simply change from cow's milk to a soy formula. Since treatments are not available that can improve the body's ability to produce lactase, lactose deficiency treatments instead, are focused on controlling the diet.

Most people affected by lactose intolerance do well if they limit their intake of lactose foods and drinks. People differ in the amounts they can handle before experiencing symptoms. Some have to stop lactose completely. People who are sensitive after ingesting small amounts of lactose can take lactase enzymes, which are available without a prescription. Using the liquid form, people can add a few drops in their milk, put the milk in the refrigerator and drink it after 24 hours, when the lactase enzymes have worked to reduce the lactose content by 70%. If the milk is heated first and double the amount of lactase liquid is added, the milk will be 90% lactose free. Recently, researchers have developed a chewable lactase enzyme tablet. By taking three to six tablets just before eating, the tablets help people digest lactose-containing solid foods. Supermarkets also carry lactose-reduced milk and other products, which contain the needed nutrients found in the regular products but without the lactose.

Foods that contain lactose are milk, low-fat milk, skim milk, chocolate milk, buttermilk, sweetened condensed milk, dried whole milk, instant nonfat dry milk, low-fat yogurts, frozen yogurts ice cream, ice milk, sherbet, cheese, cottage cheese, low-fat cottage cheese, cream and butter. Other foods that may contain hidden lactose are: nondairy creamers, powdered artificial sweeteners, foods containing milk power or nonfat milk solids, bread, cake, margarine, creamed soups, pancakes, waffles, processed breakfast cereals, salad **dressings**, luncheon meats, potato chips, puddings, custards, confections and some meat products. These forms of hidden lactose may appear on packaging labels as whey, curds, milk solids, lactoserum, dry milk solids, milk by-products, modified milk ingredients, non-fat dry milk powder, and other such terms.

Many cultured milk products, such as yogurt, contain probiotics, which are living organisms that help to maintain a well regulated digestive system. These products can be used to help with gastrointestinal problems. Probiotics also help to digest lactose, when the body cannot do so naturally.

Prognosis

Lactose intolerance is easy to manage. People of all ages however, especially children, have to replace the **calcium** lost during the reduction (or elimination) of milk products by taking supplements and eating calcium-rich foods, such as leafy vegetables (broccoli, spinach, and kale), certain seafood (canned salmon, oysters, sardines, and shrimp), calcium-fortified foods, almonds, oranges, pinto beans, rhubarb, and tofu. Many people who suffer with lactose intolerance will be able to continue eating some milk products. Some diary products may be tolerable to one's system depending on the amount of lactose contained within t hem. Many times milk can be consumed in smaller amounts to lessen the problem associated with the malady. In addition, milk consumed with meals is usually less problematic. Yogurt contains enzymes that break down lactose, so lactose-intolerant people may tolerate it. The condition is not considered dangerous. However, unless treated properly, people with lactose intolerance have to contend with weight loss and malnutrition, along with many symptoms that cause discomfort.

KEY TERMS

Galactose—Simple sugar derived from milk sugar.

Glucose—A simple sugar and the chief energy source in the body.

Lactase enzyme—The enzyme produced by cells that line the small intestine which allows the body to break down lactose.

Lactose—The primary sugar in milk.

Prevention

Often, lactose intolerance is a natural occurrence that cannot be avoided. However, people can prevent symptoms by managing the condition with diet and lactase supplements. Foods and beverages that state they are "lactose-free" can be substituted for diary products. Milk can be treated with commercially available lactase products (lactase drops) that remove almost all of the lactose contained within milk. Lactase capsules or tablets are also available, which can be taken orally before eating meals that include dairy products.

Resources

BOOKS

Coulston, Ann M, and Carol J. Boushey, editors. *Nutrition in the Prevention and Treatment of Disease*. Amsterdam: Academic Press, 2008.

Fleming, Alisa Marie. *Go Dairy Free: The Guide and Cookbook for Milk Allergies, Lactose Intolerance, and Casein-Free Living*. Henderson, NV: Fleming Ink, 2008.

Schmid, Ron. *The Untold Story of Milk: The History, Politics and Science of Nature's Perfect Food*. Washington, DC: New Trends, 2009.

OTHER

African Adaptation to Digesting Milk Is "Strongest Signal of Selection Ever". Scientific American. (December 11, 2006), http://www.scientificamerican.com/article.cfm?id=african-adaptation-to-dig&ref=sciam (accessed September 15, 2010).

Lactose Intolerance. Mayo Clinic. (February 16, 2010), http://www.mayoclinic.com/health/lactose-intolerance/DS00530 (accessed September 15, 2010).

Lactose Intolerance. MedlinePlus, National Library of Medicine and National Institutes of Health. (August 22, 2008), http://www.nlm.nih.gov/medlineplus/ency/article/000276.htm (accessed September 15, 2010).

Lactose Intolerance. National Digestive Diseases Information Clearinghouse. (June 2009), http://digestive.niddk.nih.gov/ddiseases/pubs/lactoseintolerance/; (accessed September 15, 2010).

ORGANIZATIONS

American Dietetic Association, 120 South Riverside Plaza, Suite 2000, Chicago, IL, 60606-6995, (312) 899-0040, (800) 877-1600, http://www.eatright.org/.

American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD, 20814, (301) 654-2055, (301) 654-5920, http://www.gastro.org/.

Lisette Hilton

Lambliasis *see* **Giardiasis**

Laminectomy

Definition

A laminectomy is a surgical procedure in which the surgeon removes a portion of the bony arch, or lamina, on the dorsal surface of a vertebra, which is one of the bones that make up the human spinal column. It is done to relieve back **pain** that has not been helped by more conservative treatments. In most cases a laminectomy is an elective procedure rather than emergency surgery. A laminectomy for relief of pain in the lower back is called a lumbar laminectomy or an open decompression.

Purpose

Structure of the spine

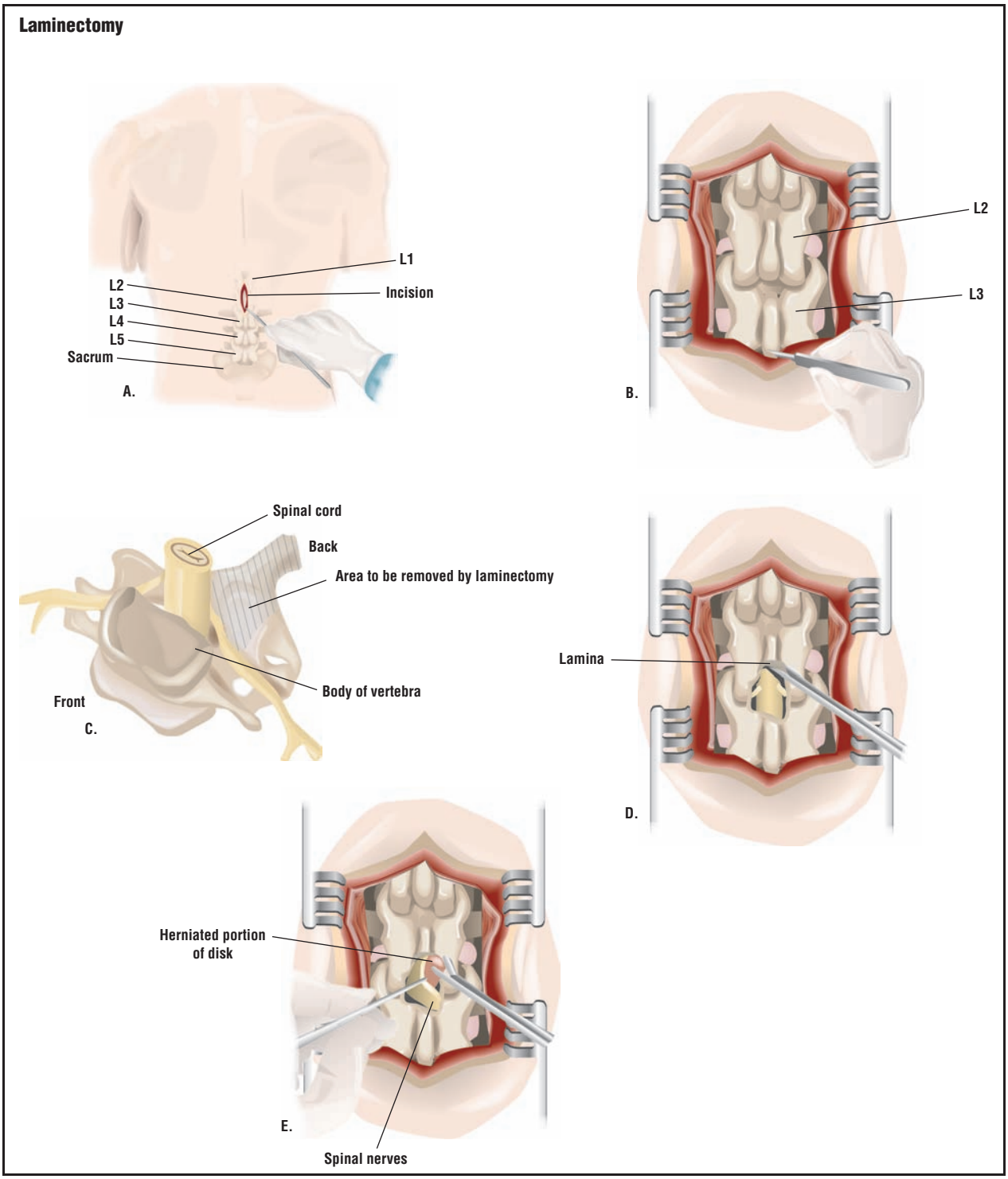
In order to understand why removal of a piece of bone from the arch of a vertebra relieves pain, it is helpful to have a brief description of the structure of the spinal column and the vertebrae themselves. In humans, the spine comprises 33 vertebrae, some of which are fused together. There are seven vertebrae in the cervical (neck) part of the spine; 12 vertebrae in the thoracic (chest) region; five in the lumbar (lower back) region; five vertebrae that are fused to form the sacrum; and four vertebrae that are fused to form the coccyx, or tailbone. It is the vertebrae in the lumbar portion of the spine that are most likely to be affected by the disorders that cause back pain.

The 24 vertebrae that are not fused are stacked vertically in an S-shaped column that extends from the tailbone below the waist up to the back of the head. This column is held in alignment by ligaments, cartilage, and muscles. About half the weight of a person's body is carried by the spinal column itself and the other half by the muscles and ligaments that hold the spine in alignment. The bony arches of the laminae on each vertebra form a canal that contains and protects the spinal cord. The spinal cord extends from the base of the brain to the upper part of the lumbar spine, where it ends in a collection of nerve fibers known as the cauda equina, which is a Latin phrase meaning "horse's tail." Other nerves branching out from the spinal cord pass through openings formed by adjoining vertebrae. These openings are known as foramina (singular, foramen).

Between each vertebra is a disk that serves to cushion the vertebrae when a person bends, stretches, or twists the spinal column. The disks also keep the foramina between the vertebrae open so that the spinal nerves can pass through without being pinched or damaged. As people age, the intervertebral disks begin to lose moisture and break down, which reduces the size of the foramina between the vertebrae. In addition, bone spurs may form inside the vertebrae and cause the spinal canal itself to become narrower. Either of these processes can compress the spinal nerves, leading to pain, **tingling** sensations, or weakness in the lower back and legs. A lumbar laminectomy relieves pressure on the spinal nerves by removing the disk, piece of bone, tumor, or other structure that is causing the compression.

Causes of lower back pain

The disks and vertebrae in the lower back are particularly vulnerable to the effects of **aging** and daily wear and tear because they bear the full weight of the upper body, even when one is sitting quietly in a chair. When a person bends forward, 50% of the motion occurs at the hips, but the remaining 50% involves the lumbar spine. The force exerted in bending is not evenly divided among the five lumbar vertebrae; the segments between the third and fourth lumbar



In this posterior (from the back) lumbar laminectomy, an incision is made in the patient's back over the lumbar vertebrae (A). The wound is opened with retractors to expose the L2 and L3 vertebrae (B). A piece of bone at the back of the vertebrae is removed (C and D), allowing a damaged disk to be repaired (E). *(Illustration by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)*

KEY TERMS

Cauda equina—The collection of spinal nerve roots that lie inside the spinal column below the end of the spinal cord. The name comes from the Latin for "horse's tail."

Cauda equina syndrome (CES)—A group of symptoms characterized by numbness or pain in the legs and/or loss of bladder and bowel control, caused by compression and paralysis of the nerve roots in the cauda equina. CES is a medical emergency.

Chiropractic—A system of therapy based on the notion that health and disease are related to the interactions between the brain and the nervous system. Treatment involves manipulation and adjustment of the segments of the spinal column. Chiropractic is considered a form of alternative medicine.

Decompression—Any surgical procedure done to relieve pressure on a nerve or other part of the body. A laminectomy is sometimes called an open decompression.

Dorsal—Referring to a position closer to the back than to the stomach. The laminae in the spinal column are located on the dorsal side of each vertebra.

Dura—A tough fibrous membrane that covers and protects the spinal cord.

Foramen (plural, foramina)—The medical term for a natural opening or passage. The foramina of the spinal column are openings between the vertebrae for the spinal nerves to branch off from the spinal cord.

Laminae (singular, lamina)—The broad plates of bone on the upper surface of the vertebrae that fuse together at the midline to form a bony covering over the spinal canal.

Laminotomy—A less invasive alternative to a laminectomy in which a hole is drilled through the lamina.

Ligamenta flava (singular, ligamentum flavum)—A series of bands of tissue that are attached to the vertebrae in the spinal column. They help to hold the spine straight and to close the spaces between the laminar arches. The Latin name means "yellow band(s)."

Lumbar—Pertaining to the part of the back between the chest and the pelvis.

Myelogram—A special type of x-ray study of the spinal cord, made after a contrast medium has been injected into the space surrounding the cord.

Osteopathy—A system of therapy that uses standard medical and surgical methods of diagnosis and treatment while emphasizing the importance of proper body alignment and manipulative treatment of musculoskeletal disorders. Osteopathy is considered mainstream primary care medicine rather than an alternative system.

Pain disorder—A psychiatric disorder in which pain in one or more parts of the body is caused or made worse by psychological factors. The lower back is one of the most common sites for pain related to this disorder.

Retractor—An instrument used during surgery to hold an incision open and pull back underlying layers of tissue.

Sciatica—Pain in the lower back, buttock, or leg along the course of the sciatic nerve.

Somatization disorder—A chronic condition in which psychological stresses are converted into physical symptoms that interfere with work and relationships. Lower back pain is a frequent complaint of patients with somatization disorder.

Spinal stenosis—Narrowing of the canals in the vertebrae or around the nerve roots, causing pressure on the spinal cord and nerves.

Vertebra (plural, vertebrae)—One of the bones of the spinal column. There are 33 vertebrae in the human spine.

vertebrae (L3-L4) and the fourth and fifth (L4-L5) are most likely to break down over time. More than 95% of spinal disk operations are performed on the fourth and fifth lumbar vertebrae.

Specific symptoms and disorders that affect the lower back include:

- Sciatica. Sciatica refers to sudden pain felt as radiating from the lower back through the buttocks and down the back of one leg. The pain, which may be experienced as weakness in the leg, a tingling feeling, or a "pins and needles" sensation, runs along the course of the sciatic nerve. Sciatica is a common symptom of a herniated disk.
- Spinal stenosis. Spinal stenosis is a disorder that results from the narrowing of the spinal canal surrounding the spinal cord and eventually compressing the cord. It may result from hereditary factors, from the effects of aging, or from changes in the pattern of blood flow to

the lower back. Spinal stenosis is sometimes difficult to diagnose because its early symptoms can be caused by a number of other conditions and because the patient usually has no history of back problems or recent injuries. Imaging studies may be necessary for accurate diagnosis.

- Cauda equina syndrome (CES). Cauda equina syndrome is a rare disorder caused when a ruptured disk, bone fracture, or spinal stenosis put intense pressure on the cauda equina, the collection of spinal nerve roots at the lower end of the spinal cord. CES may be triggered by a fall, automobile accident, or penetrating gunshot injury. It is characterized by loss of sensation or altered sensation in the legs, buttocks, or feet; pain, numbness, or weakness in one or both legs; difficulty walking; or loss of control over bladder and bowel functions. *Cauda equina syndrome is a medical emergency requiring immediate treatment*. If the pressure on the nerves in the cauda equina is not relieved quickly, permanent paralysis and loss of bladder or bowel control may result.
- Herniated disk. The disks between the vertebrae in the spine consist of a fibrous outer part called the annulus and a softer inner nucleus. A disk is said to herniate when the nucleus ruptures and is forced through the outer annulus into the spaces between the vertebrae. The material that is forced out may put pressure on the nerve roots or compress the spinal cord itself. In other cases, the chemicals leaking from the ruptured nucleus may irritate or inflame the spinal nerves. More than 80% of herniated disks affect the spinal nerves associated with the L5 vertebra or the first sacral vertebra.
- Osteoarthritis (OA). OA is a disorder in which the cartilage in the hips, knees, and other joints gradually breaks down, allowing the surfaces of the bones to rub directly against each other. In the spine, OA may result in thickening of the ligaments surrounding the spinal column. As the ligaments increase in size, they may begin to compress the spinal cord.

Factors that increase a person's risk of developing pain in the lower back include:

- Hereditary factors. Some people are born with relatively narrow spinal canals and may develop spinal stenosis fairly early in life.
- Sex. Men are at greater risk of lower back problems than women, in part because they carry a greater proportion of their total body weight in the upper body.
- Age. The intervertebral disks tend to lose their moisture content and become thinner as people get older.
- Occupation. Jobs that require long periods of driving (long-distance trucking; bus, taxi, or limousine operation) are hard on the lower back because of vibrations from the road surface transmitted upward to the spine. Occupations that require heavy lifting (nursing, child care, construction work, airplane maintenance) put extra stress on the lumbar vertebrae. Other high-risk occupations include professional sports, professional dance, assembly line work, foundry work, mining, and mail or package delivery.
- Lifestyle. Wearing high-heeled shoes, carrying heavy briefcases or shoulder bags on one side of the body, or sitting for long periods of time in one position can all throw the spine out of alignment.
- Obesity. Being overweight, particularly if the extra pounds are concentrated in the abdomen, adds to the strain on the muscles and ligaments that support the spinal column.
- Trauma. Injuries to the back from contact sports, falls, criminal assaults, or automobile accidents may lead to misalignment of the vertebrae or a ruptured disk. Traumatic injuries may also trigger the onset of cauda equina syndrome.

Demographics

Pain in the lower back is a chronic condition that has been treated in various ways from the beginnings of human medical practice. The earliest description of disorders affecting the lumbar vertebrae was written in 3000 B.C. by an ancient Egyptian surgeon. In the modern world, back pain is responsible for more time lost from work than any other cause except the **common cold**. Between 10% and 15% of workers' compensation claims are related to chronic pain in the lower back. It is estimated that the direct and indirect costs of back pain to the American economy range between $75 and $80 billion per year.

In the United States, about 13 million people seek medical help each year for the condition. According to the Centers for Disease Control, 14% of all new visits to primary care doctors are related to problems in the lower back. The CDC estimates that 2.4 million adults in the United States are chronically disabled by back pain, with another 2.4 million temporarily disabled. About 80% of people will experience pain in the lower back at some point in their lifetime; on a yearly basis, one person in every five will have some kind of back pain.

Back pain primarily affects the adult population, most commonly people between the ages of 45 and 64. It is more common among men than women, and more common among Caucasians and Hispanics than among African Americans or Asian Americans.

Description

A laminectomy is performed with the patient under **general anesthesia**, usually positioned lying on the side or stomach. The surgeon begins by making a small straight incision over the damaged vertebra.

The surgeon next uses a retractor to spread apart the muscles and fatty tissue overlying the spine. When the laminae have been reached, the surgeon cuts away part of the bony arch in order to expose the ligamentum flavum, which is a band of yellow tissue attached to the vertebra that helps to support the spinal column and closes in the spaces between the vertebral arches. The surgeon then cuts an opening in the ligamentum flavum in order to reach the spinal canal and expose the compressed nerve. At this point the cause of the compression (**herniated disk**, tumor, bone spur, or a fragment of the disk that has separated from the remainder) will be visible.

Bone spurs, if any, are removed in order to enlarge the foramina and the spinal canal. If the disk is herniated, the surgeon uses the retractor to move the compressed nerve aside and removes as much of the disk as necessary to relieve pressure on the nerve. The space that was occupied by the disk will be filled eventually by new connective tissue.

If necessary, a spinal fusion is performed to stabilize the patient's lower back. A small piece of bone taken from the hip is grafted onto the spine and attached with metal screws or plates to support the lumbar vertebrae.

Following completion of the spinal fusion, the surgeon closes the incision in layers, using different types of sutures for the muscles, connective tissues, and skin. The entire procedure takes one to three hours.

Diagnosis/Preparation

Diagnosis

The differential diagnosis of lower back pain is complicated by the number of possible causes and the patient's reaction to the discomfort. In many cases the patient's perception of back pain is influenced by poor-quality sleep or emotional issues related to occupation or family matters. A primary care doctor will begin by taking a careful medical and occupational history, asking about the onset of the pain as well as its location and other characteristics. Back pain associated with the lumbar spine very often affects the patient's ability to move, and the muscles overlying the affected vertebrae may feel sore or tight. Pain resulting from heavy lifting usually begins within 24 hours of the overexertion. Most patients who do not have a history of chronic pain in the lower back feel better after 48 hours of bed rest with pain medication and either a heating pad or ice pack to relax **muscle spasms**.

If the patient's pain is not helped by rest and other conservative treatments, he or she will be referred to an orthopedic surgeon for a more detailed evaluation. An orthopedic evaluation includes a **physical examination**, neurological workup, and imaging studies. In the physical examination, the doctor will ask the patient to sit, stand, or walk in order to see how these functions are affected by the pain. The patient may be asked to **cough** or to lie on a table and lift each leg in turn without bending the knee, as these maneuvers can help to diagnose nerve root disorders. The doctor will also palpate (feel) the patient's spinal column and the overlying muscles and ligaments to determine the external location of any tender spots, **bruises**, thickening of the ligaments, or other structural abnormalities. The neurological workup will focus on the patient's reflexes and the spinal nerves that affect the functioning of the legs. Imaging studies for lower back pain typically include an x-ray study and CT scan of the lower spine, which will reveal bone deformities, narrowing of the intervertebral disks, and loss of cartilage. An MRI may be ordered if **spinal stenosis** is suspected. In some cases the doctor may order a myelogram, which is an x ray or CT scan of the lumbar spine performed after a special dye has been injected into the spinal fluid.

Lower back pain is one of several common general medical conditions that require the doctor to assess the possibility that the patient has a concurrent psychiatric disorder. Such diagnoses as somatization disorder or pain disorder do not mean that the patient's physical symptoms are imaginary or that they should not receive surgical or medical treatment. Rather, a psychiatric diagnosis indicates that the patient is allowing the back pain to become the central focus of life or responding to it in other problematic ways. Some researchers in Europe as well as North America think that the frequency of lower back problems in workers' disability claims reflect emotional dissatisfaction with work as well as physical stresses related to specific jobs.

Preparation

Most hospitals require patients to have the following tests before a laminectomy: a complete physical examination; **complete blood count** (CBC); an electrocardiogram (EKG); a urine test; and tests that measure the speed of blood clotting.

Aspirin and arthritis medications should be discontinued seven to 10 days before a laminectomy because they thin the blood and affect clotting time. Patients should provide the surgeon and anesthesiologist with a

complete list of all medications, including over-the-counter and herbal preparations, that they take on a regular basis.

The patient is asked to stop **smoking** at least a week before surgery and to take nothing by mouth after midnight before the procedure.

Aftercare

Aftercare following a laminectomy begins in the hospital. Most patients will remain in the hospital for one to three days after the procedure. During this period the patient will be given fluids and antibiotic medications intravenously to prevent infection. Medications for pain will be given every three to four hours, or through a device known as a PCA (patient-controlled anesthesia). The PCA is a small pump that delivers a dose of medication into the IV when the patient pushes a button. To get the lungs back to normal functioning, a respiratory therapist will ask the patient to do some simple breathing exercises and begin walking within several hours of surgery.

Aftercare during the hospital stay is also intended to lower the risk of a venous thromboembolism (VTE), or blood clot in the deep veins of the leg. Prevention of VTE involves medications to thin the blood and wearing compression stockings or boots.

Most surgeons prefer to see patients one week after surgery to remove stitches and check for any postoperative complications. Patients should not drive or return to work before their checkup. A second follow-up examination is usually done four to eight weeks after the laminectomy.

Patients can help speed their recovery by taking short walks on a daily basis; avoiding sitting or standing in the same position for long periods of time; taking brief naps during the day; and sleeping on the stomach or the side. They may take a daily bath or shower without needing to cover the incision. The incision should be carefully patted dry, however, rather than rubbed.

Risks

Risks associated with a laminectomy include:

- bleeding
- infection
- damage to the spinal cord or other nerves
- weakening or loss of function in the legs
- blood clots
- leakage of spinal fluid resulting from tears in the dura, the protective membrane that covers the spinal cord
- worsening of back pain

Results

Normal results depend on the cause of the patient's lower back pain; most patients can expect considerable relief from pain and some improvement in functioning. There is some disagreement among surgeons about the success rate of laminectomies, however, which appears to be due to the fact that the operation is generally done to improve quality of life—cauda equina syndrome is the only indication for an emergency laminectomy. Different sources report success rates between 26% and 99%, with 64% as the average figure. According to one study, 31% of patients were dissatisfied with the results of the operation, possibly because they may have had unrealistic expectations of the results.

Morbidity and mortality rates

The mortality rate for a lumbar laminectomy is between 0.8% and 1%. Rates of complications depend partly on whether a spinal fusion is performed as part of the procedure; while the general rate of complications following a lumbar laminectomy is given as 6–7%, the rate rises to 12% of a spinal fusion has been done.

Alternatives

Conservative treatments

Surgery for lower back pain is considered a treatment of last resort, with the exception of cauda equina syndrome. Patients should always try one or more conservative approaches before consulting a surgeon about a laminectomy. In addition, most health insurers will require proof that the surgery is necessary, since the average total cost of a lumbar laminectomy is $85,000.

Some conservative approaches that have been found to relieve lower back pain include:

- Analgesic or muscle relaxant medications. Analgesics are drugs given to relieve pain. The most commonly prescribed pain medications are aspirin or NSAIDs. Muscle relaxants include methocarbamol, cyclobenzaprine, or diazepam.
- Epidural injections. Epidural injections are given directly into the space surrounding the spinal cord. Corticosteroids are the medications most commonly given by this route, but preliminary reports indicate that epidural injections of indomethacin are also effective in relieving recurrent pain in the lower back.
- Rest. Bed rest for 48 hours usually relieves acute lower back pain resulting from muscle strain.
- Appropriate exercise. Brief walks are recommended as a good form of exercise to improve blood circulation, particularly after surgery. In addition, there are several

simple exercises that can be done at home to strengthen the muscles of the lower back. A short pamphlet entitled *Back Pain Exercises* may be downloaded free of charge from the American Academy of Orthopaedic Surgeons (AAOS) web site.

- Losing weight. People who are severely obese may wish to consider weight reduction surgery to reduce the stress on their spine as well as their heart and respiratory system.
- Occupational modifications or change. Lower back pain related to the patient's occupation can sometimes be eased by taking periodic breaks from sitting in one position; by using a desk and chair proportioned to one's height; by learning to use the muscles of the thighs when lifting heavy objects rather than the lower back muscles; and by maintaining proper posture when standing or sitting. In some cases the patient may be helped by changing occupations.
- Physical therapy. A licensed physical therapist can be helpful in identifying the patient's functional back problems and planning a course of treatment to improve flexibility, strength, and range of motion.
- Osteopathic manipulative treatment (OMT). Osteopathic physicians (DOs) receive the same training in medicine and surgery as MDs; however, they are also trained to evaluate postural and spinal abnormalities and to perform several different manual techniques for relief of back pain. An article published in the *New England Journal of Medicine* in 1999 reported that OMT was as effective as physical therapy and standard medication in relieving lower back pain, with fewer side effects and lower health care costs. OMT is recommended in the United Kingdom as a very low-risk treatment that is more effective than bed rest or mild analgesics.
- Transcutaneous electrical nerve stimulation (TENS). TENS is a treatment technique developed in the late 1960s that delivers a mild electrical current to stimulate nerves through electrodes attached to the skin overlying a painful part of the body. It is thought that TENS works by stimulating the production of endorphins, which are the body's natural painkilling compounds.

Surgical alternatives

The most common surgical alternative to laminectomy is a minimally invasive laminotomy and/or microdiscectomy. In this procedure, which takes about an hour, the surgeon makes a 0.5 in (1.3 cm) incision in the lower back and uses a series of small dilators to separate the layers of muscle and fatty tissue over the spine rather than cutting through them with a scalpel. A tube-shaped retractor is inserted to expose the part of the lamina over the nerve root. The surgeon then uses a power drill to make a small hole in the lamina to expose the nerve itself. After the nerve has been moved aside with the retractor, a small grasping device is used to remove the herniated portion or fragments of the damaged spinal disk.

The advantages of these minimally invasive procedures are fewer complications and a shortened recovery time for the patient. The average postoperative stay is three hours. In addition, 90% of patients are pleased with the results.

Complementary and alternative (CAM) approaches

Two alternative methods of treating back disorders that have been shown to help many patients are **acupuncture** and **chiropractic**. Chiropractic is based on the belief that the body has abilities to heal itself provided that nerve impulses can move freely between the brain and the rest of the body. Chiropractors manipulate the segments of the spine in order to bring them into proper alignment and restore the nervous system to proper functioning. Many are qualified to perform acupuncture as well as chiropractic adjustments of the vertebrae and other joints. Several British and Swedish studies have reported that acupuncture and chiropractic are at least as effective as other conservative measures in relieving pain in the lower back.

Movement therapies, including **yoga**, **tai chi**, and gentle stretching exercises, may be useful in maintaining or improving flexibility and range of motion in the spine. A qualified yoga instructor can work with the patient's doctor before or after surgery to put together an individualized set of beneficial stretching and breathing exercises. The **Alexander technique** is a type of **movement therapy** that is often helpful to patients who need to improve their posture.

Resources

BOOKS

Browner BD et al. *Skeletal Trauma: Basic science, management, and reconstruction*. 3rd ed. Philadelphia: Elsevier, 2003.

Canale, ST, ed. *Campbell's Operative Orthopaedics*. 10th ed. St. Louis: Mosby, 2003.

DeLee, JC and D. Drez. *DeLee and Drez's Orthopaedic Sports Medicine*. 2nd ed. Philadelphia: Saunders, 2005.

Harris ED et al. *Kelley's Textbook of Rheumatology*. 7th ed. Philadelphia: Saunders, 2005.

PERIODICALS

Aldrete, J. A. "Epidural Injections of Indomethacin for Postlaminectomy Syndrome: A Preliminary Report." *Anesthesia and Analgesia* 96 (February 2003): 463–468.

Braverman, D. L., J. J. Ericken, R. V. Shah, and D. J. Franklin. "Interventions in Chronic Pain Management. 3. New Frontiers in Pain Management: Complementary Techniques." *Archives of Physical Medicine and Rehabilitation* 84 (March 2003) (3 Suppl 1): S45–S49.

Harvey, E., A. K. Burton, J. K. Moffett, and A. Breen. "Spinal Manipulation for Low-Back Pain: A Treatment Package Agreed to by the UK Chiropractic, Osteopathy and Physiotherapy Professional Associations." *Manual Therapy* 8 (February 2003): 46–51.

Hurwitz, E. L., H. Morgenstern, P. Harber, et al. "A Randomized Trial of Medical Care With and Without Physical Therapy and Chiropractic Care With and Without Physical Modalities for Patients with Low Back Pain: 6-Month Follow-Up Outcomes from the UCLA Low Back Pain Study." *Spine* 27 (October 15, 2002): 2193–2204.

Nasca, R. J. "Lumbar Spinal Stenosis: Surgical Considerations." *Journal of the Southern Orthopedic Association* 11 (Fall 2002): 127–134.

Pengel, H. M., C. G. Maher, and K. M. Refshauge. "Systematic Review of Conservative Interventions for Subacute Low Back Pain." *Clinical Rehabilitation* 16 (December 2002): 811–820.

Sleigh, Bryan C., MD, and Ibrahim El Nihum, MD. "Lumbar Laminectomy." *eMedicine* . August 8, 2002 [cited May 3, 2003]. http://www.emedicine.com/aaem/topic500.htm.

Wang, Michael Y., Barth A. Green, Sachin Shah, et al. "Complications Associated with Lumbar Stenosis Surgery in Patients Older Than 75 Years of Age." *Neurosurgical Focus* 14 (February 2003): 1–4.

ORGANIZATIONS

American Academy of Orthopedic Surgeons, 6300 North River Road, Rosemont, IL, 60018-4262, (847) 823-7186, (800) 346-2267, (847) 823-8125, http://www.aaos.org.

American Academy of Neurological and Orthopaedic Surgeons (AANOS), 2300 South Rancho Drive, Suite 202, Las Vegas, NV, 89102, (702) 388-7390, http://www.aanos.org.

The American Board of Neurological Surgery, 6550 Fannin Street, Suite 2139, Houston, TX, 77030, (713) 441-6015, http://www.abns.org.

American Chiropractic Association, 1701 Clarendon Boulevard, Arlington, VA, 22209, (703) 276-8800, (703) 243-2593, memberinfo@acatoday.org, http://www.acatoday.org.

American Physical Therapy Association, 1111 North Fairfax Street, Fairfax, VA, 22314-1488, (703) 684-APTA (2782), (800) 999-APTA (2782), (703) 684-7343, http://www.apta.org.

National Rehabilitation Information Center, 8201 Corporate Drive, Suite 600, Landover, MD, 20785, (301) 459-5900, (800) 346-2742, (301) 459-4263, naricinfo@heitechservices.com, http://www.naric.com/.

Rebecca Frey, Ph.D.

Laminectomy *see* **Disk removal**
Language disturbance *see* **Aphasia**
Laparoscopic cholecystectomy *see* **Cholecystectomy**

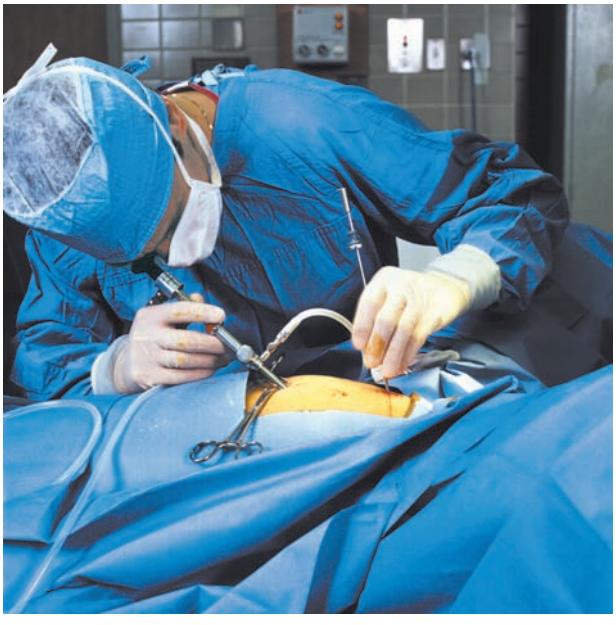
Laparoscopy

Definition

Laparoscopy is a minimally invasive procedure used as a diagnostic tool and surgical procedure that is performed to examine the abdominal and pelvic organs, or the thorax, head, or neck. Tissue samples can also be collected for biopsy using laparoscopy and malignancies treated when it is combined with other therapies. Laparoscopy can also be used for some cardiac and vascular procedures.

Purpose

Laparoscopy is performed to examine the abdominal and pelvic organs to diagnose certain conditions and—depending on the condition—can be used to perform surgery. Laparoscopy is commonly used in gynecology to examine the outside of the uterus, the fallopian tubes, and the ovaries—particularly in pelvic **pain** cases where the underlying cause cannot be determined using diagnostic imaging (ultrasound and



This surgeon is performing a laparoscopic procedure on a patient. *(Photo Researchers, Inc. Reproduced by permission.)*

KEY TERMS

Ascites—Accumulation of fluid in the abdominal cavity; laparoscopy may be used to determine its cause.

Cholecystitis—Inflammation of the gallbladder, often diagnosed using laparoscopy.

Electrosurgical device—A medical device that uses electrical current to cauterize or coagulate tissue during surgical procedures; often used in conjunction with laparoscopy.

Embolism—Blockage of an artery by a clot, air or gas, or foreign material. Gas embolism may occur as a result of insufflation of the abdominal cavity during laparoscopy.

Endometriosis—A disease involving occurrence of endometrial tissue (lining of the uterus) outside the uterus in the abdominal cavity; often diagnosed and treated using laparoscopy.

Hysterectomy—Surgical removal of the uterus; often performed laparoscopically.

Insufflation—Inflation of the abdominal cavity using carbon dioxide; performed prior to laparoscopy to give the surgeon space to maneuver surgical equipment.

Oophorectomy—Surgical removal of the ovaries; often performed laparoscopically.

Pneumothorax—Air or gas in the pleural space (lung area) that may occur as a complication of laparoscopy and insufflation.

Subcutaneous emphysema—A pathologic accumulation of air underneath the skin resulting from improper insufflation technique.

Trocar—A small sharp instrument used to puncture the abdomen at the beginning of the laparoscopic procedure.

computed tomography). Examples of gynecologic conditions diagnosed using laparoscopy include **endometriosis**, **ectopic pregnancy**, **ovarian cysts**, **pelvic inflammatory disease** [PID], **infertility**, and **cancer**. Laparoscopy is used in **general surgery** to examine the abdominal organs, including the gallbladder, bile ducts, the liver, the appendix, and the intestines.

During the laparoscopic surgical procedure, certain conditions can be treated using instruments and devices specifically designed for laparoscopy. Medical devices that can be used in conjunction with laparoscopy include surgical lasers and electrosurgical units. Laparoscopic surgery is now preferred over open surgery for several types of procedures because of its minimally invasive nature and its association with fewer complications.

Microlaparoscopy can be performed in the physician's office using smaller laparoscopes. Common clinical applications in gynecology include pain mapping (for endometriosis), sterilization, and fertility procedures. Common applications in general surgery include evaluation of chronic and acute abdominal pain (as in **appendicitis**), basic trauma evaluation, biopsies, and evaluation of abdominal masses.

Laparoscopy is commonly used by gynecologists, urologists, and general surgeons for abdominal and pelvic applications. Laparoscopy is also being used by orthopedic surgeons for spinal applications and by cardiac surgeons for minimally invasive heart surgery. Newer video-assisted laparoscopic procedures include **thyroidectomy** and **parathyroidectomy**.

Demographics

At first, laparoscopy was only been performed on young, healthy adults, but the use of this technique has greatly expanded. Populations on whom laparoscopies are now performed include infants, children, the elderly, the obese, and those with chronic disease states, such as cancer. The applications of this type of surgery have grown considerably over the years to include a variety of patient populations, and will continue to do so with the refinement of laparascopic techniques.

Description

Laparoscopy is typically performed in the hospital under **general anesthesia**, although some laparoscopic procedures can be performed using local anesthetic agents. Once under anesthesia, a urinary catheter is inserted into the patient's bladder for urine collection. To begin the procedure, a small incision is made just below the navel and a cannula or trocar is inserted into the incision to accommodate the insertion of the laparoscope. Other incisions may be made in the abdomen to allow the insertion of additional laparoscopic instrumentation. A laparoscopic insufflation device is used to inflate the abdomen with carbon dioxide gas to create a space in which the laparoscopic surgeon can maneuver the instruments. After the laparoscopic diagnosis and treatment are completed, the laparoscope, cannula, and other instrumentation are removed, and the incision is sutured and bandaged.

Laparoscopes have integral cameras for transmitting images during the procedure, and are available in various sizes depending upon the type of procedure performed. The images from the laparoscope are transmitted to a

viewing monitor that the surgeon uses to visualize the internal anatomy and guide any surgical procedure. Video and photographic equipment are also used to document the surgery, and may be used postoperatively to explain the results of the procedure to the patient.

Robotic systems are available to assist with laparoscopy. A robotic arm, attached to the operating table may be used to hold and position the laparoscope. This serves to reduce unintentional camera movement that is common when a surgical assistant holds the laparoscope. The surgeon controls the robotic arm movement by foot pedal with voice-activated command, or with a handheld control panel.

Microlaparoscopy has become more common over the past few years. The procedure involves the use of smaller laparoscopes (that is, 2 mm compared to 5–10 mm for hospital laparoscopy), with the patient undergoing **local anesthesia** with conscious **sedation** (during which the patient remains awake but very relaxed) in a physician's office. Video and photographic equipment, previously explained, may be used.

Laparoscopy has been explored in combination with other therapies for the treatment of certain types of malignancies, including pelvic and aortic lymph node dissection, **ovarian cancer**, and early **cervical cancer**. Laparoscopic radiofrequency ablation is a technique whereby laproscopy assists in the delivery of radiofrequency probes that distribute pulses to a tumor site. The pulses generate heat in malignant tumor cells and destroys them.

The introduction of items such as temperature-controlled instruments, surgical instruments with greater rotation and articulation, improved imaging systems, and multiple robotic devices will expand the utility of laparoscopic techniques in the future. The skills of surgeons will be enhanced as well, with further development of training simulators and computer technology.

Diagnosis/Preparation

Before undergoing laparoscopic surgery, the patient should be prepared by the doctor for the procedure both psychologically and physically. It is very important that the patient receive realistic counseling before surgery and prior to giving informed consent. This includes discussion about further open abdominal surgery (laparotomy) that may be required during laparoscopic surgery, information about potential complications during surgery, and the possible need for blood transfusions. In the case of diagnostic laparoscopy for chronic pelvic pain, the procedure may simply indicate that all organs are normal and the patient should be prepared for this possibility. The surgery may be explained using pictures, models, videotapes, and movies. It is especially important for the patient to be able to ask questions and express concerns. It may be helpful, for the patient to have a family member or friend present during discussions with the doctor. Such conversations could understandably cause **anxiety**, and information relayed may not be adequately recalled under such circumstances.

There is usually a presurgical exam two weeks before the surgery to gather a medical history and obtain blood and urine samples for laboratory testing. It is important that the patient inform the doctor completely about any prior surgeries, medical conditions, or medications taken on a regular basis, including **nonsteroidal anti-inflammatory drugs** (NSAIDs), such as **aspirin**. Patients taking blood thinners, like Coumadin or Heparin (generic name: warfarin) should not adjust their medication themselves, but should speak with their prescribing doctors regarding their upcoming surgery. (Patients should never adjust dosage without their doctors' approval. This is especially important for elderly patients, asthmatics, those with **hypertension**, or those who are on ACE inhibitors.) If a tubal dye study is planned during the procedure, the patient may also be required to provide information on menstrual history. For some procedures, an autologous (self) **blood donation** may be suggested prior to the surgery to replace blood that may be lost during the procedure. Chest x rays may also be required. For some obese patients, weight loss may be necessary prior to surgery.

Immediately before to surgery, there are several pre-operative steps that the patient may be advised to take. The patient should shower at least 24 hours prior to the surgery, and gently but thoroughly cleanse the umbilicus (belly button) with antibacterial soap and water using a cotton-tipped swab. Because laparoscopy requires general anesthesia in most cases, the patient may be asked to eat lightly 24 hours prior to surgery and fast at least 12 hours prior to surgery. Bowel cleansing with a laxative may also required, allowing the it to be more easily visualized and to prevent complications in the unlikely event of bowel injury. Those who are have diabetes or have **hypoglycemia** may wish to schedule their procedures early in the morning to avoid low blood sugar reactions. The patient should follow the directions of the hospital staff, arriving early on the day of surgery to sign paperwork and to be screened by the anesthesiology staff. Questions will be asked regarding current medications and dosages, **allergies** to medication, previous experiences with anesthesia (that is, allergic reactions, and previous experiences regarding time-to-consciousness),

and a variety of other questions. It is often helpful for the patient to make a list of this information beforehand so that the information can be easily retrieved when requested by the hospital staff.

Aftercare

Following laparoscopy, patients are required to remain in a recovery area until the immediate effects of anesthesia subside and until normal voiding is accomplished (especially if a urinary catheter was used during the surgery). Vital signs are monitored to ensure that there are no reactions to anesthesia or internal injuries present. There may be some **nausea** and/or **vomiting**, which may be reduced by the use of the propofol anesthetic for healthy patients undergoing elective procedures such as **tubal ligation**, diagnostic laparoscopy, or **hernia repair**. Laparoscopy is usually an outpatient procedure and patients are discharged from the recovery area within a few hours after the procedure. For elderly patients and those with other medical conditions, recovery may be slower. Patients with more serious medical conditions, or patients undergoing emergency laparoscopy, an overnight hospital stay or a stay of several days may be required.

Discharged patients will receive instructions regarding activity level, medications, postoperative dietary modifications, and possible side effects of the procedure. It may be helpful to have a friend or family member present when these instructions are given, as the after-effects of anesthesia may cause some temporary confusion. Postoperative instructions may include information on when one might resume normal activities such as bathing, housework, and driving. Depending on the nature of the laparoscopic procedure and the patient's medical condition, daily activity may be restricted for a few days and strenuous during administration of anesthesia may cause some soreness. Additionally, shoulder pain may persist as long as 36 hours after surgery. Pain-relieving medications and **antibiotics** may be prescribed for several days postoperatively.

Patients will be instructed to watch for signs of a **urinary tract infection** (UTI) or unusual pain; either may indicate organ injury. It is important to understand the difference between normal discomfort and pain, because pain may indicate a problem. Patients may also experience an elevated temperature, and occasionally "postlaparoscopy syndrome"; this condition is similar in appearance to **peritonitis** (marked by abdominal pain, **constipation**, **vomiting**, and **fever**) that disappears shortly after surgery without antibiotics. However, any postoperative symptoms that cause concern for the patient should be discussed with the doctor, so that any fears can be alleviated and recovery can be accomplished. Due to the after-effects of anesthesia, patients should not drive themselves home.

It is advisable for someone to stay with the patient for a few hours following the procedure, in case complications arise. Injury to an organ might not be readily apparent for several days after the procedure. The physical signs that should be watched for and reported immediately include:

- fever and chills
- abdominal distension
- vomiting
- difficulty urinating
- sharp and unusual pain in the abdomen or bowel
- redness at the incision site, which indicates infection
- discharge from any places where tubes were inserted or incisions were made

Additional complications may include a urinary tract infection (resulting from catheterization) and minor infection of the incision site. An injury to the ureter may be indicated by abdominal distention or a pain in the flank. Additional testing may be required if a complication is suspected.

Risks

Complications may be associated with the laparoscopy procedure in general, or may be specific to the type of operation that is performed. Patients should consult with their doctors regarding the types of risks that are specific for their procedures. The most serious complication that can occur during laparoscopy is laceration of a major abdominal blood vessel resulting from improper positioning, inadequate insufflation (inflation) of the abdomen, abnormal pelvic anatomy, and too much force exerted during scope insertion. Thin patients with well-developed abdominal muscles are at higher risk, since the aorta may only be an inch or so below the skin. Obese patients are also at higher risk because more forceful and deeper needle and scope penetration is required. During laparoscopy, there is also a risk of bleeding from blood vessels, and **adhesions** may require repair by open surgery if bleeding cannot be stopped using laparoscopic instrumentation. In laparoscopic procedures that use electrosurgical devices, **burns** to the incision site are possible due to passage of electrical current through the laparoscope caused by a fault or malfunction in the equipment.

Complications related to insufflation of the abdominal cavity include gas inadvertently entering a blood vessel and causing an **embolism**, **pneumothorax**, or subcutaneous **emphysema**. One common but not serious side effect of insufflation is pain in the shoulder

and upper chest area for a day or two following the procedure.

Any abdominal surgery, including laparoscopy, carries the risk of unintentional organ injury (punctures and perforations). For example, the bowel, bladder, ureters, or fallopian tubes may be injured during the laparoscopic procedure. Many times these injuries are unavoidable due to the patient's anatomy or medical condition. Patients at higher risk for bowel injury include those with chronic bowel disease, PID, a history of pervious abdominal surgery, or severe endometriosis. Some types of laparoscopic procedures have a higher risk of organ injury. For instance, during laparoscopic removal of endometriosis adhesions or ovaries, the ureters may be injured due to their proximity to each other.

Several clinical studies have shown that the complication rate during laparoscopy is associated with inadequate surgeon experience. Surgeons who are more experienced in laparoscopic procedures have fewer complications than those performing their first 100 cases.

Results

In diagnostic laparoscopy, the surgeon will be able to see signs of a disease or condition (for example, endometriosis adhesions; ovarian cysts; diseased gallbladder) immediately, and can either treat the condition surgically or proceed with appropriate medical management. In diagnostic laparoscopy, biopsies may be taken of tissue in questionable areas, and laboratory results will govern medical treatment. In therapeutic laparoscopy, the surgeon performs a procedure that rectifies a known medical problem, such as **hernia** repair or appendix removal. Because laparoscopy is minimally invasive compared to open surgery, patients may experience less trauma and postoperative discomfort, have fewer procedural complications, have a shorter hospital stay, and return more quickly to daily activities. The results will vary, however, depending on the patients's condition and type of treatment.

Morbidity and mortality rates

Laparoscopic surgery, like most surgeries, is not without risk. Risks should be thoroughly explained to the patient. Complications from laparoscopic surgeries arise in 1–5% of the cases, with a mortality of about 0.05%. Complications may arise from the laparoscopic entry during procedure, and the risks vary depending on the elements specific to a particular procedure. For example, the risk of injury to the common bile duct in laparoscopic biliary surgery is 0.3–0.6% of cases. The factors that contribute to morbidity are currently under study and debate. Injury may occur to blood vessels and internal organs. Some studies examining malpractice data indicate that trocar injury to the bowel or blood vessels may account up to one-fourth of laparoscopic medical claims. It has been suggested that these injuries can be reduced by alterations in the placement and use of the Verses needle, or by using an open technique of trocar insertion in which a blunt cannula (non-bladed) is inserted into the abdominal cavity through an incision. The insertion of secondary trocars may be of particular interest as a risk factor. There is still some debate, however, as to which method of trocar insertion is most appropriate in a particular situation, as no technique is without risk. The most commonly cited injury in laparoscopic malpractice claims has been injury to the bile duct (66%). Proper identification of this structure by an experienced surgeon, or by a cholangiogram, may reduce this type of injury. Other areas of the body may be injured during access including the stomach, bladder, and liver. Hemorrhages may also occur during the operation.

Laparoscopic entry injuries have been the subject of recent study. Data collected from insurance companies and medical device regulation indicate that bowel and vascular injuries may account for 76% of the injuries that occur when a primary port is created. Delayed recognition of bowel injuries was noted to be an important factor in mortality. The risk of possible injury or **death** in laparoscopy depends on such factors as the anatomy of the patient, the force of entry, and the type operative procedure being performed.

Alternatives

The alternatives to laparoscopy vary, depending on the medical condition being treated. Laparotomy (open abdominal surgery with larger incision) may be pursued when further visualization is needed to treat the condition, such as in the case of pain of severe endometriosis with deeper lesions. For those female patients with pelvic masses, transvaginal sonography may be a helpful technique in obtaining information about whether such masses are malignant, assisting in the choice between laparoscopy or laparotomy.

Resources

BOOKS

Gabbe, S. G., et al. *Obstetrics: Normal and Problem Pregnancies*. 5th ed. London: Churchill Livingstone, 2007.

Katz, V. L., et al. *Comprehensive Gynecology*. 5th ed. St. Louis: Mosby, 2007.

Khatri, V. P., and J. A. Asensio. *Operative Surgery Manual*. Philadelphia: Saunders, 2002.

Townsend, C. M., et al. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: Saunders, 2007.

OTHER

"Laparoscopy." Medline Plus, August 21, 2009.http://www.nlm.nih.gov/medlineplus/ency/article/007016.htm

ORGANIZATIONS

American College of Obstetricians and Gynecologists, P.O. Box 96920, Washington, DC, 20090-6920, (202) 638-5577, http://www.acog.org.

Society of American Gastrointestinal Endoscopic Surgeons (SAGES), 2716 Ocean Park Boulevard, Suite 3000, Santa Monica, CA, 90405, (310) 314-2404, http://www.endoscopy-sages.com.

Society of Laparoendoscopic Surgeons, 7330 SW Sixty-second Place, Suite 410, Miami, FL, 33143-4825, (305) 665-9959, http://www.sls.org.

Jennifer E. Sisk, MA
Jill Granger, MS
Brenda W. Lerner

Laryngeal cancer

Definition

Laryngeal **cancer** is cancer of the larynx or voice box.

Description

The larynx is located where the throat divides into the esophagus and the trachea. The esophagus is the tube that takes food to the stomach. The trachea, or windpipe, takes air to the lungs. The area where the larynx is located is sometimes called the Adam's apple.

The larynx has two main functions. It contains the vocal cords, cartilage, and small muscles that make up the voice box. When a person speaks, small muscles tighten the vocal cords, narrowing the distance between them. As air is exhaled past the tightened vocal cords, it creates sounds that are formed into speech by the mouth, lips, and tongue.

The second function of the larynx is to allow air to enter the trachea and to keep food, saliva, and foreign material from entering the lungs. A flap of tissue called the epiglottis covers the trachea each time a person swallows. This blocks foreign material from entering the lungs. When not swallowing, the epiglottis retracts, and air flows into the trachea. During treatment for cancer of the larynx, both of these functions may be lost.

Cancers of the larynx develop slowly. About 95% of these cancers develop from thin, flat cells similar to skin cells called squamous epithelial cells. These cells line the larynx. Gradually, the squamous epithelial cells begin to change and are replaced with abnormal cells. These abnormal cells are not cancerous but are pre-malignant cells that have the potential to develop into cancer. This condition is called dysplasia. Most people with dysplasia never develop cancer. The condition simply goes away without any treatment, especially if the person with dysplasia stops **smoking** or drinking alcohol.

The larynx is made up of three parts, the glottis, the supraglottis, and the subglottis. Cancer can start in any of these regions. Treatment and survival rates depend on which parts of the larynx are affected and whether the cancer has spread to neighboring areas of the neck or distant parts of the body.

The glottis is the middle part of the larynx. It contains the vocal cords. Cancers that develop on the vocal cords are often diagnosed very early because even small vocal cord tumors cause hoarseness. In addition, the vocal cords have no connection to the lymphatic system. This means that cancers on the vocal cord do not spread easily. When confined to the vocal cords without any involvement of other parts of the larynx, the cure rate for this cancer is 75% to 95%.

The supraglottis is the area above the vocal cords. It contains the epiglottis, which protects the trachea from foreign materials. Cancers that develop in this region are usually not found as early as cancers of the glottis because the symptoms are less distinct. The supraglottis region has many connections to the lymphatic system, so cancers in this region tend to spread easily to the lymph nodes and may spread to other parts of the body (lymph nodes are small bean-shaped structures that are found throughout the body; they produce and store infection-fighting cells). In 25% to 50% of people with cancer in the supraglottal region, the cancer has already spread to the lymph nodes by the time they are diagnosed. Because of this, survival rates are lower than for cancers that involve only the glottis.

The subglottis is the region below the vocal cords. Cancer starting in the subglottis region is rare. When it does, it is usually detected only after it has spread to the vocal cords, where it causes obvious symptoms such as hoarseness. Because the cancer has already begun to spread by the time it is detected, survival rates are generally lower than for cancers in other parts of the larynx.

About 12,000 new cases of cancer of the larynx develop in the United States each year. Each year, about 3,900 die of the disease. Laryngeal cancer is between four and five times more common in men than in women. Almost all men who develop laryngeal cancer are over age 55. Laryngeal cancer is about 50%

more common among African-American men than among other Americans.

It is thought that older men are more likely to develop laryngeal cancer than women because the two main risk factors for acquiring the disease are lifetime habits of smoking and alcohol **abuse**. More men are heavy smokers and drinkers than women, and more African-American men are heavy smokers than other men in the United States. However, as smoking becomes more prevalent among women, it seems likely that more cases of laryngeal cancer in females will be seen.

Causes and symptoms

Laryngeal cancer develops when the normal cells lining the larynx are replaced with abnormal cells (dysplasia) that become malignant and reproduce to form tumors. The development of dysplasia is strongly linked to life-long habits of smoking and heavy use of alcohol. The more a person smokes, the greater the risk of developing laryngeal cancer. It is unusual for someone who does not smoke or drink to develop cancer of the larynx. Occasionally, however, people who inhale asbestos particles, wood dust, paint or industrial chemical fumes over a long period of time develop the disease.

The symptoms of laryngeal cancer depend on the location of the tumor. Tumors on the vocal cords are rarely painful, but cause hoarseness. Anyone who is continually hoarse for more than two weeks or who has a **cough** that does not go away should be checked by a doctor.

Tumors in the supraglottal region above the vocal cords often cause more, but less distinct symptoms. These include:

- persistent sore throat
- pain when swallowing
- difficulty swallowing or frequent choking on food
- bad breath
- lumps in the neck
- persistent ear pain (called referred pain; the source of the pain is not the ear)
- change in voice quality

Tumors that begin below the vocal cords are rare, but may cause noisy or difficult breathing. All the symptoms above can also be caused other cancers as well as by less seriousness illnesses. However, if these symptoms persist, it is important to see a doctor and find their cause, because the earlier cancer treatment begins, the more successful it is.

Diagnosis

On the first visit to a doctor for symptoms that suggest laryngeal cancer, the doctor first takes a complete medical history, including family history of cancer and lifestyle information about smoking and alcohol use. The doctor also does a **physical examination**, paying special attention to the neck region for lumps, tenderness, or swelling.

The next step is examination by an otolaryngologist, or ear, nose, and throat (ENT) specialist. This doctor also performs a physical examination, but in addition will also want to look inside the throat at the larynx. Initially, the doctor may spray a local anesthetic on the back of the throat to prevent gagging, then use a long-handled mirror to look at the larynx and vocal cords. This examination is done in the doctor's office. It may cause gagging but is usually painless.

A more extensive examination involves a **laryngoscopy**. In a laryngoscopy, a lighted fiberoptic tube called a laryngoscope that contains a tiny camera is inserted through the patient's nose and mouth and snaked down the throat so that the doctor can see the larynx and surrounding area. This procedure can be done with a sedative and local anesthetic in a doctor's office. More often, the procedure is done in an outpatient surgery clinic or hospital under **general anesthesia**. This allows the doctor to use tiny clips on the end of the laryngoscope to take biopsies (tissue samples) of any abnormal-looking areas.

Laryngoscopies are normally painless and take about one hour. Some people find their throat feels scratchy after the procedure. Since laryngoscopies are done under **sedation**, patients should not drive immediately after the procedure, and should have someone available to take them home. Laryngoscopy is a standard procedure that is covered by insurance.

The locations of the samples taken during the laryngoscopy are recorded, and the samples are then sent to the laboratory where they are examined under the microscope by a pathologist who specializes in diagnosing diseases through cell samples and laboratory tests. It may take several days to get the results. Based on the findings of the pathologist, cancer can be diagnosed and staged.

Once cancer is diagnosed, other tests will probably be done to help determine the exact size and location of the tumors. This information is helpful in determining which treatments are most appropriate. These tests may include:

- Endoscopy. Similar to a laryngoscopy, this test is done when it appears that cancer may have spread to other areas, such as the esophagus or trachea.
- Computed tomography (CT or CAT) scan. Using x-ray images taken from several angles and computer modeling, CT scans allow parts of the body to be seen as a cross section. This helps locate and size the tumors, and provides information on whether they can be surgically removed.
- Magnetic resonance imaging (MRI). MRI uses magnets and radio waves to create more detailed cross-sectional scans than computed tomography. This detailed information is needed if surgery on the larynx area is planned.
- Barium swallow. Barium is a substance that, unlike soft tissue, shows up on x rays. Swallowed barium coats the throat and allows x-ray pictures to be made of the tissues lining the throat.
- Chest x ray. Done to determine if cancer has spread to the lungs. Since most people with laryngeal cancer are smokers, the risk of also having lung cancer or emphysema is high.
- Fine needle aspiration (FNA) biopsy. If any lumps on the neck are found, a thin needle is inserted into the lump, and some cells are removed for analysis by the pathologist.
- Additional blood and urine tests. These tests do not diagnose cancer, but help to determine the patient's general health and provide information to determine which cancer treatments are most appropriate.

Treatment

Staging

Once cancer of the larynx is found, more tests will be done to find out if cancer cells have spread to other parts of the body. This is called staging. A doctor needs to know the stage of the disease to plan treatment. In cancer of the larynx, the definitions of the early stages depend on where the cancer started.

STAGE I. The cancer is only in the area where it started and has not spread to lymph nodes in the area or to other parts of the body. The exact definition of stage I depends on where the cancer started, as follows:

- Supraglottis: The cancer is only in one area of the supraglottis and the vocal cords can move normally.
- Glottis: The cancer is only in the vocal cords and the vocal cords can move normally.
- Subglottis: The cancer has not spread outside of the subglottis.

STAGE II. The cancer is only in the larynx and has not spread to lymph nodes in the area or to other parts of the body. The exact definition of stage II depends on where the cancer started, as follows:

- Supraglottis: The cancer is in more than one area of the supraglottis, but the vocal cords can move normally.
- Glottis: The cancer has spread to the supraglottis or the subglottis or both. The vocal cords may or may not be able to move normally.
- Subglottis: The cancer has spread to the vocal cords, which may or may not be able to move normally.

STAGE III. Either of the following may be true:

- The cancer has not spread outside of the larynx, but the vocal cords cannot move normally, or the cancer has spread to tissues next to the larynx.
- The cancer has spread to one lymph node on the same side of the neck as the cancer, and the lymph node measures no more than 3 centimeters (just over 1 inch).

STAGE IV. Any of the following may be true:

- The cancer has spread to tissues around the larynx, such as the pharynx or the tissues in the neck. The lymph nodes in the area may or may not contain cancer.
- The cancer has spread to more than one lymph node on the same side of the neck as the cancer, to lymph nodes on one or both sides of the neck, or to any lymph node that measures more than 6 centimeters (over 2 inches).
- The cancer has spread to other parts of the body.

RECURRENT. Recurrent disease means that the cancer has come back (recurred) after it has been treated. It may come back in the larynx or in another part of the body.

Treatment

Treatment is based on the stage of the cancer as well as its location and the health of the individual. Generally, there are three types of treatments for cancer of the larynx. These are surgery, radiation, and **chemotherapy**. They can be used alone or in combination based in the stage of the caner. Getting a second opinion after the cancer has been staged can be very helpful in sorting out treatment options and should always be considered.

SURGERY. The goal of surgery is to cut out the tissue that contains malignant cells. There are several common surgeries to treat laryngeal cancer.

Stage III and stage IV cancers are usually treated with total **laryngectomy**. This is an operation to remove

the entire larynx. Sometimes other tissues around the larynx are also removed. Total laryngectomy removes the vocal cords. Alternate methods of voice communication must be learned with the help of a speech pathologist. Laryngectomy is treated in depth as a separate entry in this volume.

Smaller tumors are sometimes treated by partial laryngectomy. The goal is to remove the cancer but save as much of the larynx (and corresponding speech capability) as possible. Very small tumors or cancer in situ are sometimes successfully treated with laser excision surgery. In this type of surgery, a narrowly-targeted beam of light from a laser is used to remove the cancer.

Advanced cancer (Stages III and IV) that has spread to the lymph nodes often requires an operation called a neck dissection. The goal of a neck dissection is to remove the lymph nodes and prevent the cancer from spreading. There are several forms of neck dissection. A **radical neck dissection** is the operation that removes the most tissue.

Several other operations are sometimes performed because of laryngeal cancer. A **tracheotomy** is a surgical procedure in which an artificial opening is made in the trachea (windpipe) to allow air into the lungs. This operation is necessary if the larynx is totally removed. A **gastrectomy** tube is a feeding tube placed through skin and directly into the stomach. It is used to give **nutrition** to people who cannot swallow or whose esophagus is blocked by a tumor. People who have a total laryngectomy usually do not need a gastrectomy tube if their esophagus remains intact.

RADIATION. **Radiation therapy** uses high-energy rays, such as x rays or gamma rays, to kill cancer cells. The advantage of radiation therapy is that it preserves the larynx and the ability to speak. The disadvantage is that it may not kill all the cancer cells. Radiation therapy can be used alone in early stage cancers or in combination with surgery. Sometimes it is tried first with the plan that if it fails to cure the cancer, surgery still remains an option. Often, radiation therapy is used after surgery for advanced cancers to kill any cells the surgeon might not have removed.

There are two types of radiation therapy. External beam radiation therapy focuses rays from outside the body on the cancerous tissue. This is the most common type of radiation therapy used to treat laryngeal cancer. With internal radiation therapy, also called brachytherapy, radioactive materials are placed directly on the cancerous tissue. This type of radiation therapy is a much less common treatment for laryngeal cancer.

External radiation therapy is given in doses called fractions. A common treatment involves giving fractions five days a week for seven weeks. Clinical trials are underway to determine the benefits of accelerating the delivery of fractions (accelerated fractionation) or dividing fractions into smaller doses given more than once a day (hyperfractionation). Side effects of radiation therapy include **dry mouth**, **sore throat**, hoarseness, skin problems, trouble swallowing, and diminished ability to taste.

CHEMOTHERAPY. Chemotherapy is the use of drugs to kill cancer cells. Unlike radiation therapy, which is targeted to a specific tissue, chemotherapy drugs are either taken by mouth or intravenously (through a vein) and circulate throughout the whole body. They are used mainly to treat advanced laryngeal cancer that is inoperable or that has metastasized to a distant site. Chemotherapy is often used after surgery or in combination with radiation therapy. Clinical trials are underway to determine the best combination of treatments for advanced cancer.

The two most common chemotherapy drugs used to treat laryngeal cancer are cisplatin and 5-fluorouracil (5-FU). There are many side effects associated with chemotherapy drugs, including **nausea and vomiting**, loss of appetite, hair loss, **diarrhea**, and mouth sores. Chemotherapy can also damage the blood-producing cells of the bone marrow, which can result in low blood cell counts, increased chance of infection, and abnormal bleeding or bruising.

Alternative treatment

Alternative and complementary therapies range from herbal remedies, vitamin supplements, and special **diets** to spiritual practices, **acupuncture**, massage, and similar treatments. When these therapies are used in addition to conventional medicine, they are called complementary therapies. When they are used instead of conventional medicine, they are called alternative therapies.

Complementary or alternative therapies are widely used by people with cancer. One large study published in the *Journal of Clinical Oncology* in July, 2000 found that 83% of all cancer patients studied used some form of complementary or alternative medicine as part of their cancer treatment. No specific alternative therapies have been directed toward laryngeal cancer. However, good nutrition and activities that reduce **stress** and promote a positive view of life have no unwanted side-effects and appear to be beneficial in boosting the immune system in fighting cancer.

Unlike traditional pharmaceuticals, complementary and alternative therapies are not evaluated by the United

KEY TERMS

Dysplasia—The abnormal change in size, shape or organization of adult cells.

Lymph—Clear, slightly yellow fluid carried by a network of thin tubes to every part of the body. Cells that fight infection are carried in the lymph.

Lymphatic system—Primary defense against infection in the body. The lymphatic system consists of tissues, organs, and channels (similar to veins) that produce, store, and transport lymph and white blood cells to fight infection.

Lymph nodes—Small, bean-shaped collections of tissue found in a lymph vessel. They produce cells and proteins that fight infection, and also filter lymph. Nodes are sometimes called lymph glands.

Metastasize—Spread of cells from the original site of the cancer to other parts of the body where secondary tumors are formed.

Malignant—Cancerous. Cells tend to reproduce without normal controls on growth and form tumors or invade other tissues.

States Food and Drug Administration (FDA) for either safety or effectiveness. These therapies may have interactions with traditional pharmaceuticals. Patients should be wary of "miracle cures" and notify their doctors if they are using herbal remedies, vitamin supplements or other unprescribed treatments. Alternative and experimental treatments normally are not covered by insurance.

Prognosis

Cure rates and survival rates can predict group outcomes, but can never precisely predict the outcome for a single individual. However, the earlier laryngeal cancer is discovered and treated, the more likely it will be cured.

Cancers found in stage 0 and stage 1 have a 75% to 95% cure rate depending on the site. Late stage cancers that have metastasized have a very poor survival rate, with intermediate stages falling somewhere in between. People who have had laryngeal cancer are at greatest risk for recurrence (having cancer come back), especially in the head and neck, during the first two to three years after treatment. Check-ups during the first year are needed every other month, and four times a year during the second year. It is rare for laryngeal cancer to recur after five years of being cancer-free.

Prevention

By far, the most effective way to prevent laryngeal cancer is not to smoke. Smokers who quit smoking also significantly decrease their risk of developing the disease. Other ways to prevent laryngeal cancer include limiting the use of alcohol, eating a well-balanced diet, seeking treatment for prolonged **heartburn**, and avoiding inhaling asbestos and chemical fumes.

Resources

OTHER

"Laryngeal and Hypopharyngeal Cancer." *CancerNet*. December 2009. http://www.cancer.net/patient/Cancer+Types/Laryngeal+and+Hypopharyngeal+Cancer.

"What you Need to Know About Cancer of the Larynx." *CancerNet* November 2000. [cited July 19, 2001]. http://www.cancernet.nci.nih.gov.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

National Cancer Institute (National Institutes of Health), NCI Office of Communications and Education, 6116 Executive Blvd. Suite 300, Bethesda, MD, 20892-8322, (800) 4-CANCER (422-6237), cancergovstaff@mail.nih.gov, http://www.cancer.gov/.

National Cancer Institute Office of Cancer Complementary and Alternative Medicine, 6116 Executive Blvd., Suite 609, MSC 8339, Bethesda, MD, 20892, (301) 435-7980, (301) 480-0075, ncioccam1-r@mail.nih.gov, http://www.cancer.gov/cam/.

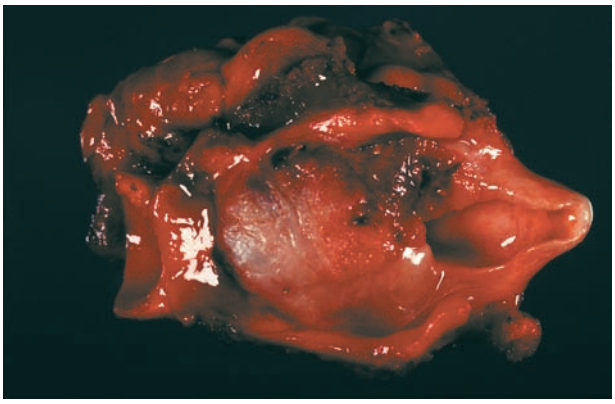
National Center for Complementary and Alternative Medicine (NCCAM), P.O. Box 7923, Gaitherburg, MD, 20898, (866) 464-3616, (888) 644-6226, info@nccam.nih.gov, http://nccam.nih.gov/.

Tish Davidson, A.M.

Laryngectomy

Definition

Laryngectomy is the partial or complete surgical removal of the larynx, usually as a treatment for **cancer** of the larynx.



A pathology photograph of an extracted tumor found on the larynx. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Purpose

Normally a laryngectomy is performed to remove tumors or cancerous tissue. In rare cases, it may be done when the larynx is badly damaged by gunshot, automobile injuries, or similar violent accidents. Laryngectomies can be total or partial. Total laryngectomies are done when cancer is advanced. The entire larynx is removed. Often if the cancer has spread, other surrounding structures in the neck, such as lymph nodes, are removed at the same time. Partial laryngectomies are done when cancer is limited to one spot. Only the area with the tumor is removed. Laryngectomies may also be performed when other cancer treatment options, such as radiation or **chemotherapy**, fail.

Precautions

Laryngectomy is done only after cancer of the larynx has been diagnosed by a series of tests that allow the otolaryngologist (a specialist often called an ear, nose, and throat doctor) to look into the throat and take tissue samples (biopsies) to confirm and stage the cancer. People need to be in good general health to undergo a laryngectomy, and will have standard preoperative blood work and tests to make sure they are able to safely withstand the operation.

Description

The larynx is located slightly below the point where the throat divides into the esophagus, which takes food to the stomach, and the trachea (windpipe), which takes air to the lungs. Because of its location, the larynx plays a critical role in normal breathing, swallowing, and speaking. Within the larynx, vocal folds (often called vocal cords) vibrate as air is exhaled past, thus creating speech. The epiglottis protects the trachea, making sure that only air gets into the lungs. When the larynx is removed, these functions are lost.

Once the larynx is removed, air can no longer flow into the lungs. During this operation, the surgeon removes the larynx through an incision in the neck. The surgeon also performs a **tracheotomy**. He makes an artificial opening called a stoma in the front of the neck. The upper portion of the trachea is brought to the stoma and secured, making a permanent alternate way for air to get to the lungs. The connection between the throat and the esophagus is not normally affected, so after healing, the person whose larynx has been removed (called a laryngectomee) can eat normally. However, normal speech is no longer possible. Several alternate means of vocal communication can be learned with the help of a speech pathologist.

Preparation

As with any surgical procedure, the patient will be required to sign a consent form after the procedure is thoroughly explained. Many patients prefer a second opinion, and some insurers require it. Blood and urine studies, along with **chest x ray** and EKG may be ordered as the doctor deems necessary. The patient also has a preoperative meeting with an anesthesiologist. If a complete laryngectomy is planned, it may be helpful to meet with a speech pathologist and/or an established laryngectomee for discussion of post-operative expectations and support.

Aftercare

A person undergoing a laryngectomy spends several days in intensive care (ICU) and receives intravenous (IV) fluids and medication. As with any major surgery, the blood pressure, pulse, and respirations are monitored regularly. The patient is encouraged to turn, **cough**, and deep breathe to help mobilize secretions in the lungs. One or more drains are usually inserted in the neck to remove any fluids that collect. These drains are removed after several days.

It takes two to three weeks for the tissues of the throat to heal. During this time, the laryngectomee cannot swallow food and must receive **nutrition** through a tube inserted through the nose and down the throat into the stomach. During this time, even people with partial laryngectomies are unable to speak.

When air is drawn in normally through the nose, it is warmed and moistened before it reaches the lungs. When air is drawn in through the stoma, it does not

have the opportunity to be warmed and humidified. In order to keep the stoma from drying out and becoming crusty, laryngectomees are encouraged to breathe artificially humidified air. The stoma is usually covered with a light cloth to keep it clean and to keep unwanted particles from accidentally entering the lungs. Care of the stoma is extremely important, since it is the person's only way to get air to the lungs. After a laryngectomy, a healthcare professional will teach the laryngectomee and his or her caregivers how to care for the stoma.

Immediately after a laryngectomy, an alternate method of communication such as writing notes, gesturing, or pointing must be used. A partial laryngectomy patient will gradually regain some speech several weeks after the operation, but the voice may be hoarse, weak, and strained. A speech pathologist will work with a complete laryngectomee to establish new ways of communicating.

There are three main methods of vocalizing after a total laryngectomy. In esophageal speech the laryngectomee learns how to "swallow" air down into the esophagus and creates sounds by releasing the air. This method requires quite a bit of coordination and learning, and produces short bursts (7 or 8 syllables) of low-volume sound.

Tracheoesophageal speech diverts air through a hole in the trachea made by the surgeon. The air then passes through an implanted artificial voice prosthesis (a small tube that makes a sound when air goes through it). Recent advances have been made in implanting voice prostheses that produce good voice quality.

The third method of artificial sound communication involves using a hand-held electronic device that translates vibrations into sounds. There are several different styles of these devices, but all require the use of at least one hand to hold the device to the throat. The choice of which method to use depends on many things including the age and health of the laryngectomee, and whether other parts of the mouth, such as the tongue, have also been removed.

Many patients resume daily activities after surgery. Special precautions must be taken during showering or shaving. Special instruction and equipment is also required for those who wish to swim or water ski, as it is dangerous for water to enter the windpipe and lungs through the stoma.

Regular follow-up visits are important following treatment for cancer of the larynx because there is a higher-than-average risk of developing a new cancer in the mouth, throat, or other regions of the head or neck.

KEY TERMS

Larynx—Also known as the voice box, the larynx is composed of cartilage that contains the apparatus for voice production. This includes the vocal cords and the muscles and ligaments that move the cords.

Lymph nodes—Accumulations of tissue along a lymph channel, which produce cells called lymphocytes that fight infection.

Tracheostomy—A surgical procedure in which an artificial opening is made in the trachea (windpipe) to allow air into the lungs.

Many self-help and support groups are available to help patients meet others who face similar problems.

Risks

Laryngectomy is often successful in curing early stage cancers. However it does cause lifestyle changes. Laryngectomees must learn new ways of speaking. They must be continually concerned about the care of their stoma. Serious infections can occur if water or other foreign material enters the lungs through an unprotected stoma. Also, women who undergo partial laryngectomy or who learn some types of artificial speech will have a deep voice similar to that of a man. For some women this presents psychological challenges.

Results

Ideally, removal of the larynx will remove all cancerous material. The person will recover from the operation, make lifestyle adjustments, and return to an active life.

Sometimes cancer has spread to surrounding tissues and it is necessary to remove lymph nodes, parts of the tongue, or other cancerous tissues. As with any major operation, post- surgical infection is possible. Infection is of particular concern to laryngectomees who have chosen to have a voice prosthesis implanted, and is one of the major reasons for having to remove the device.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

The International Association of Laryngectomees (IAL), 925B Peachtree Street - NE Suite 316 , Atlanta, GA, 30309, (866) 425-3678, http://www.theial.com/ial/.

National Institute on Deafness and Other Communication Disorders, National Institutes of Health, 31 Center Drive, MSC 2320, Bethesda, MD, 20892-2320, (301) 496-7243, (301) 402-0018, nidcdinfo@nidcd.nih.gov , http://www.nidcd.nih.gov/.

NCI Office of Communications and Education, 6116 Executive Blvd. Suite 300, Bethesda, MD, 20892-8322, (800) 4-CANCER (422-6237), cancergovstaff@mail. nih.gov, http://www.cancer.gov/aboutnci/cis.

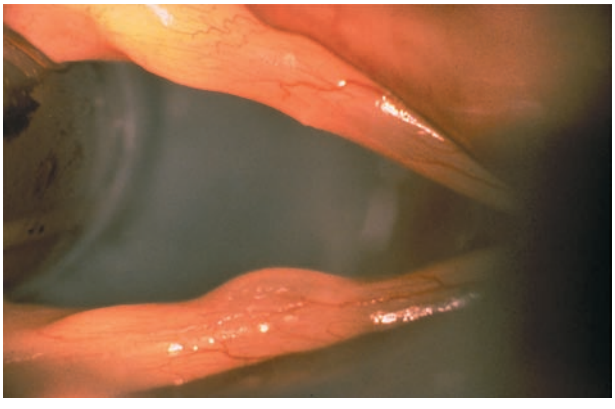
The Voice Center at Eastern Virginia Medical School, PO Box 1980, Norfolk, VA, 23501-1980, (757) 446-7360, http://www.evms.edu/evms.

Kathleen D. Wright, RN
Tish Davidson, AM

Laryngitis

Definition

Laryngitis, one type of dysphonia (disorders of the voice), is caused by inflammation of the larynx, resulting in distortion (hoarseness) of the voice. Sometimes irritation of the vocal cords, which are contained within the larynx, causes a complete, but temporary, loss of the voice. Acute laryngitis usually lasts for less than a few days and usually causes only strain on the vocal cords, while the chronic form of the inflammation can extend out to several weeks and may cause serious problems.



An endoscopic view of a patient's vocal cords with laryngitis. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Demographics

The disorder is found in both children and adults, and is equally common in all races of people all over the world. It is equally prevalent in men and women.

Description

When air is breathed in (inspired), it passes through the nose and the nasopharynx or through the mouth and the oropharynx. These are both connected to the larynx, a tube made of cartilage. The vocal cords, responsible for setting up the vibrations necessary for speech, are located within the larynx. They consist of two folds of mucous membrane, which surround muscle and cartilage. The air continues down the larynx to the trachea. The trachea then splits into two branches, the left and right bronchi (bronchial tubes). These bronchi branch into smaller air tubes which run within the lungs, leading to the small air sacs of the lungs (alveoli).

Either food, liquid, or air may be taken in through the mouth. While air goes into the larynx and the respiratory system, food and liquid are directed into the tube leading to the stomach, the esophagus. Because food or liquid in the bronchial tubes or lungs could cause a blockage or lead to an infection, the airway must be protected. The epiglottis is a leaf-like piece of cartilage extending upwards from the larynx. The epiglottis can close down over the larynx when someone is eating or drinking, preventing these substances from entering the airway.

In laryngitis, the tissues below the level of the epiglottis are swollen and inflamed. This causes swelling around the area of the vocal cords, so that they cannot vibrate normally. A hoarse sound to the voice is very characteristic of laryngitis. Laryngitis is a very common problem, and often occurs during the course of an upper respiratory tract infection (cold).

Causes and symptoms

Acute laryngitis is caused almost 100% of the time by a virus. The same viruses that cause the majority of simple upper respiratory infections (colds, **bronchitis**, etc.), along with the **mumps** and **measles**, are responsible for laryngitis. These include human parainfluenza viruses (HPIVs), influenzavirus A, human respiratory syncytial virus (RSV), human rhinovirus, coronaviruses, and enteric cytopathic human orphan virus (ECHO virus). Extremely rarely, bacteria such as Group A streptococcus bacterium (*Streptococcus pyogenes*), *Moraxella catarrhalis*, or those strains of mycobacteria (usually *Mycobacterium tuberculosis*) that cause **tuberculosis** may cause laryngitis. In people with faulty immune systems (particular due to acquired **immunodeficiency** syndrome, or **AIDS**),

infections with fungi may be responsible for laryngitis. In addition, factors that can contribute to laryngitis include **allergies**, acid reflux disease or similar problems, alcohol consumption, **smoking** tobacco products, and excessive coughing.

Chronic laryngitis is usually caused by strain to the vocal cords from inhaled irritants (chemical fumes, smoke, etc.), excessive alcohol use, chronic **sinusitis**, smoking, acid reflux, and excessive use of the voice (singers, etc.). It can also be caused, although less frequently, by bacterial, fungal, or parasitic infections. Chronic laryngitis can also be caused by **cancer** or tumors, **vocal cord paralysis** (from injuries, strokes or other health problems, and age-related problems).

Symptoms usually begin along with, or following, symptoms of a cold. A sore, scratchy, dry throat; **fever**; runny nose; achiness; and **fatigue** may all occur. Difficulty swallowing sometimes occurs with **streptococcal infections**. The patient may **cough** and wheeze. Most characteristically, the patient's voice will sound weak, strained, hoarse, and raspy. Sometimes the voice is temporarily lost. Swollen lymph nodes in the throat, face, or chest may also be present.

In extremely rare cases, the swelling of the larynx may cause symptoms of airway obstruction. This is more common in infants, because the diameter of their airways is so small. In that case, the baby may have a greatly increased respiratory rate, and exhibit loud high-pitched sounds with breathing (called **stridor**). In other cases, blood may be coughed up, increased production of saliva in the mouth may be present, and difficulties in eating may also occur.

Diagnosis

A visit to the doctor is necessary if such symptoms last for over a few days. If hoarseness remains for more than two weeks, then a trip to a physician is wise. For children, always seek medical care if the child has trouble swallowing, difficulty breathing, a body temperature of over 103°F (39°C), excessive drooling, and noisy, high-pitched sounds while inhaling. When at the health-care professional, diagnosis is usually made by learning the history of a cold followed by hoarseness. The throat usually appears red and somewhat swollen. Listening to the chest and back with a stethoscope may reveal some harsh **wheezing** sounds with inspiration (breathing in).

In long-standing (chronic laryngitis), tuberculosis may be suspected. Using a scope called a laryngoscope, examination of the airway will show redness, swelling, small bumps of tissue called nodules, and irritated pits in the tissue called ulcerations. The medical professional will examine the back of the throat with a small, lighted mirror. In some cases, a fiber-optic **laryngoscopy** may be performed. In such procedures, an endoscope with a small camera and light is inserted into the nose or mouth so that the physician can examine the throat and, especially, watch the action of the vocal cords while the patient is speaking.

In other cases, the medical team may analyze a sample of tissue suspected as part of the laryngitis. The biopsy will be removed and taken to a medical laboratory where it will be examined under a microscope. In still other cases, special skin testing (TB testing) will reveal whether the individual has been exposed to the bacteria causing tuberculosis (TB).

Treatment

Treatment of a simple, viral laryngitis simply addresses the symptoms. Gargling with warm salt water, **pain** relievers such as **acetaminophen**, the use of vaporizers to create moist air, and rest will help the illness resolve within a week. **Corticosteroids** may sometimes be used to reduce inflammation. However, such medication is usually only used in certain cases, such as when the laryngitis is more severe or there is an urgent need to recover more quickly.

Antibiotic or anti-fungal medication may be prescribed or given if the laryngitis is due to a bacterial or fungal infection, respectively.

In an infant who is clearly struggling for air, it may be necessary to put in an artificial airway for a short period of time. This is very rarely needed.

An individual with tubercular laryngitis is treated with a combination of medications used to treat classic TB. In people with fungal laryngitis, a variety of anti-fungal medications are available.

If laryngitis is caused by gastroesophageal reflux, sometimes also called **gastroesophageal reflux disease** (GERD), the person may be given ranitidine hydrochloride (Zantac) or omeprazole (Prilosec) for one to two months.

For laryngitis patients with severe hoarseness a visit to the voice pathologist or laryngologist may be necessary. In some cases **speech therapy** or a various surgical procedures may be recommended. People who sing or others who use their voices frequently (such as teachers) may be asked to rest their voice until it returns to normal.

Alternative treatment

Alternative treatments include **aromatherapy** inhalations made with benzoin, lavender, frankincense,

KEY TERMS

Epiglottis—A leaf-like piece of cartilage extending upwards from the larynx, which can close like a lid over the trachea to prevent the airway from receiving any food or liquid being swallowed.

Larynx—The part of the airway lying between the pharynx and the trachea.

Nasopharynx—The part of the airway into which the nose leads.

Oropharynx—The part of the airway into which the mouth leads.

Trachea—The part of the airway which leads into the bronchial tubes.

thyme, and sandalwood. Decoctions (extracts made by boiling an herb in water) or infusions (extracts made by steeping an herb in boiling water) can be made with red sage (*Salvia officinalis* var. *rubra*) and yarrow (*Achillea millefolium*) or with licorice (*Glycyrrhiza glabra*). These are used for gargling, and are said to reduce pain. **Echinacea** (*Echinacea* spp.) tincture taken in water every hour for 48 hours is recommended to boost the immune system. Antiviral herbs, including usnea (*Usnea* spp.), lomatium (*Lomatium dissectum*), and ligusticum (*Ligusticum porteri*), may help hasten recovery from laryngitis. Homeopathic remedies are recommended based on the patient's symptoms. Some people may get relief from placing cold compresses on the throat.

Prognosis

Prognosis for laryngitis is excellent. Recovery is complete, and usually occurs within a week's time.

Prevention

Prevention of laryngitis is the same as for any upper respiratory infections. The only way to even attempt to prevent such illnesses is by good hand washing, and by avoiding situations where one might come in contact with people who might be sick. However, even with relatively good hygiene practices, most people will get about five to six colds per year. It is unpredictable which of these may lead to laryngitis.

In addition, do not smoke and avoid situations where second-hand smoke may be present. Also, drink plenty of water daily to keep the throat moist.

Resources

BOOKS

Feigin, Ralph D. et al., editors. *Feigin ' Cherry' Textbook of Pediatric Infectious Diseases*. Philadelphia: Saunders/Elsevier, 2009.

Fried, Marvin P. et al., editors. *The Larynx*. San Diego: Plural, 2009.

OTHER

"Laryngitis." Mayo Clinic. (April 3, 2010), http://www.mayoclinic. com/health/laryngitis/DS00366. (accessed July 26, 2010).

"Laryngitis." Medline Plus, National Library of Medicine and National Institutes of Health. (October 10, 2008), http://www.nlm.nih.gov/medlineplus/ency/article/001385.htm. (accessed July 26, 2010).

ORGANIZATIONS

American Academy of Otolaryngology–Head and Neck Surgery, Inc., 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 836-4444, http://www.entnet.org.

Rosalyn Carson-DeWitt, MD

Laryngoscopy

Definition

Laryngoscopy refers to a procedure used to view the inside of the larynx (the voice box).

Description

The purpose and advantage of seeing inside the larynx is to detect tumors, foreign bodies, nerve or structural injury, or other abnormalities. Two methods allow the larynx to be seen directly during the examination. In one, a flexible tube with a fiber-optic device is threaded through the nasal passage and down into the throat. The other method uses a rigid viewing tube passed directly from the mouth, through the throat, into the larynx. A light and lens affixed to the endoscope are used in both methods. The endoscopic tube may also be equipped to suction debris or remove material for biopsy. **Bronchoscopy** is a similar, but more extensive procedure in which the tube is continued through the larynx, down into the trachea and bronchi.

Preparation

Laryngoscopy is done in the hospital with a local anesthetic spray to minimize discomfort and suppress

KEY TERMS

Endoscopic tube—A tube that is inserted into a hollow organ permitting a physician to see the inside it.

the gag reflex. Patients are requested not to eat for several hours before the examination.

Aftercare

If the throat is sore, soothing liquids or lozenges will probably relieve any temporary discomfort.

Risks

This procedure carries no serious risks, although the patient may experience soreness of the throat or **cough** up small amounts of blood until the irritation subsides.

Results

A normal result would be the absence of signs of disease or damage.

An abnormal finding, such as a tumor or an object lodged in the tissue, would either be removed or described for further medical attention.

Jill S. Lasker

Larynx removal *see* **Laryngectomy**

Laser-assisted in-situ keratomileusis *see* **Photorefractive keratectomy and laser-assisted in-situ keratomileusis**

Laser surgery

Definition

The term "laser" means light amplification by stimulated emission of radiation. Laser surgery uses a laser light source to remove tissues that are diseased or unwanted, to treat blood vessels that are bleeding, or to terminate tumors or lesions. Laser beams are strong beams of light produced by electrically stimulating a particular material, in the case of laser surgery, most often carbon dioxide, argon, or neodymium.

The special light beam is focused to treat tissues by heating the cells until they burst. There are a number of different laser types. Each has a different use and color. Three types of laser that are commonly used are: the carbon dioxide (CO_2) laser; the YAG laser (yttrium aluminum garnet); and the argon laser.

Purpose

Laser surgery is used to:

- cut or destroy tissue that is abnormal or diseased without harming healthy, normal tissue
- shrink or destroy tumors and lesions
- close off nerve endings to reduce postoperative pain
- cauterize (seal) blood vessels to reduce blood loss
- seal lymph vessels to minimize swelling and decrease spread of tumor cells
- remove moles, warts, and tattoos
- decrease the appearance of skin wrinkles

Precautions

Anyone who is thinking about having laser surgery should ask the surgeon to:

- explain why laser surgery is likely to be of greater benefit than traditional surgery
- describe the surgeon's experience in performing the laser procedure the patient is considering

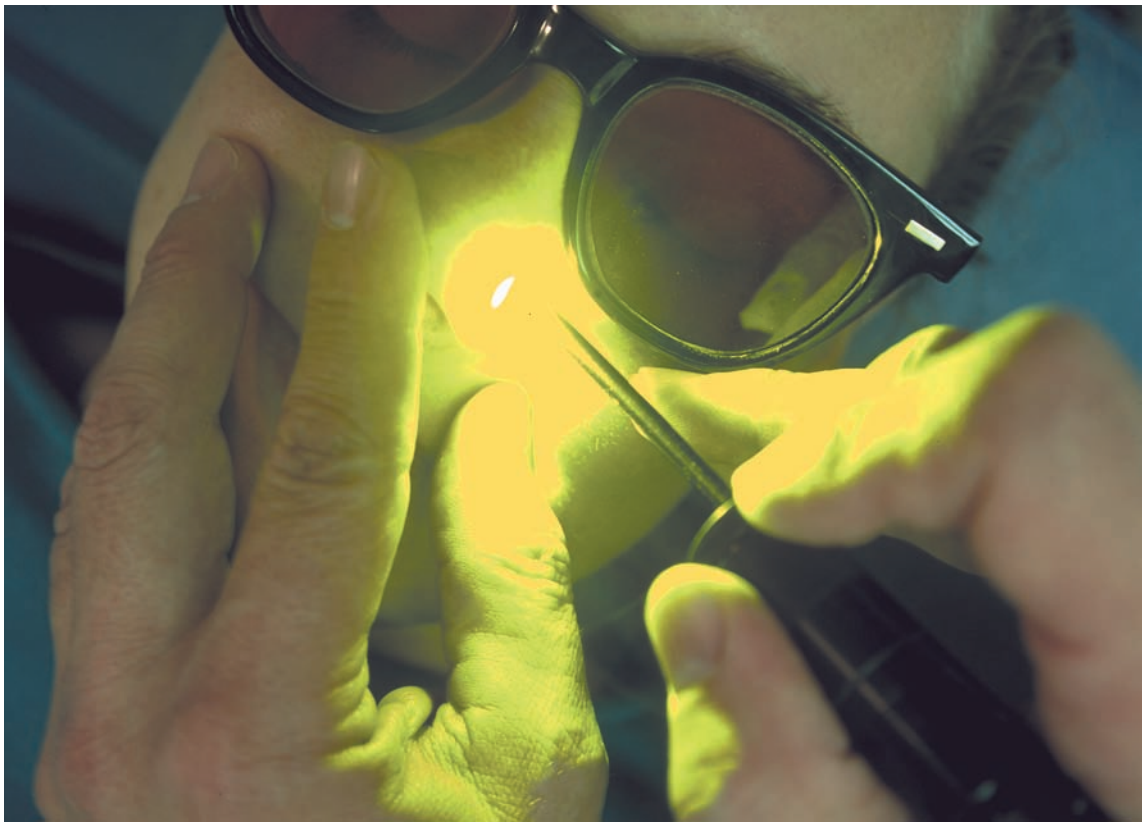
Because some lasers can temporarily or permanently discolor the skin of blacks, Asians, and Hispanics, a dark-skinned patient should make sure that the surgeon has successfully performed laser procedures on people of color. Potential problems include infection, **pain**, scarring, and changes in skin color.

Some types of laser surgery should not be performed on pregnant women or on patients with severe cardiopulmonary disease or other serious health problems.

Additionally, because some laser surgical procedures are performed under **general anesthesia**, its risks should be fully discussed with the anesthesiologist. The patient should fully disclose all over-the-counter and prescription medications that are being taken, as well as the foods and beverages that are generally consumed; some can interact with agents used in anesthesia.

Description

Lasers are used to perform many surgical procedures. Lasers of various wavelengths are used remove tissue, cut, coagulate, and vaporize. Often times, lasers can take the place of conventional surgical tools—scalpels, cryosugery probes, electrosurgical units, or



Cosmetic laser surgery in progress. The wavelengths of the laser's light can be matched to a specific target, enabling the physician to destroy the capillaries near the skin's surface without damaging the surrounding tissue. *(Will & Deni McIntyre/ Photo Researchers, Inc.)*

microwave devices—to carry out standard procedures such as **mastectomy** (breast surgery). By using lasers, surgeons can accomplish more complex tasks and reduce blood loss, decrease postoperative patient discomfort, decrease the chances of infection to the wound, reduce the spread of some cancers, minimize the extent of surgery (in some cases), and achieve better outcomes in wound healing. Also, because lasers are more precise, the laser can penetrate tissue by adjusting the intensity of the light.

Lasers are also extremely useful in both open and laparoscopic procedures. Breast surgery, **hernia repair**, **bowel resection**, hemorrhoidectomy, gallbladder removal, and solid organ surgery are among the common types of laser surgery.

The first working laser was introduced in 1960. Initially used to treat diseases and disorders of the eye, the device was first used to treat diseases and disorders of the eye, whose transparent tissues gave ophthalmic surgeons a clear view of how the narrow, concentrated beam was being directed. Dermatologic surgeons also helped to pioneer laser surgery, and developed and improved upon many early techniques and more refined surgical procedures.

Types of lasers

The three types of lasers most often used in medical treatment are the:

- Carbon dioxide (CO_2) laser. Primarily a surgical tool, this device converts light energy to heat strong enough to minimize bleeding, while cutting through or vaporizes tissue.
- Neodymium: yttrium-aluminum-garnet (Nd:YAG) laser. Capable of penetrating tissue more deeply than other lasers, the Nd:YAG laser enables blood to clot quickly, allowing surgeons to see and can enable surgeons to see and touch body parts that could otherwise be reached only through open (invasive) surgery.
- Argon laser. This laser provides the limited penetration needed for eye surgery and superficial skin disorders. In a special procedure known as photodynamic therapy (PDT), this laser uses light-sensitive dyes to shrink or dissolve tumors.

KEY TERMS

Argon—A colorless, odorless gas.

Astigmatism—A condition in which one or both eyes cannot filter light properly and images appear blurred and indistinct.

Canker sore—A blister-like sore on the inside of the mouth that can be painful but is not serious.

Carbon dioxide—A heavy, colorless gas that dissolves in water.

Cardiopulmonary disease—Illness of the heart and lungs.

Cardiopulmonary resuscitation (CPR)—An emergency procedure used to restore circulation and prevent brain death to a person who has collapsed, is unconscious, is not breathing, and has no pulse.

Cauterize—To use heat or chemicals to stop bleeding, prevent the spread of infection, or destroy tissue.

Cornea—The outer, transparent lens that covers the pupil of the eye and admits light.

Endometriosis—An often painful gynecologic condition in which endometrial tissue migrates from the inside of the uterus to other organs inside and beyond the abdominal cavity.

Glaucoma—A disease of the eye in which increased pressure within the eyeball can cause gradual loss of vision.

Invasive surgery—A form of surgery that involves making an incision in the patient's body and inserting instruments or other medical devices into it.

Laparoscopic procedures—Surgical procedures during which surgeons rely on a laparoscope—a pencil-thin instrument that has its own lighting system and miniature video camera. To perform surgeries, only small incisions are needed to insert the instruments and the miniature camera.

Nearsightedness—A condition in which one or both eyes cannot focus normally, causing objects at a distance to appear blurred and indistinct. Also called myopia.

Ovarian cyst—A benign or malignant growth on an ovary. An ovarian cyst can disappear without treatment or become extremely painful and have to be surgically removed.

Pilonidal cyst—A special kind of abscess that occurs in the cleft between the buttocks. Forms frequently in adolescence after long trips that involve sitting.

Vaporize—To dissolve solid material or convert it into smoke or gas.

Varicose veins—Swollen, twisted veins, usually occurring in the legs, that occur more often in women than in men.

Laser applications

Sometimes described as "scalpels of light," lasers are used alone or with conventional surgical instruments in a array of procedures that:

- improve appearance
- relieve pain
- restore function
- save lives

Laser surgery is often standard operating procedure for specialists in:

- cardiology (branch of medicine which deals with the heart and its diseases)
- dentistry (branch of medicine which deals with the anatomy and development and diseases of the teeth)
- dermatology (science which treats the skin, its structure, functions, and its diseases)
- gastroenterology (science which treats disorders of the stomach and intestines)
- gynecology (science which treats of the structure and diseases of women)
- neurosurgery (surgery of the nervous system)
- oncology (cancer treatment)
- ophthalmology (treatment of disorders of the eye)
- orthopedics (treatment of disorders of bones, joints, muscles, ligaments, and tendons)
- otolaryngology (treatment of disorders of the ears, nose, and throat)
- pulmonology (treatment of disorders of the respiratory system)
- urology (treatment of disorders of the urinary tract and of the male reproductive system)

Routine uses of lasers, include eliminating **birthmarks**, skin discoloration, and skin changes due to **aging**, and removing benign, precancerous, or cancerous tissues or tumors. Lasers are used to stop a patient's **snoring**, remove tonsils, remove or transplant hair, and relieve pain and restore function in patients who are too

weak to undergo major surgery. Lasers are also used to treat:

- angina (chest pain)
- cancerous or noncancerous tumors that cannot be removed or destroyed
- cold and canker sores, gum disease, and tooth sensitivity or decay
- ectopic pregnancy (development of a fertilized egg outside the uterus)
- endometriosis
- fibroid tumors
- gallstones
- glaucoma, mild-to-moderate nearsightedness and astigmatism, and other conditions that impair sight
- migraine headaches
- noncancerous enlargement of the prostate gland
- nosebleeds
- ovarian cysts
- ulcers
- varicose veins
- warts
- numerous other conditions, diseases, and disorders

Advantages of laser surgery

Often referred to as "bloodless surgery," laser procedures usually involve less bleeding than conventional surgery. The heat generated by the laser keeps the surgical site free of germs and reduces the risk of infection. Because a smaller incision is required, laser procedures often take less time (and cost less money) than traditional surgery. Sealing off blood vessels and nerves reduces bleeding, swelling, scarring, pain, and the length of the recovery period.

Disadvantages of laser surgery

Although many laser surgeries can be performed in a doctor's office, rather than in a hospital, the person guiding the laser must be at least as thoroughly trained and highly skilled as someone performing the same procedure in a hospital setting. The American Society for Laser Medicine and Surgery urges that:

- All operative areas be equipped with oxygen and other drugs and equipment required for cardiopulmonary resuscitation (CPR).
- Nonphysicians performing laser procedures be properly trained, licensed, and insured.
- A qualified and experienced supervising physician be able to respond to and manage unanticipated events or other emergencies within five minutes of the time they occur.
- Emergency transportation to a hospital or other acute care facility (ACF) be available whenever laser surgery is performed in a non-hospital setting.

Diagnosis/Preparation

Because laser surgery is used to treat so many diverse conditions, the patient should ask the physician for detailed instructions about how to prepare for a specific procedure. Diet, activities, and medications may not have to be limited prior to surgery, but some procedures require a **physical examination**, a medical history, and conversation with the patient that:

- enables the doctor to evaluate the patient's general health and current medical status
- provides the doctor with information about how the patient has responded to other illnesses, hospital stays, and diagnostic or therapeutic procedures
- clarifies what the patient expects the outcome of the procedure to be

Aftercare

Most laser surgeries can be performed on an outpatient basis, and patients are usually permitted to leave the hospital or medical office when their vital signs have stabilized. A patient who has been sedated should not be discharged until recovery from the anesthesia is complete, unless a responsible adult is available to accompany the patient home.

The doctor may prescribe analgesic (pain-relieving) medication, and should provide easy-to-understand, written instructions on how to take the medication. The doctor should also be able to give the patient a good estimate of how the patient's recovery should progress, the recovery time, and what to do in case complications or emergency arise. The amount of time it takes for the patient to recover from surgery depends on the surgery and on the individual. Recovery time for laser surgery is, for the most part, faster than for traditional surgery.

Risks

Like traditional surgery, laser surgery can be complicated by:

- hemorrhage
- infection
- perforation (piercing) of an organ or tissue

Laser surgery can also involve risks that are not associated with traditional surgical procedures. Being careless or not practicing safe surgical techniques can severely burn the patient's lungs. Patients must wear protective eye shields while undergoing laser surgery on

any part of the face near the eyes or eyelids, and the United States Food and Drug Administration has said that both doctors and patients must use special wavelength-specific, protective eyewear whenever a CO_2 laser is used.

There are other kinds of dangers that laser surgery can impose of which the patient should be aware. Laser beams have the capacity to do a great deal of damage when coupled with high enough energy and absorption. They can ignite clothing, paper, and hair. Further, the risk of fire from lasers increases in the presence of oxygen. Hair should be protected and clothing should be tied back, or removed, within the treatment areas. It is important to guard against electric shock, as lasers require the use of high voltage. Critically, installation must ensure proper wiring.

Laser beams can burn or destroy healthy tissue, cause injuries that are painful and sometimes permanent, and actually compound problems they are supposed to solve. Errors or inaccuracies in laser surgery can worsen a patient's vision, for example, and lasers can scar and even change the skin color of some patients.

All of the above risks, precautions, and potential complications should be discussed by the doctor with the patient.

Results

The nature and severity of the problem, the skill of the surgeon performing the procedure, and the patient's general health and realistic expectations are among the factors that influence the outcome of laser surgery. Successful procedures can enable patients to feel better, look younger, and enjoy longer, fuller, more active lives.

A patient who is considering any kind of laser surgery should ask the doctor to provide detailed information about what the outcome of the surgery is expected to be, what the recovery process will involve, and how long it will probably be before a normal appearance is regained and the patient can resume normal activities.

A person who is considering any type of laser surgery should ask the doctor to provide specific and detailed information about what could go wrong during the procedure and what the negative impact on the patient's health or appearance might be.

Lighter or darker skin may appear, for example, when a laser is used to remove sun damage or age spots from an olive- or dark-skinned individual. This abnormal pigmentation may or may not disappear over time.

Scarring or rupturing of the cornea is uncommon, but laser surgery on one or both eyes can:

- increase sensitivity to light or glare
- reduce night vision
- permanently cloud vision, or cause sharpness of vision to decline throughout the day

Signs of infection following laser surgery include:

- burning
- crusting of the skin
- itching
- pain
- scarring
- severe redness
- swelling

Resources

BOOKS

Berlien, Hans-Peter, et al., eds. *Applied Laser Medicine*. New York: Springer, 2004.

Goldberg, David J. *Laser Dermatology: Pearls and Problems*. Malden, MA: Blackwell, 2008.

Niemz, Markoff H., *Laser-Tissue Interactions: Fundamentals and Applications*. New York: Springer, 2007.

PERIODICALS

Parlette, Eric C., Michael S. Kaminer, and Kenneth A. Arndt. "The Art of Tattoo Removal: Of the Multiple Removal Approaches, Laser Therapy Is the Gold Standard." *Plastic Surgery Products* 18, no. 1 (Jan 2008): 18–20.

ORGANIZATIONS

American Society for Laser Medicine and Surgery, 2404 Stewart Avenue, Suite 240, Wausau, WI, 54401, (715) 845-9283, (715) 848-2493, information@aslms.org, http://www.aslms.org.

Cancer Information Service, 9000 Rockville Pike, Building 31, Suite 10A18, Bethesda, MD, 20892, http://wwwicic.nci.nih.gov.

Mayo Clinic, Division of Colon and Rectal Surgery , 200 First Street SW, Rochester, MN, 55905, (507) 284-2511, http://www.mayoclinic.org/colorectalsurgery-rst/laparoscopicsurgery.html.

Mayo Clinic, Mayo Foundation for Medical Education and Research, 200 First Street SW, Rochester, MN, 55905, (507) 284-2511, http://www.mayoclinic.com .

National Cancer Institute, NCI Public Inquiries Office, 6116 Executive Boulevard, Bethesda, MD, 20892-8322, (800) 422-6237, http://www.cancer.gov.

Laith Farid Gulli, MD, MS
Randi B. Jenkins, BA
Bilal Nasser, MD, MS
Robert Ramirez, BS
Brenda W. Lerner

LASIK *see* **Photorefractive keratectomy and laser-assisted in-situ keratomileusis**

Lassa fever *see* **Hemorrhagic fevers**

Late effects of childhood cancer and its treatment

Definition

Late effects of childhood **cancer** treatment may be defined as any adverse effect of treatment that does not resolve after treatment is completed or which appears after the completion of the treatment for cancer. Late effects can include adverse effects on major organ systems, problems with cognitive and psychosocial functioning as well as the development of second malignancies.

Demographics

Due to the effectiveness of treatment modalities in treating childhood cancers, deaths from these cancers have decreased dramatically over the last 50 years. Before 1970, virtually all children diagnosed with cancer died from the disease. Today, with current therapy, 79% of children affected by cancer are able to be cured. The numbers of survivors of childhood cancers are increasing with an estimated 1 long-term childhood cancer survivor among every 450 adolescents and young adults in the United States. There are approximately 300,000 long-term childhood cancer survivors in the U.S. alone. Two-thirds of childhood cancer survivors will develop at least one late adverse effect as a result of their treatment for cancer.

Description

As ever-increasing numbers of children are surviving cancer, follow-up of these survivors has focused attention on adverse effects which may occur sometimes years after receiving treatment for childhood cancer. Many of these adverse effects become evident as the child matures into **puberty** and young adulthood. Many young cancer survivors have at least one organ system which has been impacted either by the cancer or by treatment for the cancer.

Late effects can be caused by **chemotherapy**, **radiation therapy**, hematopoietic stem cell transplant, and/or surgery. Virtually any organ of the body can be affected. According to the Children's Oncology Group of the American Academy of Pediatrics, the risk of late effects is directly related to the intensity of the cancer therapy received as treatment. Treatment methodologies which increase risk for late effects include longer treatment with higher doses of chemotherapy and radiation therapy, therapy which includes more than one treatment modality, e.g., a combination of chemotherapy and radiation as opposed to using only one of the modalities alone, and receiving therapy to treat relapse of disease. The patient's age at the time of the treatment also influences the potential for adverse late effects with younger children being at higher risk. Young children are particularly susceptible to the effects of cancer treatments which can result in impaired growth, cognitive function, sexual development, and organ function.

Most of the time, chemotherapy results in immediate and acute effects. However, some late effects of treatment with chemotherapy can develop. For example, treatment with chemotherapy drugs classified as alkylating agents can lead to problems such as delayed or arrested puberty and **infertility** and can result in the development of a different or second cancer. Treatment with radiation therapy can impede normal growth and development, can impair organ function and can lead to the development of cancer as well.

Late Effects by Organ System

Neurocognitive effects

Tests of cognitive function and academic achievement in childhood cancer survivors confirm the negative impact of radiation therapy targeted to the brain in infants and children. The negative effects are especially pronounced in survivors of the brain cancer, medulloblastoma, because of the higher doses of radiation therapy experienced by those survivors.

Neurocognitive effects such as seizures, **memory loss**, and decrease in cognitive function as evidenced by lower IQ and mathematics scores are associated with cranial radiation therapy and intrathecal administration of chemotherapy used in the treatment of children with acute lymphoblastic leukemia (ALL). Studies of children with brain tumors who were treated with surgery and radiation to the brain reveal similar neurocognitive deficits. Children who were younger than 3 years of age when treated experience more pronounced negative neurocognitive consequences.

Cardiac effects

Damage to the heart and cardiovascular system can occur as a result of treatment with radiation therapy that includes all or part of the heart in the treatment field. Childhood survivors of Hodgkin disease or those who received radiation to the spine as treatment for some brain tumors are at increased risk. Late effects of radiation therapy which included the heart in the treatment field includes pericardial effusions, constrictive **pericarditis** and premature **coronary artery disease**.

Childhood cancer survivors, especially infants and toddlers, who were treated with chemotherapy drugs classified as anthracyclines are at higher risk for the

development of heart damage including anthracycline-induced **cardiomyopathy**. The use of anthracycline chemotherapy in children can also lead to the development of congestive **heart failure**, pericarditis, and ventricular **arrhythmias**. **Mitral valve insufficiency** can also occur as a late effect.

Pulmonary effects

Cancer treatments which can affect the lungs and result in late effects include radiation therapy and chemotherapy. Late effects of radiation therapy develop over a period of months and even years resulting in pneumonitis and **pulmonary fibrosis**.

Chemotherapy agents which can cause long-term adverse effects to the lungs include bleomycin, which is used in the treatment of children with **germ cell tumors** and lymphoma, and nitrosureas such as carmustine, which are used in the treatment of children with brain tumors. Pulmonary damage is increased when these agents are used in combination with radiation therapy. Adverse effects include pneumonitis and other pulmonary toxicities.

Endocrine and reproductive effects

Radiation therapy and treatment with chemotherapy agents classified as alkylating agents can lead to endocrine toxicity. Endocrine toxicity can negatively affect growth which can result in short stature.

Chemotherapy agents, particularly nitrogen mustard, procarbazine, and cyclophosphamide are the most damaging to the reproductive system. Young women treated with these drugs in combination with radiation may undergo **premature menopause** with the average age at **menopause** in one study at age 31 years. Young women who experience early menopause are then at increased risk of **osteoporosis** and heart disease at an earlier age than the general population.

Radiation to the reproductive organs in childhood can lead to fertility problems in men and in women in later years. Results of a study released in 2010 revealed that women who received radiation to the pelvic region prior to menarche were 12 times more likely to experience **stillbirth** and neonatal **death** of their offspring. In women treated with radiation therapy after menarche there was no significantly increased risk irregardless of the dose of radiation. In males, radiation to the testes did not affect risk for stillbirth or neonatal death rates of offspring nor was risk increased for the offspring of men and women who were treated in childhood with alkylating chemotherapy agents.

Children, particularly girls, diagnosed with acute lymphoblastic leukemia (ALL) and who were treated with higher doses of cranial irradiation, are more likely to develop **obesity** as a late effect.

Damage to the thyroid gland can also occur after radiation to the neck and/or chest.

Risk for second malignancies

Childhood cancer survivors who were treated with radiation therapy, chemotherapy or both modalities combined are at increased risk for the development of second malignant neoplasm (cancer). Risk for the development of a second cancer is related to the total dose received of chemotherapy and/or radiation therapy. Higher doses are correlated with increased risk of malignancy development.

Chemotherapy agents classified as alkylating agents especially nitrogen mustard, cyclophosphamide, ifosfamide, melphalan, and procarbazine damage DNA which can result in the development of a second malignancy such as acute myelogenous leukemia (AML). AML typically occurs 4–8 years after treatment for the first malignancy with alkylating agents.

Treatment with chemotherapy drugs classified as epipodophyllotoxins, such as etoposide and teniposide, can also result in the development of leukemia. In one study, about 12% of patients treated with acute lymphoblastic leukemia (ALL) developed secondary AML which is almost always fatal.

The risk of developing a second cancer after treatment with radiation therapy is related to the age of the patient at the time of the treatment and the total dose received. The risk of developing the second malignancy increases with time with as many as 20 years elapsing before the development of the secondary cancer. The most common second malignant neoplasms to develop include **breast cancer** after radiation to the chest as part of treatment for Hodgkin disease, brain tumors after radiation to the brain and central nervous system for the treatment of ALL, soft tissue **sarcomas**, and bone, thyroid and bladder cancers.

Prevention

Prevention of late effects of cancer therapies is receiving increased scrutiny and is generating substantial amounts of research as increased numbers of children survive cancer. Current treatment protocols attempt to treat childhood cancer while sparing normal tissues and organs as much as possible. Newer therapies and radiation techniques allow for more precise targeting of therapies. In addition, radiation therapy and some chemotherapy agents may be omitted or delayed in very young children. Other drugs, known

KEY TERMS

Cardiomyopathy—A disease or disorder which affects the heart muscle.

Intrathecal—Administration of chemotherapy drugs injected into the cerebrospinal fluids which surround the brain and spinal cord.

Pericardial effusion—An accumulation of excess fluid in the pericardial sac which surrounds the heart.

Pneumonitis—Inflammation of the lungs.

Pulmonary fibrosis—Scarring of lung tissue.

as chemoprotectants, can be utilized to lessen the known toxicities of some chemotherapy drugs.

Resources

PERIODICALS

American Academy of Pediatrics Children's Oncology Group."Long-term Follow-up Care for Pediatric Cancer Survivors."*Pediatrics*.(March 2009); 123(3): 906–15.

Berry, G.J., & Jorden, M. "Pathology of Radiation and Anthracycline Cardiotoxicity."*Pediatr Blood Cancer*. (Jun 15 2005); 44(7): 630–7.

DeBruin, M.L., Van Dulmen-den Broeder, E., Van den Berg, M.H., & Lambalk, C.B."Fertility in Childhood Cancer Survivors."*Endocr Dev*.(2009); 15: 135–58.

Edgar, A.B., Morris, E.M., Kelnar, C.J., & Wallace, H.B."Long-term Follow-up of Survivors of Childhood Cancer."*Endocr Dev*.(2009); 15: 159–80.

Maeda, M."Late Effects of Childhood Cancer: Life-threatening Issues."*J Nippon Med Sch*.(Dec 2008); 75(6): 320–4.

Robison, L.L., Green, D.M., Hudson, M., et al."Long-term Outcomes of Adult Survivors of Childhood Cancer." *Cancer*.(Dec 1, 2005); 104 (11 Suppl): 2257–64.

OTHER

Monteleone, P.M., & Meadows, A.T."Late Effects of Childhood Cancer and Treatment."eMedicine. May 6, 2009 [cited September 18, 2010].http://www.emedicine.medscape.com.

ORGANIZATIONS

CureSearch for Children's Cancer, National Childhood Cancer Foundation, 4600 East West Highway, Suite 600, Bethesda, Maryland, 20814-3457, (800) 458-6223 (U.S. and Canada), info@curesearch.org, http://www.curesearch.org.

Melinda Granger Oberleitner
RN, DNS, APRN, CNS

Laxatives

Definition

Laxatives are products that promote bowel movements.

Purpose

Laxatives are used to treat constipation—the passage of small amounts of hard, dry stools, usually fewer than three times a week. Before recommending the use of laxatives, differential diagnosis is usually performed because prolonged **constipation** may be evidence of a significant problem, such as localized **peritonitis** (an infection of the abdominal wall) or **diverticulitis** (an infection of part of the intestine). Complaints of constipation also may be associated with **obsessive-compulsive disorder**. Use of laxatives should be avoided in these cases. Individuals should be aware that patterns of defecation are highly variable. Normal patterns may vary from two to three times daily to two to three times weekly.

Laxatives may also be used prophylactically for patients recovering from a myocardial infarction (**heart attack**) or those who have had recent surgery and should not strain during defecation. Laxatives are also used to cleanse the lower bowel before a **colonoscopy** or similar diagnostic imaging procedure.

Description

Laxatives may be grouped by mechanism of action. Saline cathartics include dibasic **sodium** phosphate (Phospo-Soda), magnesium citrate, magnesium hydroxide (milk of magnesia), magnesium sulfate (Epsom salts), and sodium biphosphate. These laxatives act by attracting and holding water in the intestine and may produce a watery stool. Magnesium sulfate is the most potent of the laxatives in this group.

Stimulant and irritant laxatives increase the contracting movements of the intestine, causing stool to move faster through the bowl and giving less time for water to be absorbed. Examples of these laxatives include cascara and bisadocyl (Dulcolax.) Castor oil works in a similar fashion.

Bulk-producing laxatives increase the volume of the stool, soften the stool, and stimulate intestinal motility. Psyllium (Metamucil, Konsil) and methylcellulose (Citrucel) are examples of this type of laxative. The overall effect is similar to that of eating high-fiber foods, and this class of laxative is most suitable for regular use. Many primary care physicians suggest

KEY TERMS

Cathartic colon—A poorly functioning colon, resulting from the chronic abuse of stimulant cathartics.

Colon—The large intestine.

Diverticulitis—Inflammation of the part of the intestine known as the diverticulum.

Fiber—Carbohydrate material in food that cannot be digested.

Hyperosmotic—Hypertonic, containing a higher concentration of salts or other dissolved materials than normal tissues.

Osteomalacia—A disease of adults, characterized by softening of the bone. Similar to rickets which is seen in children.

Pregnancy category—A system of classifying drugs according to their established risks for use during pregnancy. Category A: Controlled human studies have demonstrated no fetal risk. Category B: Animal studies indicate no fetal risk, but no human studies, or adverse effects in animals, but not in well-controlled human studies. Category C: No adequate human or animal studies, or adverse fetal effects in animal studies, but no available human data. Category D: Evidence of fetal risk, but benefits outweigh risks. Category X: Evidence of fetal risk. Risks outweigh any benefits.

Steatorrhea—An excess of fat in the stool.

Stool—The solid waste that is left after food is digested. Stool forms in the intestines and passes out of the body through the anus.

that patients try laxatives in this category before using saline or stimulant laxatives.

Stool softener laxatives causes water to be retained within the fecal mass, providing a larger, softer stool. Docusate (Colace) is a representative example of the stool softener class of laxatives. It must be taken before the fecal mass forms to have any effect, so it has no effect on acute constipation. It may, however, be useful in preventing constipation in patients with recurrent problems or in those who are about to take a constipating drug, such as narcotic **analgesics**.

Mineral oil is an emollient laxative. Emollient laxatives act by retarding intestinal absorption of fecal water and moving the feces more easily through the intestine, thereby softening the stool.

The hyperosmotic laxatives are glycerin and lactulose (Chronulac, Duphalac), both of which act by holding water within the intestine. Lactulose may also increase contractions of the intestine.

Some newer options for the treatment of chronic constipation are being developed by researchers. These include alternative therapies such as **biofeedback**, newer drugs like tegaserod (Zelnorm) and prucalopride, which stimulate peristalsis (muscle contraction in the intestine), a nerve growth factor known as neurotrophin-3, and electrical stimulation of the colon.

Recommended dosage

Dosage varies widely depending on the product and whether constipation is acute or chronic. See specific products or consult a healthcare provider.

Precautions

Short-term use of laxatives is generally safe except in patients experiencing **appendicitis**, fecal impaction, or intestinal obstruction. Lactulose is composed of two sugar molecules, galactose and fructose and should not be administered to patients who require a low galactose diet.

Chronic use of laxatives may result in fluid and electrolyte imbalances, steatorrhea, osteomalacia, **diarrhea**, cathartic colon, and **liver disease**. Excessive intake of mineral oil may cause impaired absorption of the oil-soluble **vitamins** A, D, E, and K. Excessive use of magnesium salts may cause hypermagnesemia.

Lactulose and magnesium sulfate are **pregnancy** category B substances, which means that there is there is no evidence in animals of harm to a fetus from the drug, but no significant studies on humans have been performed. Casanthranol, cascara sagrada, danthron, docusate sodium, docusate **calcium**, docusate potassium, mineral oil and senna are pregnancy category C substances, meaning that either harm to the fetus has been shown in animals or there are no animal studies available, and there are no controlled human studies. Casanthranol, cascara sagrada and danthron are excreted in breast milk, resulting in the potential for increased incidence of diarrhea in a nursing infant.

The American College of Toxicology states that cathartics should *not* be used as a means of clearing poisons from the digestive tract of a **poisoning** victim. Although some physicians have administered these laxatives along with **activated charcoal** in order to

reduce the body's absorption of the poison, this treatment is no longer recommended.

Interactions

Mineral oil and docusate should not be used in combination. Docusate is an emulsifying agent that will increase the absorption of mineral oil.

Bisacodyl tablets are enteric coated, and so they should not be used in combination with **antacids**. The antacids will cause premature rupture of the enteric coating. Many medications should not be taken within two hours of taking a laxative. The patient should ask his or her doctor or pharmacist about this and other possible considerations before beginning to take a laxative.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Chew, Rusheng. *Gastrointestinal System*. 3rd ed. New York: Mosby, 2007.

Karch, A. M. *Lippincott's Nursing Drug Guide*. Springhouse, PA: Lippincott Williams & Wilkins, 2008.

Wexnerm, Steven D., and Graeme S. Duthie, eds. *Constipation: Etiology, Evaluation, and Management*. 2nd ed. New York: Springer, 2006.

ORGANIZATIONS

American Society of Health-System Pharmacists (ASHP), 7272 Wisconsin Avenue, Bethesda, MD, 20814, (301) 657-3000, (866) 279-0681, http://www.ashp.org.

National Digestive Diseases Information Clearinghouse (NDDIC), 2 Information Way, Bethesda, MD, 20892-3570, (703) 738-4929, (800) 891-5389, http://digestive.niddk.nih.gov.

United States Food and Drug Administration (FDA), 10903 New Hampshire Ave, Silver Spring, MD, 02993-0002, (888) 463-6332, http://www.fda.gov.

Rebecca J. Frey, PhD
Tish Davidson, A. M.

Lazy eye *see* **Amblyopia**

LCM *see* **Lymphocytic choriomeningitis**

LDH isoenzymes test *see* **Lactate dehydrogenase isoenzymes test**

LDH test *see* **Lactate dehydrogenase test**

Lead poisoning

Definition

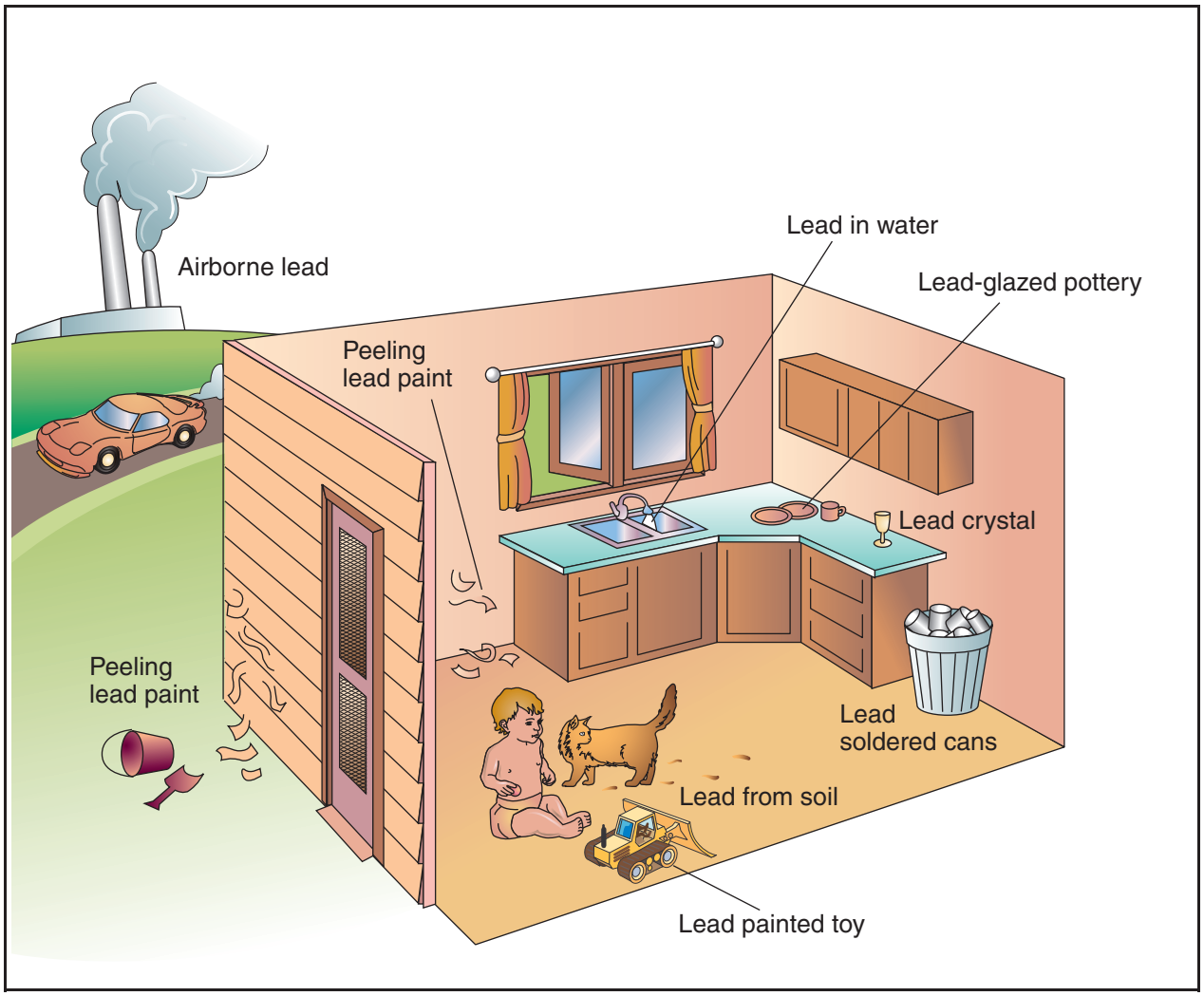
Lead poisoning occurs when a person swallows, absorbs, or inhales lead in any form. The result can be damaging to the brain, nerves, and many other parts of the body. Acute lead poisoning, which is somewhat rare, occurs when a relatively large amount of lead is taken into the body over a short period of time. Chronic lead poisoning—a common problem in children—occurs when small amounts of lead are taken in over a longer period. The Centers for Disease Control and Prevention (CDC) defines childhood lead poisoning as a whole-blood lead concentration equal to or greater than 10 micrograms/dL.

Description

Lead can damage almost every system in the human body, and it can also cause high blood pressure (**hypertension**). It is particularly harmful to the developing brain of fetuses and young children. The higher the level of lead in a child's blood, and the longer this elevated level lasts, the greater the chance of ill effects. Over the long term, lead poisoning in a child can lead to learning disabilities, behavioral problems, and even **mental retardation**. At very high levels, lead poisoning can cause seizures, **coma**, and even **death**. Most deaths are among males (74%), African Americans (67%), adults over the age of 45 (76%), and Southerners (70%).

About one out of every six children in the United States has a high level of lead in the blood, according to the Agency for Toxic Substances and Disease Registry. Many of these children are exposed to lead through peeling paint in older homes. Others are exposed through dust or soil that has been contaminated by old paint or past emissions of leaded gasoline. Since children between the ages of 12–36 months are apt to put things in their mouths, they are more likely than older children to take in lead. Pregnant women who come into contact with lead can pass it along to the fetus.

More than 80% of American homes built before 1978 have lead-based paint in them, according to the Centers for Disease Control and Prevention (CDC). The older the home, the more likely it is to contain lead paint, and the higher the concentration of lead in the paint is apt to be. Some homes also have lead in the water pipes or plumbing. People may have lead in the paint, dust, or soil around their homes or in their drinking water without knowing it, since lead can't be seen, smelled, or tasted. Because lead doesn't break down naturally, it can continue to cause problems until it is removed.



Continuous exposure to lead can damage nearly every system in the human body and is particularly harmful to the developing brain of fetuses and young children. Common sources of lead exposure include lead-based paint, dust and soil, drinking water, food from cans, and eating utensils, such as plates and drinking glasses, that are lead-based. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

Lead poisoning and the broad issue of dangerously high levels of lead in common consumer product, especially those made in China, became a major issue in 2007.The summer of 2007 saw a record number of recalls of millions of toys made in China, primarily because of high levels of lead. Affected were several of the leading United States toy companies. In August 2007, Fisher-Price recalled one million toy products, including popular Sesame Street characters, Dora the Explorer, and Go, Diego, Go. That same month, Mattel recalled millions of toys involving such high-profile brands as Barbie, Sarge die cast cars, Doggie Day Care, and Polly Pocket Play Sets, according to the U.S. Consumer Product Safety Commission. Worldwide, Mattel recalled 18.2 million Chinese-made toys as of September 2007, including nearly 10 million in the United States. In November 2007, at the start of the holiday buying season, Kmart removed jewelry from its stores that had been advertised as lead-free after extremely high concentrations of lead were found in some pieces. In some cases, more than half of the jewelry's content was lead. Kmart refused to say how many pieces were involved or where they were made. In August 2007, two U.S. law firms filed class action lawsuits against Mattel Inc. asking for more than $5 million in damages.

Causes and symptoms

Before scientists knew how harmful it could be, lead was widely used in paint, gasoline, water pipes, and many

other products. Today house paint is almost lead-free, gasoline is unleaded, and household plumbing is no longer made with lead materials. Still, remnants of the old hazards remain. Following are some sources of lead exposure:

- Lead-based paint. This is the most common source of exposure to large amounts of lead among preschoolers. Children may eat paint chips from older homes that have fallen into disrepair. They may also chew on painted surfaces such as windowsills. In addition, paint may be disturbed during remodeling.
- Dust and soil. These can be contaminated with lead from old paint or past emissions of leaded gasoline. In addition, pollution from operating or abandoned industrial sites and smelters can find its way into the soil, resulting in soil contamination.
- Drinking water. Exposure may come from lead water pipes, found in many homes built before 1930. Even newer copper pipes may have lead solder. Also, some new homes have brass faucets and fittings that can leach lead.
- Jobs and hobbies. A number of activities can expose participants to lead. These include making pottery or stained glass, refinishing furniture, doing home repairs, and using indoor firing ranges. When adults take part in such activities, they may inadvertently expose children to lead residue that is on their clothing or on scrap materials.
- Food. Imported food cans often have lead solder. Lead may also be found in leaded crystal glassware and some imported ceramic or old ceramic dishes (e.g., ceramic dishes from Mexico). A 2003 study of cases of lead poisoning in pregnant women found that 70% of the patients were Hispanics, most of whom had absorbed the lead from their pottery. In addition, food may be contaminated by lead in the water or soil.
- Folk medicines. Certain folk medicines (for example, alarcon, alkohl, azarcon, bali goli, coral, ghasard, greta, liga, pay-loo-ah, and rueda) and traditional cosmetics (kohl, for example) contain large amounts of lead.
- Moonshine whiskey. Lead poisoning from drinking illegally distilled liquor is still a cause of death among adults in the southern United States.
- Gunshot wounds. Toxic amounts of lead can be absorbed from bullets or bullet fragments that remain in the body after emergency surgery.

Chronic lead poisoning

New evidence suggests that lead may be harmful to children even at low levels that were once thought to be safe, and the risk of damage rises as blood levels of lead increase. The symptoms of chronic lead poisoning take time to develop, however. Children can appear healthy despite having high levels of lead in their blood. Over time, though, problems such as the following may arise:

- learning disabilities
- hyperactivity
- mental retardation
- slowed growth
- hearing loss
- headaches

It is also known that certain genetic factors increase the harmful effects of lead poisoning in susceptible children; however, these factors are not completely understood.

Lead poisoning is also harmful to adults, in whom it can cause high blood pressure, digestive problems, nerve disorders, **memory loss**, and muscle and joint **pain**. In addition, it can lead to difficulties during **pregnancy**, as well as cause reproductive problems in men and women.

More recently, chronic exposure to lead in the environment has been found to speed up the progression of kidney disorders in patients without diabetes.

Acute lead poisoning

Acute lead poisoning, while less common, shows up more quickly and can be fatal. Symptoms such as the following may occur:

- severe abdominal pain
- diarrhea
- nausea and vomiting
- weakness of the limbs
- seizures
- coma

Diagnosis

A high level of lead in the blood can be detected with a simple blood test. In fact, testing is the only way to know for sure if children without symptoms have been exposed to lead, since they can appear healthy even as long-term damage occurs. The CDC recommends testing all children at 12 months of age and, if possible, again at 24 months. Testing should start at six months for children at risk for lead poisoning. Based on these test results and a child's risk factors, the doctor will then decide whether further testing is needed and how often. In some states, more frequent testing is required by law.

Children at risk

Children with an increased risk of lead poisoning include those who:

- Live in or regularly visit a house built before 1978 in which chipped or peeling paint is present.
- Live in or regularly visit a house that was built before 1978 where remodeling is planned or underway.
- Have a brother or sister, housemate, or playmate that has been diagnosed with lead poisoning.
- Have the habit of eating dirt, or have been diagnosed with pica.
- Live with an adult whose job or hobby involves exposure to lead.
- Live near an active lead smelter, battery-recycling plant, or other industry that can create lead pollution.

Adults at risk

Testing is also important for adults whose job or hobby puts them at risk for lead poisoning. This includes people who take part in the following activities:

- glazed pottery or stained glass making
- furniture refinishing
- home renovation
- target shooting at indoor firing ranges
- battery reclamation
- precious metal refining
- radiator repair
- art restoration

Treatment

The first step in treating lead poisoning is to avoid further contact with lead. For adults, this usually means making changes at work or in hobbies. For children, it means finding and removing sources of lead in the home. In most states, the public health department can help assess the home and identify lead sources.

If the problem is lead paint, a professional with special training should remove it. Removal of lead paint is not a do-it-yourself project. Scraping or sanding lead paint creates large amounts of dust that can poison people in the home. This dust can stay around long after the work is completed. In addition, heating lead paint can release lead into the air. For these reasons, lead paint should only be removed by someone who knows how to do the job safely and has the equipment to clean up thoroughly. Occupants, especially children and pregnant women, should leave the home until the cleanup is finished.

Medical professionals should take all necessary steps to remove bullets or bullet fragments from patients with gunshot injuries.

Chelation therapy

If blood levels of lead are high enough, the doctor may also prescribe **chelation therapy**. This refers to treatment with chemicals that bind to the lead and help the body pass it in urine at a faster rate. There are four chemical agents that may be used for this purpose, either alone or in combination. Edetate **calcium** disodium (EDTA calcium) and dimercaprol (BAL) are given through an intravenous line or in shots, while succimer (Chemet) and penicillamine (Cuprimine, Depen) are taken by mouth. (Although many doctors prescribe penicillamine for lead poisoning, this use of the drug has not been approved by the Food and Drug Administration.)

Alternative treatment

Changes in diet are no substitute for medical treatment. However, getting enough calcium, zinc, and protein may help reduce the amount of lead the body absorbs. Iron is also important, since people who are deficient in this nutrient absorb more lead. Garlic and thiamine, a B-complex vitamin, have been used to treat lead poisoning in animals. However, their usefulness in humans for this purpose has not been proved. Nutritional, botanical, and homeopathic medicines can be administered once the source is removed, to help correct any imbalances brought on by lead toxicity.

Prognosis

If acute lead poisoning reaches the stage of seizures and coma, there is a high risk of death. Even if the person survives, there is a good chance of permanent brain damage. The long-term effects of lower levels of lead can also be permanent and severe. However, if chronic lead poisoning is caught early, these negative effects can be limited by reducing future exposure to lead and getting proper medical treatment.

Prevention

Many cases of lead poisoning can be prevented. These steps can help:

- Keep the areas where children play as clean and dust-free as possible.
- Wash pacifiers and bottles when they fall to the floor, and wash stuffed animals and toys often.
- Make sure children wash their hands before meals and at bedtime.

KEY TERMS

Chelation therapy—Treatment with chemicals that bind to a poisonous metal and help the body pass it in urine at a faster rate.

Dimercaprol (BAL)—A chemical agent used to remove excess lead from the body.

Edetate calcium disodium (EDTA calcium)—A chemical agent used to remove excess lead from the body.

Penicillamine (Cuprimine, Depen)—A drug used to treat medical problems (such as excess copper in the body and rheumatoid arthritis) and to prevent kidney stones. It is also sometimes prescribed to remove excess lead from the body.

Pica—An abnormal appetite or craving for non-food items, often such substances as chalk, clay, dirt, laundry starch, or charcoal.

Succimer (Chemet)—A drug used to remove excess lead from the body.

- Mop floors and wipe windowsills and other chewable surfaces, such as cribs, twice a week with a solution of powdered dishwasher detergent in warm water.
- Plant bushes next to an older home with painted exterior walls to keep children at a distance.
- Plant grass or another ground cover in soil that is likely to be contaminated, such as soil around a home built before 1960 or located near a major highway.
- Have household tap water tested to find out if it contains lead.
- Use only water from the cold-water tap for drinking, cooking, and making baby formula, since hot water is likely to contain higher levels of lead.
- If the cold water hasn't been used for six hours or more, run it for several seconds, until it becomes as cold as it will get, before using it for drinking or cooking. The more time water has been sitting in the pipes, the more lead it may contain.
- If you work with lead in your job or hobby, change your clothes before you go home.
- Do not store food in open cans, especially imported cans.
- Do not store or serve food in pottery meant for decorative use.

Resources

BOOKS

Legge, Thomas M., and Kenneth W. Goadby. *Lead Poisoning and Lead Absorption: The Symptoms, Pathology and Prevention*. Whitefish, MT: Kessinger Publishing, 2007.

PERIODICALS

Lanphear, Bruce P. "The Conquest of Lead Poisoning: A Pyrrhic Victory." *Environmental Health Perspectives* (October 2007): 484(2).

Parham, Marti. "Toy Recalls & Lead Poisoning: What Parents Need to Know." *Jet* (September 24, 2007): 48(2).

Pekkanen, John. "Poisonous Predator: Lead is Gone from Gasoline and Paint but Continues to Pose Danger to Kids, Particularly in Older Neighborhoods." *Children's Voice Magazine* (July-August 2007): 26(5).

Sharmer, Laurel, et al. "Newly Recognized Pathways of Exposure to Lead in the Middle-Income Home." *Journal of Environmental Health* (October 2007): 15(5).

Sloviter, Vikki. "Lead, Lead, Everywhere, What's A Parent to Do?" *Pediatrics for Parents* (August 2007): 12(2).

Walker, Misha K., and Mary Jean Brown. "Childhood Lead Poisoning Prevention." *Pediatrics for Parents* (February 2007): 4(2).

ORGANIZATIONS

Childhood Lead Poisoning Prevention Branch, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov/nceh/lead/.

Consumer Product Safety Commission, 4330 East West Highway, Bethesda, MD, 20814, (301) 504-7923, (301) 504-0124, (800) 638-2772, http://www.cpsc.gov/.

National Safety Council, 1121 Spring Lake Dr., Itasca, IL, 60143-3201, (630) 285-1121, (630) 285-1315, (800) 621-7615, customerservice@nsc.org, http://www.nsc.org.

The National Lead Information Center, 422 S. Clinton Ave., Rochester, NY, 14620, (585) 232-3111, (800) 424-5323, http://www.epa.gov/lead.

Linda Wasmer Smith
Ken R. Wells

Learning disorders

Definition

Learning disorders are academic difficulties experienced by children and adults of average to above-average intelligence. People with learning disorders have difficulty with reading, writing, mathematics, or a combination of the three. These difficulties significantly interfere with academic achievement or daily living.

Description

Learning disorders, or disabilities, affect approximately 2 million children between the ages of six and 17 (5% of public school children), although some experts think the figure may be as high as 15%. These children have specific impairments in acquiring, retaining, and processing information. Standardized tests place them well below their IQ range in their area of difficulty. The three main types of learning disorders are reading disorders, mathematics disorders, and disorders of written expression. The male: female ratio for learning disorders is about 5:1.

Reading disorders

Reading disorders are the most common type of learning disorder. Children with reading disorders have difficulty recognizing and interpreting letters and words (**dyslexia**). They aren't able to recognize and decode the sounds and syllables (phonetic structure) behind written words and language in general. This condition lowers accuracy and comprehension in reading.

Mathematics disorders

Children with mathematics disorders (dyscalculia) have problems recognizing and counting numbers correctly. They have difficulty using numbers in everyday settings. Mathematics disorders are typically diagnosed in the first few years of elementary school when formal teaching of numbers and basic math concepts begins. Children with mathematics disorders usually have a coexisting reading disorder, a disorder of written expression, or both.

Disorders of written expression

Disorders of written expression typically occur in combination with reading disorders or mathematics disorders or both. The condition is characterized by difficulty with written compositions (dysgraphia). Children with this type of learning disorder have problems with spelling, punctuation, grammar, and organizing their thoughts in writing.

Causes and symptoms

Learning disorders are thought to be caused by neurological abnormalities that trigger impairments in the regions of the brain that control visual and language processing and attention and planning. These traits may be genetically linked. Children from families with a history of learning disorders are more likely to develop disorders themselves. In 2003 a team of Finnish researchers reported finding a candidate gene for developmental dyslexia on human chromosome 15q21.

Learning difficulties may also be caused by such medical conditions as a traumatic brain injury or brain infections such as **encephalitis** or **meningitis**.

The defining symptom of a learning disorder is academic performance that is markedly below a child's age and grade capabilities and measured IQ. Children with a reading disorder may confuse or transpose words or letters and omit or add syllables to words. The written homework of children with disorders of written expression is filled with grammatical, spelling, punctuation, and organizational errors. The child's handwriting is often extremely poor. Children with mathematical disorders are often unable to count in the correct sequence, to name numbers, and to understand numerical concepts.

Diagnosis

Problems with vision or hearing, mental disorders (depression, attention-deficit/hyperactivity disorder), **mental retardation**, cultural and language differences, and inadequate teaching may be mistaken for learning disorders or complicate a diagnosis. A comprehensive medical, psychological, and educational assessment is critical to making a clear and correct diagnosis.

A child thought to have a learning disorder should undergo a complete medical examination to rule out an organic cause. If none is found, a psychoeducational assessment should be performed by a psychologist, psychiatrist, neurologist, neuropsychologist, or learning specialist. A complete medical, family, social, and educational history is compiled from existing medical and school records and from interviews with the child and the child's parents and teachers. A series of written and verbal tests are then given to the child to evaluate his or her cognitive and intellectual functioning. Commonly used tests include the Wechsler Intelligence Scale for Children (WISC-III), the Woodcock-Johnson Psychoeducational Battery, the Peabody Individual Achievement Test-Revised (PIAT-R) and the California Verbal Learning Test (CVLT). Federal legislation mandates that this testing is free of charge within the public school system.

Treatment

Once a learning disorder has been diagnosed, an individual education plan (IEP) is developed for the child in question. IEPs are based on psychoeducational test findings. They provide for annual retesting to measure a child's progress. Learning-disordered students may receive special instruction within a regular general education class or they may be taught in a special education or learning center for a portion of the day.

KEY TERMS

Dyslexia—An inability to read, write, or spell words in spite of the ability to see and recognize letters. Dyslexia is an autosomal dominant disorder thst occurs more frequently in males.

IQ—Intelligence quotient; a measure of intellectual functioning determined by performance on standardized intelligence tests.

Phonics—A system to teach reading by teaching the speech sounds associated with single letters, letter combinations, and syllables.

Common strategies for the treatment of reading disorders focus first on improving a child's recognition of the sounds of letters and language through phonics training. Later strategies focus on comprehension, retention, and study skills. Students with disorders of written expression are often encouraged to keep journals and to write with a computer keyboard instead of a pencil. Instruction for students with mathematical disorders emphasizes real-world uses of arithmetic, such as balancing a checkbook or comparing prices.

Resources

BOOKS

Beers, Mark H., MD, and Robert Berkow, MD., editors. "Learning Disorders." In *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2004.

Healy, Jane M. *Different Learners: Identifying, Preventing, and Treating Your Children's Learning Problems*.

PERIODICALS

Galaburda, D. M., and B. C. Duchaine. "Developmental Disorders of Vision." *Neurologic Clinics* 21 (August 2003): 687–707.

Gillberg, C., and H. Soderstrom. "Learning Disability." *Lancet* 362 (September 6, 2003): 811–821.

Taipale, M., N. Kaminen, J. Nopola-Hemmi, et al. "A Candidate Gene for Developmental Dyslexia Encodes a Nuclear Tetratricopeptide Repeat Domain Protein Dynamically Regulated in Brain." *Proceedings of the National Academy of Sciences in the USA* 100 (September 30, 2003): 11553–11558.

Taylor, K. E., and J. Walter. "Occupation Choices of Adults With and Without Symptoms of Dyslexia." *Dyslexia* 9 (August 2003): 177–185.

Witt, W. P., A. W. Riley, and M. J. Coiro. "Childhood Functional Status, Family Stressors, and Psychosocial Adjustment Among School-Aged Children with Disabilities in the United States." *Archives of Pediatric and Adolescent Medicine* 157 (July 2003): 687–695.

OTHER

LD Online Page. http://www.ldonline.org.

ORGANIZATIONS

Learning Disabilities Association of America, 4156 Library Road, Pittsburg, PA, 15234-1349, (412) 341-1515, (412) 344-0224, http://www.ldanatl.org/.

National Center for Learning Disabilities, 381 Park Avenue South, Suite 1401, New York, NY, 10016, (212) 545-7510, (212) 545-9665, (888) 575-7373, ncld@ncld.org, http://www.ncld.org.

The Interactive Guide to Learning Disabilities for Parents, Teachers, and Children, 2775 S. Quincy St., Arlington, VA, 22206, (703) 998-2060, http://www.ldonline.org.

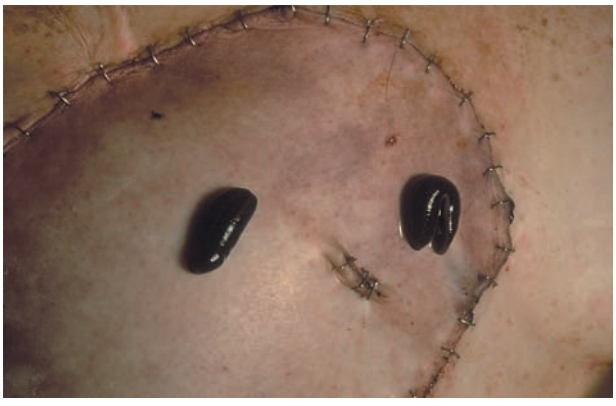
Paula Anne Ford-Martin
Rebecca J. Frey, PhD

Leeches

Definition

Leeches are bloodsucking worms with segmented bodies. They belong to the same large classification of worms as earthworms and certain oceanic worms.

Leeches can primarily be found in freshwater lakes, ponds, or rivers. They range in size from 0.2 in (5 mm) to nearly 18 in (45 cm) and have two characteristic suckers located at either end of their bodies. Leeches consume the blood of a wide variety of animal hosts, ranging from fish to humans. To feed, a leech first attaches itself to the host using the suckers. One of these suckers surrounds the leech's mouth, which contains three sets of jaws that bite into the host's flesh, making a Y-shaped incision. As the leech begins



These leeches are being used to reduce venous congestion, or excessive amounts of blood in the blood vessels. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

to feed, its saliva releases chemicals that dilate blood vessels, thin the blood, and deaden the **pain** of the bite. Because of the saliva's effects, a person bitten by a leech may not even be aware of it until afterwards, when he or she sees the incision and the trickle of blood that is difficult to stop.

For centuries, leeches were a common tool of doctors, who believed that many diseases were the result of "imbalances" in the body that could be stabilized by releasing blood. For example, leeches were sometimes attached to veins in the temples to treat headaches. Advances in medical knowledge led doctors to abandon bloodletting and the use of leeches in the mid-nineteenth century. In recent years, however, doctors have found a new purpose for leeches–helping to restore blood circulation to grafted or severely injured tissue.

Purpose

There are many occasions in medicine, mostly in surgery and trauma care, when blood accumulates and causes trouble. Leeches can be used to reduce the swelling of any tissue that is holding too much blood. This problem is most likely to occur in two situations:

- Trauma. Large blood clots resulting from trauma can threaten tissue survival by their size and pressure. Blood clots can also obstruct the patient's airway.
- Surgical procedures involving reattachment of severed body parts or tissue reconstruction following burns. In these situations it is difficult for the surgeon to make a route for blood to leave the affected part and return to the circulation. The hardest part of reattaching severed extremities like fingers, toes and ears is to reconnect the tiny veins. If the veins are not reconnected, blood will accumulate in the injured area. A similar situation occurs when plastic surgeons move large flaps of skin to replace skin lost to burns, trauma or radical surgery. The skin flaps often drain blood poorly, get congested, and begin to die. Leeches have come to the rescue in both situations.

Precautions

It is important to use only leeches that have been raised in the laboratory under sterile conditions in order to protect patients from infection. Therapeutic leeches belong to one of two species–*Hirudo michaelseni* or *Hirudo medicinalis*.

Description

One or more leeches are applied to the swollen area, depending on the size of the graft or injury, and left on for several hours. The benefits of the treatment lie not in the amount of blood that the leeches ingest, but in the anti-bloodclotting (anticoagulant) enzymes in the saliva that allow blood to flow from the bite for up to six hours after the animal is detached, effectively draining away blood that could otherwise accumulate and cause tissue **death**. Leech saliva has been described as a better anticoagulant than many currently available to treat strokes and heart attacks. Active investigation of the chemicals in leech saliva is currently under way, and one anticoagulant drug, hirudin, is derived from the tissues of *Hirudo medicinalis*.

KEY TERMS

Anemia—A blood disorder marked by low hemoglobin levels in red blood cells, which leads to a deficiency of oxygen in the blood.

Anticoagulant—A chemical or medication that prevents blood from clotting.

Aftercare

The leeches are removed by pulling them off or by loosening their grip with **cocaine**, heat, or acid. The used leeches are then killed by placing them in an alcohol solution and disposed of as a biohazard. Proper care of the patient's sore is important, as is monitoring the rate at which it bleeds after the leech is removed. Any clots that form at the wound site during treatment should be removed to ensure effective blood flow.

Risks

Infection is a constant possibility until the sore heals. It is also necessary to monitor the amount of blood that the leeches have removed from the patient, since a drop in red blood cell counts could occur in rare cases of prolonged bleeding.

Resources

PERIODICALS

Daane, S., et al. "Clinical Use of Leeches in Reconstructive Surgery." *American Journal of Orthopedics* 26, no. 8 (August 1997): 528-532.

J. Ricker Polsdorfer, MD

Left ventricular failure *see* **Heart failure**

Leg veins x ray *see* **Venography**

Legg-Calvé *see* **Osteochondroses**
Legionella pneumophila infection *see* **Legionnaires' disease**
Legionellosis *see* **Legionnaires' disease**

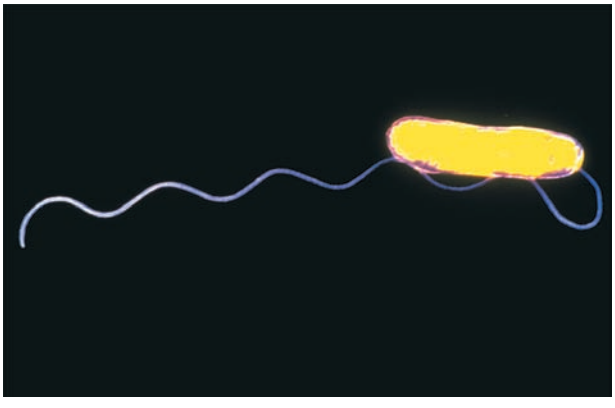
Legionnaires' disease

Definition

Legionnaires' disease is a type of **pneumonia** caused by *Legionella* bacteria. The bacterial species responsible for Legionnaires' disease is *L. pneumophila*. Major symptoms include **fever**, chills, muscle aches, and a **cough** that is initially nonproductive. Definitive diagnosis relies on specific laboratory tests for the bacteria, bacterial antigens, or antibodies produced by the body's immune system. As with other types of pneumonia, Legionnaires' disease poses the greatest threat to people who are elderly, ill, or immunocompromised.

Description

Legionella bacteria were first identified as a cause of pneumonia in 1976, following an outbreak of pneumonia among people who had attended an American Legion convention in Philadelphia, Pennsylvania. This eponymous outbreak prompted further investigation into *Legionella* and it was discovered that earlier unexplained pneumonia outbreaks were linked to the bacteria. The earliest cases of Legionnaires' disease were shown to have occurred in 1965, but samples of the bacteria exist from 1947.



A transmission electron microscopy (TEM) image of *Legionella pneumophila*, the bacteria that causes Legionnaires' disease. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Exposure to the *Legionella* bacteria doesn't necessarily lead to infection. According to some studies, an estimated 5–10% of the American population show serologic evidence of exposure, the majority of whom do not develop symptoms of an infection. *Legionella* bacteria account for 2–15% of the total number of pneumonia cases requiring hospitalization in the United States.

There are at least 40 types of *Legionella* bacteria, half of which are capable of producing disease in humans. A disease that arises from infection by *Legionella* bacteria is referred to as legionellosis. The *L. pneumophila bacterium*, the root cause of Legionnaires' disease, causes 90% of legionellosis cases. The second most common cause of legionellosis is the *L. micdadei* bacterium, which produces the Philadelphia pneumonia-causing agent.

Approximately 10,000–40,000 people in the United States develop Legionnaires' disease annually. The people who are the most likely to become ill are over age 50. The risk is greater for people who suffer from health conditions such as malignancy, diabetes, lung disease, or **kidney disease**. Other risk factors include immunosuppressive therapy and cigarette **smoking**. Legionnaires' disease has occurred in children, but typically it has been confined to newborns receiving respiratory therapy, children who have had recent operations, and children who are immunosuppressed. People with HIV infection and **AIDS** do not seem to contract Legionnaires' disease with any greater frequency than the rest of the population, however, if contracted, the disease is likely to be more severe compared to other cases.

Cases of Legionnaires' disease that occur in conjunction with an outbreak, or epidemic, are more likely to be diagnosed quickly. Early diagnosis aids effective and successful treatment. During epidemic outbreaks, fatalities have ranged from 5% for previously healthy individuals to 24% for individuals with underlying illnesses. Sporadic cases (that is, cases unrelated to a wider outbreak) are harder to detect and treatment may be delayed pending an accurate diagnosis. The overall fatality rate for sporadic cases ranges from 10–19%. The outlook is bleaker in severe cases that require respiratory support or dialysis. In such cases, fatality may reach 67%.

Causes and symptoms

Legionnaires' disease is caused by inhaling *Legionella* bacteria from the environment. Typically, the bacteria are dispersed in aerosols of contaminated water. These aerosols are produced by devices in which warm water can stagnate, such as air-conditioning cooling towers, humidifiers, shower heads, and faucets. There have also been cases linked to whirlpool spa baths and water misters in grocery store produce departments. Aspiration of contaminated water is also a potential

source of infection, particularly in hospital-acquired cases of Legionnaires' disease. There is no evidence of person-to-person transmission of Legionnaires' disease.

Once the bacteria are in the lungs, cellular representatives of the body's immune system (alveolar macrophages) congregate to destroy the invaders. The typical macrophage defense is to phagocytose the invader and demolish it in a process analogous to swallowing and digesting it. However, the *Legionella* bacteria survive being phagocytosed. Instead of being destroyed within the macrophage, they grow and replicate, eventually killing the macrophage. When the macrophage dies, many new *Legionella* bacteria are released into the lungs and worsen the infection.

Legionnaires' disease develops 2–10 days after exposure to the bacteria. Early symptoms include lethargy, headaches, fever, chills, muscle aches, and a lack of appetite. Respiratory symptoms such as coughing or congestion are usually absent. As the disease progresses, a dry, hacking cough develops and may become productive after a few days. In about a third of Legionnaires' disease cases, blood is present in the sputum. Half of the people who develop Legionnaires' disease suffer **shortness of breath** and a third complain of breathing-related chest **pain**. The fever can become quite high, reaching 104°F (40°C) in many cases, and may be accompanied by a decreased heart rate.

Although the pneumonia affects the lungs, Legionnaires' disease is accompanied by symptoms that affect other areas of the body. About half the victims experience **diarrhea** and a quarter have **nausea and vomiting** and abdominal pain. In about 10% of cases, acute renal failure and scanty urine production accompany the disease. Changes in mental status, such as disorientation, confusion, and **hallucinations**, also occur in about a quarter of cases.

In addition to Legionnaires' disease, *L. pneumophila* legionellosis also includes a milder disease, Pontiac fever. Unlike Legionnaires' disease, Pontiac fever does not involve the lower respiratory tract. The symptoms usually appear within 36 hours of exposure and include fever, **headache**, muscle aches, and lethargy. Symptoms last only a few days and medical intervention is not necessary.

Diagnosis

The symptoms of Legionnaires' disease are common to many types of pneumonia and diagnosis of sporadic cases can be difficult. The symptoms and chest x rays that confirm a case of pneumonia are not useful in differentiating between Legionnaires' disease and other pneumonias. If a pneumonia case involves multisystem symptoms, such as diarrhea and **vomiting**, and an initially dry cough, laboratory tests are done to definitively identify *L. pneumophila* as the cause of the infection.

If Legionnaires' disease is suspected, several tests are available to reveal or indicate the presence of *L. pneumophila* bacteria in the body. Since the immune system creates antibodies against infectious agents, examining the blood for these indicators is a key test. The level of immunoglobulins, or antibody molecules, in the blood reveals the presence of infection. In microscopic examination of the patient's sputum, a fluorescent stain linked to antibodies against *L. pneumophila* can uncover the presence of the bacteria. Other means of revealing the bacteria's presence from patient sputum samples include **isolation** of the organism on culture media or detection of the bacteria by DNA probe. Another test detects *L. pneumophila* antigens in the urine.

Treatment

Most cases of *Legionella* pneumonia show improvement within 12–48 hours of starting antibiotic therapy. The antibiotic of choice has been erythromycin, sometimes paired with a second antibiotic, rifampin. Tetracycline, alone or with rifampin, is also used to treat Legionnaires' disease, but has had more mixed success in comparison to erythromycin. Other **antibiotics** that have been used successfully to combat *Legionella* include doxycycline, clarithromycin, fluorinated quinolones, and trimethoprim/sulfamethoxazole.

The type of antibiotic prescribed by the doctor depends on several factors including the severity of infection, potential **allergies**, and interaction with previously prescribed drugs. For example, erythromycin interacts with warfarin, a blood thinner. Several drugs, such as **penicillins** and **cephalosporins**, are ineffective against the infection. Although they may be deadly to the bacteria in laboratory tests, their chemical structure prevents them from being absorbed into the areas of the lung where the bacteria are present.

In severe cases with complications, antibiotic therapy may be joined by respiratory support. If renal failure occurs, dialysis is required until renal function is recovered.

Prognosis

Appropriate medical treatment has a major impact on recovery from Legionnaires' disease. Outcome is also linked to the victim's general health and absence of complications. If the patient survives the infection, recovery from Legionnaires' disease is

KEY TERMS

Antibody—A molecule created by the immune system in response to the presence of an antigen. It serves to recognize the invader and help defend the body from infection.

Antigen—A molecule, such as a protein, which is associated with a particular infectious agent. The immune system uses this molecule as the identifying characteristic of the infectious invader.

Culture—A laboratory system for growing bacteria for further study.

DNA probe—An agent that binds directly to a predefined sequence of nucleic acids.

Immunocompromised—Refers to conditions in which the immune system is not functioning properly and cannot adequately protect the body from infection.

Immunoglobulin—The protein molecule that serves as the primary building block of antibodies.

Immunosuppressive therapy—Medical treatment in which the immune system is purposefully thwarted. Such treatment is necessary, for example, to prevent organ rejection in transplant cases.

Legionellosis—A disease caused by infection with a Legionella bacterium.

Media—Substance which contains all the nutrients necessary for bacteria to grow in a culture.

Phagocytosis—The "ingestion" of a piece of matter by a cell.

complete. Similar to other types of pneumonia, severe cases of Legionnaires' disease may cause scarring in the lung tissue as a result of the infection. Renal failure, if it occurs, is reversible and renal function returns as the patient's health improves. Occasionally, **fatigue** and weakness may linger for several months after the infection has been successfully treated.

Prevention

Since the bacteria thrive in warm stagnant water, regularly disinfecting ductwork, pipes, and other areas that may serve as breeding areas is the best method for preventing outbreaks of Legionnaires' disease. Most outbreaks of Legionnaires' disease can be traced to specific points of exposure, such as hospitals, hotels, and other places where people gather. Sporadic cases are harder to determine and there is insufficient evidence to point to exposure in individual homes.

Resources

PERIODICALS

Shuman, H. A., et al. "Intracellular Multiplication of Legionella pneumophila: Human Pathogen of Accidental Tourist?" *Current Topics in Microbiology and Immunology* 225 (1998): 99.

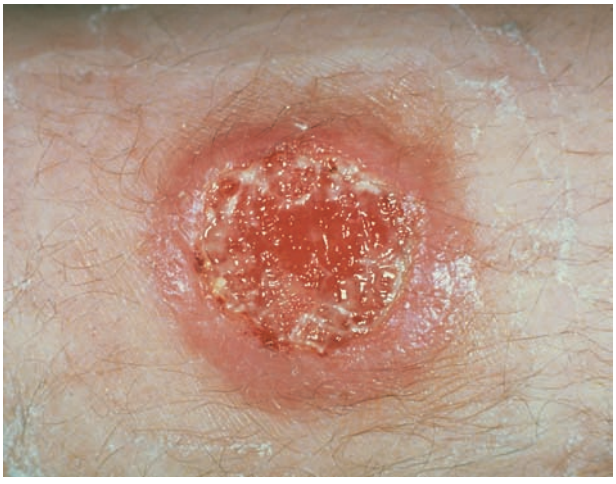
Julia Barrett

Leiomyomas *see* **Uterine fibroids**

Leishmaniasis

Definition

Leishmaniasis refers to several different illnesses caused by infection with a parasitic organism called a protozoan. Specifically, the organism belongs to the genus *Leishmania*. The disease is transmitted to humans from certain species of the infected female sand fly (order Dipteran) that are found in sandy areas. In the United States, the sand fly is often referred to by the terms of horse fly, greenhead, sand flea, sand gnats, and various others. In the Balkans the sand fly is called the



This condition, also called an oriental sore, is caused by the bacterium *L. tropica*. *(© Lester V. Bergman/Corbis.)*

Balkan sore; in India, the Delhi boil; and in Iraq the Baghdad boil; while in Afghanistan it is called saldana.

Demographics

All ages of people are susceptible to the disease. However, children are at greater risk than are adults. In addition, it is more common in rural areas than in urban settings. The disease is also of greater risk to men than it is to women, probably because males tend to be outside more frequently than females and are more likely to be exposed to sand flies at a higher rate. The risk of getting the disease is higher during nighttime because sand flies are more active in darkness then in sunlight. People also at heightened risk for the disease are adventure travelers, ecotourists, and other tourists visiting areas where leishmaniasis is more common. Volunteers, missionaries, soldiers in such areas where the disease is common are also at higher risk, as are bird watchers, ornithologists (people who study birds), and people who frequently work and play outside.

Medical studies have shown that people with acquired immune deficiency syndrome (**AIDS**) have a 100 to 1,000 greater chance of developing visceral leishmaniasis, one of the four primary types of leishmaniasis.

The disease is found primarily in the tropics, subtropics, and southern Europe. In the Western Hemisphere, it is found in parts of Mexico, Central America, and South America (but not in Chile or Uruguay). In the Eastern Hemisphere, it is frequently located in parts of Asia, the Middle East, southern Europe, and Africa.

At any one time, about 12 to 20 million people throughout the world are infected with leishmaniasis. According to the U.S. Centers for Disease Control and Prevention (CDC), about 1.5 million new cases of cutaenous leishmaniasis, the most common type of the disease, are reported yearly worldwide, while about a half million new cases of visceral leishmaniasis, the second most common type, are estimated annually. It is estimated that over 80,000 deaths occur annually from the disease.

While leishmaniasis exists as a disease in about 88 countries on five continents, some countries are hit harder than others. The vast majority of cases of cutaneous leishmaniasis take place in Afghanistan, Algeria, Brazil, Iran, Iraq, Peru, Saudi Arabia, and Syria. Almost all of the cases of visceral leishmaniasis happen in Bangladesh, Brazil, India, Nepal, and Sudan. Other areas that harbor the causative protozoa include China, many countries throughout Africa, Mexico, Central and South America, Turkey, and Greece. Cases of leishmaniasis occur in the United States but only from people who have traveled outside of the country. In addition, cases of cutaneous leishmaniasis have taken place in Texas and Oklahoma. Past cases of visceral leishmaniasis have not been reported in the United States, according to the CDC.

Description

Protozoa are considered to be the most simple organisms in the animal kingdom. They are all single-celled. The blood-sucking sand fly carries the types of protozoa that cause leishmaniasis. The sand fly is referred to as the disease vector, simply meaning that the infectious agent (the protozoan) is transported by the sand fly and passed on to other animals or humans in whom the protozoan will set up residence and cause disease. The animal or human in which the protozoan then resides is referred to as the host.

Once the protozoan is within the human host, the human's immune system is activated to try to combat the invader. Specialized immune cells called macrophages work to swallow up the protozoa. Usually, this technique kills a foreign invader, but these protozoa can survive and flourish within macrophages. The protozoa multiply within the macrophages, ultimately causing the macrophage to burst open. The protozoa are released, and take up residence within other neighboring cells.

At this point, the course of the disease caused by the protozoa is dependent on the specific type of protozoa, and on the type of reaction the protozoa elicits from the immune system. There are several types of protozoa that cause leishmaniasis, and they produce different patterns of disease progression.

There are four primary types of leishmaniasis. They are:

- Localized (simple) cutaneous leishmaniasis, which is the most common type, causes a skin sore at the site of the bite. This type can then proceed to become any of the other three types.
- Diffuse cutaneous leishmaniasis, which is difficult to treat, can produce large areas of skin lesions that resemble leprosy.
- Mucocutaneous leishmaniasis, which starts with skin ulcers, is especially troublesome for the nose and mouth.
- Visceral leishmaniasis, which is the second most common type and the most serious one because it usually affects some of the internal organs (such as liver and spleen), can be fatal if not treated promptly.

Causes and symptoms

There are a number of types of protozoa that can cause leishmaniasis. Each type exists in specific

locations, and there are different patterns to the kind of disease each causes. The overall species name is Leishmania (commonly abbreviated L.). The specific types include: *L. Donovani, L. Infantum, L. Chagasi, L. Mexicana, L. Amazonensis, L. Tropica, L. Major, L. Aethiopica, L. Brasiliensis, L. Guyaensis, L. Panamensis, L. Peruviana*. Some of the names are reflective of the locale in which the specific protozoa is most commonly found, or in which it was first discovered.

Localized cutaneous leishmaniasis

This type of disease, also called simple cutaneous leishmaniasis, occurs most commonly in China, India, Asia Minor, Africa, the Mediterranean Basin, and Central America. It has ranged in an area from northern Argentina all the way up to southern Texas. It is called different names in different locations, including chiclero ulcer, bush **yaws**, uta, oriental sore, Aleppo boil, and Baghdad sore.

This is perhaps the least drastic type of disease caused by any of the *Leishmania*. Several weeks or months after being bitten by an infected sand fly, the host may notice an itchy bump (lesion) on an arm, leg, or face. Lymph nodes in the area of this bump may be swollen. Within several months, the bump develops a crater (ulceration) in the center, with a raised, reddened ridge around it. There may be several of these lesions (sores) near each other, and they may spread into each other to form one large lesion. Often, individual lesions change in size and appearance as they develop. Eventually, they may have a raised edge and a central ulcerated area. People with sores also often have **swollen glands** near the infected areas. Although localized cutaneous leishmaniasis usually heals on its own, it may take as long as one year. A depressed, light-colored scar usually remains behind. Some lesions never heal, and may invade and destroy the tissue below. For example, lesions on the ears may slowly, but surely, invade and destroy the cartilage that supports the outer ear.

Diffuse cutaneous leishmaniasis

This type of disease occurs most often in Ethiopia, Brazil, Dominican Republic, and Venezuela.

The lesions of diffuse cutaneous leishmaniasis are very similar to those of localized cutaneous leishmaniasis, except they are spread all over the body. The body's immune system apparently fails to battle the protozoa, which are free to spread throughout. The characteristic lesions resemble those of the dread biblical disease, **leprosy**.

Mucocutaneous leishmaniasis

This type of leishmaniasis occurs primarily in the tropics of South America.

With an incubation period of from one to three months, the disease begins with the same sores noted in localized cutaneous leishmaniasis. Sometimes these primary lesions heal, other times they spread and become larger. Some years after the first lesion is noted (and sometimes several years after that lesion has totally healed), new lesions appear in the mouth and nose, and occasionally in the area between the genitalia and the anus (the perineum). These new lesions, called mucosal lesions, are particularly destructive and painful. Sometimes their appearance is delayed twenty years from the first presence of the primary lesions.

The mucosal lesions erode underlying tissue and cartilage, frequently eating through the septum (the cartilage that separates the two nostrils). If the lesions spread to the roof of the mouth and the larynx (the part of the wind pipe which contains the vocal cords), they may prevent speech. Other symptoms include **fever**, weight loss, and anemia (low red blood cell count). There is always a large danger of bacteria infecting the already open sores.

Visceral leishmaniasis

This type of leishmaniasis occurs in India, China, the southern region of Russia, and throughout Africa, the Mediterranean, and South and Central America. It is frequently called Kala-Azar or Dumdum fever.

In this disease, the protozoa use the bloodstream to travel to the liver, spleen, lymph nodes, and bone marrow. Fever may last for as long as eight weeks, disappear, and then reappear again. The lymph nodes, spleen, and liver are often quite enlarged. Weakness, **fatigue**, loss of appetite, **diarrhea**, and weight loss are common. Abnormal blood tests also result, including low red blood cell count, low **white blood cell count**, and low **platelet count**. Kala-azar translates (from the country of India) to mean "black fever." The name kala-azar comes from a characteristic of this type of leishmaniasis. Individuals with light-colored skin take on a darker, grayish skin tone, particularly of their face and hands. A variety of lesions appear on the skin.

Diagnosis

Diagnosis for each of these types of leishmaniasis involves taking a scraping from a lesion, preparing it in a laboratory, and examining it under a microscope to demonstrate the causative protozoan. Other methods that have been used include:

KEY TERMS

Host—The organism (such as a monkey or human) in which another organism (such as a virus or bacteria) is living.

Larynx—The part of the airway lying between the pharynx and the trachea.

Leishman-Donovan body—A body of a (trypanosomatid) protozoa at a particular and characteristic stage in its life cycle; the infectious (trypanosomatid) protozoa can cause leishmaniasis, and is relatively easy to identify at that stage.

Lesion—A disruption of the normal structure and function of a tissue by some disease process.

Macrophage—A cell of the immune system that engulfs and digests foreign invaders such as bacteria and viruses in an attempt to stop them from causing disease within the body.

Protozoa—A group of organisms which are the smallest members of the animal kingdom, consisting of a single cell.

Ulceration—An area of pitting and irritation.

Vector—A carrier organism (such as a fly or mosquito) that to delivers a virus (or other agent of infection) to a host.

- Culturing a sample piece of tissue in a laboratory to allow the protozoa to multiply for easier microscopic identification.
- Injecting a mouse or hamster with a solution made of scrapings from a patient's lesion to see if the animal develops a leishmaniasis-like disease.
- Demonstrating the presence in macrophages of the characteristic-appearing protozoan, called Leishman-Donovan bodies.

In some types of leishmaniasis, a skin test (similar to that given for **tuberculosis**, or TB) may be used. In this test, a solution containing a small bit of the protozoan antigen (cell marker that causes the human immune system to react) is injected or scratched into a patient's skin. In a positive reaction, cells from the immune system will race to this spot, causing a characteristic skin lesion. Not all types of leishmaniasis cause a positive skin test, however. The CDC states that diagnosis of leishmaniasis can be difficult. Results from laboratory tests frequently come back as negative even when the person has the disease.

Treatment

The treatment of choice for all types of leishmaniasis is a type of drug containing the element antimony. These include **sodium** sitogluconate, and meglumin antimonate. When these types of drugs do not work, other medications with anti-protozoal activity are utilized, including amphotericin B, pentamidine, flagyl, and allopurinol. In 2004, it was reported that the world's first non-profit drug company was seeking approval in India for a drug to cure visceral leishmaniasis. Historically, an estimated 200,000 people die annually from the disease in that country. The company, called One World Health, hoped to offer the drug called paromomycin for a three-week treatment course. In 2006, paromomycin was approved by the Drug Controller General of India for treatment of visceral leishmaniasis.

Prognosis

The prognosis for leishmaniasis is quite variable, and depends on the specific strain of infecting protozoan, as well as the individual patient's immune system response to infection. Localized cutaneous leishmaniasis may not require any treatment. Although it may take many months, these lesions usually heal themselves completely. Only rarely do these lesions fail to heal and become more destructive.

Diffuse cutaneous leishmaniasis may smolder on for years without treatment, eventually progressing to mucocutaneous leishmaniasis, and ultimately causing **death** when the large, open lesions become infected with bacteria.

Mucocutaneous leishmaniasis is often relatively resistant to treatment. Untreated visceral leishmaniasis has a 90% death rate, but only a 10% death rate with proper treatment.

Visceral leishmaniasis has been increasingly associated with human **immunodeficiency** virus (HIV). For example, the two have appeared together in southern Europe, primarily among intravenous drug users. If treated properly, the risk from death is minimal. However, the rates of mortality in untreated cases has been shown to range from 75% to 95%. Even when death does not occur from the disease, it can leave the person disfigured and with serious deformities. Advanced cases of visceral leishmaniasis can eventually cause death if left untreated.

Prevention

Prevention involves protecting against sand fly **bites**. Insect repellents used around homes, on clothing, on skin, and on bed nets (to protect people while sleeping) are effective measures.

Reducing the population of sand flies is also an important preventive measure. In areas where leishmaniasis is very common, recommendations include clearing the land of trees and brush for at least 984 feet (300 meters) around all villages, and regularly spraying the area with insecticides. Because rodents often carry the protozoan that causes leishmaniasis, careful rodent control should be practiced. Dogs, which also carry the protozoan, can be given a simple blood test.

Resources

BOOKS

Feigin, Ralph D. et al., editors.*Feigin ' Cherry' Textbook of Pediatric Infectious Diseases*. Philadelphia: Saunders/Elsevier, 2009.

Myler, Peter J., and Nicolas Fasel.*Leishmania: After the Genome*. Norfolk, UK: Caister Academic, 2008.

Tibayrenc, Michel, editor.*Encyclopedia of Infectious Diseases: Modern Methodologies*. Hoboken, NJ: Wiley-Liss, 2007.

OTHER

"Leishmaniasis." Division of Parasitic Diseases, Centers for Disease Control and Prevention. (September 22, 2008), http://www.cdc.gov/ncidod/dpd/parasites/leishmania/default.htm (accessed July 26, 2010).

"Leishmaniasis." eMedicine, WebMD. (April 20, 2010), http://emedicine.medscape.com/article/783750-overview (accessed July 26, 2010).

"New Cure For Deadly Visceral Leishmaniasis (Kala-Azar) Approved By Government Of India." Institute for One World Health. (September 8, 2006), http://www. oneworldhealth.org/press_releases/release/pr_1226360315 (accessed July 26, 2010).

ORGANIZATIONS

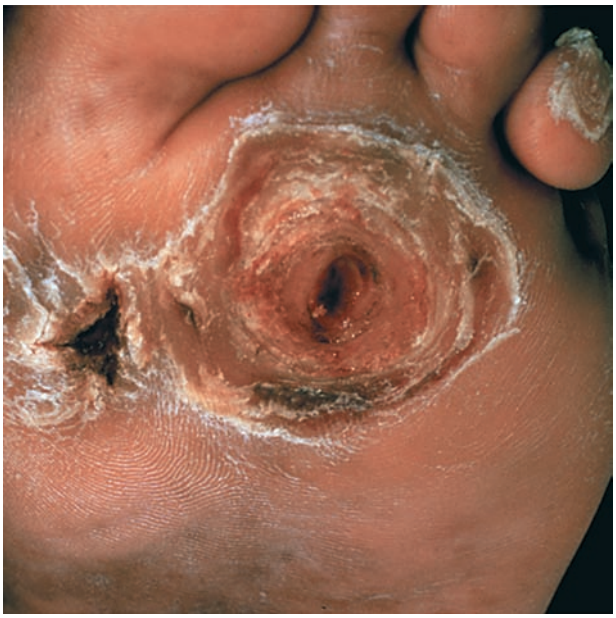
Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

Rosalyn Carson-DeWitt, MD
Teresa G. Odle

Leprosy

Definition

Leprosy is a slowly progressing chronic bacterial infection that affects the skin, peripheral nerves in the hands and feet, upper respiratory tract, and mucous membranes of the nose, throat, and eyes. Destruction of the nerve endings causes the affected areas to lose sensation. Leprosy is a progressive disease; that is, one that takes anywhere from six months to 40 years to develop. If left untreated, it can cause **skin lesions** and inflammatory nodules (granulomas) on the skin and nerves and, ultimately, permanent damage and disfigurement to the skin, nerves, limbs, eyes, and other body parts. It primarily affects the outer extremities such as the eyes, nose, earlobes, hands, testicles (in men), and feet.



Lesions such as these are characteristic of leprosy.
(© Phototake. — All rights reserved.)

Demographics

The World Health Organization (WHO) places the number of identified leprosy cases in the world at 212,802 as of the 2008. According to WHO, the number of new cases globally decreased by about 4% from 2007 to 2008. Seventy percent of all cases are located in just three countries: India, Indonesia, and Myanamar (Burma). The infection can be acquired, however, in the Western Hemisphere as well. According to the Department of Health and Human Services, there are about 6,500 reported cases in the United States (with approximately 3,300 of them requiring active medical intervention) as of last quarter of the 2000s. Almost all of the U.S. cases involve immigrants from developing countries. Cases also occur in some areas of the Caribbean. Although it was thought for many years that only humans are affected by the disease, 15% of wild

armadillos in southern Texas and Louisiana have been found to be infected with *M. leprae*.

Description

Leprosy is also known as Hansen's disease after Norwegian physician Gerhard Armauer Hansen (1841–1912), who in 1878 identified the bacillus (rod-shaped bacterium) *Mycobacterium leprae* (*M leprae*) that causes the disease.

The infection is characterized by abnormal changes of the skin. These changes, called lesions, are at first flat and red. Upon enlarging, they have irregular shapes and a characteristic appearance. The lesions are typically darker in color around the edges with discolored pale centers. Because the organism grows best at lower body temperatures, the leprosy bacillus prefers the skin, the mucous membranes, and the nerves. Infection in the nerves and their eventual destruction leads to sensory loss. The loss of sensation in the fingers and toes increases the risk of injury. Inadequate care causes infection of open **wounds**. **Gangrene** may also follow, resulting in the deformation or **death** of body tissue.

Because of the disabling deformities associated with it, leprosy has been considered one of the most dreaded diseases since Biblical times (beginning at about 1500 B.C. and ending around A.D. 100), though much of what was called leprosy in the Old Testament most likely was not the same disease. Its victims were often shunned by the community, kept at arm's length, or sent to a leper colony. Many people still have misconceptions about the disease. Contrary to popular belief, it is not highly communicable and is extremely slow to develop. Household contacts of most cases and the medical personnel caring for Hansen's disease patients are not at particular risk. It is very curable, although the treatment is long-term, requiring multiple medications.

Causes and symptoms

The organism that causes leprosy is a rod-shaped bacterium called *Mycobacterium leprae*. This bacterium is related to *Mycobacterium tuberculosis*, the causative agent of **tuberculosis**. *M. leprae* is considered an obligate intracellular bacterium; that is, a bacterium that is able to grow only inside certain human and animal cells. Because special staining techniques involving acids are required to view these bacteria under the microscope, they are referred to as acid-fast bacilli (AFB).

When *Mycobacterium leprae* invades the body, one of two reactions can take place. In tuberculoid leprosy (TT), the milder form of the disease, the body's immune cells attempt to seal off the infection from the rest of the body by surrounding the offending pathogen. Because this response by the immune system occurs in the deeper layers of the skin, the hair follicles, sweat glands, and nerves can be destroyed. As a result, the skin becomes dry and discolored and loses its sensitivity. Involvement of nerves on the face, arms, or legs can cause them to enlarge and to become easily felt by the examining doctor. This finding is highly suggestive of TT. The scarcity of bacteria in this type of leprosy leads to it being referred to as paucibacillary (PB) leprosy. Seventy to eighty percent of all leprosy cases are of the tuberculoid type.

In lepromatous (LL) leprosy, which is the second and more contagious form of the disease, the body's immune system is unable to mount a strong response to the invading organism. Hence, the organism multiplies freely in the skin. This type of leprosy is also called the multibacillary (MB) leprosy, because of the presence of large numbers of bacteria. The characteristic feature of this disease is the appearance of large nodules or lesions all over the body and face. Occasionally, the mucous membranes of the eyes, nose, and throat may be involved. Facial involvement can produce a lion-like appearance (leonine facies). This type of leprosy can lead to blindness, drastic change in voice, or mutilation of the nose. Leprosy can strike anyone; however, children seem to be more susceptible than adults.

The early symptoms of leprosy are not apparent, and they may very slowly develop over many years without much notice. Well-defined skin lesions that are numb are the first symptoms of tuberculoid leprosy. **Numbness** and a decreasing ability to sense hot and cold temperatures are two other early symptoms of leprosy. Lepromatous leprosy is characterized by a chronic stuffy nose due to invasion of the mucous membranes, and the presence of nodules and lesions all over the body and face. As the disease advances, the sense of touch, **pain**, and pressure are decreased and, eventually lost. Skin lesions of hypopigmented macules (flat and pale areas of the skin) also appear, as do nearly painless ulcers and increased dryness of the eyes. Eventually, large ulcerated areas are produced. Eventually facial disfiguration develops, along with loss of fingers and toes.

Although patients with leprosy are commonly thought not to suffer pain, neuroapthic pain caused by inflammation of peripheral nerve endings is increasingly recognized as a major complication of the disease in many patients. **Corticosteroids** may be given to reduce the inflammation.

The incubation period of the leprosy bacillus varies anywhere from six months to ten years. On an average, it takes four years for the symptoms of tuberculoid

leprosy to develop. Probably because of the slow growth of the bacillus, lepromatous leprosy develops even more slowly, taking an average of eight years for the initial lesions to appear.

It is still not very clear how the leprosy bacillus is transmitted from person to person; about 50% of patients diagnosed with the disease have a history of close contact with an infected family member. Since untreated patients have a large number of *M. leprae* bacilli in their nasal secretions, it is thought that transmission may take place via nasal droplets. The milder tubercular form of leprosy may be transmitted by insect carriers or by contact with infected soil.

Some medical researchers contend that *M. leprae* is transmitted from one human to another through nasal secretions or droplets. However, other scientists think that the bacterium enters the body through breaks in the skin. As of 2010, the specific ways that the bacterium enters the body is being investigated by scientists.

The disease appears primarily in the poorest of the world's countries. In addition, environmental factors such as overpopulated areas, unhygienic living conditions, contaminated water, risk of other immune-compromising diseases, and insufficient diet/extreme **malnutrition** may also be contributing factors adding to the risk of leprosy.

Diagnosis

Leprosy is usually diagnosed through clinical investigations. One of the hallmarks of leprosy is the presence of AFB in smears taken from the skin lesions, nasal scrapings, or tissue secretions. In patients with LL leprosy, the bacilli are easily detected; however, in TT leprosy the bacteria are very few and almost impossible to find. In such cases, a diagnosis is made based on the clinical signs and symptoms, the type and distribution of skin lesions, and history of having lived in an endemic area. Generally, laboratory analysis is not used because such labs are rarely found in these very poor countries where leprosy is mostly found.

The signs and symptoms characteristic of leprosy can be easily identified by a health worker after a short training period. There is no need for a laboratory investigation to confirm a leprosy diagnosis, except in very rare circumstances.

In an endemic area, if smears from an individual show the presence of AFB, or if he/she has typical skin lesions, then that person should definitely be regarded as having leprosy. Usually, there is slight discoloration of the skin (sometimes called hypopigmented patches of skin) and loss of skin sensitivity along with redness of the area. Thickened nerves accompanied by weakness of muscles supplied by the affected nerve are very typical of the disease. One characteristic occurrence is a foot drop where the foot cannot be flexed upwards, affecting the ability to walk.

When laboratory tests are used, such tests usually include a CBC (**complete blood count**) test, liver function test, creatinine (clearance) test, and a nerve biopsy.

Treatment

A vaccine for leprosy is still not available. The most widely used drug for leprosy is dapsone (DDS). However, the emergence of dapsone-resistant strains prompted the introduction of multidrug therapy, or MDT. MDT combines dapsone, rifampin (Rifadin; also known as rifampicin), and clofazimine (Lamprene), all of which are powerful antibacterial drugs. Patients with MB leprosy are usually treated with all three drugs, while patients with PB leprosy are only given rifampin and dapsone. Usually three months after starting treatment, a patient ceases being infectious, though not everyone with this disease is necessarily infectious before treatment. Depending on the type of leprosy, the time required for treatment may vary from six months to two years or more.

Each of the drugs has minor side effects. Dapsone can cause **nausea**, **dizziness**, **palpitations**, **jaundice**, and rash. A doctor should be contacted immediately if a rash develops. Dapsone also interacts with the second drug, rifampin. Rifampin increases the metabolizing of dapsone in the body, requiring an adjustment of the dapsone dosage. Rifampin may also cause **muscle cramps**, or nausea. If jaundice, flu-like symptoms or a rash appear, a doctor should be contacted immediately. The third drug, clofazimine may cause severe abdominal pain and **diarrhea**, as well as discoloration of the skin. Red to brownish black discoloration of the skin and bodily fluids, including sweat, may persist for months to years after use.

Thalidomide, the most famous agent of **birth defects** in the twentieth century, is now being used to treat complications of leprosy and similar diseases. Thalidomide regulates the immune response by suppressing a protein, tumor necrosis factor alpha.

Leprosy patients should be aware that treatment itself can cause a potentially serious immune system response called a lepra reaction. When **antibiotics** kill *M. leprae*, antigens (the proteins on the surface of the organism that initiate the body's immune system response) are released from the dying bacteria. In some people, when the antigens combine with the antibodies to *M. Leprae* in the bloodstream, a reaction called

KEY TERMS

Endemic area—A geographical area where a particular disease is prevalent.

Gangrene—Death of tissue due to loss of blood supply followed by bacterial invasion and putrefaction.

Incubation period—The time it takes for symptoms to develop after initial exposure to a disease-causing organism.

Lesion—Any visible, local abnormality of the tissues of the skin, such as a wound, sore, rash, or boil.

Mucous membranes—The inner tissue that covers or lines body cavities or canals open to the outside, such as nose and mouth. These membranes secrete mucus and absorb water and salts.

Nasal scraping—Pathological material obtained for clinical study by scratching the inner surface of the nose with a clinical instrument.

Nodules—A small mass of tissue in the form of a protuberance or a knot that is solid and can be detected by touch.

Pathogen—Any disease-producing agent or microorganism.

Smear—A specimen prepared for microscopic study by spreading the material across a slide and treating it with a specific stain.

erythema nodosum leprosum may occur, resulting in new lesions and peripheral nerve damage. Cortisone-type medications and, increasingly, thalidomide are used to minimize the effects of lepra reactions.

Surgery may be performed in order to make cosmetic improvements to the patient. In some cases, severe ulcers caused by leprosy may be treated surgically with small skin grafts. In other cases, some movement of the limbs can be restored or, at least, some neural function improved.

Prognosis

Leprosy is curable; however, the deformities and nerve damage associated with leprosy are often irreversible. Prevention or **rehabilitation** of these defects is an integral part of management of the disease. **Reconstructive surgery**, aimed at preventing and correcting deformities, offers the greatest hope for disabled patients. Sometimes, the deformities are such that the patients will not benefit from this type of surgery.

Comprehensive care involves teaching patients to care for themselves. If the patients have significant nerve damage or are at high risk of developing deformities, they must be taught to take care of their insensitive limbs, similar to diabetics with lower leg nerve damage. Lacking the sensation of pain in many cases, the patients should constantly check themselves to identify cuts and **bruises**. If adequate care is not taken, these wounds become festering sores and a source of dangerous infection. Physiotherapy exercises are taught to the patients to maintain a range of movement in finger joints and prevent the deformities from worsening. Prefabricated standardized splints are available and are extremely effective in correcting and preventing certain common deformities in leprosy. Special kinds of footwear have been designed for patients with insensitive feet in order to prevent or minimize the progression of foot ulcers.

The genome of *M leprae* has been sequenced as of 2010. The completion of this project has allowed much more research to be performed in the search for better treatments and a cure for leprosy. Scientists are currently working on how the bacterium infects humans, how the infection is transmitted within the body, what the period of incubation is for the disease, and many more avenues toward solving the problem.

Prevention

By early diagnosis and appropriate treatment of infected individuals, even a disease as ancient as leprosy can be controlled. People who are in immediate contact with the leprosy patient should be tested for leprosy. Annual examinations should also be conducted on these people for a period of five years following their last contact with an infectious patient. Some physicians have advocated dapsone treatment for people in close household contact with leprosy patients.

The WHO Action Program for the Elimination of Leprosy adopted a resolution calling for the elimination of leprosy around the world by the year 2005. This goal was not reached, however; a computer simulation performed for WHO by a team of Dutch researchers in 2004 indicates that leprosy is likely to persist in some parts of the world until 2020, although its incidence will continue to decline.

The WHO Action Program has now defined a strategy to eventually eliminate the disease as a public health problem. Members of the program hope to reach a rate of 1 or less leprosy case per 10,000 population. As of 2008, this "elimination" rate of 1 per 10,000 have been reached in most countries with the highest rates of leprosy. In 2007, the countries of Mozambique and the Democratic Republic of the Congo reached this elimination rate. Other nations of the world are nearing this elimination rate but still have areas of high concentration within their boundaries. Some of these countries include Angola, Brazil, Central African Republic, India, Madagascar, Nepal, and Tanzania.

Resources

BOOKS

Beers, Mark H., editors. *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Brachman, Philip S., et al. editors. *Bacterial Infections of Humans: Epidemiology and Control*. New York: Springer Science and Business Media, 2009.

Murray, Patrick R., et al. editors. *Manual of Clinical Microbiology*. Washington, DC: ASM Press, 2007.

Sehgal, Alfica. *Leprosy*. Philadelphia: Chelsea House, 2006.

OTHER

"Leprosy." HealthyMe, Blue Cross/Blue Shield of Massachusetts. (July 25, 2007), http://www.ahealthyme.com/topic/adam1001347 (accessed July 27, 2010).

"Leprosy." National Institutes of Health. (July 10, 2009), http://health.nih.gov/topic/Leprosy.(accessed July 27, 2010).

"Leprosy (Hansen's Disease)." MedicineNet. http://www.medicinenet.com/leprosy/article.htm. (accessed July 27, 2010).

"Leprosy Today." World Health Organization. http://www.who.int/lep/en/. (accessed July 27, 2010).

"National Hansen's Disease (Leprosy) Program." Health Resources and Services Administration, Department of Health and Human Services. http://www.hrsa.gov/hansens/. (accessed July 29, 2010).

ORGANIZATIONS

American Leprosy Missions, 1 ALM Way, Greenville, SC, 29601, (864) 271-7040, (800) 543-3135, (864) 271-7062, amlep@leprosy.org, http://www.leprosy.org/.

International Federation of Anti-Leprosy Associations (ILEP), 234 Blythe Road, London, United Kingdom, W14 0HJ, +44 (0) 20 7602 6925, +44 (0) 20 7371 1621, ilep@ilep.org.uk, http://www.ilep.org.uk/.

LEPRA Health in Action, 28 Middleborough, Colchester Essex, United Kingdom, CO1 1TG, +44 (0) 01206 216700, +44 (0) 01206 762151, http://www.leprahealthinaction.org/.

Leprosy Mission International, 80 Windmill Road, BrentfordMiddlesex, United Kingdom, TW8 0QH, +44 (0) 20 8326 6767, +44 (0) 20 8326 6777, friends@timint.org, http://www.leprosymission.org/.

Lata Cherath, PhD
Rebecca J. Frey, PhD

Leptospirosis

Definition

Leptospirosis is a febrile (**fever**) disease caused primarily by infection with the bacterium *Leptospira interrogans*, but also by other bacteria within the genus *Leptospira*. *L. interrogans* is sometimes classified as a spirochete because it has a spiral shape. It can be transmitted to humans by various wild animals such as rats, opossums, raccoons, foxes, and skunks. Domesticated animals such as dogs and livestock can also carry and transmit the disease. Humans may also acquire the disease through soil or water infected by such animals. This rare disease and contagious infection can range from very mild and symptomless to a more serious, even life-threatening form, that may be associated with kidney (renal) failure. German physician Adolf Weil (1848–1916) first described the disease in 1886. It was later observed in 1907 from a slice of renal tissue during a post mortem procedure.

Demographics

The disease is relatively rare in humans. Leptospirosis is usually found in tropical and subtropical areas, especially around stagnant or slow-moving waters, but can be present anywhere worldwide. It is also more likely to be a problem during the months of July through October and February through March. The infection is often transmitted to humans after they have drunk water contaminated with animal urine. It can also be contracted through such contamination of breaks in the skin and through mucous membranes such as the eyes.

Leptospirosis is rarely found in the continental part of the United States. However, when it is present in the United States, it is most often located in the state of Hawaii. According to the Centers for Disease Control and Prevention (CDC), between 100 and 200 cases of leptospirosis are reported in the United States each year. In addition, nearly 75% of cases of leptospirosis in North America occur in males. Further, about 50% of cases happen in Hawaii, followed by the southern Atlantic, Gulf, and Pacific coastal states. However, because of the nonspecific symptoms of leptospirosis, it is believed that the occurrence in the United States is

actually much higher. Leptospirosis occurs year-round in North America, but about half of the cases take place between July and October.

Description

An infection by the bacterium *Leptospira interrogans* goes by different names in different regions. Alternate names for leptospirosis include mud fever, canefield fever, Rat Catcher's Yellows, seven–day fever, swamp fever, cane cutter's fever, rice field fever, Stuttgart disease, Swineherd's disease, and Fort Bragg fever. More severe cases of leptospirosis are called Weil's syndrome or icterohemorrhagic fever.

Leptospirosis is called a **zoonosis** because it is a disease of animals that can be transmitted to humans. It can be a very serious problem in the livestock industry. *Leptospira* bacteria have been found in dogs, rats, livestock, mice, voles, rabbits, hedgehogs, skunks, possums, frogs, fish, snakes, and certain birds and insects. Infected animals pass the bacteria in their urine for months, or even years. In the United States, rats and dogs are more commonly linked with human leptospirosis than other animals.

Humans are considered accidental hosts and become infected with *Leptospira interrogans* by coming into contact with urine from infected animals. Transmission of the organism occurs through direct contact with urine, or through contact with soil, water, or plants that have been contaminated by animal urine. *Leptospira interrogans* can survive for as long as six months outdoors under favorable conditions. Leptospira bacteria can enter the body through cuts or other skin damage or through mucous membranes (such as the inside of the mouth and nose). Researchers believe that the bacteria may be able to pass through intact skin, although evidence for this hypothesis has not been obtained.

Once past the skin barrier, bacteria enter the blood stream and rapidly spread throughout the body. The infection causes damage to the inner lining of blood vessels. The liver, kidneys, heart, lungs, central nervous system, and eyes may be affected.

There are two stages in the disease process. The first stage is during the active Leptospira infection and is called the bacteremic or septicemic phase. The bacteremic phase lasts from three to seven days and presents as typical flu-like symptoms. During this phase, bacteria can be found in the patient's blood and cerebrospinal fluid. The second stage, or immune phase, takes place either immediately after the bacteremic stage or after a one to three day symptom-free period. The immune phase can last up to one month. During the immune phase, symptoms are milder but **meningitis** (inflammation of spinal cord and brain tissues) is common. Bacteria can be isolated only from the urine during this second phase.

Causes and symptoms

Leptospirosis is caused primarily by an infection with the bacterium *Leptospira interrogans*. Bacteria are spread through contact with urine from infected animals. Persons at an increased risk for leptospirosis include farmers, ranchers, slaughterhouse workers, miners, animal health care workers and veterinarians, fish farmers and processors, sewage and canal workers, cane harvesters, and soldiers. High-risk activities include care of pets (especially dogs); the raising of livestock; hunting and trapping; trail biking; freshwater swimming, rafting, canoeing, and kayaking; and participating in sports within muddy fields.

Symptoms of *Leptospira* infection appear within two to 26 days following exposure to the bacteria, with 10 days being the average number of days. Because the symptoms can be nonspecific, most people who have antibodies to *Leptospira* do not remember having had an illness. Eighty five to 90% of the cases are not serious and clear up on their own. Symptoms of the first stage of leptospirosis last three to seven days and include:

- fever (with a temperature of 100–105°F [38–41°C])
- severe headache
- muscle pain
- stomach pain
- chills
- nausea
- vomiting
- diarrhea
- back pain
- joint pain
- neck stiffness
- extreme exhaustion

Dry **cough**, **sore throat**, and body rash sometimes also occur. Other symptoms, which are usually less frequently observed, are enlarged lymph glands, liver, and spleen, abnormal sounds from the lungs, skin rash, and muscle tenderness or rigidity.

Following the first stage of disease, a brief symptom-free period ensues for most patients. The symptoms of the second stage vary in each patient. Most patients have a low-grade fever, **headache**, **vomiting**, and rash. Aseptic meningitis is common in the second stage, symptoms of which include headache and **photosensitivity**

(sensitivity of the eye to light). *Leptospira* can affect the eyes and make them cloudy and yellow to orange colored. Vision may be blurred.

Ten percent of the persons infected with *Leptospira* develop a serious disease called Weil's syndrome. The symptoms of Weil's syndrome are more severe than those described above and there is no distinction between the first and second stages of disease. The hallmark of Weil's syndrome is liver, kidney, and blood vessel disease. The signs of severe disease are apparent after 3–7 days of illness. In addition to those listed above, symptoms of Weil's syndrome include **jaundice** (yellow skin and eyes), decreased or no urine output, **hypotension** (low blood pressure), rash, anemia (decreased number of red blood cells), **shock**, and severe mental status changes. Red spots on the skin, "blood shot" eyes, and bloody sputum signal that blood vessel damage and hemorrhage have occurred.

Diagnosis

Leptospirosis can be diagnosed and treated by doctors who specialize in infectious diseases. During the bacteremic phase of the disease, the symptoms are relatively nonspecific. This often causes an initial misdiagnosis because many diseases have similar symptoms to leptospirosis. The later symptoms of jaundice and kidney failure together with the bacteremic phase symptoms suggest leptospirosis. Blood samples will be tested to look for antibodies to *Leptospira interrogans*. Blood samples taken over a period of a few days would show an increase in the number of antibodies. Isolating *Leptospira* bacteria from blood, cerebrospinal fluid (performed by spinal tap), and urine samples is diagnostic of leptospirosis. Tests for **white blood cell count** and creatine kinase may also be performed. It may take six weeks for *Leptospira* to grow in laboratory media. Most insurance companies cover the diagnosis and treatment of this infection.

Several diagnostic tests for leptospirosis have been devised that are more accurate as well as faster than standard cultures. One test uses flow cytometry light scatter analysis; this method can evaluate a sample of infected serum in as little as 90 minutes. A second technique is an IgM-enzyme-linked immunosorbent assay (ELISA), which detects the presence of IgM antibodies to *L. interrogans* in blood serum samples.

Treatment

Leptospirosis is treated with **antibiotics** (such as tetracycline or chloramphenicol), penicillin (Bicillin, Wycillin), doxycycline (Monodox, Vibramycin), or erythromycin (E-mycin, Ery-Tab). However, many doctors prefer to treat patients with ceftriaxone, which is easier to use than intravenous penicillin. Ciprofloxacin may be combined with other drugs in caring for patients who develop **uveitis**. It is generally agreed that antibiotic treatment during the first few days of illness is helpful. However, leptospirosis is often not diagnosed until the later stages of illness. The benefit of antibiotic treatment in the later stages of disease, however, is controversial. A rare complication of antibiotic therapy for leptospirosis is the occurrence of the Jarisch–Herxheimer reaction, which is characterized by fever, chills, headache, and muscle **pain**.

Patients with severe illness require hospitalization for treatment and monitoring. Medication or other treatment for pain, fever, **vomiting**, fluid loss, bleeding, mental changes, and low blood pressure may be provided. Patients with kidney failure require hemodialysis to remove waste products from the blood.

KEY TERMS

Hemodialysis—The removal of waste products from the blood stream in patients with kidney failure. Blood is removed from a vein, passed through a dialysis machine, and then put back into a vein.

Jarisch–Herxheimer reaction—A rare reaction to the dead bacteria in the blood stream following antibiotic treatment.

Meningitis—Inflammation of tissues in the brain and spinal cord. Aseptic meningitis refers to meningitis with no bacteria present in the cerebral spinal fluid.

Spirochete—Any of a family of spiral- or coil-shaped bacteria known as Spirochetae. *L. interrogans* is a spirochete, as well as are the organisms that cause syphilis and relapsing fever.

Zoonosis (plural, zoonoses)—Any disease of animals that can be transmitted to humans. Leptospirosis is an example of a zoonosis.

Prognosis

The majority of patients infected with *Leptospira interrogans* experience a complete recovery when treated promptly. Ten percent of patients develop eye inflammation (uveitis) up to one year after the illness. Other complications include excessive bleeding, meningitis, and Jarisch-Herxheimer reaction. In the United States, about one out of every 100 patients die from leptospirosis. **Death** is usually caused by kidney failure, but has

also been caused by **myocarditis** (inflammation of heart tissue), **septic shock** (reduced blood flow to the organs because of the bacterial infection), organ failure, and/or poorly functioning lungs. Mortality is highest in patients over 60 years of age.

Prevention

Persons who are at an extremely high risk (such as soldiers training in wetlands) can be pretreated with 200 milligrams (mg) of doxycycline once a week. As of the early 2010s, no vaccine is available to prevent leptospirosis in humans, although similar vaccines have been formulated by veterinarians for dogs, swine, cattle, and other animals.

There are many ways to decrease the chances of being infected by *Leptospira*. These include:

- Avoid swimming or wading in freshwater ponds and slowly moving streams, especially those located near farms.
- Do not conduct canoe or kayak capsizing drills in freshwater ponds. Use a swimming pool instead.
- Boil or chemically treat pond or stream water before drinking it or cooking with it.
- Control rats and mice around the home.
- Have pets and farm animals vaccinated against *Leptospira*.
- Wear protective clothing (gloves, boots, long pants, and long-sleeved shirts) when working with wet soil or plants.

Resources

BOOKS

Beers, Mark H., et al., editors. *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Goldman, Lee, and Dennis Ausiello, editors. *Cecil Medicine*. Philadelphia: Saunders Elsevier, 2008.

Rowland, Lewis P., et al. *Merritt's Neurology*. Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, 2010.

OTHER

"Leptospirosis." MedicineNet. http://www .medicinenet.com/leptospirosis/article.htm. (accessed September 6, 2010).

"Leptospirosis." Medline Plus, National Library of Medicine and National Institutes of Health. (August 3, 2008), http ://www.nlm.nih.gov/medlineplus/ency/article/001376.htm. (accessed September 6, 2010).

ORGANIZATIONS

American Veterinary Medical Association (AVMA), 1931 North Meacham Rd., Suite 100, Schaumburg, IL, 60173–4360, (800) 248-2862, (847) 925-1329, http://www.avma.org.

Centers for Disease Control and Prevention, 1600 Clifton Rd., Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

International Leptospirosis Society, Faculty of Medicine, Nursing and Health Sciences, Monash UniversityVictoria, Australia, 3800, +61 3 9905 4301, +61 3 9905 4302, enquiries@med.monash.edu.au, http://www.med.monash.edu.au/microbiology/staff/adler/ils.html.

Belinda Rowland, PhD
Rebecca J. Frey, PhD

Lesch-Nyhan syndrome

Definition

Lesch-Nyhan syndrome, which is also known as HPRT deficiency or Kelley-Seegmiller syndrome, is a rare genetic disorder that affects males. Males with this syndrome develop physical handicaps, **mental retardation**, and kidney problems. It is caused by a total absence of a key enzyme that affects the level of uric acid in the body. Self-injury or **self-mutilation** is a distinctive feature of this genetic disease.

Description

Lesch-Nyhan syndrome was first described in 1964 by Drs. Michael Lesch and William Nyhan. The enzyme deficiency that causes the disorder was discovered in 1967 by a researcher named Seegmiller. The syndrome is caused by a severe change (mutation) in a gene that encodes an enzyme known as hypoxanthine-guanine phosphoribosyl transferase, or HPRT. This gene was identified and sequenced by Friedmann and colleagues in 1985. HPRT catalyzes a reaction that is necessary to prevent the buildup of uric acid, a nitrogenous waste product that is ordinarily excreted from the body through the kidneys. A severe mutation in the HPRT gene leads to an absence of HPRT enzyme activity which, in turn, leads to markedly elevated uric acid levels in the blood (hyperuricemia). This buildup of uric acid is toxic to the body and is related to the symptoms associated with the disease. Absence of the HPRT enzyme activity is also thought to alter the chemistry of certain parts of the brain, such as the basal ganglia, affecting neurotransmitters (chemicals used for communication between nerve cells), acids, and other chemicals. This change in the nervous system is also related to the symptoms associated with Lesch-Nyhan syndrome.

Males with Lesch-Nyhan syndrome develop neurologic problems during infancy. Infants with Lesch-Nyhan syndrome have weak muscle tone (hypotonia) and are unable to develop normally. Affected males develop uncontrollable writhing movements (athetosis) and muscle stiffness (spasticity) over time. Lack of speech is also a common feature of Lesch-Nyhan syndrome. The most dramatic symptom of Lesch-Nyhan syndrome, however, is the compulsive self-injury seen in 85% of affected males. This self-injury involves the biting of their own lips, tongue, and finger tips, as well as head banging. This behavior leads to serious injury and scarring.

Lesch-Nyhan syndrome affects approximately one in 380,000 live births. It occurs evenly among races. Almost always, only male children are affected, although a few cases of the disorder in girls have been reported. Women carriers usually do not have any symptoms. Women carriers can occasionally develop inflammation of the joints (**gout**) as they get older.

Causes and symptoms

Severe changes (mutations) in the HPRT gene completely halt the activity of the enzyme HPRT. There have been many different severe mutations identified in the HPRT gene. These mutations may be different between families. The HPRT gene is located on the X chromosome. Since the HPRT gene is located on the X chromosome, Lesch-Nyhan syndrome is considered X-linked. This means that it only affects males.

A person's sex is determined by their chromosomes. Males have one X chromosome and one Y chromosome. Females, on the other hand, have two X chromosomes. Males who possess a severe mutation in their HPRT gene will develop Lesch-Nyhan syndrome. Females who possess a severe mutation in their HPRT gene will not. They are considered to be carriers. This is because females have another X chromosome without the mutation that prevents them from getting this disease. If a woman is a carrier, she has a 50% risk with any **pregnancy** to pass on her X chromosome with the mutation. Therefore, with every male pregnancy she has a 50% risk to have an affected son, and with every female pregnancy she has a 50% risk to have a daughter who is a carrier.

At birth, males with Lesch-Nyhan syndrome appear completely normal. Development is usually normal for the first few months. Symptoms develop between three to six months of age. Sand-like crystals of uric acid in the diapers may be one of the first symptoms of the disease. The baby may be unusually irritable. Typically, the first sign of nervous system impairment is the inability to lift their head or sit up at an appropriate age. Many patients with Lesch-Nyhan will never learn to walk. By the end of the first year, writhing motions (athetosis), and spasmodic movements of the limbs and facial muscles (chorea) are clear evidence of defective motor development.

The compulsive self-injury associated with Lesch-Nyhan syndrome begins, on average, at three years. The self-injury begins with biting of the lips and tongue. As the disease progresses, affected individuals frequently develop finger biting and head banging. The self-injury can increase during times of **stress**.

Males with Lesch-Nyhan disease may also develop kidney damage due to **kidney stones**. Swollen and tender joints (gout) is another common problem.

Diagnosis

The diagnosis of Lesch-Nyhan syndrome is based initially on the distinctive pattern of the child's symptoms, most commonly involuntary muscle movements or failure to crawl and walk at the usual ages. In some cases the first symptom is related to overproduction of uric acid; the parents notice "orange sand" in the child's diapers. The "sand" is actually crystals of uric acid tinged with blood.

Measuring the amount of uric acid in a person's blood or urine can not definitively diagnose Lesch-Nyhan syndrome. It is diagnosed by measuring the activity of the HPRT enzyme through a blood test. When the activity of the enzyme is very low it is diagnostic of Lesch-Nyhan syndrome. It can also be diagnosed by DNA testing. This is also a blood test. DNA testing checks for changes (mutations) in the HPRT gene. Results from DNA testing are helpful in confirming the diagnosis and also when the child's family is interested in prenatal testing for future pregnancies.

Prenatal diagnosis is possible by DNA testing of fetal tissue drawn by **amniocentesis** or **chorionic villus sampling** (CVS). Fetuses should be tested if the mother is a carrier of a change (mutation) in her HPRT gene. A woman is at risk of being a carrier if she has a son with Lesch-Nyhan syndrome or someone in her family has Lesch-Nyhan syndrome. Any woman at risk of being a carrier should have DNA testing through a blood test.

Treatment

There are no known treatments for the neurological defects of Lesch-Nyhan. Allopurinol (Aloprim,

KEY TERMS

Amniocentesis—A procedure performed at 16–18 weeks of pregnancy in which a needle is inserted through a woman's abdomen into her uterus to draw out a small sample of the amniotic fluid from around the baby. Either the fluid itself or cells from the fluid can be used for a variety of tests to obtain information about genetic disorders and other medical conditions in the fetus.

Athetosis—A condition marked by slow, writhing, involuntary muscle movements.

Basal ganglia—A section of the brain responsible for smooth muscular movement.

Chorea—Involuntary, rapid, jerky movements.

Chorionic villus sampling (CVS)—A procedure used for prenatal diagnosis at 10–12 weeks gestation. Under ultrasound guidance a needle is inserted either through the mother's vagina or abdominal wall and a sample of cells is collected from around the early embryo. These cells are then tested for chromosome abnormalities or other genetic diseases.

Enzyme—A protein that catalyzes a biochemical reaction or change without changing its own structure or function.

Mutation—A permanent change in the genetic material that may alter a trait or characteristic of an individual, or manifest as disease, and can be transmitted to offspring.

Neurotransmitter—Chemical in the brain that transmits information from one nerve cell to another.

Palsy—Uncontrolable tremors.

Spasticity—Increased mucle tone, or stiffness, which leads to uncontrolled, awkward movements.

Zyloprim), a drug usually prescribed to lower the risk of gout attacks, can lower blood uric acid levels. This medication is a preventive; it does not correct many of the symptoms of Lesch-Nyhan. Other drugs that are given to manage spasticity include baclofen (Lioresal), which is a muscle relaxant, and benzodiazepine tranquilizers.

Some patients with Lesch-Nyhan syndrome have their teeth removed to prevent self-injury. Restraints may be recommended to reduce self-destructive behaviors, although some patients can be managed with a combination of behavioral modification therapy and medications.

Prognosis

With strong supportive care, infants born with Lesch-Nyhan can live into adulthood with symptoms continuing throughout life. Few live beyond 40, however, with **death** usually resulting either from kidney failure or from aspiration **pneumonia**. Sudden unexpected death from **respiratory failure** is common in these patients.

At present, there are no preventive measures for Lesch-Nyhan syndrome. However, recent studies have indicated that this genetic disorder may be a good candidate for treatment with gene replacement therapy. Unfortunately, the technology necessary to implement this therapy has not yet been perfected.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Parker, Philip M. *Lesch–Nyhan Syndrome—A Bibliography and Dictionary for Physicians, Patients, and Genome Researchers*. San Diego: ICON Group International, 2007.

PERIODICALS

Willers, I. "Germline Mosaicism Complicates Molecular Diagnosis of Lesch-Nyhan Syndrome." *Prenatal Diagnosis* 24 (September 2004): 737–740.

OTHER

GeneClinics. http://www.geneclinics.org/profiles/lns/details.html.

Pediatric Database (PEDBASE). http://www.icondata.com/health/pedbase/files/LESCH-NY.HTM.

ORGANIZATIONS

Genetic Alliance, Inc., 4301 Connecticut Ave., NW, Suite 404, Washington, DC, 20008-2369, (202) 966-5557, (202) 966-8553, info@geneticalliance.org, http://www.geneticalliance.org.

Lesch-Nyhan Disease International Study Group, http://www.lesch-nyhan.org/.

LND Net, http://lndnet.ning.com/.An online Lesch-Nyhan Disease support group.

National Organization for Rare Disorders, P.O. Box 8923, New Fairfield, CT, 06812-8923, (800) 999-6673, http://www.rarediseases.org.

Holly Ann Ishmael, M.S.
Rebecca J. Frey, PhD

Leukemia stains

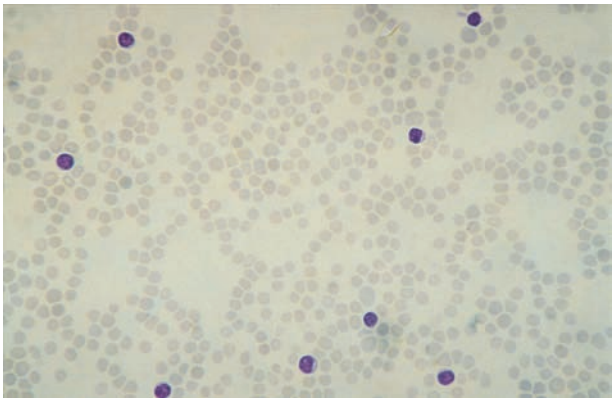
Definition

Leukemia stains are laboratory tests done on bone marrow or blood samples to help diagnose specific types of leukemia.

Purpose

Leukemia stains are done to diagnose and classify leukemia. Blood contains red cells, several varieties of white cells, and platelets. Cancerous overproduction of any one type of cell produces one of many types of leukemia. A patient's specific type of leukemia must be classified in order to provide the best treatment and most accurate prognosis.

The type and maturity of the cells involved are identified by analyzing blood and bone marrow under a microscope. Often, however, the abnormality or immaturity of the cells make it difficult to identify the cell types with certainty. Special leukemia stains help to distinguish one cell type from another.



A magnified stain of chronic lymphocytic leukemia cells. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Description

Special stains are added to bone marrow or blood that has been smeared on a microscope slide. Cell types react differently to the chemicals in the stains.

If the patient has few white cells, a buffy coat smear is made. A tube of blood is spun in a centrifuge. Red cells fall, plasma rises, and white cells settle in a thin middle layer called the buffy coat. The smear is made from this layer.

Sudan black B stain

This stain distinguishes between acute lymphoblastic leukemia (cells stain positive) and acute myeloblastic leukemia (cells stain negative).

Periodic acid-Schiff stain (PAS)

The PAS stain is primarily used to identify erythroleukemia, a leukemia of immature red blood cells. These cells stain a bright fuchsia.

Terminal deoxynucleotidyl transferase stain (TdT)

The TdT stain differentiates between acute lymphoblastic leukemia (cells stain positive) and acute myelogenous leukemia (cells stain negative).

Leukocyte alkaline phosphatase (LAP)

The LAP stain is used to determine if an increase of cells is due to chronic myelogenous leukemia or a noncancerous reaction to an infection or similar conditions. Cells from a noncancerous reaction stain positive with many intense blue granules; cells from chronic myelogenous leukemia have few blue granules.

Tartrate-resistant acid phosphatase stain (TRAP)

The TRAP stain is primarily used to identify **hairy cell leukemia** cells. These cells stain with purple to dark red granules.

Myeloperoxidase stain

The myeloperoxidase stain distinguishes between the immature cells in acute myeloblastic leukemia (cells stain positive) and those in acute lymphoblastic leukemia (cells stain negative).

Leukocyte specific esterase

This stain identifies granulocytes, which show red granules.

KEY TERMS

Bone marrow—The spongy tissue inside large bones where blood cells are formed.

Buffy coat—The thin layer of concentrated white blood cells that forms when a tube of blood is spun in a centrifuge.

Leukemia—Any of several cancers of the bone marrow characterized by the abnormal increase of a type of blood cell.

Leukemia stains—Special stains added to smears of blood or bone marrow, performed to diagnose and classify leukemia.

Leukocyte nonspecific esterase

Nonspecific esterase stain identifies monocytes and immature platelets (megakaryocytes), which show positive black granules.

Preparation

Leukemia stains are done on smears of blood or bone marrow. To collect blood, a healthcare worker draws blood from a vein in the inner elbow region. Collection of the sample takes only a few minutes.

When bone marrow is needed, the person is given **local anesthesia**. Then the physician inserts a needle through the skin and into the bone—usually the breast bone or hip bone—and 0.5–2 mL of bone marrow is withdrawn. This procedure takes approximately 30 minutes.

Aftercare

Patients sometimes feel discomfort or bruising at the puncture site after blood collection. They may also become dizzy or faint. Pressure to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort.

Collection of bone marrow is done under a physician's supervision. The patient is asked to rest after the procedure and is watched for weakness and signs of bleeding.

Results

A normal blood or bone marrow smear shows no evidence of leukemic cells. The expected reaction of cells varies with the type of stain.

Leukemia stain results that help diagnosis and classify leukemia are supported by the results of other laboratory tests and the person's clinical condition.

Resources

BOOKS

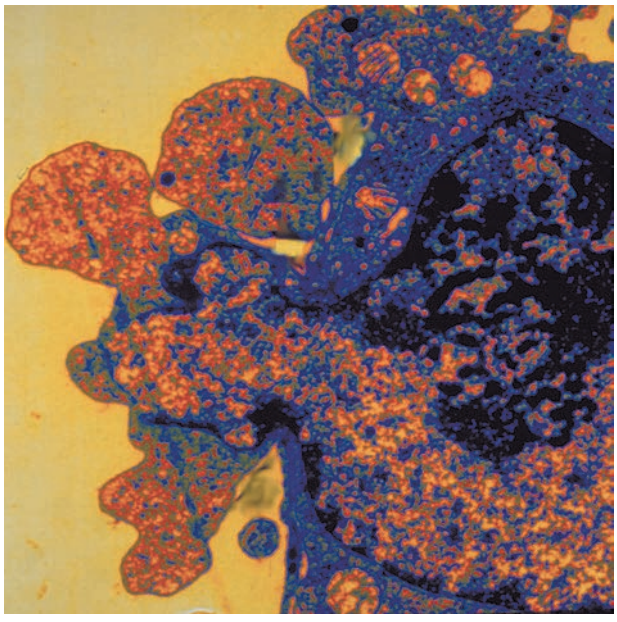
Fischbach, Frances Talaska, and Marshall Barnett Dunning. *A Manual of Laboratory and Diagnostic Tests*. 8th ed. Philadelphia: Wolters Kluwer Heath/Lippincott Williams & Wilkins, 2009.

Nancy J. Nordenson

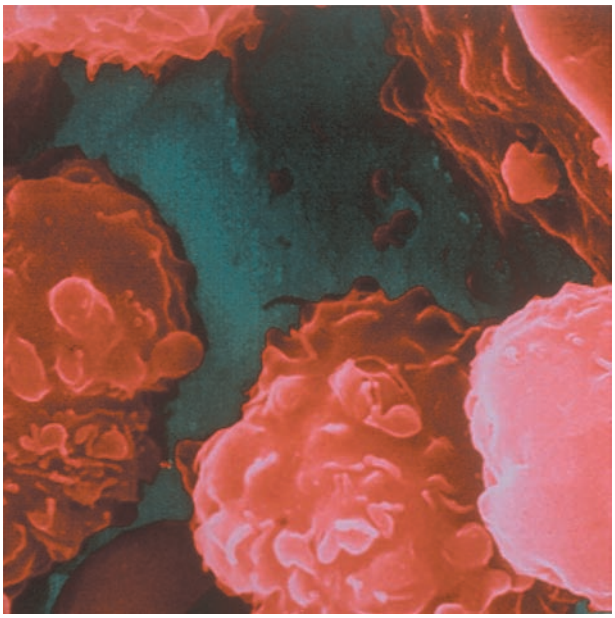
Leukemias, acute

Definition

Leukemia is a **cancer** that starts in the organs that make blood, namely the bone marrow and the lymph system. Depending on their characteristics, leukemias can be divided into two broad types. Acute leukemias are the rapidly progressing leukemias, while the **chronic leukemias** progress more slowly. The vast majority of the childhood leukemias are of the acute form.



An enhanced transmission electron microscopy (TEM) image of acute myelogenous leukemia cells. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*



An enhanced scanning electron microscopy (SEM) image of acute myelogenous leukemia cells. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Description

The cells that make up blood are produced in the bone marrow and the lymph system. The bone marrow is the spongy tissue found in the large bones of the body. The lymph system includes the spleen (an organ in the upper abdomen), the thymus (a small organ beneath the breastbone), and the tonsils (an organ in the throat). In addition, the lymph vessels (tiny tubes that branch like blood vessels into all parts of the body) and lymph nodes (pea-shaped organs that are found along the network of lymph vessels) are also part of the lymph system. The lymph is a milky fluid that contains cells. Clusters of lymph nodes are found in the neck, underarm, pelvis, abdomen, and chest.

The cells found in the blood are the red blood cells (RBCs), which carry oxygen and other materials to all tissues of the body; white blood cells (WBCs) that fight infection; and the platelets, which play a part in the clotting of the blood. The white blood cells can be further subdivided into three main types: granulocytes, monocytes, and lymphocytes.

The granulocytes, as their name suggests, have particles (granules) inside them. These granules contain special proteins (enzymes) and several other substances that can break down chemicals and destroy microorganisms, such as bacteria. Monocytes are the second type of white blood cell. They are also important in defending the body against pathogens.

The lymphocytes form the third type of white blood cell. There are two main types of lymphocytes: T lymphocytes and B lymphocytes. They have different functions within the immune system. The B cells protect the body by making "antibodies." Antibodies are proteins that can attach to the surfaces of bacteria and viruses. This "attachment" sends signals to many other cell types to come and destroy the antibody-coated organism. The T cells protect the body against viruses. When a virus enters a cell, it produces certain proteins that are projected onto the surface of the infected cell. The T cells recognize these proteins and make certain chemicals that are capable of destroying the virus-infected cells. In addition, the T cells can destroy some types of cancer cells.

The bone marrow makes stem cells, which are the precursors of the different blood cells. These stem cells mature through stages into either RBCs, WBCs, or platelets. In acute leukemias, the maturation process of the white blood cells is interrupted. The immature cells (or "blasts") proliferate rapidly and begin to accumulate in various organs and tissues, thereby affecting their normal function. This uncontrolled proliferation of the immature cells in the bone marrow affects the production of the normal red blood cells and platelets as well.

Acute leukemias are of two types: acute lymphocytic leukemia and acute myelogenous leukemia. Different types of white blood cells are involved in the two leukemias. In acute lymphocytic leukemia (ALL), it is the T or the B lymphocytes that become cancerous. The B cell leukemias are more common than T cell leukemias. Acute myelogenous leukemia, also known as acute nonlymphocytic leukemia (ANLL), is a cancer of the monocytes and/or granulocytes.

Leukemias account for 2% of all cancers. Because leukemia is the most common form of childhood cancer, it is often regarded as a disease of childhood. However, leukemias affect nine times as many adults as children. Half of the cases occur in people who are 60 years of age or older. The incidence of acute and chronic leukemias is about the same. According to the estimates of the American Cancer Society (ACS), approximately 29,000 new cases of leukemia were diagnosed in 1998.

Causes and symptoms

Leukemia strikes both sexes and all ages. The human T-cell leukemia virus (HTLV-I) is believed to be the causative agent for some kinds of leukemias. However, the cause of most leukemias is not known. Acute lymphoid leukemia (ALL) is more common

CHARLOTTE FRIEND (1921–1987)

(The Library of Congress.)

Charlotte Friend was born to Russian immigrants, Morris Friend and Cecilia (Wolpin), on March 11, 1921, in New York City. At three years of age, her father died of a heart condition. Friend's decision to pursue a career in medicine may well have been influenced by her father's death and by her mother's occupation as a pharmacist. As a child, Friend read books about bacteriologists and, by age ten, she knew that she wanted to study bacteriology. She attended Hunter College, enlisting in the U.S. Navy after her graduation in 1944.

Friend attended Yale University, earning her Ph.D. in bacteriology in 1950. After working for the Memorial Sloan-Kettering Institute for Cancer Research, she became an associate professor at Cornell University in 1952. Friend began researching cancer and became particularly interested in leukemia and its cause. She believed that a virus caused the disease and confirmed this theory by using an electron microscope to photograph the virus in mice. Her findings were initially met with much skepticism but she was able to develop a vaccine that was used successfully with mice, which added credibility to her theory. Her breakthroughs have led medical researchers to new methods of treating cancer and to a greater understanding of the disease.

Friend was a prolific writer who published 113 original papers, 49 abstracts, book chapters, and reviews, many of which she completed individually. She was diagnosed with lymphoma and died on January 13, 1987.

among Caucasians than among African-Americans, while acute myeloid leukemia (AML) affects both races equally. The incidence of acute leukemia is slightly higher among men than women. People with Jewish ancestry have a higher likelihood of getting leukemia. A higher incidence of leukemia has also been observed among persons with **Down syndrome** and some other genetic abnormalities.

Exposure to ionizing radiation and to certain organic chemicals, such as benzene, is believed to increase the risk of getting leukemia. Having a history of diseases that damage the bone marrow, such as **aplastic anemia**, or a history of cancers of the lymphatic system puts people at a high risk for developing acute leukemias. Similarly, the use of anticancer medications, immunosuppressants, and the antibiotic chloramphenicol are also considered risk factors for developing acute leukemias.

The symptoms of leukemia are generally vague and non-specific. A patient may experience all or some of the following symptoms:

- weakness or chronic fatigue
- fever of unknown origin
- weight loss that is not due to dieting or exercise
- frequent bacterial or viral infections
- headaches
- skin rash
- non-specific bone pain
- easy bruising
- bleeding from gums or nose
- blood in urine or stools
- enlarged lymph nodes and/or spleen
- abdominal fullness

Diagnosis

Like all cancers, acute leukemias are best treated when found early. There are no screening tests available.

If the doctor has reason to suspect leukemia, he or she will conduct a very thorough **physical**

examination to look for enlarged lymph nodes in the neck, underarm, and pelvic region. Swollen gums, enlarged liver or spleen, **bruises**, or pinpoint red **rashes** all over the body are some of the signs of leukemia. Urine and blood tests may be ordered to check for microscopic amounts of blood in the urine and to obtain a complete differential blood count. This count will give the numbers and percentages of the different cells found in the blood. An abnormal blood test might suggest leukemia; however, the diagnosis has to be confirmed by more specific tests.

The doctor may perform a **bone marrow biopsy** to confirm the diagnosis of leukemia. During the biopsy, a cylindrical piece of bone and marrow is removed. The tissue is generally taken out of the hipbone. These samples are sent to the laboratory for examination. In addition to diagnosis, the biopsy is also repeated during the treatment phase of the disease to see if the leukemia is responding to therapy.

A spinal tap (**lumbar puncture**) is another procedure that the doctor may order to diagnose leukemia. In this procedure, a small needle is inserted into the spinal cavity in the lower back to withdraw some cerebrospinal fluid and to look for leukemic cells.

Standard imaging tests, such as x rays, **computed tomography scans** (CT scans), and **magnetic resonance imaging** (MRI) may be used to check whether the leukemic cells have invaded other areas of the body, such as the bones, chest, kidneys, abdomen, or brain. A gallium scan or **bone scan** is a test in which a radioactive chemical is injected into the body. This chemical accumulates in the areas of cancer or infection, allowing them to be viewed with a special camera.

Treatment

There are two phases of treatment for leukemia. The first phase is called "induction therapy." As the name suggests, during this phase, the main aim of the treatment is to reduce the number of leukemic cells as far as possible and induce a remission in the patient. Once the patient shows no obvious signs of leukemia (no leukemic cells are detected in blood tests and bone marrow biopsies), the patient is said to be in remission. The second phase of treatment is then initiated. This is called continuation or maintenance therapy, and the aim in this case is to kill any remaining cells and to maintain the remission for as long as possible.

Chemotherapy is the use of drugs to kill cancer cells. It is usually the treatment of choice and is used to relieve symptoms and achieve long-term remission of the disease. Generally, combination chemotherapy, in which multiple drugs are used, is more efficient than using a single drug for the treatment. Some drugs may be administered intravenously through a vein in the arm; others may be given by mouth in the form of pills. If the cancer cells have invaded the brain, then chemotherapeutic drugs may be put into the fluid that surrounds the brain through a needle in the brain or back. This is known as intrathecal chemotherapy.

Because leukemia cells can spread to all the organs via the blood stream and the lymph vessels, surgery is not considered an option for treating leukemias.

Radiation therapy, which involves the use of x rays or other high-energy rays to kill cancer cells and shrink tumors, may be used in some cases. For acute leukemias, the source of radiation is usually outside the body (external radiation therapy). If the leukemic cells have spread to the brain, radiation therapy can be given to the brain.

Bone marrow transplantation is a process in which the patient's diseased bone marrow is replaced with healthy marrow. There are two ways of doing a bone marrow transplant. In an allogeneic bone marrow transplant, healthy marrow is taken from a donor whose tissue is either the same as or very closely resembles the patient's tissues. The donor may be a twin, a brother or sister (sibling), or a person who is not related at all. First, the patient's bone marrow is destroyed with very high doses of chemotherapy and radiation therapy. Healthy marrow from the donor is then given to the patient through a needle in a vein to replace the destroyed marrow.

In the second type of bone marrow transplant, called an autologous bone marrow transplant, some of the patient's own marrow is taken out and treated with a combination of **anticancer drugs** to kill all the abnormal cells. This marrow is then frozen to save it. The marrow remaining in the patient's body is destroyed with high-dose chemotherapy and radiation therapy. The marrow that was frozen is then thawed and given back to the patient through a needle in a vein. This mode of bone marrow transplant is currently being investigated in clinical trials.

Biological therapy or immunotherapy is a mode of treatment in which the body's own immune system is harnessed to fight the cancer. Substances that are routinely made by the immune system (such as growth factors, hormones, and disease-fighting proteins) are either synthetically made in a laboratory or their effectiveness is boosted and they are then put back into the patient's body. This treatment mode is also being investigated in clinical trials all over the country at major cancer centers.

KEY TERMS

Antibodies—Proteins made by the B lymphocytes in response to the presence of infectious agents, such as bacteria or viruses, in the body.

Biopsy—The surgical removal and microscopic examination of living tissue for diagnostic purposes.

Chemotherapy—Treatment with drugs that act against cancer.

Computerized tomography (CT) scan—A series of x rays put together by a computer in order to form detailed pictures of areas inside the body.

Cytokines—Chemicals made by the cells that act on other cells to stimulate or inhibit their function. Cytokines that stimulate growth are called "growth factors."

Immunotherapy—Treatment of cancer by stimulating the body's immune defense system.

Lumbar puncture—A procedure in which the doctor inserts a small needle into the spinal cavity in the lower back to withdraw some spinal fluid for testing. Also known as a "spinal tap."

Magnetic resonance imaging (MRI)—A medical procedure using a magnet linked to a computer to picture areas inside the body.

Maturation—The process by which stem cells transform from immature cells without a specific function into a particular type of blood cell with defined functions.

Radiation therapy—Treatment using high-energy radiation from x-ray machines, cobalt, radium, or other sources.

Remission—A disappearance of a disease as a result of treatment. Complete remission means that all disease is gone. Partial remission means that the disease is significantly improved by treatment, but residual traces of the disease are still present.

Prognosis

Like all cancers, the prognosis for leukemia depends on the patient's age and general health. According to statistics, more than 60% of the patients with leukemia survive for at least a year after diagnosis. Acute myelocytic leukemia (AML) has a poorer prognosis rate than acute lymphocytic leukemias (ALL) and the chronic leukemias. In the last 15 to 20 years, the five-year survival rate for patients with ALL has increased from 38% to 57%.

Interestingly enough, since most childhood leukemias are of the ALL type, chemotherapy has been highly successful in their treatment. This is because chemotherapeutic drugs are most effective against actively growing cells. Due to the new combinations of anticancer drugs being used, the survival rates among children with ALL have improved dramatically. Eighty percent of the children diagnosed with ALL now survive for five years or more, as compared to 50% in the late 1970s.

Prevention

Most cancers can be prevented by changes in lifestyle or diet, which will reduce the risk factors. However, in leukemias, there are no such known risk factors. Therefore, at the present time, no way is known to prevent leukemias from developing. People who are at an increased risk for developing leukemia because of proven exposure to ionizing radiation or exposure to the toxic liquid benzene, and people with Down syndrome, should undergo periodic medical checkups.

ORGANIZATIONS

American Cancer Society, 250 Williams Street, Atlanta, GA, 30303-1002, (800) ACS-2345, https://www.cancer.org/.

National Cancer Institute, 6116 Executive Blvd., Room 3036A, Bethesda, MD, 20892-8322, (800) 422-6237, http://www.cancer.gov.

Leukemia Society of America, Inc., 600 Third Ave, New York, NY, 20892-8322, (800) 955-4572, http://www.leukemia.org.

Lata Cherath, PhD

Leukemias, chronic

Definition

Chronic leukemia is a disease in which too many white blood cells are made in the bone marrow. Depending on the type of white blood cell that is

involved, chronic leukemia can be classified as chronic lymphocytic leukemia or chronic myeloid leukemia.

Description

Chronic leukemia is a **cancer** that starts in the blood cells made in the bone marrow. The bone marrow is the spongy tissue found in the large bones of the body. The bone marrow makes precursor cells called "blasts" or "stem cells" that mature into different types of blood cells. Unlike **acute leukemias**, in which the process of maturation of the blast cells is interrupted, in chronic leukemias, the cells do mature and only a few remain as immature cells. However, even though the cells appear normal, they do not function as normal cells.

The different types of cells that are produced in the bone marrow are red blood cells (RBCs), which carry oxygen and other materials to all tissues of the body; white blood cells (WBCs), which fight infection; and platelets, which play a part in the clotting of the blood. The white blood cells can be further subdivided into three main types: the granulocytes, monocytes, and the lymphocytes.

The granulocytes, as their name suggests, have granules (particles) inside them. These granules contain special proteins (enzymes) and several other substances that can break down chemicals and destroy microorganisms such as bacteria.

Monocytes are the second type of white blood cell. They are also important in defending the body against pathogens.

The lymphocytes form the third type of white blood cell. There are two main types of lymphocytes: T lymphocytes and B lymphocytes. They have different functions within the immune system. The B cells protect the body by making "antibodies." Antibodies are proteins that can attach to the surfaces of bacteria and viruses. This attachment sends signals to many other cell types to come and destroy the antibody-coated organism. The T cell protects the body against viruses. When a virus enters a cell, it produces certain proteins that are projected onto the surface of the infected cell. The T cells can recognize these proteins and produce certain chemicals (cytokines) that are capable of destroying the virus-infected cells. In addition, the T cells can destroy some types of cancer cells.

Chronic leukemias develop very gradually. The abnormal lymphocytes multiply slowly, but in a poorly regulated manner. They live much longer and thus their numbers build up in the body. The two types of chronic leukemias can be easily distinguished under the microscope. Chronic lymphocytic leukemia (CLL) involves the T or B lymphocytes. B cell abnormalities are more common than T cell abnormalities. T cells are affected in only 5% of the patients. The T and B lymphocytes can be differentiated from the other types of white blood cells based on their size and by the absence of granules inside them. In chronic myelogenous leukemia (CML), the cells that are affected are the granulocytes.

Chronic lymphocytic leukemia (CLL) often has no symptoms at first and may remain undetected for a long time. Chronic myelogenous leukemia (CML), on the other hand, may progress to a more acute form.

Chronic leukemias account for 1.2% of all cancers. Because leukemia is the most common form of childhood cancer, it is often regarded as a disease of childhood. However, leukemias affect nine times as many adults as children. In chronic lymphoid leukemia, 90% of the cases are seen in people who are 50 years or older, with the average age at diagnosis being 65. The incidence of the disease increases with age. It is almost never seen in children. Chronic myeloid leukemias are generally seen in people in their mid-40s. It accounts for about 4% of childhood leukemia cases. According to the estimates of the American Cancer Society (ACS), approximately 29,000 new cases of leukemia will be diagnosed in 1998.

Causes and symptoms

Leukemia strikes both sexes and all ages. Although the cause is unknown, chronic leukemia is linked to genetic abnormalities and environmental factors. For example, exposure to ionizing radiation and to certain organic chemicals, such as benzene, is believed to increase the risks for getting leukemia. Chronic leukemia occurs in some people who are infected with two human retroviruses (HTLV-I and HTLV-II). An abnormal chromosome known as the Philadelphia chromosome is seen in 90% of those with CML. The incidence of chronic leukemia is slightly higher among men than women.

The symptoms of chronic leukemia are generally vague and non-specific. In chronic lymphoid leukemia (CLL), a patient may experience all or some of the following symptoms:

- swollen lymph nodes
- an enlarged spleen, which could make the patient complain of abdominal fullness
- chronic fatigue
- a general feeling of ill-health
- fever of unknown origin
- night sweats
- weight loss that is not due to dieting or exercise
- frequent bacterial or viral infections

In the early stages of chronic myeloid leukemia (CML), the symptoms are more or less similar to CLL. In the later stages of the disease, the patient may experience these symptoms:

- non-specific bone pain
- bleeding problems
- mucus membrane irritation
- frequent infections
- a pale color due to a low red blood cell count (anemia)
- swollen lymph glands
- fever
- night sweats

Diagnosis

There are no screening tests available for chronic leukemias. The detection of these diseases may occur by chance during a routine **physical examination**.

If the doctor has reason to suspect leukemia, he or she will conduct a very thorough physical examination to look for enlarged lymph nodes in the neck, underarm, and pelvic region. Swollen gums, an enlarged liver or spleen, **bruises**, or pinpoint red **rashes** all over the body are some of the signs of leukemia. Urine and blood tests may be ordered to check for microscopic amounts of blood in the urine and to obtain a complete differential blood count. This count will give the numbers and percentages of the different cells found in the blood. An abnormal blood test might suggest leukemia; however, the diagnosis has to be confirmed by more specific tests.

The doctor may perform a **bone marrow biopsy** to confirm the diagnosis of leukemia. During the bone marrow biopsy, a cylindrical piece of bone and marrow is removed. The tissue is generally taken out of the hipbone. These samples are sent to the laboratory for examination. In addition to diagnosis, bone marrow biopsy is also done during the treatment phase of the disease to see if the leukemia is responding to therapy.

Standard imaging tests such as x rays, **computed tomography scans** (CT scans), and **magnetic resonance imaging** (MRI) may be used to check whether the leukemic cells have invaded other organs of the body, such as the bones, chest, kidneys, abdomen, or brain.

Treatment

The treatment depends on the specific type of chronic leukemia and its stage. In general, **chemotherapy** is the standard approach to both CLL and CML. **Radiation therapy** is occasionally used. Because leukemia cells can spread to all the organs via the blood stream and the lymph vessels, surgery is not considered an option for treating leukemias.

Bone marrow transplantation (BMT) is becoming the treatment of choice for CML because it has the possibility of curing the illness. BMT is generally not considered an option in treating CLL because CLL primarily affects older people, who are not considered to be good candidates for the procedure.

In BMT, the patient's diseased bone marrow is replaced with healthy marrow. There are two ways of doing a bone marrow transplant. In an allogeneic bone marrow transplant, healthy marrow is taken from another person (donor) whose tissue is either the same or very closely resembles the patient's tissues. The donor may be a twin, a sibling, or a person who is not related at all. First, the patient's bone marrow is destroyed with very high doses of chemotherapy and radiation therapy. To replace the destroyed marrow, healthy marrow from the donor is given to the patient through a needle in the vein.

In the second type of bone marrow transplant, called an autologous bone marrow transplant, some of the patient's own marrow is taken out and treated with a combination of **anticancer drugs** to kill all the abnormal cells. This marrow is then frozen to save it. The marrow remaining in the patient's body is then destroyed with high dose chemotherapy and radiation therapy. Following that, the patient's own marrow that was frozen is thawed and given back to the patient through a needle in the vein. This mode of bone marrow transplant is currently being investigated in clinical trials.

In chronic lymphoid leukemia (CLL), chemotherapy is generally the treatment of choice. Depending on the stage of the disease, single or multiple drugs may be given. Drugs commonly prescribed include **steroids**, chlorambucil, fludarabine, and cladribine. Low dose radiation therapy may be given to the whole body, or it may be used to alleviate the symptoms and discomfort due to an enlarged spleen and lymph nodes. The spleen may be removed in a procedure called a **splenectomy**.

In chronic myeloid leukemia (CML), the treatment of choice is bone marrow transplantation. During the slow progress (chronic phase) of the disease, chemotherapy may be given to try to improve the cell counts. Radiation therapy, which involves the use of x rays or other high-energy rays to kill cancer cells and shrink tumors, may be used in some cases to reduce the discomfort and **pain** due to an enlarged spleen. For chronic leukemias, the source of radiation is usually outside the body (external radiation therapy). If the

KEY TERMS

Antibodies—Proteins made by the B lymphocytes in response to the presence of infectious agents, such as bacteria or viruses, in the body.

Biopsy—The surgical removal and microscopic examination of living tissue for diagnostic purposes.

Chemotherapy—Treatment with drugs that act against cancer.

Computerized tomography (CT) scan—A series of x rays put together by a computer in order to form detailed pictures of areas inside the body.

Cytokines—Chemicals made by the cells that act on other cells to stimulate or inhibit their function. Cytokines that stimulate growth are called "growth factors."

Immunotherapy—Treatment of cancer by stimulating the body's immune defense system.

Lumbar puncture—A procedure in which the doctor inserts a small needle into the spinal cavity in the lower back to withdraw some spinal fluid for testing. Also known as a "spinal tap."

Magnetic resonance imaging (MRI)—A medical procedure using a magnet linked to a computer to picture areas inside the body.

Maturation—The process by which stem cells transform from immature cells without a specific function into a particular type of blood cell with defined functions.

Radiation therapy—Treatment using high-energy radiation from x-ray machines, cobalt, radium, or other sources.

Remission—A disappearance of a disease as a result of treatment. Complete remission means that all disease is gone. Partial remission means that the disease is significantly improved by treatment, but residual traces of the disease are still present.

leukemic cells have spread to the brain, radiation therapy can be directed at the brain. As the disease progresses, the spleen may be removed in an attempt to try to control the pain and to improve the blood counts.

In the acute phase of CML, aggressive chemotherapy is given. Combination chemotherapy, in which multiple drugs are used, is more efficient than using a single drug for the treatment. The drugs may either be administered intravenously through a vein in the arm or by mouth in the form of pills. If the cancer cells have invaded the central nervous system (CNS), chemotherapeutic drugs may be put into the fluid that surrounds the brain through a needle in the brain or back. This is known as intrathecal chemotherapy.

Biological therapy or immunotherapy is a mode of treatment in which the body's own immune system is harnessed to fight the cancer. Substances that are routinely made by the immune system (such as growth factors, hormones, and disease-fighting proteins) are either synthetically made in a laboratory, or their effectiveness is boosted and they are then put back into the patient's body. This treatment mode is also being investigated in clinical trials all over the country at major cancer centers.

Prognosis

The prognosis for leukemia depends on the patient's age and general health. According to statistics, in chronic lymphoid leukemia, the overall survival for all stages of the disease is nine years. Most of the deaths in people with CLL are due to infections or other illnesses that occur as a result of the leukemia.

In CML, if bone marrow transplantation is performed within one to three years of diagnosis, 50–60% of the patients survive three years or more. If the disease progresses to the acute phase, the prognosis is poor. Less than 20% of these patients go into remission.

Prevention

Most cancers can be prevented by changes in lifestyle or diet, which will reduce the risk factors. However, in leukemias, there are no known risk factors. Therefore, at the present time, there is no way known to prevent the leukemias from developing. People who are at an increased risk for developing leukemia because of proven exposure to ionizing radiation, the organic liquid benzene, or people who have a history of other cancers of the lymphoid system (Hodgkin's lymphoma) should undergo periodic medical checkups.

ORGANIZATIONS

American Cancer Society, 250 Williams Street, Atlanta, GA, 30303-1002, (800) ACS-2345, https://www.cancer.org/.

National Cancer Institute, 6116 Executive Blvd., Room 3036A, Bethesda, MD, 20892-8322, (800) 422-6237, http://www.cancer.gov.

Leukemia Society of America, Inc., 600 Third Ave, New York, NY, 20892-8322, (800) 955 4572, http://www.leukemia.org.

Lata Cherath, PhD

Leukocytosis

Definition

Leukocytosis is a condition characterized by an elevated number of white cells in the blood.

Description

Leukocytosis is a condition that affects all types of white blood cells. Other illnesses, such as neutrophilia, lymphocytosis, and granulocytosis, target specific types of white blood cells. Normal white blood cell counts are 4,300–10,800 white blood cells per microliter. Leukocyte or white blood cell levels are considered elevated when they are between 15,000–20,000 per microliter. The increased number of leukocytes can occur abnormally as a result of an infection, **cancer**, or drug intake; however, leukocytosis can occur normally after eating a large meal or experiencing **stress**.

Causes and symptoms

Leukemias can cause white blood cell counts to increase to as much as 100,000. Each kind of white cell can produce a leukemia. Apart from leukemias, nearly all leukocytosis is due to one type of white blood cell, the polymorphonuclear leukocyte (PMN). These conditions are more accurately referred to as neutrophilia.

The most common and important cause of neutrophilia is infection, and most infections cause neutrophilia. The degree of elevation often indicates the severity of the infection. Tissue damage from other causes raises the white count for similar reasons. **Burns**, infarction (cutting off the blood supply to a region of the body so that it dies), crush injuries, inflammatory diseases, poisonings, and severe diseases, like kidney failure and **diabetic ketoacidosis**, all cause neutrophilia.

Counts almost as high occur in leukemoid (leukemia-like) reactions caused by infection and non-infectious inflammation.

Drugs can also cause leukocytosis. Cortisone-like drugs (prednisone), lithium, and NSAIDs are the most common offenders.

KEY TERMS

Biopsy—Surgical removal of tissue for examination.

Inflammation—Heat, swelling, redness, and pain caused by tissue injury.

Ketoacidosis—A severe stage of diabetes where acids and ketones accumulate in the body.

NSAID—Non-steroidal anti-inflammatory drug such as ibuprofen.

Non-specific stresses also cause white blood cells to increase in the blood. Extensive testing of medical students reveals that neutrophilia accompanies every examination. Vigorous **exercise** and intense excitement also cause elevated white blood cell counts.

Diagnosis

A **complete blood count** (CBC) is one of the first tests obtained in any medical setting. More than 11,000 white cells in a cubic millimeter of blood is considered high. **Bone marrow biopsy** may help clarify the cause.

Treatment

Relieving the underlying cause returns the count to normal.

Prognosis

By treating the underlying condition, white blood cell counts usually return to normal

Resources

BOOKS

Fauci, Anthony S., et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw–Hill Professional, 2008.

J. Ricker Polsdorfer, MD

Leukotriene inhibitors

Definition

Leukotriene inhibitors are prescription medications that treat **asthma** and some **allergies** by blocking

the formation or activity of leukotrienes—small mediator chemicals produced by cells in the body.

Purpose

More than 50 million Americans suffer from asthma and allergies. Asthma is one of the most prevalent chronic diseases in the United States, affecting 9 million (12.7%) of children. Seasonal allergies affect 20–40 million (20%) of Americans, about 40% of them children. It is estimated that 60–70% of those with asthma also suffer from **allergic rhinitis**, allergies affecting the mucous membranes of the nose.

Asthma, an inflammation of the bronchial airways, and seasonal allergies and allergic **rhinitis** involve several chemical mediators including histamine and leukotrienes. Leukotrienes are a class of unsaturated fatty-acid chains containing 20 carbon atoms.

During an asthma attack or within minutes of exposure to an allergen such as dust or pollen, leukotrienes are released by a type of blood cell in the lungs, causing the following responses:

- contraction of the bronchial airway muscles
- inflammation of the airway linings
- swelling and narrowing of the airways
- production of mucus and fluid
- wheezing and shortness of breath
- nasal congestion

Leukotriene inhibitors may decrease the symptoms of mild to moderate allergen-induced asthma, improve nighttime symptoms, and reduce the number of acute asthma attacks. Taken daily on a long-term basis they may help to prevent or control the symptoms of persistent asthma—asthma with symptoms that last at least two days per week or two nights per month. They also are prescribed for children with frequent or more severe asthma attacks and for those who dislike or have difficulty using asthma inhalers. Although leukotriene inhibitors may decrease the need for inhaled beta-agonists or **corticosteroids**, they are not used to treat asthma attacks. Leukotriene inhibitors also may be used to treat symptoms of allergic rhinitis or short-term seasonal allergies, including sneezing, runny nose, **itching**, and **wheezing**.

Description

Leukotriene inhibitors are often called leukotriene:

- blockers
- modifiers
- antagonists
- pathway modifiers

When they were first introduced in 1996, leukotriene inhibitors represented the first new class of asthma medication in two decades. Classified as anti-inflammatories, they were originally developed to improve lung function in asthmatics by relaxing the smooth muscles around the bronchial airways and by reducing lung inflammation.

Types of leukotriene inhibitors

The available leukotriene inhibitors are: montelukast (Singulair), zafirlukast (Accolate), and zileuton (Zyflo).

Montelukast and zafirlukast are leukotriene-receptor antagonists that prevent leukotriene from binding to cell receptors and initiating the chain of events leading to symptoms of allergy and asthma. Montelukast works rapidly. It is the only leukotriene inhibitor that has been approved by the U.S. Food and Drug Administration (FDA) for use in children as young as two, as well as for the treatment of seasonal allergies.

Zafirlukast is a synthetic peptide that inhibits the receptor binding of three leukotreines (LTC4, LTD4, and LTE4) that cause smooth muscle constriction. It is used for mild to moderate persistent asthma, exercise-induced asthma, and the management of allergic rhinitis in those aged seven and older.

Zileuton is a 5-lipooxygenase pathway inhibitor that interferes with the synthesis of LTA4, LTC4, LTD4, and LTE4. It is used to treat chronic asthma in adolescents and adults.

Effectiveness

Leukotriene inhibitors may be prescribed along with **inhaled corticosteroids** for control of mild to moderate, persistent asthma. Used alone they are less effective than low-dose inhaled corticosteroids. However, they enable some people to reduce their doses of inhaled corticosteroids. Leukotriene inhibitors may be an option for people with mild asthma who want to avoid corticosteroids, which can cause serious side effects with long-term use. When used in conjunction with beta-agonists, leukotriene inhibitors reduce symptoms and may lower the beta-agonist usage.

Leukotriene inhibitors appear to decrease the symptoms of seasonal allergic rhinitis. Although they may relieve nasal congestion better than **antihistamines**, they are less effective than corticosteroid nasal sprays. A leukotriene inhibitor combined with

an antihistamine may be more effective than either drug alone.

Leukotriene inhibitors have helped some children who suffer from nocturnal asthma, exercise- and aspirin-induced asthma, allergic rhinitis, and seasonal allergies.

Clinical studies

Montelukast appears to be an effective asthma controller in about one-third of patients. Another one-third receives no benefit. However, most long-term studies have found that standard inhaled corticosteroids are more effective for controlling asthma than either beta-agonists or leukotriene inhibitors.

A 2003 analysis of 13 clinical studies found that Singulair and Accolate resulted in 60% more asthma flare-ups and other symptoms as compared with traditional asthma treatments. Patients using inhaled corticosteroids had fewer daytime symptoms and night awakenings than those taking Singulair or Accolate. The researchers advised against switching to a leukotriene inhibiter unless the dosage of inhaled medication is less than 400 micrograms per day.

A 2005 study sponsored by Merck, the maker of Singulair, found that a one-year course of Singulair was useful for treating two- to five-year-olds with occasional asthma attacks that were triggered by respiratory infections. Singulair reduced this type of asthma flare-up by 32% as compared with a control group receiving a placebo. Singulair also delayed the onset of the first asthma flare-up and reduced the need for inhaled medication. However, it did not reduce the length or severity of the flare-up once it had begun. The researchers suggested that children with infection-triggered asthma should begin taking a leukotriene inhibitor before the start of the flu season or at the onset of an upper-respiratory-tract infection.

Another 2005 study found that children whose asthma improved with montelukast alone were younger and had had asthma for a shorter period of time as compared with children whose asthma improved only with inhaled corticosteroids. Among the children whose lung function improved by at least 7.5%, 5% took montelukast alone, 23% were on inhaled corticosteroids only, and 17% were on both medications.

Other uses

Leukotriene inhibitors have been used successfully to treat inflammations of the esophagus (esophagitis) or stomach and intestines (**gastroenteritis**) that are caused by white blood cells called eosinophils that are involved in allergic reactions. Montelukast has been used to successfully treat symptoms of interstitial **cystitis**, a chronic inflammation of the bladder.

Recommended dosage

Montelukast is taken once per day in the evening so as to relieve morning allergy symptoms. Although dosing may vary, average daily doses of montelukast for asthma and seasonal allergies are: children aged 1–5: one 4-mg chewable tablet or 4-mg oral granules (one packet), swallowed whole or mixed in a spoonful of soft food; children aged 6–14: one 5-mg chewable tablet; children over 14 and adults: one 10-mg tablet.

The average doses of zafirlukast for children aged 7–11 are 10-mg tablets twice a day. Children aged 12 and older and adults usually take 20-mg tablets twice a day. Zafirlukast is taken one hour before or two hours after a meal, since food reduces its bioavailability by about 49%.

The average dose of zileuton is a 600-mg tablet four times per day for children aged 12 and older and adults.

Leukotriene inhibitors are expensive. Missed doses should be taken as soon as possible unless it is almost time for the next dose, in which case the dose should be skipped.

Precautions

Although leukotriene inhibitors are considered safe, they can raise the levels of liver enzymes. The FDA recommends **liver function tests** monthly for the first three months on medication, followed by quarterly monitoring for the next year, and continued interim testing. Zileuton is contraindicated for those with elevated liver enzymes, active **alcoholism**, or **liver disease**. Increased levels of liver enzymes may be detectable in the blood within two months of starting zileuton. Zileuton can affect liver function and, one rare occasions, can damage the liver.

It is unclear whether leukotriene inhibitors should be taken during **pregnancy**. Zafirlukast and zileuton should not be used by a woman who is **breastfeeding**. Both medications have been found to increase the risk of mild to moderate respiratory tract infections in patients aged 55 and older.

Medical conditions that may interfere with the use of montelukast include: allergies to **aspirin** or non-steroidal anti-inflammatories (NSAIDs); liver disease, which can increase the blood levels of the drug; and **phenylketonuria** because chewable tablets may contain aspartame.

KEY TERMS

Allergic rhinitis—Nasal symptoms caused by an allergic reaction.

Asthma—A disease that causes the bronchial airways to narrow, swell, and produce mucus, making breathing difficult.

Beta-agonist—Beta2-agonist; beta-adrenergic agonist; a bronchodilator medication—inhaled or oral—that relaxes the muscles surrounding the airways to relieve asthma symptoms.

Corticosteroids—Inhaled medications for long-term control of asthma.

Leukotrienes—A class of small molecules produced by cells in response to allergen exposure; they contribute to allergy and asthma symptoms.

Montelukast (Singulair)—An inhibitor that prevents leukotrienes from binding to cell receptors; taken over time, montelukast can reduce or prevent symptoms of asthma and allergies.

Zafirlukast (Accolate)—An inhibitor that prevents leukotrienes from binding to cell receptors; taken over time, zafirlukast can help reduce or prevent asthma symptoms.

Zileuton (Zyflo)—A medication that interferes with the biosynthetic pathway that produces leukotrienes; used to help prevent asthma attacks.

A healthcare provider should be contacted if an increased number of short-acting bronchodilator inhalations are needed to relieve an acute asthma attack or if more than the maximum number of daily inhalations are required while using zileuton.

To be effective montelukast and zafirlukast must be taken at the same time every day. Zileuton must be taken at regularly spaced intervals every day, even if asthma symptoms appear to improve. Montelukast should be continued through an acute asthma attack in addition to rescue medication.

Side effects

Although leukotriene inhibitors generally have few side effects and those may subside as the body adjusts to the drug, headaches are common with these medications. Headaches occur in 18–19% of those taking montelukast and in 25% of those taking zileutin. Among 7 to 11 year olds on zanfirlukast, 4.5% suffer from headaches, as do 12.9% of those aged 12 and over.

Other less common side effects of leukotriene inhibitors include:

- rash
- fatigue
- dizziness
- abdominal pain
- nausea and vomiting
- diarrhea

Montelukast appears to cause fewer side effects than other leukotriene inhibitors and is less likely to affect the liver. Side effects occurring in less than 4.2% of patients include:

- heartburn
- weakness
- fever
- nasal congestion
- cough
- dental pain
- rarely, pus in the urine

Rare side effects of zileuton include:

- itching
- flu-like symptoms
- upper right abdominal pain
- yellow eyes or skin (jaundice)

Interactions

Drugs that may interact with montelukast include:

- aspirin
- NSAIDs
- phenobarbital
- rifampin

Zafirlukast and zileuton can raise the blood levels of the asthma medication theophylline (Theo Dur and others) and the blood thinner warfarin (Coumarin). Theophylline levels and blood-clotting times should be monitored frequently.

Medications that may interact with zafirlukast include:

- aspirin
- blood pressure medications
- some seizure medications

Medications that may interact with zileuton include:

- the beta-blocker propanolol
- beta-agonists
- terfenadine (Seldane and others)

Resources

BOOKS

Barnes, Peter J., et al. *Asthma and COPD: Basic Mechanisms and Clinical Management*. 2nd ed. Amsterdam; London: Academic, 2009.

Firestein, Gary S., et al. *Kelley's Textbook of Rheumatology*. Philadelphia: Saunders/Elsevier, 2009.

PERIODICALS

"Asthma: Corticosteroids Are More Effective than Beta-Agonists or Leukotriene Antagonists." *Health & Medicine Week* (December 20, 2004): 77.

"Asthma: Journal Publishes Research on Tailoring Asthma Treatment in Children." *Health & Medicine Week* (February 28, 2005): 75.

Banasiak, Nancy Cantey, and Mikki Meadows-Oliver. "Leukotrienes: Their Role in the Treatment of Asthma and Seasonal Allergic Rhinitis." *Pediatric Nursing* 31, no. 1 (January/February 2005): 35–8.

Ducharme, F. M. "Inhaled Glucocorticoids Versus Leukotriene Receptor Antagonists as Single Agent Asthma Treatment: Systematic Review of Current Evidence." *British Medical Journal* 236, no. 7390 (March 22, 2003): 621–6.

OTHER

Lehnert, Paul. "Leukotriene Modifiers for Allergic Rhinitis." *Health Guide A-Z*. WebMD. October 8, 2003 [cited March 14, 2005]. http://www.webmd.com/allergies/leukotriene.

Mayo Clinic Staff. "Medications and Immunotherapy for Asthma." *Asthma Center*. MayoClinic.com. August 13, 2004 [cited March 14, 2005]. http://www.mayoclinic.com/invoke.cfm?objectid = 58BCFCCC-BB00-4E67-A29876A9D30B65ED.

ORGANIZATIONS

American Academy of Allergy, Asthma & Immunology, 555 East Wells Street, Suite 1100, Milwaukee, WI, 53202-3823, (414) 272-6071, http://www.aaaai.org.

Childhood Asthma Research and Education (CARE) Network. National Heart, Lung, and Blood Institute, 6701 Rockledge Drive, MSC 7952, Bethesda, MD, 20892-7952, (301) 435-0202, (301) 480-3557, taggartv@nhlbi.nih.gov, http://www.asthma-carenet.org.

Margaret Alic, Ph.D.

Levodopa *see* **Antiparkinson drugs**

Levothyroxine *see* **Thyroid hormones**

LGV *see* **Lymphogranuloma venereum**

Lice infestation

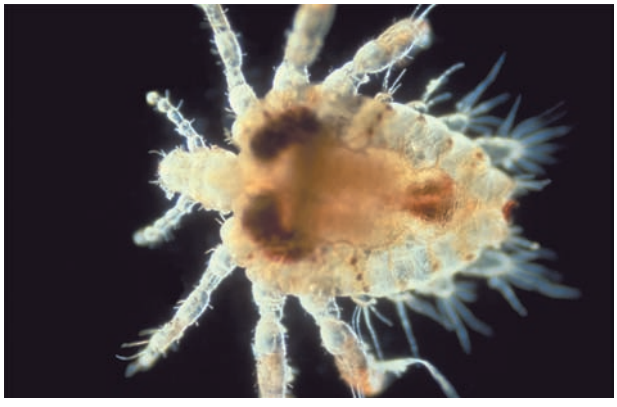
Definition

Lice infestation is a condition in which large numbers of lice are present on a person's scalp, body, or pubic area. It is called an infestation rather than an infection because the parasites live on the skin and outside of the body rather than in the internal organs. Lice are tiny insects that can spread from one person to another through close contact; through sharing such personal items as clothing, hats, combs, or hairbrushes; or through lying on a bed, pillow, or carpet that has been in contact with someone with lice.

Demographics

The demographics of lice infestation vary depending on the type of lice involved. On the whole, lice infestations are common in the general population; there are at least 12 million cases in the United States each year, although this figure is only an estimate. Head lice infestations are often not reported because people find them socially embarrassing—even though the Centers for Disease Control and Prevention (CDC) states that "Personal hygiene or cleanliness in the home or school has nothing to do with getting head lice." The number of all three types of lice infestations in Europe as well as North America has increased in recent years; a recent study of schoolchildren in Belgium, Turkey, and the Czech Republic found that rates of head lice infestations ranged from 9–16%.

Head lice are most common in schoolchildren between the ages of 3 and 11, and their families. Girls are more likely to be infested than boys because



A close-up view of a body louse. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

they are more likely to share clothing and other personal items with friends. It can be difficult to prevent a child from picking up head lice at school because of the amount of close contact among children and their belongings.

Body lice infest both children and adults; there is no difference in frequency between men and women. Homeless people and others who live in crowded conditions without opportunities to bathe or shower regularly are at greatest risk of getting body lice. Pubic lice are most common in people between the ages of 14 and 40 who are sexually active.

There is some seasonal difference in lice infestations in temperate climates; head lice infestations are more common during the warmer months while body and pubic lice infestations are more common in the fall and winter.

Description

Lice are a long-standing pest, having infested prehistoric humans as well as ancient humans after the invention of writing; the oldest known fossils of lice eggs are at least 10,000 years old. In modern societies, there are three related species of human lice that live on different parts of the body:

- head lice, *Pediculus humanus capitis*
- body lice, *Pediculosis humanus corporis*
- pubic lice, *Phthirus pubis,* commonly called "crab" lice

The three types of lice that infest humans are somewhat different in size and outward appearance. Head lice are 1–2 mm long, white or gray in color, and have flattened abdomens. The female louse lays her nits (eggs) close to the base of a hair shaft and attaches them to it with a sticky glue-like substance. The glue is what makes it so difficult to remove the nits from the hair shaft.

Body lice are about twice the size of head lice, between 2 and 4 mm long. The body louse lives in the seams of clothing, emerging at night to feed on the person's body. Pubic lice are smaller and broader, about 1.2 mm long. They have larger front claws, which is why pubic lice are sometimes called "crabs." The claws enable pubic lice to cling to the coarse hairs in the human groin and armpit areas.

Pediculosis capitis is an infestation of head lice. A body lice infestation is called pediculosis corporis. Pediculosis palpebrarum or Phthiriasis palpebrarum, caused by crab lice, is an infestation of the eyebrows and eyelashes.

Lice infestations are not usually dangerous. However, head lice infestations present a serious public health problem because they spread easily among schoolchildren. In general, lice infestations occur in crowded, unsanitary facilities including prison, military, and refugee camps. Lice infestations also occur frequently among the homeless.

Lice are transmitted through personal contact or infected clothing, bedding, or towels. Pubic lice are sexually transmitted. Lice do not jump, hop, or fly and they do not live on pets.

Risk factors

Risk factors for lice infestation include:

- Close body-to-body contact between family members or playmates.
- Sharing personal belongings, including headphones, combs, brushes, hats, scarves, and other personal items.
- Contact with contaminated furniture or bedding. Couch cushions and upholstery can harbor lice as well as pillows and sheets or blankets.
- Homelessness or imprisonment.
- Sexual contact with a large number of partners.

Causes and symptoms

Causes

The cause of lice infestations is the presence of head, body, or pubic lice on a person's body or in their clothing. The life cycle of lice helps to explain some of the symptoms of an infestation. When the nit or egg hatches, about 8–10 days after being laid, it produces an immature louse called a nymph. The nymph needs blood to survive. It has sucking mouth parts on its head that can pierce the skin and draw blood to feed on. Human lice feed about five times a day for 35 to 45 minutes at a time. The nymph becomes a mature adult about ten days after hatching. Its complete life cycle is between 30 and 35 days in length.

Symptoms

Lice infestations are characterized by intense **itching** caused by an allergic reaction to a toxin in the lice saliva. The itching can interfere with sleep and concentration. Repeated **bites** can lead to generalized skin eruptions or inflammation. Scratching or scraping at the bites can cause **hives** or abrasions that may lead to bacterial skin infections. Swelling or inflammation of the neck glands are common complications of head lice.

KEY TERMS

Crabs—An informal term for pubic lice.

Endemic—A condition that is always present in a given population, such as human lice infestation.

Host—An organism that is infected by a virus, bacterium, or parasite.

Infestation—A condition in which a parasite develops and multiplies on the body of its host rather than inside the body.

Insecticide—A pesticide that kills insects.

Lindane—An organic chloride, neurotoxic insecticide that kills lice.

Malathion—An organic phosphate, neurotoxic insecticide that kills lice.

Neurotoxin—A chemical compound that is toxic to the central nervous system.

Nit—The egg sac laid by adult female lice.

Nymph—The immature louse that hatches from the nit.

Pediculicide—Any substance that kills lice.

Pediculosis (plural, pediculoses)—A lice infestation.

Permethrin—A synthetic pyrethroid for killing lice.

Petroleum jelly or ointment—Petrolatum, a gelatinous substance obtained from oil that is used as a protective dressing.

Piperonyl butoxide—A liquid organic compound that enhances the activity of insecticides.

Pyrethrin, pyrethroid—Naturally-occurring insecticide extracted from chrysanthemum flowers. It paralyzes lice so that they cannot feed.

Wood's lamp—A special lamp that uses ultraviolet light to detect certain types of skin infections and infestations. It was invented in 1903 by a physicist named Robert Wood.

Some symptoms of a lice infestation depend on the area of the body that is affected:

- Head lice: Itchy scalp due to an allergic reaction to the bites of the lice; small red bumps on the head or neck; sensation of something moving over the scalp; an irritated rash caused by scratching the itchy parts of the scalp.
- Body lice: Itching and a rash caused by an allergic reaction to the bites of the lice. A long-term infestation may cause discoloration of the skin of the waist area and upper thighs. There may also be open sores caused by scratching the itching areas; these raw areas can become infected by other disease organisms.
- Pubic lice: Itching in the genital area or other body areas with coarse hair (armpits, mustache area, eyebrows, eyelashes), and visible nits or lice crawling in the affected area. Crab lice in children may be an indication of sexual activity or abuse.

Diagnosis

Examination

The steady increase in all three types of lice infestations since 1980 means that the diagnosis and treatment of such infestations is one of the most common tasks in a general medical practice. A diagnosis of lice infestation can be made in the doctor's office by examining the skin, hair, pubic area, or clothing of the affected person. The doctor can collect nits from the hair by using a fine-toothed comb or remove lice from the body with a piece of cellulose tape. The organisms can then be studied under the microscope to determine the type of lice involved. Lice usually are diagnosed by the itching. However, itching may not occur until several weeks after infestation, if at all. The tickling caused by moving lice may be noticeable. Definite diagnosis requires identification of lice or their nits.

Head lice may cause irritability in children. Scalp irritations or sores may be present. Although head lice in children are usually limited to the scalp, in adults, head lice can spread to eyebrows, eyelashes, mustaches, and beards. An adult louse may be visible as movement on the scalp, especially around the ears, nape of the neck, and center line of the crown—the warmest parts of the head. Since less than 20 mature lice may be present at a given time during infestation, the nits often are easier to spot. Nits vary in color from grayish-white to yellow, brown, or black. They are visible at the base or on the shaft of individual hairs. Applying about 10 oz (280 g) of isopropyl (rubbing) alcohol to the hair and rubbing with a white towel for about 30 seconds releases lice onto the towel for identification.

Body lice appear similar to head lice; however, they burrow into the skin and are rarely seen except

on clothing, where they lay their nits in seams. Over time, body lice infestations can lead to a thickening and discoloring of the skin around the waist, groin, and upper thighs. Scratching may cause sores that become infected with bacteria or fungi.

Pubic lice usually appear first on genital hair, although they may spread to other body hair. In young children, pubic lice are usually seen on the eyebrows or eyelashes. Pubic lice appear as brown or gray moving dots on the skin. There are usually only a few live lice present and they move very quickly away from light. Their white nits can be seen on hair shafts close to the skin. Although pubic lice sometimes produce small, bluish spots called maculae ceruleae on the trunk or thighs, usually it is easier to spot scratching marks. Small dark-brown specks of lice excretion may be visible on underwear.

Since pediculicides (medications for treating lice) are usually strong insecticides with potential side effects, it is important to rule out other causes of scratching and skin inflammation. The oval-shaped head lice nits can be distinguished from dandruff because they are glued at an angle to the hair shaft. In contrast, flat, irregularly shaped flakes of dandruff shake off easily. A healthcare professional needs to distinguish between body lice and scabies—a disease caused by skin mites—and between pubic lice and **eczema**, a skin condition.

Tests

Another test that can be performed to diagnose lice infestations involves the use of a Wood's lamp, which is a device that uses ultraviolet light to detect lice, fungal infections, and a few other types of skin infections. The patient is taken into a dark room while the doctor shines the lamp on the area that may be infested. If lice or nits are present, they will glow greenish-yellow.

Patients diagnosed with an infestation of pubic lice may be given a blood test to check for HIV and other **sexually transmitted diseases**.

Treatment

Traditional

Most treatments apply to all types of lice infestation and, particularly with head lice, treatments are an area of great controversy. The questionable safety and effectiveness of allopathic (fighting disease with remedies that produce effects different from those produced by the disease) treatments has spurred the search for alternative therapies. As of 2010, there is no single product or method that assures 100% destruction of the eggs and hatched lice after just one treatment. With any type of treatment, itching may not subside for several days.

Head lice

Most authorities believe that head lice should be treated immediately upon discovery. Before beginning any treatment:

- test a small scalp section for allergic reactions to the medication
- a vinegar rinse may help to loosen nits
- wash hair with regular shampoo

Treatments that are applied to the scalp and hair include:

- olive oil or petroleum ointment to smother the lice; cover the head with a shower cap, four to six hours per day for three to four days
- olive oil (three parts) and essential oil of lavender (one part)
- herbal shampoos or pomades
- a mixture of paw paw, thymol, and tea tree oil
- a combination of coconut oil, anise, and ylang ylang
- other mixtures of essential oils
- RID Pure Alternative, a nontoxic, hypoallergenic, dye and fragrance-free product
- a spray containing phenethyl propionate, cedar oil, peppermint oil, and sodium lauryl sulfate (LiceFreee)
- cocamide DEA (a lathering agent), triethanolamine (a local irritant), and disodium EDTA (a chelator), (SafeTek) is both a nontoxic pediculicide and a conditioner for combing out lice and nits

Cutting the hair or shaving the head may be effective. Aromatherapies also are available. Infested eyelashes and eyebrows should be treated with petroleum jelly for several days and the nits should be plucked off with tweezers or fingernails.

Body lice

Treatment for body lice is a thorough washing of the entire body and replacing infected clothing. Clothing and bedding should be washed at 140°F (60°C) and dried at high temperature, or dry-cleaned.

Pubic lice

A common herbal treatment for pubic lice consists of:

- oil of pennyroyal, *Mentha pulegium*, 25%
- oil of garlic, *Allium sativum*, 25%
- distilled water, 50%

The mixture is applied to the pubic hair once a day for three days. Anyone with pubic lice should be tested for other sexually transmitted diseases.

Nit removal

Neither alternative nor allopathic treatments will kill all lice nits. Hair and pubic lice nits must be removed manually to prevent re-infestation as the eggs hatch. Manual removal alone may effectively treat a lice infestation.

Before removing nits, one of the following procedures may be used:

- 50% vinegar rinse to loosen the nits
- wiping individual locks of hair from base to tip with a cloth soaked in vinegar
- 8% formic acid solution applied to the hair for 10 minutes, rinsed out, and towel-dried
- catching live lice with a comb, tweezers, fingernails, or by sticking them with double-sided tape
- enzymatic lice-egg remover

Furthermore, hair should be clean, damp, and untangled and hair conditioner should not be used on hair treated allopathically. Clothing should be removed and a towel placed between the hair and shoulders. Divide hair into 6 square-inch (6 sq.-cm.) sections. Clips or elastics can be used to divide long hair. This will help ensure that the entire scalp is inspected.

Nits are manually removed with:

- any fine-toothed comb, including pet flea combs
- a specialized nit comb (LiceMeister, LiceOut)
- a battery-powered vibrating or anti-static comb
- tweezers
- baby safety scissors
- fingernails

To comb out nits, comb along each hair section from scalp to tip. Between each passing, dip the comb in water and wipe with a paper towel to remove lice and nits. Hold the comb to the light to be sure it is clean. If necessary, clean comb with a tooth or fingernail brush or dental floss. Work under a good light using a magnifying glass if necessary. Do not rush—long, thick hair may take an hour to comb out thoroughly. Wash towels and clothing after combing. This treatment should be repeated at least twice a week for at least two weeks.

Reinfestation

Reinfestation occurs often with all types of lice due to:

- ineffective or incomplete treatment
- chemical-resistant lice
- failure to remove live nits
- failure to treat all infected household members, playmates, or sexual partners
- failure to remove nits from clothing, bedding, towels, or other items
- reinfestation from another source

Reinfestation with body or pubic lice can be prevented by washing underclothes, sleepwear, bedding, and towels in hot, soapy water and drying with high heat for at least 20 minutes. Clothing infected with body lice should be ironed under high heat. Sexual partners should be treated for public lice simultaneously and should re-examine themselves for several days.

To prevent head lice reinfestation:

- Repeat lice checks and nit removal daily until none are found.
- Notify school, camp, or day care center, and parents of playmates.
- Check and if necessary treat household members, playmates, schoolmates, school or daycare staff, and others in close contact with an infestation.
- Treat combs and brushes with rubbing alcohol, Lysol, or soapy water above 130°F (54°C).
- Wash all bedding, clothing, headgear, scarves, and coats with soapy water at 130°F (54°C) and dry with high heat for at least 20 minutes.
- Wash or vacuum stuffed animals and other toys.
- Vacuum all helmets, carpets, rugs, mattresses, pillows, upholstery, and car seats.
- Remove the vacuum cleaner bag after use, seal in a plastic bag, and place in the outside garbage.
- Non-washable items should be dry cleaned or sealed in a plastic bag for up to four weeks.
- Lice pesticide sprays for inanimate objects are toxic and are not recommended.
- Repeat treatment if necessary.

Infested eyelashes are treated with a thick coating of prescription petroleum ointment, applied twice daily for ten days.

Drugs

All types of lice are treated allopathically with insecticidal lotions, shampoos, or cream rinses.

This woman's eyelashes are infested with nits, or eggs, of a body louse. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Experts disagree about the effectiveness and/or safety of pediculicides. Pediculicides do not kill nits, so nit removal and a second application in seven to 10 days may be necessary. Pediculicides can be poisonous if used improperly or too frequently and overuse can lead to the proliferation of chemically resistant lice. The residue may remain on the hair for several weeks and can cause skin or eye irritations.

Pediculicides should *not* be used:

- near broken skin, eyes, or mucous membranes
- in the bathtub or shower
- by pregnant or nursing women or children under two
- by those with allergies, asthma, epilepsy, or some other medical conditions

PYRETHROIDS. All U.S. Food and Drug Administration (FDA)-approved nonprescription pediculicides contain relatively safe and effective pyrethroids. Insecticidal pyrethrins (0.33%) (RID, A-200) are extracts from chrysanthemum flowers. Permethrin (1%) (Nix) is a more stable synthetic pyrethrin. Pyrethroid pediculicides usually contain 4% piperonyl butoxide.

To treat with pyrethroids:

- Apply for specified time, usually ten minutes.
- Thoroughly rinse out.
- Do not wash hair for one or two days after treatment.
- Do not use cream rinse, hair spray, mousse, gels, mayonnaise, or vinegar before or within one week after treatment. These products may reduce pediculicide effectiveness.

During the 1990s, as schools began requiring children to be lice and nit-free, the use of pyrethroids rose significantly and the FDA began receiving reports of ineffectiveness. The FDA ordered new labeling of pyrethroid pediculicides on the outside of the carton, in simpler language, and with more information in 2006. Permethrin sprays for treating mattresses, furniture, and other items are not recommended.

OTHER INSECTICIDES. Prescription insecticides are used when other lice treatments fail or cannot be used. These pesticides include:

- Malathion (0.5% in Ovide), a neurotoxic organophosphate, was withdrawn from the U.S. market due to an increase in malathion-resistant lice and re-introduced in 1999. It is foul-smelling and flammable. Sometimes infested clothing is treated with a 1% malathion powder. The chief advantage of malthion is that it is effective against lice that have developed resistance to lindane and permethrin.
- Lindane (1% or higher; Kwell), an organochloride neurotoxin, can induce seizures and death in susceptible people, even when used according to the directions. In 2003 the FDA required new labeling and a reduction in bottle size.
- Ivermectin (Stromectol), an oral treatment for intestinal parasites, is effective against head lice but has not been approved for that use by the FDA as of 2010. It is approved in Europe for the treatment of head lice, and a recent clinical trial reported in the *New England Journal of Medicine* in March 2010 that oral ivermectin is superior to malathion for difficult-to-treat head lice.

Prognosis

Despite the presence of chemically resistant lice and the thoroughness required to prevent reinfestation, essentially all lice infestations can be eradicated eventually. Lice infestations by themselves are not fatal; however, body lice are dangerous because they can transmit three potentially fatal illnesses: **typhus**, **relapsing fever**, and **trench fever**. Pubic lice are not known to spread other diseases as of 2010. In 2009, 25% of head lice from homeless persons in San Francisco were found to be carrying *Bartonella quintana*, the bacterium that causes trench **fever**. This finding suggests that head lice as well as body lice are potential carriers of emerging diseases.

Prevention

Prevention of lice infestation depends on adequate personal hygiene and the following public health measures:

- avoid sharing combs, brushes, hair accessories, hats, towels, or bedding
- check hair and scalp weekly for lice and nits
- limit the number of sexual partners

Regular lice checks in schools and "no nit" reentry policies have not been shown to be effective. The American Academy of Pediatrics, the Harvard School of Public Health, and the National Association of School Nurses recommend their elimination, although many healthcare professionals disagree.

Scientists have identified both the gene that enables head and body lice to digest blood and the gene that helps lice combat deadly infections, with the potential for new treatments and preventatives for lice infestation.

Resources

BOOKS

Dlugosz, Cynthia Knapp. *The Practitioner's Quick Reference to Nonprescription Drugs*. Washington, DC: American Pharmacists Association, 2009.

Goroll, Allan H., and Albert G. Mulley, Jr., eds. *Primary Care Medicine: Office Evaluation and Management of the Adult Patient*. 6th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, 2009.

Marquardt, William C., ed. *Biology of Disease Vectors*. 2nd ed. Burlington, MA: Elsevier Academic Press, 2005.

Somervill, Barbara A. *Lice: Head Hunters*. New York: PowerKids Press, 2008.

PERIODICALS

Bonilla, D.L., et al. "*Bartonella quintana* in Body Lice and Head Lice from Homeless Persons, San Francisco, California, USA." *Emerging Infectious Diseases* 15 (June 2009): 912–15.

Burgess, I.F. "Current Treatments for Pediculosis Capitis." *Current Opinion in Infectious Diseases* 22 (April 2009): 131–36.

Chosidow, O., et al. "Oral Ivermectin Versus Malathion Lotion for Difficult-to-treat Head Lice." *New England Journal of Medicine* 362 (March 11, 2010): 896–905.

Falagas, M.E., et al. "Worldwide Prevalence of Head Lice." *Emerging Infectious Diseases* 14 (September 2008): 1493–94.

Galiczynski, E.M., Jr., and D.M. Elsteon. "What's Eating You? Pubic Lice (*Pthirus pubis*)." *Cutis* 81 (February 2008): 109–14.

Idriss, S., and J. Levitt. "Malathion for Head Lice and Scabies: Treatment and Safety Considerations." *Journal of Drugs in Dermatology* 8 (August 2009): 715–20.

Pilger, D., et al. "Household-wide Ivermectin Treatment for Head Lice in an Impoverished Community: Randomized Observer-blinded Controlled Trial." *Bulletin of the World Health Organization* 88 (February 2010): 90–96.

OTHER

Buxton, Patrick. *Lousology 101: Images and Biology of Head Lice*. National Pediculosis Association (NPA). http://www.headlice.org/faq/lousology.htm (accessed September 23, 2010).

Centers for Disease Control and Prevention (CDC). *Lice*. May 16, 2008. http://www.cdc.gov/lice (accessed September 23, 2010).

Guenther, Lyn, et al. "Pediculosis." *eMedicine* May 5, 2009. http://emedicine.medscape.com/article/225013-overview (accessed September 23, 2010).

"Lice." *MayoClinic.com*. February 18, 2010. http://www.mayoclinic.com/health/lice/DS00368 (accessed September 23, 2010).

Rapini, Ronald P. "Parasitic Infestations." American Academy of Dermatology. http://www.aad.org/education/students/parainfest.htm (accessed September 23, 2010).

ORGANIZATIONS

American Academy of Dermatology, PO Box 4014, Schaumburg, IL, 60168-4014, (847) 330-0230, (866) 503-SKIN (503-7546), (847) 240-1859, http://www.aad.org.

American Academy of Family Physicians (AAFP), PO Box 11210, Shawnee Mission, KS, 66207, (913) 906-6000, (800) 274-2237, (913) 906-6075, contactcenter@aafp.org, http://www.aafp.org.

American Academy of Pediatrics (AAP), 141 Northwest Point Boulevard, Elk Grove Village, IL, 60007, (847) 434-4000, (847) 434-8000, http://www.aap.org.

Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

National Pediculosis Association (NPA), 1005 Boylston Street, Suite 343, Newton, MA, 02461, (800) 323-1305 ext 7971, (800) 235-1305, npa@headlice.org, http://www.headlice.org.

U.S. Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD, 20993, (888) 463-6332, http://www.fda.gov.

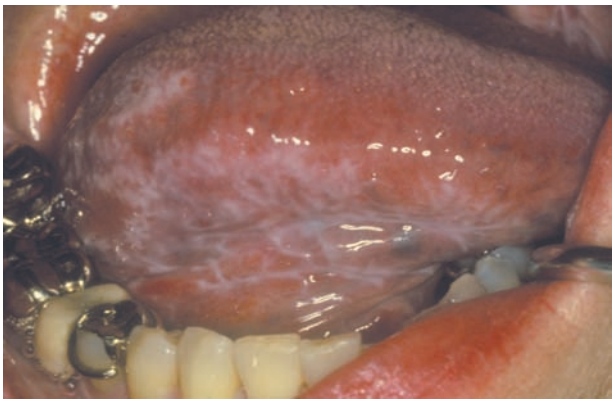
World Health Organization (WHO), Avenue Appia 20, 1211 Geneva 27, Switzerland, + 41 22 791 21 11, + 41 22 791 31 11, info@who.int, http://www.who.int/en/.

Rebecca J. Frey, PhD
Margaret Alic, PhD

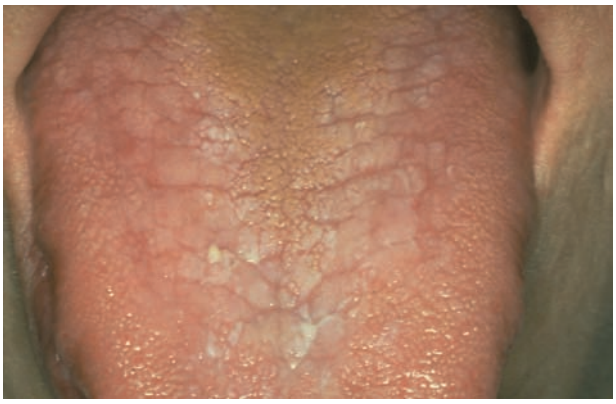
Lichen planus

Definition

Lichen planus is a chronic mucocutaneous (relating to the skin and mucous membrane) condition of unknown origin that produces rows of small, shiny,



Lichen planus appearing under the tongue. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*



One example of lichen planus on the tongue. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

flat–topped, itchy pink or purple raised papules or lesions (bumps) or **rashes** (spots) on the wrists, forearms or lower legs, especially in middle-aged patients. It sometimes also affects the mucous membranes, such as those within the mouth and genitals. The name refers to the inflammatory appearance of the skin.

Demographics

The condition affects females more than males, in an approximate ratio of three to two. It also affects middle-aged people more often than younger or older people. Infants and children rarely get the condition. Lichen planus is found throughout the world and is equally distributed among races. It affects between one and two percent of the world' population. The majority of the people affected by licken planus consist of middle-aged women. People with **hepatitis C** or **cirrhosis** (liver scarring) are also more likely to get lichen planus.

Description

The condition is not contagious nor infectious. However, it is difficult to treat, with reoccurrences coming back for years even with proper treatment. Lesions are found on the skin, genitals, and in the mouth. Most cases resolve spontaneously within two years. These features usually characterize the affected skin: purple in color, shape of polygonal papules, without depth (flat to the skin's surface), and itchy but without any apparent reason (pruritic). They are most often located on the wrists and ankles. When the condition begins to heal, the skin turns a brownish or blue–black color, which may remain for a long time.

Causes and symptoms

No one knows what causes lichen planus, although some experts suspect that it is an abnormal immune reaction following a viral infection, probably aggravated by **stress**. The condition does not involve any known pathogens and it cannot be passed from one person to another (not contagious). The condition is similar to symptoms caused by exposure to arsenic, bismuth, gold, iodides, quinide, **diuretics**, or developers used in color photography. The rashes that it produces are called lichenoid reactions. These reactions are further classified as lichenoid mucositis (of the mucosa) or lichenoid **dermatitis** (of the skin). Either one can be caused by heart disease, arthritis, medications used to control high blood pressure, and reactions to **allergies**. Occasionally, lichen planus in the mouth appears to be an allergic reaction to medications, filling material, dental hygiene products, chewing gum, or candy.

Symptoms can appear suddenly, or they may gradually develop, usually as a rash on the insides of the wrists, forearms, ankles, or legs. The rash may also be present on the scalp, neck, lower back, nails of the fingers and toes, or on the mucous membranes of the nose, mouth, vagina, penis, and anus. Lesions on the skin may be preceded by a dryness and metallic taste or burning in the mouth.

Once lesions appear, usually in rows, they change over time into flat, glistening, purple lesions marked with white lines or spots. Color may change from purple to pink, and then to red. Mild to severe **itching** is common. White, lacy lesions are usually painless, but eroded lesions often burn and can be painful. A soreness or burning sensation can emerge when symptoms involve the mucous membranes. When the nails are affected, their appearance often becomes split, thin, and grooved. The nails may eventually be lost. Hair on the scalp, when lichen planus is apparent,

KEY TERMS

PUVA—A type of phototherapy that combines the oral or topical photosensitizing chemical psoralen, plus long–wave ultraviolet light-A (UVA).

becomes thin, with the scalp itself appearing red and irritated. All of the hair on the scalp may be lost. As the lesions clear up, they usually leave a brown or gray discoloration behind, especially in dark skinned people. Rashes on the nails or scalp may leave permanent scarring.

Lichen planus in the mouth, sometimes called oral lichen planus, occurs in six different forms with a variety of symptoms. They may appear as lacy-white streaks, white plaques, or eroded ulcers. The streaks consist of small, pale reddish, slightly raised bumps, often on the tongue or inside the cheeks. Often the gums are affected, so that the surface of the gum peels off, leaving the gums red and raw. The area around the mouth may be painful and tender, with a burning or itching sensation. It may also feel dry and have a metallic taste to it. Food and beverages may have a diminished taste to them.

Diagnosis

A medical history of the patient is gathered, along with the performance of a **physical examination**. A doctor can probably diagnose the condition simply from looking at the characteristic lesions, but a **skin biopsy**, usually from a punch biopsy test, may be needed to confirm the diagnosis. A punch biopsy test removes a tiny section of the deeper layers of the skin. The biopsy, which is of an average depth of 0.25 inch (6 millimeters), is examined under a microscope to detect whether lichen planus is present.

Treatment

There is no cure for lichen planus. Treatment, which is usually difficult and long-term, is aimed at easing symptoms. Itching can be treated with steroid creams and oral **antihistamines**. Cool compresses and baths containing colloidal oatmeal can also help. Cortisosteroid ointment may be applied to the skin for minor irritations. Severe lesions can be treated with **corticosteroids** by mouth, or combinations of photochemotherapy (such as PUVA) and griseofulvin. PUVA, which stands for psoralen (also called psoralene) plus UVA treatment, is used when the patient takes an oral dose of psoralen to sensitize the skin and then the skin is exposed to ultraviolet-A (UVA) light. Griseofulvin (also called grisovin) is an antifungal drug.

Immunosuppressant medications may also be used. Hydroxychloroquine (Plaquenil), an antimalaria drug, is sometimes provided to reduce inflammation. Tacrolimus (FK-506 or Fujimycin), an immunosuppressive drug, is often taken to reduce allergic symptoms. Immune-modulating medication, such as imiquimod (Aldara) or tacrolimus (Protoic) may also be used. Dapsone, which is often given to treat **acne**, is sometimes used too. Aloe vera is applied to help return the damaged skin to its normal state.

Patients with lesions in the mouth may find that regular professional cleaning of the teeth and conscientious dental care improve the condition. Using milder toothpastes instead of tartar control products also seems to lessen the number of ulcers and makes them less sensitive. A combination of oral corticosteroids and extra-strength corticosteroid ointments applied to the affected areas are often used for mucous membranes.

Even though lichen planus may go away with treatment, it can come back, sometimes years later.

Prognosis

While lichen planus can be annoying, it is usually fairly benign and clears up on its own. It may take months to reach its peak, but it usually clears up within 18 months. Normally, lichen planus is non–cancerous. However, long-term lesions associated with lichen planus can result in increased risk from squamous cell carcinoma, which is a type of skin **cancer**.

Prevention

It is recommended that people with at increased risk from lichen planus do not use tobacco products, such as cigarettes, because tobacco adds to the risk of squamous cell carcinoma. Regular examinations are advised for people more likely to contract lichen planus so that any changes to mucous membranes or the skin can be regularly monitored by medical professionals.

Resources

BOOKS

Beers, Mark H., et al., editors. *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Sollecito, Thomas P., editor. *Oral Soft Tissue Lesions*. Philadelphia: Saunders, 2005.

Trozak, Daniel J., Dan J. Tennenhouse, and John J. Russell. *Dermatology Skills for Primary Care: An Illustrated Guide*. Totowa, NJ: Humana Press, 2006.

OTHER

"Lichen Planus." Mayo Clinic. (August 15, 2008), http://www.mayoclinic.com/health/lichen–planus/DS00782. (accessed September 6, 2010).

"Lichen Planus." Medline Plus, National Library of Medicine and National Institutes of Health. (October 8, 2008), http ://www.nlm.nih.gov/medlineplus/ency/article/000867.htm. (accessed September 6, 2010).

Carol A. Turkington

Lichen simplex chronicus

Definition

Lichen simplex chronicus (LSC) is a chronic inflammation of the skin (**dermatitis**) characterized by small, round itchy spots that thicken and become leathery as a result of scratching. Various degrees of scaling also occur from repeated scratching or rubbing. The inflammation occurs most frequently in the following areas: scalp, outer lower part of lower leg, knee, wrist, ankle, side and back of neck, forearm, elbow, scrotum, vulva, anal area, upper eyelid, ear opening, and fold behind ear. The itchiness felt by the person may be so intense that he or she is unable to stop. Soon, the patient continues to scratch out of habit, when begins the progression of the brown, thick, leathery skin.

Demographics

The chronic inflammation can occur in any human. It is not known to occur more or less frequently with respect to race. Its exact frequency has not been identified by the medical community. However, it is more common in women than in men. It is also more prevalent in adults age 30 to 50 years. People with previous skin conditions or with a family history of skin disorders, such as **psoriasis** and **eczema**, are more likely to develop lichen simplex chronicus. People are not at risk from dying of lichen simplex chronicus.

Description

Also termed neurodermatis and scratch dermatitis, lichen simplex chronicus is the result of chronic skin irritation. Initial irritation causes **itching**, and in turn, itching causes scratching. Scratching usually leads to further irritation, which damages the skin. The possibility of infection is greatly increased when the outer layer of protective skin is broken. Skin usually repairs itself quickly. However, in the case of lichen simplex chronicus, healing skin causes more itching and more scratching causes a thickening of the skin (lichen). The small skin patches are usually one to 10 inches (3–25 centimeters) in diameter.

Some complications from the condition if present for long periods include bacterial skin infection, permanent scarring, and permanent changes in the color of the skin.

Causes and symptoms

The cause of lichen simplex chronicus is not known. It is seen as often being caused by constant rubbing of the skin, such as in disorders like psoriasis and eczema. It may also occur when something continually irritates the skin, such as clothing. It may also result when such conditions as **anxiety**, depression, or nervousness occurs. The rubbing begins the chain of events that leads from itching to scratching and then to the presence of leather-like skin patches. Children are susceptible to the disorder because they often rub and scratch their skin, such as when insect **bites** occur. Mentally disabled children that have repetitive motions as part of their disability are also at higher risk for contracting lichen simplex chronicus.

Symptoms include chronic itching, which is often accompanied by nervous tension. The appearance of scratch marks and leathery skin patches can be found anywhere on the body. A prolonged lichen simplex chronicus can result in brown-colored pigmentation at the site of irritation. Signs of infection include a yellowish, thick fluid coming from the excessively scratched areas. **Pain** may also be another sign of infection. Other symptoms include **skin lesions** that are often located on the wrist, neck, wrist, forearms, inner elbow, thighs, lower leg, back of knee, and rectum/anus area. The lesions are usually raw looking and darkened or reddened, and include scratch marks, defined borders, and extended skin lines.

Diagnosis

A dermatologist, a physician specializing in the study and treatment of skin disorders, can make a diagnosis after a visual examination. Specifically, the medical professional looks at the appearance of the skin, and determines the period that itching and scratching have occurred. A patch test, sometimes also called a contact delayed hypersensitivity allergy

test, is used to eliminate other disorders that may be the cause. Small drops of various diluted chemicals are placed onto the skin to see if an allergic reaction occurs.

A skin lesion biopsy, also called a punch biopsy, may be needed to confirm a diagnosis of lichen simplex chronicus. The biopsy (a tiny piece of removed skin) is sent to a laboratory so it can be analyzed under a microscope. The result will confirm whether or not the condition is due to lichen simplex chronicus or another disorder such as **lichen planus**.

Treatment

Treatment of the itching is necessary to stop the scratching and resulting skin damage. There are a number of ways to stop itching. Perhaps the most important is to cut fingernails very short. Ice can substitute for the relief of scratching. Heat and fuzzy clothing worsen itching; cold and smooth clothing pacify it. If the itching is persistent, **dressings** may be applied to the affected areas.

Among the topical medications that relieve itching are a number of commercial preparations containing menthol, camphor, eucalyptus oil, and aloe. Topical cortisone is also available without a prescription. Some preparations also contain **antihistamines**, which penetrate intact skin poorly. All these medicines work better under occlusion, which means putting a waterproof barrier like a rubber glove, plastic wrap, or cloth dressing over them. For broken skin, **topical antibiotics** like bacitracin help prevent infection. These preparations should be used early to forestall further damage to the skin.

Reducing the buildup of thick skin or thickened lesions may require medicines that dissolve or melt keratin, the major chemical in skin's outer layer. These keratolytics include urea, lactic acid, and salicylic acid. Lotions or soaps containing coal tar may also be recommended.

Resistant cases of lichen simplex chronicus will often respond to cortisone-like drugs injected directly into the lesions.

Sedatives or tranquilizers may be prescribed to combat the nervous tension and anxiety that often accompanies the condition.

In addition, counseling with a dermatologist may be necessary to minimize or eliminate the need to scratch and itch. Consultation with an allergist may also be needed. Specific psychological counseling in **stress** management or behavior modification should be sought for people with anxiety and stress.

KEY TERMS

Antihistamine—A chemical that interferes with the action of histamine. Histamine is part of an inflammatory response and helps to cause itching.

Callus—Thickened skin due to chronic rubbing or irritation.

Lesion—Abnormal change in tissue caused by localized disease.

Prognosis

Diligent adherence to treatment is usually rewarded with a resolution of the condition. The original cause of itching may be gone, or it may reappear. Preventive treatment in its early stages will arrest the process. Reducing stress and anxiety in one' life will help to minimize or eliminate the problem.

Prevention

Ways to prevent lichen simplex chronicus include keeping nails cut close so less damage is done to the skin when scratching occurs. Also, cover areas prone to scratching, especially if they are unconsciously scratched while sleep. Use over-the-counter creams or medications to eliminate the itchiness. Prevent dry skin by using moisturizing creams and ointments. Also, take cool baths filled with baking soda, colloidal oatmeal, or other similar ingredients that help to relieve skin irritants. When using cleansing products, such as clothing detergents, choose ones that do not contain perfumes and dyes. Maintain a healthy lifestyle that includes reducing stress and anxiety.

Resources

BOOKS

Beers, Mark H., et al., editors. *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Fauci, Anthony S. *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill, 2008.

Schwarzenberger, Kathryn, Andrew E. Werchniak, and Christine J. Ko, editors. *General Dermatology*. Edinburgh, Scotland: Saunders Elsevier, 2009.

Sollecito, Thomas P., editor. *Oral Soft Tissue Lesions*. Philadelphia: Saunders, 2005.

Trozak, Daniel J., Dan J. Tennenhouse, and John J. Russell. *Dermatology Skills for Primary Care: An Illustrated Guide*. Totowa, NJ: Humana Press, 2006.

OTHER

"Lichen Simplex Chronicus. " eMedicine, WebMD. (June 4, 2010), ht tp://emedicine.medscape.com/article/1123423–overview. (accessed September 8, 2010).

"Lichen Simplex Chronicus. " Medline Plus, National Library of Medicine and National Institutes of Health. (October 3, 2008), http ://www.nlm.nih.gov/medlineplus/ency/article/000872.htm. (accessed September 8, 2010).

"Neurodermatitis. " Mayo Clinic. (May 5, 2010), http://www.mayoclinic.com/health/neurodermatitis/DS00712. (accessed September 8, 2010).

J. Ricker Polsdorfer, MD

Life support

Definition

Life support refers to a spectrum of techniques and therapies used to maintain life after the failure of one or more vital organs. When someone is critically injured or seriously ill, life-saving techniques and therapies (such as a feeding tube, organ transplantation, heart and lung bypass machine, **cardiopulmonary resuscitation** [CPR], dialysis, defibrillator, and artificial pacemaker) are used in the attempt to sustain and save the patient' life. Such measures are often performed in such places as an operating room, emergency room (ER), intensive care unit (ICU), and ambulance. However, as such measures become more technically advanced, some become available in every day places. One such device is called the portable defibrillator, or automated external defibrillator. Bought by companies and governments, they are often ready to be used at a moment's notice in business settings and public areas.

Purpose

A patient requires life support when one or more vital organs fail, due to causes such as trauma, infection, **cancer**, **heart attack**, or chronic disease. Among the purposes of life support are to:

- Establish and maintain the ABCs of resuscitation—airway, breathing, and circulation.
- Restore the patient's homeostasis—the internal chemical and physical balance of the body.
- Protect the patient from complications of the underlying disease and its treatment.

The ABCs of life support is supported by a part of medical care that is commonly called basic life support (BLS). Within BLS, the medical professionals are called upon to care for patients with life-threatening illnesses and injuries until the patients can be provided with more comprehensive medical care. For instance, medical personnel inside an ambulance at the scene of a traffic accident are one type of person involved in BLS. These people receive BLS training in order to be certified at their position. Other people trained in BLS include firefighters, police officers, teachers, and security guards. Specific portions of the training involve guidelines of action that are to be used when coming across specific emergencies such as drowning, massive bleeding, or cardiac arrest. Once the BLS personnel transport the patient to the hospital or other medical facility, the next phase of medical care is begun—that of the advanced life support (ALS).

Precautions

Patients and families need to recognize that life support is an extremely painful, expensive, and emotionally wrenching experience. Life support exposes a patient to vast risks of further medical complications, and offers no guarantee of a positive outcome. Even in successful cases, recovery may be slow and frustrating.

Description

Successful life support begins with establishing the ABC's of resuscitation—airway, breathing, and circulation.

The airway refers to a clear and unobstructed passageway for air (primarily oxygen) to enter the lungs from outside the body and for primarily carbon dioxide to exit the lungs through the mouth and nose. The patient's airway may become blocked by:

- Foreign body obstruction, as by food or dentures
- Injury-related damage and swelling, as from a wound or surgery
- Loss of protective reflexes due to coma of any origin

Life support may begin with basic cardiopulmonary resuscitation (CPR), as in cases of cardiac arrest. Thereafter, the most common technique used to create a secure airway is insertion of an endotracheal (ET) tube through the mouth or nose into the windpipe (trachea). An alternative method of securing an airway is by **tracheotomy**, a surgical procedure in which a tube is inserted into the trachea through an incision made in the base of the throat. Of the two options, placement of an ET tube is usually quicker and more convenient, and thus occurs much more commonly. Doctors perform a tracheotomy when they cannot establish an ET

airway, or when the patient will require an artificial airway for more than a week or two.

Breathing refers to the movement of air in and out of the lungs (respiration). Inadequate breathing may result from:

- Heart disease, as in congestive heart failure
- Primary diseases of the lungs, such as pneumonia, asthma, or emphysema
- Coma of any cause, such as narcotic overdose or stroke
- Muscle fatigue or neuromuscular disease (spinal cord injury or polio)
- Pain, from rib fractures or surgery on the chest

When the patient cannot breathe sufficiently, the physician will use a ventilator, a machine that pumps air in and out of the patient's lungs. For many doctors and members of the public, the term "life support" calls up the image of an ET tube and ventilator.

Circulation refers to the adequate flow of blood around the body from the heart to vital organs. The blood delivers oxygen to all cells of the body and removes carbon dioxide from all cells. Circulation can fail due to:

- Primary disease of the heart (heart attack)
- Blood loss (trauma or internal bleeding of any cause)
- Severe infection (sepsis)
- Drug reactions or overdoses
- Extreme allergic reaction
- Severe dehydration (gastroenteritis or heat-related illness)

In order to ensure adequate circulation, the patient will require one or more intravenous (IV) tubes (catheters). The IVs may include both the short needle and tube commonly used in the hand or forearm, and longer catheters inserted into the larger and more central veins of the body. Catheters inserted into these larger veins are known as central lines. Through the IVs the patient receives fluids, drugs, and blood transfusions as needed to support the circulation.

Once the ABC's are secure, life support is directed at maintaining homeostasis, the body's delicate chemical and physical balance. In a healthy person, the body keeps precise control over many components of its makeup, such as its fluids, nutrients, and pressures. When vital organs fail, the body can no longer regulate these components, and the doctor must take steps to restore the normal state.

Preserving the body's internal equilibrium requires careful monitoring of innumerable indicators of the patient's well-being. These indicators include:

- Vital signs (heartbeats per minute, breaths per minute, blood pressure, body temperature, and weight)
- Fluids (input and output of the body)
- Blood cell counts
- Chemical substances of the body (sodium, potassium, sugar, and many others)
- Pressures in the circulation, lungs, and perhaps even the brain
- Presence of germs (bacteria, fungi) causing infection in body systems (lungs, blood, urine)

This intensive monitoring usually takes place in an intensive care unit (ICU) or critical care unit (CCU) and requires:

- Specialized physicians, such as cardiologists, intensivists, and surgeons
- Highly-skilled nursing care, often one nurse per patient around-the-clock
- Extensive support staff, such as respiratory therapists, laboratory technicians, radiology technicians, dieticians, and pharmacists
- Constant measurement of basics such as pulse, heart rhythm, and oxygen level in the blood
- Frequent inspection of the patient's alertness, color, and level of pain
- Use of catheters in the veins and arteries to withdraw blood samples and measure pressures in the circulation
- Use of tubes in the bladder (Foley catheter), stomach (nasogastric tube), and other body cavities
- Frequent laboratory tests on blood, urine, drainage from wounds, and other body specimens
- X-ray, ultrasound, computerized tomography (CT), and other imaging procedures
- Electrocardiograms

The treatments of life support include:

- Oxygen
- Intravenous fluids with sugar and basic salts
- Drugs to improve circulation and other body functions
- Antibiotics
- Transfusions
- Surgery
- Nutritional supplements by vein or stomach tube
- Tubes in body cavities (chest or abdomen) to relieve fluid buildup
- Dialysis
- Pacemaker

KEY TERMS

Cardiopulmonary—Relating to the heart and lungs.

Central line—A tube placed by needle into a large, central vein of the body.

Coma—Unconsciousness.

Defibrillation—Use of an electric shock to restore a normal heartbeat.

Endotracheal tube—A tube placed into the windpipe through the nose or mouth.

Foley catheter—A tube that drains urine from the bladder.

Homeostasis—The internal chemical and physical balance of the body.

Nasogastric tube—A tube placed through the nose into the stomach.

Neuromuscular—Relating to nerves and muscles.

Resuscitation—Treatments to restore an adequate airway, breathing, and circulation.

Sepsis—An overwhelming infection with effects throughout the body.

Tracheotomy—A surgical procedure in which a tube is inserted into the trachea through an incision made in the base of the throat.

Trauma—Serious physical injury.

Ventilator—A machine that pumps air in and out of the lungs.

Vital signs—Basic indicators of body function, usually meaning heartbeats per minute, breaths per minute, blood pressure, body temperature, and weight.

- Electrical defibrillation
- Various machines to assist heart or lung function
- Transplantation of organs or mechanical substitutes (artificial heart)
- Sedation or even temporary paralysis to enable the patient to tolerate these procedures

Preparation

The need for life support may arise suddenly and with little warning. All people should discuss in advance with family and doctor their wishes for the use of life support should a medical crisis develop. The doctor will note the preferences in the patient's record. Patients should sign documents such as an Advance Directive and Durable Power of Attorney for Health Care to express their wishes and designate a surrogate decision-maker in case of incapacitation.

Physicians and medical care providers must anticipate the possibility that a patient will require life support, perhaps suddenly. In preparation, doctors and medical staff must:

- Receive training in resuscitation skills
- Monitor patients carefully
- Maintain proper supplies and equipment
- Discuss in advance with patients and patients' families whether or not to begin life support

Aftercare

If a patient survives life support treatments, doctors will cautiously try to wean the patient from the support systems. Being able to breathe adequately without the ventilator is one major hurdle. Patients commonly fail in their first attempts to breathe on their own, often tiring out after a few hours. Thus, the doctor will reconnect the ventilator, give the patient a rest, and try again in a day or two.

As the patient regains organ function, there is less need for monitors, tests, and treatments that require an intensive care setting. The doctor may transfer the patient to a lower level of hospital care, a skilled nursing facility (SNF), or perhaps directly to home. Physical and occupational therapists may help the patient improve strength and endurance. The patient will receive continuing care from the primary doctor and specialists as needed. The patient may require prescription drugs, assist devices, and psychological therapists.

Risks

The risks and consequences of life support are enormous. These risks include:

- Physical dangers
- Emotional suffering
- Financial costs
- Societal discord

The physical dangers of life support encompass all the hazards of the patient's underlying disease and treatments. Among these risks are:

- Permanent damage to the brain, kidneys, and other vital organs caused by poor circulation or low oxygen content of the blood
- Direct damage to organs from use of medical instruments and procedures
- Infections, often with organisms that are highly resistant to antibiotics
- Abnormal blood clots
- Skin ulcers from lying immobilized for long periods
- Extreme pain
- Exposure of medical personnel to communicable diseases

The emotional consequences of life support touch patients, families, and medical caregivers. These repercussions arise from:

- The frightening environment of an ICU
- The need to make life-and-death decisions
- The anger, guilt, and grief that relate to life-threatening illness
- The fact that many lengthy and difficult treatments will end in failure

The financial costs of life support are huge. A single day of life support costs many thousands of dollars. These expenses fall on individual payers, insurance companies, health plans, and governments. All such payers face difficult decisions regarding the allotment of money for such treatment, especially in cases that are likely to be futile.

Although the removal of life support from a seriously ill or injured person may be seen as a rare occurrence in society, it has been found to be relatively common. In fact, in a 2008 study funded by the National Institute of Nursing Research, and appearing in the *American Journal of Respiratory and Critical Care Medicine*, a gradual removal of life support, called sequential withdrawal, was found to be quite common. In fact, Dr. J. Randall Curtis, the principal investigator of the study, states that the sequential withdrawal of life support: "...occurred in nearly half of the patients we studied." The study also found that, when necessary, sequential withdrawal was less traumatic to the patient's family than was the immediate removal of all life-support measures.

Society as a whole faces difficult decisions surrounding life support. Some governments have enacted regulations that establish priorities for the spending of health care resources. Patients who do not receive treatment under such rules may feel victimized by society's choices.

Resources

BOOKS

Cameron, Peter, et al., editors. *Textbook of Adult Emergency Medicine*. Edinburgh, Scotland, Churchill Livingstone/Elsevier, 2009.

Irwin, Richard S., and James M. Rippe, editors. *Irwin and Rippe's Intensive Care Medicine*. Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, 2008.

Knoop, Kevin J., et al, editors. *The Atlas of Emergency Medicine*. New York: McGraw-Hill Medical, 2010.

Marx, John A., et al, editors. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. Philadelphia: Mosby/Elsevier, 2010.

OTHER

CPR and ECC. American Heart Association. www.heart.org/HEARTORG/CPRAndECC/CPR_UCM_001118_SubHomePage.jsp. (accessed August 2, 2010).

Prolonging the Withdrawal of Life Support in the ICU Affects Family Satisfaction with Care. NIH News, National Institutes of Health. (October 15, 2008), www.nih.gov/news/health/oct2008/ninr-15.htm. (accessed August 2, 2010).

Isaac R. Berniker

Light sensitivity *see* **Photosensitivity**

Light therapy

Definition

Light therapy, or **phototherapy**, is the administration of doses of bright light in order to treat a variety of sleep and **mood disorders**. It is most commonly used to re-regulate the body's internal clock and/or relieve depression.

Purpose

Light therapy is most often prescribed to treat **seasonal affective disorder**, a form of depression most often associated with shortened daylight hours in northern latitudes from the late fall to the early spring. It is also occasionally employed to treat such sleep-related disorders as **insomnia** and **jet lag**. Recently, light therapy has also been found effective in the treatment of such nonseasonal forms of depression as **bipolar disorder**. One 2001 study found that bright light reduced depressive symptoms 12–35% more than a placebo treatment in nine out of 10 randomized controlled trials.

When used to treat SAD or other forms of depression, light therapy has several advantages over prescription antidepressants. Light therapy tends to work faster than medications, alleviating depressive symptoms within two to 14 days after beginning light therapy as opposed to an average of four to six weeks with medication. And unlike antidepressants, which can cause a variety of side effects from **nausea** to concentration problems, light therapy is extremely well tolerated. Some side effects are possible with light but are generally not serious enough to cause discontinuation of the therapy.

There are several other different applications for light therapy, including:

- Full-spectrum/UV light therapy for disorders of the skin. A subtype of light therapy that is often prescribed to treat skin diseases, rashes, and jaundice.
- Cold laser therapy. The treatment involves focusing very low-intensity beams of laser light on the skin, and is used in laser acupuncture to treat a myriad of symptoms and illnesses, including pain, stress, and tendinitis.
- Colored light therapy. In colored light therapy, different colored filters are applied over a light source to achieve specific therapeutic effects. The colored light is then focused on the patient, either with a floodlight which covers the patient with the colored light, or with a beam of light that is focused on the area of the illness.
- Back of knee light therapy. According to a 1998 study published in the journal *Science*, the area behind the human knee known as the popliteal region contains photoreceptors that can help to adjust the body's circadian rhythms. The authors of the study found that they could manipulate circadian rhythms by focusing a bright light on the popliteal region. Further studies are underway to determine the efficacy of this treatment on disorders such as SAD and diabetic nerve pain.

Description

Light therapy is generally administered at home. The most commonly used light therapy equipment is a portable lighting device known as a light box. The light box may be a full-spectrum box, in which the lighting element contains all wavelengths of light found in natural light (including UV rays), or it may be a bright light box, in which the lighting element emits non-UV white light. The box may be mounted upright to a wall, or slanted downwards towards a table.

The patient sits in front of the box for a prescribed period of time (anywhere from 15 minutes to several hours). For patients just starting on the therapy, initial sessions are usually only 10–15 minutes in length. Some patients with SAD undergo light therapy session two or three times a day, others only once. The time of day and number of times treatment is administered depends on the physical needs and lifestyle of the individual patient. If light therapy has been prescribed for the treatment of SAD, it typically begins in the fall months as the days begin to shorten, and continues throughout the winter and possibly the early spring. Patients with a long-standing history of SAD are usually able to establish a time-table or pattern to their depressive symptoms, and can initiate treatment accordingly before symptoms begin.

The light from a slanted light box is designed to focus on the table it sits upon, so patients may look down to read or do other sedentary activities during therapy. Patients using an upright light box must face the light source, and should glance toward the light source occasionally without staring directly into the light. The light sources in these light boxes typically range from 2,500–10,000 lux (in contrast, average indoor lighting is 300–500 lux; a sunny summer day is about 100,000 lux).

Light boxes can be purchased for between $200 and $500. Some healthcare providers and healthcare supply companies also rent the fixtures. This gives a patient the opportunity to have a trial run of the therapy before making the investment in a light box. Recently, several new light box products have become available. Dawn simulators are lighting devices or fixtures that are programmed to turn on gradually, from dim to bright light, to simulate the sunrise. They are sometimes prescribed for individuals who have difficulty getting up in the morning due to SAD symptoms. Another device known as a light visor is designed to give an individual more mobility during treatment. The visor is a lighting apparatus that is worn like a sun visor around the crown of the head. Patients with any history of eye problems should consult their healthcare professional before attempting to use a light visor.

Origins

Light, both natural and artificial, has been prescribed throughout the ages for healing purposes. Sunlight has been used medicinally since the time of the ancient Greeks; Hippocrates, the father of modern medicine, prescribed exposure to sunlight for a number of illnesses. In the late nineteenth and early twentieth centuries, bright light and fresh air were

KEY TERMS

Dawn simulation—A form of light therapy in which the patient is exposed while asleep to gradually brightening white light over a period of an hour and a half.

Lux—The International System unit for measuring illumination, equal to one lumen per square meter.

Neurotransmitter—A chemical in the brain that transmits messages between neurons, or nerve cells.

Seasonal affective disorder (SAD)—A mood disorder characterized by depression, weight gain, and sleepiness during the winter months. An estimated 4–6% of the population of Canada and the northern United States suffers from SAD.

Serotonin—A neurotransmitter that is involved in mood disorders as well as transmitting nerve impulses.

frequently prescribed for a number of mood and **stress** related disorders. In fact, prior to World War II (1939–1945), hospitals were regularly built with solariums, or sun rooms, in which patients could spend time recuperating in the sunlight.

Precautions

Patients with eye problems should see an ophthalmologist regularly both before and during light therapy. Because UV rays are emitted by the light box, patients taking photosensitizing medications should consult with their healthcare provider before beginning treatment. In addition, patients with medical conditions that make them sensitive to UV rays should also be seen by a healthcare professional before starting phototherapy.

Patients beginning light therapy for SAD may need to adjust the length, frequency, and timing of their phototherapy sessions in order to achieve the maximum benefits. Patients should keep their healthcare provider informed of their progress and the status of their depressive symptoms. Occasionally, additional treatment measures for depression (e.g, antidepressants, herbal remedies, **psychotherapy**) may be recommended as an adjunct, or companion treatment, to light therapy.

Preparation

Full-spectrum light boxes do emit UV rays, so patients with sun-sensitive skin should apply a sun screen before sitting in front of the box for an extended period of time.

Risks

Some patients undergoing light therapy treatments report side effects of eyestrain, headaches, insomnia, **fatigue**, **sunburn**, and dry eyes and nose. Most of these effects can be managed by adjusting the timing and duration of the light therapy sessions. A strong sun block and eye and nose drops can alleviate the others. Long-term studies have shown no negative effects to eye function of individuals undergoing light therapy treatment.

A small percentage of light therapy patients may experience hypomania, a feeling of exaggerated, hyperelevated mood. Again, adjusting the length and frequency of treatment sessions can usually manage this side effect.

Research and general acceptance

Light therapy is widely accepted by both traditional and complementary medicine as an effective treatment for SAD. The exact mechanisms by which the treatment works are not known, but the bright light employed in light therapy may act to readjust the body's circadian rhythms, or internal clock. Other popular theories are that light triggers the production of serotonin, a neurotransmitter believed to be related to **depressive disorders**, or that it influences the body's production of melatonin, a hormone that may be related to circadian rhythms. A recent British study suggests that dawn simulation, a form of light therapy in which the patient is exposed to white light of gradually increasing brightness (peaking at 250 lux after 90 minutes) may be even more effective in treating depression than exposure to bright light. Dawn simulation is started around 4:30 or 5 a.m., while the patient is still asleep.

Wide-spectrum UV light treatment for skin disorders such as **psoriasis** is also considered a standard treatment option in clinical practice. However, such other light-related treatments as cold laser therapy and colored light therapy are not generally accepted, since few or no scientific studies exist on the techniques.

Training and certification

Psychiatrists, psychologists, and other mental healthcare professional prescribe light therapy treatment for SAD. Holistic healthcare professionals and light therapists who specialize in this treatment are also available; in some states, these professionals

require a license, so individuals should check with their state board of health to ensure their practitioner has the proper credentials. Light therapy for skin disorders should be prescribed by a dermatologist or other healthcare professional with expertise in skin diseases and light therapy treatment.

Resources

BOOKS

Lam, Raymond W. and Edwin M. Tam. *A Clinician's Guide to Using Light Therapy*. Cambridge: Cambridge University Press, 2009.

Rosenthal, N.E. *Winter Blues: Everything You Need to Know to Beat Seasonal Affective Disorder* New York: Guilford Press, 2006.

PERIODICALS

Lurie, S.J., et al. "Seasonal Affective Disorder." *American Family Physician* 74 (November 1, 2006): 1521–1524.

Even, C., et al. "Efficacy of Light Therapy in Nonseasonal Depression: A Systematic Review." *Journal of Affective Disorders*. 108 (May 2008):11–23.

ORGANIZATIONS

National Depressive and Manic Depressive Association, 730 Franklin Street, Suite 501, Chicago, IL, 60610, (800) 826–3632, http://www.ndmda.org.

Society for Light Treatment and Biological Rhythms, 824 Howard Ave., New Haven, CT, 60610, (203) 764–4324, http://www.sltbr.org.

Paula Ford-Martin
Rebecca J. Frey, PhD
Brenda W. Lerner

Light treatment *see* **Ultraviolet light treatment**

Lipase test

Definition

The lipase test is a blood test performed to determine the serum level of a specific protein (enzyme) involved in digestion. Lipase is an enzyme produced by the pancreas, which is a large gland situated near the stomach. Lipase works to break down a certain type of blood lipid (**triglycerides**) into fatty acids.

Lipase appears in the blood together with another enzyme called amylase following damage to or diseases affecting the pancreas. It was once thought that abnormally high lipase levels were associated only with diseases of the pancreas. Other conditions are now known to be associated with high lipase levels, especially kidney failure and intestinal obstruction. Diseases involving the pancreas, however, produce much higher lipase levels than diseases of other organs. Lipase levels in pancreatic disorders are often 5–10 times higher than normal.

Purpose

The lipase test is most often used in evaluating inflammation of the pancreas (**pancreatitis**), but it is also useful in diagnosing kidney failure, intestinal obstruction, **mumps**, and peptic ulcers. Doctors often order amylase and lipase tests at the same time to help distinguish pancreatitis from ulcers and other disorders in the abdomen. If the patient has acute (sudden onset) pancreatitis, the lipase level usually rises somewhat later than the amylase level—about 24–48 hours after onset of symptoms—and remains abnormally high for 5–7 days. Because the lipase level peaks later and remains elevated longer, its determination is more useful in late diagnosis of acute pancreatitis. Conversely, however, lipase levels are not as useful in diagnosing chronic pancreatic disease.

Precautions

Patients should be asked whether they are taking certain prescription drugs that can affect the accuracy of the lipase test. Drugs that can cause elevated lipase levels include bethanechol, cholinergics, codeine, indomethacin, meperidine, methacholine, and morphine. Drugs that may decrease levels include **calcium** ions.

Description

A lipase test is performed on a sample of the patient's blood, withdrawn from a vein into a vacuum tube. The procedure, which is called a venipuncture, takes about five minutes.

Preparation

The patient should have nothing to eat or drink for 12 hours before the lipase test.

Risks

Risks for this test are minimal, but may include slight bleeding from the puncture site, a small bruise or swelling in the area, **fainting**, or feeling lightheaded.

Results

Reference values for lipase determination are laboratory- and method-specific. In general, normal results are usually less than 200 units/L (triolein methods by titration or turbidimetry).

KEY TERMS

Amylase—A digestive enzyme that breaks down starch.

Lipid—A greasy organic compound that cannot be dissolved in water. Triglycerides, which are broken down by lipase, are one type of blood lipid.

Pancreas—An elongated gland situated across the back of the abdomen behind the stomach. It secretes both digestive enzymes and hormones. Pancreatic hormones regulate the level of sugar in the blood.

Pancreatitis—Inflammation of the pancreas, frequently caused by gallstones, alcohol abuse, viral infection, or injury.

Turbidimetry—A technique of measurement that analyzes the amount of sediment in a liquid.

Increased lipase levels are found in acute pancreatitis, chronic relapsing pancreatitis, and pancreatic **cancer**. High lipase levels also occur in certain liver diseases, kidney failure, bowel obstruction, peptic ulcer disease, and tumors or inflammation of the salivary glands.

Resources

BOOKS

Pagana, Kathleen Deska, and Timothy J. Pagana. *Mosby's Manual of Diagnostic and Laboratory Tests*. 4th ed. St. Louis: Mosby, 2009.

Janis O. Flores

Lipidoses

Definition

Lipidoses are heredity metabolic disorders, passed from parents to their children, characterized by defects of the digestive system that impair the way the body uses fats (a type of lipid) from the diet. When the body is unable to properly digest fats, one or more enzymes used to metabolize lipids are not produced in sufficient amounts or are improperly produced. Consequently, lipids accumulate in body tissues in abnormal amounts. Lipids are molecules that include fats, waxes, oils, fat-soluble **vitamins**, sterols (such as estrogen and cholesterol), and other related compounds whose primary task is to store energy. Consequently, lipidoses are also called by the name of lipid storage disorders or diseases. When lipids excessively accumulate over time they can eventually lead to cell and tissue damage, especially affecting the brain, peripheral nervous system, spleen, liver, and bone marrow.

Demographics

This group of diseases is inherited from one or both parents. In each case of lipidoses, the parent carries a gene that is unable to regulate a particular protein. In some cases, neither parent has the disorder but passes it on to their offspring, equally affecting both males and females. In other instances, the mother carries the damaged gene and passes it on to her offspring, with the males more severely affected by the disorder than the females.

Description

The digestion, storage, and use of fats from foods is a complex process that involves hundreds of chemical reactions in the body. In most people, the body is already programmed by its genetic code to produce all of the enzymes and chemicals necessary to carry out these functions. These genetic instructions are passed from parents to their offspring during reproduction.

People with lipidoses are born without the genetic codes needed to tell their bodies how to complete a particular part of the fat digestion process. In most of these disorders, the body does not produce a certain enzyme or chemical. Over 30 different disorders of fat metabolism are related to genetic defects. Although the defects are passed from parents to children, the parents often do not have the disorders themselves.

The symptoms, available treatments, and long-term consequences of these conditions vary greatly. Some of the conditions become apparent shortly after the infant is born; in others, symptoms may not develop until adulthood. For most of the lipidoses, diagnosis is suspected based on the symptoms and family history. Blood tests, urine tests, and tissue tests can be used to confirm the diagnosis. **Genetic testing** can be used, in some cases, to identify the defective gene. Some of these disorders can be controlled with changes in the diet, medications, or

enzyme supplements. For many, treatment is not available. Some may cause **death** in childhood or contribute to a shortened life expectancy. Some of the most common or most serious lipidoses are discussed below.

Fabry's disease

Causes and symptoms

Approximately one in every 40,000 males is born with Fabry's disease, which is also called Fabry disease and alpha-galactosidase-A deficiency. This condition has an X-linked, recessive pattern of inheritance, meaning that the defective gene is carried on the X chromosome. A female who carries a defective recessive gene on one of her two X chromosomes has a 50% chance of passing the defective gene to her sons who will develop the disorder associated with the defective gene (a male receives one X chromosome from his mother and one Y chromosome from his father). She also has a 50% chance of passing the defective recessive gene to her daughters who will be carriers of the disorder (like their mother). Some female carriers of Fabry's disease show mild signs of the disorder, especially cloudiness of the cornea.

The gene that is defective in Fabry's disease causes a deficiency of the enzyme alpha-galactosidase A. Without this enzyme, fatty compounds start to line the blood vessels. The collection of fatty deposits eventually affects blood vessels in the skin, heart, kidneys, and nervous system. The first symptoms in childhood are **pain** and discomfort in the hands and feet brought on by **exercise**, **fever**, **stress**, or changes in the weather. A raised rash of dark red-purple non-cancerous, spots (called angiokeratomas) is common, especially on skin between the waistline and the knees. Other symptoms include a decreased ability to sweat and changes in the cornea or outer layer of the eye. Other symptoms include gastrointestinal problems, heart enlargement, and progressive kidney damage. Although the disease begins in childhood, it progresses very slowly. Kidney and heart problems develop in adulthood.

Diagnosis

The diagnosis can be confirmed by a blood test to measure for alpha-galactosidase A. Women who are carries of the defective gene can also be identified by a blood test.

Treatment

Treatment focuses on prevention of symptoms and long-term complications and slowing down the progression of the disease. Daily doses of phenytoin **sodium** (Phenytek, Dilantin, Infatabs), diphenylhydantoin (Dilantin), or carbamazapine (Tegretol) can prevent or reduce the severity of pain in the hands and feet associated with the condition. To help with gastrointestinal problems, metoclopramide (Maxolon, Primperan, Pramin) may be given and, to help digest fats, the nutritional supplement called Lipisorb may be provided. A low-sodium, low-protein diet may be beneficial to those patients who have some kidney complications. If kidney problems progress, **kidney dialysis** or **kidney transplantation** may be required. Enzyme replacement therapy is currently being explored at helping to ease pain, reduce storage problems, and to improve organ capabilities.

Prognosis

Although patients with Fabry's disease usually survive to adulthood, they are at increased risk for **stroke**, heart attacks, and kidney damage. They usually die prematurely from complications of these high-risk conditions.

Drugs such as phenytoin and carbamazepine are often prescribed to treat pain that accompanies Fabry's disease. Metoclopramaide or Lipisorb (a nutritional supplement) can ease gastrointestinal distress that often occurs in Fabry's patients, and some individuals may require kidney transplant or dialysis. Recent experiments indicate that enzyme replacement can reduce storage, ease pain, and improve organ function in patients with Fabry's disease.

Gaucher disease

Causes and symptoms

Gaucher (pronounced go-shay) disease, also called Gaucher's disease, is the most common of the lipid storage disorders. It is found in populations all over the world (20,000 to 40,000 people have a type of the disease), and it occurs with equal frequency in males and females. **Gaucher disease** has a recessive pattern of inheritance, meaning that a person must inherit a copy of the defective gene from both parents in order to have the disease. The genetic defect causes a deficiency of the enzyme glucocerebrosidase that is responsible for breaking down a certain type of fat and releasing it from fat cells. These fat cells begin to crowd out healthy cells in the liver, spleen, bones, and nervous system. Symptoms of Gaucher disease can start in infancy, childhood, or adulthood.

Three types of Gaucher disease have been identified, but there are many variations in how

symptoms develop. Type 1 (non-neuropathic type) is the most common and affects both children and adults. It occurs much more often in people of Eastern European and Russian Jewish (Ashkenazi) ancestry, affecting 1 out of every 450 live births. The first signs of the disease include an enlarged liver and spleen, causing the abdomen to swell. Children with this condition may be shorter than the normal height. Other symptoms include tiredness, pain, bone deterioration, bone lesions, broken bones, lymph node swelling, anemia, low blood **platelet count**, and bruising. It also may include yellow spots on the eyes and a brownish color to the skin. People with Gaucher disease are more prone to infections than are other people. Type 2 Gaucher disease (acute infantile neuropathic type) is more serious. It normally begins within the first few months after birth. Symptoms, which are similar to those in Type 1, progress rapidly, but also include nervous system damage, limb rigidity, and decreased ability to swallow or suck. Symptoms of Type 3 Gaucher disease (chronic neuronopathic type) begin during early childhood with symptoms like Type 1. Unlike Type 2, the progress of the disease is slower, although it also includes nervous system damage. Anemia, respiratory problems, and poor coordination are some of its specific symptoms.

Diagnosis

Gaucher disease may be suspected based on symptoms and is confirmed with a blood test for levels of the enzyme. Samples of tissue from an affected area may also be used to confirm a diagnosis of the disease.

Treatment

The symptoms of Gaucher disease in Type 1 and Type 3 Gaucher disease can be stopped and even reversed by treatment with injections of enzyme replacements. Such treatment has been found to counter many of the symptoms such as abnormal blood count, and liver and spleen size. Two enzyme drugs currently available are alglucerase (Ceredase) and imiglucerase (Cerezyme). Other treatments address specific symptoms such as anemia, broken bones, or pain. Type 1 and Type 3 Gaucher disease often results in brain and nervous system damage. There is not a way to reverse such damage.

Prognosis

The pain and deformities associated with symptoms can make coping with this illness very challenging for individuals and families. With treatment and control of symptoms, people with Type 1 Gaucher disease may lead fairly long and normal lives. Most infants with Type 2 die before the age of 2 years. Children with Type 3 Gaucher disease may survive to adolescence and early adulthood.

Krabbe's disease

Causes and symptoms

Krabbe's disease, also called Krabbe disease, is caused by a deficiency of the enzyme galactoside beta-galactosidase. It has a recessive pattern of inheritance and is believed to occur in 1 of 40,000 births in the United States. This condition, which is also called globoid cell leukodystrophy or Krabbe leukodystrophy, is characterized by acute central and peripheral nervous system degeneration. It develops in early infancy with initial symptoms of irritability, **vomiting**, and episodes of partial unconsciousness. Symptoms progress rapidly to seizures, muscle weakness, difficulty swallowing, blindness, deafness, **mental retardation**, and **paralysis**. Other symptoms include muscle weakness,

Treatment

A cure for Krabbe's disease is not available. Treatment is supportive at best, with actions that help to relieve symptoms. Some clinical trials have shown that children who receive umbilical cord blood stem cells from non-family members before any symptoms are present develop lessened neurological impairment than other children with the disease. Bone marrow transplants have also been tried in the more modest cases of Krabbe's disease.

Prognosis

Children born with Krabbe's disease die in infancy, usually before the age of 2 years. As shown by recent trials, children who have received umbilical cord blood stem cells or bone marrow transplants before symptoms are present show better prognosis than other children with the disease. People who get the disease later in later usually have a less severe form of it and live longer, too.

Niemann-Pick disease

Causes and symptoms

At least five different forms of Niemann-Pick disease (NPD) have been identified. The different types seem to be related to the activity level of the enzyme sphingomyelinase. In patients with Types A and B NPD, there is a build up of sphingomyelin in cells of

the brain, liver, spleen, kidney, and lung. Type A is the most common form of NPD and the most serious, with death usually occurring by the age of 18 months. Symptoms develop within the first few months of life and include poor appetite, failure to grow, enlarged liver and spleen, and the appearance of cherry red spots in the retina of the eye. Type B (also labeled juvenile onset) develops in infancy or childhood with symptoms of mild liver or spleen enlargement and lung problems. Some adults with this form (Type E) may also show a loss of muscle coordination. Types C or D NPD are related to cholesterol transfer out of cells. Children with Types C or D grow normally in early childhood, but eventually develop difficulty in walking and loss of muscle coordination. Ultimately, the nervous system becomes severely damaged and these patients die. Type C occurs in any population, while Type D has been identified only in patients from Nova Scotia, Canada.

Diagnosis

Diagnosis is confirmed by analyzing a sample of tissue. Prenatal diagnosis of Types A and B of NPD can be done with **amniocentesis** or **chorionic villus sampling**.

Treatment

There is not a cure for Niemann-Pick disease. Treatment consists of supportive care to deal with symptoms and the development of complications. **Bone marrow transplantation** is being investigated as a possible treatment for Type B. So far, the results have shown promise, but additional trials are necessary. Low-cholesterol **diets** may be helpful for patients with Types C and D, but clinical trials have not been promising.

Prognosis

Patients with Type A NPD usually die within the first year and a half of life, usually from infection or neurological problems. Type B patients generally live to adulthood but suffer from significant liver and lung problems. They usually require supplemental oxygen due to decreased function in their lungs. Bone marrow transplants have been attempted with such Type B patients. With Types C and D NPD, there is significant nervous system damage leading to severe **muscle spasms**, seizures, and eventually, to **coma** and death. Some patients with Types C and D die in childhood, while less severely affected patients may survive to adulthood.

Refsum's disease

Causes and symptoms

Refsum's disease, also called Refsum disease and Adult Refsum disease (ARD), has a recessive pattern of inheritance and affects populations from Northern Europe, particularly Scandinavians most frequently. It is due to a deficiency of phytanic acid hydroxylase, an enzyme that breaks down a fatty acid called phytanic acid. This condition affects the nervous system, eyes, bones, and skin. Symptoms, which usually appear by age 20 years, include vision problems (retinitis pigmentosa and rhythmic eye movements [nystagmus]), loss of muscle coordination, loss of sense of smell (**anosmia**), pain, **numbness**, and elevated protein in the cerebrospinal fluid. Later symptoms include deafness, abnormalities with the heartbeat (cardiac arrnythmias), lack of coordination (ataxis), weakness and numbness (peripheral neuropath), and scaly, dry skin (**ichthyosis**). Still other people may have shortened toes or fingers. If symptoms do not appear in the 20s, they may begin appearing in the 40s or 50s.

Treatment

A diet free of phytanic acid (found in dairy products, fatty fish [such as tuna, cod, and haddock], lamb, stewed beef and lamb, white bread, white rice, boiled potatoes, and egg yolk) can reduce some of the symptoms. **Plasmapheresis**, a process where whole blood is removed from the body, processed through a filtering system, and then return to the body, may be used to filter phytanic acid from the blood.

Prognosis

Refsum's disease is the lipidoses that is most treatable because a change in diet can control the disease. By removing phytanic acid from the diet, the symptoms associated with it usually disappear. Problems with hearing, vision, and smell may continue even with treatment. If left untreated, the disease may eventually lead to death from irregularities of the heart.

Tay-Sachs disease

Causes and symptoms

Tay-Sachs disease (TSD) is a fatal condition caused by a deficiency of the enzyme beta-hexosaminidase A, which allows excessive amounts of the fatty material called ganglioside G_{M2} to build up in tissues and nerve cells within the brain. The defective gene that causes this disorder is found in roughly 1 in 250 people in the general population. However, certain populations

KEY TERMS

Amniocentesis—A procedure where a needle is inserted through the abdomen into the uterus of a pregnant woman to remove a small amount of the fluid that surrounds the developing fetus. This test can be performed at about week 16 of the pregnancy. Cells from the fetus can be tested for genetic defects.

Chorionic villi sampling—A procedure to remove a small tissue sample of the placenta, the sac that surrounds the developing fetus. This test can be performed as early as week 10 of the pregnancy. The tissue can be tested for genetic defects.

Lipids—Organic compounds not soluble in water, but soluble in fat solvents such as alcohol. Lipids are stored in the body as energy reserves and are also important components of cell membranes.

Recessive—Refers to an inherited characteristic or trait that is expressed only when two copies of the gene responsible for it are present.

X-linked—Refers to a gene carried on the X chromosome, one of the two sex chromosomes.

have significantly higher rates of TSD. French-Canadians living near the St. Lawrence River and in the Cajun regions of Louisiana are at higher risk of having a child with TSD. The highest risk seems to be in people of Eastern European and Russian Jewish (Ashkenazi) descent. Tay-Sachs disease has a recessive pattern of inheritance, and approximately 1 in every 27 people of Jewish ancestry in the United States carries the TSD gene. Symptoms develop in infancy and are due to the accumulation of a fatty acid compound in the nervous system. Early symptoms include reduced vision and physical coordination, deafness, seizures, red spots on retina of eyes, and mental retardation. Eventually, the child develops problems with breathing and swallowing. Blindness, paralysis, and death follow. In another type of the disease, it occurs in people in their 20s or early 30s. They begin to have problems walking. Eventually, their nervous system progressively deteriorates.

Diagnosis

Carriers of the Tay-Sachs related gene can be identified with a blood test. Amniocentesis or chorionic villi sampling can be used to determine if the fetus has Tay-Sachs disease.

Treatment

Treatment options are not available for Tay-Sachs disease. Parents who are identified as carriers may want to seek **genetic counseling**. If a fetus is identified as having TSD, parents may consider termination of the **pregnancy**. If a person contracts the disease, anticonvulsant medication can be prescribed to control seizures. As neurological problems continue, swallowing may be difficult, and a feeding tube may be inserted to help in providing nutrient.

Prognosis

Children born with Tay-Sachs disease become increasingly debilitated; most die by about age four years, usually from infections.

Wolman's disease

Causes and symptoms

Wolman's disease, a type of acid lipase deficiency and acid lipase disease, is caused by a genetic defect (with a recessive pattern of inheritance) that results in deficiency of an enzyme that breaks down cholesterol. It occurs in both males and females. This causes large amounts of fat to accumulate in body tissues. Infants are born without symptoms and they appear to be normal. However, symptoms begin in the first few weeks of life and include an enlarged liver and spleen, adrenal calcification (hardening of adrenal tissue due to deposits of **calcium** salts), **vomiting**, anemia, **jaundice**, and fatty stools.

Treatment

Treatment is not currently available.

Prognosis

Infants usually die by the age of one year. They usually die from **malnutrition**. However, if they survive as children, they may live into adulthood

Prevention

Couples who have family histories of genetic defects can undergo genetic testing and counseling to see if they are at risk for having a child with one of the lipidoses disorders. During pregnancy, cell samples can be collected from the fetus using amniocentesis or chorionic villi sampling. The results of these tests

can indicate if the developing fetus has a lipidosis disorder. Termination of the pregnancy may be considered in some cases.

Resources

BOOKS

Lawrence, Glen D. *The Fats of Life: Essential Fatty Acids in Health and Disease*. New Brunswick, NJ: Rutgers University Press, 2010.

Mouritsen, Ole. *Life: As a Matter of Fat the Emerging Science of Lipidomics*. New York: Springer, 2005.

Nicholls, Stephen J., and Pia Lundman. *Practical Approach to Diagnosis and Management of Lipid Disorders*. Sudbury: MA: Jones and Bartlett, 2011.

Tonkin, Andrew M., editor. *Lipid Disorders*. Oxford, UK: Clinical, 2009.

OTHER

Acid Lipase Disease. National Institute of Neurological Diseases and Stroke. (April 23, 2010), www.ninds.nih.gov/disorders/acid_lipase/acid_lipase.htm. (accessed August 2, 2010).

Blood Diseases Program. Harvard Stem Cell Institute, Harvard University. www.hsci.harvard.edu/research/blood-diseases-program. (accessed August 2, 2010).

Fabry Disease. National Institute of Neurological Diseases and Stroke. (March 8, 2010), www.ninds.nih.gov/disorders/fabrys/fabrys.htm. (accessed August 2, 2010).

Gaucer' Disease. National Institute of Neurological Diseases and Stroke. (October 30, 2009), www.ninds.nih.gov/disorders/gauchers/gauchers.htm. (accessed August 2, 2010).

Krabbe Disease. National Institute of Neurological Diseases and Stroke. (July 1, 2008), www.ninds.nih.gov/disorders/krabbe/krabbe.htm. (accessed August 2, 2010).

Niemann-Pick disease. National Institute of Neurological Diseases and Stroke. (June 18, 2007), www.ninds.nih.gov/disorders/niemann/niemann.htm. (accessed August 2, 2010).

Lipid Storage Diseases. National Institute of Neurological Diseases and Stroke. (May 28, 2010), www.ninds.nih.gov/disorders/lipid_storage_diseases/detail_lipid_storage_diseases.htm. (accessed August 2, 2010).

Refsum Disease. National Institute of Neurological Diseases and Stroke. (February 14, 2007), www.ninds.nih.gov/disorders/refsum/refsum.htm. (accessed August 2, 2010).

Tay-Sachs Disease. National Institute of Neurological Diseases and Stroke. (February 14, 2007), www.ninds.nih.gov/disorders/taysachs/taysachs.htm. (accessed August 2, 2010).

ORGANIZATIONS

Fabry Support and Information Group, 108 N.E. Second Street, Suite C; P. O. Box 510, Concordia, MO, 64020-0510, (660) 463-1355, (660) 463-1356, http://www.fabry.org/.

National Institute of Neurological Disorders and Stroke, Post Office Box 20824, Bethesda, MD, 20824, (301) 496-5751, (800) 352-9424, http://www.ninds.nih.gov/.

National Niemann-Pick Foundation, 401 Madison Avenue, Suite B; P.O. Box 49, Fort Atkinson, WI, 53538, (920) 563-0930, (877) 287-3672, (920) 563-0931, nnpdf@nnpdf.org, http://www.nnpdf.org/.

National Organization for Rare Disorders, 55 Kanosia Avenue; P. O. Box 1968, Danbury, CT, 06813-1968, (203) 744-0100, (203) 798-2291, http://www.rarediseases.org/.

National Tay-Sachs and Allied Diseases Association, 2001 Beacon Street, Suite 204, Boston, MA, 02135, (800) 906-8723, (617) 277-0134, http://www.ntsad.org/.

Altha Roberts Edgren

Lipoproteins test

Definition

Lipoproteins are the "packages" in which cholesterol and **triglycerides** travel throughout the body. Measuring the amount of cholesterol carried by each type of lipoprotein helps determine a person's risk for cardiovascular disease (disease that affects the heart and blood vessels, also called CVD).

Purpose

Cholesterol and triglycerides are fat-like substances called lipids. Cholesterol is used to build cell membranes and hormones. The body makes cholesterol and gets it from food. Triglycerides provide a major source of energy to the body tissues. Both cholesterol and triglycerides are vital to body function, but an excess of either one, especially cholesterol, puts a person at risk of cardiovascular disease.

Because cholesterol and triglycerides can't dissolve in watery liquid, they must be transported by something that can dissolve in blood serum. Lipoproteins contain cholesterol and triglycerides at the core and an outer layer of protein, called apolipoprotein.

There are four major classes of lipoproteins: chylomicrons, very low-density lipoproteins (VLDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL). There also are less commonly measured classes such as lipoprotein(a) and subtypes of the main classes. Each lipoprotein has characteristics that make the cholesterol it carries a greater or lesser risk. Measuring each type of lipoprotein helps determine a person's risk for cardiovascular disease more

accurately than cholesterol measurement alone. When a person is discovered to be at risk, treatment by diet or medication can be started and his or her response to treatment monitored by repeated testing.

Description

Chylomicrons

Chylomicrons are made in the intestines from the triglycerides in food. They contain very little cholesterol. Chylomicrons circulate in the blood, getting smaller as they deposit the triglycerides in fatty tissue. Twelve hours after a meal, they are gone from circulation. Serum collected from a person directly after eating will form a creamy layer on the top if left undisturbed and refrigerated overnight. This creamy layer is the chylomicrons.

Very low-density lipoproteins (VLDL)

VLDL are formed in the liver by the combination of cholesterol, triglycerides formed from circulating fatty acids, and apolipoprotein. This lipoprotein particle is smaller than a chylomicron, and contains less triglyceride but more cholesterol (10–15% of a person's total cholesterol). As the VLDL circulates in the blood, triglycerides are deposited and the particle gets smaller, eventually becoming a low-density lipoprotein (LDL). Serum from a person with a large amount of VLDL will be cloudy.

Low-density lipoproteins (LDL)

LDL, often called "bad" cholesterol, is formed primarily by the breakdown of VLDL. LDL contains little triglycerides and a large amount of cholesterol (60–70% of a person's total cholesterol). Although the particles are much smaller than chylomicrons and VLDL, LDL particles can vary in size and chemical structure. These variations represent subclasses within the LDL class. Serum from a person with a large amount of LDL will be clear.

LDL carries cholesterol in the blood and deposits it in body tissues and in the walls of blood vessels, a condition known as **atherosclerosis**. The amount of LDL in a person's blood is directly related to his or her risk of cardiovascular disease. The higher the LDL level, the greater the risk. LDL is the lipoprotein class most used to trigger and monitor cholesterol lowering therapy.

High-density lipoproteins (HDL)

HDL is often called "good" cholesterol. HDL removes excess cholesterol from tissues and vessel walls and carries it to the liver, where it is removed from the blood and discarded. The amount of HDL in a person's blood is inversely related to his or her risk of cardiovascular disease. The lower the HDL level, the greater the risk; the higher the level, the lower the risk. The smallest lipoprotein, it contains 20–30% of a person's total cholesterol and can be separated into two major subclasses.

Lipoprotein(a)

Lipoprotein(a) is found in lower concentrations than other lipoproteins, yet it carries a unique and significant risk for cardiovascular disease. Because of its similarity to LDL, test methods often don't measure it separately, but include it within the LDL class. Testing specifically for this class may uncover why a person is not responding to standard cholesterol-lowering treatment. High lipoprotein(a) levels may not respond to treatment aimed at high LDL.

Measurement guidelines

The Expert Panel of the National Cholesterol Education Program (NCEP) sponsored by the National Institutes of Health has published guidelines for the detection of high cholesterol in adults. The NCEP panel recommends that adults over the age of 20 be tested for cholesterol and HDL every five years. If the cholesterol is high, the HDL is low (below 35 mg/dL), or other risk factors are present, a complete lipoprotein profile that includes total cholesterol, triglycerides, HDL, and calculated LDL should be done.

Measurement methods

There are a variety of methods to measure the lipoprotein classes. All require separation of the classes before they can be measured. One way to separate them is by spinning serum (the yellow, watery liquid that separates from the cells when **blood clots**) for a long time in a high-speed centrifuge (called ultracentrifugation). The most dense classes will settle toward the bottom, the least dense toward the top. Following centrifugation, the most complete measurement of all the lipoprotein classes is done using electrophoresis. This procedure measures the quantity of each lipoprotein class based on its movement in an electrical field.

In 2003, a new test called the vertical auto profile or VAP, was developed that provides detailed measurements of cholesterol subclasses. These subclasses play important roles in patients later developing heart disease. The new tests were predicted to help identify important, emerging risk factors for heart disease.

KEY TERMS

Atherosclerosis—Disease of blood vessels caused by deposits of cholesterol on the inside walls of the vessels.

Cardiovascular disease—Disease that affects the heart and blood vessels.

Cholesterol—A fat-like substance called a lipid. It is used to build cell membranes and hormones. The body makes cholesterol and gets it from food.

Lipoproteins—The packages in which cholesterol and triglycerides travel throughout the body.

Other, less extensive procedures also are used. For example, if only HDL is to be measured, a chemical is added to the serum that will clump the other classes, leaving HDL free in the serum to be measured by a chemical method. LDL often is not measured directly but its level is calculated based on the measurements of total cholesterol, HDL, and triglycerides. The formula is called the Friedewald formula: LDL = total cholesterol - HDL - (triglycerides/5). The calculated result will be inaccurate in a person with high triglycerides. Results usually are available the same or following day.

Preparation

The patient must fast for 12 hours before the test, eating nothing and drinking only water. The person should not have alcohol for 24 hours before the test. There should be a stable diet and no illnesses occurring in the preceding two weeks.

A lipoproteins test requires 5 mL (milliliters) of blood. A person's physical position while having blood collected affects the results. Values from blood drawn while a person is sitting may be different from those while the person is standing. If repeated testing is done, the person should be in the same position each time.

Aftercare

Discomfort or bruising may occur at the puncture site or the person may feel dizzy or faint. Pressure to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort.

Results

People with HDL levels between 45 mg/dL and 59 mg/dL carry an average risk for cardiovascular disease. People with HDL levels above 60 mg/dL have a negative risk factor and appear to be protected from cardiovascular disease.

LDL levels below 130 mg/dL are desirable.

Some people have normal variations in their lipoprotein and total cholesterol levels. Repeat testing may be necessary, especially if a value is at a borderline risk category point.

Abnormal results

People with HDL levels of 36–44 mg/dL have a moderate risk of cardiovascular disease. HDL levels below 35 mg/dL are a major risk.

LDL levels of 130–159 mg/dL place a person at a borderline high risk of cardiovascular disease; levels above 160 mg/dL place a person at high risk. Relative proportions between HDL and LDL are important also. Results of a large clinical trial in 2003 showed that the new VAP cholesterol tests increased lipid-lowering therapy by 59% in high-risk patients with diabetes.

Resources

PERIODICALS

"Doctors Laboratory to Offer VAP Expanded Cholesterol Test." *Heart Diseases Weekly* September 7, 2003: 35.

"Results of a Prospective, Multi-center Study Showed that the Availability of Lipoprotein Subclass Testing (Vertical Auto profile (VAP) Cholesterol Test) Increased Use of Lipid-lowering Therapy by 59% in High-risk Patients with Type 2 Diabetes." *Diagnostics & Imaging Week* June 19, 2003: 6.

ORGANIZATIONS

American Heart Association National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, Review.personal.info@heart.org.

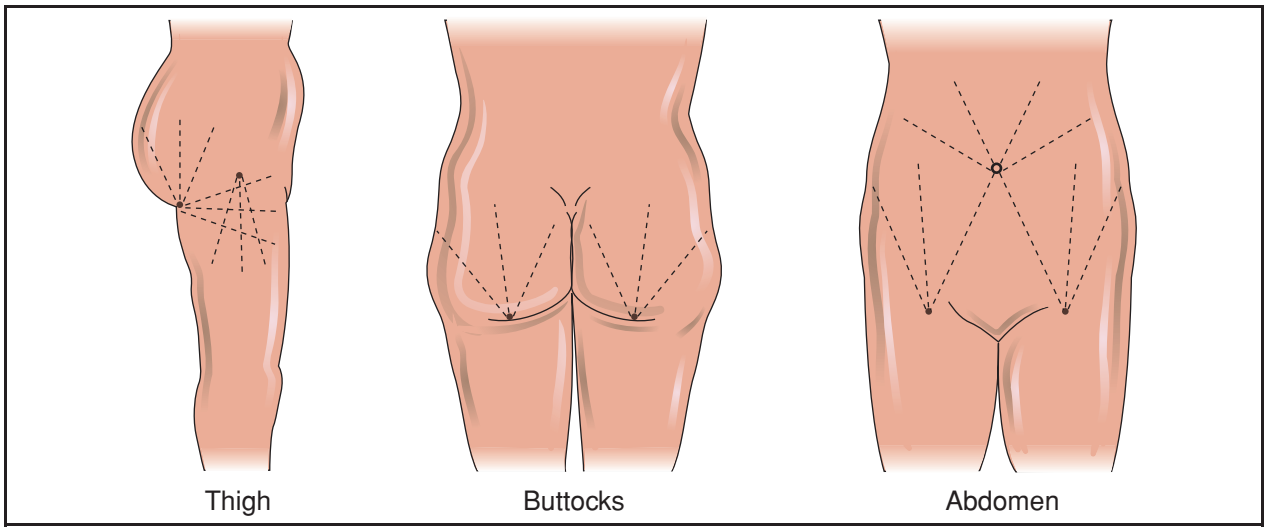
National Heart Lung and Blood Institute Health Information Center, P.O. Box 30105, Bethesda, MD, 20824-0105, (301) 592-8573, (240) 629-3246, http://www.nhlbi. nih.gov.

Nancy J. Nordenson
Teresa G. Odle

Liposuction

Definition

Liposuction, also known as lipoplasty or suction-assisted lipectomy, is **cosmetic surgery** performed to remove unwanted deposits of fat from under the skin. The surgeon sculpts and re-contours a person's body by removing excess fat deposits that have been



Common entry sites for liposuction procedures. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

"Before" photo of patient undergoing liposuction. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

"After" photo of same patient following liposuction. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

resistant to reduction by diet or **exercise**. Removal of fat cells is permanent.

Purpose

Liposuction is intended to reduce and smooth the contours of the body and improve a person's appearance. Its goal is cosmetic improvement. Liposuction does not remove large quantities of fat and is not intended as a weight-reduction technique. The average amount of fat removed is about 1 quart (1 liter). Although liposuction is not intended to remove cellulite (lumpy fat), some doctors believe that it improves the appearance of areas that contain cellulite, including thighs, hips, buttocks, abdomen, and chin. A technique called liposhaving shows more promise at reducing cellulite. Liposhaving can be done under **local anesthesia** and is reported to be less traumatic to the skin than liposuction. Liposuction is most often performed by board-certified plastic surgeons.

Demographics

Liposuction is the most commonly performed cosmetic procedure for men in the United States and the second most common cosmetic procedure (after breast augmentation) for women. In 2006, about 403,680 liposuction procedures were performed in the United States. This is more than double the amount performed ten years earlier.

Description

Most liposuction procedures are performed under local anesthesia. Local anesthesia produces loss of sensation without loss of consciousness. The tumescent, or wet, technique is used most often. In this technique, a large volume of very dilute anesthetic is injected under the person's skin, making the tissue swollen (tumescent) and firm. Epinephrine is added to the solution to reduce bleeding, which allows the removal of larger amounts of fat.

The physician first numbs the skin with an injection of local anesthetic. After the skin is desensitized, the doctor makes a series of tiny incisions no larger than 0.12–0.25 in (3–6 mm) in length. Flooding the area with more dilute anesthetic, fat is then extracted with suction through a long, blunt hollow tube called a cannula. The doctor repeatedly pushes the cannula through the fat layers in a radiating pattern creating tunnels, thus removing fat and re-contouring the area.

Some newer modifications to the procedure include the use of a cutting cannula called a liposhaver. Formerly some surgeons used ultrasound to help break up the fat deposits, but this technique has largely been abandoned because it created greater safety risks than the tumescent technique. Larger incisions may be closed with a suture or staple, while micro incisions are covered with **bandages** but do not need sutures. Incisions usually heal completely within two weeks and should leave few or no **scars**

KEY TERMS

Cellulite—Dimpled skin that is caused by uneven fat deposits beneath the surface.

Epinephrine—Epinephrine, also called adrenalin, occurs naturally in the body and causes blood vessels to constrict or narrow. As a drug, it is used to reduce bleeding.

Hemoglobin—The component of blood that carries oxygen to the tissues.

Liposhaving—Involves removing fat that lies closer to the surface of the skin by using a needle-like instrument that contains a sharp-edged shaving device.

The length of time required to perform the procedure varies with the amount of fat that is to be removed and the number of areas to be treated. Most operations take from 30 minutes up to two hours, but extensive procedures can take longer. Risk of complications increases the more extensive the procedure. The length of time required also varies with the manner in which the anesthetic is injected.

The cost of liposuction varies depending upon the fees commonly charged in the region of the country where it is performed, the extent of the area being treated, and the person performing the procedure. In the mid-2000s, an increasing trend was for Americans to go overseas to have cosmetic procedures performed in countries where they cost substantially less than in the United States. These procedures are cosmetic and are not covered by most insurance policies.

Diagnosis/Preparation

Liposuction is most successful when performed on persons who have firm, elastic skin and concentrated pockets of fat in areas that are characterized by cellulite. To get good results after fat removal, the skin must contract to conform to the new contours without sagging. Older persons have less elastic skin and, consequently, may not be good candidates for this procedure. People with generalized fat distribution, rather

than localized pockets, are not good candidates. Candidates should be in good general health and free of heart or lung disease. People who have poor circulation or who have had recent surgery at the intended site of fat reduction are not good candidates.

The doctor will conduct a **physical examination** and may order blood work to determine clotting time and hemoglobin level for transfusions, in case the need should arise. The person may be placed on **antibiotics** before surgery to ward off potential infection.

Aftercare

Liposuction is normally an outpatient procedure. Patients should plan to have someone available to drive them home and stay with them for the next 12–24 hours. If the tumescent technique is used, the patient will feel little or no **pain** for 24 hours following the procedure but after that may have soreness and swelling for several weeks. After some liposuction surgery, the patient may need to wear a support garment continuously for 2–3 weeks. If ankles or calves were treated, support hose should be worn for up to 6 weeks. The support garments can be removed during bathing. A drainage tube placed under the skin in the area of the procedure may be needed to prevent fluid build-up.

The incisions involved in this procedure are tiny, but the surgeon may close them with metal sutures or staples. These will be removed a few days surgery. Some micro-incisions are small enough that the doctor may not need to close them with sutures. Minor bleeding or seepage through the incision site(s) is common after this procedure. Wearing the elastic bandage or support garment helps reduce fluid loss.

The patient usually can return to normal activity within a week. Any postoperative bruising is expected to go away within 10–14 days. Postoperative swelling begins to go down after a week. It may take 3–6 months for the final contour to be reached depending on the extent of the surgery.

Risks

Liposuction under local anesthesia using the tumescent technique is exceptionally safe so long as the patient is in good health. The main hazards associated with this surgery involve migration of a blood clot or fat globule to the heart, brain, or lungs. Such an event can cause a **heart attack** or **stroke**. Ultrasound assisted liposuction has largely been abandoned because of safety concerns such as **burns** and complications such as scarring.

Staying in bed increases the risk of clot formation, but too much activity can result in increased swelling of the surgical area. Such swelling is a result of excess fluid and blood accumulation, and generally comes from not wearing the compression garments. If necessary, this excess fluid can be drained with a needle in the doctor's office.

Infection is another complication, but this rarely occurs. If the physician is skilled and works in a sterile environment, infection should not be much of a concern.

The greatest risk of complications arises when too much fat is removed or too many parts of the body are worked on at one time. If too much fat is removed, the skin may peel in that area. Smokers are at increased risk for shedding skin because their circulation is impaired. Removing too much fat may also cause the patient to go into **shock**.

Results

The loss of fat cells is permanent, and the patient should have smoother, more pleasing body contours without excessive bulges. Nevertheless, if the patient overeats, the remaining fat cells will grow in size. Although the patient may gain weight, the body should retain the new proportions and the suctioned area should remain proportionally smaller.

Tiny scars at the site of incision are normal. The doctor usually makes the incisions in places where the scars are not likely to show.

In some instances, the skin may appear rippled, wavy, or baggy after surgery. Pigmentation spots may develop. The re-contoured area may be uneven. This unevenness can be corrected with a second procedure that is less extensive than the first.

Morbidity and mortality rates

The morbidity rate from liposuction is less than 1%. Mortality is exceedingly rare.

Alternatives

Some of the alternatives to liposuction include modifying diet to lose excess body fat, exercise, accepting one's body and appearance as it is, or using clothing or makeup to downplay or emphasize body or facial features.

Resources

BOOKS

Loftus, Jean M. *The Smart Woman's Guide to Plastic Surgery*., 2nd ed. New York: McGraw-Hill, 2008.

Olesen, R. Merrell. *Cosmetic Surgery for Dummies*. Hoboken, NJ: Wiley, 2005.
Perry, Arthur W. *Straight Talk About Cosmetic Surgery*. New Haven, CT: Yale University Press, 2007.
Shelton, Ron M., and Terry Malloy. *Liposuction: A Question and Answer Guide to Today's Popular Cosmetic Procedure*. New York: Berkley Books, 2004.

OTHER

"Liposuction." United States Food and Drug Administration. 2005. [cited January 24, 2008]. http://www.fda.gov/womens/getthefacts/liposuction.html.

ORGANIZATIONS

American Board of Plastic Surgery, Seven Penn Center, Suite 400, 1635 Market Street, Philadelphia, PA, 19103-2204, (215) 587-9322, http://www.abplsurg.org.
American College of Surgeons, 633 North Saint Claire Street, Chicago, IL, 60611, (312) 202-5000, http://www.facs.org.
American Society for Aesthetic Plastic Surgery, 11081 Winners Circle, Los Alamitos, CA, 90720, (888) 272-7711, http://www.surgery.org.
American Society for Dermatologic Surgery, 5550 Meadowbrook Drive, Suite 120, Rolling Meadows, IL, 60006, (847) 956-0900, http://www.asds-net.org.
American Society of Plastic and Reconstructive Surgeons, 444 E. Algonquin Road, Arlington Heights, IL, 60005, (847) 228-9900, http://www.plasticsurgery.org.

L. Fleming Fallon, Jr., MD, PhD
Tish Davidson, AM
Brenda W. Lerner

Listeria monocytogenes infection *see* **Listeriosis**

Listeriosis

Definition

Listeriosis is an **infectious disease** caused by a bacterium, *Listeria monocytogenes*, which is most commonly acquired by eating contaminated food. The organism can spread to the blood stream and central nervous system. During **pregnancy**, listeriosis often causes **miscarriage** or **stillbirth**. It is also more likely to cause serious illness in the elderly, in newborns, or in people with weakened immune systems. Although listeriosis is infectious (caused by a disease organism), it is not contagious; that is, it is not spread by direct contact with other infected persons, with the exception of vaginal transmission during **childbirth**.

Demographics

Listeriosis, also called listeria infection, is usually an uncommon disease in the general human population in North America and Western Europe. There are on average 9.7 cases per million persons per year in Canada and the United States, and five cases per million per year in Europe; however, European doctors have reported as of early 2010 that the rate of listeriosis in Europe has been rising since 2005. Listeriosis is far more common among domestic animals, farm animals (particularly cattle and sheep), game animals, poultry, and wild birds than among humans. Listeriosis outbreaks are sporadic (rare and scattered in occurrence) rather than epidemic; they are, however, more common in cold or temperate climates than in the tropics, and more likely to occur in the summer in North America. The most recent foodborne outbreak in the United States occurred in Massachusetts in 2007 and involved contaminated milk.

Description

Listeriosis is caused by an infection with the gram-positive bacterium *Listeria monocytogenes*. The bacterium was named for Joseph Lister (1827–1912), a British surgeon honored as the pioneer of antiseptic surgery. The bacterium is rod-shaped and moves about with the help of a small flagellum. It secretes a chemical that causes the destruction of red blood cells.

This bacterium is carried by at least 64 different species of animals, and it has also been found in soil, water, sewage, and animal feed. Five out of every 100 people carry *L. monocytogenes* in their intestines. The bacterium is hardy and can survive in a wide temperature range, from 39°F (3.9°C) to 111°F (43.9°C). It is found almost everywhere in the world in plants and soils.

Listeriosis is considered a foodborne disease because most people become infected after eating food contaminated with *L. monocytogenes*. However, a woman can pass the bacteria to her baby during pregnancy. In addition, there have been a few cases in which veterinarians or farm workers have developed *Listeria* skin infections by touching infected calves or poultry.

There are five distinct clinical forms of listeriosis:

- Infection during pregnancy, most commonly in the third trimester.
- Neonatal (newborn) infection, which can take two forms: an early-onset inflammation of the entire body (sepsis), which usually results in premature

birth; and a late-onset infection of the central nervous system, which the baby acquires during vaginal delivery.

- Central nervous system (CNS) infection. *L. monocytogenes* has a special predilection for the central nervous system of humans. The infection may take the form of inflammation of the membranes covering the brain (meningitis), paralysis of the cranial nerves, inflammation of the brain tissue itself (encephalitis), or abscesses. Patients may suffer from seizures and changes in mental status.
- Gastroenteritis (inflammation of the digestive tract). *L. monocytogenes* can cause diarrhea lasting one to three days.
- Cutaneous listeriosis. This is an infection of the skin most likely to affect veterinarians and others who handle infected farm or wild animals.

Risk factors

Persons at particular risk for listeriosis include the elderly, pregnant women, newborns, those who take glucocorticosteroid medications (which suppress immune responses to infection), and those with a weakened immune system (immunocompromised). Risk is increased when a person suffers from diseases such as **AIDS**, **cancer**, **kidney disease**, **diabetes mellitus**, or by the use of certain medications. Infection is most common in babies younger than one month old and adults over 60 years of age. Pregnant women account for 27% of the cases and immunocompromised persons account for almost 70%. Persons with AIDS are 280 times more likely to get listeriosis than others.

With the exception of pregnant women, sex is not a risk factor for listeriosis; neither is race nor ethnicity.

Causes and symptoms

As noted, persons become infected with *L. monocytogenes* by eating contaminated food. *Listeria* has been found on raw vegetables, fish, poultry, raw (unpasteurized) milk, fresh meat, processed meat (such as deli meat, hot dogs, and canned meat), and certain soft cheeses—particularly Brie, Camembert, feta cheese, and bleu cheese. Listeriosis outbreaks in the United States since the 1980s have been linked to cole slaw, milk, Mexican–style cheese, undercooked hot dogs, undercooked chicken, and delicatessen or salad bar–type foods.

Unlike most other bacteria, *L. monocytogenes* does not stop growing when food is in the refrigerator—its growth is merely slowed. Although initial levels of the bacterium in contaminated foods are usually low, its ability to survive and multiply at low temperatures allows it to reach levels high enough to cause human disease, particularly if contaminated foods that allow for the growth of the organism are stored for prolonged times under refrigeration. Fortunately, typical cooking temperatures and the pasteurization process in milk do kill this bacterium.

Listeria bacteria can pass through the wall of the intestines, and from there they can get into the blood stream. Once in the blood stream, they can be transported anywhere in the body, but are commonly found the central nervous system (brain and spinal cord). In pregnant women they are often found in the placenta (the organ which connects the baby's umbilical cord to the uterus). *Listeria monocytogenes* live inside specific white blood cells called macrophages. Inside macrophages, the bacteria can hide from immune responses and become inaccessible to certain **antibiotics**. *Listeria* bacteria are capable of multiplying within macrophages, and then may spread to other macrophages.

Gastrointestinal listeriosis

After consuming food contaminated with this bacteria, symptoms of infection may appear anywhere from 11–70 days later. Most people do not get any noticeable symptoms. Scientists are unsure, but they believe that *L. monocytogenes* can cause upset stomach and intestinal problems just like other food-borne illnesses. Persons with listeriosis may develop such flu-like symptoms as **fever**, **headache**, **nausea and vomiting**, tiredness, and **diarrhea**.

Listeriosis in pregnancy

Pregnant women experience a mild, flu–like illness with fever, muscle aches, upset stomach, and intestinal problems. They recover, but the infection can cause miscarriage, **premature labor**, early rupture of the birth sac, and stillbirth. Unfortunately, half of the newborns infected with *Listeria* will die from the illness.

Neonatal listeriosis

There are two types of listeriosis in the newborn baby: early-onset disease and late-onset disease. Early-onset disease refers to a serious illness that is present at birth and usually causes the baby to be born prematurely. Babies infected during pregnancy usually have a blood infection (**sepsis**) and may have a serious, whole body infection called granulomatosis infantisepticum. When a full-term baby becomes infected with *Listeria* during childbirth, that situation is called late-onset disease. Commonly, symptoms of late–onset listeriosis

KEY TERMS

Abscess—An accumulation of pus caused by localized infection in tissues or organs. *L. monocytogenes* can cause abscesses in many organs, including the brain, spleen, and liver.

Brain stem—The posterior portion of the brain that connects directly to the spinal cord. It regulates breathing, heart function, and the sleep-wake cycle as well as maintaining consciousness.

Cutaneous—Pertaining to the skin.

Encephalitis—Acute inflammation of brain tissue.

Endocarditis—Inflammation of the endocardium, the inner layer of heart tissue.

Flagellum—A tail-like projection extending from the cell walls of certain bacteria. Its name is the Latin word for "whip."

Glucocorticosteroids—Also called glucocorticoids, a class of steroid hormones that play important roles in metabolism and the immune system. Synthetic glucocorticosteroids are drugs given to control certain allergic and immune system disorders; they include cortisone, prednisone, aldosterone, and dexamethasone. These drugs suppress the immune response to infection; thus they can increase a person's risk of listeriosis.

Immunocompromised—To have a poor immune system due to disease or medication. Immunocompromised persons are at risk for developing infections because they can not fight off microorganisms as can healthy persons.

Macrophages—White blood cells whose job is to destroy invading microorganisms. *Listeria monocytogenes* avoids being killed and can multiply within the macrophage.

Meningitis—Inflammation of the meninges, the layers of membranes that cover and protect the brain and spinal cord.

Sepsis—An inflammatory response of the whole body to an infection. Listeriosis in newborns may take the form of sepsis.

Sporadic—Rare and occasional in occurrence. Listeriosis in humans is a sporadic disease.

appear about two weeks after birth. Babies with late-term disease typically have **meningitis** (inflammation of the brain and spinal tissues); yet they have a better chance of surviving than those with early-onset disease.

Central nervous system involvement

Immunocompromised adults are at risk for a serious infection of the blood stream and central nervous system (brain and spinal cord). Meningitis occurs in about half of the cases of adult listeriosis. Symptoms of listerial meningitis occur about four days after the flu-like symptoms and include fever, personality change, uncoordinated muscle movement, **tremors**, muscle contractions, seizures, and slipping in and out of consciousness.

L. monocytogenes causes **endocarditis** in about 7.5% of cases of listeriosis. Endocarditis is an inflammation of heart tissue due to bacterial infection. Listerial endocarditis causes **death** in about half of patients. Other diseases which have been caused by *Listeria monocytogenes* include **brain abscess**, eye infection, hepatitis (**liver disease**), **peritonitis** (abdominal infection), lung infection, joint infection, arthritis, heart disease, bone infection, and gallbladder infection.

Diagnosis

Listeriosis may be diagnosed and treated by infectious disease specialists and internal medicine specialists. The diagnosis and treatment of this infection should be covered by most insurance providers.

Examination

The doctor may or may not suspect listeriosis on the basis of an office examination, as the symptoms of a gastrointestinal listeria infection are not unique to *L. monocytogenes*. A patient with listerial meningitis or **encephalitis** may have seizures, problems with movement, or mental status changes. But again, these can be caused by other disease organisms affecting the CNS. Laboratory tests are required to rule out other causes of the patient's symptoms.

Tests

The only way to confirm a diagnosis of listeriosis as of 2010 is to isolate *L. monocytogenes* from blood, cerebrospinal fluid (CSF), urine, or stool. A sample of cerebrospinal fluid is removed from the spinal cord using a needle and syringe. This procedure is commonly called a spinal tap. The amniotic fluid (the fluid that surrounds the unborn baby inside the uterus) may be tested in pregnant women with listeriosis.

This sample is obtained by inserting a needle through the abdomen into the uterus and withdrawing fluid. *L. monocytogenes* grows well in laboratory media, and test results can be available within a few days. Blood cultures and CSF tests are more reliable for identifying *L. monocytogenes* than stool tests.

Imaging tests may be performed if endocarditis or involvement of the brain stem are suspect. **Transesophageal echocardiography** is used to diagnose endocarditis. MRI is the most accurate form of imaging for identifying listeria infections in the brain stem.

Treatment

Traditional

Medications are the treatment of choice for listeriosis. Intravenous antibiotics must be started immediately as soon as the diagnosis is suspected or confirmed.

Drugs

Listeriosis is treated with antibiotics, most often ampicillin (Omnipen), chloramphenicol (Chloromycetin), or sulfamethoxazole-trimethoprim (Bactrim, Septra). Because the bacteria live within macrophage cells, treatment may be difficult and the treatment periods may vary. Usually, pregnant women are treated for two weeks; newborns, two to three weeks; adults with mild disease, two to four weeks; persons with meningitis, three weeks; persons with brain abscesses, six weeks; and persons with endocarditis, four to six weeks.

Patients are often hospitalized for treatment and monitoring. However, it is not necessary to isolate them because listeriosis is not spread by human contact. Other drugs may be provided to relieve **pain** and fever and to treat other reactions to the infection.

Prognosis

Although listeriosis is a relatively uncommon infectious disease, it does cause significant mortality; the overall mortality rate for listeria infections in humans in 20–30%. Listeriosis is the most virulent form of foodborne disease in North America, with fatality rates higher than those of **botulism** or *Salmonella***food poisoning**. According to the Centers for Disease Control and Prevention (CDC), there are on average 500 deaths from listeriosis each year in the United States.

Prevention

The CDC recommends the following precautions to prevent getting listeriosis:

- Cook all raw food thoroughly, and wash all raw vegetables carefully.
- Wash hands, knives, and cutting boards in hot soapy water after handling uncooked foods.
- Avoid drinking raw (unpasteurized) milk or consuming dairy products made from raw milk.
- Pregnant women or immunocompromised people should avoid Brie, Camembert, feta, Mexican queso blanco or queso fresco, and bleu cheese. Cream cheese, yogurt, and cottage cheese are safe to eat.
- Reheat leftovers or ready-to-eat foods like hot dogs until they are steaming hot.
- Avoid delicatessen foods unless they can be thoroughly reheated.
- Cook all fish and meat to safe internal temperatures.

Resources

BOOKS

Ryser, Elliott T., and Elmer H. Marth, editors. *Listeria, Listeriosis, and Food Safety*, 3rd ed. Boca Raton, FL: CRC Press, 2007.

Walker, W. Allan. *The Harvard Medical School Guide to Healthy Eating during Pregnancy*. New York: McGraw–Hill, 2006.

PERIODICALS

Allerberger, F., and M. Wagner. "Listeriosis: A Resurgent Foodborne Infection." *Clinical Microbiology and Infection* 16 (January 2010): 16–23.

Chan, Y.C., and M. Wiedmann. "Physiology and Genetics of *Listeria monocytogenes* Survival and Growth at Cold Temperatures." *Critical Reviews in Food Science and Nutrition* 49 (March 2009): 237–53.

Freitag, N.E., et al. "*Listeria monocytogenes*—From Saprophyte to Intracellular Pathogen." *Nature Reviews. Microbiology* 7 (September 2009): 623–28.

McClure, E.M., and R.L. Goldenberg. "Infection and Stillbirth." *Seminars in Fetal and Neonatal Medicine* 14 (August 2009): 182–89.

Posfay–Barbe, K.M., and E.R. Wald. "Listeriosis." *Seminars in Fetal and Neonatal Medicine* 14 (August 2009): 228–33.

Sleator, R.D., et al. "The Interaction between *Listeria monocytogenes* and the Host Gastrointestinal Tract." *Microbiology* 155 (August 2009): 2463–75.

Wilson, J., and J.S. Brownstein. "Early Detection of Disease Outbreaks Using the Internet." *Canadian Medical Association Journal* 180 (April 14, 2009): 829–31.

OTHER

Centers for Disease Control and Prevention (CDC). "Listeriosis". http://www.cdc.gov/nczved/divisions/dfbmd/diseases/listeriosis/ (accessed September 26, 2010).

Food and Drug Administration (FDA). "Listeria". http://www.fda.gov/ForConsumers/ByAudience/ForWomen/ucm118542.htm (accessed September 26, 2010).

Mayo Clinic. "Listeria Infection." http://www.mayoclinic.com/health/listeria–infection/DS00963 (accessed September 26, 2010).
Weinstein, Karen B., and Joanna Ortiz. "*Listeria monocytogenes*." eMedicine. (June 23, 2008). http://emedicine.medscape.com/article/220684–overview (accessed September 26, 2010).

ORGANIZATIONS

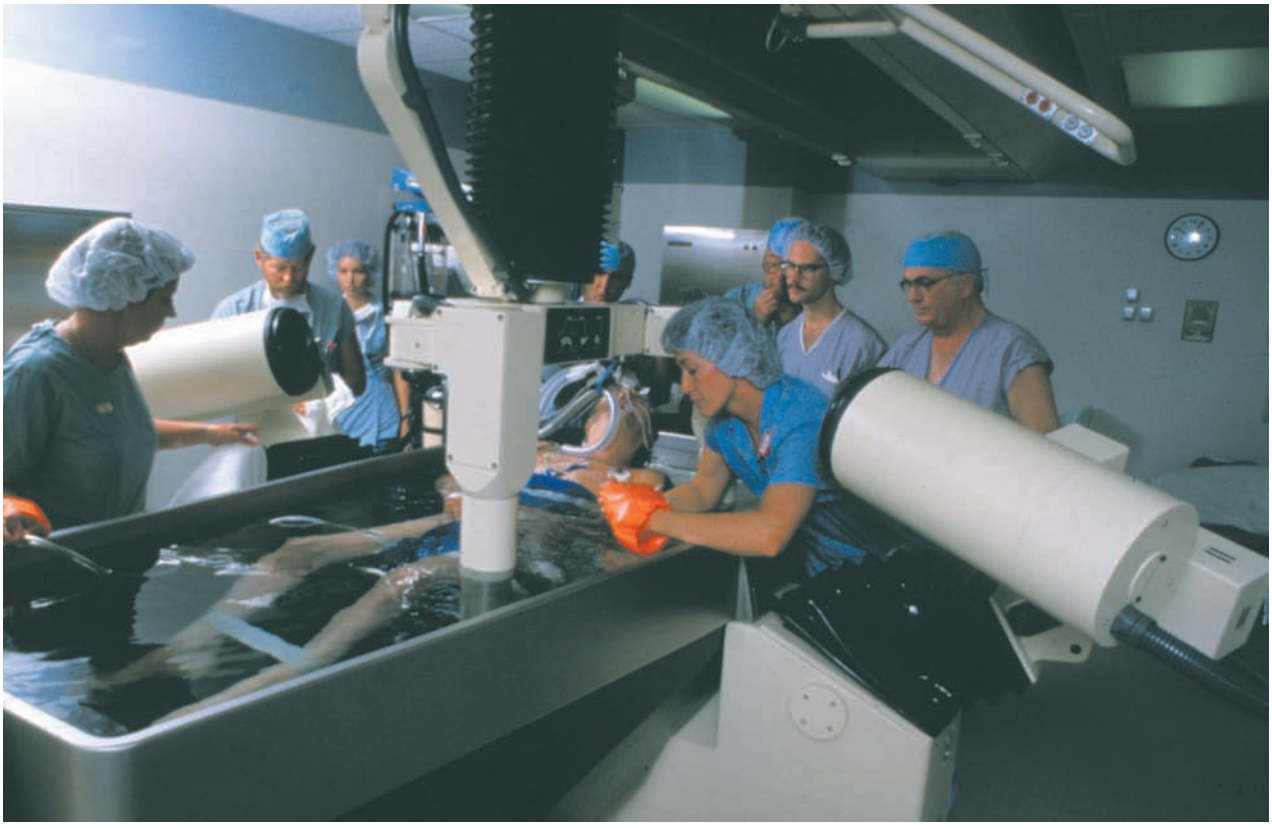
American College of Emergency Physicians (ACEP), 1125 Executive Circle, Irving, TX, 75038-2522, (972) 550-0911, (800) 798-1822, (972) 580-2816, http://www.acep.org/.
American Veterinary Medical Association (AVMA), 1931 North Meacham Rd., Suite 100, Schaumburg, IL, 60173-4360, (847) 925-8070, (847) 925-1329, avmainfo@avma.org, http://www.avma.org/.
Centers for Disease Control and Prevention (CDC), 1600 Clifton Rd., Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.
National Institute of Allergy and Infectious Diseases (NIAID), 6610 Rockledge Dr., MSC 6612, Bethesda, MD, 20892-6612, (301) 496-5717, (866) 284-4107, (301) 402-3573, http://www3.niaid.nih.gov.
U.S. Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD, 20993, (888) 463-6332, http://www.fda.gov/.
World Health Organization (WHO), Avenue Appia 20, 1211 Geneva 27, Switzerland, + 41 22 791 21 11, + 41 22 791 31 11, info@who.int, http://www.who.int/en/.

Belinda Rowland, PhD
Rebecca J. Frey, PhD

Lithotripsy

Definition

Lithotripsy is the use of high-energy shock waves to fragment and disintegrate **kidney stones**. The shock wave, created by using a high-voltage spark or an electromagnetic impulse, is focused on the stone. This shock wave shatters the stone and this allows the fragments to pass through the urinary system. Since the shock wave is generated outside the body, the procedure is termed extracorporeal shock wave lithotripsy, or ESWL.



A lithotripter in use by patient in tub. This noninvasive method crushes kidney stones through shock waves. *(Photo Researchers, Inc.)*

KEY TERMS

Aneurysm—A dilation of the wall of an artery which causes a weak area prone to rupturing.

Bladder—Organ in which urine is stored prior to urination.

Bleeding disorder—Problems in the clotting mechanism of the blood.

Cardiologist—A physician who specializes in problems of the heart.

EKG—A tracing of the electrical activity of the heart.

ESWL (Extracorporeal shock wave lithotripsy)—The use of focused shock waves, generated outside the body, to fragment kidney stones.

Gravel—The debris which is formed from a fragmented kidney stone.

IVP (Intravenous pyelogram)—The use of a dye, injected into the veins, used to locate kidney stones. Also used to determine the anatomy of the urinary system.

Kidney stone—A hard mass that forms in the urinary tract and which can cause pain, bleeding, obstruction, or infection. Stones are primarily made up of calcium.

Stent—A plastic tube placed in the ureter prior to the ESWL procedure which facilitates the passage of gravel and urine.

Ultrasound—Sound waves used to determine the internal structures of the body.

Ureter—A tube which carries urine from the kidney to the bladder.

Urethra—A tube through which urine passes during urination.

Urologist—A physician who specializes in problems of the urinary system.

Purpose

ESWL is used when a kidney stone is too large to pass on its own, or when a stone becomes stuck in a ureter (a tube which carries urine from the kidney to the bladder) and will not pass. Kidney stones are extremely painful and can cause serious medical complications if not removed.

Precautions

ESWL should not be considered for patients with severe skeletal deformities, patients weighing over 300 lbs (136 kg), patients with abdominal aortic aneurysms, or patients with uncontrollable bleeding disorders. Patients who are pregnant should not be treated with ESWL. Patients with cardiac **pacemakers** should be evaluated by a cardiologist familiar with ESWL. The cardiologist should be present during the ESWL procedure in the event the pacemaker needs to be overridden.

Description

Lithotripsy uses the technique of focused shock waves to fragment a stone in the kidney or the ureter. The patient is placed in a tub of water or in contact with a water-filled cushion, and a shock wave is created which is focused on the stone. The wave shatters and fragments the stone. The resulting debris, called gravel, then passes through the remainder of the ureter, through the bladder, and through the urethra during urination. There is minimal chance of damage to skin or internal organs because biologic tissues are resilient, not brittle, and because the the shock waves are not focused on them.

Preparation

Prior to the lithotripsy procedure, a complete **physical examination** is done, followed by tests to determine the number, location, and size of the stone or stones. A test called an intravenous pyelogram, or IVP, is used to locate the stones. An IVP involves injecting a dye into a vein in the arm. This dye, which shows up on x ray, travels through the bloodstream and is excreted by the kidneys. The dye then flows down the ureters and into the bladder. The dye surrounds the stones, and x rays are then used to evaluate the stones and the anatomy of the urinary system. (Some people are allergic to the dye material, so it cannot be used. For these people, focused sound waves, called ultrasound, can be used to see where the stones are located.) Blood tests are done to determine if any potential bleeding problems exist. For women of childbearing age, a **pregnancy** test is done to make sure the patient isn't pregnant; and elderly patients have an EKG done to make sure no potential heart problems exist. Some patients may have a stent placed prior to the lithotripsy procedure. A stent is a plastic tube placed in the ureter which allows the passage of gravel and urine after the ESWL procedure is completed.

Aftercare

Most patients have a lot of blood in their urine after the ESWL procedure. This is normal and should clear

after several days to a week or so. Lots of fluids should be taken to encourage the flushing of any gravel remaining in the urinary system. The patient should follow up with the urologist in about two weeks to make sure that everything is going as planned. If a stent has been inserted, it is normally removed at this time. Patients may return to work whenever they feel able.

Risks

Abdominal **pain** is not uncommon after ESWL, but it is usually not cause to worry. However, persistent or severe abdominal pain may imply unexpected internal injury. Colicky renal pain is very common as gravel is still passing. Other problems may include perirenal hematomas (**blood clots** near the kidneys) in 66% of the cases; nerve palsies; **pancreatitis** (inflammation of the pancreas); and obstruction by stone fragments. Occasionally, stones may not be completely fragmented during the first ESWL treatment and further ESWL procedures may be required.

ORGANIZATIONS

American Urological Association (AUA), 1000 Corporate Boulevard, Linthicum, MD, 21090, (410) 689-3700, (410) 689-3800, (866) 746-4282, aua@AUAnet.org, http://www.auanet.org.

Joseph Knight, PA

Live cell therapy *see* **Cell therapy**

Liver-spleen scan *see* **Liver nuclear medicine scan**

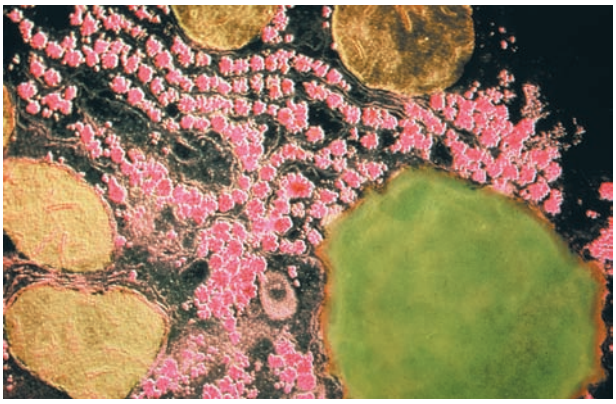
Liver biopsy

Definition

A liver biopsy is a medical procedure performed to obtain a small piece of liver tissue for diagnostic testing. Liver biopsies are sometimes called percutaneous liver biopsies, because the tissue sample is obtained by going through the patient's skin.

Purpose

A liver biopsy is usually done to diagnose a tumor, or to evaluate the extent of damage that has occurred to the liver because of chronic disease. Biopsies are often performed to identify abnormalities in liver tissues after imaging studies have failed to yield clear results.



A false color image of hepatocyte cells of the liver that secrete bile. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

A liver biopsy may be ordered to evaluate any of the following conditions or disorders:

- jaundice
- cirrhosis
- hemochromatosis—a condition of excess iron in the liver.
- repeated abnormal results from liver function tests
- unexplained swelling or enlargement of the liver
- primary cancers of the liver, such as hepatomas, cholangiocarcinomas, and angiosarcomas
- metastatic cancers of the liver

Precautions

Some patients should not have percutaneous liver biopsies. They include patients with any of the following conditions:

- platelet count below 60,000
- longer-than-normal prothrombin time
- liver tumor that contains a large number of blood vessels
- history of unexplained bleeding
- watery (hydatid) cyst
- infection in either the cavity around the lungs, or the diaphragm

Description

Percutaneous liver biopsy is done with a special hollow needle, called a Menghini needle, attached to a suction syringe. Doctors who specialize in the digestive system or liver will sometimes perform liver biopsies. But in most cases, a radiologist (a doctor who specializes in x rays and imaging studies) performs the

biopsy. The radiologist will use computed tomography scan (CT scan) or ultrasound to guide the choice of the site for the biopsy.

An hour or so before the biopsy, the patient may be given a sedative to help relaxation. He or she is then asked to lie on the back with the right elbow to the side and the right hand under the head. The patient is instructed to lie as still as possible during the procedure. He or she is warned to expect a sensation resembling a punch in the right shoulder, but to hold still in spite of the momentary feeling.

The doctor marks a spot on the skin where the needle will be inserted and thoroughly cleanses the right side of the upper abdomen with an antiseptic solution. The patient is then given an anesthetic at the biopsy site.

The needle with attached syringe is inserted into the patient's chest wall. The doctor then draws the plunger of the syringe back to create a vacuum. At this point the patient is asked to take a deep breath, exhale the air and hold their breath at the point of complete exhalation. The needle is inserted into the liver and withdrawn quickly, usually within two seconds or less. The negative pressure in the syringe draws or pulls a sample of liver tissue into the biopsy needle. As soon as the needle is withdrawn, the patient can breathe normally. Pressure is applied at the biopsy site to stop any bleeding, and a bandage will be placed over it. The entire procedure takes 10 to 15 minutes. Test results are usually available within a day.

KEY TERMS

Biopsy—A procedure where a piece of tissue is removed from a patient for diagnostic testing.

Menghini needle—A special needle used to obtain a sample of liver tissue.

Percutaneous biopsy—A biopsy in which a needle is inserted and a tissue sample removed through the skin.

Prothrombin time—A blood test that determines how quickly a person's blood will clot.

Vital signs—A person's essential body functions, usually defined as the pulse, body temperature, and breathing rate.

Preparation

Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen are known to thin the blood and interfere with clotting. These medications should be avoided for at least a week before the biopsy. Four to eight hours before the biopsy, patients should stop eating and drinking.

The patient's blood will be tested prior to the biopsy to make sure that it is clotting normally. Tests will include a **platelet count** and a **prothrombin time**. Doctors will also ensure that the patient is not taking any other medications, such as blood thinners like Coumadin, that might affect blood clotting.

Aftercare

Liver biopsies are outpatient procedures in most hospitals. After the biopsy, patients are usually instructed to lie on their right side for about two hours. This provides pressure to the biopsy site and helps prevent bleeding. A nurse will check the patient's vital signs at regular intervals. If there are no complications, the patient is sent home within about four to eight hours.

Patients should arrange to have a friend or relative take them home after discharge. Bed rest for a day is recommended, followed by a week of avoiding heavy work or strenuous **exercise**. The patient can resume eating a normal diet.

Some mild soreness in the area of the biopsy is normal after the anesthetic wears off. Irritation of the muscle that lies over the liver can also cause mild discomfort in the shoulder for some patients. Tylenol can be taken for minor soreness, but aspirin and NSAIDs are best avoided. Patients should call their doctor if they have severe **pain** in the abdomen, chest or shoulder, difficulty breathing, or persistent bleeding. These signs may indicate that there has been leakage of bile into the abdominal cavity, or that air has been introduced into the cavity around the lungs.

Risks

The risks of a liver biopsy are usually very small. When complications do occur, over 90% are apparent within 24 hours after the biopsy. The most significant risk is internal bleeding. Bleeding is most likely to occur in elderly patients, in patients with **cirrhosis**, or in patients with a tumor that has many blood vessels. Other complications from percutaneous liver biopsies include the leakage of bile or the introduction of air into the chest cavity (**pneumothorax**). There is also a small chance that an infection may occur, or an internal organ such as the lung, gall bladder, or kidney could be punctured.

Results

After the biopsy, the liver sample is sent to the pathology laboratory for study under a microscope. A normal (negative) result would find no evidence of **cancer** or other disease in the tissue sample.

Changes in liver tissue that are visible under the microscope indicate abnormal results. Possible causes for the abnormality include the presence of a tumor, or a disease such as hepatitis.

Resources

BOOKS

Kanel, Gary C., and Jacob Korula. *Atlas of Liver Pathology*. 3rd ed. Philadelphia; London: Saunders, 2011.

Lefkowitch, Jay H., and Peter J. Scheuer. *Scheuer's Liver Biopsy Interpretation*. Edinburgh: Saunders, 2010.

PERIODICALS

Bravo, Arturo A., et al. "Liver Biopsy" *New England Journal of Medicine* 344, no. 7 (February 15, 2001): 495-500.

Lata Cherath, PhD

Liver cancer

Definition

Liver **cancer** is a relatively rare form of cancer but has a high mortality rate. Liver cancers can be classified into two types. They are either primary, when the cancer starts in the liver itself, or metastatic, when the cancer has spread to the liver from some other part of the body.

Description

Primary liver cancer

Primary liver cancer is a relatively rare disease in the United States, representing about 2% of all malignancies and 4% of newly diagnosed cancers. Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world. It is much more common outside the United States, representing 10% to 50% of malignancies in Africa and parts of Asia. Rates of HCC in men are at least two to three times higher than for women. In high–risk areas (East and Southeast Asia, sub-Saharan Africa), men are even more likely to have HCC than women.

According to the American Cancer Society, 18,920 people in the United States will be diagnosed with primary liver cancer in 2004, and 14,270 persons will die from the disease. The incidence of primary liver cancer has been rising in the United States and Canada since the mid-1990s, most likely as a result of the rising rate of **hepatitis C** infections.

TYPES OF PRIMARY LIVER CANCER. In adults, most primary liver cancers belong to one of two types: hepatomas, or hepatocellular carcinomas (HCC), which start in the liver tissue itself; and cholangiomas, or cholangiocarcinomas, which are cancers that develop in the bile ducts inside the liver. About 80% to 90% of primary liver cancers are hepatomas. In the United States, about five persons in every 200,000 will develop a hepatoma (70% to 75% of cases of primary liver cancers are HCC). In Africa and Asia, over 40 persons in 200,000 will develop this form of cancer (more than 90% of cases of primary liver are HCC). Two rare types of primary liver cancer are mixed-cell tumors and Kupffer cell **sarcomas**.

One type of primary liver cancer, called a hepatoblastoma, usually occurs in children younger than four years of age and between the ages of 12 and 15. Unlike liver cancers in adults, hepatoblastomas have a good chance of being treated successfully. Approximately 70% of children with hepatoblastomas experience complete cures. If the tumor is detected early, the survival rate is over 90%.

Metastatic liver cancer

The second major category of liver cancer, metastatic liver cancer, is about 20 times as common in the United States as primary liver cancer. Because blood from all parts of the body must pass through the liver for filtration, cancer cells from other organs and tissues easily reach the liver, where they can lodge and grow into secondary tumors. Primary cancers in the colon, stomach, pancreas, rectum, esophagus, breast, lung, or skin are the most likely to metastasize (spread) to the liver. It is not unusual for the metastatic cancer in the liver to be the first noticeable sign of a cancer that started in another organ. After **cirrhosis**, metastatic liver cancer is the most common cause of fatal **liver disease**.

Causes and symptoms

Risk factors

The exact cause of primary liver cancer is still unknown. In adults, however, certain factors are known to place some individuals at higher risk of developing liver cancer. These factors include:

- Male sex.
- Age over 60 years.

- Ethnicity. Asian Americans with cirrhosis have four times as great a chance of developing liver cancer as Caucasians with cirrhosis, and African Americans have twice the risk of Caucasians. In addition, Asians often develop liver cancer at much younger ages than either African Americans or Caucasians.
- Exposure to substances in the environment that tend to cause cancer (carcinogens). These include: a substance produced by a mold that grows on rice and peanuts (aflatoxin); thorium dioxide, which was once used as a contrast dye for x rays of the liver; vinyl chloride, used in manufacturing plastics; and cigarette smoking.
- Use of oral estrogens for birth control.
- Hereditary hemochromatosis. This is a disorder characterized by abnormally high levels of iron storage in the body. It often develops into cirrhosis.
- Cirrhosis. Hepatomas appear to be a frequent complication of cirrhosis of the liver. Between 30% and 70% of hepatoma patients also have cirrhosis. It is estimated that a patient with cirrhosis has 40 times the chance of developing a hepatoma than a person with a healthy liver.
- Exposure to hepatitis viruses: Hepatitis B (HBV), Hepatitis C (HCV), Hepatitis D (HDV), or Hepatitis G (HGV). It is estimated that 80% of worldwide HCC is associated with chronic HBV infection. In Africa and most of Asia, exposure to hepatitis B is an important factor; in Japan and some Western countries, exposure to hepatitis C is connected with a higher risk of developing liver cancer. In the United States, nearly 25% of patients with liver cancer show evidence of HBV infection. Hepatitis is commonly found among intravenous drug abusers. The 70% increase in HCC incidence in the United States is thought to be due to increasing rates of HBV and HCV infections due to increased sexual promiscuity and illicit drug needle sharing. The association between HDV and HGV and HCC is unclear at this time.

Symptoms of liver cancer

The early symptoms of primary, as well as metastatic, liver cancer are often vague and not unique to liver disorders. The long period between the beginning of the tumor's growth and the first signs of illness is the major reason why the disease has such a high mortality rate. At the time of diagnosis, patients are often fatigued, with **fever**, abdominal **pain**, and loss of appetite. They may look emaciated and generally ill. As the tumor enlarges, it stretches the membrane surrounding the liver (the capsule), causing pain in the upper abdomen on the right side. The pain may extend into the back and shoulder. Some patients develop a collection of fluid, known as **ascites**, in the abdominal cavity. Others may show signs of bleeding into the digestive tract. In addition, the tumor may block the ducts of the liver or the gall bladder, leading to **jaundice**. In patients with jaundice, the whites of the eyes and the skin may turn yellow, and the urine becomes dark-colored.

Diagnosis

Physical examination

If the doctor suspects a diagnosis of liver cancer, he or she will check the patient's history for risk factors and pay close attention to the condition of the patient's abdomen during the **physical examination**. Masses or lumps in the liver and ascites can often be felt while the patient is lying flat on the examination table. The liver is usually swollen and hard in patients with liver cancer; it may be sore when the doctor presses on it. In some cases, the patient's spleen is also enlarged. The doctor may be able to hear an abnormal sound (bruit) or rubbing noise (friction rub) if he or she uses a stethoscope to listen to the blood vessels that lie near the liver. The noises are caused by the pressure of the tumor on the blood vessels.

Laboratory tests

Blood tests may be used to test liver function or to evaluate risk factors in the patient's history. Between 50% and 75% of primary liver cancer patients have abnormally high blood serum levels of a particular protein (alpha-fetoprotein or AFP). The AFP test, however, cannot be used by itself to confirm a diagnosis of liver cancer, because cirrhosis or chronic hepatitis can also produce high alpha–fetoprotein levels. Tests for alkaline phosphatase, bilirubin, lactic dehydrogenase, and other chemicals indicate that the liver is not functioning normally. About 75% of patients with liver cancer show evidence of hepatitis infection. Again, however, abnormal liver function test results are not specific for liver cancer.

Imaging studies

Imaging studies are useful in locating specific areas of abnormal tissue in the liver. Liver tumors as small as an inch across can now be detected by ultrasound or computed tomography scan (CT scan). Imaging studies, however, cannot tell the difference between a hepatoma and other abnormal masses or lumps of tissue (nodules) in the liver. A sample of liver tissue for biopsy is needed to make the definitive

diagnosis of a primary liver cancer. CT or ultrasound can be used to guide the doctor in selecting the best location for obtaining the biopsy sample.

Chest x rays may be used to see whether the liver tumor is primary or has metastasized from a primary tumor in the lungs.

Liver biopsy

Liver biopsy is considered to provide the definite diagnosis of liver cancer. A sample of the liver or tissue fluid is removed with a fine needle and is checked under a microscope for the presence of cancer cells. In about 70% of cases, the biopsy is positive for cancer. In most cases, there is little risk to the patient from the biopsy procedure. In about 0.4% of cases, however, the patient develops a fatal hemorrhage from the biopsy because some tumors are supplied with a large number of blood vessels and bleed very easily.

Laparoscopy

The doctor may also perform a **laparoscopy** to help in the diagnosis of liver cancer. First, the doctor makes a small cut in the patient's abdomen and inserts a small, lighted tube called a laparoscope to view the area. A small piece of liver tissue is removed and examined under a microscope for the presence of cancer cells.

Treatment

Treatment of liver cancer is based on several factors, including the type of cancer (primary or metastatic); stage (early or advanced); the location of other primary cancers or metastases in the patient's body; the patient's age; and other coexisting diseases, including cirrhosis. For many patients, treatment of liver cancer is primarily intended to relieve the pain caused by the cancer but cannot cure it.

Surgery

Few liver cancers in adults can be cured by surgery because they are usually too advanced by the time they are discovered. If the cancer is contained within one lobe of the liver, and if the patient does not have either cirrhosis, jaundice, or ascites, surgery is the best treatment option. Patients who can have their entire tumor removed have the best chance for survival. Unfortunately, only about 5% of patients with metastatic cancer (from primary tumors in the colon or rectum) fall into this group. If the entire visible tumor can be removed, about 25% of patients will be cured. The operation that is performed is called a partial hepatectomy, or partial removal of the liver. The surgeon will remove either an entire lobe of the liver (a **lobectomy**) or cut out the area around the tumor (a wedge resection).

A newer technique that is reported to be safe and effective is laparoscopic radiofrequency ablation (RFA). RFA is a technique in which the surgeon places a special needle electrode in the tumor under guidance from MRI or CT scanning. When the electrode has been properly placed, a radiofrequency current is passed through it, heating the tumor and killing the cancer cells. RFA can be used to treat tumors that are too small or too inaccessible for removal by conventional open surgery.

Chemotherapy

Some patients with metastatic cancer of the liver can have their lives prolonged for a few months by **chemotherapy**, although cure is not possible. If the tumor cannot be removed by surgery, a tube (catheter) can be placed in the main artery of the liver and an implantable infusion pump can be installed. The pump allows much higher concentrations of the cancer drug to be carried to the tumor than is possible with chemotherapy carried through the bloodstream. The drug that is used for infusion pump therapy is usually floxuridine (FUDR), given for 14-day periods alternating with 14-day rests. Systemic chemotherapy can also be used to treat liver cancer. The medications usually used are 5-fluorouracil (Adrucil, Efudex) or methotrexate (MTX, Mexate). Systemic chemotherapy does not, however, significantly lengthen the patient's survival time.

Radiation therapy

Radiation therapy is the use of high-energy rays or x rays to kill cancer cells or to shrink tumors. Its use in liver cancer, however, is only to give short–term relief from some of the symptoms. Liver cancers are not sensitive to radiation, and radiation therapy will not prolong the patient's life.

Liver transplantation

Removal of the entire liver (total hepatectomy) and **liver transplantation** can be used to treat liver cancer. However, there is a high risk of tumor recurrence and metastases after transplantation. In addition, most patients have cancer that is too far advanced at the time of diagnosis to benefit from liver transplantation.

Other therapies

Other therapeutic approaches include:

- Hepatic artery embolization with chemotherapy (chemoembolization).

KEY TERMS

Aflatoxin—A substance produced by molds that grow on rice and peanuts. Exposure to aflatoxin is thought to explain the high rates of primary liver cancer in Africa and parts of Asia.

Alpha-fetoprotein—A protein in blood serum that is found in abnormally high concentrations in most patients with primary liver cancer.

Cirrhosis—A chronic degenerative disease of the liver, in which normal cells are replaced by fibrous tissue. Cirrhosis is a major risk factor for the later development of liver cancer.

Cryoablation—A technique for removing cancerous tissue by killing it with extreme cold.

Hepatitis—A viral disease characterized by inflammation of the liver cells (hepatocytes). People infected with hepatitis B or hepatitis C virus are at an increased risk for developing liver cancer.

Metastatic cancer—A cancer that has spread to an organ or tissue from a primary cancer located elsewhere in the body.

Radiofrequency ablation—A technique for removing a tumor by heating it with a radiofrequency current passed through a needle electrode.

- Alcohol ablation via ultrasound-guided percutaneous injection.
- Ultrasound-guided cryoablation.
- Immunotherapy with monoclonal antibodies tagged with cytotoxic agents.
- Gene therapy with retroviral vectors containing genes expressing cytotoxic agents.

Alternative treatment

Many patients find that alternative and complementary therapies help to reduce the **stress** associated with illness, improve immune function, and boost spirits. While there is no clinical evidence that these therapies specifically combat disease, activities such as **biofeedback**, relaxation, **therapeutic touch**, **massage therapy** and **guided imagery** have no side effects and have been reported to enhance well–being.

Several other healing therapies are sometimes used as supplemental or replacement cancer treatments, such as antineoplastons, cancell, cartilage (bovine and shark), laetrile, and mistletoe. Many of these therapies have not been the subject of safety and efficacy trials by the National Cancer Institute (NCI). The NCI has conducted trials on cancell, laetrile, and other alternative therapies and found no anticancer activity. These treatments have varying effectiveness and safety considerations. Patients using any alternative remedy should first consult their doctor in order to prevent harmful side effects or interactions with traditional cancer treatment.

Prognosis

Liver cancer has a very poor prognosis because it is often not diagnosed until it has metastasized. Fewer than 10% of patients survive three years after the initial diagnosis; the overall five-year survival rate for patients with hepatomas is around 4%. Most patients with primary liver cancer die within six months of diagnosis, usually from liver failure; fewer than 5% are cured of the disease. Patients with liver cancers that metastasized from cancers in the colon live slightly longer than those whose cancers spread from cancers in the stomach or pancreas.

African American and Hispanic patients have much lower 5-year survival rates than Caucasian patients. It is not yet known, however, whether cultural differences as well as biological factors may be partly responsible for the variation in survival rates.

Prevention

There are no useful strategies at present for preventing metastatic cancers of the liver. Primary liver cancers, however, are 75% to 80% preventable. Current strategies focus on widespread **vaccination** for **hepatitis B**, early treatment of hereditary **hemochromatosis**, and screening of high-risk patients with alpha–fetoprotein testing and ultrasound examinations.

Lifestyle factors that can be modified in order to prevent liver cancer include avoidance of exposure to toxic chemicals and foods harboring molds that produce aflatoxin. Most important, however, is avoidance of alcohol and drug **abuse**. Alcohol abuse is responsible for 60% to 75% of cases of cirrhosis, which is a major risk factor for eventual development of primary liver cancer. Hepatitis is a widespread disease among persons who abuse intravenous drugs.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Berber, E., A. Senagore, F. Remzi, et al. "Laparoscopic Radiofrequency Ablation of Liver Tumors Combined with Colorectal Procedures." *Surgical Laparoscopy, Endoscopy and Percutaneous Techniques* 14 (August 2004): 186–190.

Cahill, B. A., and D. Braccia. "Current Treatment for Hepatocellular Carcinoma." *Clinical Journal of Oncology Nursing* 8 (August 2004): 393–399.

Decadt, B., and A. K. Siriwardena. "Radiofrequency Ablation of Liver Tumours: Systematic Review." *Lancet Oncology* 5 (September 2004): 550–560.

Harrison, L. E., T. Reichman, B. Koneru, et al. "Racial Discrepancies in the Outcome of Patients with Hepatocellular Carcinoma." *Archives of Surgery* 139 (September 2004): 992–996.

Nguyen, M. H., A. S. Whittemore, R. T. Garcia, et al. "Role of Ethnicity in Risk for Hepatocellular Carcinoma in Patients with Chronic Hepatitis C and Cirrhosis." *Clinical Gastroenterology and Hepatology* 2 (September 2004): 820–824.

OTHER

American Cancer Society (ACS). *Cancer Facts & Figures 2010*. http://www.cancer.org/Research/CancerFacts-Figures/index?ssSourceSiteId = null

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

American College of Gastroenterology, PO Box 342260, Bethesda, MD, 20827-2260, (30·) 263-9000, http://www.acg.gi.org.

American Institute for Cancer Research (AICR), 1759 R St. NW, Washington, DC, 20009, (202) 328-7744, (202) 328-7226, (800) 843-8114, aicrweb@aicr.org, http://aicr.org.

American Liver Foundation, 75 Maiden Lane, Suite 603, New York, NY, 10038, (212) 668-1000, (212) 483-8179, http://www.liverfoundation.org/.

CancerCare, National Office, 275 Seventh Ave., Floor 22, New York, NY, 10001, (212) 712-8400, (212) 712-8495, (800) 813-HOPE, info@cancercare.org, http://www.cancercare.org/.

Cancer Hope Network, 2 North Road - Suite A, Chester, NJ, 07930, (908) 879-4039, (908) 879-6518, (800) 552-4366, http://www.cancerhopenetwork.org/.

Hospice Education Institute, 3 Unity Square; P.O. Box 98, Machiasport, ME, 04655-0098, (207) 255-8800, (207) 255-8008, (800) 331-1620, info@hospiceworld.org, http://www.hospiceworld.org/.

National Cancer Institute (National Institutes of Health), NCI Office of Communications and Education, 6116 Executive Blvd. Suite 300, Bethesda, MD, 20892-8322, (800) 4-CANCER (422-6237), cancergovstaff@mail.nih.gov, http://www.cancer.gov/.

Rebecca J. Frey, PhD
Laura Ruth, PhD

Liver cirrhosis *see* **Cirrhosis**

Liver disease

Definition

Liver disease is a general term for any damage that reduces the functioning of the liver.

Description

The liver is a large, solid organ located in the upper right-hand side of the abdomen. Most of the liver lies under the rib cage, which helps protect it from physical injury. The liver is made up of two main lobes and two minor lobes and has a total weight in adults of about 3.5 lb (1.6 kg).

Within the liver are tiny ducts (tubes) that collect bile, a product secreted by the liver. Bile is stored in to the gall bladder and then released into the intestines after meals to help in the digestion of fats and the absorption of certain **vitamins**. This system of bile production by the liver, transport through the bile ducts, and storage in the gall bladder is called the biliary system. Damage to this system is called biliary disease.

The liver receives blood that comes directly from the intestines. At any given time the liver contains about 13% of the blood circulating in the body. This blood is rich in nutruents (food, vitamins, and **minerals**) that the body needs to function. Some of the most important functions of the liver are to process these nutrients.

Important functions of the liver include:

- manufacturing and regulating the production of proteins. The most important proteins made in the liver are albumin, which helps maintain blood volume, and clotting factors to help regulate blood clotting.
- making and storing fatty acids and cholesterol.
- forming and releasing bile
- processing and storing sugars in the form of glycogen, which can then be re-converted into energy
- Storing iron, an important element in blood formation

- Breaking down (detoxifying) alcohol, drugs, and environmental poisons so that they can be removed from the body.
- Processing and removing bilirubin, a product released when red blood cells break down, and ammonia, a toxic waste product of protein breakdown.
- Defending against infection by removing bacteria from the blood and making chemicals necessary to the functioning of the immune system.

Although the liver is the only organ that has the capacity to grow back, or regenerate, after injury or damage, sometimes the damage is too great for it to heal. The American Association for the Study of Liver Disease estimates that about 25 million Americans experience a liver-related disease each year. Individuals cannot live without a functioning liver. The ability to transplant livers is improving, **liver transplantation** is not nearly as common or successful as **kidney transplantation**.

Because the liver has many vital functions, there are many types of liver disease. The American Liver Foundation estimates that over 20,000 Americans die of chronic liver disease each year and another 360,000 are hospitalized. Individuals cannot live without a functioning liver.

Congenital Liver Diseases

Congenital liver diseases are disorders that are present at birth. Inherited liver diseases and disorders include:

- Alagile syndrome, a disorder that causes withering of the bile ducts. This disease occurs in less than 1 in 100,000 individuals.
- Alpha 1-antitrypsin deficiency, an inborn error in metabolism and the most common type of genetic liver disease.
- Galactosemia, a hereditary metabolic disease in which the liver is unable to break down the sugar galactose found in milk. It occurs in about one in every 20,000 births.
- Hematochromatosis, a hereditary metabolic disorder in which too much iron is absorbed from the diet and stored in the liver. This disease affects over one million Americans.
- Porphyria, a disorder in which the component of blood that contains iron is not correctly formed.
- Tyrosinemia, a rare inherited error in metabolism that causes severe liver disease in infants and children. It affects fewer than 200,000 individuals in the United States.
- Type I glycogen storage disease, a lack of the enzyme that helps regulate blood glucose (sugar) levels.
- Wilson's disease, an inherited disorder in which copper is accumulated in the liver and nervous system.

Acquired Liver Diseases

Many liver diseases are acquired from infection and exposure of the liver to toxic substances such as alcohol or drugs. In some areas of the world (although not the United States) liver parasites are a common cause of liver disease. In the United States, the most common acquired liver diseases are **hepatitis A**, B, and C and **cirrhosis**. Hepatitis A causes an acute (short-term) illness and is caused by a virus found in food or drinking water contaminated with feces. Hepatitis A infects between 125,000 and 250,000 people in the United States each year and causes about 100 deaths annually.

Hepatitis B is a viral infection spread by blood exchange and sexual contact with an infected person. It can be passed from an infected mother to her fetus. In most people hepatitis B is a short-term illness that causes mild symptoms such as **fatigue**, but in 2–6% of people, the disease lasts a long time and causes permanent liver damage. More than 75,000 people in the United States become infected with hepatitis B each year. Chinese Americans have a hepatitis B infection rate five times that of Caucasian Americans.

Hepatitis C is caused by a virus spread mainly through contact with the blood of an infected person, such as through sharing needles to inject drugs or from a mother to a fetus. Individuals infected with hepatitis C virus may not feel sick or know that they are infected for many years, but the disease can increase the likelihood of developing **liver cancer** of cirrhosis. The American Liver Foundation estimates that 4 million Americans are infected with hepatitis C, resulting in 10,000–12,000 deaths each year. About 70% of individuals who are infected do not know that they have the virus. African Americans have the highest rate of hepatitis C infections and are twice as likely to be infected with hepatitis C as Caucasian Americans.

Cirrhosis of the liver involves the formation of permanent scar tissue in the liver and loss of liver function. It is often caused by chronic alcohol **abuse** (alcoholic liver disease), but it can also be caused by diseases such as hepatitis. Cirrhosis interferes with blood flow through the liver and can raise pressure in blood vessels supplying the liver and decrease the absorption of nutrients from the blood, leading to **malnutrition**. The liver of individuals with cirrhosis

KEY TERMS

Biliary—Relating to the system that produces and transports bile.

Bile—A yellowish-green material secreted by the liver, stored by the gall bladder, and emptied into the small intestine to aid in the digestion and absorption of fats.

Bilirubin—A reddish-yellow substance that results from the breakdown of aging red blood cells. It is found in blood and bile, and if it accumulates in large quantities can cause jaundice.

Biopsy—A diagnostic procedure in which a small sample of tissue is obtained and examined under the microscope to determine they type and stage of a disease.

Congenital—Present at birth.

Feces—Waste products eliminated from the large intestine; excrement.

Jaundice—A yellowish tinge to the skin and whites of the eyes that indicates malfunction of the biliary system and/or liver and build up of bile components in the blood.

is also less effective in removing toxic wastes from the blood. Cirrhosis can be fatal.

Over 800 over-the-counter and prescription drugs, as well as illicit street drugs, can cause liver damage. One of the most common drugs to cause liver damage is **acetaminophen** (Tylenol) when taken at high doses or by individuals who already have some liver damage. Exposure to toxic chemicals, physical injury, and blockage of the bile ducts call also cause liver damage.

Liver **cancer** can either develop first in the liver (primary liver cancer) or spread there from another site (metastasized cancer). About 16,000 new cases of primary liver cancer are diagnosed each year, most commonly in middle age and older men. Although the cause of liver cancer is unclear, it appears to be associated with chronic infections of hepatitis B and C.

Causes and symptoms

The causes of liver disease are many and varied. Leading causes are viral infection, alcohol abuse, and inherited disease. A common symptoms of liver disease are **jaundice**. With jaundice, the skin and the whites of the eyes take on a yellowish color as a result of the accumulation of bilirubin and bile pigments in the blood. This is a sign that the liver or the biliary system is not functioning properly. Other symptoms of liver disease include an enlarged liver and swollen abdomen, **nausea**, **vomiting**, weight loss, and fatigue. Some infections cause flu-like symptoms of **fever**, **headache**, and weakness.

Diagnosis

Liver function tests, sometimes called a liver panel, measure various enzymes, proteins, and waste products in the blood. These readings can tell a physician whether the liver is damaged and give an idea of how well it is functioning. Liver function tests are the most common way to diagnose liver damage. Based on the results of a liver panel, additional blood tests for infection, a **liver biopsy**, or liver scan may be done to pinpoint the reason for loss of function.

Treatment

Treatments depend on the type of liver disease an individual has. Many liver diseases are treated with altered **diets**, abstinence from alcohol, and medication. Hepatitis can be treated with antiviral medications such as interferon or ribavirin. Liver cancer is treated with **chemotherapy**, radiation, and surgery. More than 300 clinical trials are enrolling patients with various types of liver disease in experimental treatment programs. Information on current clinical trials can be found at www.clinicaltrials.gov.

If the liver fails completely, a liver transplant is possible. About 5,600 liver transplants were performed in the United States in 2003. Donors and recipients are matched on the basis of blood type and must also be about the same weight. There is no machine like a **kidney dialysis** machine to perform the functions of the liver while individuals are awaiting a transplant. In 2003, 1,800 people died awaiting a liver donor, and about 18,000 more are on the waiting list awaiting a donated liver. Livers to be transplanted can come from either a living donor or a deceased donor.

Alternative treatment

A great deal of interest in alternative treatments for hepatitis C has resulted in a review of alternative and complementary treatments by the National Center for Complementary and Alternative Medicine (NCCAM), a division of the United States National Institutes of Health. Although there was in 2003 not

enough solid experimental evidence to show that any herbal treatments cured hepatitis C, the most promising herbal treatment was an extract of milk thistle (*Silybum marianum*), a plant in the aster family that has been used for centuries in Europe to treat liver disease and jaundice. Some studies suggested that extracts of milk thistle promoted the growth of certain types of liver cells and acted as an anti-oxidant to protect the liver while producing few unwanted side effects. Other studies showed no protective effects.

Licorice root (*Glycyrrhiza glabra*) was also reviewed by NCCAM. Some studies suggested that licorice root had antiviral properties, however this herb did not reduce the amount of hepatitis C virus circulating in the blood. Long term use of licorice root can have serious, health-threatening side effects.

Other alternative treatments studied by NCCAM include **ginseng** (*Panax quinquefolius* and *Panax ginseng*), which they concluded might possibly have a positive effect on the liver, especially in the elderly, and schisandra (*Schisandra chinensis* and *Schisandra sphenanthera*) used in Chinese medicine, which seemed to have a liver-protective effect in laboratory animals. Thymus extract and colloidal silver were found to be ineffective in treating liver disease.

Prognosis

The course of liver disease depends on the type of disease. Many individuals recover completely from infections of hepatitis A and B. However, if liver scarring occurs, the effects are irreversible. The initial success rate for liver transplants is good, with about 90% of individuals receiving a liver transplant are alive one year after the transplant operation. However, no alternative treatments produced a better outcome than traditional treatments of hepatitis C.

Prevention

Prevention is an effective way to avoid liver disease. Vaccines exist for hepatitis A and B (but not hepatitis C), although many individuals remain unvaccinated. In addition to **vaccination**, individuals can decrease the likelihood of developing liver disease by

- practicing safe sex
- avoiding sharing needles
- eating a healthy, balanced diet
- taking medications as prescribed
- avoiding drinking alcohol.

Resources

OTHER

"CAM and Hepatitis C: Focus on Herbal Supplements." National Center for Complementary and Alternative Medicine. May 6, 2010 [cited October 15, 2010]. http://nccam.nih.gov/health/hepatitisc/.

"Liver Function Test Factsheet" liverfoundation.org. 2003 [cited 23 March 2005]. http://www.liverfoundation.org/db/articles/1077.

ORGANIZATIONS

American Association for the Study of Liver Diseases, 1001 North Fairfax Street, Suite 400, Alexandria, VA, 22314, (703) 299-9766, (703) 299-9622, aasld@aasld.org, http://www.aasld.org.

American Liver Foundation, 75 Maiden Lane, Suite 603, New York, NY, 10038, (212) 668-1000, (212) 483-8179, http://www.liverfoundation.org/.

Tish Davidson, A.M.

Liver encephalopathy

Definition

Liver encephalopathy is a potentially life-threatening disease in which toxic substances accumulate in the blood. Also known as hepatic encephalopathy or hepatic **coma**, this condition can cause confusion, disorientation, abnormal neurological signs, loss of consciousness, and **death**.

Description

A normally functioning liver metabolizes and detoxifies substances formed in the body during the digestive process. Impaired liver function allows substances like ammonia (formed when the body digests protein), some fatty acids, phenol, and mercaptans to escape into the bloodstream. From there, they may penetrate the blood-brain barrier, affect the central nervous system (CNS), and lead to hepatic coma.

Hepatic coma is most common in patients with chronic **liver disease**. It occurs in 50–70% of all those with **cirrhosis**.

Causes and symptoms

The cause of hepatic coma is unknown, but the condition is frequently associated with the following conditions:

- Acute or chronic liver disease
- Gastrointestinal bleeding

- Azotemia, the accumulation of nitrogen-containing compounds (such as urea) in the blood
- Inherited disorders that disrupt the process by which nitrogen is decomposed and excreted
- The use of shunts (devices implanted in the body to redirect the flow of fluid from one vessel to another)
- Electrolyte imbalances, including low levels of potassium (hypokalemia) and abnormally alkaline blood pH (alkalosis). These imbalances may result from the overuse of sedatives, analgesics, or diuretics; reduced levels of oxygen (hypoxia), or withdrawal of excessive amounts of body fluid (hypovolemia)
- Constipation, which may increase the body's nitrogen load
- Surgery
- Infection
- Acute liver disease.

Binge drinking and acute infection are common causes of hepatic coma in patients with long-standing liver disease.

Symptoms of hepatic encephalopathy range from almost unnoticeable changes in personality, energy levels, and thinking patterns to deep coma.

Inability to reproduce a star or other simple design (**apraxia**) and deterioration of handwriting are common symptoms of early encephalopathy. Decreased brain function can also cause inappropriate behavior, lack of interest in personal grooming, mood swings, and uncharacteristically poor judgment.

The patient may be less alert than usual and develop new sleep patterns. Movement and speech may be slow and labored.

As the disease progresses, patients become confused, drowsy, and disoriented. The breath and urine acquires a sweet, musky odor. The hands shake, the outstretched arms flap (asterixis or "liver flap"), and the patient may lapse into unconsciousness. As coma deepens, reflexes may be heightened (hyperreflexia). The toes sometimes splay when the sole of the foot is stroked (Babinski reflex).

Agitation occasionally occurs in children and in adults who suddenly develop severe symptoms. Seizures are uncommon.

Diagnosis

The absence of sensitive, reliable tests for encephalopathy make the physician's personal observations and professional judgment the most valuable diagnostic tools.

KEY TERMS

Cirrhosis—A serious disease of the liver caused by chronic damage to its cells and the eventual formation of scar tissue (fibrosis).

Coma—A condition of deep unconsciousness from which the person cannot be aroused.

Electrolytes—Substances that conduct electricity when they are in solution. In the body, electrolytes in the blood and tissues enable nerve impulses to flow normally.

Encephalopathy—A dysfunction of the brain. Hepatic encephalopathy is brain dysfunction that occurs because the liver isn't removing harmful substances from the blood.

Confusion, disorientation, and other indications of impaired brain function strongly suggest encephalopathy in patients known to have liver disease. CAT scans and examination of spinal fluid don't provide diagnostic clues. Elevated arterial ammonia levels are almost always present in hepatic coma, but levels are not necessarily correlated with the severity or extent of the disease.

Magnetic resonance imaging (MRI) can show severe brain swelling that often occurs prior to coma, and **electroencephalography** (EEG) detects abnormal brain waves even in patients with early, mild symptoms. Blood and urine analyses can provide important information about the cause of encephalopathy in patients suspected of taking large quantities of sedatives or other drugs.

Treatment

This condition may disappear if the cause of symptoms is eliminated. In other cases, treatment is designed to improve liver function as much as possible; remove or relieve factors that worsen symptoms; and decrease the body's production of poisonous substances.

All non-essential medications are discontinued. Soft restraints are recommended in place of sedatives for patients who become agitated.

Enemas or **laxatives** are used to stimulate expulsion of toxic intestinal products. All or most protein is eliminated from the diet, and supplemental feeding may be necessary to replenish lost calories. Regular doses of neomycin (Neobiotic), taken orally or administered to comatose patients in liquid form through a tube, may be used to decrease production of protein-digesting bacteria in the bowel.

Lactulose, a synthetic sugar, changes the characteristics of intestinal bacteria, decreases the amount of ammonia accumulated in the body, and has laxative properties. The patient is given hourly doses of lactulose syrup until **diarrhea** occurs, then dosage is adjusted to maintain regular bowel function. Lactulose and dietary-protein restrictions may be used to control chronic encephalopathy.

Prognosis

Encephalopathy may be reversible if the responsible factor is identified and removed or treated. Patients whose condition is the result of chronic liver disease may recover completely after the underlying cause is corrected.

Despite intensive treatment, encephalopathy caused by acute liver inflammation (fulminant hepatitis) is fatal for as many as 80% of patients. Those with chronic liver failure often die in hepatic coma.

ORGANIZATIONS

American Liver Foundation, 75 Maiden Lane, Suite 603, New York, NY, 10038, (212) 668-1000, (212) 483-8179, http://www.liverfoundation.org/.

Maureen Haggerty

Liver fluke infections *see* **Fluke infections**

Liver function tests

Definition

Liver function tests, or LFTs, include tests that are routinely measured in all clinical laboratories. LFTs include bilirubin, a compound formed by the breakdown of hemoglobin; ammonia, a breakdown product of protein that is normally converted into urea by the liver before being excreted by the kidneys; proteins that are made by the liver, including total protein, albumin, prothrombin, and fibrinogen; cholesterol and **triglycerides**, which are made and excreted via the liver; and the enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and lactate dehydrogenase (LDH). Other liver function tests include serological tests (to demonstrate antibodies); DNA tests for hepatitis and other viruses; and tests for antimitochondrial and smooth muscle antibodies, transthyretin (prealbumin), **protein electrophoresis**, bile acids, alpha-fetoprotein, and a constellation of other enzymes that help differentiate necrotic (characterized by the **death** of tissue) versus obstructive **liver disease**.

Purpose

Liver function tests done individually do not give the physician much information, but used in combination with a careful history, **physical examination**, and imaging studies, they contribute to making an accurate diagnosis of the specific liver disorder. Different tests will show abnormalities in response to liver inflammation; liver injury due to drugs, alcohol, toxins, or viruses; liver malfunction due to blockage of the flow of bile; and liver cancers.

Precautions

Blood for LFTs is collected by sticking a needle into a vein. The nurse or phlebotomist (person trained to draw blood) performing the procedure must be careful to clean the skin before sticking in the needle.

Bilirubin: Drugs that may cause increased blood levels of total bilirubin include anabolic **steroids**, **antibiotics**, antimalarials, ascorbic acid, Diabinese, codeine, **diuretics**, epinephrine, **oral contraceptives**, and vitamin A.

Ammonia: Muscular exertion can increase ammonia levels, while cigarette **smoking** produces significant increases within one hour of inhalation. Drugs that may cause increased levels include alcohol, **barbiturates**, **narcotics**, and diuretics. Drugs that may decrease levels include antibiotics, levodopa, lactobacillus, and potassium salts.

ALT: Drugs that may increase ALT levels include **acetaminophen**, ampicillin, codeine, dicumarol, indomethacin, methotrexate, oral contraceptives, **tetracyclines**, and verapamil. Previous intramuscular injections may cause elevated levels.

GGT: Drugs that may cause increased GGT levels include alcohol, phenytoin, and phenobarbital. Drugs that may cause decreased levels include oral contraceptives.

LDH: Strenuous activity may raise levels of LDH. Alcohol, anesthetics, **aspirin**, narcotics, procainamide, and fluoride may also raise levels. Ascorbic acid (vitamin C) can lower levels of LDH.

Description

The liver is the largest and one of the most important organs in the body. As the body's "chemical factory," it regulates the levels of most of the biomolecules found in the blood, and acts with the kidneys to clear the blood of drugs and toxic substances. The liver metabolizes these products, alters their chemical structure, makes them water soluble, and excretes them in

KEY TERMS

Bile acid—A detergent that is made in the liver and excreted into the intestine to aid in the absorption of fats.

Biliary—Relating to bile.

Cirrhosis—A liver disease where there is a loss of normal liver tissues, replaced by scar tissue. This is usually caused by chronic alcohol abuse, but also can be caused by blockage of the bile ducts.

Detoxification—A process of altering the chemical structure of a compound to make it less toxic.

Hepatitis—Inflammation of the liver.

Hepatocyte—Liver cell.

Isoenzyme—One of a group of enzymes that brings about the same reactions on the same chemicals, but are different in their physical properties.

Jaundice—Hyperbilirubinemia, or too much bilirubin in the blood. Bilirubin will be deposited in the skin and the mucosal membranes. The whites of the eyes and the skin appear yellow.

Lipoprotein—A chemical combination of a protein and a lipid (fats).

Neonatal jaundice—A disorder in newborns where the liver is too premature to conjugate bilirubin, which builds up in the blood.

bile. Laboratory tests for total protein, albumin, ammonia, transthyretin, and cholesterol are markers for the synthetic (chemical-producing) function of the liver. Tests for cholesterol, bilirubin, ALP, and bile salts are measures of the secretory (excretory) function of the liver. The enzymes ALT, AST, GGT, LDH, and tests for viruses are markers for liver injury.

Some liver function tests are used to determine if the liver has been damaged or its function impaired. Elevations of these markers for liver injury or disease tell the physician that something is wrong with the liver. ALT and bilirubin are the two primary tests used largely for this purpose. Bilirubin is measured by two tests, called total and direct bilirubin. While total bilirubin is elevated in various liver diseases, it is also increased in certain (hemolytic) **anemias** caused by increased red blood cell turnover. Neonatal hyperbilirubinemia (**jaundice**) is a condition caused by an immature liver than cannot conjugate (process) the bilirubin. The level of total bilirubin in the blood becomes elevated and must be monitored closely in order to prevent damage to the brain caused by unconjugated bilirubin, which has a high affinity for brain tissue. Bilirubin levels can be decreased by exposing the baby to UV light. Direct bilirubin is formed only by the liver, and therefore, it is specific for hepatic or biliary disease. Its concentration in the blood is very low (0–0.2 mg/dL) and therefore, even slight increases are significant. Highest levels of direct bilirubin are seen in obstructive liver diseases. However, direct bilirubin is not sensitive to all forms of liver disease and is not always elevated in the earliest stages of disease. Therefore, ALT is needed to exclude a diagnosis.

Although ALT is present in other tissues, its concentration in the liver is far greater than any other tissue. The enzyme is very sensitive to liver injury. Consequently, if ALT or direct bilirubin is increased, then some form of liver disease is likely. If both are normal, then liver disease is unlikely.

These two tests, along with others, are used to help make a diagnosis. The most useful tests for this purpose are the liver function enzymes and the ratio of direct to total bilirubin. These tests are used to differentiate diseases characterized primarily by hepatocellular damage (necrosis, or cell death) from those characterized by obstructive damage (**cholestasis** or blockage of bile flow). Liver cell damage may be caused by viral hepatitis, hepatitis induced by drugs or poisons (toxic hepatitis), **alcoholic hepatitis**, hypoxic necrosis (a consequence of congestive **heart failure**), chronic hepatitis, and **cirrhosis** of the liver. Obstructive liver diseases include intrahepatic (within the liver) obstructive disease or extrahepatic (outside the liver) obstruction. In both cases, the direct bilirubin is often greatly elevated because the liver can conjugate the bilirubin, but this direct bilirubin cannot be excreted via the bile. In such cases the ratio of direct to total bilirubin is greater than 0.4.

Aspartate aminotransferase (AST) is not as specific for liver disease as ALT is. However, differentiation of acute and chronic forms of liver disease is aided by examining the ratio of ALT to AST, called the DeRitis ratio. In acute hepatitis, **Reye's syndrome**, and **infectious mononucleosis**, the ALT predominates. However, in alcoholic liver disease, chronic hepatitis, and cirrhosis, the AST predominates.

Alkaline phosphatase (ALP) is increased in obstructive liver diseases, but it is not specific for the liver. Increases are commonly seen in bone diseases,

late **pregnancy**, leukemia, and some other malignancies. The enzyme gamma-glutamyl transferase (GGT) is used to help differentiate the source of an elevated ALP. GGT is greatly increased in obstructive jaundice, alcoholic liver disease, and hepatic **cancer**. When the increase in GGT is two or more times greater than the increase in ALP, the source of the ALP is considered to be from the liver. When the increase in GGT is five or more times the increase in ALP, this points to a diagnosis of alcoholic hepatitis. GGT, but not AST and ALT, is elevated in the first stages of liver inflammation due to alcohol consumption, and GGT is useful as a marker for excessive drinking. GGT has been shown to rise after acute persistent alcohol ingestion and then fall when alcohol is avoided.

Lactate dehydrogenase (LDH) is found in almost all cells in the body. LDH is increased in megaloblastic and hemolytic anemias, leukemias and lymphomas, myocardial infarction, infectious mononucleosis, muscle wasting diseases, and both necrotic and obstructive jaundice. LDH is markedly increased in most cases of **liver cancer**. An enzyme pattern showing a marked increase in LDH and to a lesser degree ALP with only slightly increased transaminases (AST and ALT) is seen in cancer of the liver.

Some liver function tests are not sensitive enough to be used for diagnostic purposes, but are elevated in severe or chronic liver diseases. These tests are used primarily to indicate the extent of damage to the liver. Tests falling into this category are ammonia, total protein, albumin, cholesterol, transthyretin, fibrinogen, and the **prothrombin time**.

Analysis of blood ammonia aids in the diagnosis of severe liver diseases and helps to monitor the course of these diseases. Together with the AST and the ALT, ammonia levels are used to confirm a diagnosis of Reye's syndrome, a rare disorder usually seen in children and associated with infection and aspirin intake. Reye's syndrome is characterized by brain and liver damage following an upper respiratory tract infection, **chickenpox**, or **influenza**. Ammonia levels are also helpful in the diagnosis and treatment of hepatic encephalopathy, a serious brain condition caused by the accumulated toxins that result from liver disease and liver failure. Ammonia levels in the blood are normally very low. Increasing ammonia signals end-stage liver disease and a high risk of hepatic **coma**.

Albumin is the protein found in the highest concentration in blood, making up over half of the protein mass. A persistently low albumin in liver disease is a sign of progressive liver failure. In the acute stages of liver disease, proteins such as transthyretin (prealbumin) may be measured to give an indication of the severity of the disease.

Cholesterol is synthesized by the liver. Its balance is maintained by the liver's ability to remove cholesterol from lipoproteins, and use it to produce bile acids and salts that it excretes into the bile ducts. In obstructive jaundice caused by stones, biliary tract scarring, or cancer, the bile cannot be eliminated. Cholesterol and triglycerides may accumulate in the blood as low-density lipoprotein (LDL) cholesterol. In acute necrotic liver diseases, triglycerides may be elevated. In liver failure caused by necrosis, the liver's ability to synthesize cholesterol is reduced, and blood levels may be low.

The liver is responsible for production of the vitamin K clotting factors. In obstructive liver diseases a deficiency of vitamin K-derived clotting factors results from failure to absorb vitamin K. In obstructive jaundice, an intramuscular injection of vitamin K will be given. In severe necrotic disease, the liver cannot synthesize clotting factors from vitamin K.

The most prevalent liver disease is viral hepatitis. Tests for this condition include a variety of antigen and antibody markers and nucleic acid tests. In addition to hepatitis A-E, viral hepatitis may be caused by **Epstein-Barr virus** (EBV) and cytomegalovirus (CMV) infections of the liver. Tests for these viruses such as the infectious mononucleosis antibody test, anti-viral capsid antigen test (anti-VCA), and anti-CMV test are useful in diagnosing these infections.

Liver disease may be caused by autoimmune mechanisms in which autoantibodies destroy liver cells. Autoimmune necrosis is associated with **systemic lupus erythematosus** and chronic viral hepatitis, usually caused by **hepatitis B** and **hepatitis C** virus infections. These conditions give rise to anti-smooth muscle antibodies and anti-nuclear antibodies, and tests for these are useful markers for chronic hepatitis. Antibodies to mitochondrial antigens (antimitochondrial antibodies) are found in the blood of more than 90% of persons with **primary biliary cirrhosis**.

Preparation

Patients are asked to fast and to inform clinicians of all drugs, even over-the-counter drugs, that they are taking. Many times liver function tests are done on an emergency basis. Thus **fasting** and obtaining a medical history may not be possible.

Aftercare

Patients will have blood drawn into a vacuum tube and may experience some **pain** and burning at

the site of injection. A gauze bandage may be placed over the site to prevent further bleeding. If the patient is suffering from severe liver disease, he or she may lack clotting factors. The nurse or caregiver should be careful to monitor bleeding in these patients after obtaining blood.

Results

Reference ranges vary from laboratory to laboratory and also depend upon the method used. However, normal values are generally framed by the ranges shown below.

- ALT: 5–35 IU/L. (Values for the elderly may be slightly higher, and values also may be higher in men and in African-Americans.)
- AST: 0–35 IU/L.
- ALP: 30–120 IU/LALP is higher in children, older adults and pregnant females.
- GGT: males 2–30 U/L; females 1–24 U/L.
- LDH: 0–4 days old: 290–775 U/L; 4–10 days: 545–2000 U/L; 10 days–24 months: 180–430 U/L; 24 months–12 years: 110–295 U/L; 12–60 years: 100–190 U/L; 60 years: 110–210 U/L.
- Bilirubin: (Adult, elderly, and child) Total bilirubin: 0.1–1.0 mg/dL; indirect bilirubin: 0.2–0.8 mg/dL; direct bilirubin: 0.0–0.3 mg/dL. (Newborn) Total bilirubin: 1–12 mg/dL. Note: critical values for adult: greater than 1.2 mg/dL. Critical values for newborn (requiring immediate treatment): greater than 15 mg/dL.
- Ammonia: 10–70 micrograms per dL (heparinized plasma). Normal values for this test vary widely, depending upon the age of the patient and the type of specimen.
- Albumin: 3.2–5.4 g/L.

Abnormal results

ALT: Values are significantly increased in cases of hepatitis, and moderately increased in cirrhosis, liver tumor, obstructive jaundice, and severe **burns**. Values are mildly increased in **pancreatitis**, **heart attack**, infectious mononucleosis, and **shock**. Most useful when compared with ALP levels.

AST: High levels may indicate liver cell damage, hepatitis, heart attack, heart failure, or gall stones.

ALP: Elevated levels occur in diseases that impair bile formation (cholestasis). ALP may also be elevated in many other liver disorders, as well as some lung cancers (bronchogenic carcinoma) and Hodgkin's lymphoma. However, elevated ALP levels may also occur in otherwise healthy people, especially among older people.

GGT: Increased levels are diagnostic of hepatitis, cirrhosis, liver tumor or metastasis, as well as injury from drugs toxic to the liver. GGT levels may increase with alcohol ingestion, heart attack, pancreatitis, infectious mononucleosis, and Reye's syndrome.

LDH: Elevated LDH is seen with heart attack, **kidney disease**, hemolysis, viral hepatitis, infectious mononucleosis, Hodgkin's disease, abdominal and lung cancers, **germ cell tumors**, progressive **muscular dystrophy**, and **pulmonary embolism**. LD is not normally elevated in cirrhosis.

Bilirubin: Increased indirect or total bilirubin levels can indicate various serious anemias, including hemolytic disease of the newborn and **transfusion** reaction. Increased direct bilirubin levels can be diagnostic of bile duct obstruction, **gallstones**, cirrhosis, or hepatitis. It is important to note that if total bilirubin levels in the newborn reach or exceed critical levels, exchange transfusion is necessary to avoid kernicterus, a condition that causes brain damage from bilirubin in the brain.

Ammonia: Increased levels are seen in primary liver cell disease, Reye's syndrome, severe heart failure, hemolytic disease of the newborn, and hepatic encephalopathy.

Albumin: Albumin levels are increased due to **dehydration**. They are decreased due to a decrease in synthesis of the protein which is seen in severe liver failure and in conditions such as burns or renal disease that cause loss of albumin from the blood.

Patient education

Healthcare providers should inform the patient of any abnormal results and explain how these values reflect the status of their liver disease. It is important to guide the patient in ways to stop behaviors such as taking drugs or drinking alcohol, if these are the causes of the illness.

Resources

BOOKS

Feldman, M, et al. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease*, 8th ed. St. Louis: Mosby, 2005.

McPherson RA et al. *Henry's Clinical Diagnosis and Management By Laboratory Methods*, 21st ed. Philadelphia: Saunders, 2007.

ORGANIZATIONS

American Association for the Study of Liver Disease, 1001 North Fairfax, Suite 400, Alexandria, VA, 22314, (703)

299-9766, (703) 299-9622, aasld@aasld.org, http://www.aasld.org.

American Liver Foundation, 75 Maiden Lane, Suite 603, New York, NY, 10038, (212) 668-1000, (212) 483-8179, http://www.liverfoundation.org.

National Cancer Institute, NCI Public Inquiries Office, 6116 Executive Boulevard, Bethesda, MD, 20892-8322, (800) 422-6237, http://www.cancer.gov.

Rosalyn Carson-DeWitt, MD
Brenda W. Lerner

Liver nuclear medicine scan

Definition

A liver scan is a diagnostic procedure to evaluate the liver for suspected disease. A radioactive substance which concentrates in the liver is injected intravenously and the image of its distribution in the body is analyzed to diagnose certain abnormalities.

Purpose

In the past, liver scans were used to evaluate the liver in a wide variety of situations. It was considered a useful study to detect abnormalities, but was often not able to establish a specific diagnosis. In the 1990s, radionuclide imaging of the liver (use of a radioactive form of cobalt or iodine) evolved into a more specialized study, used to identify individual diseases or conditions. This is accomplished by using different radioisotopes precisely designed to further evaluate a particular case. Isotopes are different forms of the same substance, such as radioactive iodine, that are injected into the body. This allows the physician to trace the process of the substance throughout the part of the body that is being tested for disease.

A liver scan is usually ordered after blood studies and other imaging procedures have shown a liver abnormality. It is most often used to further evaluate masses or tumors. These may be benign growths in the liver, or **cancer** which has developed in the liver or has spread (or metastasized) from another organ.

A liver scan may also be helpful in diagnosing specific disorders, by detecting features which are characteristic of a disorder, such as **cirrhosis** of the liver. This study may also be part of the battery of tests used to evaluate potential candidates for liver transplant.

KEY TERMS

Radioisotope—A radioactive, or radiation-emitting form of an element.

Radionuclide—A substance which emits radiation that can be detected by a scanner as the substance disintegrates.

Precautions

Women who are pregnant or breast feeding should not have this test.

Description

This test can be performed in an outpatient setting or a hospital x-ray department. The patient usually lies down while a radioactive substance (radioactive isotope) which accumulates in the liver is injected through a vein in the arm. Scanning times may vary, depending on the specific radioisotope used. It most often begins within minutes after injection. The radionuclide scanner, sometimes called a gamma camera or scintillation camera, is positioned above the upper abdomen and may lightly touch the patient. It is important for the patient to lie quietly. Position changes and brief periods of breath holding may be required. The test usually takes approximately one hour.

A specialized liver scan used to assess blood flow is frequently used. It may be referred to as a radionuclide blood pool or volume study, a labeled red cell scintigram, or some combination of these terms. Other studies may be named for the radioisotope used. This test may also be called a liver-spleen scan.

Preparation

No physical preparation is required. A liver scan should be performed before doing any study that uses iodinated or barium-containing contrast agents, to prevent inaccurate results.

The patients should understand that there is no danger of radioactive exposure to themselves or others. Only small amounts of radionuclide are used. The total amount of radiation absorbed is often less than the dose received from ordinary x rays. The scanner does not emit any radiation, but detects and records it from the patient.

Aftercare

No special precautions are needed.

Results

A normal scan will show a liver of normal size, shape, and position.

An abnormal liver scan may result from a mass. Depending on the radioisotope and technique used, the scan may identify particular types of tumors or certain cancers. Too much radioisotope in the spleen and bones, compared to the liver, can indicate potential **hypertension** or cirrhosis. Liver diseases such as cirrhosis or hepatitis may also cause an abnormal scan, but are rarely diagnosed from the information revealed by this study alone.

Resources

PERIODICALS

Drane, Walter E. "Scintigraphic Techniques for Hepatic Imaging." *Radiologic Clinics of North America* 36 (March 1998): 309-318.

Ellen S. Weber, MSN

National transplant waiting list by organ type (June 2010)

Organ needed	Persons waiting
Kidney	85,296
Liver	16,031
Heart	3,141
Kidney/Pancreas	2,199
Lung	1,802
Pancreas	1,450
Intestine	242
Heart/Lung	79

SOURCE: U.S. Department of Health and Human Services, Organ Procurement and Transplantation Network. Available online at: http://optn.transplant.hrsa.gov/data/default.asp (accessed June 8, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

Liver transplantation

Definition

Liver transplantation is a surgery that removes a diseased liver and replace it with a healthy donor liver.

Purpose

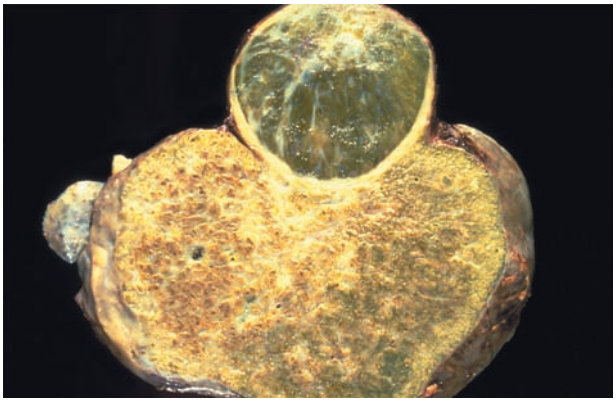
The liver is the body's principle chemical factory. It receives all nutrients, drugs, and toxins absorbed from the intestines and performs the final stages of digestion, converting food into energy and replacement parts for the body. The liver also filters the blood of all waste products, removes and detoxifies poisons and excretes many of these into the bile. It processes other chemicals for excretion by the kidneys. The liver is also an energy storage organ, changing food energy to a chemical called glycogen that can be rapidly converted to fuel.

As the liver fails, all of its functions diminish. **Nutrition** suffers, toxins build up, and waste products accumulate. Scar tissue builds up on the liver if disease is of long duration. As the liver **scars**, blood flow is progressively restricted in the portal vein, which carries blood from the stomach and abdominal organs to the liver. The resulting high blood pressure (**hypertension**) causes swelling of and bleeding from the blood vessels of the esophagus. Severe **jaundice**, fluid accumulation in the abdomen (**ascites**), and deterioration of mental function, due to the build-up of toxins in the blood (**liver encephalopathy**), eventually occur, leading to **death**.

Among the many causes of liver failure that bring patients to **transplant surgery** are:

- Progressive hepatitis (mostly due to virus infection) accounts for more than a third.
- Alcohol damage brings in about 20%.
- Scarring or abnormality of the biliary system accounts for roughly another 20%.
- The remainder comes from selected cancers, other uncommon diseases, and a situation called fulminant liver failure.

Fulminant liver failure most commonly happens during acute viral hepatitis, but it is also the result of **mushroom poisoning** by *Amanita phalloides* and toxic reactions to some medicines, like an overdose of



The diseased liver of a patient ready for transplantation. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

KEY TERMS

Acetaminophen—A common pain reliever (Tylenol).

Antigen—Any chemical that provokes an immune response.

Bile ducts—Tubes carrying bile from the liver to the intestines.

Biliary system—The tree of tubes that carries bile.

Hepatic artery—The blood vessel supplying arterial blood to the liver.

Inferior vena cava—The biggest vein in the body, returning blood to the heart from the lower half of the body.

Leukemia—A cancer of the white blood cells.

Lymphoma—A cancer of lymphatic tissue.

Portal vein—The blood vessel carrying venous blood from the abdominal organs to the liver.

acetaminophen. This is a special category of candidates for liver transplant because of the speed of their disease and the immediate need of treatment.

The first human liver transplant was performed in 1963, and since then, thousands of liver transplants are done every year. Since the introduction of of cyclosporine (a drug that suppresses the immune response that rejects the donor organ), success rates for liver transplantation have reached 85%.

Precautions

Patients with advanced heart and lung disease, who are HIV positive, and who abuse drugs and alcohol are poor candidates for liver tranplantation. Their ability to survive the surgery and the difficult recovery period, as well as their longterm prognosis, is hindered by their conditions.

Description

There are three types of liver transplantation methods. They include:

- Orthotopic transplantation is the replacement of a whole diseased liver with a healthy donor liver.
- Heterotopic transplantation is the addition of a donor liver at another site, while the diseased liver is left intact.
- Reduced-size liver transplantation is the replacement of a whole diseased liver with a portion of a healthy donor liver. Reduced-size liver transplants are most often performed on children.

When an orthotopic transplantation is performed, a segment of the inferior vena cava attached to the liver is taken from the donor as well. The same parts are removed from the recipient and replaced by connecting the inferior vena cava, the hepatic artery, the portal vein and the bile ducts.

When there is a possibility that the afflicted liver may recover, a heterotopic tranplantation is performed. The donor liver is placed in a different site, but it still has to have the same connections. It is usually attached very near the original liver, and if the original liver recovers, the donor shrivels away. If the original liver does not recover, it will shrivel, leaving the donor in place.

Reduced-size liver transplantation tranplants part of a donor liver into a patient. It is possible to divide the liver into eight pieces, each supplied by a different set of blood vessels. Two of these pieces have been enough to save a patient in liver failure, especially if the patient is a child. It is therefore possible to transplant one liver into at least two patients and to transplant part of a liver from a living donor and have both donor and recipient survive. Liver tissue grows to accommodate its job so long as there is initially enough of the organ to use. Patients have survived with only 15–20% of their original liver, provided that 15–20% was healthy.

Availability of organs for transplant is a current crisis in the transplantation business. In October 1997, a national distribution system was established that gives priority to the sickest patients closest in location to the donor liver, but makes livers available nationally. It is now possible to preserve a liver out of the body for 10–20 hours by flushing it with cooled solutions of special chemicals and nutrients, so it can be transported across the country.

Preparation

Before transplantation takes place, the patient is first determined to be a good candidate for transplantation by going through rigorous medical examination. A suitable candidate boosts their nutritional intake in order to ensure that they are as healthy as possible before surgery. Drugs are administered that will decrease rejection after surgery. Consultation with the patient, as well as any

family, is conducted to explain the surgery and its complications. Psychological counciling is recommended.

Aftercare

In order to prevent organ rejection, immunosuppressive drugs will be taken. Hospitalization ranges from four weeks to five months, depending on the rate of recovery.

Successfully receiving a transplanted liver is only the beginning of a life-long process. Patients with transplanted livers have to stay on **immunosuppressant drugs** for the rest of their lives to prevent organ rejection. Although many can reduce the dosage after the initial few months, virtually none can discontinue drugs altogether. Prednisone, azathioprine, and tacrolimus are often combined with cyclosporine for better results. Newer immunosuppressive agents are coming that promise even better results. In spite of immunosuppressants, rejection occurs most of the time and requires additional medication. In some cases it cannot be reversed, and retransplantation becomes necessary.

Risks

Early failure of the transplant occurs once in four surgeries and has to be repeated. Some transplants never work, some succumb to infection, and some suffer immune rejection. Primary failure is apparent within one or two days. Infections happen in half the patients and often appear during the first week. Rejection usually starts at the end of the first week. The surgery itself may need revision because of narrowing, leaking, or **blood clots** at the connections.

There are potential social and economic problems, psychological problems, and a vast array of possible medical and surgical complications. Close medical surveillance must continue for the rest of the patient's life. Infections are a constant risk while on immunosuppressive agents, because the immune system is supposed to prevent them. A way has not yet been devised to control rejection without hampering immune defenses against infections. Not only do ordinary infections pose a threat, but because of the impaired immunity, transplant patients are susceptible to the same "opportunistic" infections that threaten **AIDS** patients–pneumocystis **pneumonia**, herpes and cytomegalovirus infections, fungi, and a host of bacteria.

Immunosuppression also hinders the body's ability to resist **cancer**. All the drugs used to prevent rejection increase the risk of leukemias and lymphomas.

There is also a risk of the original disease returning. Hepatitis virus still inhabits the patient, as does the urge to drink alcohol. Newer **antiviral drugs** hold out promise for dealing with hepatitis, and Alcoholics Anonymous (AA) is the most effective treatment known for **alcoholism**.

Drug reactions are also a continuing threat. Every drug used to suppress the immune system has potential problems.

ORGANIZATIONS

American Liver Foundation, 75 Maiden Lane, Suite 603, New York, NY, 10038, (212) 668-1000, (212) 483-8179, http://www.liverfoundation.org/.

J. Ricker Polsdorfer, MD

Ller-Christi *see* **Histiocytosis X**

Loaiasis *see* **Filariasis**

Lobectomy

Definition

A lobectomy is the removal of a lobe of one of the organs, usually referring to the brain, the lung, or the liver.

Purpose

Lobectomies are usually performed to prevent the spread of **cancer** from one part of an organ to other parts or to other parts of the body. Lobectomies also are performed on patients with severe seizure disorders (such as some forms of **epilepsy**) to prevent further seizures. However, there are differences in each of the three organs on which lobectomies may be performed.

Description

The brain

Each lobe of the brain performs a different function, and when part of the brain is removed, it does not grow back. However, other parts of the brain can take over some, or all, of the function of the missing part of the brain. Depending on the part of the brain removed, the effects may be quite severe, or nearly nonexistent.

The most commonly referenced brain lobectomy in the medical literature is the removal of the temporal lobe. Temporal lobectomy usually is performed to prevent debilitating seizures. Seizures are commonly caused by temporal lobe epilepsy, but can also be caused by brain tumors in the temporal lobe. Thus,

lobectomy of the temporal lobe in patients with a temporal lobe tumor reduces or eliminates seizures, and has the beneficial side effect of removing the tumor mass.

The lung

Lobectomies of the lung also are called pulmonary lobectomies. Each part of the lung performs the same function: it exchanges oxygen for carbon dioxide in the blood. There are many different lobes of the lung, however, and some lobes exchange more oxygen than others. Lobes of the lung do not regenerate after they are removed. Therefore, removal of a large portion of the lung may cause a person to need oxygen or ventilator support for the rest of his or her life. However, removal of a small portion of the lung may result in very little change to the patient's quality of life. A test (a quantitative ventilation/perfusion scan, or quantitative V/Q scan) may be used before surgery to help determine how much of the lung can safely be removed.

The outcome of lung lobectomies also depends on the general health of the entire lung; **emphysema** and **smoking** would have a negative impact on the health of a patient's lung. The surgeon may perform the surgery with video assistance and special tools to decrease **pain** and speed patient recovery following surgery.

The liver

A lobectomy of the liver is also called a hepatic lobectomy. The liver plays a major role in digestion, in the transformation of food into energy, and in filtering and storing blood. It processes nutrients and drugs, produces bile, controls the level of glucose (sugar) in the blood, detoxifies blood, and regulates blood clotting. Unlike the brain and the lung, the liver may regrow, or regenerate, after part of the liver has been removed. In addition, since every part of the liver performs the same functions, the liver is the organ whose function is least likely to be severely affected by lobectomy, in the long term, because it regenerates. However, as the liver is central to the body's functions, removal of too much of the liver at once may result in **coma** or **death**.

Precautions

Brain lobectomies should not be performed unless the patient has been unable to control seizures through medication. Additionally, the seizures must be caused by a single, relatively small, localized part of the brain that can be resected without severe damage. Lung lobectomies should only be performed on patients with early stage non-small cell carcinoma of the lung, or as part of a combination of therapies at later stages. Since even a "complete removal" of the tumor does not result in an overwhelming survival rate after five years, other therapies also may be considered. Small cell cancer of the lung does not respond to surgical intervention. Patients with **liver disease** that is too extensive may need a liver transplant rather than a liver lobectomy. Patients with blood clotting problems, either due to chemotherapeutic agents or for other reasons, should have these problems addressed before surgery.

Preparation

Before surgery, patients should not take **aspirin** or ibuprofen for one week. Patients also should consult their physician about any blood-thinning medications such as coumadin or warfarin. The night before surgery, patients will usually be asked not to eat or drink after a certain time.

Aftercare

Each surgery offers different aftercare challenges. Patients may need to be hospitalized for some time after the operation. Patients with portions of their brain removed may require **rehabilitation** of a physical, mental, or emotional nature depending on the portion of the brain that has been removed. Patients who have had portions of their lungs removed probably will require a tube in their chest to drain fluid, and may require a machine to help them breathe. They also may require oxygen, either on a temporary or permanent basis. Patients who have had hepatic lobectomies also may have drainage tubes, and may also have initial dietary restrictions. Physicians should be consulted for the specifics of aftercare in each individual situation.

Risks

Specific risks vary from surgery to surgery and should be discussed with a physician. In general, any surgery requiring a general anesthetic may, uncommonly, result in death. Improperly performed brain surgery may result in permanent brain damage. Depending on the surgeon and the size of the tissue removed, patients may be at risk for some types of brain damage. As previously mentioned, patients having part of a lung removed may have difficulty breathing and may require the use of oxygen. Patients also may experience infection (**pneumonia**), or **blood clots**. Liver resection (surgery) may result in the following

complications: coma, slow return of normal bowel function, and biliary leakage.

Results

Most patients who undergo temporal lobectomy experience few or no seizures after surgery (some estimates range from about 70% to about 90% success rate). Unfortunately, lung lobectomy is not as successful. 50% of cancer patients with completely removable stage I non-small cell cancer of the lung survive five years after the procedure. If the cancer has progressed beyond this stage, or if the cancer is not completely removable, the chances for survival drop significantly. The results of liver resection vary. The possible outcomes of each surgical type should be discussed with the patient's physician. Generally, the less severe the cancer, and the less tissue that needs to be removed, the better the outcome.

Abnormal results vary from operation to operation and should be discussed thoroughly with the patient's physician before surgery. Patients who undergo temporal lobectomy may, rarely, die as a result of the operation (a complication in less than 1% of patients). Patients also may have problems with their vision, or problems with speech. Abnormal results from the removal of part of the lung could include pneumonia or blood clots (which may result in **stroke**, **heart attack**, or other problems) after the surgery. Also, a small percentage of patients undergoing lung lobectomy die during or soon after the surgery. The percentage of patients who suffer death varies from about 3–6% depending on the amount of lung tissue removed. Finally, abnormal outcomes from liver resection can include coma, death, and problems with liver function.

Resources

PERIODICALS

Namori, Hiroaki, et al. "Thoracoscopic Lobotomy for Lung Cancer with a Largely Fused Fissure." *Chest* 9, no. 10 (February 2003): 19–23.

Tatum, W. O., and S. R. Benbadis. "The Neurosurgical Treatment of Epilepsy." *Archives of Family Medicine* 9, no. 10 (November–December 2000): 1142–1147.

OTHER

Harrison's Principles of Internal Medicine online, Chapter 90: Neoplasms of the lung.http://www.harrisonsonline.com/.

Koike, Atsushi, M.A., Hiroyuki Shimizu, M.D., Ichiro Suzuki, M.D., Buichi Ishijima, M.D., and Morihiro Sugishita, Dr. H.S., Dr. M.S. "Preserved musical abilities following right temporal lobectomy." *Journal of Neurosurgery*. December 1996. [cited July 24, 2005]. http://www.c3.hu/~mavideg/jns/1-4-prev1.html.

"Lung Surgery." *Healthsquare.com*.http://www.healthsquare.com/htm.

Michael Zuck, Ph.D.
Teresa G. Odle

Lobectomy *see* **Lung surgery**

Lobotomy *see* **Psychosurgery**

Local anesthetic *see* **Anesthesia, local**

Localized scratch dermatitis *see* **Lichen simplex chronicus**

Lockjaw *see* **Tetanus**

Loperamide *see* **Antidiarrheal drugs**

Loratadine *see* **Antihistamines**

Lou Gehrig's disease *see* **Amyotrophic lateral sclerosis**

Louis-Bar syndrome *see* **Ataxia-telangiectasia**

Low back pain

Definition

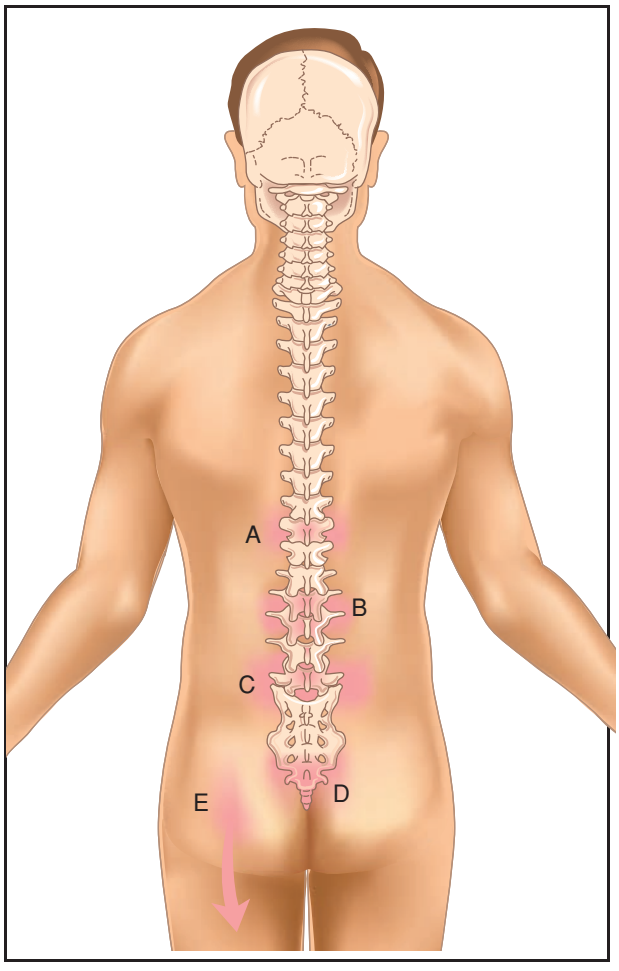
Low back **pain** is a common musculoskeletal symptom that may be either acute or chronic. It may be caused by a variety of diseases and disorders that affect the lumbar spine. Low back pain is often accompanied by **sciatica**, which is pain that involves the sciatic nerve and is felt in the lower back, the buttocks, and the backs of the thighs.

Description

Low back pain is a symptom that affects 80% of the general United States population at some point in life with sufficient severity to cause absence from work. It is the second most common reason for visits to primary care doctors, and is estimated to cost the American economy $75 billion every year.

Low back pain may be experienced in several different ways:

- Localized. In localized pain the patient will feel soreness or discomfort when the doctor palpates, or presses on, a specific surface area of the lower back.
- Diffuse. Diffuse pain is spread over a larger area and comes from deep tissue layers.



Sites of low back pain. Pain anywhere along the spine (A) can be caused by osteoarthritis. Pain along one or the other side of the spine may be (B) a kidney infection. Trauma to back muscles, joints, or disks (C) causes low back pain. Damage to the coccyx (D) can occur during a fall. Sciatica (E) can cause pain to run down from the back and buttocks area down a leg. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

- Radicular. The pain is caused by irritation of a nerve root. Sciatica is an example of radicular pain.
- Referred. The pain is perceived in the lower back but is caused by inflammation elsewhere—often in the kidneys or lower abdomen.

Causes and Symptoms

Acute pain

Acute pain in the lower back that does not extend to the leg is most commonly caused by a sprain or muscle tear, usually occurring within 24 hours of heavy lifting or overuse of the back muscles. The pain is usually localized, and there may be **muscle spasms** or soreness when the doctor touches the area. The patient usually feels better when resting.

Chronic pain

Chronic low back pain has several different possible causes:

MECHANICAL. Chronic strain on the muscles of the lower back may be caused by **obesity**; **pregnancy**; or job-related stooping, bending, or other stressful postures.

MALIGNANCY. Low back pain at night that is not relieved by lying down may be caused by a tumor in the cauda equina (the roots of the spinal nerves controlling sensation in and movement of the legs), or a **cancer** that has spread to the spine from the prostate, breasts, or lungs. The risk factors for the spread of cancer to the lower back include a history of **smoking**, sudden weight loss, and age over 50.

ANKYLOSING SPONDYLITIS. Ankylosing spondylitis is a form of arthritis that causes chronic pain in the lower back. The pain is made worse by sitting or lying down and improves when the patient gets up. It is most commonly seen in males between 16 and 35. Ankylosing spondylitis is often confused with mechanical back pain in its early stages.

HERNIATED SPINAL DISK. Disk herniation is a disorder in which a spinal disk begins to bulge outward between the vertebrae. Herniated or ruptured disks are a common cause of chronic low back pain in adults.

PSYCHOGENIC. Back pain that is out of proportion to a minor injury, or that is unusually prolonged, may be associated with a somatoform disorder or other psychiatric disturbance.

Low back pain with leg involvement

Low back pain that radiates down the leg usually indicates involvement of the sciatic nerve. The nerve can be pinched or irritated by herniated disks, tumors of the cauda equina, abscesses in the space between the spinal cord and its covering, **spinal stenosis**, and compression **fractures**. Some patients experience **numbness** or weakness of the legs as well as pain.

Diagnosis

The diagnosis of low back pain can be complicated. Most cases are initially evaluated by primary care physicians rather than by specialists.

Initial workup

PATIENT HISTORY. The doctor will ask the patient specific questions about the location of the pain, its characteristics, its onset, and the body positions or activities that make it better or worse. If the doctor suspects that the pain is referred from other organs, he or she will ask about a history of diabetes, peptic ulcers, **kidney stones**, urinary tract infections, or **heart murmurs**.

PHYSICAL EXAMINATION. The doctor will examine the patient's back and hips to check for conditions that require surgery or emergency treatment. The examination includes several tests that involve moving the patient's legs in specific positions to test for nerve root irritation or disk herniation. The flexibility of the lumbar vertebrae may be measured to rule out ankylosing spondylitis.

Imaging studies

Imaging studies are not usually performed on patients whose history and **physical examination** suggest routine muscle strain or overuse. X rays are ordered for patients whose symptoms suggest cancer, infection, inflammation, pelvic or abdominal disease, or bone fractures. MRIs are usually ordered only for patients with certain types of masses or tumors.

It is important to know that the appearance of some abnormalities on imaging studies of the lower back does not necessarily indicate that they cause the pain. Many patients have minor deformities that do not create symptoms. The doctor must compare the results of imaging studies very carefully with information from the patient's history and physical examination.

Treatment

All forms of treatment of low back pain are aimed either at symptom relief or to prevent interference with the processes of healing. None of these methods appear to speed up healing.

Acute pain

Acute back pain is treated with **nonsteroidal anti-inflammatory drugs** (NSAIDs), such as ibuprofen, **muscle relaxants**, or **aspirin**. Applications of heat or cold compresses are also helpful to most patients. If the patient has not experienced some improvement after several weeks of treatment, the doctor will reinvestigate the cause of the pain.

Chronic pain

Patients with chronic back pain are treated with a combination of medications, **physical therapy**, andoccupational or lifestyle modification. The medicationsgiven are usually NSAIDs, although patients withhypertension, kidney problems, or stomach ulcers should not take these drugs. Patients who take NSAIDs for longer than six weeks should be monitored periodically for complications.

Physical therapy for chronic low back pain usually includes regular **exercise** for fitness and flexibility, and massage or application of heat if necessary.

Lifestyle modifications include giving up smoking, weight reduction (if necessary), and evaluation of the patient's occupation or other customary activities.

Patients with herniated disks are treated surgically if the pain does not respond to medication.

Patients with chronic low back pain sometimesbenefit from **pain management** techniques, including **biofeedback**, **acupuncture**, and **chiropractic** manipulation of the spine.

Psychotherapy is recommended for patients whose back pain is associated with a somatoform, **anxiety**, or depressive disorder.

Low back pain with leg involvement

Treatment of sciatica and other disorders that involve the legs may include NSAIDs. Patients with long-standing sciatica or spinal stenosis that do not respond to NSAIDs are treated surgically. Although some doctors use cortisone injections to relieve the pain, this form of treatment is still debated.

Alternative treatment

A thorough differential diagnosis is important before any treatment is considered. There are times when alternative therapies are the most beneficial, and other times when more invasive treatments are needed.

Chiropractic

Chiropractic treats patients by manipulating or adjusting sections of the spine. It is one of the most popular forms of alternative treatment in the United States for relief of back pain caused by straining or lifting injuries. Some osteopathic physicians, physical therapists, and naturopathic physicians also use spinal manipulation to treat patients with low back pain.

KEY TERMS

Ankylosing spondylitis—A type of arthritis that causes gradual loss of flexibility in the spinal column. It occurs most commonly in males between 16 and 35.

Cauda equina—The roots of the spinal nerves controlling movement and sensation in the legs. These nerve roots are located in the lower spine and resemble a horse's tail (*cauda equina* in Latin).

Chiropractic—A method of treatment based on the interactions of the spine and the nervous system. Chiropractors adjust or manipulate segments of the patient's spinal column in order to relieve pain.

Lumbar spine—The segment of the human spine above the pelvis that is involved in low back pain. There are five vertebrae, or bones, in the lumbar spine.

Radicular—Pain that is caused by the root of a nerve.

Referred pain—Pain that is experienced in one part of the body but originates in another organ or area. The pain is referred because the nerves that supply the damaged organ enter the spine in the same segment as the nerves that supply the area where the pain is felt.

Sciatica—Pain caused by irritation of the sciatic nerve. Sciatica is felt in the lower back, the buttocks, and the backs of the upper legs.

Spinal stenosis—A form of sciatica that is caused by a narrowing of the spinal canal in the lumbar vertebrae. The narrowing puts pressure on the roots of the sciatic nerve.

Traditional Chinese medicine

Practitioners of **traditional Chinese medicine** treat low back pain with acupuncture, *tui na* (push-and-rub) massage, and the application of herbal poultices.

Herbal medicine

Herbal medicine can utilize a variety of antispasmodic herbs in combination to help relieve low back pain due to spasm. Lobelia (*Lobelia inflata*) and myrrh (*Commiphora molmol*) are two examples of antispasmodic herbs.

Homeopathy

Homeopathic treatment for acute back pain consists of applications of *Arnica* oil to the sore area or oral doses of *Arnica* or *Rhus toxicodendron*. *Bellis perennis* is recommended for deep muscle injuries. Other remedies may be recommended based on the symptoms presented by the patient.

Body work and yoga

Massage and the numerous other body work techniques can be very effective in treating low back pain. **Yoga**, practiced regularly and done properly, can be most useful in preventing future episodes of low back pain.

Prognosis

The prognosis for most patients with acute low back pain is excellent. About 80% of patients recover completely in 4–6 weeks. The prognosis for recovery from chronic pain depends on the underlying cause.

Prevention

Low back pain due to muscle strain can be prevented by lifestyle choices, including regular physical exercise and weight control, avoiding smoking, and learning the proper techniques for lifting and moving heavy objects. Exercises designed to strengthen the muscles of the lower back, and chairs or car seats with lumbar supports are also recommended.

Resources

BOOKS

Hellman, David B. "Arthritis & Musculoskeletal Disorders." In *Current Medical Diagnosis and Treatment, 1998*, edited by Stephen McPhee, et al., 37th ed. Stamford: Appleton & Lange, 1997.

Rebecca J. Frey, PhD

Low blood magnesium *see* **Magnesium imbalance**

Low blood phosphate level *see* **Phosphorus imbalance**

Low blood pressure *see* **Orthostatic hypotension; Hypotension**

Low blood sugar *see* **Hypoglycemia**

Low calcium blood level *see* **Hypocalcemia**

Low potassium blood level *see* **Hypokalemia**

Low sodium blood level *see* **Hyponatremia**

Low sugar diet

Definition

Low-sugar **diets** are a specialized form of low-carbohydrate diets for diabetes management or weight loss. Some are derived from general guidelines drawn up by such organizations as the American Diabetes Association (ADA) or the American Heart Association (AHA); others, like the Sugar Busters diet, are diet plans published by individuals or groups for the general public. Low-sugar diets are based on reducing the total amount of sugar obtained in the diet from fruits, starches, and other foods, not just from table sugar and such other sweeteners as honey, molasses, or corn syrup.

Standard classifications and definitions of dietary sugars are as follows:

- Simple sugars. These include monosaccharides (glucose, galactose, and fructose) and disaccharides (sucrose [glucose plus fructose], found in sugar cane, sugar beets, honey, and corn syrup; lactose [glucose plus galactose], found in milk products; and maltose [glucose plus glucose], found in malt.
- Complex carbohydrates (starches). These foods contain glucose.
- Naturally occurring or intrinsic sugars. These sugars occur naturally in whole fruit, vegetable, and milk products.
- Added or extrinsic sugars. These are sugars or syrups added during food processing or at the table.
- Total sugars. This term refers to the sum total of naturally occurring and added sugars in a specific food.
- High-fructose corn syrup. This is a sweetener that is produced from corn syrup that undergoes enzymatic processing to increase its fructose content and is then mixed with glucose.

Purpose

The purpose of low-sugar diets is to assist in the long-term management of **diabetes mellitus**, to enable weight loss or weight management, or both.

Demographics

It is difficult to estimate how many diabetics or dieters in North America are trying to manage their respective conditions on low-sugar diets. At one point in the early 2000s, some writers thought that as many as 18% of American adults were using low-carbohydrate diets of one type or another; another estimate published in 2006 is that 3.4% of American adults are following one of these diets at any given time. What is known, however, is that the average American diet as of 2009 is much higher in sugar than is permitted by low-carbohydrate or low-sugar diets.

According to the American Heart Association (AHA), the average American consumes 355 calories per day (22.5 teaspoons) in the form of sugars added to foods, mostly soft drinks and other sweetened beverages. The demographic with the highest daily sugar intake is males between the ages of 14 and 19, who consume an average of 34 teaspoons of sugar per day. The AHA stated in August 2009 that a prudent sugar intake for the average American woman is less than a third of this amount (100 calories or 6 teaspoons) and less than half of it for the average man (150 calories or 9 teaspoons).

Precautions

The most important precautions for low-sugar diets, as for any other diet intended for weight control or diabetes management, are making sure that the diet is based on accurate medical information and sound nutritional advice, and that it includes foods and recipes that the individual patient enjoys, for the sake of long-term compliance.

Several specific precautions recommended for low-sugar diets include the following:

- Read food labels carefully. Required nutritional labeling lists the ingredients in a food product in the order of their amount within the product. The higher an ingredient's position in the list, the larger the amount of it in the food. People on a low-sugar diet should not consume any product in which sugar is listed as one of the top 3 ingredients.
- Remember that there are many different forms of sugar in food products: high-fructose corn syrup, brown sugar, beet sugar, cane sugar, sorbitol, mannitol, raw sugar, agave nectar, cane sugar juice, turbinado sugar, honey, maltodextrin, molasses, dextrose, and sucrose.
- Drink water instead of soda pop or sugary fruit juice. These products can contain as much as 4 tablespoons of sugar per can.
- Avoid adding table sugar to cereals, tea, coffee, grapefruit, and other foods that many people habitually sweeten. One suggestion often made is to cut the usual amount of sugar added at the table in half, then in half again the following week until the craving for it disappears.
- Be aware that sugar is often added to such products as bread, catsup, canned soup, tomato sauce, and

other canned foods even though it is not needed. Look for brands of these items that do not contain added sugar.

- Try cutting the amount of sugar called for in some cookie or pie recipes. In many cases the recipe will work just as well with half the amount of sugar.

Description

General low-sugar diets

Most diabetic diet plans are based on some form of carbohydrate counting or carbohydrate measurement because carbohydrates are the nutrients with the greatest impact on blood glucose levels. A low-sugar diet is based on the assumption that sugars are to be avoided as much as possible in favor of starchy carbohydrates.

Some low-sugar diets are based on the glycemic index (GI), an approach to carbohydrate counting based on the knowledge that the body does not convert all carbohydrates in food to glucose with the same speed or efficiency. The glycemic index (GI) is a classification of foods according to the speed at which the body converts their carbohydrate to glucose. Glucose itself is assigned a value of 100 on the glycemic index and other foods are measured against it. Any food below 55 is considered to have a low GI. Examples include grapefruit juice (48), oatmeal (42), and spaghetti (41).

Sugar Busters diet

The Sugar Busters diet is a popularized version of a low-GI diet available in an inexpensive paperback edition and supported by a website with a chat forum. There is a child's version of the diet available as well as a book for adults, written by a team of three doctors and the CEO of a Fortune 500 energy company (who is listed as the first author).

The Sugar Busters diet is essentially a diet that eliminates sources of sugar and other high-GI carbohydrates in order to lower blood insulin levels. It requires the dieter to eliminate all refined sugar, honey, and molasses; white flour and products made with it (white bread, cake, bagels, crackers, and tortillas); potatoes; most forms of white rice; corn flour; sugared soft drinks; beer; and other foods that are high on the GI index. The general rule is that any permissible food must contain 3 grams of sugar or less per serving. A more detailed list of acceptable and unacceptable foods can be found at the "Newbie Tips" link listed below. The published book contains little information on tailoring the diet to individual needs; a common criticism of it is that it is a one-size-fits-all approach to carbohydrate counting.

Origins

Low-carbohydrate diets for both diabetes management and weight loss have been produced by various organizations and individual authors in North America since the 1960s. Low-sugar diets, however, did not gain much attention from the general public until the 1990s. The concept of the glycemic index was introduced by David Jenkins, a Canadian physician, in 1981. The first version of the Sugar Busters diet, based on the glycemic index, was published in New Orleans in 1998, with a revised version following in 2003.

Preparation

Preparation for using a low-sugar or any other diet plan for weight loss includes consulting a primary care physician. Persons wishing to try the Sugar Busters diet should read the introduction to the book first and understand the theory underlying this diet before making food purchases and meal plans based on the diet.

Preparation for following a low-sugar or any other diabetic diet usually involves meeting with a dietitian or diabetes counselor as well as the doctor in order to plan a diet that will work well with the patient's food preferences and lifestyle. Children and adolescents, athletes, and all type 1 diabetics need to take particular care regarding the timing of their meals as well as the total calories and specific foods included in the diet.

Aftercare

A low-sugar, low-carbohydrate, or any other diabetes diet is a lifelong part of diabetes management. Follow-up includes regular medical checkups, home monitoring of blood glucose levels, and consultations with a dietitian if adjustments are needed.

A low-sugar or any other specific diet for weight management is also a lifelong undertaking and should be followed under a doctor's and/or a dietitian's supervision.

Risks

As of 2009, there are no known risks to health in following a low-sugar diet under a doctor's supervision provided the diet is nutritionally sound. Some researchers note, however, that the long-term effects of low-sugar or low-carbohydrate diets are still

KEY TERMS

Agave nectar—A sweetener produced commercially in Mexico from the leaves of the agave, a succulent plant with thick fleshy leaves.

Bariatric—Related to or specializing in the treatment of obesity.

Blood glucose—The main sugar that the body makes from the food in the diet.

Disaccharide—Any sugar formed when two monosaccharides are joined together and a molecule of water is removed.

Fructose—A monosaccharide sugar found in many fruits.

Glycemic index (GI)—A measurement of the speed at which the body converts carbohydrates in foods to blood glucose. The more rapidly a food's carbohydrates are converted to glucose, the higher its GI.

Insulin—A hormone secreted by the pancreas that causes the cells in the liver, muscle and fatty tissues of the body to use the glucose carried in the bloodstream after a meal.

Monosaccharide—The simplest form of sugar. Monosaccharides combine to form disaccharides and such complex carbohydrates as starch and cellulose.

Pancreas—A small organ that lies between the stomach and the liver and secretes insulin.

Sucrose—The scientific name for table sugar. Sucrose is a disaccharide derived from glucose and fructose.

Turbinado sugar—A type of sugar made from sugar cane extract. It resembles light brown sugar in color but is paler and has larger crystals. It is called demerara sugar in the United Kingdom.

unknown, as no studies of the benefits of these diets have been conducted over long enough periods of time to determine whether they may increase the risk of such conditions as heart disease, **cancer**, and kidney or bone problems—which take years to develop. Over the short term, diabetics are at risk of complications from their disease if they try extreme fad diets for rapid weight loss or if they fail to stay within their individual dietary guidelines.

One group of people who should be particularly careful in trying a low-sugar diet is athletes, particularly long-distance or marathon runners. Athletes (or people who **exercise** vigorously for long periods of time) require more high-glycemic index foods in the diet that supply large quantities of glucose quickly to meet the body's needs for energy. Even the authors of the Sugar Busters diet recognize that "this diet may not be exactly right for [athletes and fitness buffs]."

Results

The results of a properly designed low-sugar diabetic diet include improved stability in blood glucose levels; weight loss when needed; lowered risk of the complications of diabetes; and patient satisfaction with the food choices and dishes allowed on the diet. The major problem with low-sugar diets as well as low-carbohydrate diets in general is the difficulty most patients have in sticking with them over the long term because of their restrictiveness. Researchers at the Mayo Clinic have noted that the dropout rate for these diets is the same as that for low-fat diets and other restrictive diet plans.

Another problem associated with the Sugar Busters diet and other diet plans based on the glycemic index is their complexity. Doctors at the Joslin Diabetes Center comment, "The more complex a meal plan is, the less likely people are to follow it. The glycemic index is a fairly complex meal planning tool." In addition, different people's bodies respond differently to so-called "high" and "low" GI foods. A registered dietitian may be able to help patients determine their own individual glycemic index of foods based on how their blood glucose level responds to the various meals and snacks they usually eat.

Health care team roles

All members of the health care team may come into contact with diabetic patients. The nurse plays a particularly important role in teaching patients the skills necessary to manage this complex disease, and educating them about the effects of their medications. Registered dietitians and diabetes counselors are also important participants in nutritional planning and patient education. Diabetes education is an ongoing process that may require periodic consultation with a specialized diabetes counselor as well as participation in a diabetes support group.

Persons following a low-sugar diet for weight loss or weight management rather than diabetes management should consult their primary care physician to

make sure that such a diet is appropriate for them, particularly if they participate in sports or other forms of vigorous exercise. They may also wish to consult a registered dietitian to help them plan an individualized low-sugar diet based on the glycemic index.

Alternatives

Bariatric (weight-loss) surgery is sometimes recommended for severely obese patients with type 2 diabetes and a body mass index (BMI) over 35. Blood sugar levels return to normal in 55 to 95% of people with diabetes depending on the procedure performed. The most effective type of weight-loss surgery for type 2 diabetics appears to be a procedure in which part of the small intestine is bypassed. This procedure is expensive, however, and involves the possibility of such long-term complications as **osteoporosis** and nutritional deficiencies. It also requires major adjustments in the patient's lifestyle.

Research and general acceptance

There is little consensus on the merits of low-sugar diets as of 2009. Studies of low-GI diets have yielded conflicting results regarding their effectiveness; and as previously noted, many of these diets are sufficiently complex as to discourage many people from using them. Although the Sugar Busters diet is reported to help people lose weight, at least in the short term, the Clinical Trials website notes that this diet has not been evaluated for either long-term safety or efficacy as of late 2009. There is one clinical trial under way as of 2009 of a general low-sugar diet in obese adolescents.

Caregiver concerns

Caregivers need to make sure that a diabetic or obese person in their care adheres to the food choices, meal plans, calorie allotment, and timing of meals in their diet. "Cheating" on one's diet can have severe short-term as well as long-term consequences for a poorly controlled diabetic.

Caregivers caring for a person trying to manage diabetes or lose weight on a low-sugar diet should also make sure that they understand the theories underlying these diets and encourage the dieter to stick with the plan.

Resources

BOOKS

Maccaro, Janet. *Change Your Food, Change Your Mood.* Lake Mary, FL: 2008.

Steward, H. Leighton, et al. *The New Sugar Busters! : Cut Sugar to Trim Fat*. New York: Ballantine Books, 2003.

Wise, S. J. *The Sugar Addict's Diet: A Primer for the Low Sugar Lifestyle, a Path of Healing, Wellness, and Weight Loss*. New Canaan, CT: New Century Publishing, 2001.

PERIODICALS

Blanck, H.M., et al. "Use of Low-carbohydrate, High-protein Diets among Americans: Correlates, Duration, and Weight Loss." *Medscape General Medicine* 8 (April 5, 2006): 5.

Collins, J.K., et al. "Consumer Acceptability of Low-sugar Watermelon Sweetened with Non-calorie Sweetener by a Native American Community." *International Journal of Food Sciences and Nutrition* 57 (August-September 2006): 363–68.

Gellar, L.A., et al. "Healthy Eating Practices: Perceptions, Facilitators, and Barriers among Youth with Diabetes." *Diabetes Educator* 33 (July-August 2007): 671–79.

Johnson, R.K., et al. "Dietary Sugars Intake and Cardiovascular Health: A Scientific Statement from the American Heart Association." *Circulation* 120 (September 15, 2009): 1011–20.

Vega-Lopez, S., and S.N. Mayol-Kreiser. "Use of the Glycemic Index for Weight Loss and Glycemic Control: A Review of Recent Evidence." *Current Diabetes Reports* 9 (October 2009): 379–88.

Ventura, E., et al. "Reduction in Risk Factors for Type 2 Diabetes Mellitus in Response to a Low-sugar, High-fiber Dietary Intervention in Overweight Latino Adolescents." *Archives of Pediatric and Adolescent Medicine* 163 (April 2009): 320–27.

OTHER

American Diabetes Association (ADA). "Position Statement: Nutrition Recommendations and Interventions for Diabetes." *Diabetes Care* 31 (January 2008), Suppl. 1, 561–578. http://care.diabetesjournals.org/content/31/Supplement_1/S61.full.pdf+html

Joslin Diabetes Center. *The Glycemic Index and Diabetes*. http://www.joslin.org/info/the_glycemic_index_and_diabetes.html

Sugar Busters! *Newbie Tips*. This is a summary of the food restrictions and other recommendations of the Sugar Busters diet. http://www.sugarbusters.com/filessb/newbietips.htm

ORGANIZATIONS

American Diabetes Association, 1701 North Beauregard Street, Alexandria, VA, 22311, 800-DIABETES (800-342-2383), AskADA@diabetes.org, http://www.diabetes.org/.

American Dietetic Association, 120 South Riverside Plaza, Suite 2000, Chicago, IL, 60606-6995, (800) 877-1600, http://www.eatright.org/cps/rde/xchg/ada/hs.xsl/index.html.

American Society for Metabolic and Bariatric Surgery (ASMBS), 100 SW 75th Street, Suite 201, Gainesville, FL, 32607, (352) 331-4900, (352) 331-4975, info@asmbs.org, http://www.asbs.org/.

Joslin Diabetes Center, One Joslin Place, Boston, MA, 02215, (617) 732-2400, (800) JOSLIN-1, diabetes@joslin.harvard.edu, http://www.joslin.org/index.html.

National Diabetes Education Program (NDEP), One Diabetes Way, Bethesda, MD, 20814-9692, (301) 496-3583, http://ndep.nih.gov/.
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Building 31. Rm 9A06, 31 Center Drive, MSC 2560, Bethesda, MD, 20892-2560, (301) 496-3583, http://www2.niddk.nih.gov/Footer/ContactNIDDK.htm, http://www2.niddk.nih.gov/.
Sugar Busters!, http://www.sugarbusters.com/index.html.

Rebecca J. Frey, PhD

Lower esophageal ring

Definition

Lower esophageal ring is a condition in which there is a ring of tissue inside the lower part of the esophagus (the tube connecting the throat with the stomach). This tissue causes narrowing and partial blockage of the esophagus. Lower esophageal ring can also refer to the ring itself.

Description

Lower esophageal ring (also called Schatzki's ring and B-ring) affects about 10–14% of the population. Normally, the lower part of the esophagus, near where the esophagus meets the stomach, has an inside diameter of 1.5–2 inches. The diameter of this part of the esophagus is less when lower esophageal ring is present, and diameters as small as one-eighth inch have been seen. When the inside diameter is less than about three-fourths of an inch, intermittent difficulty with swallowing can result. About 96% of people with lower esophageal ring have no symptoms.

Causes and symptoms

Causes

Lower esophageal ring seems to result from infoldings of tissue near the bottom of the esophagus, but the underlying cause is unknown. Although some specialists speculate they are due to a congenital defect, most people do not develop symptoms until they reach their forties or later. Although lower esophageal ring is generally associated with **hiatal hernia**, and sometimes with **heartburn**, the cause/effect relationship is unclear.

Symptoms

Intermittent difficulty swallowing solid food is the primary symptom of this condition. The degree of difficulty in swallowing is directly related to the degree the esophagus is narrowed. Certain foods, especially tough or fibrous foods like meat, are more likely to cause swallowing difficulties.

Diagnosis

Gastroenterologists and internists are best equipped to diagnose and treat lower esophageal ring. The diagnosis is based on the patient's history of swallowing difficulties and a barium x ray of the upper gastrointestinal tract. For a barium x ray, the patient swallows a liquid containing barium, a substance that is opaque to x rays. Subsequent x-ray photography reveals the shape of the esophagus and any narrow regions present.

The presence of a lower esophageal ring can also be shown with a test called an esophagoscopy. This procedure visualizes the inside of the esophagus with an inserted, thin, flexible tube. However, this test is less sensitive for lower esophageal ring and costs about five times as much as barium x ray. However, if the findings of a barium x ray are not definitive, esophagoscopy should be done. Biopsies can then be done on questionable areas.

Treatment

Dietary change

Swallowing difficulties due to lower esophageal ring can often be relieved by chewing food more thoroughly. Soft foods and liquids may also be recommended.

Dilation

Lower esophageal rings can be corrected by passing a bougie (a cylindrical, mercury-filled dilator) through the esophagus. This procedure, called bougienage, is effective most of the time, but may need to be repeated every few years. Complications and adverse reactions are extremely rare.

Surgery

If bougienage is unsuccessful, lower esophageal ring tissue can be surgically removed.

Prognosis

The probability of a favorable outcome is high. Swallowing difficulties can be alleviated in almost every case, and the rate of complications from bougienage or surgery is less than 1%.

KEY TERMS

Bougie—A mercury-filled dilator in the shape of a cylinder or tapered cylinder. Bougies come in a range of different sizes.

Bougienage—The procedure of dilating tubal organs, like the esophagus, with a bougie or bougies.

Congenital—Existing at birth.

Dysphagia—Difficulty swallowing.

Esophagoscopy (also esophagoendoscopy)—Examination of the inside of the esophagus using a flexible tube that transmits video images.

Esophagus—The tube connecting the throat to the stomach, which is about ten inches long in adults. It is coated with mucus and surrounded by muscles, and pushes food to the stomach by sequential waves of contraction. It functions to transport food from the throat to the stomach and to keep the contents of the stomach in the stomach.

Heartburn—A burning sensation in the chest that can extend to the neck, throat, and face, caused by the movement of stomach acid into the esophagus.

Hiatal hernia—A condition where part of the stomach extends through the diaphragm into the chest cavity.

Prevention

Since the cause of lower esophageal ring is not known, there are no definitive preventive measures. Nevertheless, anyone with lower esophageal ring who also suffers from heartburn would be wise to prevent or treat the heartburn. It is possible that the stomach acid in the esophagus associated with heartburn contributes to esophageal ring.

ORGANIZATIONS

American College of Gastroenterology, P. O. Box 342260, Bethesda, MD, 20827-2260, (301) 263-9000, http://www.acg.gi.org.

American Gastroenterological Association (AGA), 4930 Del Ray Avenue, Bethesda, MD, 20814, (301) 654-2055, (301) 654-5920, member@gastro.org, http://www.gastro.org.

American Society for Gastrointestinal Endoscopy, 1520 Kensington Road, Suite 202, Oak Brook, IL, 60523, (630) 573-0600, (630) 573-0691, (866) 353-2743, info!asge.org, http://www.asge.org/.

National Digestive Diseases Information Clearinghouse (NDDIC), 2 Information Way, Bethesda, MD, 20892-3570, (703) 738-4929, (800) 891-5389, http://digestive.niddk.nih.gov.

Lorraine Lica, PhD

Lower GI exam *see* **Barium enema**

LSD *see* **Lysergic acid diethylamide**

Lues *see* **Syphilis**

Lumbar puncture

Definition

Lumbar puncture (LP) is the technique of using a needle to withdraw cerebrospinal fluid (CSF) from the spinal canal. CSF is the clear, watery liquid that protects the central nervous system from injury and cushions it from the surrounding bone structure. It contains a variety of substances, particularly glucose (sugar), protein, and white blood cells from the immune system.

Purpose

Lumbar puncture, or spinal tap, is used to diagnose some malignancies, such as certain types of brain **cancer** and leukemia, as well as other medical conditions that affect the central nervous system. It is sometimes used to assess patients with certain psychiatric symptoms and conditions.

It is also used for injecting **chemotherapy** directly into the CSF. This type of treatment is called intrathecal therapy. Other medical conditions diagnosed with lumbar puncture include:

- viral and bacterial meningitis
- syphilis, a sexually transmitted disease
- bleeding (hemorrhaging) around the brain and spinal cord
- multiple sclerosis, a disease that affects the myelin coating of the nerve fibers of the brain and spinal cord
- Guillain-Barré syndrome, an inflammation of the nerves

KEY TERMS

Acute lymphoblastic leukemia (ALL)—A type of leukemia, also called acute lymphocytic leukemia, primarily in children, affecting lymphocytes.

Encephalitis—An inflammation or infection of the brain and spinal cord caused by a virus or as a complication of another infection.

Guillain-Barré syndrome—An inflammation involving nerves that affects the extremities. The inflammation may spread to the face, arms, and chest.

Immune system—Protects the body against infection.

Intrathecal therapy—Injecting chemotherapy directly into the CSF using lumbar puncture.

Manometer—A device used to measure fluid pressure.

Meningitis—An infection or inflammation of the membranes or tissues that cover the brain and spinal cord, and caused by bacteria or a virus.

Multiple sclerosis—A disease that destroys the covering (myelin sheath) of nerve fibers of the brain and spinal cord.

Spinal canal—The cavity or hollow space within the spine that contains cerebrospinal fluid.

Thrombocytopenia—Reduced platelet levels.

Vertebrae—The bones of the spinal column. There are 33 along the spine, with five (called L1–L5) making up the lower lumbar region.

Precautions

In some circumstances, a lumbar puncture to withdraw a small amount of CSF for analysis may lead to serious complications. Lumbar puncture should be performed only with extreme caution, and only if the benefits are thought to outweigh the risks, in certain conditions. For example, in people who have blood clotting (coagulation) or bleeding disorders or who are on anticoagulant treatment, lumbar puncture can cause bleeding that can compress the spinal cord. The term for this condition is spinal **subdural hematoma**, and it is a rare complication. However, it is of concern to some cancer patients whose low platelet counts (**thrombocytopenia**) make them more susceptible to bleeding. In some cases, these patients are given a platelet **transfusion** prior to lumbar puncture, but this procedure is still under investigation. A four-year study, supported in part by the National Cancer Institute, researched the risk of lumbar puncture on children with acute lymphoblastic leukemia (ALL). No serious lumbar puncture complications were observed in this study of over 5,000 children.

Lumbar puncture has been shown to be less precise than some other methods in monitoring intracranial fluid pressure. A transducer provides more accurate information about changes in the flow of blood and cerebrospinal fluid within the brain.

A traumatic lumbar puncture (TLP) occurs when a blood vessel is inadvertently ruptured during the procedure. If this happens as part of a diagnostic leukemia workup, there is the potential of contaminating the CSF specimen that has been removed with leukemia cells, causing a false positive test result.

If there is a large **brain tumor** or other mass, removal of CSF can cause pressure shifts within the brain (herniation), causing compression of the brain stem and other vital structures, and leading to irreversible brain damage or **death**. These problems are easily avoided by checking blood coagulation through a blood test and by doing a computed tomography scan (CT) or **magnetic resonance imaging** (MRI) scan before attempting the lumbar puncture. In addition, a lumbar puncture procedure should never be performed at the site of a localized skin infection on the lower back because the infection may be introduced into the CSF and may spread to the brain or spinal cord.

Description

In a lumbar puncture, the area of the spinal column used to obtain the CSF sample is in the lumbar spine, or lower section of the back. In rare instances, such as a spinal fluid blockage in the middle of the back, a doctor may perform a spinal tap in the neck. The lower lumbar spine (usually between the vertebrae known as L4–5) is preferable because the spinal cord stops near L2, and a needle introduced below this level will miss the spinal cord and encounter only nerve roots, which are easily pushed aside.

A lumbar puncture takes about 15–30 minutes. Patients can undergo the test in a doctor's office, laboratory, or outpatient hospital setting. Sometimes it requires an inpatient hospital stay. If the patient has severe **osteoarthritis** of the spine, is extremely

uncooperative, or obese, it may be necessary to introduce the spinal needle using x-ray guidance.

In order to get an accurate sample of cerebrospinal fluid, it is critical that a patient is in the proper position. The spine must be curved to allow as much space as possible between the lower vertebrae, or bones of the back, for the doctor to insert a lumbar puncture needle between the vertebrae and withdraw a small amount of fluid. The most common position is for the patient to lie on his or her side with the back at the edge of the exam table, head and chin bent down, knees drawn up to the chest, and arms clasped around the knees. (Small infants and people who are obese may need to curve their spines in a sitting position.) People should talk to their doctors if they have any questions about their position because it is important to be comfortable and to remain still during the entire procedure. In fact, the doctor will explain the procedure to the patient (or guardian) so that the patient can agree in writing to have it done (informed consent). If the patient is anxious or uncooperative, a short-acting sedative may be given.

During a lumbar puncture, the doctor drapes the back with a sterile covering that has an opening over the puncture site and cleans the skin surface with an antiseptic solution. Patients receive a local anesthetic to minimize any **pain** in the lower back.

The doctor inserts a thin hollow needle in the space between two vertebrae of the lower back and slowly advances it through ligamentous tissues toward the spine. A steady flow of clear cerebrospinal fluid, normally the color of water, will begin to fill the needle as soon as it enters the spinal canal. The doctor measures the cerebrospinal fluid pressure with a special instrument called a manometer and withdraws several vials of fluid for laboratory analysis. The amount of fluid collected depends on the type and number of tests needed to diagnose a particular medical disorder.

In some cases, the doctor must remove and reposition the needle. This occurs when there is not an even flow of fluid, the needle hits bone or a blood vessel, or the patient reports sharp, unusual pain.

Preparation

Patients can go about their normal activities before a lumbar puncture. Experts recommend that patients relax before the procedure to release any muscle tension, since the lumbar puncture needle must pass through muscle tissue before it reaches the spinal canal. A patient's level of relaxation before and during the procedure plays a critical role in the test's success. Relaxation may be difficult for those patients who face frequent lumbar punctures, such as children with leukemia. In these cases, it is especially important for the child to receive psychological support before and after each procedure. It may be helpful to praise a child who remained still and quiet during the procedure, and to remind the child of his or her good behavior before the next lumbar puncture.

Aftercare

After the procedure, the doctor covers the site of the puncture with a sterile bandage. Patients must avoid sitting or standing and remain lying down for as long as six hours after the lumbar puncture. They should also drink plenty of fluids to help prevent lumbar puncture **headache**, which is discussed in the next section.

Risks

The most common side effect of lumbar puncture is a headache. This problem occurs in 10–20% of adult patients and in up to 40% of children. It is caused by decreased CSF pressure related to a small leak of CSF through the puncture site. These headaches usually are a dull pain, although some people report a throbbing sensation. A stiff neck and **nausea** may accompany the headache. A lumbar puncture headache typically begins within a few hours to two days after the procedure and usually persists a few days, although it can last several weeks or months.

In some cases, the headache can be prevented by lying flat for an hour after the lumbar puncture, and taking in more fluids for 24 hours after the procedure. Since an upright position worsens the pain, lying flat also helps control the pain, along with prescription or non–prescription pain relief medication, preferably one containing **caffeine**. In rare cases, the puncture site leak is "patched" using the patient's own blood. People may also experience back pain. Headaches and backaches appear to be more common in adolescents than in younger children, and more common in girls than in boys.

Patients who receive **anticancer drugs** through lumbar puncture sometimes have **nausea and vomiting**. Intrathecal methotrexate can cause mouth sores. Some of these symptoms may be relieved by antinausea drugs prescribed by the physician.

In a very few cases, lumbar puncture in infants can lead to such complications as paraplegia. These complications are associated with the smaller size of the

infant's central nervous system and increased difficulty in avoiding certain parts of the spinal cord when performing an LP.

People should talk to their doctors about complications from a lumbar puncture. In most cases, this procedure is safe and effective. Some patients experience pain, difficulty urinating, infection, or leakage of cerebrospinal fluid from the puncture site after the procedure.

Results

Normal CSF is clear and colorless. It may be straw or yellow–colored if there is excess protein, which may occur with cancer or inflammation. It may be cloudy in infections; blood–tinged if there was recent bleeding; or yellow to brown (xanthochromic) if caused by an older instance of bleeding.

A series of laboratory tests analyze the CSF for a variety of substances to rule out cancer or other medical disorders of the central nervous system. The following are normal values for commonly tested substances:

- CSF pressure: 50–180 mmH_2O
- Glucose: 40–85 mg/dL
- Protein: 15–50 mg/dL
- Leukocytes (white blood cells): total less than 5 per mL
- Lymphocytes (specific type of white blood cell): 60–70%
- Monocytes (a kind of white blood cell): 30–50%
- Neutrophils (another kind of white blood cell): none

Normally, there are no red blood cells in the CSF unless the needle passes though a blood vessel on route to the CSF. If this is the case, there should be more red blood cells in the first tube collected than in the last.

Abnormal results

A lumbar puncture is sometimes used as part of a diagnostic cancer workup. Abnormal test result values in the pressure or any of the substances found in the cerebrospinal fluid may suggest a number of medical problems including a tumor or spinal cord obstruction; hemorrhaging or bleeding in the central nervous system; infection from bacterial, viral, or fungal microorganisms; or an inflammation of the nerves. If there is a tumor in the meninges (membranes around the brain and spinal cord), the CSF may have higher protein levels, lower glucose levels, and a mild increase in lymphocytes (pleocytosis). It is important for patients to review the results of a **cerebrospinal fluid analysis** with their doctor and to discuss any treatment plans.

Resources

BOOKS

Fauci, Anthony S., et al. *Harrison's Principles of Internal Medicine*, 17th ed. New York: McGraw-Hill, 2008.

OTHER

"Cerebral spinal fluid (CSF) collection." *Medline Plus*, June 24, 2009. http://www.nlm.nih.gov/medlineplus/ency/article/003428.htm

ORGANIZATIONS

American Academy of Neurology, 1080 Montreal Avenue, St. Paul, MN, 55116-2325, (800) 879-1960, (651) 695-2791, membersservices@aan.com, http://www. aan.com.

Rebecca J. Frey, PhD
Brenda W. Lerner

Lumbar stenosis *see* **Spinal stenosis**
Lumbosacral radiculopathy *see* **Sciatica**

Lumpectomy

Definition

Lumpectomy is a type of surgery for **breast cancer**. It is considered "breast-conserving" surgery because only the malignant tumor and a surrounding margin of normal breast tissue are removed. Lymph nodes in the armpit (axilla) may also be removed. This procedure is also called lymph node dissection.

Purpose

Lumpectomy is a surgical treatment for newly diagnosed breast **cancer**. It is estimated that at least 50% of women with breast cancer are good candidates for this procedure. The location, size, and type of tumor are of primary importance when considering breast cancer surgery options. The size of the breast is another factor the surgeon considers when recommending surgery. The patient's psychological outlook, as well as her lifestyle and preferences, should also be taken into account when treatment decisions are being made.

The extent and severity of a cancer is evaluated, or "staged," according to a fairly complex system. Staging considers the size of the tumor and whether the cancer has spread (metastasized) to adjacent tissues, such as the chest wall, the lymph nodes, and/or to distant parts of the body. Women with early stage

breast cancers are usually better candidates for lumpectomy. In most cases, a course of **radiation therapy** after surgery is part of the treatment. **Chemotherapy** or hormone treatment may also be prescribed.

In some instances, women with later stage breast cancer may be able to have lumpectomies. Chemotherapy may be administered before surgery to decrease tumor size and the chance of metastasis in selected cases.

Contraindications to lumpectomy

There are a number of factors that may prevent or prohibit a breast cancer patient from having a lumpectomy. The tumor itself may be too large or located in an area where it would be difficult to remove with good cosmetic results. Sometimes several areas of cancer are found in one breast, so the tumor cannot be removed as a single lump. A cancer that has already attached itself to nearby structures, such as the skin or the chest wall, needs more extensive surgery.

Demographics

The American Cancer Society estimated that in 2010, 250,500 new cases of breast cancer will be diagnosed in the United States and 40,200 women will die as a result of the disease. Approximately one in eight women will develop breast cancer at some point in her life. The risk of developing breast cancer increases with age: women aged 30 to 40 have a one in 252 chance of developing breast cancer; women aged 40 to 50 have a one in 68 chance; women aged 50 to 60 have a one in 35 chance; and women aged 60 to 70 have a one in 27 chance—and these statistics do not even account for genetic and environmental factors. Also, about one percent of all breast cancers are diagnosed in men.

Description

Any amount of tissue, from 1–50% of the breast, may be removed and called a lumpectomy. Breast conservation surgery is a frequently used synonym for lumpectomy. Partial **mastectomy**, quadrantectomy, segmental excision, wide excision, and tylectomy are other, less commonly used names for this procedure.

The surgery is usually done while the patient is general anesthetic. Local anesthetic with additional **sedation** may be used for some patients. The tumor and surrounding margin of tissue is removed and sent to a pathologist for examination. The surgical site is then closed. Newer techniques may use **magnetic resonance imaging** guidance to more accurately identify the breast tissue to be removed. Additionally, laser instruments may be used to perform the actual lumpectomy.

If axillary lymph nodes were not removed before, a second incision may be made in the armpit. The fat pad that contains lymph nodes is removed from this area and is also sent to the pathologist for analysis. This portion of the procedure is called an axillary lymph node dissection; it is critical for determining the stage of the cancer. Typically, 10 to 15 nodes are removed, but the number may vary. A newer alternative to axillary lymph node dissection involves removal of only one lymph node. This technique, called sentinel node biopsy, samples just the first lymph node to which the breast tissue drains. If the sentinel node is negative, it is likely that no cancer has spread to more distant lymph nodes. If the sentinel node is positive, then the surgeon may have to proceed with an axillary lymph node dissection. Surgical drains may be left in place in either location to prevent fluid accumulation. The surgery may last from one to three hours.

Alternatives to lumpectomy

Certain medical or physical circumstances may also eliminate lumpectomy as a treatment option. Sometimes lumpectomy may be attempted, but the surgeon is unable to remove the tumor with a sufficient amount of surrounding normal tissue. This may be termed "persistently positive margins," or "lack of clear margins." Lumpectomy is suitable for women who have had previous lumpectomies and have a recurrence of breast cancer.

Because of the need for radiation therapy after lumpectomy, this surgery may be medically unacceptable. A breast cancer discovered during **pregnancy** is not amenable to lumpectomy because radiation therapy is part of the treatment. Radiation therapy cannot be administered to pregnant women because it may injure the fetus. If, however, delivery would be completed prior to the need for radiation, pregnant women may undergo lumpectomy. A woman who has already had therapeutic radiation to the chest area for other reasons cannot undergo additional exposure for breast cancer therapy.

The need for radiation therapy may also be a barrier due to nonmedical concerns. Some women simply fear this type of treatment and choose more extensive surgery so that radiation will not be required. The commitment of time, usually five days a week for six weeks, may not be acceptable for others. This may be due to financial, personal, or job-related constraints. Finally, in geographically isolated areas, a course of radiation therapy may require lengthy travel and perhaps unacceptable amounts of time away from family and other responsibilities.

A procedure in which the entire affected breast is removed, called a mastectomy, has been shown to be equally effective in treating breast cancer as lumpectomy, in terms of rates of recurrence and survival. Some women may choose to have a mastectomy because they strongly fear a recurrence of breast cancer, and may consider a lumpectomy too risky. Others may feel uncomfortable with a breast that has had a cancer, and would experience more peace of mind with the entire breast removed.

Preparation

Routine preoperative preparations, such as having nothing to eat or drink the night before surgery, are typically ordered for a lumpectomy. Information about expected outcomes and potential complications is also part of preparation for lumpectomy, as it is for any surgical procedure. It is especially important that women know about sensations they might experience after the operation, so the they are not misinterpreted as signs of further cancer or poor healing.

If the tumor is not able to be felt (not palpable), a pre-operative localization procedure is needed. A fine wire, or other device, is placed at the tumor site, using x ray or ultrasound for guidance. This is usually done in the radiology department of a hospital. The woman is most often sitting up and awake, although some sedation may be administered.

Aftercare

The patient may stay in the hospital one or two days, or return home the same day. This generally depends on the extent of the surgery, the medical condition of the patient, and physician and patient preferences. A woman usually goes home with a small bandage. The inner part of the surgical site usually has dissolvable stitches. The skin may be sutured or stitched; or the skin edges may be held together with steristrips, which are special thin, clear pieces of tape.

After a lumpectomy, patients are usually cautioned against lifting anything that weighs over five pounds for several days. Other activities may be restricted (especially if the axillary lymph nodes were removed) according to individual needs. **Pain** is often enough to limit inappropriate motion. Women are often instructed to wear a well-fitting support bra both day and night for approximately one week after surgery.

Pain is usually well controlled with prescribed medication. If it is not, the patient should contact the surgeon, as severe pain may be a sign of a complication, which needs medical attention. A return visit to the surgeon is normally scheduled approximately ten days to two weeks after the operation.

KEY TERMS

Axillary lymph node—Lymph nodes under the arm.

Lymph node—A small mass of tissue in the form of a knot or protuberance. They are the primary source of lymph fluid, which serves in the body's defense by removing toxic fluids and bacteria.

Quadrantectomy—Removal of a quadrant, or about a quarter of the breast.

Radiation therapy is usually started as soon as possible after lumpectomy. Other additional treatments, such as chemotherapy or hormone therapy, may also be prescribed. The timing of these is specific to each individual patient.

Risks

The risks are similar to those associated with any surgical procedure. Risks include bleeding, infection, breast asymmetry, anesthesia reaction, or unexpected scarring. A lumpectomy may also cause loss of sensation in the breast. The size and shape of the breast will be affected by the operation. Fluid can accumulate in the area where tissue was removed, requiring drainage.

If lymph node dissection is performed, there are several potential complications. A woman may experience decreased feeling in the back of her armpit. She may also experience other sensations, including **numbness**, **tingling**, or increased skin sensitivity. An inflammation of the arm vein, called phlebitis, can occur. There may be injury to the nerves controlling arm motion.

There is a risk of developing **lymphedema** (swelling of the arm) after axillary lymph node dissection. This swelling can range from mild to very severe. It can be treated with elastic **bandages** and specialized **physical therapy**, but it is a chronic condition, requiring continuing care. Lymphedema can arise at any time, even years after surgery.

Approximately 17% of patients develop lymphedema after axillary lymph node dissection, while only 3% of patients develop lymphedema after sentinel node biopsy. Five percent of women are unhappy with the cosmetic effects of the surgery.

Results

When lumpectomy is performed, it is anticipated that it will be the definitive surgical treatment for breast cancer. Other forms of therapy, especially radiation, are often prescribed as part of the total treatment plan. The expected outcome is no recurrence of the breast cancer.

The outcome of breast cancer is very dependent of the stage at the time of diagnosis. For stage 0 disease, the five-year survival is almost 100%. For stage I (early/lymph node negative), the five-year survival is alsom almost 100%. For stage II (early/lymph node positive), the five-year survival decreases to 81–92%. For stage III disease (locally advanced), the five-year survival is 54-67%. For women with stage IV (metastatic) breast cancer, the five-year survival is about 20%.

Resources

BOOKS

Abeloff, MD et al. *Clinical Oncology*. 3rd ed. Philadelphia: Elsevier, 2004.

Townsend, CM et al. *Sabiston Textbook of Surgery*.17th ed. Philadelphia: Saunders, 2004.

Miller, Kenneth D. *Choices in Breast Cancer Treatment: Medical Specialists and Cancer Survivors Tell You What You Need to Know*. Baltimore: Johns Hopkins, 2008.

PERIODICALS

Sabel M.S., et al. "Residual Disease After Re-Excision Lumpectomy for Close Margins." *Journal of Surgical Oncology*. 99 (2009): 2, 99–103.

Ziogas, D., E. Ignatiadou, and M. Fatouros. "Lumpectomy and Partial Breast Irradiation - Risks and Benefits for Early Breast Cancer." *Annals of Surgical Oncology*. 15 (2008): 8, 2352–2353.

OTHER

Breastcancer.org. "Lumpectomy." http://www.breastcancer.org/treatment/surgery/lumpectomy/ (accessed February 4, 2010).

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329-4251, (800) 227–2345, http://www.cancer.org.

National Lymphedema Network, 2211 Post St., Suite 404, San Francisco, CA, 94115–3427, (415) 921–1306, (800) 541–3259, http://www.wenet.net/~lymphnet.

Susan G. Komen for the Cure, 5005 LBJ Freeway, Suite 250, Dallas, TX, 75244, (877) GO–KOMEN, (877) 465–6636, http://ww5.komen.org.

Ellen S. Weber, MSN
Stephanie Dionne Sherk
Brenda W. Lerner

Lumpy breasts *see* **Fibrocystic condition of the breast**

Lumpy jaw *see* **Actinomycosis**

Lung abscess

Definition

Lung **abscess** is an acute or chronic infection of the lung, marked by a localized collection of pus within cavities, inflammation, and destruction of the pulmonary tissue (necrosis of the lung). Sometimes small abscesses form, which are called lung **gangrene** or necrotizing **pneumonia**. Acute abscesses last for only four to six weeks, while chronic abscesses last much longer.

Demographics

The infection of the lung called lung abscess can affect anyone in the world at any age. Males are more prone to it than females. The frequency of its occurrence in the United States is unknown.

Description

Lung abscess is the end result of a number of different disease processes ranging from fungal and bacterial infections to **cancer**. The following aerobic bacterial species can lead to lung abscess:

- *Pseudomonas aeruginosa*
- *Klebsiella pneumoniae*
- *Haemophilus influenzae*
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- Species within the genus *Nocardia*
- Species within the genus *Actinomyces*
- Fungal species.

The following non-bacterial and atypical bacterial pathogen species can also lead to lung abscess:

- Parasitic species within the genera *Paragonimus* (flatworms) and *Entamoeba* (amoeba).
- Species within the genus *Mycobacterium*.
- Fungi species within the genera *Aspergillus, Histoplasma, Blastomyces,* and *Coccidioides*.

Patients who are most vulnerable include those weakened by cancer and other chronic diseases; patients with a history of **substance abuse** including alcohol,

diabetes, **epilepsy** and seizures, and poor dental hygiene; patients who have recently had operations under anesthesia; and **stroke** patients. The elderly are more likely to have lung abscess than any other age group because of increased risk from **periodontal disease** (disorders in and around the teeth), dysphagia (difficulties with swallowing), and aspiration (entry of foreign material into trachea and lungs). In children, the most vulnerable patients are those with weakened immune systems, **malnutrition**, or blunt injuries to the chest.

Causes and symptoms

The immediate cause of most lung abscesses is infection caused by bacteria. About 65% of these infections are produced by anaerobes, which are bacteria that do not need air or oxygen to live. The remaining cases are caused by a mixture of anaerobic and aerobic (air breathing) bacteria and other pathogens. When the bacteria arrive in the lung, special cells called phagocytes engulf or eat them. The phagocytes release chemicals that contribute to inflammation and eventual necrosis, or **death**, of a part of the lung tissue. Several different ways are available for bacteria to get into the lungs. Some of them are: aspiration, bronchial obstruction, and spread of infection.

Aspiration

Aspiration refers to the accidental inhalation of material from the mouth or throat into the airway and lungs. It is responsible for about 50% of cases of lung abscess. The human mouth and gums contain large numbers of anaerobic bacteria; patients with periodontal disease or poor **oral hygiene** have higher concentrations of these organisms. Aspiration is most likely to occur in patients who are unconscious or semi-conscious due to anesthesia, seizures, alcohol and drug **abuse**, or stroke. Patients who have problems swallowing or coughing, or who have nasogastric tubes in place are also at risk of aspiration.

Bronchial obstruction

The bronchi are the two branches of the windpipe that lead into the lungs. If they are blocked by tissue swelling, cancerous tumors, or **foreign objects**, a lung abscess may form from infection trapped behind the blockage.

Spread of infection

About 20% of cases of pneumonia that cause the death of lung tissue (necrotizing pneumonia) will develop into lung abscess. Lung abscess can also be caused by the spread of other infections from the liver, abdominal cavity, or open chest **wounds**. Rarely, acquired immune deficiency syndrome (**AIDS**) patients can develop lung abscess from *Pneumocystis carinii* and other organisms that take advantage of a weakened immune system.

Lung abscess is usually slow to develop. It may take about two weeks after aspiration or bronchial obstruction for an abscess to produce noticeable symptoms. The patient may be acutely ill for two weeks to three months. In the beginning, the symptoms of lung abscess are difficult to distinguish from those of severe pneumonia. Adults will usually have moderate **fever** (101 to 102°F/38 to 39°C), chills, chest **pain**, and general weakness. Children may or may not have chest pain, but usually suffer weight loss and high fevers. As the illness progresses, about 75% of patients will **cough** up foul or musty-smelling sputum; some also cough up blood.

Lung abscess can lead to serious complications, including **emphysema**, spread of the abscess to other parts of the lung, hemorrhage, **adult respiratory distress syndrome**, rupture of the abscess, inflammation of the membrane surrounding the heart, or chronic inflammation of the lung.

Symptoms of lung abscess is dependent on whether the abscess is caused by anaerobic bacterial infection or other pathogens. If it is caused by anaerobic bacterial infection, patients often have symptoms that slowly appear over a matter of weeks to months. Common symptoms are cough with mucus, fever, night sweats, weight loss, and anorexia. If lung abscess is caused by other pathogens, the symptoms come on more quickly. However, abscesses from fungi and species within the bacterial genera *Nocardia* and *Mycobacteria* often produce more gradual symptoms that progressively worsen.

Diagnosis

The diagnosis is made on the basis of the patient's medical history (especially recent operations under **general anesthesia**) and general health as well as imaging studies. Smears and cultures taken from the patient's sputum for microbiologic diagnosis are not usually very helpful because they will be contaminated with bacteria from the mouth. The doctor will first use a bronchoscope (lighted tube inserted into the windpipe) to rule out the possibility of lung cancer. In some cases of serious infection, the doctor can use a fiberoptic bronchoscope with a protected specimen brush to take material directly from the patient's lungs, for identification of the organism. This technique is time- consuming and expensive, and requires the patient to be taken off **antibiotics** for 48 hours. It is usually used only to evaluate severely ill patients with weakened immune systems.

KEY TERMS

Abscess—An area of injured body tissue that fills with pus, as in lung abscess.

Anaerobe—A type of bacterium that does not require air or oxygen to live. Anaerobic bacteria are frequent causes of lung abscess.

Aspiration—Inhalation of fluid or foreign bodies into the airway or lungs. Aspiration often happens after vomiting.

Bronchoscope—A lighted, flexible tube inserted into the windpipe to view the bronchi or withdraw fluid samples for testing. Bronchoscopy with a protected brush can be used in the diagnosis of lung abscess in severely ill patients.

Bronchus—One of the two large tubes connecting the windpipe and the lungs.

Leukocytosis—An increased level of white cells in the blood. Leukocytosis is a common reaction to infections, including lung abscess.

Necrotizing pneumonia—Pneumonia that causes the death of lung tissue. It often precedes the development of lung abscess.

Sputum—The substance that is brought up from the lungs and airway when a person coughs or spits. It is usually a mixture of saliva and mucus, but may contain blood or pus in patients with lung abscess or other diseases of the lungs.

In most cases, the doctor will use the results of a **chest x ray** to help distinguish lung abscess from **empyema**, cancer, **tuberculosis**, or cysts. In patients with lung abscess, the x ray scan will show a thick-walled unified clear space or cavity surrounded by solid tissue. There is often a visible air-fluid level. The doctor may also order a computed tomography (CT) scan of the chest, in order to have a clearer picture of the exact location of the abscess.

Blood tests cannot be used to make a diagnosis of lung abscess, but they can be useful in ruling out other conditions. Patients with lung abscess usually have abnormally high white blood cell counts (**leukocytosis**) when their blood is tested, but this condition is not unique to lung abscess.

Treatment

Lung abscess is treated with a combination of antibiotic drugs, **oxygen therapy**, and surgery. The antibiotics that are usually given for lung abscess are penicillin G, penicillin V, and clindamycin. They are given intravenously until the patient shows signs of improvement, and then they are continued in oral form. The patient may need to take antibiotics for a month or longer, until the chest x ray indicates that the abscess is healing. Oxygen may be given to patients who are having trouble breathing.

Surgical treatment

Most patients with lung abscess will not need surgery. About 5% of patients—usually those who do not respond to antibiotics or are coughing up large amounts of blood (500 milliliters or more)—may have emergency surgery for removal of the diseased part of the lung or for insertion of a tube to drain the abscess. Antibiotic treatment is considered to have failed if fever and other symptoms continue after ten to 14 days of treatment; if chest x rays indicate that the abscess is not shrinking; or if the patient has pneumonia that is spreading to other parts of the lung.

Supportive care

Because lung abscess is a serious condition, patients need quiet and bed rest. Hospital care usually includes increasing the patient's fluid intake to loosen up the secretions in the lungs, and **physical therapy** to strengthen the patient's breathing muscles.

Follow-up

Patients with lung abscess need careful follow-up care after the acute infection subsides. Follow-up usually includes a series of chest x rays to make sure that the infection has cleared up. Treatment with antibiotics may continue for as long as four months, to prevent recurrence.

Prognosis

About 90 to 95% of lung abscess patients can be treated successfully with antibiotics alone. Patients who need surgical treatment have a mortality rate of 10 to 15%. Those that have higher risks of death from lung abscess are anyone with malnutrition, human **immunodeficiency** virus (HIV), or mental debilitation, and the elderly. Those with HIV and other immunocompromised conditions also have a high mortality rate.

Prevention

Some of the conditions that make people more vulnerable to lung abscess concern long-term lifestyle behaviors, such as substance abuse and lack of dental care. Others, however, are connected with chronic illness and hospitalization. Aspiration can be prevented with proper care of unconscious patients, which includes suctioning of throat secretions and positioning patients to promote drainage. Conscious patients can be given physical therapy to help them cough up material in their lungs and airways. Patients with weakened immune systems can be isolated from patients with pneumonia or fungal infections.

Resources

BOOKS

Fishman, Alfred P. et al. editors. *Fishman' Pulmonary Diseases and Disorders*. New York: McGraw-Hill Medical, 2008.

McPhee, Stephen J., and Maxine A. Papadakis, editors. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw-Hill, 2010.

Petty, Thomas L. and James S. Seebass, editors. *Pulmonary Disorders of the Elderly: Diagnosis, Prevention, and Treatment*. Philadelphia: American College of Physicians, 2007.

Watchie, Joanne. *Cardiovascular and Pulmonary Physical Therapy: A Clinical Manual*. St. Louis: Saunders/Elsevier, 2010.

OTHER

Lung Absess. eMedicine, WebMD. (August 19, 2009), emedicine.medscape.com/article/299425-overview. (accessed August 3, 2010).

Rebecca J. Frey, PhD

Lung biopsy

Definition

Lung biopsy is a procedure for obtaining a small sample of lung tissue for examination. The tissue is usually examined under a microscope, and may be sent to a microbiological laboratory for culture. Microscopic examination is performed by a pathologist.

Purpose

A lung biopsy is usually performed to determine the cause of abnormalities, such as nodules that appear on chest x rays. It can confirm a diagnosis of **cancer**, especially if malignant cells are detected in the patient's sputum or bronchial washing. In addition to evaluating lung tumors and their associated symptoms, lung biopsies may be used to diagnose lung infections, especially **tuberculosis** and **Pneumocystis pneumonia**, drug reactions, and chronic diseases of the lungs such as **sarcoidosis** and **pulmonary fibrosis**.

A lung biopsy can be used for treatment as well as diagnosis. **Bronchoscopy**, a type of lung biopsy performed with a long, flexible slender instrument called a bronchoscope, can be used to clear a patient's air passages of secretions and to remove airway blockages.

Demographics

Lung cancer is the leading cause of cancer-related deaths in the United States. About 219,440 patients were newly diagnosed with lung cancer in 2009 (about 116,090 in men and 103,350 in women). It claimed nearly 159,390 lives in 2009 (86,990 in men and 70,490 in women). Worldwide, lung cancer kills more people than cancers of the breast, prostate, colon, and pancreas combined. Cigarette **smoking** accounts for nearly 90% of cases of lung cancer in the United States.

Description

Overview

The right and left lungs are separated by the mediastinum, which contains the heart, trachea, lymph nodes, and esophagus. Lung biopsies sometimes involve **mediastinoscopy**.

Types of lung biopsies

Lung biopsies are performed using a variety of techniques, depending on where the abnormal tissue is located in the lung, the health and age of the patient, and the presence of lung disease. A bronchoscopy is ordered if a lesion identified on the x ray seems to be located on the wall (periphery) of the chest. If the suspicious area lies close to the chest wall, a needle biopsy can be done. If both methods fail to diagnose the problem, an open lung biopsy may be performed. When there is a question about whether the lung cancer or suspicious mass has spread to the lymph nodes in the mediastinum, a mediastinoscopy is performed.

BRONCHOSCOPIC BIOPSY. During the bronchoscopy, a thin, lighted tube (bronchoscope) is passed from the nose or mouth, down the windpipe (trachea) to the air passages (bronchi) leading to the lungs. Through the bronchoscope, the physician views the airways, and is able to clear mucus from blocked

airways, and collect cells or tissue samples for laboratory analysis.

NEEDLE BIOPSY. The patient is mildly sedated, but awake during the needle biopsy procedure. He or she sits in a chair with arms folded in front on a table. An x-ray technician uses a computerized axial tomography (CAT) scanner or a fluoroscope to identify the precise location of the suspicious areas. Markers are placed on the overlying skin to identify the biopsy site. The skin is thoroughly cleansed with an antiseptic solution, and a local anesthetic is injected to numb the area. The patient will feel a brief stinging sensation when the anesthetic is injected.

The physician makes a small incision, about half an inch (1.25 cm) in length. The patient is asked to take a deep breath and hold it while the physician inserts the biopsy needle through the incision into the lung tissue to be biopsied. The patient may feel pressure, and a brief sharp **pain** when the needle touches the lung tissue. Most patients do not experience severe pain. The patient should refrain from coughing during the procedure. The needle is withdrawn when enough tissue has been obtained. Pressure is applied at the biopsy site and a sterile bandage is placed over the incision. A **chest x ray** is performed immediately after the procedure to check for potential complications. The entire procedure takes 30–60 minutes.

OPEN BIOPSY. Open biopsies are performed in a hospital operating room under **general anesthesia**. Once the anesthesia has taken effect, the surgeon makes an incision over the lung area, a procedure called a thoracotomy. Some lung tissue is removed and the incision is closed with sutures. Chest tubes are placed with one end inside the lung and the other end protruding through the closed incision. Chest tubes are used to drain fluid and blood, and re-expand the lungs. They are usually removed the day after the procedure. The entire procedure normally takes about an hour. A chest x ray is performed immediately after the procedure to check for potential complications.

VIDEO-ASSISTED THORACOSCOPIC SURGERY. A minimally invasive technique, video-assisted thoracoscopic surgery (VATS) can be used to biopsy lung and mediastinal lesions. VATS may be performed on selected patients in place of open lung biopsy. While the patient is under general anesthesia, the surgeon makes several small incisions in the chest wall. A thorascope, a thin, hollow, lighted tube with a tiny video camera mounted on it, is inserted through one of the small incisions. The other incisions allow the surgeon to insert special instruments to retrieve tissue for biopsy.

MEDIASTINOSCOPY. This procedure is performed under general anesthesia. A 2–3 inch (5–8 cm) incision is made at the base of the neck. A thin, hollow, lighted tube, called a mediastinoscope, is inserted through the incision into the space between the right and the left lungs. The surgeon removes any lymph nodes or tissues that look abnormal. The mediastinoscope is then removed, and the incision is sutured and bandaged. A mediastinoscopy takes about an hour.

Preparation

Before scheduling a lung biopsy, the physician performs a careful evaluation of the patient's medical history and symptoms, and performs a **physical examination**. Chest x rays and sputum cytology (examination of cells obtained from a deep-cough mucus sample) are other diagnostic tests that may be performed. An electrocardiogram (EKG) and laboratory tests may be performed before the procedure to check for blood clotting problems, anemia, and blood type, should a **transfusion** become necessary.

During a preoperative appointment, usually scheduled within one to two weeks before the procedure, the patient receives information about what to expect during the procedure and the recovery period. During this appointment or just before the procedure, the patient usually meets with the physician (or physicians) performing the procedure (the pulmonologist, interventional radiologist, or thoracic surgeon).

A chest x ray or CAT scan of the chest is used to identify the area to be biopsied.

About an hour before the biopsy procedure, the patient receives a sedative. Medication may also be given to dry up airway secretions. General anesthesia is not used for this procedure.

For at least 12 hours before the open biopsy, VATS, or mediastinoscopy procedures, the patient should not eat or drink anything. Prior to these procedures, an intravenous line is placed in a vein in the patient's arm to deliver medications or fluids as necessary. A hollow tube, called an endotracheal tube, is passed through the patient's mouth into the airway leading to the lungs. Its purpose is to deliver the general anesthetic. The chest area is cleansed with an antiseptic solution. In the mediastinoscopy procedure, the neck is also cleansed to prepare for the incision.

Smoking cessation

Patients who will undergo surgical diagnostic and treatment procedures should be encouraged to stop

KEY TERMS

Bronchoscopy—A medical test that enables the physician to see the breathing passages and the lungs through a hollow, lighted tube.

Chest x ray—Brief exposure of the chest to radiation to produce an image of the chest and its internal structures.

Endotracheal tube—A hollow tube that is inserted into the windpipe to administer anesthesia.

Lung nodule—See pulmonary nodule.

Lymph nodes—Small, bean-shaped structures that serve as filters, scattered along the lymphatic vessels. Lymph nodes trap bacteria or cancer cells that are traveling through the lymphatic system.

Malignant—Cancerous.

Mediastinoscopy—A procedure that allows the physician to see the organs in the mediastinal space using a thin, lighted, hollow tube (a mediastinoscope).

Mediastinum—The area between the lungs, bounded by the spine, breastbone, and diaphragm.

Pleural cavity—The space between the lungs and the chest wall.

Pneumothorax—A condition in which air or gas enters the pleura (area around the lungs) and causes a collapse of the lung.

Pulmonary nodule—A lesion surrounded by normal lung tissue. Nodules may be caused by bacteria, fungi, or a tumor (benign or cancerous).

Sputum—A mucus-rich secretion that is coughed up from the passageways (bronchial tubes) and the lungs.

Sputum cytology—A lab test in which a microscope is used to check for cancer cells in the sputum.

Thoracentesis—Removal of fluid from the pleural cavity.

smoking and stop using tobacco products. The patient needs to make the commitment to be a nonsmoker after the procedure. Patients able to stop smoking several weeks before surgical procedures have fewer postoperative complications. Smoking cessation programs are available in many communities. The patient should ask a health care provider for more information if he or she needs help with smoking cessation.

Informed consent

Informed consent is an educational process between health care providers and patients. Before any procedure is performed, the patient is asked to sign a consent form. Prior to signing the form, the patient should understand the nature and purpose of the diagnostic procedure or treatment, its risks and benefits, and alternatives, including the option of not proceeding with the test or treatment. During the discussions, the health care providers are available to answer the patient's questions about the consent form or procedure.

Aftercare

Needle biopsy

Following a needle biopsy, the patient is allowed to rest comfortably. He or she may be required to lie flat for two hours following the procedure to prevent the risk of bleeding. The nurse checks the patient's status at two-hour intervals. If there are no complications after four hours, the patient can go home once he or she has received instructions about resuming normal activities. The patient should rest at home for a day or two before returning to regular activities, and should avoid strenuous activities for one week after the biopsy.

Open biopsy, VATS, or mediastinoscopy

After an open biopsy, VATS, or mediastinoscopy, the patient is taken to the recovery room for observation. The patient receives oxygen via a face mask or nasal cannula. If no complications develop, the patient is taken to a hospital room. Temperature, blood oxygen level, pulse, blood pressure, and respiration are monitored. Chest tubes remain in place after surgery to prevent the lungs from collapsing, and to remove blood and fluids. The tubes are usually removed the day after the procedure.

The patient may experience some grogginess for a few hours after the procedure. He or she may have a **sore throat** from the endotracheal tube. The patient may also have some pain or discomfort at the incision site, which can be relieved by pain medication. It is common for patients to require some pain medication for up to two weeks following the procedure.

After receiving instructions about resuming normal activities and caring for the incision, the patient usually goes home the day after surgery. The

patient should not drive while taking narcotic pain medication.

Patients may experience **fatigue** and muscle aches for a day or two because of the general anesthesia. The patient can gradually increase activities, as tolerated. Walking is recommended. Sutures are usually removed after one to two weeks.

The physician should be notified immediately if the patient experiences extreme pain, light-headedness, or difficulty breathing after the procedure. Sputum may be slightly bloody for a day or two after the procedure. Heavy or persistent bleeding requires evaluation by the physician.

Risks

Lung biopsies should not be performed on patients who have a bleeding disorder or abnormal blood clotting because of low platelet counts, or prolonged **prothrombin time** (PT) or **partial thromboplastin time** (PTT). Platelets are small blood cells that play a role in the blood clotting process. PT and PTT measure how well blood is clotting. If clotting times are prolonged, it may be unsafe to perform a biopsy because of the risk of bleeding. If the **platelet count** is lower than 50,000/cubic mm, the patient may be given a platelet transfusion as a temporary relief measure, and a biopsy can then be performed.

In addition, lung biopsies should not be performed if other tests indicate the patient has enlarged alveoli associated with **emphysema**, **pulmonary hypertension**, or enlargement of the right ventricle of the heart (**cor pulmonale**).

The normal risks of any surgical procedure include bleeding, infection, or **pneumonia**. The risk of these complications is higher in patients undergoing open biopsy procedures, as is the risk of **pneumothorax** (lung collapse). In rare cases, the lung collapses because of air that leaks in through the hole made by the biopsy needle. A chest x ray is done immediately after the biopsy to detect the development of this potential complication. If a pneumothorax occurs, a chest tube is inserted into the pleural cavity to re-expand the lung. Signs of pneumothorax include **shortness of breath**, rapid heart rate, or blueness of the skin (a late sign). If the patient has any of these symptoms after being discharged from the hospital, it is important to call the health care provider or emergency services immediately.

Bronchoscopic biopsy

Bronchoscopy is generally safe, and complications are rare. If they do occur, complications may include spasms of the bronchial tubes that can impair breathing, irregular heart rhythms, or infections such as pneumonia.

Needle biopsy

Needle biopsy is associated with fewer risks than open biopsy because it does not involve general anesthesia. Some **hemoptysis** (coughing up blood) occurs in 5% of needle biopsies. Prolonged bleeding or infection may also occur, although these are very rare complications.

Open biopsy

Possible complications of an open biopsy include infection or pneumothorax. If the patient has very severe breathing problems before the biopsy, breathing may be further impaired following the operation. Patients with normal lung function prior to the biopsy have a very small risk of respiratory problems resulting from or following the procedure.

Mediastinoscopy

Complications due to mediastinoscopy are rare. Possible complications include pneumothorax or bleeding caused by damage to the blood vessels near the heart. Mediastinitis, infection of the mediastinum, may develop. Injury to the esophagus or larynx may occur. If the nerves leading to the larynx are injured, the patient may be left with a permanently hoarse voice. All of these complications are rare.

Results

Normal results indicate no evidence of infection in the lungs, no detection of lumps or nodules, and cells that are free from cancerous abnormalities.

Abnormal results of needle biopsy, VATS, and open biopsy may be associated with diseases other than cancer. Nodules in the lungs may be due to active infections such as tuberculosis, or may be **scars** from a previous infection. In 33% of biopsies using a mediastinoscope, the biopsied lymph nodes prove to be cancerous. Abnormal results should always be considered in the context of the patient's medical history, physical examination, and other tests such as sputum examination, and chest x rays before a final diagnosis is made.

The risk of **death** from needle biopsy is rare. The risk of death from open biopsy is one in 3,000 cases. In mediastinoscopy, death occurs in fewer than one in 3,000 cases.

Alternatives

The type of alternative diagnostic procedures available depend upon each patient's diagnosis.

Some people may be eligible to participate in clinical trials, research programs conducted with patients to evaluate a new medical treatment, drug, or device. The purpose of clinical trials is to find new and improved methods of treating different diseases and special conditions. For more information on current clinical trials, visit the National Institutes of Health's ClinicalTrials.gov at http://www.clinicaltrials.gov or call (888) FIND-NLM [(888) 346-3656] or (301) 594-5983.

The National Cancer Institute (NCI) has conducted a clinical trial to evaluate a technology—low-dose helical computed tomography—for its effectiveness in screening for lung cancer. One study concluded that this test is more sensitive in detecting specific conditions related to lung cancer than other screening tests.

Resources

BOOKS

Ernst, Armin. *Introduction to Bronchoscopy*. Cambridge: Cambridge University Press, 2009.

Mason, R.J., et al. *Murray & Nadel's Textbook of Respiratory Medicine*. 4th ed. Philadelphia: Saunders, 2007.

Mehta, Atul C. *Therapeutic Bronchoscopy*. London: Informa Healthcare, 2008.

PERIODICALS

Antonelli, Massimo, and Franco Cavaliere. "Introduction to Bronchoscopy." *Intensive Care Medicine*. 35, (2009) 10: 1822–1823.

Chhajed. P.N., Eberhardt, R., Dienemann, H., Azzola, A., Brutsche, M.H., Tamm, M., and F.J. Herth. "Therapeutic Bronchoscopy Interventions Before Surgical Resection of Lung Cancer." *The Annals of Thoracic Surgery*. 81 (2006) 5: 1839–1843.

Qureshi, R.A., Stamenkovic, S.A., Carnochan, F.M., and W.S. Walker. "Video-Assisted Thoracoscopic Lung Biopsy in Patients with Interstitial Lung Disease." *The Annals of Thoracic Surgery*. 84, (2007) 6: 2136–2137.

Sano, Yoshifumi, et al. "Percutaneous Computed Tomography-Guided Lung Biopsy and Pleural Dissemination." *Cancer*. 115, (2009) 23: 5526.

Weiser, Todd, Hyman, S. Kevin, Yun, Jamie, Litle, Virginia, Chin, Cynthia, and Scott J. Swanson. "Electromagnetic Navigational Bronchoscopy: A Surgeon's Perspective." *The Annals of Thoracic Surgery*. 85, (2008) 2: S797.

OTHER

National Institutes of Health. "Bronchoscopy with transbronchial biopsy." *Medline Plus*.http://www.nlm.nih.gov/medlineplus/ency/article/003859.htm(accessed February 5, 2010).

National Institutes of Health. "Lung needle biopsy." *Medline Plus*.http://www.nlm.nih.gov/medlineplus/ency/article/003860.htm(accessed February 5, 2010).

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329–4251, (800) 227–2345, info@cancer.org, http://www.cancer.org.

American Lung Association, 1301 Pennsylvania Ave., NW, Suite 800, Washington, DC, 20004, (800) 548–8252, webmaster@lungusa.org, http://www.lungusa.org.

National Heart, Lung and Blood Institute, P.O. Box 30105, Bethesda, MD, 20824–0105, (301) 251–2222, nhlbiinfo@nhlbi.nih.gov, http://www.nhlbi.nih.gov.

Rosalyn Carson-DeWitt, MD
Brenda W. Lerner

Lung cancer, non-small cell

Definition

Non-small cell lung **cancer** (NSCLC) is a disease in which the cells of the lung tissues grow uncontrollably and form tumors.

Demographics

Worldwide, lung cancer is the most common cancer in males, and the fifth most common cancer in women. The worldwide mortality rate for patients with lung cancer is 86%. In the United States, lung cancer is the leading cause of **death** from cancer among both men and women. The World Health Organization estimates that the worldwide mortality from lung cancer will increase to three million by the year 2025. Of those three million deaths, almost two and a half million will result from non-small cell lung cancer.

The American Cancer Society (ACS) estimates that 219,440 Americans will develop lung cancer in 2009, 116,090 men and 103,350 women. Of these patients, 159,000 will die of the disease.

The incidence of lung cancer is beginning to fall in developed countries. This may be a result of antismoking campaigns. In developing countries, however, rates continue to rise, which may be a consequence of both industrialization and the increasing use of tobacco products.

Description

There are two kinds of lung cancers, primary and secondary. Primary lung cancer starts in the lung itself, and is divided into **small cell lung cancer** and non-small cell lung cancer. Small cell lung cancers are shaped like an oat and called oat-cell cancers; they are aggressive, spread rapidly, and represent 20% of lung cancers. Non-small cell lung cancer represents almost 80% of all primary lung cancers. Secondary lung cancer is cancer that starts somewhere else in the body (for example, the breast or colon) and spreads to the lungs.

The lungs

The lungs are located along with the heart in the chest cavity. The lungs are not simply hollow balloons but have a very organized structure consisting of hollow tubes, blood vessels and elastic tissue. The hollow tubes, called bronchi, are highly branched, becoming smaller and more numerous at each branching. They end in tiny, blind sacs made of elastic tissue called alveoli. These sacs are where the oxygen a person breathes in is taken up into the blood, and where carbon dioxide moves out of the blood to be breathed out.

Normal healthy lungs are continually secreting mucus that not only keeps the lungs moist, but also protects the lungs by trapping foreign particles like dust and dirt in breathed air. The inside of the lungs is covered with small hairlike structures called cilia. The cilia move in such a way that mucus is swept up out of the lungs and into the throat.

Lung cancer

Most lung cancers start in the cells that line the bronchi, and can take years to develop. As they grow larger they prevent the lungs from functioning normally. The tumor can reduce the capacity of the lungs, or block the movement of air through the bronchi in the lungs. As a result, less oxygen gets into the blood and patients feel short of breath. Tumors may also block the normal movement of mucus up into the throat. As a result, mucus builds up in the lungs and infection may develop behind the tumor. Once lung cancer has developed it frequently spreads to other parts of the body.

The speed at which non-small cell tumors grow depends on the type of cells that make up the tumor. The following three types account for the vast majority of non-small cell tumors:

- Adenocarcinomas are the most common and often cause no symptoms. Frequently they are not found until they are advanced.
- Squamous cell carcinomas usually produce symptoms because they are centrally located and block the lungs.
- Undifferentiated large cell and giant cell carcinomas tend to grow rapidly, and spread quickly to other parts of the body.

Causes and symptoms

Causes

Tobacco **smoking** accounts for 87% of all lung cancers. Giving up tobacco can prevent most lung cancers. Smoking **marijuana** cigarettes is considered another risk factor for cancer of the lung. Second hand smoke also contributes to the development of lung cancer among nonsmokers.

Certain hazardous materials that people may be exposed to in their jobs have been shown to cause lung cancer. These include asbestos, coal products, and radioactive substances. Air pollution may also be a contributing factor. Exposure to radon, a colorless, odorless gas that sometimes accumulates in the basement of homes, may cause lung cancer in a tiny minority of patients. In addition, patients whose lungs are scarred from other lung conditions may have an increased risk of developing lung cancer.

Symptoms

Lung cancers tend to spread very early, and only 15% are detected in their early stages. The chances of early detection, however, can be improved by seeking medical care at once if any of the following symptoms appear:

- a cough that does not go away
- chest pain
- shortness of breath
- recurrent lung infections, such as bronchitis or pneumonia
- bloody or brown-colored spit or phlegm (sputum)
- persistent hoarseness
- significant weight loss that is not due to dieting or vigorous exercise; fatigue and loss of appetite
- unexplained fever

Although these symptoms may be caused by diseases other than lung cancer, it is important to consult a doctor to rule out the possibility of lung cancer.

If lung cancer has spread to other organs, the patient may have other symptoms such as headaches, bone **fractures**, **pain**, bleeding, or **blood clots**.

Diagnosis

Physical examination and diagnostic tests

The doctor will first take a detailed medical history and assess risk factors. During a complete **physical examination** the doctor will examine the patient's throat to rule out other possible causes of hoarseness or coughing, and will listen to the patient's breathing and chest sounds.

If the doctor has reason to suspect lung cancer, particularly if the patient has a history of heavy smoking or occupational exposure to irritating substances, a **chest x ray** may be ordered to see if there are any masses in the lungs. Special imaging techniques, such as computed tomography (CT) scans or **magnetic resonance imaging** (MRI), may provide more precise information about the size, shape, and location of any tumors.

Sputum analysis

Sputum analysis is a noninvasive test that involves microscopic examination of cells that are coughed up from the lungs. This test can diagnose at least 30% of lung cancers, even if tumors are not visible on chest x rays. In addition, the test can detect cancer in its very early stages, before it spreads to other regions. The sputum test does not provide any information about the location of the tumor.

Lung biopsy

Lung biopsy is the most definitive diagnostic tool for cancer. It can be performed in three different ways. **Bronchoscopy** involves the insertion of a slender, lighted tube, called a bronchoscope, down the patient's throat and into the lungs. This test allows the doctor to see the tubes inside the lungs, and to obtain samples of lung tissue. If a needle biopsy is to be performed, the location of the tumor is first identified using a computerized tomography (CT) scan or magnetic resonance imaging (MRI). The doctor then inserts a needle through the chest wall and collects a sample of tissue from the tumor. In the third procedure, known as surgical biopsy, the chest wall is opened up and a part of the tumor, or all of it, is removed. A doctor who specializes in the study of diseased tissue (a pathologist) examines the tumor to identify the cancer's type and stage.

Treatment

Staging

Treatment for non-small cell lung cancer depends primarily on the stage of the cancer. Staging is a process that tells the doctor if the cancer has spread and the extent of its spread. The most commonly used treatments are surgery, **radiation therapy**, and **chemotherapy**.

Non-small cell lung cancer has six stages:

- Occult carcinoma. Cancer cells have been found in the sputum, but no tumor has yet been found.
- Stage 0. A small group of cancerous cells have been found in one location.
- Stage I. The cancer is only in the lung and has not spread anywhere else.
- Stage II. The cancer has spread to nearby lymph nodes.
- Stage III. The cancer has spread to more distant lymph nodes, and/or other parts of the chest like the diaphragm.
- Stage IV. The cancer has spread to other parts of the body.

Surgery

Surgery is the standard treatment for the earlier stages of non-small cell lung cancer. The surgeon will decide on the type of surgery, depending on how much of the lung is affected. There are three different types of surgical procedures:

- Wedge resection is the removal of a small part of the lung.
- Lobectomy is the removal of one lobe of the lung. (The right lung has three lobes and the left lung has two lobes.)
- Pneumonectomy is the removal of an entire lung.

Lung surgery is a major procedure and patients can expect to experience pain, weakness in the chest, and **shortness of breath**. Air and fluid collect in the chest after surgery. As a result, patients will need help to turn over, **cough**, and breath deeply. Patients should be encouraged to perform these activities because they help get rid of the air and fluid and speed up recovery. It can take patients several months before they regain their energy and strength.

Radiotherapy

Patients whose cancer has progressed too far for surgery (Stages III and IV) may receive radiotherapy. Radiotherapy involves the use of high-energy rays to

KEY TERMS

Bronchi—The tubes that carry air into the lungs.

Lymph—Clear fluid containing white blood cells that is collected from the tissues of the body and flows in vessels called the lymphatic system.

Lymph node—Small oval-shaped filters in the lymphatic system that trap bacteria and other unwanted particles to ensure their removal from the body.

Palliative—Referring to any type of treatment that is given to relieve the symptoms of a disease rather than to cure it.

Respiratory distress—A condition in which patients with lung disease are not able to get enough oxygen.

kill cancer cells. It is used either by itself or in combination with surgery or chemotherapy. The amount of radiation used depends on the size and the location of the tumor.

Radiation therapy may produce such side effects as tiredness, skin **rashes**, upset stomach, and **diarrhea**. Dry or sore throats, difficulty in swallowing, and loss of hair in the treated area are all minor side effects of radiation. These may disappear either during the course of the treatment or after the treatment is over.

Chemotherapy

Chemotherapy is also given to patients whose cancer has progressed too far for surgery. Chemotherapy is medication that is usually given intravenously to kill cancer cells. These drugs enter the bloodstream and travel to all parts of the body, killing cancer cells that have spread to different organs. Chemotherapy is used as the primary treatment for cancers that have spread beyond the lung and cannot be removed by surgery. It can also be used in addition to surgery or radiation therapy.

Chemotherapy for NSCLC has made significant advances since the early 1980s in improving the patient's quality of life as well as length of survival. Newer cytotoxic (cell-killing) agents developed in the 1990s, such as the taxanes, are typically combined with either cisplatin or carboplatin as first-line therapy for non-small cell lung cancer.

Newer drugs for lung cancer developed since 2000 include gefinitib (Iressa) and pemetrexed (Alimta). The FDA approved gefinitib in May 2003 as a treatment for patients with NSCLC who have not responded to platinum-based or taxane chemotherapy. It is taken by mouth and works by inhibiting an enzyme involved in the growth of tumor cells. Pemetrexed, which is given by injection, was approved by the FDA in February 2004 for the treatment of **mesothelioma**, a type of lung cancer caused by exposure to asbestos fibers. However, the drug appears to be effective in treating other types of lung cancer as well.

Chemotherapy is also used as palliative treatment for non-small cell lung cancer. Palliative refers to any type of therapy that is given to relieve the symptoms of a disease but not to cure it.

Clinical trials

Patients diagnosed with non-small cell lung cancer should discuss participating in clinical trials with their doctor. There are many clinical trials currently underway that are investigating all different stages of the disease. These trials are studying various new treatment options including:

- Chemotherapy with new drugs, and combinations of drugs
- Courses of chemotherapy prior to surgery
- Radiotherapy after surgery
- Chemotherapy and radiotherapy in combination

Information on open clinical trials is available on the Internet from the National Cancer Institute at http://cancertrials.nci.nih.gov.

Alternative and complementary therapies

Because non-small cell lung cancer has a poor prognosis with conventional medical treatment, many patients are willing to try complementary and alternative therapies. These therapies are used to try to reduce **stress**, ease side effects and symptoms, or control disease. Two treatments sometimes used are shark cartilage and mistletoe. Although shark cartilage is thought to interfere with the tumor's blood supply, clinical trials have so far been inconclusive. Mistletoe is a poisonous plant that has been shown to kill cancer cells in the laboratory. Again, however, clinical trials with cancer patients have been inconclusive.

Patients who decide to try complementary and alternative therapies should tell their doctors. Some of these therapies may interfere with conventional treatment.

Coping with cancer treatment

The side effects associated with treatment of non-small cell lung cancer can be severe. Patients should ask their doctors about medications to treat **nausea and vomiting**, and other side effects. It is particularly important to eat a nutritious diet and to drink plenty of fluids. In addition, most patients report feeling very tired and should get plenty of rest.

Patients should consider joining local support groups with people who are coping with the same experiences. Many people with cancer find they can share thoughts and feelings with group members that they do not feel comfortable sharing with friends or family. Support groups are also a good source of information about coping with cancer.

Prognosis

The prognosis for non-small cell lung cancer is better if the disease is found early, and removed surgically. For patients whose disease is caught in Stage I, the survival rate five years after surgery ranges from 60% to 80%. Up to 55% of Stage II patients are alive after five years, but only about 30% of Stage III patients make it to five years. Unfortunately, 85% of patients already have at least Stage III cancer by the time they are diagnosed. Many of these patients have disease that is too advanced for surgery. Despite treatment with radiotherapy and chemotherapy, the five-year survival for patients with inoperable disease is extremely low.

Prevention

The best way to prevent lung cancer is not to start smoking or to quit smoking. Secondhand smoke from other people's tobacco should also be avoided. Appropriate precautions should be taken when working with cancer-causing substances (**carcinogens**). Testing houses for the presence of radon gas, and removing asbestos from buildings have also been suggested as preventive strategies.

Resources

BOOKS

Abeloff, MD et al. *Clinical Oncology*. 3rd ed. Philadelphia: Elsevier, 2004.

Goldman L, Ausiello D., eds.*Cecil Textbook of Internal Medicine*. 23rd ed. Philadelphia: Saunders, 2008.

Mason, RJ et al. *Murray & Nadel's Textbook of Respiratory Medicine*. 4th ed. Philadelphia: Saunders, 2007.

PERIODICALS

Cohen, M. H., G. A. Williams, R. Sridhara, et al. "United States Food and Drug Administration Drug Approval Summary: Gefitinib (ZD1839; Iressa) Tablets." *Clinical Cancer Research* 10 (February 15, 2004): 1212–1218.

Fossella, F. V. "Pemetrexed for Treatment of Advanced Non-Small Cell Lung Cancer." *Seminars in Oncology* 31 (February 2004): 100–105.

Frampton, J. E., and S. E. Easthope. "Gefitinib: A Review of Its Use in the Management of Advanced Non-Small-Cell Lung Cancer." *Drugs* 64 (2004): 2475–2492.

Ramalingam, S., and C. P. Belani. "State-of-the-Art Chemotherapy for Advanced Non-Small Cell Lung Cancer." *Seminars in Oncology* 31 (February 2004): 68–74.

Rigas, J. R. "Taxane-Platinum Combinations in Advanced Non-Small Cell Lung Cancer: A Review." *Oncologist* 9, Supplement 2 (2004): 16–23.

OTHER

American Cancer Society (ACS). *Cancer Facts & Figures 2004*.http://www.cancer.org/downloads/STT/CAFF_inalPWSecured.pdf.

FDA News, February 5, 2004. "FDA Approves First Drug for Rare Type of Cancer." http://www.fda.gov/bbs/topics/NEWS/2004/NEW01018.html.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329–4251, (800) 227-2345, info@cancer.org, http://www.cancer.org.

American Lung Association, 1301 Pennsylvania Ave., NW, Suite 800, Washington, DC, 20004, (800) 548-8252, webmaster@lungusa.org, http://www.lungusa.org.

National Heart, Lung and Blood Institute, P.O. Box 30105, Bethesda, MD, 20824–0105, (301) 251-2222, nhlbiinfo@nhlbi.nih.gov, http://www.nhlbi.nih.gov.

Lata Cherath, PhD
Alison McTavish, M.Sc.
Rebecca J. Frey, PhD

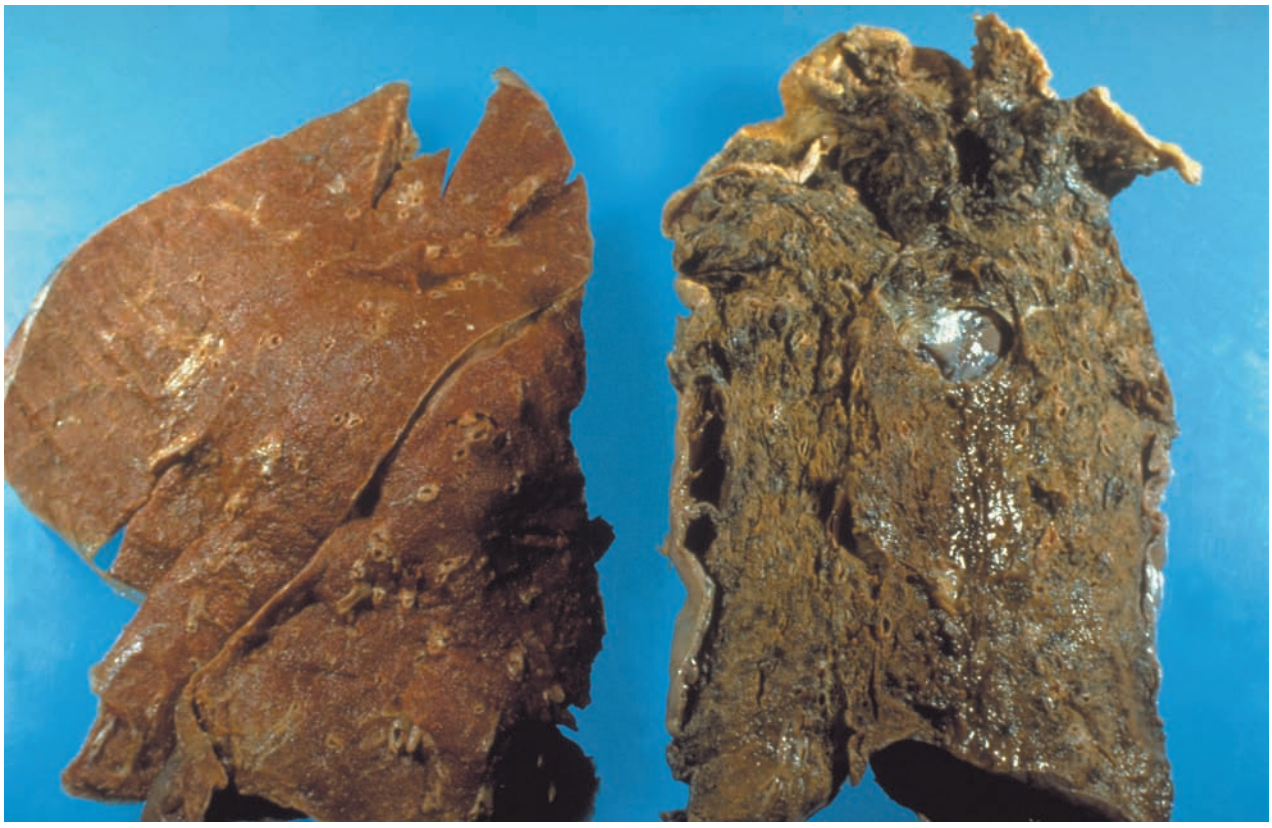
Lung cancer, small cell

Definition

Small cell lung **cancer** is a disease in which the cells of the lung tissues grow uncontrollably and form tumors.

Demographics

Lung cancer is a growing global epidemic. Worldwide, lung cancer is the second most common cancer among both men and women and is the leading cause of cancer **death** in both sexes. The worldwide mortality rate for patients with lung cancer is 86%. Of the 160,000 deaths from lung cancer that occur annually



A normal lung (left) and the lung of a cigarette smoker (right). *(A. Glauberman/Photo Researchers, Inc.)*

in the United States, about 40,000 are caused by small cell lung cancer. Although there are differences in mortality rates between ethnic groups, this is mainly due to differences in **smoking** habits.

Description

Lung cancer is divided into two main types: small cell and non-small cell. Small cell lung cancer is the least common of the two, accounting for only about 10% to 15% of all lung cancers. In the past, the disease was called oat cell cancer because, when viewed under a microscope, the cancer cells resemble oats. This type of lung cancer grows quickly and is more likely to spread to other organs in the body.

The lungs are located along with the heart in the chest cavity. The lungs are not simply hollow balloons, but have a very organized structure consisting of hollow tubes, blood vessels, and elastic tissue. The hollow tubes, called bronchi, are multi-branched, becoming smaller and more numerous at each branching. They end in tiny, blind sacs made of elastic tissue called alveoli. These sacs are where the oxygen a person breathes in is taken up into the blood, and where carbon dioxide moves out of the blood to be breathed out.

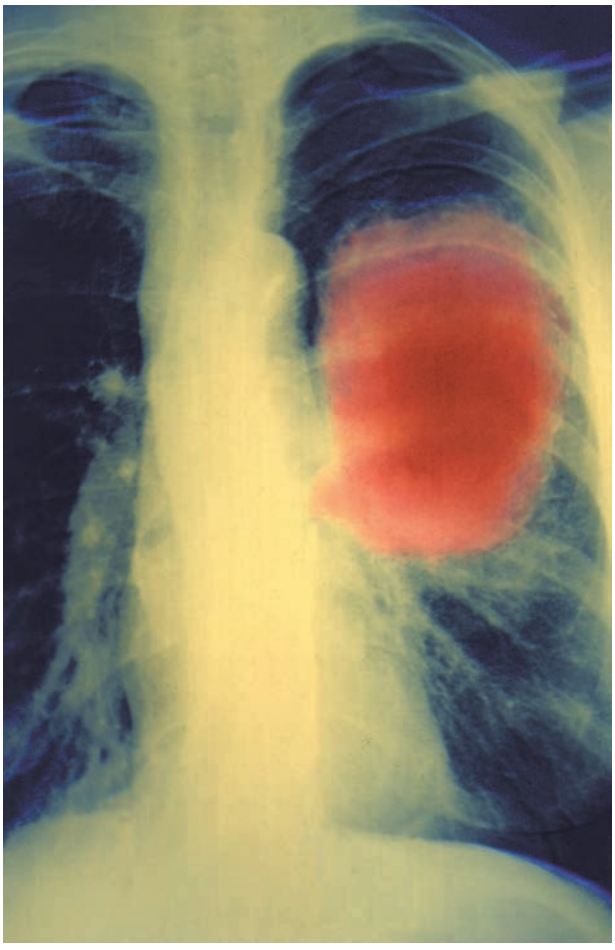
Normal, healthy lungs are continually secreting mucus that not only keeps the lungs moist, but also protects the lungs by trapping foreign particles like dust and dirt in breathed air. The inside of the lungs is covered with small, hair-like structures called cilia. The cilia move in such a way that mucus is swept up out of the lungs and into the throat.

Small cell lung tumors usually start to develop in the central bronchi. They grow quickly and prevent the lungs from functioning at their full capacity. Tumors may block the movement of air through the bronchi in the lungs. As a result, less oxygen gets into the blood and patients feel short of breath. Tumors may also block the normal movement of mucus into the throat. As a result, mucus builds up in the lungs and infection may develop behind the tumor.

Causes and symptoms

Causes

Tobacco smoking accounts for nearly 90% of all lung cancers. The risk of developing lung cancer is increased for smokers who start at a young age, and for those who have smoked for a long time. The risk



An x-ray image showing an oval-shaped carcinoma in the left lung (right of image). *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

also increases as more cigarettes are smoked, and when cigarettes with higher tar content are smoked. Smoking **marijuana** cigarettes is also a risk factor for lung cancer. These cigarettes have a higher tar content than tobacco cigarettes.

Certain hazardous materials that people may be exposed to in their jobs have been shown to cause lung cancer. These include asbestos, coal products, and radioactive substances. Air pollution may also be a contributing factor. Exposure to radon, a colorless, odorless gas that sometimes accumulates in the basement of homes, may cause lung cancer in some patients. In addition, patients whose lungs are scarred from other lung conditions may have an increased risk of developing lung cancer.

Although the exact cause of lung cancer is not known, people with a family history of lung cancer appear to have a slightly higher risk of contracting the disease.

Symptoms

Small cell lung cancer is an aggressive disease that spreads quickly. Symptoms depend on the tumor's location within the lung, and on whether the cancer has spread to other parts of the body. More than 80% of small cell lung cancer patients have symptoms for only three months or less, and few cases are detected early. The following symptoms are the most commonly reported by small cell lung cancer patients at the time of their diagnosis:

- a persistent cough
- chest pain
- shortness of breath and wheezing
- persistent hoarseness
- fatigue and loss of appetite

Although some patients may experience bloody spit or phlegm, this symptom is more commonly seen in patients with other types of lung cancer.

Small cell tumors often press against a large blood vessel near the lungs called the superior vena cava (SVC), causing a condition known as SCV syndrome. This condition may cause patients to retain water, **cough**, and have **shortness of breath**. Because small cell lung cancer often spreads quickly to the bones and central nervous system, patients may also have bone **pain**, headaches, and seizures.

Small cell lung cancer can cause several hormonal disorders. About 40% of patients begin to secrete an anti-diuretic hormone at the wrong time. This hormone causes the body to retain water, which may result in the patient experiencing confusion, seizures, or **coma**. Less common are the development of **Cushing's syndrome** and the Eaton-Lambert syndrome. Symptoms of Cushing's syndrome include **obesity**, severe **fatigue**, high blood pressure, backache, high blood sugar, easy bruising, and bluish-red stretch marks on the skin. Eaton-Lambert syndrome is a neuromuscular disorder that causes muscle weakness, fatigue, and a **tingling** sensation on the skin. All of these hormonal disorders usually diminish after the lung tumor is successfully treated.

Diagnosis

If lung cancer is suspected, the doctor will take a detailed medical history that checks both symptoms and risk factors. During a complete **physical examination**, the doctor will examine the patient's throat to rule out other possible causes of hoarseness or coughing, and listen to the patient's breathing and the sounds made when the patient's chest and upper back are tapped. A **chest x ray** may be ordered to

check for masses in the lungs. Special imaging techniques, such as computed tomography (CT) scans or **magnetic resonance imaging** (MRI), may provide more precise information about the size, shape, and location of any tumors.

Sputum analysis involves microscopic examination of the cells that are either coughed up from the lungs, or are collected through a special instrument called a bronchoscope. The sputum test does not, however, provide any information about the location of the tumor and must be followed by other tests.

Lung biopsy is the most definitive diagnostic tool for cancer. It can be performed in several different ways. The doctor can perform a **bronchoscopy**, which involves the insertion of a slender, lighted tube, called a bronchoscope, down the patient's throat and into the lungs. In addition to viewing the passageways of the lungs, the doctor can use the bronchoscope to obtain samples of the lung tissue. In another procedure known as a needle biopsy, the location of the tumor is first identified using a CT scan or MRI. The doctor then inserts a needle through the chest wall and collects a sample of tissue from the tumor. In the third procedure, known as surgical biopsy, the chest wall is opened up and a part of the tumor, or all of it, is removed for examination.

Treatment

Staging

Staging procedures are important in lung cancer because they tell doctors whether patients have disease only in their lungs, or whether the cancer has spread to other parts of the body. To establish the cancer stage, doctors have to perform various tests. These may include **bone marrow aspiration and biopsy**, CT scans of the chest and abdomen, MRI scans of the brain, and radionuclide bone scans. All of these tests determine the extent to which the cancer has spread. Once the stage is determined, doctors can decide on a course of treatment, and can have a better idea of the patient's prognosis.

Unlike other types of lung cancer, the staging of small cell lung cancer is relatively simple. This is because approximately 70% of patients already have metastatic disease when they are diagnosed, and small differences in the amount of tumor found in the lungs do not change the prognosis. Small cell lung cancer is usually divided into three stages:

- Limited stage: The cancer is found only in one lung and in lymph nodes close to the lung.
- Extensive stage: The cancer has spread beyond the lungs to other parts of the body.
- Recurrent stage: The cancer has returned following treatment.

Without treatment, small cell lung cancer has the most aggressive clinical course of any type of pulmonary tumor, with median survival from diagnosis of only 2–4 months. Compared with other cell types of lung cancer, small cell lung cancer has a greater tendency to be widely disseminated by the time of diagnosis, but is much more responsive to **chemotherapy** and irradiation.

Treatment of small cell lung cancer depends on whether the patient has limited, extensive, or recurrent disease. Treatment usually involves radiotherapy and chemotherapy. Surgery is rarely used for this type of lung cancer because the tumor is usually too advanced.

Patients with limited-stage disease are usually treated with chemotherapy. Combinations of two or more drugs have a better effect than treatment with a single drug. Up to 90% of patients with this stage of disease will respond to chemotherapy. The chemotherapy most commonly prescribed is a combination of the drugs etoposide (Vepesid) and cisplatin (Platinol). Combining chemotherapy with chest radiotherapy and/or occasionally surgery has also prolonged survival for limited-stage patients.

In addition to chest radiotherapy, some patients are also treated with **radiation therapy** to the brain, even if no cancer is found there. This treatment, called prophylactic cranial irradiation (PCI), is given to prevent tumors from forming in the brain. The combination of etoposide and cisplatin chemotherapy with chest radiation therapy and PCI has increased the two-year survival of limited-stage small cell lung cancer patients to almost 50%.

Combinations of different chemotherapy agents are also used for treating extensive-stage small cell lung cancer. However, compared with limited-stage patients, the percentage of extensive-stage patients who respond to therapy is lower. Commonly used drug combinations include cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), and vincristine (Oncovin), or etoposide and cisplatin. The addition of radiation therapy to chemotherapy does not improve survival in these patients. However, radiation therapy is used for the palliative (pain relief) treatment of symptoms of metastatic lung cancer, particularly brain and bone tumors.

Patients who have recurrent small cell lung cancer often become resistant to chemotherapy. These patients

are treated with palliative radiotherapy. Their doctor may also recommend that they take part in a clinical trial of a new therapy. Patients whose relapse occurs more than six months after their initial treatment, however, may still respond to traditional chemotherapy.

Coping with cancer treatment

The side effects associated with treatment of small cell lung cancer can be severe. Patients should ask their doctor about medications to treat **nausea and vomiting** and other side effects. It is particularly important to eat a nutritious diet and to drink plenty of fluids. In addition, most patients report feeling very tired and should get plenty of rest.

Clinical trials

Most of the improvements in the survival of patients with small cell lung cancer are the result of clinical trials. Ongoing trials are investigating new chemotherapy and radiotherapy regimens. In addition, entirely new types of therapy, such as **gene therapy** and biological therapy, are now being tested. Patients with a lung cancer diagnosis should ask their doctor about participating in a clinical trial.

Information on open clinical trials is available on the Internet from the National Cancer Institute at http://cancertrials.nci.nih.gov.

Alternative treatment

Many cancer patients have tried using shark cartilage to treat their disease. Shark cartilage is thought to interfere with the tumor's blood supply. A clinical trial using this treatment in lung cancer patients is ongoing. Information on this and other alternative treatments is available on the Internet from the National Center for Complementary and Alternative Medicine.

Patients who decide to try complementary and alternative therapies should tell their doctor. Some of these therapies may interfere with conventional treatment.

Prognosis

Small cell lung cancer is a very aggressive disease. Without treatment, limited-stage patients will survive for three to six months, while extensive-stage patients will survive six to 12 weeks. However, small cell lung cancer is much more responsive to chemotherapy and radiation therapy than other types of lung cancer. Among patients treated with chemotherapy, 70–90% have a major response to treatment.

KEY TERMS

Bronchi—Hollow tubes that carry air into the lungs.

PCI—A type of radiotherapy that is used to prevent tumors from growing in the brain.

Radionuclide bone scan—A test that tells if cancer has spread to the bones.

Superior vena cava (SVC) syndrome—A condition seen in lung cancer patients where the tumor presses against a large blood vessel and causes various symptoms.

Survival in patients responding to therapy is four to five times longer than in patients without treatment. In addition, two years after the start of therapy, about 10% of patients remain free of disease. In general, women tend to have a better prognosis than men. Patients whose disease has spread to the central nervous system or liver have a much worse prognosis. Although the overall survival at five years is 5% to 10%, survival is higher in patients with limited stage disease. About 70% of patients who are disease free after two years do not relapse. After five to 10 disease-free years, relapses are rare.

Prevention

The best way to prevent lung cancer is either not start smoking, or quit smoking. Secondhand smoke from other people's tobacco should also be avoided. Appropriate precautions should be taken when working with substances that can cause cancer (**carcinogens**). Testing houses for the presence of radon gas, and removing asbestos from buildings have also been suggested as preventive strategies.

Resources

BOOKS

Abeloff, MD et al. *Clinical Oncology*. 3rd ed. Philadelphia: Elsevier, 2004.

Goldman L, Ausiello D., eds.*Cecil Textbook of Internal Medicine*. 23rd ed. Philadelphia: Saunders, 2008.

Mason, RJ et al. *Murray & Nadel's Textbook of Respiratory Medicine*. 4th ed. Philadelphia: Saunders, 2007.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329-4251, (800) 227-2345, info@cancer.org, http://www.cancer.org.

American Lung Association, 1301 Pennsylvania Ave., NW, Suite 800, Washington, DC, 20004, (800) 548-8252, webmaster@lungusa.org, http://www.lungusa.org.

National Heart, Lung and Blood Institute, P.O. Box 30105, Bethesda, MD, 20824-0105, (301) 251-2222, nhlbiinfo@nhlbi.nih.gov, http://www.nhlbi.nih.gov.

Alliance for Lung Cancer Advocacy, Support, and Education, P.O. Box 849, Vancouver, WA, 98666, (800) 298-2436., nhlbiinfo@nhlbi.nih.gov, http://www.alcase.org.

Lata Cherath, PhD
Alison McTavish, MSc

Lung diseases due to gas or chemical exposure

Definition

Lung diseases due to gas or chemical exposure are conditions that can be acquired from indoor and outdoor air pollution and from ingesting tobacco smoke.

Description

The lungs are susceptible to many airborne poisons and irritants. Mucus present in the airways blocks foreign particles of a certain size; however it is unable to filter all airborne particulates. There are hundreds of substances that can pollute air and harm lungs. Harmful gases and chemicals are just one type of airborne pollutant that can adversely affect the lungs. They include:

- Vehicle exhaust
- Localized pollutants such as arsenic, asbestos, lead, and mercury
- Outdoor pollutants caused by industry and intensified by weather conditions
- Household heating devices, such as wood–burning stoves
- Household chemical products
- Tobacco smoke.

Lungs respond to irritants in four ways, each of which can occur separately or, more often, trigger other responses.

- Asthma occurs when irritation causes the smooth muscles surrounding the airways to constrict.
- Increased mucus comes from irritated mucus glands lining the airway. Excess mucus clogs the airway and prevents air from circulating.
- Constriction of the lungs results from scarring when supporting tissues are damaged.
- Cancer is caused by certain irritants, such as asbestos and tobacco smoke.

The major categories into which airborne irritants fall are allergic, organic, inorganic, and poisonous, with many agents occupying more than one category.

- Allergic irritants bother only people who are sensitive to them. Cat hair, insect parts, and pollen are common allergens. Chemicals called sulfites, which are widely used as food preservatives, also cause asthma.
- There are many organic dusts that irritate the lungs. Most of them occur on the job and cause occupational lung disease. Grain dust causes silo filler's disease. Cotton and other textile dusts cause byssinosis. Mold spores in hay cause farmer's lung.
- Inorganic dusts and aerosolized chemicals also are found mostly on the job. Classic among them are asbestos and coal dust. Many metals (cadmium, arsenic, chromium, and phosphorus), various other fine particles (cement, mica, rock), acid fumes, ammonia, ozone, and automobile and industrial emissions are part of a very long list.
- While tobacco smoke is a culprit in many smokers, a 2003 report found that those who work in the tobacco industry experience higher incidence of lung disease from tobacco dust in their work environment.
- Most intentional poisons (cyanide, nerve gas) that enter through the lungs pass through and damage other parts of the body. Mustard gas, used during World War I and banned since that time, directly and immediately destroys lungs.
- Tobacco use scars the lungs and causes emphysema and lung cancer.

Causes and symptoms

Lung disease generates three major symptoms: coughing, **wheezing**, and **shortness of breath**. It also predisposes the lungs to infections such as **bronchitis** and **pneumonia**. **Cancer** is a late effect, requiring prolonged exposure to an irritant. In the case of tobacco, an average of a pack of cigarettes a day for forty years, or two packs a day for twenty years, greatly increases the risk of lung cancer.

Diagnosis

A history of exposure combined with a **chest x ray** and lung function studies completes the diagnostic evaluation in most cases. Lung function measures the amount of air breathed in and out, the speed it moves, and the effectiveness of oxygen exchange within the

KEY TERMS

Allergen—A substance that causes an allergic reaction in those who are sensitive to it.

Asthma—Temporary airway narrowing that causes wheezing and shortness of breath due to allergies.

Bronchitis—Infection in the bronchi (breathing tubes).

Pneumonia—Infection or inflammation in the lung itself.

blood. If the cause still is unclear, a **lung biopsy** aids diagnosis.

Treatment

Eliminating the offending irritant and early **antibiotics** for infection are primary. There are many techniques available to remove excess mucus from the lungs. Respiratory therapists are trained in these methods. Finally, there are several machines available to enrich the oxygen content of breathed air.

A surgical treatment called lung reduction volume surgery is emerging as a treatment for certain people over age 65 with severe **emphysema**. It promises substantial return of lung function for selected patients by cutting away diseased parts of the lungs so that healthy tissue functions better. In the fall of 2003, Medicare announced that it would begin paying for the surgery.

Prognosis

Many of these diseases are progressive, because the irritants stay in the lungs forever. Others remain stable after the offensive agents are removed from the environment. Lungs do not heal from destructive damage, but they can clean out infection and excess mucus, and function better.

Prevention

Industrial air filters, adequate ventilation, and respirators in polluted work sites now are mandatory. Tobacco smoke is the world's leading cause of lung disease and many other afflictions. **Smoking** cessation programs are widely available.

Resources

BOOKS

Mays, Thomas Jefferson. *Pulmonary Consumption, Pneumonia, and Allied Diseases of the Lungs*. New York, NY: General Books LLC, 2009.

Miller, Max. *The Quit Smoking Companion: The Daily Guide to Freedom from Cigarettes*. Charleston, SC: BookSurge Publishing, 2009.

Petty, Thomas and James S. Seebass, editors. *Pulmonary Disorders of the Elderly: Diagnosis, Prevention, and Treatment*. Philadelphia, PA: American College of Physicians, 2007.

PERIODICALS

"Medicare Will Cover Lung Volume Reduction Surgery for Certain Patients." *Health & Medicine Week* October 20, 2003: 245.

Mustajbegovic, Jadranka, et al. "Respiratory Findings in Tobacco Workers." *Chest* May 2003: 1740–49.

ORGANIZATIONS

American Lung Association, 1301 Pennsylvania Ave. NW , Washington, DC, 20004, (202) 785-3355 , (202) 452-1805, http://www.lungusa.org.

American Thoracic Society, 61 Broadway, 6th floor, New York, NY, 10000, (212) 315-8600, http://www.thoracic.org.

Centers for Disease Control and Prevention, 1600 Clifton Rd., NE, Atlanta, GA, 30333, (404) 639-3311, (800) 311-3435, http://www.cdc.gov.org.

National Heart, Lung, and Blood Institute, PO Box 30105, Bethesda, MD, 20824-0105, (301) 592-8573. TTY: (240) 629-3255, http://www.nhlbi.nih.gov.

Smoking Cessation, 466 14th St., Suite 10, San Francisco, CA, 94103, http://www.smoking–cessation.org.

World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland, +41 (22) 791 4140, http://www.who.int/gtb.

Teresa G. Odle
J. Ricker Polsdorfer, MD
Laura Jean Cataldo, RN, Ed.D.

Lung fluke infections *see* **Fluke infections**

Lung function tests *see* **Pulmonary function test**

Lung perfusion and ventilation scan

Definition

A lung perfusion scan is a nuclear medicine test that produces a picture of blood flow to the lungs. A lung ventilation scan measures the ability of the lungs to take in air and uses radiopharmaceuticals to produce a picture of how air is distributed in the lungs.

Purpose

Lung perfusion scans and lung ventilation scans are usually performed in the same session. They are done to detect pulmonary embolisms, determine how much blood is flowing to lungs, determine which areas of the lungs are capable of ventilation, and assess how well the lungs are functioning after surgery. These tests are called by different names, including perfusion lung scan, aerosol lung scan, radionucleotide ventilation lung scan, ventilation lung scan, xenon lung scan, ventilation/perfusion scanning (VPS), pulmonary scintiphotography, or, most commonly, V/Q scan.

Description

In a lung perfusion scan, a small amount of a protein labeled with a radioisotope is injected into the patient's hand or arm vein. The patient is positioned under a special camera that can detect radioactive material, and a series of photographs are made of the chest. When these images are projected onto a screen (oscilloscope), they show how the radioactive protein has been distributed by the blood in the blood vessels running through the lungs.

In a lung ventilation scan, a mask is placed over the nose and mouth, and the patient is asked to inhale and exhale a combination of air and radioactive gas. Pictures are then taken that show the distribution of the gas in the lungs. Each test takes 15–30 minutes.

Preparation

There is little preparation needed for these tests. The patient may eat and drink normally before the procedure. Tests to check for **pulmonary embolism** are often performed on an emergency basis.

The amount of radioactivity to which a person is exposed during these tests is very low and is not harmful. However, if the patient has had other recent radionuclear tests, it may be necessary to wait until other radiopharmaceuticals have been cleared from the body so that they do not interfere with these tests.

Aftercare

No special aftercare is needed. The patient may resume normal activities immediately. The patient may be asked to consume increased amounts of fluids (unless contraindicated because of a medical condition) for one to two days after the procedures to help speed up the elimination of the radioactive material from the body.

KEY TERMS

Pulmonary embolism—A blood clot in the arteries that is traveling to the lungs.

Radiopharmaceutical—A radioactive isotope that can be injected or inhaled into the body and then traced for radiologic purposes. For example, the radioactive isotope technetium-99m (Tc-99m) is injected into the body as part of the lung perfusion scan procedure.

Risks

There are practically no risks associated with these tests.

Results

Normal results

Normal results in both tests show an even distribution of radioactive material in all parts of the lungs.

Abnormal results

In the lung perfusion scan, an absence of radioactive marker material suggests decreased blood flow to that part of the lung, which could indicate a pulmonary **embolism**. However, **pneumonia**, **emphysema**, or lung tumors can create readings on the lung perfusion scan that falsely suggest a pulmonary embolism is present.

In the lung ventilation scan, absence of marker material when the lung perfusion scan for the area is normal suggests lung disease.

Certain combinations of abnormalities in lung perfusion and ventilation scans suggest pulmonary embolism.

Resources

BOOKS

Van Leeuwen, A.M. and D.J. Poelhuis–Leth, *Davis'sComprehensive Handbook of Laboratory and Diagnostic Tests with Nursing Implications,* 3rd ed. Philadelphia: F.A. Davis Company, 2009.

Tish Davidson, A.M.
Melinda Granger Oberleitner
RN, DNS, APRN, CNS

Lung surgery

Definition

Lung surgery includes a variety of procedures used to diagnose or treat diseases of the lungs. Biopsies are performed to extract a small amount of tissue for diagnosis, resections remove a portion of lung tissue, and other surgeries are aimed at reducing the volume of the lungs, removing cancerous tumors, or improving lung function.

Purpose

The type of lung surgery performed will depend upon the underlying disease or condition, as well as other factors.

- Pneumonectomy usually refers to the removal of a lung, or sometimes one or more lobes (sections containing lung tissue, air sacs, ducts, and respiratory bronchiole). It is most commonly indicated in certain forms and stages of lung cancer.
- Thoracotomy, or surgical incision of the chest wall, is used primarily as a diagnostic tool when other procedures have failed to provide adequate diagnostic information.
- Lobectomy is the term used to describe removal of one lobe of a lung. It is most commonly indicated for lung cancer, but may also be used for cystic fibrosis patients if other treatments have failed.
- Other surgical procedures include segmental resection or wedge resection. A resection is the removal of a part of the lung, often in order to remove a tumor. Wedge resection is removal of a wedge-shaped portion of lung tissue.
- Volume reduction surgery is a newer surgery used to help relieve shortness of breath and increase tolerance for exercise in patients with chronic obstructive pulmonary disease, such as emphysema.
- Other surgeries are continuously improved upon to make biopsy less invasive and surgery more effective, such as video-assisted lobectomy. Other purposes for lung surgery may include severe abscess, areas of long-term infection, or permanently enlarged or collapsed lung tissue.

Precautions

Thoracotomy should not be performed on patients whose general health status will not tolerate major surgery. Any surgery carries with it risks associated with **general anesthesia** and possibility of infection. Patients whose risk for these complications outweighs benefit may not be considered candidates for lung surgery. Each individual patient's condition will be reviewed prior to the treatment decision.

Description

Lung surgery procedures will vary depending on the underlying cause of the surgical test or intervention. A patient will be placed under general anesthesia during the surgery. An incision is made to examine the lungs. Diseased tissue is removed and may be sent for biopsy. Following the surgery, drainage tubes may be placed in the chest to drain fluids, blood, and air from the chest cavity. Tubes will most likely remain in place for one to two days, depending on the surgery and the patient's condition. The chest cavity, ribs, and skin are closed and the incision will be sutured. Hospital stay averages from three to 10 days.

Pneumonectomy consists of removal of all of one lung. It may often be indicated only when a **lobectomy** does not successfully remove the cancerous or damaged tissue. Thoracotomy consists of reaching the lung tissue through incision and obtaining tissue for a biopsy. The biopsy is used to diagnose or stage **cancer**, and thoracotomy may be avoided until other less invasive methods have failed. Volume reduction surgery involves incision and removal of those parts of the lung or lungs which are the most destroyed, in order to allow for full function of the remaining lung structure. This procedure is still being studied.

Lobectomy is performed in the same general manner as other lung surgeries, but will involve removal of an entire lobe of the lung. Most patients with Stage I or II **non-small cell lung cancer** will receive this treatment for their disease, or a less extensive resection. Lobectomy may only be performed if a wedge or segmental resection is ineffective, but is generally preferred as treatment for primary lung cancer in any patient who can tolerate the procedure. Wedge and segmental resections are still major surgery, but remove less tissue and may be the first choice for some patients, such as those with Stage I and Stage II non-small cell lung cancer. Patients who do not have enough pulmonary function to undergo a lobectomy will receive a wedge or segmental resection instead. This may lead to a higher recurrence rate of cancer. In general, the surgery method chosen will depend on specific circumstances and consideration of benefit versus risk.

Preparation

Preparation for lung surgery is much like that for any major surgery. Patients will receive instructions

from a physician concerning limit of food or water intake prior to the surgery, as well as risks and expected recovery. Patients should continue to follow treatment for the underlying condition, unless instructed otherwise by the physician, and should discuss medications and changes in condition with their physician prior to the surgery.

Aftercare

The chest tube inserted at the end of surgery will remain in place until the lung has fully expanded. Patients will be carefully monitored in the hospital for complications and infection. Deep breathing is recommended to help lessen the risk of **pneumonia** and infection. Breathing exercises will also help expand the lung. After discharge from the hospital, the patient may still receive some **pain** or infection-fighting medications and should recover within one to three months of the operation.

Risks

Risks of lung surgery follows those of any major surgery involving general anesthesia. These risks include reactions to anesthetics or medications, bleeding, infection, and problems restoring breathing. Lung surgery, in particular, offers the risk of pneumonia and **blood clots**. Thoracotomy, as a biopsy procedure, offers greater risk than most biopsy procedures.

Results

Outcome for any lung surgery depends on many factors and the severity of disease. In general, the predicted benefits, which justified the surgery, are normal expected results. Thoracotomy results in a definitive diagnosis in more than 90% of patients. Volume reduction surgery has been shown to result in relief of some symptoms and improvement in quality of life for selected patients with severe **emphysema** and have shown short-term promise.

Mortality from lung surgery improves as procedures move from the more complete pneumonectomy to lobectomy, and the lowest rate for segmental resection.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

American Lung Association, 1301 Pennsylvania Ave. NW, Suite 800, Washington, DC, 20001, (202) 758-3355, (202) 452-1805, (800) 548-8252, info@lungusa.org, http://www.lungusa.org/.

National Heart Lung and Blood Institute Health Information Center, P.O. Box 30105, Bethesda, MD, 20824-0105, (301) 592-8573, (240) 629-3246, http://www.nhlbi.nih.gov.

Teresa Odle

Lung transplantation

Definition

Lung transplantation involves removal of one or both diseased lungs from a patient and the replacement of the lungs with healthy organs from a donor. Lung transplantation may refer to single, double, or even heart-lung transplantation.

Purpose

The purpose of lung transplantation is to replace a lung that no longer functions, or is cancerous, with a healthy lung. In order to qualify for lung transplantation, a patient must suffer from severe lung disease which limits activities of daily living. There should be potential for rehabilitated breathing function. Attempts at other medical treatments should be exhausted before transplantion is considered. Many candidates for this procedure have end-stage fibrotic

National transplant waiting list by organ type (June 2010)

Organ needed	Persons waiting
Kidney	85,296
Liver	16,031
Heart	3,141
Kidney/Pancreas	2,199
Lung	1,802
Pancreas	1,450
Intestine	242
Heart/Lung	79

SOURCE: U.S. Department of Health and Human Services, Organ Procurement and Transplantation Network. Available online at: http://optn.transplant.hrsa.gov/data/default.asp (accessed June 8, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

lung disease, are dependent on **oxygen therapy**, and are likely to die of their disease in 12–18 months.

Patients with **emphysema** or **chronic obstructive pulmonary disease** (COPD) should be under 60 years of age, have a life expectancy without transplantation of two years or less, progressive deterioration, and emotional stability in order to be considered for lung transplantation. Young patients with end-stage **silicosis** (a progressive lung disease) may be candidates for lung or heart-lung transplantation. Patients with Stage III or Stage IV **sarcoidosis** (a chronic lung disease) with **cor pulmonale** should be considered as early as possible for lung transplantation. Other indicators of lung transplantation include pulmonary **vascular disease** and chronic pulmonary infection.

Precautions

Patients who have diseases or conditions which may make them more susceptible to organ rejection should not receive a lung transplant. This includes patients who are acutely ill and unstable; who have uncontrolled or untreatable pulmonary infection; significant dysfunction of other organs, particularly the liver, kidney, or central nervous system; and those with significant coronary disease or left ventricular dysfunction. Patients who actively smoke cigarettes or are dependent on drugs or alcohol may not be selected. There are a variety of protocols that are used to determine if a patient will be placed on a transplant recipient list, and criteria may vary depending on location.

Description

Once a patient has been selected as a possible organ recipient, the process of waiting for a donor organ match begins. The donor organ must meet clear requirements for tissue match in order to reduce the chance of organ rejection. It is estimated that it takes an average of one to two years to receive a suitable donor lung, and the wait is made less predictable by the necessity for tissue match. Patients on a recipient list must be available and ready to come to the hospital immediately when a donor match is found, since the life of the lungs outside the body is brief.

Single lung transplantation is performed via a standard thoracotomy (incision in the chest wall) with the patient under **general anesthesia**. Cardiopulmonary bypass (diversion of blood flow from the heart) is not always necessary for a single lung transplant. If bypass is necessary, it involves re-routing of the blood through tubes to a heart-lung bypass machine. Double lung transplantation involves implanting the lungs as two separate lungs, and cardiopulmonary bypass is usually required. The patient's lung or lungs are removed and the donor lungs are stitched into place. Drainage tubes are inserted into the chest area to help drain fluid, blood, and air out of the chest. They may remain in place for several days. Transplantation requires a long hospital stay and recovery can last up to six months.

Heart-lung transplants always require the use of cardiopulmonary bypass. An incision is made through the middle of the sternum. The heart, lung, and supporting structures are transplanted into the recipient at the same time.

Preparation

In addition to tests and criteria for selection as a candidate for transplantation, patients will be prepared by discussing the procedure, risks, and expected prognosis at length with their doctor. Patients should continue to follow all therapies and medications for treatment of the underlying disease unless otherwise instructed by their physician. Since lung transplantation takes place under general anesthesia, normal surgical and anesthesia preparation should be taken when possible. These include no food or drink from midnight before the surgery, discussion of current medications with the physician, and informing the physician of any changes in condition while on the recipient waiting list.

Aftercare

Careful monitoring will take place in a recovery room immediately following the surgery and in the patient's hospital room. Patients must take immunosuppression, or anti-rejection, drugs to reduce the risk of rejection of the transplanted organ. The body considers the new organ an invader and will fight its presence. The **anti-rejection drugs** lower the body's immune function in order to improve acceptance of the new organs. This also makes the patient more susceptible to infection.

Frequent check-ups with a physician, including x ray and blood tests, will be necessary following surgery, probably for a period of several years.

Risks

Lung transplantation is a complicated and risky procedure, partly because of the organs and systems involved, and also because of the risk of rejection by the recipient's body. Acute rejection most often occurs within the first four months following surgery, but may occur years later. Infection is a substantial risk

KEY TERMS

Pulmonary—Refers to the respiratory system, or breathing function and system.

Sarcoidosis—A chronic disease with unknown cause that involves formation of nodules in bones, skin, lymph nodes, and lungs.

Silicosis—A progressive disease that results in impairment of lung function and is caused by inhalation of dust containing silica.

for organ recipients. An early complication of the surgery can be poor healing of the bronchial and tracheal openings created during the surgery. A late complication and risk is chronic rejection. This can result in inflammation of the bronchial tubes or in late infection from the prolonged use of **immunosuppressant drugs** to fight rejection. Overall, lung transplant recipients have demonstrated average one and two-year survival rates of more than 70%.

Results

The outcome of lung transplantation can be measured in survival rates, and also in improved quality of life for recipients. Studies have reported improved quality of life after lung and heart-lung transplants. One study showed that at the two-year follow-up period, 86% of studied recipients reported no limitation to their activity. Demonstration of normal results for patients may include quality of life measurements, as well as testing to ensure lack of infection and rejection.

ORGANIZATIONS

Children's Organ Transplant Association, Inc. , 2501 COTA Drive, Bloomington, IN, 47403, (812) 336-8885, (800) 366-2682, cota@cota.org, http://www.cota.org.

Second Wind Lung Transplant Association, 3440 Halliday Ave., St. Louis, MO, 63118-1102, (888) 855-9463, http://www.2ndwind.org.

Teresa Odle

Lupus erythematosus *see* **Systemic lupus erythematosus**

Luque rod *see* **Spinal instrumentation**

Luteinizing hormone test

Definition

The luteinizing hormone (LH) test is a test of the blood or urine to measure the level of luteinizing hormone (lutropin). This hormone level is highest immediately before a woman ovulates during her menstrual cycle.

Purpose

The LH test is frequently used to determine the timing of ovulation. Couples who are trying to become pregnant may use information about the timing of ovulation to improve their chance of conception. The LH test and other hormone tests may be used during **infertility** screening to chart a woman's menstrual cycle. It may also be used during preparation for **in vitro fertilization**, to determine when eggs are mature and ready to be removed from the ovary.

Description

Lutenizing hormone is a hormone released by the pituitary gland, a small gland at the base of the brain. The hormone stimulates the ovaries to produce and release eggs each month during the menstrual cycle. The level of LH in the blood is highest before ovulation. This increase in hormone level is sometimes called a "surge." A urine or blood sample can be analyzed by a laboratory for the level of LH present. An LH test may be used as part of an infertility screening to determine if there is a hormonal imbalance that might make it difficult to become pregnant. If fertility drugs are given to stimulate ovulation, an LH test can help determine the best time for sexual intercourse. The LH test may also be used to determine when eggs are mature enough to be surgically removed from the ovary as part of the in vitro fertilization process. LH tests may also aid in the diagnoses of polycystic ovary disease, premature ovarian failure, and **menopause**.

A urine LH detection kit is also available for use at home. These are sometimes called "ovulation tests" and are similar to home **pregnancy** test kits. A sample of the woman's first morning urine is tested with the materials provided in the kit. These home tests are often used by women who want to become pregnant. By monitoring levels of LH and watching for the "surge," they can time sexual intercourse to coincide with ovulation, increasing the chance that the egg will be fertilized.

KEY TERMS

Lutropin—Another term for luteinizing hormone, this hormone stimulates the development and release of the egg from the ovary.

Preparation

If a blood sample is taken, the skin around the vein where the needle will be inserted is swabbed with an antiseptic. No special preparation is necessary for collection of a urine sample.

Aftercare

No special aftercare is required. If the blood is tested, as with any blood sampling, the area where the needle was inserted should be kept clean.

Risks

There are no significant risks associated with either the blood or urine test for LH.

Results

The level of LH in the blood or urine will vary depending on when the sample was taken during the menstrual cycle. LH levels will be highest around the time of ovulation, about halfway between a woman's menstrual periods. Levels will be lower during the rest of the month. Women who have already experienced menopause will normally have lower LH levels.

LH levels that remain low throughout the menstrual cycle may indicate a hormonal imbalance that could prevent ovulation. Additional testing may be required if this test is done as part of an infertility screening.

Resources

BOOKS

Lowrance, James M. *Thyroid Hormones and the Tests that Monitor Them: Hormonal Functions, Imbalances and Treatments*. Seattle: CreateSpace, 2010.

Altha Roberts Edgren

Lyme borreliosis *see* **Lyme disease**

Lyme disease

Definition

Lyme disease is an infection transmitted by the bite of ticks carrying the spiral-shaped bacterium *Borrelia burgdorferi*. The effects of this infection can be long-term and disabling unless it is recognized and treated properly with **antibiotics**.

Demographics

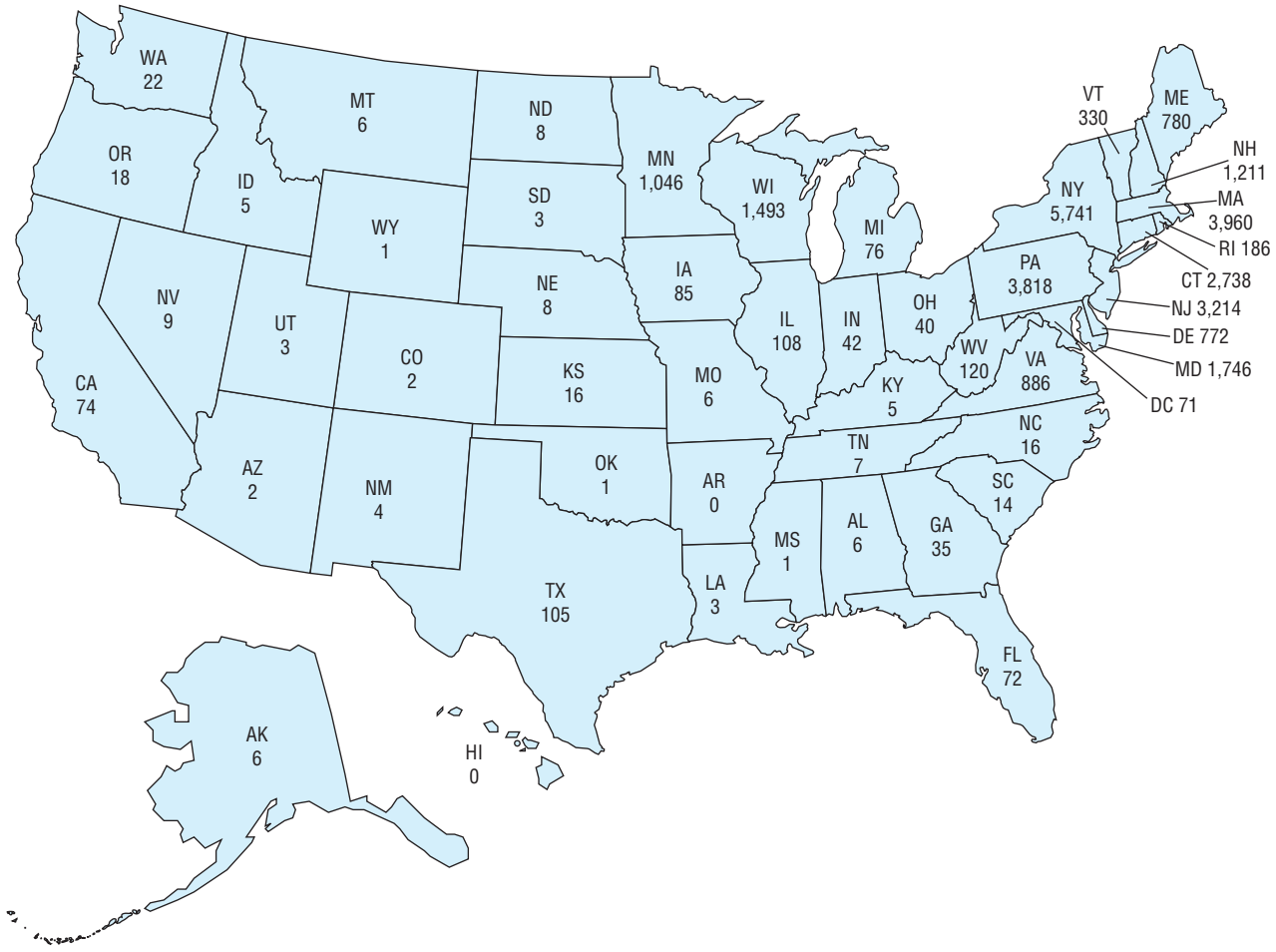
Controversy clouds the true incidence of Lyme disease because no test is 100% diagnostic for the disease, and many of its symptoms mimic those of so many other diseases. Cases of Lyme disease have been reported in 49 of the 50 states; however, distribution is not uniform. The United States Centers for Disease Control and Prevention (CDC) report that 93% of cases come from 10 states: Connecticut, Delaware, Maryland, Massachusetts, Minnesota, New Jersey, New York, Pennsylvania, Rhode Island, and Wisconsin. Oregon and northern California also report a significant number of cases.

Prevalence estimates range for 4 in 100,000 population to 9.1 per 100,000 population. In states where Lyme disease is more common, the rate can be as high as 37.4 per 100,000 population. In 2007, 27,000 new cases were reported in the United States. Some epidemiologists believe that the actual incidence of Lyme disease in the United States may be 5–10 times greater than that reported by the CDC. The reasons for this difference include the narrowness of the CDC's case definition as well as frequent misdiagnoses of the disease.

Lyme disease has also been found in Canada, most countries in continental Europe, some countries of the former Soviet Union, Japan, China, and Australia. In Europe the disease has been found in Austria,

Adult male deer tick. *(Kent Wood/Photo Researchers, Inc.)*

Confirmed Lyme disease cases by state, 2008



Total confirmed cases: 28,921

SOURCE: Centers for Disease Control and Prevention, Division of Vector-Borne Infectious Diseases, "Reported Lyme disease cases by state, 1999-2008." Available online at: http://www.cdc.gov/ncidod/dvbid/lyme/ld_rptdLymeCasesbyState.htm (accessed June 9, 2010).

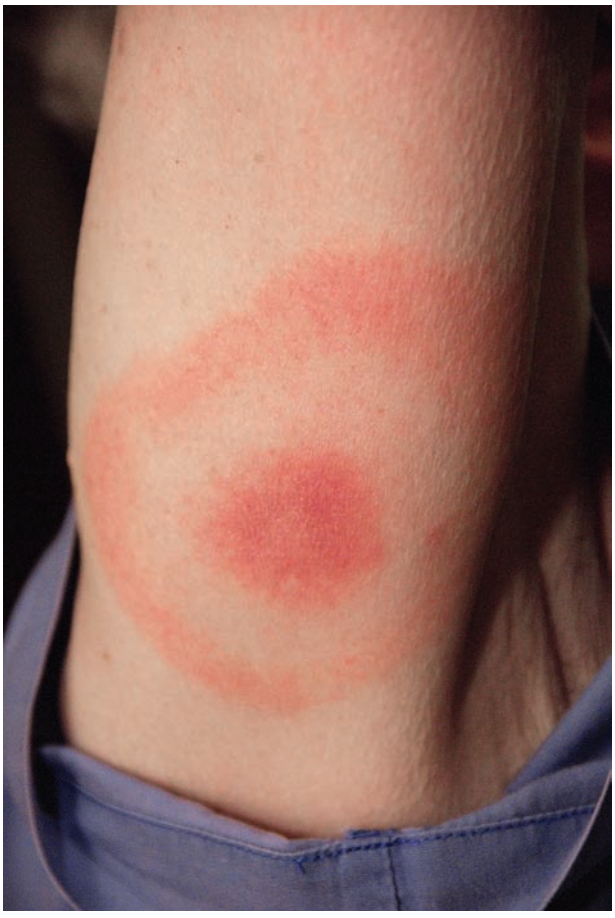
Lyme disease is caused by an infection transmitted by the bite of ticks carrying the *Borrelia burgdorferi* bacterium. *(Map by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)*

Germany, Poland, Finland, and Norway, The highest rate reported as of mid-2010 was in Slovenia, where there were an estimated 206 cases per 100,000 population and in Austria where there were 135 cases per 100,000 population.

Lyme disease affects men and women equally. People ages 5–14 and 50–59 are most likely to contract Lyme disease because these groups are more likely to participate in outdoor activities where they are exposed to ticks. About one-quarter of cases occur in children under age 5, while the fewest cases are reported in the 20–24 year old age group.

Description

Lyme is named for Lyme, Connecticut, the town where it was first diagnosed in 1975 after a puzzling outbreak of arthritis. The organism causing the disease is named for its discoverer, Willy Burgdorfer. Lyme disease, which is also called Lyme borreliosis, is a vector-borne disease. This term means that it is delivered from one host to another. It is also classified as a **zoonosis**, which means that it is a disease of animals that can be transmitted to humans under natural conditions. In this case, a tick bearing the *B. burgdorferi* organism inserts it into a host's bloodstream when it



The first sign of Lyme disease is usually an itchy, bull's-eye rash around the site of the tick bite. *(© Scott Camazine/Alamy.)*

bites the host to feed on its blood. It is important to note that neither *B. burgdorferi* nor Lyme disease can be transmitted directly from one person to another or from pets to humans.

In the United States, Lyme disease accounts for more than 90% of all reported vector-borne illnesses. It is a significant public health problem and continues to be diagnosed in increasing numbers. The CDC attributes this increase to the growing size of the deer herd and the geographical spread of infected ticks rather than to improved diagnosis.

Risk factors

People who spend a lot of time outdoors in wooded areas are at greatest risk of encountering ticks and developing Lyme disease. The risk for acquiring Lyme disease also depends on what stage in its life cycle a tick has reached. A tick passes through three stages of development—larva, nymph, and adult—each of which is dependent on a live host for food. In the United States, *B. burgdorferi* is borne by ticks of several species in the genus *Ixodes*, which usually feed on the white-footed mouse and deer (and are often called deer ticks). In the summer, the larval ticks hatch from eggs laid in the ground and feed by attaching themselves to small animals and birds. At this stage they are not a problem for humans. It is the next stage—the nymph—that causes most cases of Lyme disease. Nymphs are very active from spring through early summer, at the height of outdoor activity for most people. Because they are still quite small (less than 2 mm), they are difficult to spot, giving them ample opportunity to transmit *B. burgdorferi* while feeding. Although far more adult ticks than nymphs carry *B. burgdorferi*, the adult ticks are much larger, more easily noticed, and more likely to be removed before the 24 hours or more of continuous feeding needed to transmit *B. burgdorferi*.

Causes and symptoms

Lyme disease is caused by *B. burgdorferi*. Once *B. burgdorferi* gains entry to the body through a tick bite, it can move through the bloodstream quickly. Only 12 hours after entering the bloodstream, *B. burgdorferi* can be found in cerebrospinal fluid (which means it can affect the nervous system). Treating Lyme disease early and thoroughly is important because Lyme disease can hide for long periods within the body in a clinically latent state. That ability explains why symptoms can recur in cycles and can flare up after months or years, even over decades. It is important to note, however, that many people who are exposed to *B. burgdorferi* do not develop the disease.

Lyme disease usually is described in terms of length of infection (time since the person was bitten by a tick infected with Lyme disease) and whether *B. burgdorferi* is localized or disseminated (spread through the body by fluids and cells carrying *B. burgdorferi*). When and how symptoms of Lyme disease appear can vary widely from patient to patient. People who experience recurrent bouts of symptoms over time are said to have chronic Lyme disease.

Early localized Lyme disease

The most recognizable indicator of Lyme disease is a rash around the site of the tick bite. Often, the tick exposure has not been recognized. The eruption might be warm or itch. The rash—erythema migrans (EM)—generally develops within 3–30 days and usually begins as a round, red patch that expands outward. About 75% of patients with Lyme disease develop EM. Clearing may take place from the center out,

KEY TERMS

Antibody—A protein normally produced by the immune system to fight infection or rid the body of foreign material. The material that stimulates the production of antibodies is called an antigen. Specific antibodies are produced in response to each different antigen and can only inactivate that particular antigen.

Antigen—Any foreign substance, usually a protein, that stimulates the body's immune system to produce antibodies.

Babesiosis—A disease caused by protozoa of the genus *Babesia* characterized by a malaria-like fever, anemia, vomiting, muscle pain, and enlargement of the spleen. Babesiosis, like Lyme disease, is carried by a tick.

Bell's palsy—Facial paralysis or weakness with a sudden onset, caused by swelling or inflammation of the seventh cranial nerve, which controls the facial muscles. Disseminated Lyme disease sometimes causes Bell's palsy.

Blood-brain barrier—A specialized, semi-permeable layer of cells around the blood vessels in the brain that controls which substances can leave the circulatory system and enter the brain.

Cerebrospinal fluid—A clear fluid that fills the hollow cavity inside the brain and spinal cord. The cerebrospinal fluid has several functions, including providing a cushion for the brain against shock or impact, and removing waste products from the brain.

Disseminated—Scattered or distributed throughout the body. Lyme disease that has progressed beyond the stage of localized EM is said to be disseminated.

ELISA protocols—ELISA is an acronym for "enzyme-linked immunosorbent assay"; it is a highly sensitive technique for detecting and measuring antigens or antibodies in a solution.

Erythema migrans (EM)—A red skin rash that is one of the first signs of Lyme disease in about 75% of patients.

Lymph nodes—Small, bean-shaped masses of tissue scattered along the lymphatic system that act as filters and immune monitors, removing fluids, bacteria, or cancer cells that travel through the lymph system.

Opportunistic infection—An infection by organisms that usually do not cause infection in people whose immune systems are working normally.

Vector—An animal carrier that transfers an infectious organism from one host to another. The vector that transmits Lyme disease from wildlife to humans is the deer tick or black-legged tick.

Zoonosis (plural, zoonoses)—Any disease of animals that can be transmitted to humans under natural conditions. Lyme disease and babesiosis are examples of zoonoses.

leaving a bull's-eye effect; in some cases, the center gets redder instead of clearing. The rash may look like a bruise on people with dark skin. Of those who develop Lyme disease, about 50% notice flu-like symptoms, including **fatigue**, **headache**, chills and **fever**, muscle and joint **pain**, and lymph node swelling. However, a rash at the site can also be an allergic reaction to the tick saliva rather than an indicator of Lyme disease, particularly if the rash appears in *less* than three days and disappears only days later.

Late disseminated disease and chronic Lyme disease

Weeks, months, or even years after an untreated tick bite, symptoms can appear in several forms, including:

- fatigue, forgetfulness, confusion, mood swings, irritability, numbness.
- neurologic problems, such as pain (unexplained and not triggered by an injury), Bell's palsy (facial paralysis, usually one-sided but may be on both sides), and a mimicking of the inflammation of brain membranes known as meningitis; (fever, severe headache).
- arthritis (short episodes of pain and swelling in joints) and other musculoskeletal complaints. Arthritis eventually develops in about 60% of patients with untreated Lyme disease.

Less common effects of Lyme disease are heart abnormalities such as irregular rhythm (**arrhythmias**) or cardiac block and eye abnormalities such as swelling of the cornea, tissue, or eye muscles and nerves.

A late-stage complication of Lyme disease that affects the skin is acrodermatitis chronica atrophicans, a disorder in which the skin on the person's lower legs or hands becomes inflamed and paper-thin. This disorder is seen more frequently in Europe than in the United States.

Diagnosis

Examination

A clear diagnosis of Lyme disease can be difficult and relies on information the patient provides and the doctor's clinical judgment, particularly through elimination of other possible causes of the symptoms. Lyme disease may mimic other conditions, including **chronic fatigue syndrome** (CFS), **multiple sclerosis** (MS), and other diseases with many symptoms involving multiple body systems. Differential diagnosis (distinguishing Lyme disease from other diseases) is based on clinical evaluation with laboratory tests used for clarification, when necessary.

Doctors generally know which disease-causing organisms are common in their geographic area. The most helpful piece of information is whether a tick bite or rash was noticed and whether it happened locally or while traveling. Doctors may not consider Lyme disease if it is rare locally, but will take it into account if a patient mentions vacationing in an area where the disease is commonly found.

Children may have difficulty effectively verbalizing their symptoms and as such, their symptoms may be misdiagnosed. Parents who suspect Lyme disease in their children should inform their doctor about the possibility of the disease and be proactive in requesting further medical evaluation and treatment.

Tests

As of 2010, the United States Food and Drug Administration (FDA) had approved two blood tests for Lyme disease. This these looks for antigens (substances that stimulate the production of antibodies) produced by *B. burgdorferi* rather than for the bacterium itself. Prevue B is a rapid test that can give results within one hour. The C6 Lyme Peptide ELISA (enzyme-linked immunosorbent assay) test takes longer to give results, but is more sensitive. A positive result from either test can be confirmed by a second blood test known as the Western blot test, which must be done in a laboratory.

Early diagnosis and prompt treatment are critical to preventing the neurologic complications of Lyme disease. Fewer than 50% of children realize that they have been bitten by a tick. Any child that develops a round, bull's-eye skin rash, joint pain, flu-like symptoms, and/or neurologic symptoms should see a doctor. Because the rash may not be readily visible (e.g., on the scalp under hair), children living in or visiting areas with a high incidence of Lyme disease and those participating in frequent outdoor activities during active tick months who develop joint pain and neurologic symptoms should see a doctor.

Treatment

Traditional

Immediate removal of an attached tick is the first step in treatment for people who know they have been bitten. Because black-legged ticks are slow feeders, it takes about 36 hours for *B. burgdorferi* to make its way into the body; infection is unlikely if the tick is removed within 24 hours of attachment. People who find ticks on themselves should *not* use a hot match, petroleum jelly, nail polish, or similar items to remove the tick. They should use fine-tipped tweezers, grasp the tick as close to the skin as possible, and pull the tick away from the skin with a steady motion. The area should then be cleansed with an antiseptic.

Because most children do not realize they have been in tick-infested areas or been bitten by a tick and because deer ticks can be the size of a poppy seed or smaller, parents should be diligent about checking children for ticks, especially if the family lives in or visits an area with a high incidence of Lyme disease or an area near tick habitats.

Drugs

For most patients, initial therapy consists of oral antibiotics such as doxycycline (Doryx, Vibramycin) or amoxicillin (Amoxil, Trimox) for 14–21 days. If there poor response, alternative antibiotics such as Cefuroxime axetil (Ceftin), Clarithromycin (Biaxin), or azithromycin (Zithromax) are tried. When symptoms indicate nervous system involvement or a severe episode of Lyme disease, intravenous antibiotics such as ceftriaxone (Rocephin), cefotaxime (Claforan), or intravenous penicillin may be given for 14–30 days.

The physician may have to adjust the treatment regimen or change medications based on the patient's response. Treatment can be difficult because *B. burgdorferi* comes in several strains, some may react to different antibiotics than others. Also, *B. burgdorferi* can shut itself up in cell niches, allowing it to hide from antibiotics. Finally, antibiotics can kill *B. burgdorferi* only while it is active rather than dormant.

Complementary and Alternative

Antibiotic therapy is essential in treating Lyme disease, however, complementary therapies may minimize symptoms of Lyme disease or improve the immune response. These include vitamin and **nutritional supplements**, mostly for chronic fatigue and increased

susceptibility to infection. For example, yogurt and *Lactobacillus acidophilus* preparations help fight yeast infections, which are common in people on long-term antibiotic therapy. In addition, botanical medicine and homeopathy can be considered to help bring the body's systems back to a state of health and well being. A Western herb, spilanthes (*Spilanthes* spp.), may have an effect on diseases like Lyme disease that are caused by spirochetes (spiral-shaped bacteria), although this effect has not been proven to the satisfaction of practitioners of conventional medicine.

Other complementary and alternative therapies used in treating Lyme disease include:

- Chinese medicine. Formulae used to treat systemic bacterial infections include Wu Wei Xiao Du Yin (Five-Ingredient Decoction to Eliminate Toxin), Yin Hua Jie Du Tang (Honeysuckle Decoction to Relieve Toxicity), and Huang Lian Jie Du Tang (Coptis Decoction to Relieve Toxicity). Inflammation at the site of infection may be treated externally with Yu Lu San (Jade Dew Extract) or Jin Huang San (Golden Yellow Powder). Specific Chinese herbs and treatments can be used for specific symptoms. For examples, for systemic bacterial infection, one may use honeysuckle flower, forsythia, isatidis, scutellaria, and phellodendron. Acupuncture and ear acupuncture treatments are also used.
- Herbals. Botanical remedies include Echinacea (*Echinacea* species) to clear infection and boost the immune system, goldenseal (*Hydrastis canadensis*) to clear infection and boost the immune system, garlic to clear bacterial infection, and spilanthes (*Spilanthes* species) for spirochete infections.
- Hydrotherapy. The joint pain associated with Lyme disease can be treated with hydrotherapy. Dull, penetrating pain may be relieved by applying a warm compress to the affected area. Sharp, intense pain may be relieved by applying an ice pack to the affected area.
- Guided imagery. The patient may treat Lyme disease by visualizing Bb as looking like ticks swimming in the bloodstream being killed by the flame of a candle.
- Probiotics. Probiotics is treatment with beneficial microbes either by ingestion or through a suppository. Probiotics can restore a healthy balance of bacteria to the body in cases in which long-term antibiotic use has caused diarrhea or yeast infection. Yogurt or *Lactobacillus acidophilus* preparations may be ingested.

Prognosis

If aggressive antibiotic therapy is given early, and the patient cooperates fully and sticks to the medication regimen, recovery should be complete. Only a small percentage of Lyme disease patients fail to respond or relapse (have recurring episodes). Most long-term effects of the disease result when diagnosis and treatment is delayed or missed. Co-infection with other infectious organisms spread by ticks in the same areas as *B. burgdorferi* (**babesiosis** and **ehrlichiosis**, for instance) may be responsible for treatment failures or more severe symptoms. Most fatalities reported with Lyme disease involved patients co-infected with babesiosis.

Prevention

Minimizing risk of exposure

Precautions to avoid contact with ticks include moving leaves and brush away from living quarters. Most important are personal protection techniques when outdoors, such as:

- spraying tick repellent on clothing and exposed skin.
- wearing light-colored clothing to maximize ability to see ticks.
- tucking pant legs into socks or boot top.
- checking children and pets frequently for ticks.
- inspecting each individual living in high-risk areas daily for ticks in the spring and summer.

Minimizing risk of disease

The two most important factors are removing the tick quickly and carefully, and seeking a doctor's evaluation at the first sign of symptoms of Lyme disease. When in an area that may be tick-populated:

- Check for ticks, particularly in the area of the groin, underarm, behind ears, and on the scalp.
- Stay calm and grasp the tick as near to the skin as possible, using tweezers.
- To minimize the risk of squeezing more bacteria into the bite, pull straight back steadily and slowly to remove the tick.
- Do not try to remove the tick by using petroleum jelly, alcohol, or a lit match.
- Place the tick in a closed container (for species identification later, should symptoms develop) or dispose of it by flushing.
- See a physician immediately for any sort of rash or patchy discoloration that appears three to 30 days after a tick bite.

A vaccine for Lyme disease was available from 1998 to 2002, when it was removed from the United States market. Protection provided by the vaccine fades over time. Anyone who was vaccinated at the time the vaccine was available likely no longer has

any protection against the disease. A vaccine still exists for dogs, although veterinarians have mixed ideas about its use.

Resources

BOOKS

Weintraub, Pamela. *Cure Unknown: Inside the Lyme Epidemic*. New York: St. Martin's Press, 2008

OTHER

Learn About Lyme Disease. United States Centers for Disease Control and Prevention. March 10, 2010. http://www.cdc.gov/ncidod/dvbid/lyme

Lyme Disease. MedlinePlus. March 29, 2010. http://www.nlm.nih.gov/medlineplus/lymedisease.html

Meyerhoff, John O. Lyme Disease. eMedicine.com. July 24, 2009. http://emedicine.medscape.com/article/330178-overview

ORGANIZATIONS

American Lyme Disease Foundation, P. O. Box 466, Lyme, CT, 06371, inquire@adlf.com, http://www.aldf.com.

Lyme Disease Network of NJ. , 43 Winton Road, East Brunswick, NJ, 08816, http://www.lymenet.org.

National Institute of Allergy and Infectious Diseases Office of Communications and Government Relations, 6610 Rockledge Drive, MSC 6612, Bethesda, MD, 20892-6612, (301) 496-5717, (866) 284-4107 or TDD: (800)877-8339 (for hearing impaired), (301) 402-3573, http://www3.niaid.nih.gov.

United States Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (404) 639-3534, 800-CDC-INFO (800-232-4636). TTY: (888) 232-6348, inquiry@cdc.gov, http://www.cdc.gov.

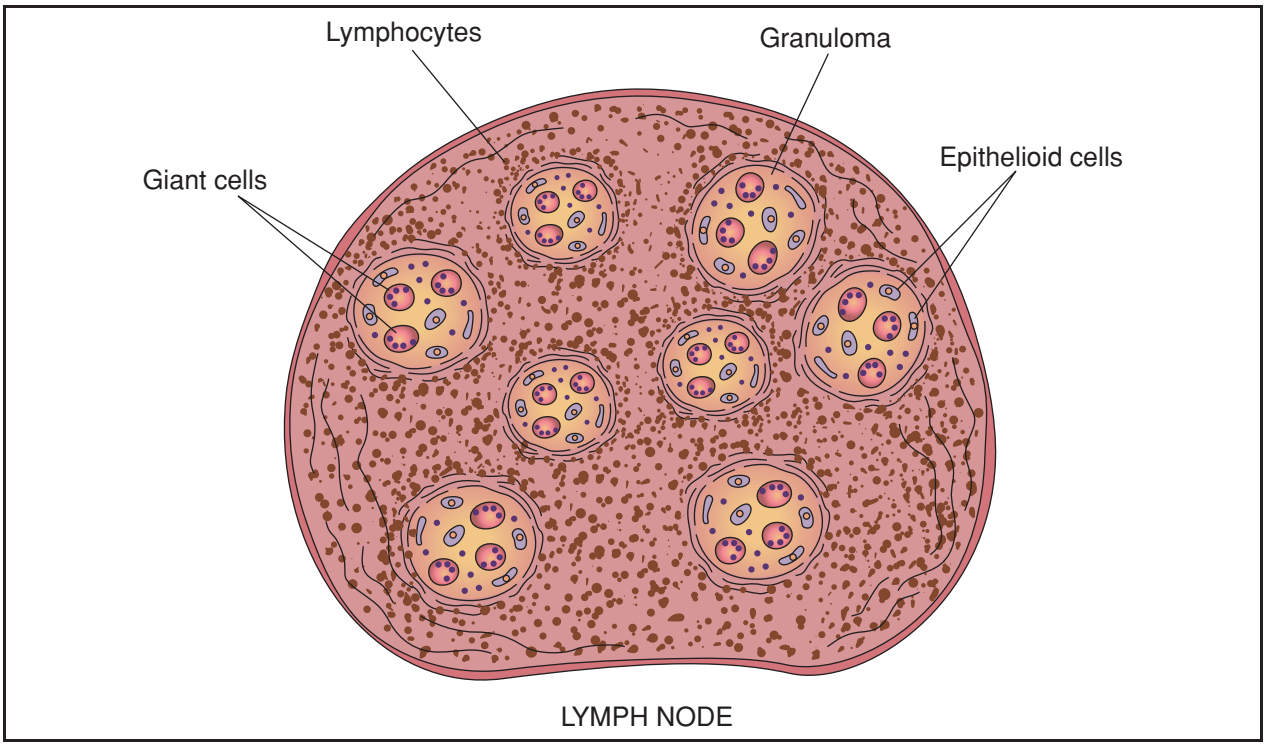
Rebecca J. Frey, Ph.D.
Jennifer E. Sisk, M.A.
Tish Davidson, A.M.

Lymph node angiogram *see* **Lymphangiography**

Lymph node biopsy

Definition

A lymph node biopsy is a procedure in which all or part of a lymph node is removed and examined to determine whether there is **cancer** within the node, or to determine the cause of **swollen glands** in the head and neck region.



Lymph node biopsy is a procedure in which a sample of lymph node tissue is removed for laboratory analysis. It is generally performed on an outpatient basis. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

KEY TERMS

Lymph nodes—Small bean-shaped organs located throughout the lymphatic system. The lymph nodes store special cells that can trap cancer cells or bacteria that are traveling through the body in lymph. Also called lymph glands.

Lymphocytes—Small white blood cells that bear the major responsibility for carrying out the activities of the immune system; they number about 1 trillion.

Malignant—Cancerous. Cells tend to reproduce without normal controls on growth and form tumors or invade other tissues.

Sentinel node—The first lymph node or group of nodes to which cancer cells are likely to spread from a primary tumor.

Spleen—An organ located at the left side of the stomach that acts as a reservoir for blood cells and produces lymphocytes and other products involved in fighting infection.

Thymus—An organ near the base of the neck that produces cells that fight infection. It is at its largest at puberty, then declines in size and function during adult life.

Tonsils—Small masses of tissue at the back of the throat.

Purpose

The lymph system is the body's primary defense against infection. It consists of the spleen, tonsils, thymus, lymph nodes, lymph vessels, and the clear, slightly yellow fluid called lymph. These components produce and transport white blood cells called lymphocytes and macrophages that rid the body of infection. The lymph system is also involved in the production of antibodies. Antibodies are proteins that fight bacteria, viruses, and other foreign materials that enter the body.

The lymph vessels are similar to veins, only instead of carrying blood as veins do, they circulate lymph to most tissues in the body. Lymph nodes are about 600 small, bean-shaped collections of tissue found along the lymph vessel. They produce cells and proteins that fight infection, and clean and filter lymph. Lymph nodes are sometimes called lymph glands, although they are not true glands. When someone talks about having swollen glands, they are actually referring to lymph nodes.

Normal lymph glands are no larger than 0.5 in (1.3 cm) in diameter and are difficult to feel. However, lymph nodes can enlarge to greater than 2.5 in (6 cm) and can become sore. Most often the swelling is caused by an infection, but it can also be caused by cancer.

Cancers can metastasize (spread) through the lymph system from the site of the original tumor to distant parts of the body where secondary tumors are formed. The purpose of a lymph node biopsy is to determine the cause of the swelling and/or to see whether cancer has begun to spread through the lymph system. This information is important in staging the cancer and devising a treatment plan.

Precautions

Women who are pregnant should inform their doctor before a lymph node biopsy, although **pregnancy** will not affect the results.

Description

There are three kinds of lymph node biopsy. Fine-needle aspiration (FNA) biopsy, often just called needle biopsy, is done when the lymph node of interest is near the surface of the body. A hematologist (a doctor who specializes in blood diseases) usually performs the test. In FNA biopsy, a needle is inserted through the skin and into the lymph node, and a sample of tissue is drawn from the node. This material is preserved and sent to the laboratory for examination.

Advantages of a needle biopsy are that the test is minimally invasive. Only a local anesthetic is used, the procedure generally takes less than half an hour, and there is little **pain** afterwards. The disadvantage is that cancer may not be detected in the small sample of cells removed by the needle.

Open lymph node biopsy is a surgical procedure. It is done by a surgeon under **general anesthesia** on lymph nodes in the interior of the body and under **local anesthesia** on surface lymph nodes where FNA biopsy is considered inadequate. Once there is adequate anesthesia, the surgeon makes a small cut and removes either the entire lymph node or a slice of tissue that is then sent to the laboratory for examination. Results in both kinds of biopsies take one to three days.

Open biopsy can be advantageous in that it is easier to detect and identify the type of cancer in a large piece of tissue. Also, lymph nodes deep in the body can be

sampled. Disadvantages include a longer recovery time, soreness at the biopsy site for several days, and the use of deeper anesthesia, increasing the risks to the patient. The procedure is done in a hospital or outpatient surgery center and takes about an hour, with additional time to recover from general anesthesia.

The third type of lymph node biopsy is known as sentinel node biopsy or sentinel node procedure. A sentinel node is the first lymph node or group of nodes reached by a cancer metastasizing from a primary tumor. This type of biopsy was pioneered at the John Wayne Cancer Institute in the 1990s. It is done as part of cancer staging, to determine whether a cancer has spread to a nearby lymph node. Sentinel node biopsy is most commonly done in patients with **breast cancer** or **malignant melanoma**, although it has also been used in patients with **colon cancer**, cancer of the cervix, or **vulvar cancer**.

To perform a sentinel node biopsy, the surgeon injects a radioactive form of technetium near the tumor several hours before the biopsy. About 15 minutes before the biopsy, a blue dye is injected in the same manner. The nodes that take up the dye and radioactive tracer are the sentinel lymph nodes. The surgeon then removes the sentinel nodes and sends them to a pathologist for examination, which takes less than 30 minutes. If cancer is detected in the sentinel node, the surgeon can remove additional lymph nodes. The advantage of the sentinel node procedure is to avoid the unnecessary removal of lymph tissue. This type of biopsy can be done as an outpatient procedure or require a short hospital stay.

Preparation

No particular preparation is necessary for a needle biopsy. For an open biopsy, patients need standard preoperative blood tests and other tests to evaluate general health. The doctor should be informed about any medications (prescription, non-prescription, or herbal) the patient is taking, as well as past bleeding problems or **allergies** to medication or anesthesia.

Aftercare

Little aftercare is needed in a needle biopsy other than a bandage to keep the biopsy site clean. Patients who have general anesthesia for an open biopsy often feel drowsy and tired for several days following the procedure, and should not plan to drive home after biopsy. The incision site must be kept clean and dry, and a follow-up visit to check on healing is usually necessary.

Risks

There are few risks associated with lymph node biopsy. The main risks are excessive bleeding (usually only in people with blood disorders) and allergic reaction to general anesthesia (rare). Occasionally the biopsy site becomes infected. In a few cases there may be **numbness** or nerve damage when the lymph node being tested lies close to a nerve. Some patients who have sentinel node biopsies develop an allergic reaction to the blue dye or find their urine or skin temporarily discolored by the dye.

Results

Normal lymph nodes are small and flat. When examined under the microscope, they show no signs of cancer or infection.

Abnormal lymph nodes are usually enlarged and contain cancerous (malignant) cells and/or show signs of infection.

Resources

BOOKS

Klimberg, V. Suzanne, ed. *Atlas of Breast Surgical Techniques*. Philadelphia: Saunders/Elsevier, 2010.

Koch, Wayne M., ed. *Head and Neck Cancer*. Philadelphia: Saunders/Elsevier, 2010.

PERIODICALS

Califano, J., and M. Nance. "Malignant Melanoma." *Facial Plastic Surgery Clinics of North America* 17 (August 2009): 337–48.

Crosbie, E.J., et al. "The Management of Vulvar Cancer." *Cancer Treatment Reviews* 35 (November 2009): 533–39.

Stadelmann, W.K. "The Role of Lymphatic Mapping and Sentinel Lymph Node Biopsy in the Staging and Treatment of Melanoma." *Clinics in Plastic Surgery* 37 (January 2010): 79–99.

Wilson, L.L. "Sentinel Lymph Node Biopsy from the Vantage Point of an Oncologic Surgeon." *Clinics in Dermatology* 27 (November-December 2009): 594–96.

Zivanovic, O., et al. "Sentinel Lymph Node Biopsy in the Management of Vulvar Carcinoma, Cervical Cancer, and Endometrial Cancer." *Oncologist* 14 (July 2009): 695–705.

OTHER

Cleveland Clinic. *Breast Cancer: Sentinel Node Biopsy*. http://my.clevelandclinic.org/services/biopsy/hic_sentinel_node_biopsy.aspx

Keshtgar, M. *Surgical Procedure: Sentinel Node Biopsy in Breast Cancer Using Radiocolloid and Blue Dye*. This is a nine-minute video by a senior lecturer in surgery at University College London.http://www.youtube.com/watch?v=4JtWk9brMRE

MedlinePlus Medical Encyclopedia. *Lymph Node Biopsy*. http://www.nlm.nih.gov/medlineplus/ency/article/003933.htm

National Cancer Institute (NCI). *Sentinel Lymph Node Biopsy: Questions and Answers*. http://www.cancer.gov/cancertopics/factsheet/therapy/sentinel-node-biopsy

ORGANIZATIONS

Alliance for Lung Cancer Advocacy, Support, and Education, P.O. Box 849, Vancouver, WA, 98666, (800) 298-2436., nhlbiinfo@nhlbi.nih.gov, http://www.alcase.org.

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329–4251, (800) 227–2345, info@cancer.org, http://www.cancer.org.

American Lung Association, 1301 Pennsylvania Ave., NW, Suite 800, Washington, DC, 20004, (800) 548–8252, webmaster@lungusa.org, http://www.lungusa.org.

National Heart, Lung and Blood Institute, P.O. Box 30105, Bethesda, MD, 20824–0105, (301) 251–2222, nhlbiinfo@nhlbi.nih.gov, http://www.nhlbi.nih.gov.

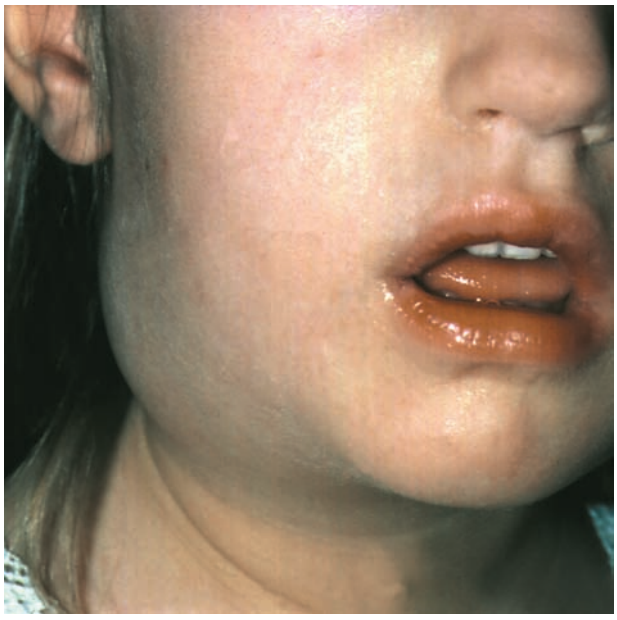
Tish Davidson, A.M.
Rebecca J. Frey, PhD
Brenda W. Lerner

Lymphadenitis

Definition

Lymphadenitis is the inflammation of a lymph node, also sometimes called a lymph gland. The inflammation happens usually in the presence of swollen or enlarged lymph node(s). Because of this symptom, lymphadenitis is commonly called swollen lymph nodes. It is often a complication of a bacterial infection of a wound, although viruses or other disease agents can also cause it. Lymphadenitis may be either one that involving a number of lymph nodes all over the body (what is called generalized lymphadenitis) or limited to a few nodes in the area of a localized infection (what is termed localized lymphadenitis). Most of the time, the infection of lymph nodes occur in the head and neck, or in the areas of the armpits and groin.

The condition is sometimes accompanied by lymphangitis, which is the inflammation of the lymphatic vessels that connect the lymph nodes. When the disease of a lymph node is caused by an autoimmune disease or a malignancy, in addition to infection, the disease is called lymphadenopathy.



Swollen lymph node glands in a young girl's neck. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Demographics

Anyone from anywhere in the world can contract lymphadenitis.

Description

Lymphadenitis is marked by swollen lymph nodes that are painful, in most cases, when the doctor touches them. If the lymphadenitis is related to an infected wound, the skin over the nodes may be red and warm to the touch. If the lymphatic vessels are also infected, there will be red streaks extending from the wound in the direction of the lymph nodes. In most cases, the infectious organisms are hemolytic *Streptococci* or *Staphylococci*.

The lymphatic system consists of a vast network or organs, lymph vessels (channels), lymph ducts, and lymph nodes that stretch throughout the human body. The system moves fluid, called lymph, from the tissues to the bloodstream. About 600 lymph nodes exist in the body, with most of them located in the head and neck. They are used to filter the lymph fluid, and to help counter infection, with the use of white blood cells. This extensive network of lymphatic vessels throughout the body and their relation to the lymph nodes helps to explain why bacterial infection of the nodes can spread rapidly to or from other parts of the body. Lymphadenitis in children often occurs in the neck area because these lymph nodes are close to

the ears and throat, which are frequent locations of bacterial infections in children.

Causes and symptoms

Streptococcal and staphylococcal bacteria are the most common causes of lymphadenitis, although viruses, protozoa, rickettsiae, fungi, and the **tuberculosis** bacillus can also infect the lymph nodes. Diseases or disorders that involve lymph nodes in specific areas of the body include rabbit **fever** (**tularemia**), **cat-scratch disease**, **lymphogranuloma venereum**, **toxoplasmosis**, **chancroid**, **sexually transmitted diseases** such as **genital herpes** and **syphilis**, **strep throat**, ear infections, mononucleosis, infected **acne**, infections from **wounds**, dental abscesses, and bubonic **plague**.

In children, **tonsillitis** or bacterial sore throats are the most common causes of lymphadenitis in the neck area. Diseases that involve lymph nodes throughout the body include mononucleosis, **cytomegalovirus infection**, toxoplasmosis, and **brucellosis**. Because lymph nodes play a critical role in fighting off bacteria, viruses, and other foreign invaders within the human body, it is especially important to see a medical professional when these glands become swollen and enlarged.

The early symptoms of lymphadenitis are swelling of the nodes caused by a buildup of tissue fluid and an increased number of white blood cells resulting from the body's response to the infection. The enlargement of the nodes may reach upwards of 0.4 inch (about 1 centimeter). These nodes are also usually tender to the touch. Further developments include fever, often as high as 101 to 102°F (38 to 39°C) together with chills, runny nose, **sore throat**, loss of appetite and weight loss, heavy perspiration or night sweats, difficult in swallowing and breathing, a rapid pulse, red and inflamed skin over the swollen gland, and general weakness.

If lymph nodes become swollen throughout the body, then such a situation may indicate the infection is one involving mononucleosis, **measles**, or **mumps**; or an immune disorder such as **rheumatoid arthritis**, human **immunodeficiency** virus (HIV), or lupus. In rare cases, the lymph node may grow larger and become hard to the touch—a condition that is rare but may indicate a tumor.

Diagnosis

Physical examination

The diagnosis of lymphadenitis is usually based on a combination of the patient's history, the external symptoms, and laboratory cultures. The doctor will press (palpate) the affected lymph nodes to see if they are sore or tender. Swollen nodes without soreness are often caused by cat-scratch disease. In children, the doctor will need to rule out mumps, tumors in the neck region, and congenital cysts that resemble swollen lymph nodes.

Although lymphadenitis is usually diagnosed in lymph nodes in the neck, arms, or legs, it can also occur in lymph nodes in the chest or abdomen. If the patient has acutely swollen lymph nodes in the groin, the doctor will need to rule out a **hernia** in the groin that has failed to reduce (incarcerated inguinal hernia). Hernias occur in 1% of the general population; 85% of patients with hernias are male.

Laboratory tests

The most significant tests are a **white blood cell count** (WBC) and a **blood culture** to identify the organism. A high proportion of immature white blood cells indicates a bacterial infection. Blood cultures may be positive, most often for a species of staphylococcus or streptococcus. In some cases, the doctor may order a biopsy of the lymph node.

Other tests the doctor may order include an x ray or computerized tomography (CT) scan of the effected area. A **lymph node biopsy** may also be performed so that a small sample of the lymph node can be examined within a laboratory setting.

Treatment

Medications

The medications given for lymphadenitis vary according to the bacterium or virus that is causing it. If the patient also has lymphangitis, he or she will be treated with **antibiotics**, usually penicillin G (Pfizerpen, Pentids), nafcillin (Nafcil, Unipen), or **cephalosporins**. Erythromycin (Eryc, E-Mycin, Erythrocin) is given to patients who are allergic to penicillin.

Over-the-counter **pain** relievers (analgesics/analgesics) may also be used to reduce pain and relieve some of the symptoms. Anti-inflammatory drugs help to reduce inflammation and swelling.

Treatment of swollen lymph nodes where the underlying cause is an immune disorder revolves around treating the underlying condition itself.

If the swollen lymph nodes are caused by different types of **cancer** (such as lymphoma, leukemia, or other cancers that spread to the lymph nodes), then treatment depends on the recommended treatment for

KEY TERMS

Hemolytic—Able to break down or dissolve red blood cells. The bacteria that cause lymphadenitis are hemolytic.

Hernia—The bulging of a part of the intestine or other organ through its surrounding wall of tissue. Most hernias are in the abdominal cavity. An inguinal hernia is located in the groin area.

Lymph nodes—The gland-like masses of tissue in the lymphatic system that contain lymphocytes. The lymph nodes also filter lymph, which is a clear yellowish tissue fluid that carries lymphocytes and fats throughout the body.

Lymphangitis—Inflammation of the lymphatic vessels. It often occurs together with lymphadenitis.

Septicemia—The presence of bacteria and their toxins in the bloodstream. Septicemia is sometimes called blood poisoning.

Staphylococcus—Any of several species of spherical bacteria that occur in groups of four or irregular clusters. *Staphylococci* frequently cause skin infections.

Streptococcus—Any of several species of bacteria that are spherical in shape and form pairs or chains. *Streptococci* cause scarlet fever, tonsillitis, and pneumonia, and are often involved in lymphadenitis.

the cancer, such as **chemotherapy**, radiation, or surgery.

If lymphadenitis is not treated properly the formation of abscesses may occur. These abscesses contain fluid, white blood cells, bacteria, dead tissue, and other materials. When such abscesses occur, a doctor usually drains them, along with prescribing antibiotics. In addition, when a bacterial infection occurs within the lymphatic system, such a condition can lead to **sepsis**, which is a serious infection found within the bloodstream. Hospitalization is usually required because intravenous antibiotics are needed to combat the widespread infection.

Supportive care

Supportive care of lymphadenitis includes resting the affected limb and treating the area with hot, moist compresses.

Surgery

Cellulitis associated with lymphadenitis should *not* be treated surgically because of the risk of spreading the infection. Pus is drained only if there is an **abscess** and usually after the patient has been started on antibiotic treatment. In some cases, a biopsy of an inflamed lymph node is necessary if a diagnosis has not been made and response to treatment has not occurred.

Prognosis

The prognosis for a full recovery is good if the patient is treated promptly with antibiotics. In most cases, the infection can be brought under control in three or four days. However, it may take several weeks, or even months, for the swelling to subside and the area to return to normal. Patients with untreated lymphadenitis may develop blood poisoning (septicemia), which is sometimes fatal.

Prevention

Prevention of lymphadenitis depends on prompt treatment of bacterial and viral infections. The practice of living healthy, with special concern on good hygiene, is especially helpful in preventing lymphadenitis, as it is in any infection.

Resources

BOOKS

Feign, Ralph D. et al., editors. *Feign ' Cherry' Textbook of Pediatric Infectious Diseases*. Philadelphia: Saunders/Elsevier, 2009.

Ioachim, Harry L, and L. Jeffrey Medeiros. *Ioachim's Lymph Node Pathology*. Philadelphia: Wolters Kluwer Health/Lippincott Williams and Wilkins, 2009.

McPhee, Stephen, and Maxine A. Papadakis, editors. *Current Medical Diagnosis and Treatment, 2009*. New York: McGraw-Hill Medical, 2008.

OTHER

Lymphadenitis. Medline Plus, National Library of Medicine and National Institutes of Health. (May 30, 2009), www.nlm.nih.gov/medlineplus/ency/article/001301.htm. (accessed August 5, 2010).

Swollen Lymph Nodes. Mayo Clinic. (January 24, 2009), www.mayoclinic.com/health/swollen-lymph-nodes/DS00880. (accessed August 4, 2010).

Rebecca J. Frey, PhD

Lymphangiography

Definition

Lymphangiography, or lymph node angiogram, is a test which utilizes x-ray technology, along with the injection of a contrast agent, to view lymphatic circulation and lymph nodes for diagnostic purposes.

Purpose

The lymphatic system is a one way circulation that channels tissue fluid back into the heart. The watery fluid called lymph seeps out of the blood into tissues, and while journeying back to the heart, it picks up germs, **cancer** cells, and some waste products. Lymph passes through the lymph nodes, which are major arsenals of immune defense that attack germs carried in the lymph. Cancer cells are also subject to attack in lymph nodes.

Cancers of the lymph system, such as Hodgkin's disease and non-Hodgkin's lymphomas, spread throughout the body. Treatment often depends upon finding all the disease and directing radiation to each location. Planning other kinds of treatment, such as surgery or **chemotherapy**, may also require that the full extent of the disease be known.

The lymphatic circulation may become clogged by infection, injury, or several other types of cancer that have spread through lymphatic channels. Swelling, sometimes massive, can result from blocked lymphatics. The most outstanding example of this is the tropical disease **filariasis**, which results in the swelling of the legs termed elephangiasis.

Lymphangiography gives precise information on the extent and location of lymph vessels and lymph nodes. Oftentimes, it is performed to evaluate the extent of a lymphatic cancer. Rarely, it is a tool, which aids surgeons attempting to reconstruct the lymphatics.

Precautions

Lymphangiography should not be performed on patients with dye or shellfish **allergies** or on patients with chronic lung disease, **kidney disease**, heart disease, or **liver disease**.

Description

A lymphangiogram begins by injecting a blue dye into a hand or foot. The lymph system picks up dye, which in turn will highlight the lymph vessels. This process may take a full day. When the lymphatic channel is clearly visible, the radiologist will insert an even tinier needle into that vessel and inject a contrast agent. X rays outline the journey of the contrast agent as it travels to the heart through lymph vessels and nodes.

KEY TERMS

Contrast agent—A substance that makes shadows on x rays.

Filariasis—A tropical disease caused by worms that live in lymph channels.

Hodgkin's disease—A cancer of the lymphatic system.

Lymphoma—A type of lyphatic cancer.

Preparation

Unless a dye allergy is suspected, no special preparation is need. If an allergy is suspected, a non-ionic contrast agent can be administered instead.

Aftercare

Prior to suture removal seven to 10 days after the procedure, the patient should watch for any sign of infection around the site.

Risks

Lipid **pneumonia** can occur if the contrast agent penetrates the thoracic duct. An allergic reaction to the contrast agent is possible, causing a range of symptoms that can range from innocuous to life threatening.

Resources

BOOKS

Tretbar, Lawrence, L., et al., eds. *Lymphedema: Diagnosis and Treatment*. Berlin: Springer, 2007.

J. Ricker Polsdorfer, MD

Lymphedema

Definition

Lymphedema involves blockage of the lymph vessels, with a resulting accumulation of lymphatic fluid in the interstitial tissues of the body.

Demographics

Lymphedema affects approximately 100 million people worldwide, including at least 3 million people in the United States. It is estimated to affect approximately 10–40% of women affected by **breast cancer**. Women who undergo surgery to remove lymph nodes under the arm (axillary area) are at risk for lymphedema, as are those who have radiation in the underarm area.

Description

The lymphatic system consists of lymph vessels and lymph nodes throughout the body. The lymph vessels collect lymphatic fluid, which consists of protein, water, fats, and wastes from cells. The lymph vessels transport the fluid to the lymph nodes, where waste materials and foreign materials are filtered out from the fluid. The fluid is then returned to the blood. When the vessels are damaged or missing, the lymph fluid cannot move freely throughout the system but accumulates. This accumulation of fluid results in abnormal swelling of the arm(s) or leg(s), and occasionally swelling in other parts of the body.

Causes

Primary lymphedema is an inherited condition, where the patient is born without lymph vessels and nodes. The swelling associated with primary lymphedema usually occurs during adolescence and affects the foot or calf. A rare form of primary lymphedema, called Milroy's Disease, occurs in **pregnancy**. However, secondary lymphedema, or acquired lymphedema, develops as a result of an injury to the lymph system. Specific causes include surgical treatments for certain types of cancers, especially those cancers that currently require the removal of lymph nodes. Radiation treatment for **cancer** or for some AIDs-related diseases such as Kaposi-Sarcoma may also result in lymphedema, as radiation may damage or destroy lymph nodes or cause the formation of scar tissue that can interrupt the normal flow of the lymphatic fluid. Specific cancers and their treatment that may result in lymphedema include **malignant melanoma**, breast (in both women and men), gynecological, head and neck, prostate, testicular, bladder, and **colon cancer**. Other causes of lymphedema include trauma to the lymphatic system from **burns**, **liposuction**, tattooing, injuries, surgery, radiation, **obesity**, heart or circulatory disease, and **multiple sclerosis**. Lymphedema in people at risk may not develop the condition immediately, but develop the condition weeks, months, or even years later. Aircraft travel has been linked to the development of lymphedema in patients after cancer surgery, possible due to the decreased cabin pressure.

In Western countries, one of the most common causes of lymphedema is **mastectomy** with axillary dissection (removal of the breast and underarm lymph tissue for treatment of breast cancer), which may result in lymphedema of the breast, underarm, or arm on the side of the surgery in 10–20% of patients. This occurs because the lymphatic drainage of the arm passes through the axilla (armpit), and tissue in the axilla is removed during the mastectomy. To reduce the risk of developing lymphedema after breast cancer treatment, there is an alternative treatment that avoids axillary lymph node dissection. Sentinel **lymph node biopsy** is a new diagnostic procedure used to determine whether the breast cancer has spread (metastasized) to axillary lymph nodes. A sentinel lymph node biopsy requires the removal of only one to three lymph nodes for close review by a pathologist. If the sentinel nodes do not contain tumor (cancer) cells, this may eliminate the need to remove additional lymph nodes in the axillary area. Early research on this technique indicates that sentinel lymph node biopsy may be associated with less **pain** and fewer complications than standard axillary dissection. Because the procedure is so new, long term data are not yet available. However, there is still a risk for developing lymphedema because of follow-up radiation treatments or **chemotherapy**, which may also damage the lymph nodes.

Symptoms of lymphedema include:

- swelling of an affected limb, which may develop gradually or suddenly
- tightness of the skin and a feeling of heaviness in the affected area
- discomfort or a feeling of "pins and needles" in the affected area
- pitting edema, which can be identified by observing a temporary indentation in the swollen area when pressure is placed on the affected area
- aching in the adjacent shoulder or hip due to the increasing weight of the swelling limb
- tight fitting of a ring, wristwatch, or bracelet, without a gain in weight.

Diagnosis

In 90% of the cases, lymphedema is diagnosed through observations, measurements, and symptoms. The remaining 10% require the use of more complex diagnostic tests such as lymphoscintigraphy. Lymphoscintigraphy is a technique in which a radioactive

KEY TERMS

Axillary nodes—Lymph nodes found in the armpit that drain the lymph channels from the breast.

Clinical aromatherapy—Aromatherapy is the therapeutic use of plant-derived, aromatic essential oils to promote physical and psychological well-being. It is sometimes used in combination with massage and other therapeutic techniques as part of a holistic treatment approach.

Debulking—General term used for surgeries in which subcutaneous tissue is removed from a lymphodemous limb.

Fibrosis—Formation of fibrous tissue as a reaction or as a repair process; may occur due to treatment and/or disease. in lymphedema condition known as hardening of the limb with resulting restriction of circulatory flow, increased infection, and weeping sores.

Fibrotic—Pertaining to or characterized by fibrosis. In dermatological description, "fibrotic" would be used to describe leathery, bound-down, or thickened, scarred skin.

Interstitial fluid—The fluid between cells in tissues. Referred to as the liquid substance of the body.

Interstitial space—The fluid filled areas that surround the cells of a given tissue; also known as tissue space.

Long-stretch bandages—Specialized bandages, similar to an Ace bandage, that have 100 to 200% stretch.

Low-stretch bandage—Specialized bandages, with 30 to 90% stretch, that are used to obtain the correct compression during the treatment of lymphedema; also known as short-stretch bandages.

Lymph—The almost colorless fluid that bathes body tissues and is found in the lymphatic vessels that drain the tissues of the fluid that filters across the blood vessel walls from blood. Lymph carries antibodies and lymphocytes (white blood cells that help fight infection) that have entered the lymph nodes from the blood.

Lymph nodes—Small bean-shaped organs of the immune system, distributed widely throughout the body and linked by lymphatic vessels. Lymph nodes are garrisons of B, T, and other immune cells.

Lymph System—When sickness or infection invades the body, the immune system is the first line of defense. A big part of that defense is the lymph system. Lymph is carried through the body by lymph vessels that have valves and muscles to help move the fluid. Along the route are lymph nodes that serve as filters for harmful substances. This network of vessels and nodes together is called the lymph system.

Lymphatic fluid—The clear fluid found outside the cells which bathes the tissues. It is collected, filtered, and transported by the lymphatic system from around the tissues to the blood circulatory system. Fluid that collects as a result of lymphedema.

Nail beds—The underlying connective tissue that nourishes the finger and toenails.

Pitting edema—When a swollen area is pressed, the pressure leaves an indentation (pit) that takes time to fill back in.

Sentinel node biopsy—A newer procedure performed in order to determine whether breast cancer has spread to auxiliary (underarm) lymph nodes. A blue radioactive tracer and/or blue dye is injected into the area of the breast tumor. The lymphatic vessels carry the dye or radioactive material, to a "sentinel node". This sentinel node is thought to be the first lymph node receiving fluid from the tumor and the one most likely to contain cancer cells if the cancer has spread. Only if the sentinel node contains cancer cells are more lymph nodes removed.

Skin contracture—A permanent tightening of the skin that prevents normal movement of the associated body part and that can cause permanent deformity. A contracture develops when the normally elastic connective tissues are replaced by inelastic fibrous tissue. This makes the affected area resistant to stretching and prevents normal movement.

substance that concentrates in the lymphatic vessels is injected into the affected tissue and is mapped using a gamma camera, which images the location of the radioactive tracer. **Magnetic resonance imaging** (MRI), computed tomography (CT) scanning, and duplex ultrasound are imaging techniques that are also sometimes used as diagnostic tools for lymphedema.

Persons who have developed lymphedema after cancer treatment should be checked for a diagnosis of possible reoccurrence of cancer, if they experience a sudden increase of swelling, since the tumor growth may be responsible for blocking lymphatic flow.

There are three stages associated with the diagnosis of lymphedema:

- Stage 1 (spontaneously reversible) - tissue is still at the pitting stage and soft to the touch. Upon waking in the morning, the limbs or affected areas are of normal or almost normal size.
- Stage 2 (spontaneously irreversible) - tissue is non-pitting and no longer soft to the touch, fibrosis begins to form, and the limbs increase in size.
- Stage 3 (lymphostatic elephantiasis) - swelling is irreversible and the affected areas are very swollen. The skin hardens and begins to break down, fibrosis is more extensive, and patients may need surgery to remove some of the swollen tissues.

Treatments

Lymphedema is a chronic condition that cannot be cured but can be improved with treatment. There are several major components of a lymphedema treatment program, which should be administered by the health care provider in cooperation with a physical therapist trained in lymphedema treatment. Complete Decongestive Therapy (CDT; also referred to as Complex Decongestive Therapy (CDT) or as Complete Decongestive Physiotherapy (CDP)) combines manual lymph drainage (MLD) with compression techniques and with patient education on self-care needs. The goals of the treatment program are to:

- remove the stagnant lymph fluids out of the tissues
- reduce and help control swelling
- soften fibrotic tissue
- improve the overall health of the patient

However, some lymphedema specialists feel that lymphedema patients with metastatic cancer should not be treated with CDT, to prevent the spreading of the cancer.

MLD was developed in 1932 in Denmark by a doctor and his wife. It was widely used in Europe and now is accepted as a therapy for lymphedema patients in the United States. In MLD a series of rhythmic, light strokes are made in a specific sequence along the lymphatic vessels and the adjoining tissues. These movements remove the lymph fluids from the tissues and return them to the circulatory system, thus reducing swelling in the affected area.

Compression techniques include the use of compression garments, compression aids, and compression **bandages**. These techniques encourage natural drainage and prevent swelling by supporting tissues in a way that aids in drainage. Compression garments are knit, stretch sleeves or stockings. Compression aids are custom-fitted sleeves, stockings, or pads made of fabric-covered foam. Bandages are an effective and flexible means of compression. They work when the patient is active or is resting and can easily be adjusted to fit changing limb sizes. However, the bandage should be a special type of short-stretch bandage and not the long-stretch bandage that is commonly known as Ace bandages. Only persons who are trained in lymphedema therapy should tape or wrap swollen areas.

Self-care techniques are practiced by the patient or his or her caregiver at home, between visits to the therapist. Self-care techniques include self-massage, skin care to maintain healthy tissue, nutritious diet, and **exercise** to increase lymph flow, increase mobility, and to improve the patient's general health.

Exposure to extreme heat has the potential to increase lymphedema swelling, so an affected person or a person at risk of developing lymphedema should avoid hot tubs, saunas, and steam rooms.

To keep the affected extremities as healthy as possible, a person with lymphedema should keep the swollen areas clean and avoid heavy lifting and pulling as well as avoid any type of trauma, such as cuts, **bruises**, **sunburn** or other burns, injections, **sports injuries**, insect **bites**, or cat scratches. Some doctors and lymphedema therapists recommend that a person with lymphedema use a preventative course of **antibiotics** when having dental treatment, that is, starting antibiotics several days before the appointment and continuing several days afterwards. A person at risk of developing lymphedema (for example, a woman who has been treated for breast cancer) should also observe the same type of precautions to prevent the development of the condition.

If infections occur, then all treatments for lymphedema should be discontinued while the infection is present, and the infection treated with antibiotics.

Surgery is sometimes used to remove excess tissue ("debulking") if the swollen limb becomes so large and heavy as to interfere with movement.

Exercise is important for a person with lymphedema, but only in moderation. If the extremity starts to ache, the person should lie down and elevate the swollen limb. Recommended exercises include walking, swimming, light aerobics, bike riding, and **yoga**.

Persons with lymphedema should wear a lymphedema alert bracelet or necklace for safety during a medical emergency, explaining the risk of infections. They may also benefit from counseling and membership in support groups to deal with the psychological impact of the disease. Sometimes patients with lymphedema will be denied insurance coverage for treatment; as a result patient advocacy groups in 2005

are attempting to get a law passed through the U.S. Congress guaranteeing insurance coverage for lymphedema.

Alternative and complementary therapies

The use of clinical **aromatherapy** in conjunction with CDT may improve the quality of life for persons with lymphedema. Clinical aromatherapy involves the use of essential oils to improve the functioning of the immune system, for the immune system is closely associated with the lymphatic system. Also a massage oil comprised of a blend of frankincense, grapefruit, hyssop, and lavender, may be used to soften scarred and fibrotic tissues. Radiation treatments can cause skin **contractures**, which can be helped by massage with a blend of cajeput, frankincense, hyssop, lavender, sage, and tea tree. Radiation can also have adverse effects on the bowel, resulting in poor bowel functioning, scarring, and activity restrictions. Massaging the abdomen with a blend of grapefruit, fennel, helichrysum, lavender, myrrh, and sage may improve intestinal functions. When compression techniques are used, the underlying skin can be treated with a blend of bay laurel, chamomile, geranium, helchrysum, lavender, patchouli, and vetiver in a combination of castor oil, safflower oil, and grapeseed oil as carrier oils. Good skin care is important in preventing infections. Body oils that contain cajeput, cypress, lavender, marjoram, and rosewood can be applied after bathing to keep the skin moist and healthy. Finger nail beds can be a portal of entry for infections, so can be kept moist with an essential oil blend of chamomile, geranium, lavender, lemon, sage, tea tree, and ylang ylang.

Prognosis

Lymphedema is a very serious condition. There is no cure for lymphedema and once it develops, it can be a long-term, uncomfortable, and sometimes painful condition requiring daily treatment. When lymphedema is not treated, the protein-rich fluid continues to accumulate, leading to even more swelling and hardening (referred to as fibrosis) of the tissues. This fluid is a good culture medium for bacteria, thus resulting in reoccurring infections when there are injuries to the skin, decrease or loss of functioning of the affected limbs, and skin breakdown. Infections, referred to lymphangitis, can affect the connective tissue under the skin. Repeated infections may result in scarring, which in turn makes the tissue susceptible to more swelling and infection. Over time, these infections result in tissue hardening (i.e., fibrosis), which is a characteristic of advanced chronic lymphedema. In very severe cases, untreated lymphedema may even result in a rare form of lymphatic cancer called lymphangiosarcoma.

Resources

BOOKS

Bardia, Aditya and Eric Seifter. *Johns Hopkins Patients' Guide to Lymphoma*.Sudbury, MA: Jones and Bartlett Publishers, Inc, 2010.

Burt, Jeannie, and White, Gwen. *Lymphedema: A Breast Cancer Patient's Guide to Prevention and Healing,* 2nd ed. Alameda, CA: Hunter House, 2005.

French, Ramona Moody. *Milady's Guide to Lymph Drainage Massage*. Clifton Park, NY: Milady Publishing, 2003.

Maisano, Gina. *Intimacy After Breast Cancer: Dealing With Your Body, Relationships and Sex*. Garden City Park, NY: Square One Publishers, 2010.

PERIODICALS

Heckathorn, Peg. *"Use of Aromatherapy in Lymphedema Management." Lymph Link*. Oct-Dec. 2003, Vol. 15, No. 4, 6-12

OTHER

Lymph Notes, an online information resource and support group for those with lymphedema and for the family, friends, and therapists who care for them. Web site: www.lymphnotes.com/index.php

Lymphatic Research Foundation. http://www.lymphaticresearch. org

Lymphedema Awareness Foundation. http://www.elymphnotes. org/

Lymphedema People. Web site: www.lymphedemapeople.com/

National Lymphedema Network, Latham Square Building, Suite 1111, 1611 Telegraph Avenue, Oakland, CA 94612-2138. Telephone: (800) 541-3259. Fax: (510) 208-3110. Web site: www.lymphnet.org

Judith Sims, Ed.D.
Laura Jean Cataldo, RN, Ed.D.

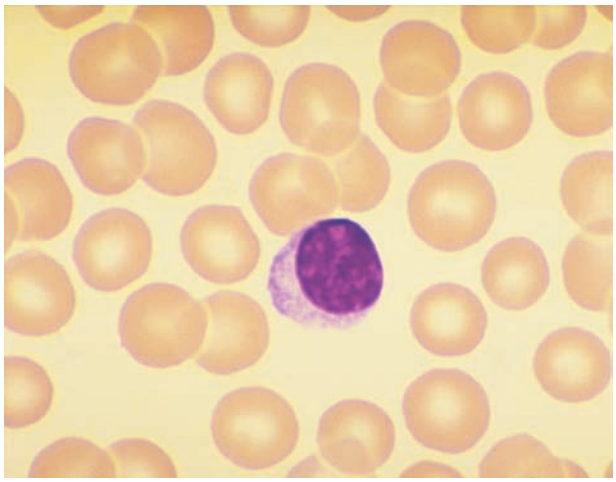
Lymphocyte typing

Definition

Lymphocyte typing focuses on identifying the numbers and relative percentages of lymphocytes in an individual's bloodstream. Lymphocytes, primarily T cells and B cells, are types of white blood cells, the underlying supports of the immune system in the bloodstream.

Purpose

Determining the numbers and relative percentages of T cells and B cells provides information on



A lymphocyte cell. *(© Lester V. Bergman/Corbis.)*

KEY TERMS

Immune system—The body's system of defenses against infectious diseases.

Lymphocytosis—A condition in which the number of lymphocytes increases above normal levels.

Lymphopenia—A condition in which the number of lymphocytes falls below normal levels.

White blood cell—A class of cells in the blood that form the foundation of the body's immune system.

the state of a person's immune system. By comparing these values to normal numbers and percentages, the presence of disease and the side effects of certain drugs can be revealed. Lymphocyte typing can also show whether a person has been exposed to certain poisonous substances.

Description

To do a **white blood cell count**, a small amount of blood is drawn from a vein. The total number of white blood cells is calculated, either through microscopic examination of a blood smear or by using automated counting equipment. For a white blood cell count with differential, 100 white blood cells are counted and the proportion of each type is calculated. Since T cells and B cells have similar appearances, a differential can only give the proportion of lymphocytes in the blood, not the proportion of specific lymphocyte types.

For more specific information on B cells and T cells, it is necessary to divide the blood into its separate components. In this procedure, a tube of blood is placed in a centrifuge, a piece of equipment that spins the tube in circles at high speed. The force generated by the spinning causes the various elements in the bloodstream to settle at different levels of the tube.

The lymphocytes are extracted from the tube and treated with special dyes, or stains. Each stain is equipped with an antibody portion that adheres to a specific type of lymphocyte, such as a B cell or a T cell. The stains make the cells visible to an automated counting machine, called a flow cytometer. Based on the number of times the machine detects a particular stain, it can calculate the number of the associated cell type. This procedure can also be used to classify T cells and B cells into their subtypes.

Preparation

If possible, a person should avoid eating a heavy meal within hours of the test or engaging in strenuous **exercise** for the 24 hours preceding the blood test.

Results

In general, normal levels of white blood cells vary slightly by age and gender. Normal values are lower in children under the age of 15 and in young adults between the ages of 20 and 30. After age 30, men have slightly higher levels of white blood cells than women.

Normal adult levels of white blood cells are 4,500–11,000 cells per microliter of blood. Lymphocytes account for approximately 25–45% of the total white blood cell count; the normal range is 1,000–4,800 lymphocytes per microliter of blood. Of the total lymphocytes, 60–80% are T cells and approximately 15% are B cells. (There are two other types of lymphocytes; natural killer and K-type; that constitute a minor proportion of the total lymphocyte numbers.)

Abnormal results

A higher-than-normal level of lymphocytes is called lymphocytosis. Lymphocytosis occurs if a person has a viral, bacterial, or other type of infection. It can also occur with certain blood disorders, such as leukemia.

Lower-than-normal levels of lymphocytes is called lymphopenia. Lymphopenia can be an indicator of certain cancers, bone marrow failure, or immune system deficiency. Medical treatments, such as **chemotherapy** and **radiation therapy**, can also deplete the body's supply of lymphocytes, as can exposure to poisonous substances.

Resources

BOOKS

Corbett, Jane Vincent. *Laboratory Tests and Diagnostic Procedures with Nursing Diagnoses*. 6th ed. Upper Saddle River, NJ: Pearson/Prentice Hall, 2004.

Turgeon, Mary Louise. *Immunology & Serology in Laboratory Medicine*. 4th ed. St. Louis: Mosby, 2009.

Julia Barrett

Lymphocytic choriomeningitis

Definition

Lymphocytic choriomeningitis (LCM) is a viral infection of the membranes surrounding the brain and spinal cord and of the cerebrospinal fluid.

Description

Lymphocytic choriomeningitis virus infection is relatively rare and recovery usually occurs spontaneously within a couple of weeks. Many cases are probably not even identified because the symptoms range from extremely mild to those resembling severe flu. A few patients develop symptoms of **meningitis**. In some rare cases, the LCM viral infection can spread throughout the central nervous system, and may even be fatal.

Causes and symptoms

LCM is caused by an arenavirus, which is an RNA virus and is a mild cousin in the family containing the much more threatening arenaviruses that cause hemmorrhagic **fever**. Humans acquire LCM virus from infected rodents by coming in contact with the animals or their excretions. Exposure to the virus is not as unlikely to occur as it seems, because the viral hosts can be common house mice and even pets, such as hamsters and chinchillas. Most cases of LCM occur in fall and winter, when mice seek warmth inside dwellings. Food and dust can become contaminated by the excretions of rodents infected with LCM virus. In 1997, French scientists alerted physicians to suspect LCM viral infection in people who had contact with Syrian hamsters.

The symptoms of LCM occur in two phases. The first (prodrome) stage can produce fever, chills, muscle aches, **cough**, and **vomiting**. In the second phase, characteristic meningitis symptoms of **headache**, stiff neck, listlessness, and **nausea and vomiting** may occur. In adults, complications are rare and recovery may even occur before the second phase.

KEY TERMS

Prodrome—Symptom(s) experienced prior to the onset of a disease. For example, visual disturbances may precede and signal the onset of a migraine headache.

The virus is not spread from person to person, except through **pregnancy**. LCM virus is one of the few viruses that can cross the placenta from mother to child during pregnancy and may be an underrecognized cause of congenital infection in newborns. Infection with cytomegalovirus, *Toxoplasma gondii*,or LCM virus can appear similar enough in infants to be confused when diagnosed. In cases that have been recognized among infants, LCM viral infection has a high mortality rate (about one-third of the babies studied died).

Diagnosis

LCM can be distinguished from bacterial meningitis by the history of prodrome symptoms and the period of time before meningitis symptoms begin, which is about 15–21 days for LCM.

Treatment

No antiviral agents exist for LCM virus. Treatment consists of supporting the patient and treating the symptoms until the infection subsides, generally within a few weeks.

Jill S. Lasker

Lymphocytic leukemia, acute *see* **Leukemias, acute**

Lymphocytic leukemia, chronic *see* **Leukemias, chronic**

Lymphocytopenia

Definition

Lymphocytopenia is a condition marked by an abnormally low level of lymphocytes in the blood.

Lymphocytes are a specific type of white blood cell with important functions in the immune system.

Description

Lymphocytes normally account for 15–40% of all white cells in the bloodstream. They help to protect the body from infections caused by viruses or fungi. They also coordinate the activities of other cells in the immune system. In addition, lymphocytes fight **cancer** and develop into antibody-producing cells that neutralize the effect of foreign substances in the blood.

Lymphocytopenia is the result of abnormalities in the way lymphocytes are produced, make their way through the bloodstream, or are lost or destroyed. These conditions can result from congenital or drug-induced decreases in the body's ability to recognize and attack invaders.

Causes and symptoms

Lymphocytopenia has a wide range of possible causes:

- AIDS and other viral, bacterial, and fungal infections
- Chronic failure of the right ventricle of the heart (this chamber of the heart pumps blood to the lungs)
- Hodgkin's disease and cancers of the lymphatic system
- A leak or rupture in the thoracic duct. The thoracic duct removes lymphatic fluid from the legs and abdomen.
- Leukemia
- Side effects of prescription medications
- Malnutrition. Diets that are low in protein and overall calorie intake may cause lymphocytopenia.
- Radiation therapy
- High stress levels
- Trauma.

The symptoms of lymphocytopenia vary. Lymphocytes constitute only a fraction of the body's white blood cells, and a decline in their number may not produce any symptoms. A patient who has lymphocytopenia may have symptoms of the condition responsible for the depressed level of lymphocytes.

Diagnosis

Lymphocytopenia is most often detected when blood tests are performed to diagnose other diseases.

KEY TERMS

B lymphocyte—A type of lymphocyte that circulates in the blood and lymph and produces antibodies when it encounters specific antigens. B lymphocytes are also called B cells.

Lymph—A clear yellowish fluid circulated by the lymphatic system. The lymph carries mostly lymphocytes and fats.

Lymphocyte—A specific type of white blood cell that is important in the production of antibodies.

Treatment

Treatment for lymphocytopenia is designed to identify and correct the underlying cause of the condition.

Drug-depressed lymphocyte levels usually return to normal a few days after the patient stops taking the medication.

A deficiency of B lymphocytes, which mature into antibody-producing plasma cells, can result in abnormally low lymphocyte levels. When the number of B lymphocytes is low, the patient may be treated with **antibiotics**, antifungal medications, antiviral agents, or a substance containing a high concentration of antibodies (**gamma globulin**) to prevent infection.

It is not usually possible to restore normal lymphocyte levels in **AIDS** patients. Drugs like AZT (azidothymidine, sold under the trade name Retrovir) can increase the number of helper T cells, which help other cells wipe out disease organisms.

Prognosis

Very low levels of lymphocytes make patients vulnerable to life-threatening infection. Researchers are studying the effectiveness of transplanting bone marrow and other cells to restore normal lymphocyte levels. **Gene therapy**, which uses the body's own resources or artificial substances to counter diseases or disorders, is also being evaluated as a treatment for lymphocytopenia.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Maureen Haggerty

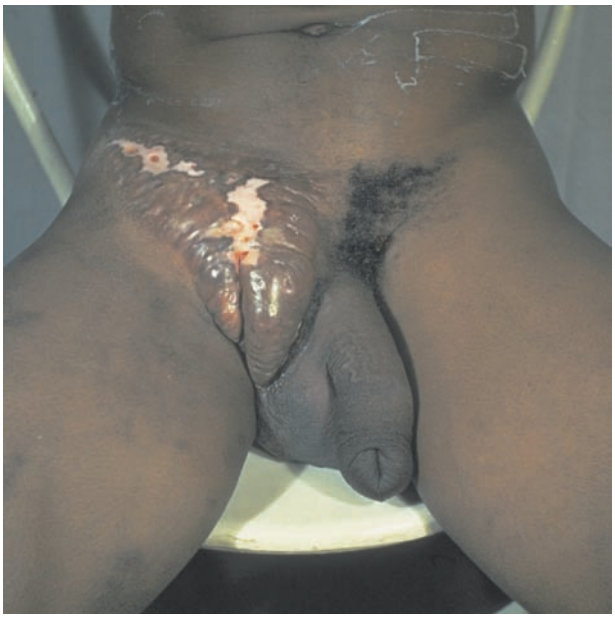
Lymphogranuloma venereum

Definition

Lymphogranuloma venereum (LGV) is a sexually transmitted systemic disease (STD) caused by a parasitic organism closely related to certain types of bacteria. It affects the lymph nodes and rectal area, as well as the genitals, in humans. The name comes from two Latin words that mean a swelling of granulation tissue in the lymph nodes resulting from sexual intercourse. Granulation tissue is tissue that forms during wound or ulcer healing that has a rough or lumpy surface.

Description

Although LGV is easily treated in its early stages, it can produce serious complications in its later stages. LGV is most likely to occur among people living in tropical or subtropical countries and among military personnel or tourists in countries or large cities with high rates of the disease. Prostitutes play a major role in carrying and transmitting LGV, as was documented during an outbreak in Florida in the late 1980s. There are about 1000 documented cases of LGV in the United States in an average year.



This man suffers from lymphogranuloma venereum, a venereal disease that is caused by the bacterium *Chlamydia trachomatis.* *(© Dr. Milton Reisch/Corbis.)*

Causes and symptoms

LGV is caused by *Chlamydia trachomatis*, a globe-shaped parasitic organism that reproduces only inside of living cells. *C. trachomatis* has 17 subtypes and is responsible for a wide range of infections in both men and women; however, only subtypes L1, L2, and L3 cause lymphogranuloma venereum. The parasite has a two-part lifecycle. In the first stage, it is inert and can survive outside of cells. In its second stage, it lacks a cell wall and actively reproduces after gaining entry to a cell. As the chlamydia organism reproduces inside the cell, it pushes the nucleus aside and forms an inclusion that can be identified with tissue staining. LGV differs from other diseases caused by *C. trachomatis* in that it affects the body's lymphatic system and not just the moist tissues of the genital region. In humans, the chlamydia organism is transmitted through vaginal or anal intercourse, oral sex, or contact with fluid from open ulcers or infected tissues.

Lymphogranuloma venereum has three stages. In its primary stage, the disease is more likely to be detected in men; it may go unnoticed in women. After an incubation period of four to 30 days, a small painless ulcer or blister develops in the genital area. Second-stage LGV develops between one and six weeks later. In this stage, the infection spreads to the lymphatic system, forming buboes (swellings) in the lymph nodes of the groin area. The buboes often merge, soften, and rupture, forming sinuses and fistulas (hollow passages and ducts) that carry an infectious bloody discharge to the outside of the body. Patients with second-stage LGV may also have **fever**, **nausea**, headaches, pains in their joints, skin **rashes**, and enlargement of the spleen or liver. Third-stage LGV, which is sometimes called anogenitorectal syndrome, develops in about 25% of patients. In men, this stage is usually seen in homosexuals. Third-stage LGV is marked by rectal **pain**, **constipation**, a discharge containing pus or bloody mucus, and the development of strictures (narrowing or tightening of a body passage) in the rectum or vagina.

LGV can have a number of serious complications. *C. trachomatis* infections of any subtype are associated with long-term fertility problems in women. Strictures in the rectum can completely close off the lower bowel, producing eventual rupture of the bowel and inflammation of the abdominal cavity. The patient can develop chronic abscesses or fistulae in the anal area or in the vagina in women. Long-term blockages in the lymph nodes can produce **elephantiasis**, a condition in which the patient's upper legs and groin area become greatly enlarged. Patients with chronic LGV infection

KEY TERMS

Anogenitorectal syndrome—Another name for third-stage LGV.

Aspiration—A procedure in which pus or other fluid is removed from a body cavity through a hollow needle connected to a syringe.

Bubo—An inflamed swelling inside a lymph node, characteristic of second-stage LGV.

Elephantiasis—Abnormal enlargement of the legs and groin area caused by blockage of the lymphatic system, as a complication of LGV.

Fistula—A passageway formed by a disease or injury that drains fluid from an infected area to the outside or to other parts of the body.

Lymph—A clear yellowish fluid that circulates throughout the body, carrying white blood cells and fats. The system that produces and circulates lymph is called the lymphatic system; it includes lymph vessels, lymph nodes, the thymus gland, and the spleen.

Proctitis—Inflammation of the anus and rectum.

Stricture—An abnormal narrowing or tightening of a body passage. LGV can cause strictures to form in the patient's rectum, or in the vagina of female patients.

have a higher risk of developing **cancer** in the inflamed areas.

Chronic LGV can be reactivated in patients who become infected with the **AIDS** virus. These patients develop open ulcers in the groin that are difficult to treat.

Diagnosis

The diagnosis of LGV is usually made on the basis of the patient's history, careful examination of the genital area and lymph nodes, and blood tests or cultures to confirm the diagnosis. In the early stages of the disease, the doctor will need to distinguish between LGV and such other STDs as **syphilis** and herpes. If the patient has developed buboes, the doctor will need to rule out **tuberculosis**, **cat-scratch disease**, bubonic **plague**, or **tularemia** (a disease similar to plague that is carried by rabbits and squirrels). If the patient has developed rectal strictures, the doctor will need to rule out tumors or **colitis**.

There are several blood tests that can be used to confirm the diagnosis of LGV. The most commonly used are the complement fixation (CF) test and the microimmunofluorescence (micro-IF) tests. Although the micro-IF test is considered more sensitive than the CF test, it is less widely available. An antibody titer (concentration) of 1:64 or greater on the CF test or 1:512 or greater on the micro-IF test is needed to make the diagnosis of LGV. In some cases, the diagnosis can be made from culturing *C. trachomatis* taken from samples of tissue fluid from ulcers or buboes, or from a tissue sample from the patient's rectum.

Treatment

LGV is treated with oral **antibiotics**, usually tetracycline or doxycycline for 10–20 days, or erythromycin or trimethoprim sulfamethoxazole for 14 days. Pregnant women are usually treated with erythromycin rather than the **tetracyclines**, because this class of medications can harm the fetus.

Patients who have developed second- and third-stage complications may need surgical treatment. The doctor can treat buboes by withdrawing fluid from them through a hollow needle into a suction syringe. This procedure is called aspiration. Fistulas and abscesses also can be treated surgically. Patients who develop elephantiasis are usually treated by plastic surgeons. Patients with rectal strictures may need surgery to prevent bowel obstruction and rupture into the abdomen.

Prognosis

The prognosis for recovery for most patients is good, with the exception of AIDS patients. Prompt treatment of the early stages of LGV is essential to prevent transmission of the disease as well as fertility problems and other serious complications of the later stages.

Prevention

Prevention of lymphogranuloma venereum has four important aspects:

- Avoidance of casual sexual contacts, particularly with prostitutes, in countries with high rates of the disease.

- Observance of proper safeguards by health professionals. Doctors and other healthcare workers should wear gloves when touching infected areas of the patient's body or handling soiled dressings and other contaminated items. All contaminated materials and instruments should be double-bagged before disposing.
- Tracing and examination of an infected person's recent sexual contacts.
- Monitoring the patient for recurring symptoms for a period of six months after antibiotic treatment.

Resources

BOOKS

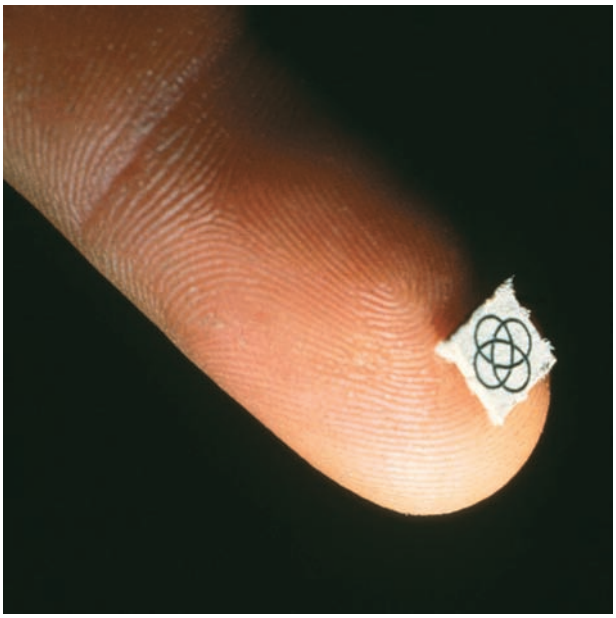
McPhee, Stephen, and Maxine Papadakis. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw–Hill Medical, 2009.

Rebecca J. Frey, PhD

Lymphomas *see* **Hodgkin's disease**

Lymphopenia *see* **Lymphocytopenia**

Lymphosarcomas *see* **Malignant lymphomas**



LSD on blotter paper. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Lysergic acid diethylamide (LSD)

Definition

Lysergic acid diethylamide (LSD), also known as "acid," belongs to a class of drugs known as hallucinogens, which distort perceptions of reality. LSD is the most potent mood and perception-altering drug known: doses as small as 30 micrograms can produce effects lasting six to 12 hours.

Purpose

In the United States, LSD has no accepted medical use and its manufacture and possession are illegal.

Description

LSD is produced synthetically from ergot, a fungus that grows on rye grass and some grains. This odorless, colorless, and slightly bitter-tasting chemical can be absorbed through the skin, but is usually taken orally. It is commonly distributed in small squares of drug-soaked absorbent paper which are chewed and swallowed. LSD and other hallucinogen use by secondary school students has decreased since 1998, but has increased among older teens and young adults attending dance clubs, raves, and concerts, according to the National Institute on Drug **Abuse**.

LSD alters perceptions by disrupting the action of serotonin, a neurotransmitter. How this happens is unknown. Its effects are most prominent in the cerebral cortex, the brain area involved in mood and perception, and the locus ceruleus, an area in the brain stem where sensory signals converge from all parts of the body. Mescaline and psilocybin, natural hallucinogens resembling LSD, have been used in social and religious rituals for thousands of years.

After its discovery in 1938, LSD was used experimentally to treat neuroses, narcotic **addiction**, **autism**, **alcoholism**, terminal **cancer**, and to study psychoses and **schizophrenia**. Nearly 30 years after its discovery, manufacture, possession, sale and use of LSD was restricted in the United States under the Drug Abuse Control Amendment of 1965.

Effects from LSD begin within an hour and last up to 12 hours. It is absorbed from the intestinal tract, circulates throughout the body and brain, is metabolized in the liver, and excreted in the urine within 24 hours. Physical effects of LSD may include loss of appetite, sleeplessness, pupil dilation, **dry mouth**, salivation, **palpitations**, perspiration, **nausea**, **dizziness**,

KEY TERMS

Acid—Common street name for LSD.

Cerebral cortex—Brain region responsible for reasoning, mood, and perception.

Hallucinogen—A drug that distorts sensory perceptions and disturbs emotion, judgment, and memory.

Hallucinogen persisting perception disorder (HPPD)—The recurrence of LSD effects after the drug experience has ended.

Locus ceruleus—Area in the brain stem that processes sensory signals from all areas of the body.

Neurotransmitter—Chemical compound in the brain that transmits signals from one nerve cell to another.

Serotonin—A neurotransmitter that modulates the actions of other neurotransmitters in the brain.

blurred vision, **anxiety**, and increases in body temperature, heartbeat, blood pressure and blood sugar.

The major mental effects of LSD are emotional and sensory. Emotions may quickly shift from euphoria to confusion and despair. Users may simultaneously experience several emotions. Colors, smells, and sounds may be intense. Users may see sounds or smell colors. Time may seem to stand still. Users may have out-of-body sensations or feel as though their bodies have changed shape or merged with another person or object.

Precautions

Though it is a dangerous drug, LSD is not addictive like **cocaine**, amphetamines, heroin, alcohol, and nicotine. Its effects are unpredictable and vary with the amount taken and other underlying factors like personality, mood, expectations and environment. Users may have enjoyable experiences with some LSD trips and terrifying anxiety and despair with others. Most LSD-related deaths stem from panic reactions during intense LSD-triggered illusions.

Side Effects

There are two long-term effects associated with LSD use. One is **psychosis**; the other is "flashbacks.", hallucinogen persisting perception disorder (HPPD). The causes and how LSD produces these effects is unknown. They have been seen in chronic hallucinogen users with underlying personality problems and in individuals with no history of psychological disorders. Flashbacks can last from a few seconds to several hours. They generally involve seeing bright flashes, halos or trails attached to moving objects. LSD-induced psychosis may include dramatic mood swings, loss of cognitive and communication skills, and **hallucinations**.

According to the Drug Abuse Warning Network (DAWN), the number of LSD-related hospital emergencies is low compared to those related to cocaine, heroin, **marijuana**, **methamphetamine**, and other illicit drugs. One reason for this trend may be that LSD currently sold on the black market is less potent than in the past. LSD dose strengths tend to range from 20 to 80 micrograms today, compared to 100 to 200 micrograms reported during the 1960s and early 1970s.

Interactions

LSD flashbacks can be spurred by use of drugs such as marijuana. Preliminary evidence suggests serotonin reuptake inhibitors like Prozac and Zoloft may also exacerbate the LSD flashback syndrome.

ORGANIZATIONS

National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD, 20847-2345, (877) 726-4727, http://store.samhsa.gov/.

National Institute on Drug Abuse, 6001 Executive Blvd., Room 5213, Bethesda, MD, (301) 443-1124, information@nida.nih.gov, http://drugabuse.gov.

United States Drug Enforcement Administration, Dr Mailstop: AXS, 2401 Jefferson Davis Highway, Alexandria, VA, 22301, (202) 307-1000, http://www.dea.gov.

Ann Quigley
James E. Waun, MD, RPh

M

Macular degeneration

Definition

Macular degeneration is the progressive deterioration of a critical region of the retina called the macula. Age-related macular degeneration (ARMD) is the most common form of macular degeneration. It is also known as age-related maculopathy (ARM), aged macular degeneration, and senile macular degeneration.

Demographics

Macular degeneration is the most common cause of legal blindness in people over 60, and accounts for approximately 11.7% of blindness in the United States or about 10 million Americans. Estimates of the frequency of macular degeneration vary widely by how the disorder is defined by researchers. Some studies estimate that more than 20% of Americans over the age of 60 are affected by the disorder. Other studies, with more rigorous criteria, have found that about 2% of Americans over age 70 and 6% over age 80 have significant macular degeneration.

Caucasians are most likely to be affected by macular degeneration. Individuals of Asian or African descent are less frequently affected, although the incidence has begun to rise in some Asian countries. Individuals of Inuit descent are at a higher risk. Females are slightly more likely to develop macular degeneration than males. People who have light colored eyes tend to have more severe degeneration than those with dark colored eyes. The reason for this is not known. Individuals who smoke, are obese, or have cardiovascular problems are also at increased risk for macular degeneration.

Description

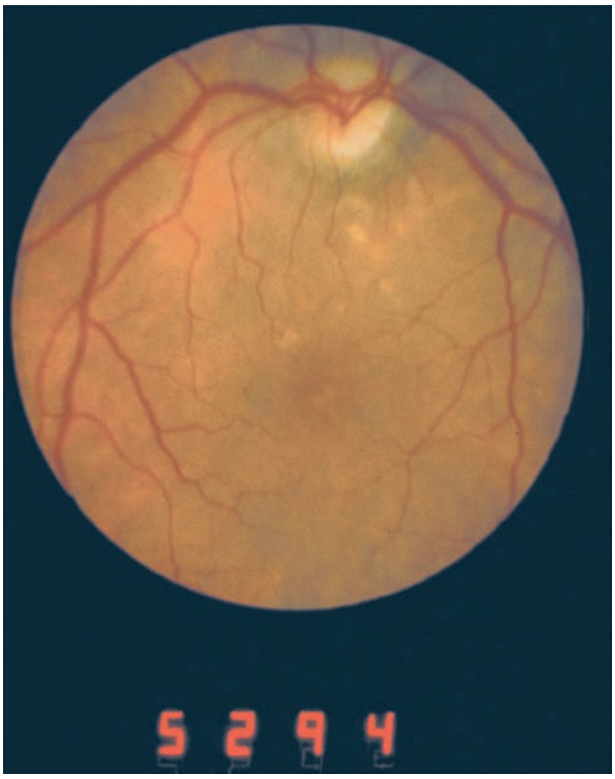
The macula is a 3–5 mm area in the central part of the retina. It is very sensitive to light and is the part of the eye that allows people to see sharp, crisp details. In ARMD, central vision becomes blurry and may be completely lost. Peripheral vision (seeing "out of the corner of your eye") is not affected, so although people with ARMD may become legally blind (visual acuity of 20/200 or worse), ARMD does not lead to a complete absence of sight. Damage done to the retina by ARMD cannot be repaired. Vision cannot be restored to normal levels, but vision loss can often be slowed, especially if the disease is diagnosed early.

ARMD is subdivided into a dry (atrophic) and a wet (exudative) form. The dry form is more common and accounts for 70–90% of cases of ARMD. It progresses more slowly than the wet form and vision loss is less severe. In the dry form, the macula thins over time as part of the **aging** process and the pigmented retinal epithelium (a dark-colored cell layer at the back of the eye) is gradually lost. Words may appear blurred or hazy and colors may appear dim or gray.

In the wet form of ARMD, new blood vessels grow underneath the retina and distort the retina. These blood vessels can leak, causing scar tissue to form on the retina. The wet form may cause visual distortion and make straight lines appear wavy. A central blind spot develops. The wet type progresses more rapidly and vision loss is more pronounced. Treatments are available for some, but not most, cases of the wet form.

Other less common forms of macular degeneration include:

- Cystoid macular degeneration. Loss of vision in the macula due to fluid-filled areas (cysts) in the macular region. This may be a result of other disorders, such as aging, inflammation, or high myopia.
- Diabetic macular degeneration. Deterioration of the macula due to diabetes.
- Senile disciform degeneration (also known as Kuhnt-Junius macular degeneration). A specific and severe type of the wet form of ARMD that involves leaking blood vessels (hemorrhaging) in the macular region. It usually occurs in people over 40 years old.



A slit-lamp view showing macular degeneration of the eye. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Causes and symptoms

Causes

The root cause of ARMD is not known, but scientists have found multiple genes that appear to be associated with the disease and there appears to be an inherited tendency toward developing the disorder. Dry ARMD develops because waste products build up in the retina. The outermost layer of the retina is called the retinal pigment epithelium (RPE). Under this is a layer of blood vessels called the choroid. Nutrients for the retina pass from the choroid blood vessels into the RPE. Waste products from the retina pass in the opposite direction, enter the bloodstream, and are removed. As individuals age, the RPE begins break down and thin out (atrophy). The waste-disposal system slows down, and waste begins to accumulate faster than it can be removed. Waste buildup causes clumps of yellow pigment, called drusen, to develop under the retina. Drusen are common in people over age 60. Ultimately this failure to dispose of retinal waste causes cells in the macula to become damaged, leading to a loss of central vision.

Some of the same things that are bad for the heart are thought to contribute to the development of macular degeneration. These risk factors include **smoking** and a diet that is rich in saturated fat. Smokers have a risk of developing ARMD that is approximately 2.4–3 times that of non-smokers. Smoking increases the risk of developing wet-type ARMD, and may increase the risk of developing dry-type as well. Dietary fat also increase the risk. In one study of older (aged 45–84) Americans, signs of early ARMD were 80% more common in the group who ate the most saturated fat compared to those who ate the least. Low consumption of **antioxidants**, such as foods rich in vitamin A, is associated with a higher risk for developing ARMD. Consumption of moderate amounts of red wine and foods rich in vitamin A is associated with a lower risk. It is generally believed that exposure to ultraviolet (UV) light may contribute to disease development, but this has not been proven.

Wet ARMD develops because the new blood vessels suddenly grow in the choroid layer. These are called choroidal neovascularizations (CNVs). They appear to grow in response to an accumulation of waste or lack of **nutrition** in the retina when the RPE begins to break down. The CNVs leak blood and fluid into the retina (thus the name "wet") causing disruption of the nutrition system and damaging the cells of the macula.

Another less common form of wet ARMD called retinal pigment epithelial detachment occurs when the choroid layer does not grown any CNVs, but fluid from the blood vessels already present leaks and collects under the RPE. Symptoms are the same as for other wet ARMD, but vision deteriorates much more slowly (months or years instead of days or weeks). Eventually new CNVs develop and this form of wet ARMD progresses to the more common form of wet ARMD.

Symptoms

Symptoms of dry and wet ARMD differ. Often dry ARMD shows no symptoms, and neither wet nor dry ARMD cause **pain**. In other cases, individuals with dry ARMD may:

- need more light for reading.
- find the colors look paler or washed out.
- have difficulty doing detailed work, such as needlepoint or model-making.
- have slightly hazy vision.
- take longer for their vision to adapt to low lighting.
- develop a blurry or blind spot in the center of their field of vision.

KEY TERMS

Antioxidant—A molecule that prevents oxidation. In the body antioxidants attach to other molecules called free radicals and prevent the free radicals from causing damage to cell walls, DNA, and other parts of the cell.

Drusen—Clumps of pigment that accumulate under the retina when wastes build up faster than they can be removed. Drusen are a sign of dry age-related macular degeneration.

Fovea—A tiny pit in the macula that is responsible for sharp vision.

Macula—The sensitive center of the retina that is responsible for detailed central vision.

Neovascularization—Growth of new capillaries.

Off-label use—Drugs in the United States are approved by the Food and Drug Administration (FDA) for specific uses based on the results of clinical trials. However, it is legal for physicians to administer these drugs for other "off-label" uses. It is not legal for pharmaceutical companies to advertise drugs for off-label uses.

Photoreceptors—Specialized nerve cells (rods and cones) in the retina that are responsible for vision.

Retina—The light-sensitive membrane at the back of the eye that images are focused on. The retina sends the images to the brain via the optic nerve.

The main symptoms of wet ARMD are that straight lines appear distorted and central vision deteriorates rapidly. Sudden onset of symptoms, particularly vision distortion, requires immediate evaluation by an ophthalmologist.

A few people with ARMD develop visual **hallucinations**. They may see patterns, animals, faces, or other objects. This is called Charles Bonnet syndrome, and it is a neurological side effect of ARMD. Although these hallucinations can be upsetting they are not a sign of mental illness.

Diagnosis

To make the diagnosis of macular degeneration, the doctor (an ophthalmologist or a retinal specialist) dilates the pupil with eye drops and examines the interior of the eye, looking at the retina for the presence of yellow bumps called drusen and for gross changes in the macula such as thinning. The doctor also administers a visual field test, looking for blank spots in the central vision. The doctor may call for fluorescein **angiography** (intravenous injection of fluorescent dye followed by visual examination and photography of the back of the eye) to determine if blood vessels in the retina are leaking.

A central visual field test called an Amsler grid is usually given to patients who are suspected of having ARMD. It is a grid printed on a sheet of paper (so it is easy to take home). When looking at a central dot on the page, the patient should call the doctor right away if any of the lines appear to be wavy or missing. This may be an indication of fluid and the onset of wet ARMD. Patients may also be asked to come in for more frequent checkups.

Treatment

ARMD cannot be reversed or cured. The goal of treatment is to slow vision loss. Treatment depends on the type, location, and stage of ARMD. For mild (early-stage) dry ARMD, often the process only involves watchful waiting. Individuals should have regular eye examinations and see their eye care professional immediately if they note any vision changes. They can monitor their vision at home for signs that dry ARMD is converting to wet ARMD by using an Amsler grid obtainable from their physician. This is a simple checkerboard line grid with a dot in the middle. While staring at the dot, individuals with ARMD may notice that some of the lines appear to be missing. If the lines appear wavy, this is a sign that wet ARMD may be developing.

In wet-type ARMD and in senile disciform macular degeneration, new capillaries grow in the macular region and leak. Treatment for wet ARMD, involves procedures and drug therapy. Not every procedure is appropriate for every patient. Many clinical trials are currently underway to test new drugs and treatments for ARMD. Individuals interested in participating in a clinical trial at no cost can find a list of trials currently enrolling new patients at http://www.clinicaltrials.gov.

Photocoagulation is an outpatient procedure in which the doctor uses a laser to burn the CNVs and seal or destroy them so that they will not leak fluid. This is an outpatient procedure. This procedure is often unsuccessful or produces less than the desired results.

Photodynamic therapy (PDT) involves the injection of the drug verteporfin (Visudyne) followed by laser treatment. The drug accumulates in the CNVs and is activated by laser light. Once activated, it destroys the CNVs. The procedure is not particularly painful. It takes about half an hour and can be done a in the doctor's office.

Drug injections can be given to stop the growth of CNVs and to reduce fluid leakage. These drugs are called anti-vascular endothelial growth factor (anti-VEGF) medications or anti-angiogenesis drugs. These include:

- pegaptanib (Macugen). This drug is approved for use in wet ARMD. It requires a series of injections.
- ranibizumab (Lucentis). This drug is approved for use in ARMD. It destroys new blood vessels and decreases leakage. It has shown some signs of improving vision. In 2008, Lucentis was very expensive (about $2,000 per treatment) and was not covered by all insurance carriers.
- bevacizumab (Avastin). This drug is approved for treatment of colorectal cancer. Its use in treating ARMD is an off-label use. However, it appears to have some of the benefits of Lucentis at a much lower price.

kenalog is a steroid drug that is used to treat inflammation. Using it to treat ARMD is an off-label use, however, it appears to be somewhat effective in reducing fluid, especially if used in combination with photodynamic therapy.

Alternative and Complementary treatment

A large research study called the Age-Related Eye Disease Study (ARED) found that certain dietary supplements slowed the progression of vision loss by up to 25% in cases of moderate to advanced ARMD. The question of preventing ARMD was not addressed. The ARED supplements included the antioxidants vitamin C, vitamin E, beta-carotene (which is converted in the body to vitamin A), and the **minerals** zinc, and copper. More recent studies have suggested lutein and zeaxanthin may also be beneficial.

The ARED supplements are to be taken in specific amounts that are often at higher levels than can be acquired through diet alone or than are found in standard multivitamin tablets. Individuals should not begin taking these dietary supplements on their own. They should consult their physician about whether they would benefit from ARED supplementation and review with their physician all medications they are taking in order to prevent harmful interactions.

Home Remedies

Consumption of a diet rich in antioxidants (beta carotene and the mixed carotenoids that are precursors of vitamin A, **vitamins** C and E, selenium, and zinc), or taking antioxidant **nutritional supplements**, may help prevent macular degeneration, particularly if started early in life. Good dietary sources of antioxidants include citrus fruits, cauliflower, broccoli, nuts, seeds, orange and yellow vegetables, cherries, blackberries, and blueberries.

Prognosis

The dry form of ARMD is self-limiting and eventually stabilizes. The loss of vision is permanent. About 15% of people with dry ARMD develop wet ARMD. Wet ARMD can progress rapidly and result in legal blindness with only coarse peripheral vision remaining, thus limiting daily activities.

Many patients with macular degeneration lose their central vision permanently and may become legally blind. However, macular degeneration rarely causes total loss of vision. Peripheral vision is usually retained. The patient can compensate, to some extent, for the loss of central vision, even though macular degeneration may render them legally blind. Improved lighting and special low-vision aids may help even if sharpness of vision (visual acuity) is poor. Vision aids include special magnifiers that allow the patient to read and telescopic aids for long-distance vision. The use of these visual aids plus the retained peripheral vision usually allow the patient to remain independent. Registration as a legally blind person will enable a patient to obtain special services and considerations.

Prevention

Avoiding the risk factors for macular degeneration may help prevent it. This includes avoiding tobacco smoke and eating a diet low in saturated fat. Some other behaviors that may help reduce the risk of wet-type ARMD are eating a diet rich in green, leafy vegetables and yellow vegetables such as carrots, sweet potatoes, and winter squash; drinking moderate amounts of alcohol, such as one or two glasses of red wine a day; and taking an antioxidant vitamin supplement, especially vitamin A. Some vitamins may be toxic in large doses, so patients should speak with their doctors. Vitamins C and E have not been shown to reduce risk, nor did selenium in one large study. The use of zinc is controversial: some studies showed a benefit, others showed no benefit, and one actually showed an increased risk of ARMD with increased levels of zinc in the blood. Some doctors suggest that wearing UV-blocking sunglasses reduces risk.

Resources

BOOKS

Gilbert, Patricia. *Coping with Macular Degeneration*. London: Sheldon Press, 2006.

Heier, Jeffrey. *100 Questions & Answers About Macular Degeneration*. Sudbury, MA: Jones and Bartlett Publishers, 2010

Roberts, Daniel L. *The First Year: Age-Related Macular Degeneration: An Essential Guide for the Newly Diagnosed*. New York: Marlowe & Co., 2006.

OTHER

Medline Plus. Macular Degeneration. December 28 2009. http://www.nlm.nih.gov/medlineplus/maculardegeneration.html

ORGANIZATIONS

American Macular Degeneration Foundation, P.O. Box 515, Northampton, MA, 01061-0515, (413) 268-7660, amdf@macular.org, http://www.macular.org/.

American Optometric Association, 243 N. Lindbergh Blvd., St. Louis, MO, 63141, (800) 365-2219, http://www.aao.org.

EyeCare America Foundation of the American Academy of Ophthalmology, P. O. Box 429098, San Francisco, CA, 94142-9098, (877) 887-6327, (800) 324-EYES (3937), (415) 561-8567, pubserv@aao.org, http://www.eyecare america.org.

The Macular Degeneration Partnership, 8733 Beverly Blvd. #201, Los Angeles, CA, 90048, (888) 430-9898, (301) 623-1837, http://www.amd.org.

National Eye Institute, 31 Center Drive MSC 2510, Bethesda, MD, 20992-3655, (301) 496-5248, 2020@nei.nih.gov, http://www.nei.nih.gov.

Prevent Blindness America, 211 West Wacker Drive Suite 1700, Chicago, IL, 60606, (800) 331-2020, http://www.preventblindness.org.

Louann W. Murray, PhD
Tish Davidson, A.M.

Macule *see* **Skin lesions**

Mad cow disease *see* **Creutzfeldt-Jakob disease**

Madura foot *see* **Mycetoma**

Maduromycosis *see* **Mycetoma**

Magnesium hydroxide *see* **Antacids**

Magnesium imbalance

Definition

As a mineral found in the fluid that surrounds cells, magnesium (Mg) is an essential component of more than 300 enzymes that regulate many body functions. Imbalances occur when the blood contains more or less magnesium than it should. When in balance, adults ingest approximately 310 to 420 milligrams of magnesium each day, with differences in daily nutritional requirements based primarily on gender and weight.

Specifically, the recommended dietary allowance (RDA), from the Institute of Medicine (which is part of the U.S. National Academies), for males and females one to three years of age is 80 milligrams; four to eight years, 130 milligrams; and nine to 13 years, 240 milligrams. For 14 to 18 years of age, the daily RDA is 410 milligrams for males and 360 milligrams for females; 19 to 30 years, 400 milligrams for males and 310 milligrams for females; and 31 years or older, 420 milligrams for males and 320 milligrams for females.

Demographics

An imbalance of magnesium in the human body can occur to anyone regardless of gender, race, or nationality.

Description

Magnesium is essential for good health. Being the fourth most abundant mineral in the human body, it is necessary for the formation and functioning of healthy bones, teeth, muscles, and nerves. The average adult contains about 25 grams of magnesium. About half of all magnesium in the body is located in the bones. However, it is also found in cells within tissues, organs, and blood. It converts food into energy, builds proteins, and is instrumental in maintaining adequate levels of **calcium** in the blood. Magnesium helps prevent cardiovascular disease and irregular heartbeat, reduces the risk of bone loss (**osteoporosis**), and increases an individual's chance of surviving a **heart attack**. It may also help prevent **stroke** and lessen the effects of existing osteoporosis.

Fish, dairy products, leafy green vegetables such as spinach, broccoli, and peas, legumes, nuts (especially almonds and cashews), seeds (especially sesame seeds), blackstrap molasses, and whole grain cereals (especially buckwheat) are especially good sources of magnesium, but varying amounts of this mineral are found in almost all foods. A wide variety of healthy foods helps to assure adequate amounts of magnesium in the body. For instance, about 80 milligrams of magnesium is contained in one-half cup of spinach, while 25 milligrams is found in one slice of whole wheat bread, and about 50 milligrams in two tablespoons of peanut butter.

Unhealthy foods, such as highly processed foods (such as what is often found in fast food restaurants),

contain very low amounts of magnesium because it is usually eliminated from such foods during processing. Most foods contain only low concentrations of magnesium. In the human body, some is stored in the kidneys, and excess amounts of magnesium are excreted in the urine or stools.

Magnesium deficiency (hypomagnesemia) or excess (hypermagnesemia) is rare, but either condition can be serious.

Causes and symptoms

Hypomagnesemia

Magnesium deficiency most often occurs in people who have been fed intravenously for a long time, whose diet does not contain enough magnesium, or who are unable to absorb and excrete the mineral properly.

Secreting too much aldosterone (the hormone that regulates the body's salt-fluid balance), ADH (a hormone that inhibits urine production), or thyroid hormone can cause hypomagnesemia.

Other factors associated with hypomagnesemia include:

- Loss of body fluids as a result of stomach suctioning or chronic diarrhea
- Cisplatin (a chemotherapy drug)
- Long-term diuretic therapy
- Hypercalcemia (abnormally high levels of calcium in the blood)
- Diabetic acidosis (a condition in which the body's tissues have a higher-than-normal acid content)
- Complications of bowel surgery
- Chronic alcoholism
- Malnutrition
- Starvation
- Severe dehydration.

People who have hypomagnesemia usually experience loss of weight and appetite, bloating, and muscle **pain**, and they pass stools that have a high fat content. In addition, they may be listless, disoriented, confused, and very irritable. Other symptoms of hypomagnesemia are:

- Nausea
- Vomiting
- Muscle weakness, along with stiffness, aches, cramps, and spasms
- Tremor
- Irregular heart beat, angina
- Back pain
- Headaches
- Joint and bone pain
- Constipation
- Nervousness
- Delusions and hallucinations
- Leg and foot cramps
- Muscle twitches (spasms)
- Changes in blood pressure.

Severe magnesium deficiency can cause seizures, especially in children. It can also contribute to cardiovascular disease, osteoporosis, high blood pressure, migraine headaches, diabetes, **anxiety disorders**, and other such diseases.

Neonatal hypomagnesemia can occur in premature babies and in infants who have genetic parathyroid disorders or who have had blood transfusions. This condition also occurs in babies born to magnesium-deficient mothers or to women who have:

- Diabetes mellitus
- Hyperparathyroidism (overactive parathyroid glands)
- Toxemia (a pregnancy-related condition characterized by high blood pressure and fluid retention).

Hypermagnesemia

Hypermagnesemia is most common in patients whose kidneys cannot excrete the magnesium they derive from food or take as medication. This condition can also develop in patients who take magnesium salts, or in healthy people who use large quantities of magnesium-containing **antacids**, **laxatives**, or **analgesics** (pain relievers).

Magnesium **poisoning** can cause severe **diarrhea** in young people, and mask the symptoms of other illnesses. Very high overdoses can lead to **coma**. The risk of complications of magnesium poisoning is greatest for:

- Elderly people with inefficient kidney function
- Patients with kidney problems or intestinal disorders
- People who use antihistamines, muscle relaxants, or narcotics.

Severe **dehydration** or an overdose of supplements taken to counteract hypomagnesemia can also cause this condition.

People who have hypermagnesemia may feel flushed and drowsy, perspire heavily, and have diarrhea. Breathing becomes shallow, reflexes diminish, and the patient becomes unresponsive. Muscle weakness and **hallucinations** are common. The patient's heart beat slows dramatically and blood pressure

KEY TERMS

Hypermagnesemia—An abnormally high concentration of magnesium in the blood.

Hypomagnesemia—An abnormally low concentration of magnesium in the blood.

plummets. Extreme toxicity, which can lead to coma and cardiac arrest, can be fatal.

Diagnosis

Blood tests are used by physicians and other medical professionals to measure magnesium levels.

Treatment

The goal of treatment is to identify and correct the cause of the imbalance. Oral magnesium supplements or injections are usually prescribed to correct mild magnesium deficiency. If the deficiency is more severe or does not respond to treatment, magnesium sulfate or magnesium chloride may be administered intravenously.

Doctors usually prescribe **diuretics** (urine-producing drugs) for patients with hypermagnesemia and advise them to drink more fluids to flush the excess mineral from the body. Patients whose magnesium levels are extremely high may need mechanical support to breathe and to circulate blood throughout their bodies.

Intravenously administered calcium gluconate may reverse damage caused by excess magnesium. Intravenous furosemide (Lasix) or ethacrynic acid (Edecrin) can increase magnesium excretion in patients who get enough fluids and whose kidneys are functioning properly.

In an emergency, dialysis can provide temporary relief for patients whose kidney function is poor or who are unable to excrete excess **minerals**.

Prognosis

Because imbalances may recur if the underlying condition is not eliminated, monitoring of magnesium levels should continue after treatment has been completed.

Prevention

Most people consume adequate amounts of magnesium in the food they eat. The eating of fruits, vegetables, and whole grains is important to maintain healthy levels of magnesium in the body. Dietary supplements can be used safely, but should only be used under a doctor's care and supervision.

Resources

BOOKS

Bernhardt, Nancy E., and Arthur M. Kasko, editors. *Nutrition for the Middle Aged and Elderly*. New York: Nova Biomedical, 2008.

Boron, Walter F. and Emile L. Boulpaep, editors. *Medical Physiology: A Cellular and Molecular Approach*. Philadelphia: Saunders/Elsevier, 2009.

Kleinman, Ronald E., editor. *Pediatric Nutrition Handbook*. Elk Grove Village, IL: American Academy of Pediatrics, 2009.

OTHER

Magnesium. National Institutes of Health, Office of Dietary Supplements. (July 13, 2009), http://ods.od.nih.gov/factsheets/magnesium.asp. (accessed August 5, 2010).

Magnesium. WebMD. (August 5, 2010), http://www.webmd.com/vitamins-supplements/ingredientmono-998-MAGNESIUM.aspx?activeIngredientId=998&activeIngredientName=MAGNESIUM (accessed August 5, 2010).

Maureen Haggerty

Magnetic field therapy

Definition

Magnetic therapy is the use of magnets to relieve **pain** in various areas of the body.

Purpose

Some of the benefits that magnetic therapy claims to provide include:

- pain relief
- reduction of swelling
- improved tissue alkalinization
- more restful sleep
- increased tissue oxygenation
- relief of stress
- increased levels of cellular oxygen
- improved blood circulation
- anti-infective activity

Description

Origins

Magnetic therapy dates as far back as the ancient Egyptians. Magnets have long been believed to have healing powers associated with muscle pain and stiffness. Chinese healers as early as 200 B.C. were said to use magnetic lodestones on the body to correct unhealthy

imbalances in the flow of *qi,* or energy. The ancient Chinese medical text known as *The Yellow Emperor's Canon of Internal Medicine* describes this procedure. The *Vedas*, or ancient Hindu scriptures, also mention the treatment of diseases with lodestones. The word "lodestone" or leading stone, came from the use of these stones as compasses. The word "magnet" probably stems from the Greek *Magnes lithos*, or "stone from Magnesia," a region of Greece rich in magnetic stones. The Greek phrase later became *magneta* in Latin.

Sir William Gilbert's 1600 treatise, *De Magnete*, was the first scholarly attempt to explain the nature of magnetism and how it differed from the attractive force of static electricity. Gilbert allegedly used magnets to relieve the arthritic pains of Queen Elizabeth I. Contemporary American interest in magnetic therapy began in the 1990s, as several professional golfers and football players offered testimony that the devices seemed to cure their nagging aches and injuries.

Many centuries ago, the earth was surrounded by a much stronger magnetic field than it is today. Over the past century and a half, scientists have been studying the decline of this magnetic field and the effects it has had on human health. When the first cosmonauts and astronauts went into space, physicians noted that they experienced bone **calcium** loss and **muscle cramps** when they were out of the Earth's magnetic field for any extended period of time. After this discovery was made, artificial magnetic fields were placed in the space capsules.

There are two theories that are used to explain magnetic therapy. One theory maintains that magnets produce a slight electrical current. When magnets are applied to a painful area of the body, the nerves in that area are stimulated, thus releasing the body's natural painkillers. The other theory maintains that when magnets are applied to a painful area of the body, all cells in that area react in such a way as to increase blood circulation, ion exchange, and oxygen flow to the area. Magnetic fields attract and repel charged particles in the bloodstream, increasing blood flow and producing heat. Increased oxygen in the tissues and blood stream is thought to make a considerable difference in the speed of healing.

Preparations

There are no special preparations for using magnetic therapy other than purchasing a product that is specific for the painful area being treated. Products available in a range of prices include necklaces and bracelets; knee, back, shoulder and wrist braces; mattress pads; gloves; shoe inserts; and more.

Precautions

The primary precaution involved with magnetic therapy is to recognize the expense of this therapy. The use of magnets for therapy has become big business. They can be found in mail–order catalogs and stores ranging from upscale department stores to specialty stores. As is the case with many popular self–administered therapies, many far–fetched claims are being made about the effectiveness of magnetic therapy. Consumers should adopt a "let the buyer beware" approach to magnetic therapy. Persons who are interested in this form of treatment should try out a small, inexpensive item to see if it works for them before investing in the more expensive products.

Side effects

There are very few side effects from using magnetic therapy. Generally, patients using this therapy find that it either works for them or it does not. Patients using transcranial magnetic stimulation for the treatment of depression reported mild **headache** as their only side effect.

Research and general acceptance

Magnetic therapy is becoming more and more widely accepted as an alternative method of pain relief. Since the late 1950s, hundreds of studies have demonstrated the effectiveness of magnetic therapy. In 1997, a group of physicians at Baylor College of Medicine in Houston, Texas studied the use of magnetic therapy in 50 patients who had developed **polio** earlier in life. These patients had muscle and joint pain that standard treatments failed to manage. In this study, 29 of the patients wore a magnet taped over a trouble spot, and 21 others wore a nonmagnetic device. Neither the researchers nor the patients were told which treatment they were receiving (magnetic or nonmagnetic). As is the case with most studies involving a placebo, some of the patients responded to the nonmagnetic therapy, but 75% of those using the magnetic therapy reported feeling much better.

In another study at New York Medical College in Valhalla, New York, a neurologist tested magnetic therapy on a group of 19 men and women complaining of moderate to severe burning, **tingling**, or **numbness** in their feet. Their problems were caused by diabetes or other conditions present such as **alcoholism**. This group of patients wore a magnetic insole inside one of their socks or shoes for 24 hours a day over a two–month period, except while bathing. They wore a nonmagnetic insert in their other sock or shoe. Then for two months they wore magnetic inserts on both feet. By the end of the

KEY TERMS

Fibromyalgia—A chronic syndrome characterized by fatigue, widespread muscular pain, and pain at specific points on the body.

Lodestone—A variety of magnetite that possesses magnetic polarity.

Transcranial magnetic stimulation—A procedure used to treat patients with depression.

study, nine out of ten of the diabetic patients reported relief, while only three of nine non–diabetic patients reported relief. The neurologist in charge of the study believes that this study opens the door to additional research into magnetic therapy for diabetic patients.

A federally funded study is underway at the University of Virginia. This study is evaluating the effectiveness of magnetic mattress pads in easing the muscle pain, stiffness and **fatigue** associated with fibromyalgia.

Magnetic therapy is now being offered for the treatment of patients suffering from depression. A procedure called transcranial magnetic stimulation (TMS) has been beneficial for patients with depression when standard depression treatments, such as anti–depression medication and therapy, have not worked. Patients undergoing TMS have experienced a lower relapse rate than those using **electroconvulsive therapy**. Unlike electroconvulsive therapy, patients using magnetic therapy have not suffered from seizures, memory lapses, or impaired thinking. Mayo Clinic, a large teaching hospital in Rochester, Minnesota has offered TMS as a treatment option for depression since 2002.

Resources

BOOKS

Mayo Clinic. *Mayo Clinic Book of Alternative Medicine: Integrating the Best of Natural Therapies with Conventional Medicine,* 2nd ed. New York, NY: Time Home Entertainment, Inc., 2010.

Pelletier, Kenneth R. *The Best Alternative Medicine*. New York, NY: Simon & Schuster, 2007.

Peters, David, and Kenneth R. Pelletier. *New Medicine (DK Complete Family Health Guides)*. New York, NY: DK ADULT, 2009.

Philpott, William, and Dwight K. Kalita. *Magnet Therapy: The Self–help Guide to Magnets–Clinically Proven to Relieve 35 Health Problems*. Garden City Park, NY: Square One Publishers, 2010.

Weintraub, Michael I., Ravinder Mamtani, and Marc S. Micozzi, editors. *Complementary and Integrative Medicine in Pain Management*. New York: Springer, 2008.

OTHER

"Transcranial Magnetic Stimulation." http://www.mayoclinic.com/health/transcranial–magnetic–stimulation/MY00185. (accessed September 11, 2010).

ORGANIZATIONS

American Holistic Medical Association (AHMA), 23366 Commerce Park, Suite 101B, Beachwood, OH, 44122, (216) 292–6644, http://www.holisticmedicine.org.

American Pain Society, 700 W. Lake Ave., Glenview, IL, 60025, (847) 375–4715. , http://www.ampainsoc.org.

Benson–Henry Institute for Mind Body Medicine at Massachusetts General Hospital, 151 Merrimac St., 4th Floor, Boston, MA, 02114, (617) 643–6090, http://www.massgeneral.org/bhi.

Kim A. Sharp
Laura Jean Cataldo, RN, Ed.D.

Magnetic resonance imaging

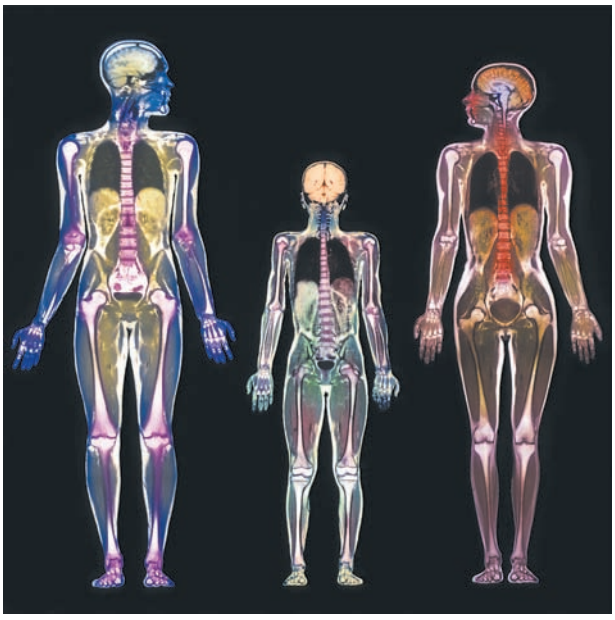
Definition

Magnetic resonance imaging (MRI) is the newest, and perhaps most versatile, medical imaging technology available. Doctors can get highly refined images of the body's interior without surgery, using MRI. By using strong magnets and pulses of radio waves to manipulate the natural magnetic properties in the body, this technique makes better images of organs and soft tissues than those of other scanning technologies. MRI is particularly useful for imaging the brain and spine, as well as the soft tissues of joints and the interior structure of bones. The entire body is visible to the technique, which poses few known health risks.

Purpose

MRI was developed in the 1980s. The latest additions to MRI technology are **angiography** (MRA) and spectroscopy (MRS). MRA was developed to study blood flow, while MRS can identify the chemical composition of diseased tissue and produce color images of brain function. The many advantages of MRI include:

- Detail. MRI creates precise images of the body based on the varying proportions of magnetic elements in different tissues. Very minor fluctuations in chemical composition can be determined. MRI images have greater natural contrast than standard x rays, computed tomography scan (CT scan), or ultrasound, all of which depend on the differing physical properties



MRI body scans of a man, woman, and child. *(Simon Fraser/ Photo Researchers, Inc.)*

of tissues. This sensitivity lets MRI distinguish fine variations in tissues deep within the body. It also is particularly useful for spotting and distinguishing diseased tissues (tumors and other lesions) early in their development. Often, doctors prescribe an MRI scan to more fully investigate earlier findings of the other imaging techniques.

- Scope. The entire body can be scanned, from head to toe and from the skin to the deepest recesses of the brain. Moreover, MRI scans are not obstructed by bone, gas, or body waste, which can hinder other imaging techniques. (Although the scans can be degraded by motion such as breathing, heartbeat, and normal bowel activity.) The MRI process produces cross-sectional images of the body that are as sharp in the middle as on the edges, even of the brain through the skull. A close series of these two-dimensional images can provide a three-dimensional view of a targeted area.
- Safety. MRI does not depend on potentially harmful ionizing radiation, as do standard x-ray and CT scans. There are no known risks specific to the procedure, other than for people who might have metal objects in their bodies.

MRI is being used increasingly during surgical operations, particularly those involving very small structures in the head and neck, as well as for preoperative assessment and planning. Intraoperative MRIs have shown themselves to be safe as well as feasible, and to improve the surgeon's ability to remove the entire tumor or other abnormality.

Given all the advantages, doctors would undoubtedly prescribe MRI as frequently as ultrasound scanning, but the MRI process is complex and costly. The process requires large, expensive, and complicated equipment; a highly trained operator; and a doctor specializing in radiology. Generally, MRI is prescribed only when serious symptoms and/or negative results from other tests indicate a need. Many times another test is appropriate for the type of diagnosis needed.

Doctors may prescribe an MRI scan of different areas of the body.

- Brain and head. MRI technology was developed because of the need for brain imaging. It is one of the few imaging tools that can see through bone (the skull) and deliver high quality pictures of the brain's delicate soft tissue structures. MRI may be needed for patients with symptoms of a brain tumor, stroke, or infection (like meningitis). MRI also may be needed when cognitive and/or psychological symptoms suggest brain disease (like Alzheimer's or Huntington's diseases, or multiple sclerosis), or when developmental retardation suggests a birth defect. MRI can also provide pictures of the sinuses and other areas of the head beneath the face. Recent refinements in MRI technology may make this form of diagnostic imaging even more useful in evaluating patients with brain cancer, stroke, schizophrenia, or epilepsy. In particular, a new 3-D approach to MRI imaging known as diffusion tensor imaging, or DTI, measures the flow of water within brain tissue, allowing the radiologist to tell where the normal flow of fluid is disrupted, and to distinguish more clearly between cancerous and normal brain tissue. The introduction of DTI has led to a technique known as fiber tracking, which allows the neurosurgeon to tell whether a space-occupying brain tumor has damaged or displaced the nerve pathways in the white matter of the brain. This information in turn improves the surgeon's accuracy during the actual operation.
- Spine. Spinal problems can create a host of seemingly unrelated symptoms. MRI is particularly useful for identifying and evaluating degenerated or herniated spinal discs. It can also be used to determine the condition of nerve tissue within the spinal cord.
- Joint. MRI scanning is most commonly used to diagnose and assess joint problems. MRI can provide clear images of the bone, cartilage, ligament, and tendon that comprise a joint. MRI can be used to diagnose joint injuries due to sports, advancing age,

or arthritis. MRI can also be used to diagnose shoulder problems, like a torn rotator cuff. MRI can also detect the presence of an otherwise hidden tumor or infection in a joint, and can be used to diagnose the nature of developmental joint abnormalities in children.

- Skeleton. The properties of MRI that allow it to see through the skull also allow it to view the inside of bones. It can be used to detect bone cancer, inspect the marrow for leukemia and other diseases, assess bone loss (osteoporosis), and examine complex fractures.
- The rest of the body. While CT and ultrasound satisfy most chest, abdominal, and general body imaging needs, MRI may be needed in certain circumstances to provide better pictures or when repeated scanning is required. The progress of some therapies, like liver cancer therapy, needs to be monitored, and the effect of repeated x-ray exposure is a concern.

Description

In essence, MRI produces a map of hydrogen distribution in the body. Hydrogen is the simplest element known, the most abundant in biological tissue, and one that can be magnetized. It will align itself within a strong magnetic field, like the needle of a compass. The earth's magnetic field is not strong enough to keep a person's hydrogen atoms pointing in the same direction, but the superconducting magnet of an MRI machine can. This comprises the "magnetic" part of MRI.

Once a patient's hydrogen atoms have been aligned in the magnet, pulses of very specific radio wave frequencies are used to knock them back out of alignment. The hydrogen atoms alternately absorb and emit radio wave energy, vibrating back and forth between their resting (magnetized) state and their agitated (radio pulse) state. This comprises the "resonance" part of MRI.

The MRI equipment records the duration, strength, and source location of the signals emitted by the atoms as they relax and translates the data into an image on a television monitor. The state of hydrogen in diseased tissue differs from healthy tissue of the same type, making MRI particularly good at identifying tumors and other lesions. In some cases, chemical agents such as gadolinium can be injected to improve the contrast between healthy and diseased tissue.

A single MRI exposure produces a two-dimensional image of a slice through the entire target area. A series of these image slices closely spaced (usually less than half an inch) makes a virtual three-dimensional view of the area.

Magnetic resonance spectroscopy (MRS) is different from MRI because MRS uses a continuous band of radio wave frequencies to excite hydrogen atoms in a variety of chemical compounds other than water. These compounds absorb and emit radio energy at characteristic frequencies, or spectra, which can be used to identify them. Generally, a color image is created by assigning a color to each distinctive spectral emission. This comprises the "spectroscopy" part of MRS. MRS is still experimental and is available in only a few research centers.

Doctors primarily use MRS to study the brain and disorders, like **epilepsy**, **Alzheimer's disease**, brain tumors, and the effects of drugs on brain growth and metabolism. The technique is also useful in evaluating metabolic disorders of the muscles and nervous system.

Magnetic resonance angiography (MRA) is another variation on standard MRI. MRA, like other types of angiography, looks specifically at fluid flow within the blood (vascular) system, but does so without the injection of dyes or radioactive tracers. Standard MRI cannot make a good picture of flowing blood, but MRA uses specific radio pulse sequences to capture usable signals. The technique is generally used in combination with MRI to obtain images that show both vascular structure and flow within the brain and head in cases of **stroke**, or when a blood clot or aneurysm is suspected.

Regardless of the exact type of MRI planned, or area of the body targeted, the procedure involved is basically the same and occurs in a special MRI suite. The patient usually lies on a narrow table and is made as comfortable as possible. Transmitters are positioned on the body and the cushioned table that the patient is laying on moves into a long tube that houses the magnet. The tube is as long as an average adult lying down, and the tube is narrow and open at both ends. Once the area to be examined has been properly positioned, a radio pulse is applied. Then a two-dimensional image corresponding to one slice through the area is made. The table then moves a fraction of an inch and the next image is made. Each image exposure takes several seconds and the entire exam will last anywhere from 30–90 minutes. During this time, the patient is not allowed to move. If the patient moves during the scan, the picture will not be clear.

An open MRI scanner is less restrictive, and is usually open on two or three sides. Although this type of machine accommodates larger or claustrophobic persons with greater ease, high-field or "closed"

KEY TERMS

Angiography—Any of the different methods for investigating the condition of blood vessels, usually via a combination of radiological imaging and injections of chemical tracing and contrasting agents.

Diffusion tensor imaging (DTI)—A refinement of magnetic resonance imaging that allows the doctor to measure the flow of water and track the pathways of white matter in the brain. DTI is able to detect abnormalities in the brain that do not show up on standard MRI scans.

Gadolinium—A very rare metallic element useful for its sensitivity to electromagnetic resonance, among other things. Traces of it can be injected into the body to enhance the MRI pictures.

Hydrogen—The simplest, most common element known in the universe. It is composed of a single electron (negatively charged particle) circling a nucleus consisting of a single proton (positively charged particle). It is the nuclear proton of hydrogen that makes MRI possible by reacting resonantly to radio waves while aligned in a magnetic field.

Ionizing radiation—Electromagnetic radiation that can damage living tissue by disrupting and destroying individual cells. All types of nuclear decay radiation (including x rays) are potentially ionizing. Radio waves do not damage organic tissues they pass through.

Magnetic field—The three-dimensional area surrounding a magnet, in which its force is active. During MRI, the patient's body is permeated by the force field of a superconducting magnet.

Radio waves— Electromagnetic energy of the frequency range corresponding to that used in radio communications, usually 10,000 cycles per second to 300 billion cycles per second. Radio waves are the same as visible light, x rays, and all other types of electromagnetic radiation, but are of a higher frequency.

MRI machines usually generate more accurate and detailed images. The stand-up type of open MRI generates images of the spine, allowing the physician to evaluate images made in the weight-bearing state.

Depending on the area to be imaged, the radiowave transmitters will be positioned in different locations.

- For the head and neck, a helmet-like hat is worn.
- For the spine, chest, and abdomen, the patient will be lying on the transmitters.
- For the knee, shoulder, or other joint, the transmitters will be applied directly to the joint.

Additional probes will monitor vital signs (like pulse, respiration, etc.).

The process is very noisy and confining. The patient hears a thumping sound for the duration of the procedure. Since the procedure is noisy, music supplied via earphones is often provided. Some patients become anxious or panic because they are in the small, enclosed tube. This is why vital signs are monitored and the patient and medical team can communicate between each other. If the chest or abdomen are to be imaged, the patient will be asked to hold his/her breath as each exposure is made. Other instructions may be given to the patient, as needed. In many cases, the entire examination will be performed by an MRI operator who is not a doctor. However, the supervising radiologist should be available to consult as necessary during the exam, and will view and interpret the results sometime later.

Preparation

In some cases (such as for MRI brain scanning or an MRA), a chemical designed to increase image contrast may be given by the radiologist immediately before the exam. If a patient suffers from **anxiety** or claustrophobia, drugs may be given to help the patient relax.

The patient must remove all metal objects (watches, jewelry, **eye glasses**, hair clips, etc). Any magnetized objects (like credit and bank machine cards, audio tapes, etc.) should be kept far away from the MRI equipment because they can be erased. Patients cannot bring their wallet or keys into the MRI machine. The patient may be asked to wear clothing without metal snaps, buckles, or zippers, unless a medical gown is worn during the procedure. The patient may be asked to remove any hair spray, hair gel, or cosmetics that may interfere with the scan.

Aftercare

No aftercare is necessary, unless the patient received medication or had a reaction to a contrast agent. Normally, patients can immediately return to

their daily activities. If the exam reveals a serious condition that requires more testing and/or treatment, appropriate information and counseling will be needed.

Risks

MRI poses no known health risks to the patient and produces no physical side effects. Again, the potential effects of MRI on an unborn baby are not well known. Any woman who is, or may be, pregnant, should carefully discuss this issue with her doctor and radiologist before undergoing a scan. The most common problems are minor bleeding and bruising at the site of contrast injection. Since neither are reportable events, morbidity can only be estimated. Occasionally, an unknown allergy to seafood is discovered after injecting contrast. No deaths have been reported from MRI tests.

MRI scanning should not be used when there is the potential for an interaction between the strong MRI magnet and metal objects that might be imbedded in a patient's body. The force of magnetic attraction on certain types of metal objects (including surgical steel) could move them within the body and cause serious injury. Metal may be imbedded in a person's body for several reasons.

- Medical. People with implanted cardiac pacemakers, metal aneurysm clips, or who have had broken bones repaired with metal pins, screws, rods, or plates must tell their radiologist prior to having an MRI scan. In some cases (like a metal rod in a reconstructed leg) the difficulty may be overcome.
- Injury. Patients must tell their doctors if they have bullet fragments or other metal pieces in their body from old wounds. The suspected presence of metal, whether from an old or recent wound, should be confirmed before scanning.
- Occupational. People with significant work exposure to metal particles (working with a metal grinder, for example) should discuss this with their doctor and radiologist. The patient may need pre-scan testing—usually a single, regular x ray of the eyes to see if any metal is present.

Chemical agents designed to improve the picture and/or allow for the imaging of blood or other fluid flow during MRA may be injected. In rare cases, patients may be allergic to or intolerant of these agents, and these patients should not receive them. If these chemical agents are to be used, patients should discuss any concerns they have with their doctor and radiologist.

The potential side effects of magnetic and electric fields on human health remain a source of debate. In particular, the possible effects on an unborn baby are not well known. Any woman who is, or may be, pregnant should carefully discuss this issue with her doctor and radiologist before undergoing a scan.

As with all medical imaging techniques, **obesity** greatly interferes with the quality of MRI.

Results

Normal results

A normal MRI, MRA, or MRS result is one that shows the patient's physical condition to fall within normal ranges for the target area scanned.

Abnormal results

Generally, MRI is prescribed only when serious symptoms and/or negative results from other tests indicate a need. There often exists strong evidence of a condition that the scan is designed to detect and assess. Thus, the results will often be abnormal, confirming the earlier diagnosis. At that point, further testing and appropriate medical treatment is needed. For example, if the MRI indicates the presence of a **brain tumor**, an MRS may be prescribed to determine the type of tumor so that aggressive treatment can begin immediately without the need for a surgical biopsy.

Resources

BOOKS

Culbreth, L. J., and C. Watson. *Magnetic Resonance Imaging Technology*. New York: Cambridge University Press, 2007.

Kastler, B. *Understanding MRI*. 2nd ed. Berlin: Springer-Verlag, 2008.

McRobbie, D. W., E. A. Moore, M. J. Graves, and M. R. Prince. *MRI from Picture to Proton*. 2nd ed. New York: Cambridge University Press, 2007.

Weishaupt, D., V. D. Koechli, and B. Marincek. *How Does MRI Work?: An Introduction to the Physics and Function of Magnetic Resonance Imaging*. 2nd ed. Berlin: Springer-Verlag, 2008.

PERIODICALS

Hara, H., T. Akisue, T. Fujimoto et al. "Magnetic Resonance Imaging of Medullary Bone Infarction in the Early Stage." *Clinical Imaging* 32, no. 2 (2008): 147–151.

Rumboldt, Z. "Imaging of Topographic Viral CNS Infections." *Neuroimaging Clinics of North America* 18, no. 1 (2002): 85–92.

Wada, R., and W. Kucharczyk. "Prion Infections of the Brain." *Neuroimaging Clinics of North America* 18, no. 1 (2008): 183–191.
Zhao, W., J. H. Choi, G. R. Hon, and M. A. Vannan. "Left Ventricular Relaxation." *Heart Failure Clinics* 4, no. 1 (2008): 37–46.

OTHER

International Society for Magnetic Imaging in Medicine. "Information about MRI Tests."http://www.ismrm.org/ (accessed February 5, 2010).
National Library of Medicine. "MRI imaging." *Medline Plus*. http://www.nlm.nih.gov/medlineplus/ency/article/003335.htm(accessed February 5, 2010).

ORGANIZATIONS

American College of Radiology, 1891 Preston White Drive, Reston, VA, 22091, (800) 227–5463, info@acr.org, http://www.acr.org.

Kurt Richard Sternlof
L. Fleming Fallon, Jr, MD, DrPH
Rosalyn Carson-DeWitt, MD
Brenda W. Lerner

Magnetic resonance spectroscopy *see* **Magnetic resonance imaging**
Major depression *see* **Depressive disorders**
Major tranquilizers *see* **Antipsychotic drugs**

Malabsorption syndrome

Definition

Malabsorption syndrome is a broad term for numerous conditions that alter the ability of the intestines, primarily the small intestines, to absorb nutrients, such as fats, proteins, and carbohydrates, adequately into the bloodstream. It may refer to malabsorption of one specific nutrient or for specific fats, proteins, carbohydrates, or trace elements (micronutrients). Malabsorpotion syndrome is not a disease but a set of symptoms that is the result of the presence of some type of disorder.

Demographics

Anyone of any age, gender, or nationality can be subjected to malabsorption syndrome.

Description

The purpose of the gastrointestinal (GI) tract, which includes the stomach and the intestines, is to digest and absorb nutrients, such as fats, proteins, and carbohydrates, water, **vitamins**, and trace **minerals**. Secretions within the GI tract break down foods ingested by humans so that eventually the final digestible products are absorbed through the intestinal cells. However, in a state involving malabsorpition syndrome, the food nutrients are abnormally absorbed across the GI tract, primarily the small intestine (or, small bowel), which can lead to **malnutrition** and many of the various forms of anemia.

Causes and symptoms

Protein, fats, and carbohydrates (macronutrients) normally are absorbed in the small intestine; the small bowel also absorbs about 80% of the eight to ten liters of fluid ingested daily. Many different conditions affect fluid and nutrient absorption by the intestine. A fault in the digestive process may result from failure of the body to produce the enzymes needed to digest certain foods. Congenital structural defects or diseases of the pancreas, gall bladder, or liver may alter the digestive process. Inflammation, infection, injury, or surgical removal of portions of the intestine may also result in absorption problems; reduced length or surface area of intestine available for fluid and nutrient absorption can result in malabsorption. **Radiation therapy** may injure the mucosal lining of the intestine, resulting in **diarrhea** that may not become evident until several years later. The use of some **antibiotics** can also affect the bacteria that normally live in the intestine and affect intestinal function.

Risk factors for malabsorption syndrome include:

- premature birth
- family history of malabsorption or cystic fibrosis
- use of certain drugs, such as mineral oil or other laxatives
- travel to foreign countries
- intestinal surgery, including bowel transplantation
- excess alcohol consumption.

The most common symptoms of malabsorption include:

- Anemia, with weakness and fatigue due to inadequate absorption of vitamin B_{12}, iron, and folic acid
- Diarrhea, steatorrhea (excessive amount of fat in the stool), and abdominal distention with cramps, bloating, and gas (flatulence) due to impaired water and carbohydrate absorption, and irritation from unabsorbed fatty acids. The individual may also report explosive diarrhea with greasy, foul-smelling stools.
- Edema (fluid retention in the body's tissues) due to decreased protein absorption

- Malnutrition and weight loss due to decreased fat, carbohydrate, and protein absorption. Weight may be 80% to 90% of usual weight despite increased oral intake of nutrients.
- Muscle cramping due to decreased vitamin D, calcium, and potassium levels
- Muscle wasting and atrophy due to decreased protein absorption and metabolism
- Perianal skin burning, itching, or soreness due to frequent loose stools.

Irregular heart rhythms may also result from inadequate levels of potassium and other electrolytes. Blood clotting disorders may occur due to a **vitamin K deficiency**. A person with malabsorption syndrome may over time lack sufficient amounts of iron, proteins, and various vitamins and minerals in the body. Consequently, malnutrition may result, along with such **anemias** involving deficiencies with vitamin K (which can cause excess bleeding), vitamin A (weakening of the eyes), vitamin D (muscle cramping), **calcium** (weakening of the bones), vitamin B_{12}, iron, and folate (**fatigue** and general weakness). Children with malabsorption syndrome often exhibit a failure to grow and thrive.

Malabsorption syndrome can be caused by poor production of enzymes used in the digestive process by the pancreas. Such problems can cause pancreatic diseases. Too much acid in the stomach or not enough bile in the liver can contribute to digestive disorders.

Several disorders can lead to malabsorption syndrome including **cystic fibrosis**, chronic **liver disease**, chronic **pancreatitis**, **Crohn's disease**, **lactose intolerance**, **cholestasis**, abetalipoproteinemia, and **biliary atresia**. Other disorders can include the following.

Tropical sprue is a malabsorptive disorder that is uncommon in the United States, but seen more often in people from the Caribbean, India, or southeast Asia. Although its cause is unknown, it is thought to be related to environmental factors, including infection, intestinal parasites, or possibly the consumption of certain food toxins. Symptoms often include a sore tongue, anemia, weight loss, along with diarrhea and passage of fatty stools.

Celiac disease (also called gluten enteropathy and non-tropical sprue) is another disorder within the classification of malabsorption syndrome. In this disorder people are intolerant to food that contain gluten, or a protein contained in grains such as barley, rye, and wheat. When such foods are eaten, the body's immune system begins to fight off what it thinks are foreign materials. Consequently, the small intestines are damaged Symptoms include diarrhea, abdominal **pain**, and irritability. However, some people with Celiac disease have few symptoms, and sometimes symptoms are nonexistent.

Whipple's disease is a relatively rare malabsorptive disorder, affecting mostly middle-aged men. The cause is thought to be related to bacterial infection, resulting in nutritional deficiencies, chronic low-grade **fever**, diarrhea, joint pain, weight loss, and darkening of the skin's pigmentation. Other organs of the body may be affected, including the brain, heart, lungs, and eyes.

Short bowel syndromes—which may be present at birth (congenital) or the result of surgery—reduce the surface area of the bowel available to absorb nutrients and can also result in malabsorption syndrome. Congenital short bowel syndrome occurs in about 24 out of 100,000 live births and has a high mortality rate (about 38%).

Other conditions that can bring on malabsorption syndrome include: acquired immune deficiency syndrome (**AIDS**), some medications (such as tetracycline, **antacids**, and some that treat **obesity**), radiation treatments, and parasites.

Diagnosis

The diagnosis of malabsorption syndrome and identification of the underlying cause can require extensive diagnostic testing. The first phase involves a thorough medical history and **physical examination** by a physician, who will then determine the appropriate laboratory studies and x rays to assist in diagnosis. A 72-hour stool collection may be ordered for fecal fat measurement; increased fecal fat in the stool collected indicates malabsorption. A biopsy of the small intestine may be done to assist in differentiating between malabsorption syndrome and small bowel disease. Diagnostic sonographic (what is commonly called ultrasound) scans, computed tomography (CT) scans, **magnetic resonance imaging** (MRI) scans, and x ray scans, along with barium **enemas**, may also be ordered to identify abnormalities of the gastrointestinal tract and pancreas.

A newer method of obtaining diagnostic information about the small intestine was approved by the Food and Drug Administration (FDA) in 2001 and is known as capsule **endoscopy**. It includes the use of an imaging capsule, a portable belt-pack image receiver and recorder, and a specially modified computer. The patient swallows the capsule, which is the size of a large pill. A miniature lens in the capsule transmits images through an antenna/transmitter to the belt-pack receiver, which the patient wears under ordinary clothing as he or she goes about daily activities. The belt-pack recording device is returned after seven or eight

KEY TERMS

Anemia—A decrease in the number of red blood cells in the bloodstream, characterized by pallor, loss of energy, and generalized weakness.

Atrophy—A wasting away of a tissue or organ, often because of insufficient nutrition.

Biopsy—A tissue sample removed from the body for examination under the microscope.

Cystic fibrosis—A hereditary genetic disorder that occurs most often in Caucasians. Thick, sticky secretions from mucus-producing glands cause blockages in the pancreatic ducts and the airways.

Edema—From the Greek word meaning swelling, an excessive accumulation of fluid in the tissue spaces. Excessive generalized edema may also be referred to as ascites.

Gluten enteropathy—A hereditary malabsorption disorder caused by sensitivity to gluten, a protein found in wheat, rye, barley, and oats. Also called non-tropical sprue or Celiac disease.

Intestines—The intestines, also known as the bowels, are divided into the large and small intestines. They extend from the stomach to the anus.

Short bowel syndrome—A condition in which the bowel is not as long as normal, either because of surgery or because of a congenital defect. Because the bowel has less surface area to absorb nutrients, it can result in malabsorption syndrome.

Steatorrhea—An excessive amount of fat in the stool.

Trace elements—A group of elements that are present in the human body in very small amounts but are nonetheless important to good health. They include chromium, copper, cobalt, iodine, iron, selenium, and zinc. Trace elements are also called micronutrients.

hours to the doctor, who then examines the images recorded as a digital video. The capsule itself is simply allowed to pass through the digestive tract.

Preparation requires only **fasting** the night before capsule endoscopy and taking nothing but clear liquids for two hours after swallowing the capsule. After four hours the patient can eat food without interfering with the test. As of the early 2010s, capsule endoscopy is used to evaluate gastrointestinal bleeding from unknown causes, inflammatory bowel disease, some malabsorption syndromes, and to monitor surgical patients following small-bowel transplantation.

Laboratory studies of the blood may include:

- Serum cholesterol. May be low due to decreased fat absorption and digestion.
- Serum sodium, potassium, and chloride. May be low due to electrolyte losses with diarrhea.
- Serum calcium. May be low due to vitamin D and amino acid malabsorption.
- Serum protein and albumin. May be low due to protein losses.
- Serum vitamin A and carotene. May be low due to bile salt deficiency and impaired fat absorption.
- D-xylose test. Decreased excretion may indicate malabsorption.
- Schilling test. May indicate malabsorption of vitamin B_{12}.

Treatment

Fluid and nutrient monitoring and replacement is essential for any individual with malabsorption syndrome. Hospitalization may be required when severe fluid and electrolyte imbalances occur. Consultation with a dietitian to assist with nutritional support and meal planning is helpful. If the patient is able to eat, the diet and supplements should provide bulk and be rich in carbohydrates, proteins, fats, minerals, and vitamins. The patient should be encouraged to eat several small, frequent meals throughout the day, avoiding fluids and foods that promote diarrhea. Intake and output should be monitored, along with the number, color, and consistency of stools.

The individual with malabsorption syndrome must be monitored for **dehydration**, including dry tongue, mouth and skin; increased thirst; low, concentrated urine output; or feeling weak or dizzy when standing. Pulse and blood pressure should be monitored, observing for increased or irregular pulse rate, or **hypotension** (low blood pressure). The individual should also be alert for signs of nutrient, vitamin, and mineral depletion, including **nausea** or **vomiting**; fissures at corner of mouth; fatigue or weakness; dry, pluckable hair; easy bruising; **tingling** in fingers or toes; and **numbness** or burning sensation in legs or feet. Fluid volume excess, as a result of diminished protein stores, may require fluid intake restrictions. The physician should also be notified of any **shortness of breath**.

Other specific medical management for malabsorption syndrome is dependent upon the cause. Treatment for tropical sprue consists of **folic acid** supplements and long-term antibiotics. Depending on the severity of the disorder, this treatment may be continued for six months or longer. Whipple's disease also may require long-term use of antibiotics, such as tetracycline. Management of some individuals with malabsorption syndrome may require injections of vitamin B_{12} and oral iron supplements. The doctor may also prescribe enzymes to replace missing intestinal enzymes, or antispasmodics to reduce abdominal cramping and associated diarrhea. People with cystic fibrosis and chronic pancreatitis require pancreatic supplements. Those with lactose intolerance or gluten enteropathy (non-tropical sprue, or Celiac disease) will have to modify their **diets** to avoid foods that they cannot properly digest.

Prognosis

The expected course for the individual with malabsorption syndrome varies depending on the cause. The onset of symptoms may be slow and difficult to diagnose. Treatment may be long, complicated, and changed often for optimal effectiveness. Patience and a positive attitude are important in controlling or curing the disorder. Careful monitoring is necessary to prevent additional illnesses caused by nutritional deficiencies. Without proper treatment for malabsorption syndrome the following conditions can result: **heart failure**, **gallstones**, **kidney stones**, anemia, **osteoporosis**, and malnutrition.

Prevention

The type of preventive measures used for malabsorption syndrome depends on the specific condition that causes it.

Resources

BOOKS

Beers, Mark H., et al., editors. *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2008.

Matarese, Laura E., Ezra Steiger, and Douglas L. Seidner, editors. *Intestinal Failure and Rehabilitation: A Clinical Guide*. Boca Raton, FL: CRC Press, 2005.

Talley, Nicholas J., Isidor Segal, and Martin D. Weltman, editors. *Gastroenterology and Hepatology: A Clinical Handbook*. Sydney, Australia: Churchill Livingstone/Elsevier, 2008.

Wangen, Stephen. *Healthier without Wheat: A New Understanding of Wheat Allergies, Celiac Disease, and Non-Celiac Gluten Intolerance*. Seattle: Innate Health, 2009.

OTHER

Malabsorption Syndromes. eMedicine, WebMD. (October 23, 2009), emedicine.medscape.com/article/931041-overview. (accessed August 6, 2010).

Malabsorption Syndromes. Medline Plus, National Library of Medicine and National Institutes of Health. (August 4, 2010), www.nlm.nih.gov/medlineplus/malabsorptionsyndromes.html (accessed August 6, 2010).

ORGANIZATIONS

National Digestive Diseases Information Clearinghouse, 2 Information Way, Bethesda, MD, 20892-3570, (800) 891-5389, (703) 738-4929, nddic@info.niddk,nih.gov, http://digestive.niddk.nih.gov/.

Kathleen D. Wright, RN
Rebecca J. Frey, PhD

Malaria

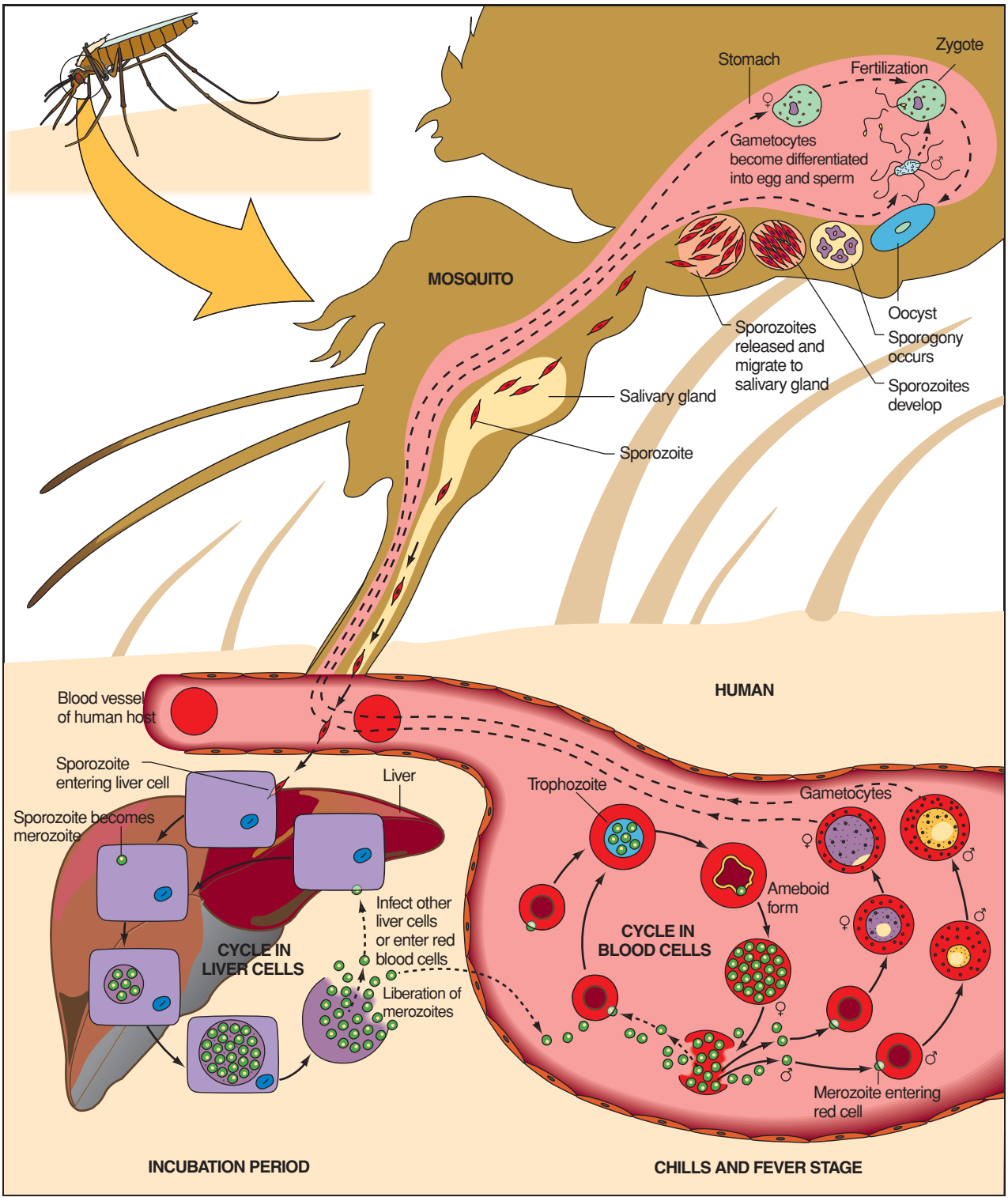
Definition

Malaria is a serious **infectious disease** spread by certain mosquitoes. It is most common in tropical climates. It is characterized by recurrent symptoms of chills, **fever**, and an enlarged spleen. The disease can be treated with medication, but it often recurs. Malaria is endemic (occurs frequently in a particular locality) in many third world countries. Isolated, small outbreaks sometimes occur within the boundaries of the United States.

Description

Malaria is a growing problem in the United States. Although only about 1400 new cases were reported in the United States and its territories in 2000, many involved returning travelers. In addition, locally transmitted malaria has occurred in California, Florida, Texas, Michigan, New Jersey, and New York City. While malaria can be transmitted in blood, the American blood supply is not screened for malaria. Widespread malarial epidemics are far less likely to occur in the United States, but small localized epidemics could return to the Western world. As of late 2002, primary care physicians are being advised to screen returning travelers with fever for malaria, and a team of public health doctors in Minnesota is recommending screening immigrants, refugees, and international adoptees for the disease—particularly those from high-risk areas.

The picture is far more bleak, however, outside the territorial boundaries of the United States. A



The life cycle of *Plasmodium vivax*, the parasite that causes malaria. *(Illustration by Hans & Cassady, Inc. Reproduced by permission of Gale, a part of Cengage Learning.)*

Malaria

Malaria caused an estimated 863,000 deaths in the world in 2008 (most recent year for which the World Health Organization [WHO] had statistics).

The majority of deaths occurred in the following regions:

- 89% in the African region
- 6% in the Eastern Mediterranean region
- 5% in the South-East Asia region

- The estimated death toll in Africa declined by 34,000 compared to 2006, mainly due to a decrease in the total number of deaths from all causes in children younger than 5.
- Thirty-one percent of African households were estimated to own at least one insecticide-treated net (ITN) in 2008, compared to 17% in 2006. More children under 5 years of age used an ITN in 2008 (24%) than in previous years, but the World Health Assembly target for usage in children is 80%.

SOURCE: World Health Organization, *World Malaria Report 2009*. Available online at: http://whqlibdoc.who.int/publications/2009/9789241563901_eng.pdf (accessed August 13, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

recent government panel warned that disaster looms over Africa from the disease. Malaria infects between 300 and 500 million people every year in Africa, India, southeast Asia, the Middle East, Oceania, and Central and South America. A 2002 report stated that malaria kills 2.7 million people each year, more than 75 percent of them African children under the age of five. It is predicted that within five years, malaria will kill about as many people as does **AIDS**. As many as half a billion people worldwide are left with chronic anemia due to malaria infection. In some parts of Africa, people battle up to 40 or more separate episodes of malaria in their lifetimes. The spread of malaria is becoming even more serious as the parasites that cause malaria develop resistance to the drugs used to treat the condition. In late 2002, a group of public health researchers in Thailand reported that a combination treatment regimen involving two drugs known as dihydroartemisinin and azithromycin shows promise in treating multidrug-resistant malaria in southeast Asia.

Causes and symptoms

Human malaria is caused by four different species of a parasite belonging to genus *Plasmodium*: *Plasmodium falciparum* (the most deadly), *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium ovale*. The last two are fairly uncommon. Many animals can get malaria, but human malaria does not spread to animals. In turn, animal malaria does not spread to humans.

A person gets malaria when bitten by a female mosquito that is looking for a blood meal and is infected with the malaria parasite. The parasites enter the blood stream and travel to the liver, where they multiply. When they re-emerge into the blood, symptoms appear. By the time a patient shows symptoms, the parasites have reproduced very rapidly, clogging blood vessels and rupturing blood cells.

Malaria cannot be casually transmitted directly from one person to another. Instead, a mosquito **bites** an infected person and then passes the infection on to the next human it bites. It is also possible to spread malaria via contaminated needles or in blood transfusions. This is why all blood donors are carefully screened with questionnaires for possible exposure to malaria.

It is possible to contract malaria in non-endemic areas, although such cases are rare. Nevertheless, at least 89 cases of so-called airport malaria, in which travelers contract malaria while passing through crowded airport terminals, have been identified since 1969.

The amount of time between the mosquito bite and the appearance of symptoms varies, depending on the strain of parasite involved. The incubation period is usually between 8 and 12 days for falciparum malaria, but it can be as long as a month for the other types. Symptoms from some strains of *P.vivax* may not appear until 8–10 months after the mosquito bite occurred.

The primary symptom of all types of malaria is the "malaria ague" (chills and fever). In most cases, the fever has three stages, beginning with uncontrollable shivering for an hour or two, followed by a rapid spike in temperature (as high as 106°F), which lasts three to six hours. Then, just as suddenly, the patient begins to sweat profusely, which will quickly bring down the fever. Other symptoms may include **fatigue**, severe **headache**, or **nausea and vomiting**. As the sweating subsides, the patient typically feels exhausted and falls asleep. In many cases, this cycle of chills, fever, and sweating occurs every other day, or every third day, and may last for between a week and a month. Those with the chronic form of malaria may have a relapse as long as 50 years after the initial infection.

Falciparum malaria is far more severe than other types of malaria because the parasite attacks all red blood cells, not just the young or old cells, as do other types. It causes the red blood cells to become very "sticky." A patient with this type of malaria can die within hours of the first symptoms. The fever is prolonged. So many red blood cells are destroyed that they block the blood vessels in vital organs (especially

the kidneys), and the spleen becomes enlarged. There may be brain damage, leading to **coma** and convulsions. The kidneys and liver may fail.

Malaria in **pregnancy** can lead to premature delivery, **miscarriage**, or **stillbirth**.

Certain kinds of mosquitoes (called anopheles) can pick up the parasite by biting an infected human. (The more common kinds of mosquitoes in the United States do not transmit the infection.) This is true for as long as that human has parasites in his/her blood. Since strains of malaria do not protect against each other, it is possible to be reinfected with the parasites again and again. It is also possible to develop a chronic infection without developing an effective immune response.

Diagnosis

Malaria is diagnosed by examining blood under a microscope. The parasite can be seen in the blood smears on a slide. These blood smears may need to be repeated over a 72-hour period in order to make a diagnosis. Antibody tests are not usually helpful because many people developed antibodies from past infections, and the tests may not be readily available. A new laser test to detect the presence of malaria parasites in the blood was developed in 2002, but is still under clinical study.

Two new techniques to speed the laboratory diagnosis of malaria show promise as of late 2002. The first is acridine orange (AO), a staining agent that works much faster (3–10 min) than the traditional Giemsa stain (45–60 min) in making the malaria parasites visible under a microscope. The second is a bioassay technique that measures the amount of a substance called histadine-rich protein II (HRP2) in the patient's blood. It allows for a very accurate estimation of parasite development. A dip strip that tests for the presence of HRP2 in blood samples appears to be more accurate in diagnosing malaria than standard microscopic analysis.

Anyone who becomes ill with chills and fever after being in an area where malaria exists must see a doctor and mention their recent travel to endemic areas. A person with the above symptoms who has been in a high-risk area should insist on a blood test for malaria. The doctor may believe the symptoms are just the common flu virus. Malaria is often misdiagnosed by North American doctors who are not used to seeing the disease. Delaying treatment of falciparum malaria can be fatal.

Treatment

Falciparum malaria is a medical emergency that must be treated in the hospital. The type of drugs, the method of giving them, and the length of the treatment depend on where the malaria was contracted and how sick the patient is.

For all strains except falciparum, the treatment for malaria is usually chloroquine (Aralen) by mouth for three days. Those falciparum strains suspected to be resistant to chloroquine are usually treated with a combination of quinine and tetracycline. In countries where quinine resistance is developing, other treatments may include clindamycin (Cleocin), mefloquin (Lariam), or sulfadoxone/pyrimethamine (Fansidar). Most patients receive an antibiotic for seven days. Those who are very ill may need intensive care and intravenous (IV) malaria treatment for the first three days.

Anyone who acquired falciparum malaria in the Dominican Republic, Haiti, Central America west of the Panama Canal, the Middle East, or Egypt can still be cured with chloroquine. Almost all strains of falciparum malaria in Africa, South Africa, India, and southeast Asia are now resistant to chloroquine. In Thailand and Cambodia, there are strains of falciparum malaria that have some resistance to almost all known drugs.

A patient with falciparum malaria needs to be hospitalized and given **antimalarial drugs** in different combinations and doses depending on the resistance of the strain. The patient may need IV fluids, red blood cell transfusions, **kidney dialysis**, and assistance breathing.

A drug called primaquine may prevent relapses after recovery from *P. vivax* or *P. ovale*. These relapses are caused by a form of the parasite that remains in the liver and can reactivate months or years later.

Another new drug, halofantrine, is available abroad. While it is licensed in the United States, it is not marketed in this country and it is not recommended by the Centers for Disease Control and Prevention in Atlanta.

Alternative treatments

The Chinese herb qiinghaosu (the Western name is artemisinin) has been used in China and southeast Asia to fight severe malaria, and became available in Europe in 1994. Because this treatment often fails, it is usually combined with another antimalarial drug (mefloquine) to boost its effectiveness. It is not available in the United States and other parts of the

KEY TERMS

Arteminisinins—A family of antimalarial products derived from an ancient Chinese herbal remedy. Two of the most popular varieties are artemether and artesunate, used mainly in southeast Asia in combination with mefloquine.

Chloroquine—An antimalarial drug that was first used in the 1940s, until the first evidence of quinine resistance appeared in the 1960s. It is now ineffective against falciparum malaria almost everywhere. However, because it is inexpensive, it is still the antimalarial drug most widely used in Africa. Native individuals with partial immunity may have better results with chloroquine than a traveler with no previous exposure.

Mefloquine—An antimalarial drug that was developed by the United States Army in the early 1980s. Today, malaria resistance to this drug has become a problem in some parts of Asia (especially Thailand and Cambodia).

Mefloquine—An antimalarial drug that was developed by the United States Army in the early 1980s. Today, malaria resistance to this drug has become a problem in some parts of Asia (especially Thailand and Cambodia).

Quinine—One of the first treatments for malaria, quinine is a natural product made from the bark of the Cinchona tree. It was popular until being superseded by the development of chloroquine in the 1940s. In the wake of widespread chloroquine resistance, however, it has become popular again. Quinine, or its close relative quinidine, can be given intravenously to treat severe *Falciparum* malaria.

Sulfadoxone/pyrimethamine (Fansidar)—An antimalarial drug developed in the 1960s. It is the first drug tried in some parts of the world where chloroquine resistance is widespread. It has been associated with severe allergic reactions due to its sulfa component.

developed world due to fears of its toxicity, in addition to licensing and other issues.

A Western herb called wormwood (*Artemesia annua*) that is taken as a daily dose can be effective against malaria. Protecting the liver with herbs like goldenseal (*Hydrastis canadensis*), Chinese goldenthread (*Coptis chinensis*), and milk thistle (*Silybum marianum*) can be used as preventive treatment. Preventing mosquitoes from biting you while in the tropics is another possible way to avoid malaria.

As of late 2002, researchers are studying a traditional African herbal remedy against malaria. Extracts from *Microglossa pyrifolia*, a trailing shrub belonging to the daisy family (Asteraceae), show promise in treating drug-resistent strains of *P. falciparum*.

Prognosis

If treated in the early stages, malaria can be cured. Those who live in areas where malaria is epidemic, however, can contract the disease repeatedly, never fully recovering between bouts of acute infection.

Prevention

Several researchers are currently working on a malarial vaccine, but the complex life cycle of the malaria parasite makes it difficult. A parasite has much more genetic material than a virus or bacterium. For this reason, a successful vaccine has not yet been developed.

Malaria is an especially difficult disease to prevent by **vaccination** because the parasite goes through several separate stages. One recent promising vaccine appears to have protected up to 60% of people exposed to malaria. This was evident during field trials for the drug that were conducted in South America and Africa. It is not yet commercially available.

The World Health Association (WHO) has been trying to eliminate malaria for the past 30 years by controlling mosquitoes. Their efforts were successful as long as the pesticide DDT killed mosquitoes and antimalarial drugs cured those who were infected. Today, however, the problem has returned a hundredfold, especially in Africa. Because both the mosquito and parasite are now extremely resistant to the insecticides designed to kill them, governments are now trying to teach people to take antimalarial drugs as a preventive medicine and avoid getting bitten by mosquitoes.

A newer strategy as of late 2002 involves the development of genetically modified non-biting mosquitoes. A research team in Italy is studying the feasibility of this means of controlling malaria.

Travelers to high-risk areas should use insect repellant containing DEET for exposed skin. Because DEET is toxic in large amounts, children should not

use a concentration higher than 35%. DEET should not be inhaled. It should not be rubbed onto the eye area, on any broken or irritated skin, or on children's hands. It should be thoroughly washed off after coming indoors.

Those who use the following preventive measures get fewer infections than those who do not:

- Between dusk and dawn, remain indoors in well-screened areas.
- Sleep inside pyrethrin or permethrin repellent-soaked mosquito nets.
- Wear clothes over the entire body.

Anyone visiting endemic areas should take antimalarial drugs starting a day or two before they leave the United States. The drugs used are usually chloroquine or mefloquine. This treatment is continued through at least four weeks after leaving the endemic area. However, even those who take antimalarial drugs and are careful to avoid mosquito bites can still contract malaria.

International travelers are at risk for becoming infected. Most Americans who have acquired falciparum malaria were visiting sub-Saharan Africa; travelers in Asia and South America are less at risk. Travelers who stay in air conditioned hotels on tourist itineraries in urban or resort areas are at lower risk than backpackers, missionaries, and Peace Corps volunteers. Some people in western cities where malaria does not usually exist may acquire the infection from a mosquito carried onto a jet. This is called airport or runway malaria.

Resources

BOOKS

Beers, Mark H., MD, and Robert Berkow, MD, editors. "Extraintestinal Protozoa: Malaria." Section 13, Chapter 161. In *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2004.

Rocco, Fiammetta. *Quinine: Malaria and the Quest for a Cure That Changed the World*. New York: Harper Perennial, 2004.

World Health Organization. *World malaria report 2008*. Geneva: World Health Organization, 2008.

PERIODICALS

van Lieshout, M., et al. "Climate Change and Malaria: Analysis of the SRES Climate and Socio-Economic Scenarios." *Global Environmental Change* 14 (2004): 87–99.

ORGANIZATIONS

Centers for Disease Control Malaria Hotline. (770) 332–4555.

Centers for Disease Control Travelers Hotline. (770) 332–4559.

OTHER

Malaria Foundation Page.http://www.malaria.org.

OTHER

Bill & Melinda Gates Foundation. "Malaria." http://www.gatesfoundation.org/GlobalHealth/Pri_Diseases/Malaria/ (accessed August 2, 2009).

Centers for Disease Control and Prevention (CDC). "Malaria." http://www.cdc.gov/malaria (accessed August 2, 2009).

Global Fund to Fight AIDS, Tuberculosis, and Malaria. "Homepage." http://www.theglobalfund.org/en/ (accessed August 2, 2009).

World Health Organization (WHO). "Malaria: Global Malaria Programme (GMP)." WHO Programs and Projects. http://www.who.int/malaria (accessed August 2, 2009).

World Health Organization (WHO). "Malaria: Roll Back Malaria Partnership." WHO Programs and Projects. http://www.rbm.who.int/ (accessed August 2, 2009).

Carol A. Turkington
Rebecca J. Frey, PhD

Malaya *see* **Elephantiasis**
Male breast enlargement *see* **Gynecomastia**
Male condom *see* **Condom**
Male infertility *see* **Infertility**
Male pattern baldness *see* **Alopecia**

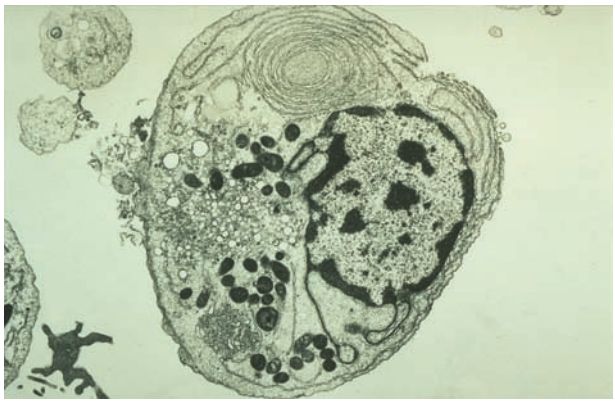
Malignant lymphomas

Definition

Lymphomas are a group of cancers in which cells of the lymphatic system become abnormal and start to grow uncontrollably. Because there is lymph tissue in many parts of the body, lymphomas can start in almost any organ of the body.

Description

The lymph system is made up of ducts or tubules that carry lymph to all parts of the body. Lymph is a milky fluid that contains the lymphocytes or white blood cells. These are the infection-fighting cells of the blood. Small pea-shaped organs are found along the network of lymph vessels. These are called the lymph nodes, and their main function is to make and store the lymphocytes. Clusters of lymph nodes are found in the pelvis region, underarm, neck, chest, and abdomen.



A malignant lymph cell. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

The spleen (an organ in the upper abdomen), the tonsils, and the thymus (a small organ found beneath the breastbone) are part of the lymphatic system.

The lymphocyte is the main cell of the lymphoid tissue. There are two main types of lymphocytes: the T lymphocyte and the B lymphocyte. Lymphomas develop from these two cell types. B cell lymphomas are more common among adults, while among children, the incidence of T and B cell lymphomas are almost equal.

The T and the B cell perform different jobs within the immune system. When an infectious bacterium enters the body, the B cell makes proteins called "antibodies." These antibodies attach themselves to the bacteria, and flag them for destruction by other immune cells. The T cells help protect the body against viruses. When a virus enters the cell, it generally produces certain proteins that are projected on the surface of the infected cell. T cells recognize these proteins and produce certain substances (cytokines) that destroy the infected cells. Some of the cytokines made by the T cells attract other cell types, which are capable of digesting the virus-infected cell. The T cells can also destroy some types of cancerous cells.

Lymphomas can be divided into two main types: Hodgkin's lymphoma or Hodgkin's disease, and non-Hodgkin's lymphomas. There are at least 10 types of non-Hodgkin's lymphomas. They are grouped (staged) by how aggressively they grow; slow growing (low grade), intermediate growing, and rapidly growing (high grade); and how far they spread.

A majority of non-Hodgkin's lymphomas begin in the lymph nodes. About 20% start in other organs, such as the lungs, liver or the gastrointestinal tract. Malignant lymphocytes multiply uncontrollably and do not perform their normal functions. Hence, the body's ability to fight infections is affected. In addition, these malignant cells may crowd the bone marrow, and, depending on the stage, prevent the production of normal red blood cells, white blood cells, and platelets. A low red blood cell count causes anemia, while a reduction in the number of platelets makes the person susceptible to excessive bleeding. Cancerous cells can also invade other organs through the circulatory system of the lymph, causing those organs to malfunction.

Causes and symptoms

The exact cause of non-Hodgkin's lymphomas is not known. However, the incidence has increased significantly in the recent years. Part of the increase is due to the **AIDS** epidemic. Individuals infected with the AIDS virus have a higher likelihood of developing non-Hodgkin's lymphomas. In general, males are at a higher risk for having non-Hodgkin's lymphomas than are females. The risk increases with age. Though it can strike people as young as 40, people between the ages of 60 and 69 are at the highest risk.

People exposed to certain pesticides and ionizing radiation have a higher than average chance of developing this disease. For example, an increased incidence of lymphomas has been seen in survivors of the atomic bomb explosion in Hiroshima, and in people who have undergone aggressive **radiation therapy**. People who suffer from immune-deficient disorders, as well as those who have been treated with immune suppressive drugs for heart or kidney transplants, and for conditions such as **rheumatoid arthritis** and autoimmune diseases, are at an increased risk for this disease.

There have been some studies that have shown a loose association between retroviruses, such as HTLV-I, and some rare forms of lymphoma. The **Epstein-Barr virus** has been linked to Burkitt's lymphoma in African countries. However, a direct cause-and-effect relationship has not been established.

The symptoms of lymphomas are often vague and non-specific. Patients may experience loss of appetite, weight loss, **nausea**, **vomiting**, abdominal discomfort, and **indigestion**. The patient may complain of a feeling of fullness, which is a result of enlarged lymph nodes in the abdomen. Pressure or **pain** in the lower back is another symptom. In the advanced stages, the patient may have bone pain, headaches, constant coughing, and abnormal pressure and congestion in the face, neck, and upper chest. Some may have fevers and night sweats. In most cases, patients go to the doctor

because of the presence of **swollen glands** in the neck, armpits, or groin area. Since all the symptoms are common to many other illnesses, it is essential to seek medical attention if any of the conditions persist for two weeks or more. Only a qualified physician can correctly diagnose if the symptoms are due to lymphoma or some other ailment.

Diagnosis

Like all cancers, lymphomas are best treated when found early. However, it is often difficult to diagnose lymphomas. There are no screening tests available, and, since the symptoms are non-specific, lymphomas are rarely recognized in their early stages. Detection often occurs by chance during a routine **physical examination**.

When the doctor suspects lymphoma, a complete medical history is taken, and a thorough physical examination is performed. Enlargement of the lymph nodes, liver, or spleen may suggest lymphomas. Blood tests will determine the cell counts and obtain information on how well the organs, such as the kidney and liver, are functioning.

A biopsy of the enlarged lymph node is the most definitive diagnostic tool for staging purposes. The doctor may perform a **bone marrow biopsy**. During the biopsy, a cylindrical piece of bone and marrow fluid is removed. They are generally taken out of the hipbone. These samples are sent to the laboratory for examination. In addition to diagnosis, the biopsy may also be repeated during the treatment phase of the disease to see if the lymphoma is responding to therapy.

Once the exact form of lymphoma is known, it is then staged to determine how aggressive it is, and how far it has spread. Staging is necessary to plan appropriate treatment.

Conventional imaging tests, such as x rays, **computed tomography scans** (CT scans), **magnetic resonance imaging**, and abdominal sonograms, are used to determine the extent of spread of the disease.

Lymphangiograms are x rays of the lymphatic system. In this procedure, a special dye is injected into the lymphatic channels through a small cut (incision) made in each foot. The dye is injected slowly over a period of three to four hours. This dye clearly outlines the lymphatic system and allows it to stand out. Multiple x rays are then taken and any abnormality, if present, is revealed.

Rarely, a **lumbar puncture** or a spinal tap is performed to check if malignant cells are present in the fluid surrounding the brain. In this test, the physician inserts a needle into the epidural space at the base of the spine and collects a small amount of spinal fluid for microscopic examination.

Treatment

Treatment options for lymphomas depend on the type of lymphoma and its present stage. In most cases, treatment consists of **chemotherapy**, radiotherapy, or a combination of the two methods.

Chemotherapy is the use of anti-cancer drugs to kill **cancer** cells. In non-Hodgkin's lymphomas, combination therapy, which involves the use of multiple drugs, has been found more effective than single drug use. The treatment may last about six months, but in some cases may last as long as a year. The drugs may either be administered intravenously (through a vein) in the arm or given orally in the form of pills. If cancer cells have invaded the central nervous system, then chemotherapeutic drugs may be instilled, through a needle in the brain or back, into the fluid that surrounds the brain. This procedure is known as intrathecal chemotherapy.

Radiation therapy, where high-energy ionizing rays are directed at specific portions of the body, such as the upper chest, abdomen, pelvis, or neck, is often used for treatment of lymphomas. External radiation therapy, where the rays are directed from a source outside the body, is the most common mode of radiation treatment.

Bone marrow transplantation is used in cases where the lymphomas do not respond to conventional therapy, or in cases where the patient has had a relapse or suffers from recurrent lymphomas.

There are two ways of doing bone marrow transplantation. In a procedure called "allogeneic bone marrow transplant," a donor is found whose marrow matches that of the patient. The donor can be a twin (best match), a sibling, or a person who is not related at all. High-dose chemotherapy or radiation therapy is given to eradicate the lymphoma. The donor marrow is then given to replace the marrow destroyed by the therapy.

In "autologous bone marrow transplantation," some of the patient's own bone marrow is harvested, chemically purged, and frozen. High-dose chemotherapy and radiation therapy are given. The marrow that was harvested, purged, and frozen is then thawed and put back into the patient's body to replace the destroyed marrow.

KEY TERMS

Antibodies—Proteins made by the B lymphocytes in response to the presence of infectious agents such as bacteria or viruses in the body.

Biopsy—The surgical removal and microscopic examination of living tissue for diagnostic purposes.

Growth factors (cytokines)—Chemicals made by the cells that act on other cells to stimulate or inhibit their function. Cytokines that stimulate growth are called "growth factors."

A new treatment option for patients with lymphoma is known as "peripheral stem cell transplantation." In this treatment approach, cells that normally circulate in the blood are collected when the patient has normal blood counts taken, and these cells are saved via a process called "pheresis." Researchers are exploring whether these cells can be used to restore the normal function and development of blood cells, rather than using a bone marrow transplant.

Prognosis

Like all cancers, the prognosis for lymphoma depends on the stage of the cancer, and the patient's age and general health. When all the different types and stages of lymphoma are considered together, only 50% of patients survive 5 years or more after initial diagnosis. This is because some types of lymphoma are more aggressive than others.

The survival rate among children is definitely better than among older people. About 90% of the children diagnosed with early stage disease survive 5 years or more, while only 60-70% of adults diagnosed with low grade lymphomas survive for 5 years or more. The survival rate for children with the more advanced stages is about 75-85%, while among adults it is 40-60%.

Prevention

Although many cancers may be prevented by making diet and life style changes which reduce risk factors, there is currently no known way to prevent lymphomas. Protecting oneself from developing AIDS, which may be a risk factor for lymphomas, is the only preventive measure that can be practiced.

At present, there are no special tests that are available for early detection of non-Hodgkin's lymphomas. Paying prompt attention to the signs and symptoms of this disease, and seeing a doctor if the symptoms persist, are the best strategies for an early diagnosis of lymphoma. Early detection affords the best chance for a cure.

Resources

OTHER

"Adults Non-Hodgkin's Lymphoma." *National Cancer Institute Page*. http://www.nci.nih.gov.

"Childhood Non-Hodgkin's Lymphoma." *National Cancer Institute Page*. http://www.nci.nih.gov.

"Hodgkin's Disease" and Non-Hodgkin's Lymphoma." *The Leukemia Society*. http://www.leukemia-lymphoma.org/hm_lls.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

Cancer Research Institute (National Headquarters), One Exchange Plaza, 55 Broadway, Suite 1802, New York, NY, (212) 688-7515, (212) 832-9376, (800) 992-2623, http://www.cancerresearch.org/.

Leukemia and Lymphoma Society, 1311 Mamaroneck Avenue, Suite 310, White Plains, NY, 10605, (800) 955-4572, http://www.leukemia-lymphoma.org.

Lymphoma Research Foundation, 8800 Venice Boulevard, Suite 207, Los Angeles, CA, 90034, (212) 349-2910, (212) 349-2886, (800) 235-6848, Helpline@lymphoma.org, http://www.lymphoma.org.

National Cancer Institute (National Institutes of Health), NCI Office of Communications and Education, 6116 Executive Blvd. Suite 300, Bethesda, MD, 20892-8322, (800) 4-CANCER (422-6237), cancergovstaff@mail.nih.gov, http://www.cancer.gov/.

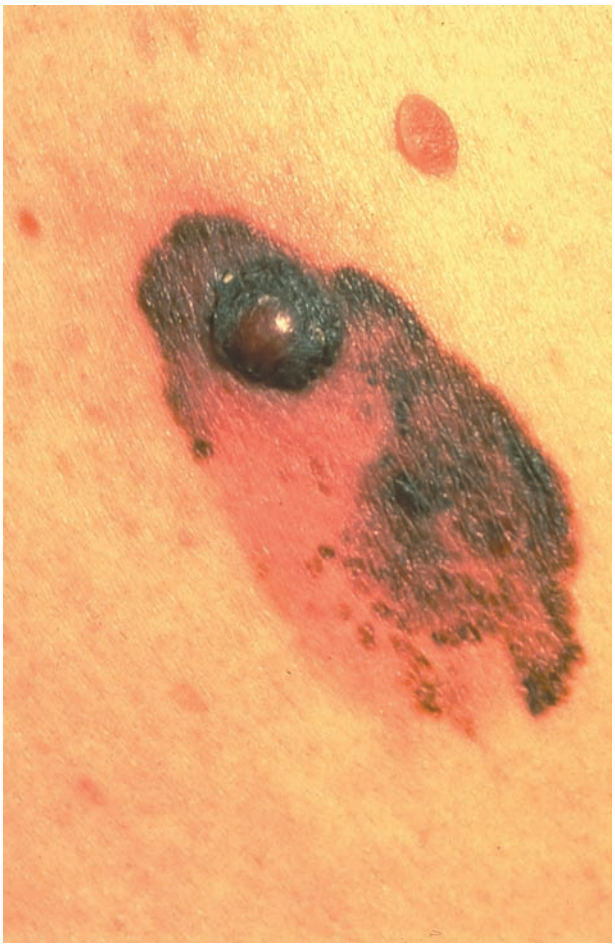
Oncolink. University of Pennsylvania Cancer Center, 3400 Spruce Street, 2 Donner, Philadelphia, PA, 19104, (215) 349-8895, (215) 349-5445, hampshire@uphs.upenn.edu, http://oncolink.org.

Lata Cherath, PhD

Malignant melanoma

Definition

Malignant melanoma is a type of **cancer** arising from the melanocyte cells of the skin. Melanocytes are cells in the skin that produce a pigment called melanin. Malignant melanoma develops when the melanocytes no longer respond to normal control mechanisms of cellular growth. They may then invade nearby structures or spread to other organs in the body



A close-up image of a malignant melanoma on a patient's back. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

(metastasis), where again they invade and compromise the function of that organ.

Description

Melanocytes are derived from a structure in the human embryo called the neural crest. They are distributed in the epidermis and thus are found throughout the skin. They produce a brown pigment known as melanin and are responsible for racial variation in skin color as well as the color of **moles**. Malignant degeneration of the melanocyte gives rise to the tumor known as melanoma, which has four subtypes. These are: superficial spreading, nodular, lentigo maligna, and acral lentiginous melanomas, accounting for 70%, 15% to 30%, 4% to 10%, and 2% to 8% of cases, respectively. Malignant melanoma may develop anywhere on the body. In men, it is most common on the trunk. In women, it is most common on the back or legs. The subtype also may influence where the tumor develops; lentigo melanoma is more common on the face while acral lentiginous melanoma is more common on the palms of the hand, soles of the feet, or in the nail beds.

The locally invasive characteristic of this tumor involves vertical penetration through the skin and into the dermis and subcutaneous (under-the-skin) tissues of the malignant melanocytes. With the exception of the nodular variety of melanoma, there is often a phase of radial or lateral growth associated with these tumors. Since it is the vertical growth that characterizes the malignancy, the nodular variant of melanoma carries the worst prognosis. Fortunately, the superficial spreading type is most common.

The primary tumor begins in the skin, often from the melanocytes of a pre-existing mole. Once it becomes invasive, it may progress beyond the site of origin to the regional lymph nodes or travel to other organ systems in the body and become systemic in nature.

Lymph is the clear, protein-rich fluid that bathes the cells throughout our body. Lymph will work its way back to the bloodstream via small channels known as lymphatics. Along the way, the lymph is filtered through cellular stations known as nodes, thus they are called lymph nodes. Nearly all organs in the body have a primary lymph node group filtering the tissue fluid, or lymph, that comes from that organ. Different areas of the skin have different primary nodal stations. For the leg, they are in the groin. For the arm, the armpit or axilla. For the face, it is the neck. Depending where on the torso the tumor develops, it may drain into one groin or armpit, or both.

Cancer, as it invades in its place of origin, may also work its way into blood vessels. If this occurs, it provides yet another route for the cancer to spread to other organs of the body. When the cancer spreads elsewhere in the body, it has become systemic in extent and the tumor growing elsewhere is known as a metastasis.

Untreated malignant melanoma follows a classic progression. It begins and grows locally, penetrating vertically. It may be carried via the lymph to the regional nodes, known as regional metastasis. It may go from the lymph to the bloodstream or penetrate blood vessels, directly allowing it a route to go elsewhere in the body. When systemic disease or distant metastasis occur, melanoma commonly involves the lung, brain, liver, or occasionally bone. The malignancy causes **death** when its uncontrolled growth compromises vital organ function.

Of the anticipated new cases of cancer for the year 2003 in the United States, malignant melanoma will account for 5% of malignancies in men and 4% in

women, being the sixth most common cancer in men and the seventh in women. It is estimated there will be 560,000 total cancer deaths in the United States in 2007. Malignant melanoma will account for 8.110 of these deaths.

The incidence of primary cutaneous malignant melanoma has been steadily increasing, possibly related to increase of sun exposure. Currently, the risk is about 13 per 100,000 of the population. It affects all age groups but is most commonly seen in patients between 30 and 60 years of age.

Sun exposure definitely increases the risk of developing melanoma, particularly in older males. The melanocytes are part of the integument's photoprotective mechanism; in response to sunlight, they produce melanin that has a protective role from the sun's ultraviolet rays. For Caucasians, the amount of melanin present in the skin is directly related to sun exposure. However, it is not so much the total sun exposure that seems important, rather it is the history of **sunburn**, (especially if severe or at an early age), that correlates with the increased risk. On this basis populations of fair-skinned people living in areas of high sun exposure such as the southwest United States or Australia are subject to increased risk. Malignant melanoma also affects non-Caucasians—though sun exposure probably does not play a role—at a rate of 10% that of Caucasians. The most common form of melanoma in African Americans is acral lentiginous melanoma.

Malignant melanoma may arise in the skin anywhere on the body. It is estimated that 50%–70% develop spontaneously while the remainder start in a pre-existing mole.

Causes and symptoms

The predisposing causes to the development of malignant melanoma are environmental and genetic. The environmental factor is excessive sun exposure. There are also genetically transmitted familial syndromes with alterations in the CDKN2A gene, which encodes for the tumor-suppressing proteins p16 and p19. In 2003 a group of Swedish researchers reported that 63 out of a group of 71 melanoma patients, or 89% of the group, had mutations in either the NRAS or the BRAF gene. The researchers found that these mutations occur at an early point in the development of melanoma and remain as the tumor progresses.

As of early 2003, some researchers think there may be two pathways to malignant melanoma, one involving exposure to sunlight and the other with melanocyte proliferation triggered by other factors. This hypothesis is based on the difference in distribution of moles on the body between patients who develop melanomas on the face and neck, and those who develop melanomas on the trunk.

A small percentage of melanomas arise within burn scar tissue. Researchers do not fully understand the relationship between deep **burns** and an increased risk of skin cancer.

As mentioned previously, melanin production in fair-skinned people is induced by sun exposure. An exposure substantial enough to result in mild sunburn will be followed by melanin producing a tan that may last a few weeks. Both ultraviolet radiation and damaging oxygen radicals caused by sun exposure may damage cells, particularly their DNA. It is suspected that this damage induces mutations that result in the development of malignant melanoma. Though these mutations are alterations of the genome causing the melanoma, they are environmentally induced and account for sporadic or spontaneous cases of this disease.

A positive family history of one or two first-degree relatives having had melanoma substantially increases the risk on a genetic basis. A family tendency is observed in 8% to 12% of patients. There is a syndrome known as the dysplastic (atypical) nevus syndrome that is characterized by atypical moles with bothersome clinical features in children under age 10. Such individuals have to be observed closely for the development of malignant melanoma. Chromosome 9p has been identified as being involved in familial predisposition. There are mutations in up to 50% of familial melanoma patients of the tumor-suppressing gene CDKN2A. The actual number of moles increases risk, but the size of the moles needs be considered. Those with 10 larger moles of over 1 cm (0.4 in.) are at more risk than those with a higher number (50-99) of smaller moles. Finally, when a child is born with a large congenital mole, careful observation for change is appropriate because of increased risk.

An excellent way of identifying changes of significance in a mole is the ABCDE rule:

- Asymmetry
- Border irregularity
- Color variegation
- Diameter greater than 6 mm (0.24 in)
- Elevation above surrounding tissue.

Notice that three of the criteria refer to variability of the lesion (color variegation refers to areas of light color and black scattered within the mole). Thus small, uniform regular lesions have less cause for concern. It is important to realize that change in a mole or the

rapid development of a new one are very important symptoms.

Another summary of important changes in a mole is the Glasgow 7-point scale. The symptoms and signs below can occur anywhere on the skin, including the palms of the hands, soles of the feet, and also the nail beds:

- Change in size
- Change in shape
- Change in color
- Inflammation
- Crusting and bleeding
- Sensory change
- Diameter greater than 7 mm (0.28 in.

In this scheme, change is emphasized along with size. Bleeding and sensory changes are relatively late symptoms.

Symptoms related to the presence of regional disease are mostly those of nodules or lumps in the areas containing the lymph nodes draining the area. Thus nodularity can be found in the armpit, the groin, or the neck if regional nodes are involved. There is also a special type of metastasis that can occur regionally with malignant melanoma; it is known as an in-transit metastasis. If the melanoma is spreading through the lymph system, some of the tumor may grow there, resulting in a nodule part way between the primary site and the original lymph node. These in-transit metastasis are seen both at the time of original presentation or later after primary treatment has been rendered, the latter being a type of recurrence.

Finally, in those who either present with or progress to widespread or systemic disease, symptoms and signs are related to the affected organ. Thus neurological problems, lung problems, or liver problems develop depending on the organ involved.

Diagnosis

None of the clinical signs or symptoms discussed above are absolute indications that a patient has malignant melanoma. The actual diagnosis is accomplished by biopsy, a procedure that removes tissue to examine under a microscope. It is important that the signs and symptoms are used to develop a suspicion of the diagnosis because the way the biopsy is performed for melanoma may be different than for other lesions of the skin.

The doctor may also use a dermatoscope to examine the mole prior to removal. The dermatoscope, which can be used to distinguish between benign moles and melanomas, is an instrument that resembles an ophthalmoscope. An immersion oil is first applied to the mole to make the outer layers of skin transparent.

When dealing with an early malignant melanoma, it is very important to establish the exact thickness of penetration of the primary tumor. Any biopsy that does not remove the full vertical extent of the primary is inadequate. Therefore, if a skin lesion is suspicious, full thickness excisional biopsy is the approach recommended. Shave biopsies and biopsies that remove only a portion of the suspect area are inappropriate. Often, in an early case, the excision involves just the suspicious lesion with minimal normal skin, but it should be a full vertical excision of the skin. If a melanoma is diagnosed, further treatment of this area will often be necessary but does not compromise outcome (prognosis). In some special areas of the body, minor modifications may be necessary about initial total excision, but full thickness excision should always be the goal. (See staging, below.)

Once the diagnosis is obtained, careful examination of the patient for regional lymph node involvement should be done. A careful review to uncover any symptoms of widespread disease is also appropriate.

The more common patient has an early melanoma, and extensive testing is not usually warranted. Routine testing in this situation involves a **complete blood count**, a **chest x ray**, and determinations of blood enzymes including lactic dehydrogenase and alkaline phosphatase.

If the patient has signs or symptoms of more advanced disease, or if the lesion's depth of penetration is sizeable, further imaging studies may be appropriate. These would involve CAT scans of the abdomen, the chest, or regional nodal areas, or a CT or MRI of the brain.

Treatment

The key to successful treatment is early diagnosis. Patients identified with localized, thin, small lesions (typified by superficial spreading subtype) nearly always survive. For those with advanced lesions, the outcome is poor in spite of progress in systemic therapy.

Clinical staging

Malignant melanoma is locally staged based on the depth of penetration through the skin and its appendages. There are two ways of looking at the depth of penetration. The Clarke system utilizes the layers of the dermis and the skin appendages present at that layer to identify the depth of penetration. The

Breslow system uses the absolute measurement of depth. Though useful conceptually, the Clarke system is used less frequently because of the fact that skin is of different thickness in different regions of the body. The depth of penetration is much greater when the tumor reaches the subcutaneous fat when the skin involved is the back as opposed to the face. It turns out that the Breslow measurement is more reproducible and thus more useful; therefore, for purposes here, depth of penetration by absolute measurement (Breslow) is used in local staging.

These stages are subdivided on the basis of penetration. Stage Ia is 0.75 mm or less (1 mm = 0.04 in), and Stage Ib is 0.75–1.5 mm penetration. Stage IIa is 1.5–4.0 mm and Stage IIb is over 4.0 mm or into the subcutaneous fat. In stage III and IV, there is disease beyond the primary site. Stage III is defined by the presence of in-transit or regional nodal metastasis or both. Stage IV is defined by the presence of distant metastasis.

Once the diagnosis of malignant melanoma has been established by biopsy and the stage has been identified using the results of the examination and studies, a treatment plan is developed. Melanoma is not cured unless it is diagnosed at a stage when it can be isolated and removed surgically. Considerations revolve around the extent of the local and regional nodal surgery for stages I through III. For stage IV patients, or those that are treated and then develop recurrence at distant sites, **chemotherapy** or immunotherapy is planned. Studies are in progress to improve the results from traditional chemotherapeutic regimens. Adjuvant therapy (auxiliary drug treatment used to make possibility of relapse less for those at high risk) is also considered.

Surgical therapy for the primary site is that of wide local removal of the skin including subcutaneous tissue surrounding the lesion. In the past, wide excisions were large and encompassed 2 in. of tissue in all directions wherever feasible. It has been shown that such wide local excisions are not necessary and the issue has become: how wide is enough? Studies from the World Health Organization Melanoma Group and by the Melanoma Intergroup Committee in the United States have provided general guidelines based on the depth of penetration of the melanoma. These guidelines and anatomic considerations need to be kept in mind by the surgeon.

The next issue in primary management is whether the patient should have the regional lymph nodes removed in addition to treatment of the primary tumor. The problems associated with the resection of regional lymph nodes are those of lifelong **edema** or swelling in the extremity. Though it does not occur in all patients (5% to 20%, depending on the extremity and extent of the dissection), it can be a disabling symptom. Certainly, if it could be ascertained that there was disease in the nodes, resection (removal) would be appropriate. However, if there was no disease, the risk of edema should be avoided. In patients with no signs of regional disease, depth of penetration of the primary tumor helps guide the decision. If the tumor penetrates less than 1mm, dissection is not usually done. If it is 1-2 mm, node dissection may be done at the time of primary treatment or the patient may be observed and only undergo lymph node dissection if the area later shows signs of disease. If the patient has enlarged lymph nodes or the depth of the tumor has led to the evaluation by CAT scan showing enlarged nodes, resection of the nodes will be considered. In the latter case, more extensive imaging of the lung, liver, or brain may be appropriate to be sure the patient does not already have stage IV disease.

Questions related to which patients should have resection of regional lymph nodes have led to an intermediary procedure known as sentinel node mapping and biopsy. Intermediate thickness melanomas between 1 and 4 mm deep (0.04 and 0.16 in.) may have nodal involvement even if the examination and any other studies done are normal. If a radioisotope tracer or blue dye is injected into the area of the primary tumor, very shortly it will travel to the lymph nodes draining that area. These sentinel nodes are thus identifiable and are the most likely to harbor any regional metastatic disease. If these nodes alone are biopsied and are normal, the rest of the lymph node group can be spared. If they show microscopic deposits of tumor, then the full resection of the lymph node group may be completed. This procedure allows selection of those patients with intermediate thickness melanoma who will benefit from the regional lymph node dissection.

Patients with metastatic melanoma who do not respond well to other therapies may be candidates for treatment with aldesleukin. Aldesleukin is a form of interleukin, a specific kind of biological response modifier that promotes the development of T-cells. These cells are part of the lymphatic system and can directly interact with and fight cancer cells. Although aldesleukin is produced naturally in the body, its therapeutic form is developed via biotechnology in a laboratory setting. Treatment is considered palliative, which means that it provides comfort but does not produce a cure. Side effects, however, can be severe, and range from flu-like symptoms to whole-body infection (**sepsis**) and **coma**.

KEY TERMS

Adjuvant therapy—Treatment given to patients who are at risk of having microscopic untreated disease present but have no obvious symptoms.

Dermis—The deeper portion or layer of the skin beneath the epidermis.

Dysplastic nevus syndrome—A familial syndrome characterized by the presence of multiple atypical appearing moles, often at a young age.

Epidermis—The uppermost layer of skin cells.

Genome—The genetic makeup of a cell, composed of DNA.

Immunotherapy—A form of treatment that uses biologic agents to enhance or stimulate normal immune function.

Integument—The medical name for the skin.

Lymph node dissection—Surgical removal of a group of lymph nodes.

Lymphedema—Swelling of an arm or leg following surgical removal of the lymph nodes that drain the limb.

Melanocytes—Skin cells derived from the neural crest that produce the protein pigment melanin.

Metastasis (plural, metastases)—A tumor growth or deposit that has spread via lymph or blood to an area of the body remote from the primary tumor.

Nevus (plural, nevi)—A medical term for mole.

Resection—The act of removing something surgically.

Skin appendages—Structures related to the integument such as hair follicles and sweat glands.

Variegation—Patchy variation in color.

Some patients, such as those with IIb or stage III melanoma, are at high risk for the development of recurrence after treatment. Although these patients are clinically free of disease after undergoing primary treatment, they are more likely to have some microscopic disease in the body that studies have not yet been able to identify. In an effort to decrease the rate of relapse, adjuvant therapy may be considered. Interferon alpha 2a is an agent that stimulates the immune system. This adjuvant therapy may slightly increase the duration of a patient's disease-free state and lengthen overall survival. However, interferon alpha 2a has high toxicity and patients may not tolerate the side effects.

Unfortunately, treatment for those patients who present with or go on to develop systemic disease usually fails; melanoma that has metastasized to the brain is particularly difficult to treat. The chemotherapeutic agent dacarbazine, or DTIC, seems to be the most active agent. Overall responses are noted in about 20% of patients, and they last only two to six months. Combination therapy may be an option. The regimen of DTIC + BCNU (carmustine) + cisplatin + tamoxifen delivers a response rate of 40%. Combining biologic or immunologic agents such as interferon with standard chemotherapeutic agents is under study and showing improved response rates, though toxicity is substantial and only the healthier, younger patients tolerate the treatment.

Some researchers are investigating the reasons why melanomas are so resistant to chemotherapy. One suggestion is that the genes ordinarily responsible for apoptosis (cell self-destruction) do not function normally in melanomas. The development of new drugs to treat melanoma depends on a better understanding of the complex processes involved in apoptosis. As of 2007, several new drugs were in development. The most promising seemed to be Zadazin (thymalfasin) when used in combination with standard dacarbazine (DTIC) chemotherapy.

Alternative treatment

Though **radiation therapy** has a minimal role in the primary treatment of malignant melanoma, for patients who have metastatic disease, radiation may be helpful. This is true in patients who have developed tumor deposits in such areas as the brain or bone.

Prognosis

Almost all patients survive stage Ia malignant melanoma, and the survivorship for stage I overall is more than 90%. Survival drops in stage IIa to about 65% at five years and is worse yet for stage IIb at slightly over 50%. Stage III has a survival rate at 5 years of 10%–47%, depending on the size and number of regional nodes involved. Stage IV malignant melanoma is almost always a fatal disease.

Coping with cancer treatment

For those with familial tendencies for malignant melanoma, **genetic counseling** may be appropriate. Psychological counseling may be appropriate for

anyone having trouble coping with a potentially fatal disease. Local cancer support groups may be helpful and are often identified by contacting local hospitals or the American Cancer Society.

Prevention

Though it is difficult to prove that **sunscreens** statistically reduce the frequency of malignant melanoma at this time, most authorities recommend their use as protection from ultraviolet light (considered a major factor in the development of melanoma.) Avoidance of severe sunburns is recommended.

Resources

BOOKS

Hearing, Vincent J., and Stanley P.L. Leong. *From Melanocytes to Malignant Melanoma: The Progression to Malignancy*. Totowa, NJ: Humana Press, 2005.

Kaufman, Howard L. *The Melanoma Book: A Complete Guide to Prevention and Treatment, Including the Early Detection Self–Exam Body Map*. New York: Gotham, 2005.

Robins, Perry, and Maritza Perez. *Understanding Melanoma: What You Need to Know*. New York: The Skin Cancer Foundation, 2006.

PERIODICALS

Crotty, Kerry. "Dermoscopy and Malignant Melanoma." *Australian Doctor* (June 22, 2007): 33.

"Importance of Monitoring Children for Malignant Melanoma Stressed." *Dermatology Nursing* (December 2005): 466.

Secko, David. "Why Is Melanoma So Malignant?" *CMAJ: Canadian Medical Association Journal* (October 25, 2005): 1023.

Tuchman, Micole, and Jeffrey M. Weinberg. "Why Everyone's Skin Needs to be Examined: The Earlier a Malignant Melanoma is Diagnosed, the Higher the Cure Rate. Two Dermatologists Tell How to Find, Treat, and Prevent the Disease." *Clinical Advisor* (Feb ruary 2006): 33–36.

Wachter, Kerri. "UVA Mutations Tied to Malignant Melanoma." *Skin & Allergy News* (February 2007): 46.

Wheeler, Tracey. "Psychological Consequences of Malignant Melanoma: Patients' Experiences and Preferences." *Nursing Standard* (November 15, 2006): 42–46.

ORGANIZATIONS

American Academy of Dermatology, PO Box 4014, Schaumburg, IL, 60168-4014, (847) 240-1859, (866) 503-SKIN (7546), http://www.aad.org.

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

British Association for Cancer Research. Institute of Cancer Research, McElwain Laboratories, St. James's University Hospital, Beckett Street, Leeds, Great Britain, LS9 7TF, 440 113 206-5611, 440 113 242-9886, bacr@leeds.ac.uk, http://www.bacr.org.uk.

Canadian Cancer Society, 10 Alcorn Ave., Suite 200, Toronto, CanadaOntario, M4V 3B1, (426) 961-7223, (416) 961-4189, http://www.cancer.ca.

National Cancer Institute (National Institutes of Health), NCI Office of Communications and Education, 6116 Executive Blvd. Suite 300, Bethesda, MD, 20892-8322, (800) 4-CANCER (422-6237), cancergovstaff@mail.nih.gov, http://www.cancer.gov/.

Skin Cancer Foundation, 149 Madison Avenue Suite 901, New York, NY, 10016, (212) 725-5176, http://www.skincancer.org.

Richard A. McCartney, MD
Ken R. Wells

Malignant plasmacytoma *see* **Multiple myeloma**

Malingering

Definition

In the context of medicine, malingering is the act of intentionally feigning or exaggerating physical or psychological symptoms for motives involving personal or financial gain. Various examples of malingering include fabricating mental or physical disorders in order to avoid school, work, or military service; or to obtain financial compensation, avoid criminal prosecution, or obtain **narcotics** and other drugs.

Demographics

Malingering can occur within any individual all over the world. Because it is often impossible to determine who is malingering and who is not, it is very difficult to statistically measure how frequently malingering occurs.

Description

People may feign physical or psychological illness for any number of reasons. Faked illness can get them out of work, military duty, or criminal prosecution. It can also help them obtain financial compensation through insurance claims, lawsuits, or workers' compensation. Feigned symptoms may also be a way of getting the doctor to prescribe certain drugs.

According to the American Psychiatric Association, patients who malinger are different from people who invent symptoms for sympathy (factitious diseases). Patients who malinger clearly have something tangible to gain. People with factitious diseases appear to have a need to play the "sick" role. They may feign illness for attention or sympathy.

KEY TERMS

Antisocial personality—A personality characterized by attitudes and behaviors at odds with society's customs and moral standards, including illegal acts.

Factitious diseases—Conditions in which symptoms are deliberately manufactured by patients in order to gain attention and sympathy. Patients with factitious diseases do not fake symptoms for obvious financial gain or to evade the legal system.

Post-traumatic stress disorder (PTSD)—A disorder that occurs among survivors of severe environmental stress such as a tornado, an airplane crash, or military combat. Symptoms include anxiety, insomnia, flashbacks, and nightmares. Patients with PTSD are unnecessarily vigilant; they may experience survivor guilt, and they sometimes cannot concentrate or experience joy.

Malingering may take the form of complaints of chronic **whiplash pain** from automobile accidents. Whiplash claims are controversial. Although some people clearly do suffer from whiplash injury, others may be exaggerating the pain for insurance claims or lawsuits. Some intriguing scientific studies have shown that chronic whiplash pain after automobile accidents is almost nonexistent in countries where the legal systems do not encourage personal injury lawsuits or financial settlements. The psychological symptoms experienced by survivors of disaster (**post-traumatic stress disorder**) are also faked by malingerers.

Causes and symptoms

People malinger for personal gain. The symptoms may vary, but generally are similar to symptoms involving **chronic fatigue syndrome** or chronic pain. Generally, malingerers complain of psychological disorders such as **anxiety**. They may also complain of chronic pain for which objective tests such as x rays cannot find any physical cause.

Many dishonest methods are used by individuals feigning symptoms of malingering. Some of these include harming oneself, trying to convince medical professionals one has a disease after learning about its details (such as symptoms) in medical textbooks, taking drugs that provoke certain symptoms common in some diseases, performing excess **exercise** to induce muscle strain or other physical types of ailments, and overdosing on drugs.

Diagnosis

Malingering may be suspected:

- When a patient is referred for examination by an attorney
- When the onset of illness coincides with a large financial incentive, such as a new disability policy
- When objective medical tests do not confirm the patient's complaints
- When the patient does not cooperate with the diagnostic work-up or prescribed treatment
- When the patient has antisocial attitudes and behaviors (antisocial personality).

The diagnosis of malingering is a challenge for doctors. On the one hand, the doctor does not want to overlook a treatable disease. On the other hand, he or she does not want to continue ordering tests and treatments if the symptoms are faked. Malingering is difficult to distinguish from certain legitimate **personality disorders**, such as factitious diseases or post-traumatic distress syndrome. In legal cases, malingering patients may be referred to a psychiatrist. Psychiatrists use certain written tests to try to determine whether the patient is faking the symptoms.

Treatment

In a sense, malingering cannot be treated because the American Psychiatric Association does not recognize it as a personality disorder. Patients who are purposefully faking symptoms for gain do not want to be cured. Often, the malingering patient fails to report any improvement with treatment, and the doctor may try many treatments without success. Treatment may include cognitive behavioral therapy, **psychotherapy**, **family therapy**, or other such types of psychological treatments. However, treatment sessions may be difficult because the malingerer may not accept such treatment when confronted with it. The malingerer may then go to another medical facility where their symptoms and medical history are not known, and they are free to once again pursue their acts of malingering.

Prognosis

If the malingerer accepts his/her malady, then treatment can be positively received, and malingering

minimized or even eliminated. However, if the malingerer does not accept his/her own predicament, then treatment is often difficult and lengthy, with the outcome often times coming out without a resolution. Treatment of malingers by the medical profession has found that most patients do not accept psychiatric help. In addition, the recovery of malingers, who do not accept and acknowledge their problem, is rarely accomplished.

Prevention

The ability to accurately prevent people from malingering is difficult at best. When not detected and allowed to persist in society, the act of malingerers placed enormous financial burdens on any country's health care system. According to the Texas Department of Insurance, fraud that includes malingering costs the U.S. insurance industry approximately $150 billion each year.

Resources

BOOKS

Dell, Paul F., and John A. O'Neil, editors. *Dissociation and the Dissociative Disorders: DSM-V and Beyond*. New York: Routledge, 2009.

Morgan, Joel E., and Jerry J. Sweet, editors. *Neuropsychology of Malingering Casebook*. New York: American Academy of Clinical Neuropsychology, 2009.

Rogers, Richard, editor. *Clinical Assessment of Malingering and Deception*. New York: Guilford Press, 2008.

OTHER

Malingering. PsychNet-UK. www.psychnet-uk.com/dsm_iv/malingering.htm. (accessed August 9, 2010).

Malingering in the Clinical Setting. *Psychiatric Times*. (March 1, 2007), www.psychiatrictimes.com/display/article/10168/55286. (accessed August 9, 2010).

ORGANIZATIONS

American Psychiatric Association, 1000 Wilson Boulevard, Suite 1825, Arlington, VA, 22209, (703) 907-7300, (880) 357-7924, apa@psych.org, http://www.psych.org/.

Robert Scott Dinsmoor

Mallet finger

Definition

Mallet finger refers to the involuntary flexion (bending) of the distal phalanx of a finger caused by the disruption or tearing of its extensor digitorum tendon at the distal interphalangeal joint (DIPJ). That is, a deformity has occurred in the finger when a tendon within that finger is damaged (lacerated) by a blunt impact. The result is that instead of being in a resting position, the outermost joint on the back of the finger remains abnormally flexed. Because of this description, it is also called extensor tendon injury. Mallet finger is also called dropped finger.

Demographics

Anyone who attempts to catch a ball (such as a football) or contacts an object (such as hitting the finger against a hard, stationary table or cabinet) has the potential of getting mallet finger. A sprain of the interphalangeal joint is common in sports. The most common injury of the interphalangeal joints is a sprain of the proximal interphalangeal joint (PIPJ). This injury is often called a jammed finger. Mallet finger occurs less frequently than a jammed finger.

Description

Tendons are the strong "cables" between muscles and bones that help control movements of the body. They consist of white, glistening, fibrous cords of various length and thickness, either round or flattened, and lacking in elasticity. In mallet finger, which often occurs as a sports–related injury, the tendon on the back of the finger becomes damaged or torn near the outermost joint. Without the support provided by the tendon, the short bone at the tip of the finger drops downward at an awkward angle. This bone, referred to as the "distal phalanx" of a finger, is the one furthest from the palm. In addition to tendon damage, mallet finger may involve a fracture of the distal phalanx.

Because the injury often occurs in such sports as baseball and softball (along with basketball and volleyball), it is commonly called baseball finger. The injury occurs when a ball (or some other object such as a knife) strikes the tip of the finger on the outstretched hand, jams the finger, and damages the tendon within the finger so it can no longer straighten the finger. This contact causes rupturing (hyperflexion) of the extensor digitorum tendon. In some incidences, the force of the ball or object causes a part of the bone along the tendon to pull away.

Causes and symptoms

Mallet finger usually occurs while playing a sport that involves a ball—for example, reaching out to catch a hard pass in basketball or bare–handing a baseball. Instead of landing on the palm of the hand, the ball accidentally hits the tip of an extended (or partially extended) finger. This straight–on impact causes instantaneous stretch of the tendon, which

may overextend or tear away. Mallet finger can also result from hitting the hand against a hard object or receiving a cut from a sharp edge such as a knife.

Symptoms of mallet finger include **pain** and swelling around the top part of the finger, near the outermost joint. These symptoms occur immediately after the injury. Redness, bruising, and further swelling develop soon afterward. The finger may be unable to be extended; however, it still may be moved with help. Sometimes blood collects beneath the nail of the affected finger. If the object also strikes the nail, it may become detached. The tip of the finger has an abnormal–looking downward droop.

Diagnosis

Mallet finger is usually diagnosed after a relatively brief **physical examination** conducted by an emergency care physician or by an orthopedist, the type of doctor who specializes in such injuries. The downward droop of the fingertip is the major indication of mallet finger, along with the tenderness and pain that occurs in the affected area. X rays will be taken to determine if the bone at the top of the finger has been fractured. Mallet finger is typically covered by medical insurance.

Treatment

If symptoms of mallet finger appear, the affected individual should consult a physician or seek emergency care. In the meantime, ice (wrapped in a towel or cloth) can be applied to the affected area to help reduce swelling and tenderness, and to alleviate pain.

Treatment usually involves first applying ice to the finger, with the affected hand elevated above the heart. The medical professional will in almost all cases attach a splint, sometimes called a Mallet splint, around the top of the affected finger in order to keep it extended and allow the injury to heal. The splint must be worn at all times for six to eight weeks, though it may be briefly removed to wash the finger, but with extreme care so as not to allow the fingertip to bend. For the next six to eight weeks after that, the splint need only be worn during sleep or athletic activities.

Two other treatment option include the wearing of a small plaster cast or the wearing of an extension block k–wire for approximately four weeks. In all cases, the device helps to immobilize the finger so that the tendon can reattach itself.

After the full amount of time has expired for wearing the device, it is then usually worn less often, but for another three to four weeks.

KEY TERMS

Distal phalanx—The outermost bone of any finger or toe.

Fracture—A break in bone.

Orthopedist—A doctor who specializes in disorders of the musculoskeletal system.

Phalanx—Any of the digital bones of the hand or foot. Humans have three phalanges to each finger and toe with the exception of the thumb and big toe which have only two each.

Tendon—A tough cord of dense white fibrous connective tissue that connects a muscle with some other part, especially a bone, and transmits the force which the muscle exerts.

If the bone at the top of the finger has sustained a large fracture, surgery may be necessary. An orthopedic surgeon or a hand specialist will usually perform the surgery. If the tendon was damaged due to a cut, stitches may be required both to repair the tendon and to adequately close the wound. In addition, if blood is present underneath the nail, or if the nail is detached, the possibility of a nail laceration or a compound fracture is present, and medical help should be sought immediately.

Over-the-counter (OTC) or prescription pain medication can be used to alleviate pain.

Alternative treatment

Acupuncture, therapeutic massage, and **yoga** are believed by some practitioners of alternative medicine to have generalized pain–relieving effects. Any of these therapies may provide additional comfort while the finger heals.

Prognosis

With proper treatment, most people regain full use of the affected finger. However, in some cases, although the finger regains its normal position, the person never regains full extension of the fingertip. In such cases, a deformity called “swan neck” results. While treatment is in progress, the device to hold the finger stationary sometimes causes a pressure sore over the distal interphalengeal joint. When damage to the bone or nail occurs, complications can result, such as stiffness, infection, and tenderness.

Prevention

There is not a specific way to prevent mallet finger, other than using extreme care and caution when performing routine activities and catching objects during sporting events and activities.

Resources

BOOKS

Judd, Sandra J. *Sports Injuries Sourcebook*. Detroit: Omnigraphics, 2007.

Madden, Christopher C., et al., editors. *Netter' Sports Medicine*. Philadelphia: Saunders/Elsevier, 2010.

Prentice, William E., editor. *Rehabilitation Techniques for Sports Medicine and Athletic Training*. New York: McGraw-Hill, 2011.

OTHER

"Mallet Finger." eMedicine. (February 17, 2009), http://emedicine.medscape.com/article/1242305-overview (accessed September 26, 2010).

"Mallet Finger." WebMD. www. webmd.com/fitness–exercise/mallet–finger (accessed September 26, 2010).

"Mallet Finger (Baseball Finger)." American Academy of Orthopaedic Surgeons. (October 2007), http://orthoinfo.aaos.org/topic.cfm?topic = A00018 (accessed September 26, 2010).

ORGANIZATIONS

American Academy of Orthopaedic Surgeons (AAOS), 6300 North River Rd., Rosemont, IL, 60018–4262, (847) 823–7186, (847) 823–8125, http://www.aaos.org/.

American Society for Surgery of the Hand (ASSH), 6300 North River Rd., Suite 600, Rosemont, IL, 60018, (847) 384–8300, (847) 384–1435, info@assh.org, http://www.assh.org/.

Greg Annussek

Mallory-Weiss syndrome

Definition

Mallory-Weiss syndrome is bleeding from an arterial blood vessel in the upper gastrointestinal tract, caused by a mucosal gastric tear at or near the point where the esophagus and stomach join.

Description

Mallory-Weiss syndrome causes about 5% of all upper gastrointestinal bleeding. The condition was originally diagnosed in alcoholics and is associated with heavy alcohol use, although it can also be found in patients who are not alcoholics. Earlier episodes of heavy hiccupping, **vomiting**, and retching are reported by about half the patients who are diagnosed with Mallory-Weiss syndrome. It is thought that the tear or laceration occurs when there is a sudden increase in intra-abdominal pressure. Patients with increased pressure in the vein leading into the liver (portal **hypertension**) are more likely to bleed heavily from an esophageal laceration than those whose blood pressure is normal.

KEY TERMS

Electrolytes—Salts and minerals that can conduct electrical impulses in the body. Common human electrolytes are sodium chloride, potassium, calcium, and sodium bicarbonate. Electrolytes control the fluid balance of the body and are important in muscle contraction, energy generation, and almost every major biochemical reaction in the body.

Endoscopy—A procedure in which an instrument containing a camera and a light source is inserted into the gastrointestinal tract so that the doctor can visually inspect the gastrointestinal system.

Esophageal varix—An enlarged vein of the esophagus. (Plural: esophageal varices.)

Portal hypertension—High blood pressure in the portal vein, which carries blood from the abdominal organs to the liver.

Causes and symptoms

In Mallory-Weiss syndrome, a tear occurs in the gastric mucosa, near where the esophagus and stomach join. About 10% of the tears are in the esophagus. Most are either right at the junction of the esophagus and stomach or in the stomach just slightly below the junction.

Bleeding from the tear causes a disruption in fluid and electrolyte balance of the body. The patient often produces vomit tinged with either fresh blood or older, blackish blood. Blood loss can be considerable.

Diagnosis

A Mallory-Weiss syndrome tear is not visible on standard upper gastrointestinal x rays. A tear about one-eighth to one and one-half inches long (0.5–4 cm) is revealed by **endoscopy**. Endoscopy also shows that in 35% of patients there is another potential cause for gastrointestinal bleeding, such as peptic ulcer, erosive **gastritis**, or esophageal varices.

Treatment

The patient is resuscitated and stabilized with blood transfusions and intravenous fluids to restore the fluid and electrolyte balance. Most of the time, esophageal bleeding stops spontaneously. When bleeding does not stop, patients are treated with an injection of epinephrine (adrenaline) and/or the bleeding artery is cauterized with heat. If these treatments fail, surgery is performed to stop the bleeding.

Prognosis

In 90-95% of patients whose bleeding does not stop spontaneously, cauterization without surgery will stop the bleeding. Patients at highest risk for a recurrence of bleeding are those with portal hypertension.

Prevention

Mallory-Weiss syndrome is associated with **alcoholism**. Limiting alcohol intake may help prevent the disorder.

Resources

BOOKS

McPhee, Stephen, and Maxine Papadakis. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw-Hill Medical, 2009.

Tish Davidson, A.M.

Malnutrition

Definition

Malnutrition is the condition that develops when the body acquires a disproportionate, inadequate, or unbalanced amount of the **vitamins**, **minerals**, and other nutrients it needs to maintain healthy tissues and organ function. It may also develop when the body has problems digesting or absorbing nutrients, or has certain medical conditions. When malnutrition occurs, many different disorders may arise depending on the specific nutrient(s) involved in the malnutrition. One form of malnutrition is called **starvation**.

Demographics

Malnutrition is a major problem all over the world, but it is more likely to occur in the poorest countries of the world where natural disasters, political instabilities and wars, and poverty are more likely to be present. It is an exceptionally serious problem with infants, children, and adolescents because such nutrients are exceptionally important during this period of extreme physical and mental growth. Malnutrition is estimated is occur in over 70% of children living in Asia, about 26% in Africa, and around four percent in Latin America and the Caribbean. In the United States, about one percent of children suffer from chronic malnutrition. According to the United Nations' Food Programme (UNFP), a child dies every six seconds somewhere in the world from malnutrition and related causes.

According to the United Nations Food and Agriculture Organization (FAO), approximately 1.02 billion people in the world are considered to be below standards provided by international nutritional guidelines, from data presented on October 14, 2009. This 2009 figure is greater than in 2006, when the number stood at 854 million. In this same period of time, it is estimated that poor **nutrition** is a contributing factor in approximately five million of the 10.9 million deaths each year of children.

Description

Undernutrition

Infants, young children, and teenagers need additional nutrients. So do women who are pregnant or **breastfeeding**. Nutrient loss can be accelerated by **diarrhea**, excessive sweating, heavy bleeding (hemorrhage), or kidney failure. Nutrient intake can be restricted by age–related illnesses and conditions, excessive dieting, **food allergies**, severe injury, serious illness, a lengthy hospitalization, or **substance abuse**.

For instance, someone who has a untreated medical disorder—such as **celiac disease** in which gluten (a protein found in barley, rye, and wheat) is not digestible; or **lactose intolerance**, in which milk and other dairy products are difficult to digest—is at a higher risk for malnutrition than someone without such disorders.

The leading cause of **death** in children in developing countries is **protein–energy malnutrition**. This type of malnutrition is the result of inadequate intake of calories from proteins, vitamins, and minerals. Children who are already undernourished can suffer from protein–energy malnutrition (PEM) when rapid growth, infection, or disease increases the need for protein and essential minerals. These essential minerals are known as micronutrients or trace elements. The World Health Organization (WHO) estimates that two billion people around the world do not consume sufficient amounts of iron in their daily diet. Iron is an

important nutrient that is found in red meat, eggs, and foods fortified with iron.

Two types of protein–energy malnutrition have been described—kwashiorkor and marasmus. Kwashiorkor occurs with fair or adequate calorie intake but inadequate protein intake, while marasmus occurs when the diet is inadequate in both calories and protein. A kwashiorkor diet may consist of only vegetables. In such cases, a wide variety of vegetables is needed to obtain all the necessary nutrients in one's diet. With a marasmus diet the body may receive so little protein that it eventually cannot digest any protein, with irreversible and fatal results.

Overnutrition

In the United States, nutritional deficiencies have generally been replaced by dietary imbalances or excesses associated with many of the leading causes of death and disability. Overnutrition results from eating too much, eating too many of the wrong things, not exercising enough, or taking too many vitamins or other dietary replacements.

Risk of overnutrition is also increased by being more than 20% overweight, consuming a diet high in fat and salt, and taking high doses of:

- Nicotinic acid (niacin) to lower elevated cholesterol levels
- Vitamin B_6 to relieve premenstrual syndrome
- Vitamin A to clear up skin problems
- Iron or other trace minerals not prescribed by a doctor.

Nutritional disorders can affect any system in the body and the senses of sight, taste, and smell. They may also produce **anxiety**, changes in mood, and other psychiatric symptoms. Malnutrition begins with changes in nutrient levels in blood and tissues. Alterations in enzyme levels, tissue abnormalities, and organ malfunction may be followed by illness and death.

Causes and symptoms

Causes

Poverty and lack of food are the primary reasons why malnutrition occurs in the United States. Ten percent of all members of low–income households do not always have enough healthful foods to eat. Protein–energy malnutrition occurs in 50% of surgical patients and in 48% of all other hospital patients.

Another cause of malnutrition is loss of appetite associated with the **aging** process. Malnutrition affects one in four elderly Americans, in part because they may lose interest in eating. In addition, such dementia–type illnesses as **Alzheimer's disease** may cause elderly persons to forget to eat.

There is an increased risk of malnutrition associated with chronic diseases, especially disease of the intestinal tract, kidneys, and liver. Patients with chronic diseases like **cancer**, acquired immune deficiency syndrome (**AIDS**), intestinal parasites, and other gastric disorders may lose weight rapidly and become susceptible to undernourishment because they cannot absorb valuable vitamins, calories, and iron.

People with drug or alcohol dependencies are also at increased risk of malnutrition. These people tend to maintain inadequate **diets** for long periods of time, and their ability to absorb nutrients is impaired by the alcohol or drug's affect on body tissues, particularly the liver, pancreas, and brain.

Eating disorders are another cause of malnutrition. People with anorexia or bulimia may restrict their food intake to such extremes that they become malnourished.

Food **allergies** may also lead to malnutrition. Some people with food allergies may find it difficult to obtain food that they can digest. In addition, people with food allergies often need additional calorie intake to maintain their weight.

Failure to absorb nutrients in food following bariatric (weight loss) surgery are yet another cause of malnutrition. **Bariatric surgery** includes such techniques as stomach stapling (gastroplasty) and various intestinal bypass procedures to help people eat less and lose weight. Malnutrition is, however, a possible side effect of bariatric surgery.

Symptoms

Unintentionally losing 10 pounds (4.5 kilograms of mass) or more in weight may be a sign of malnutrition. Malnourished people may appear to be skinny or bloated. Their skin is pale, thick, dry, and **bruises** easily. **Rashes** and changes in pigmentation are common.

Hair is thin, tightly curled, and pulls out easily. Joints ache and bones are soft and tender. The gums bleed easily, and they are swollen. The tongue may be swollen or shriveled and cracked. Visual disturbances include night blindness and increased sensitivity to light and glare.

Symptoms may vary depending on the specific cause of the malnutrition. However, some other general symptoms of malnutrition include:

KEY TERMS

Anemia—Not enough red blood cells in the blood.

Anorexia nervosa—Eating disorder marked by malnutrition and weight loss, commonly occurring in young women.

Bariatric—Pertaining to the study, prevention, or treatment of overweight.

Calorie—A unit of heat measurement used in nutrition to measure the energy value of foods. A Calorie is the amount of heat energy needed to raise the temperature of 1 kilogram of water 1°C.

Kwashiorkor—Severe malnutrition in children primarily caused by a protein–poor diet, characterized by growth retardation.

Marasmus—Severe malnutrition in children caused by a diet lacking in calories as well as protein. Marasmus may also be caused by disease and parasitic infection.

Micronutrients—Essential dietary elements that are needed only in very small quantities. Micronutrients are also known as trace elements. They include copper, zinc, selenium, iodine, magnesium, iron, cobalt, and chromium.

- anemia
- fatigue
- diarrhea
- disorientation and dizziness
- fragile bones, osteoporosis
- irritability, anxiety, and attention deficits
- goiter (enlarged thyroid gland)
- loss of reflexes and lack of muscular coordination
- muscle twitches
- poor immune function (which hinders the body' ability to fight infections)
- difficulty learning
- slow growth, both physically and mentally, in children
- amenorrhea (cessation of menstrual periods)
- scaling and cracking of the lips and mouth
- dry, scaly skin
- bloated stomach.

Malnourished children may be short for their age, thin, listless, and have weakened immune systems.

Diagnosis

Overall appearance, behavior, body–fat distribution, and organ function can alert a family physician, internist, or nutrition specialist to the presence of malnutrition. Patients may be asked to record what they eat during a specific period. X rays can determine bone density and reveal gastrointestinal disturbances, and heart and lung damage.

Blood and urine tests are used to measure the patient's levels of vitamins, minerals, and waste products. Nutritional status can also be determined by:

- Comparing a patient's weight to standardized charts
- Calculating body mass index (BMI) according to a formula that divides height into weight
- Measuring skin–fold thickness or the circumference of the upper arm.

Treatment

Normalizing nutritional status starts with a nutritional assessment. This process enables a clinical nutritionist or registered dietician to confirm the presence of malnutrition, assess the effects of the disorder, and formulate diets that will restore adequate nutrition.

Patients who cannot or will not eat, or who are unable to absorb nutrients taken by mouth, may be fed intravenously (parenteral nutrition) or through a tube inserted into the gastrointestinal (GI) tract (enteral nutrition).

Tube feeding is often used to provide nutrients to patients who have suffered **burns** or who have inflammatory bowel disease. This procedure involves inserting a thin tube through the nose and carefully guiding it along the throat until it reaches the stomach or small intestine. If long–term tube feeding is necessary, the tube may be placed directly into the stomach or small intestine through an incision in the abdomen.

Tube feeding cannot always deliver adequate nutrients to patients who:

- Are severely malnourished
- Require surgery
- Are undergoing chemotherapy or radiation treatments
- Have been seriously burned
- Have persistent diarrhea or vomiting
- Whose gastrointestinal tract is paralyzed.

Intravenous feeding can supply some or all of the nutrients these patients need.

Prognosis

The prognosis for malnutrition depends directly on its cause. Most cases of malnutrition can be corrected. However, if the cause is an illness, then the condition must be first eliminated so that the patient can completely recover from malnutrition. In some cases, the damage done by malnutrition may be irreversible even though it is not severe enough to cause death. Up to 10% of a person's body weight can be lost without side effects, but if more than 40% is lost, the situation is almost always fatal. Death usually results from **heart failure**, electrolyte imbalance, or low body temperature. Patients with semi–consciousness, persistent diarrhea, **jaundice**, or low blood **sodium** levels have a poorer prognosis.

Some children with protein–energy malnutrition recover completely. Others have many health problems throughout life, including **mental retardation** and the inability to absorb nutrients through the intestinal tract. Prognosis for all patients with malnutrition seems to be dependent on the age of the patient, and the length and severity of the malnutrition, with young children and the elderly having the highest rate of long–term complications, including both physical and mental disabilities and illnesses, and death.

Prevention

Breastfeeding a baby for at least six months is considered the best way to prevent early-childhood malnutrition. The U.S. Department of Agriculture and the Department of Health and Human Services recommend that all Americans over the age of two years:

- Consume plenty of fruits, grains, and vegetables
- Eat a well–balanced variety of foods that are low in fats and cholesterols and contain only moderate amounts of salt, sugars, and sodium
- Engage in moderate physical activity for at least 30 minutes, at least several times a week
- Achieve or maintain their ideal weight
- Use alcohol sparingly or avoid it altogether.

Every patient admitted to a hospital should be screened for the presence of illnesses and conditions that could lead to protein–energy malnutrition. Patients with higher–than–average risk for malnutrition should be more closely assessed and reevaluated often during long–term hospitalization or nursing–home care.

Resources

BOOKS

Haerens, Margaret, editor. *Malnutrition*. Detroit: Greenhaven Press, 2009.

Kalhan, Satish C., Andrew M. Prentice, and Chittaranjan S. Yajnik, editors. *Emerging Societies: Coexistence of Childhood Malnutrition and Obesity*. Basel, Switzerland: Karger, 2009.

Lomborg, Bjorn. *Global Crises, Global Solutions*. Cambridge, UK: Cambridge University Press, 2009.

OTHER

"Hunger and Malnutrition." KidsHealth.org http://kidshealth.org/parent/nutrition_fit/nutrition/hunger.html (accessed September 26, 2010).

"Malnutrition." Medline Plus, National Library of Medicine and National Institutes of Health. (May 12, 2009), http ://www.nlm.nih.gov/medlineplus/ency/article/000404.htm. (accessed September 26, 2010).

"World Hunger Facts 2010." WorldHunger.org. www.worldhunger.org/articles/Learn/world%20hunger%20facts%20 2002.htm. (accessed September 26, 2010).

ORGANIZATIONS

American Institute of Nutrition (AIN), 9650 Rockville Pike, Bethesda, MD, 20814, (301) 634–7050, (301) 634–7892, http://www.nutrition.org/.

Mary K. Fyke
Rebecca J. Frey, PhD

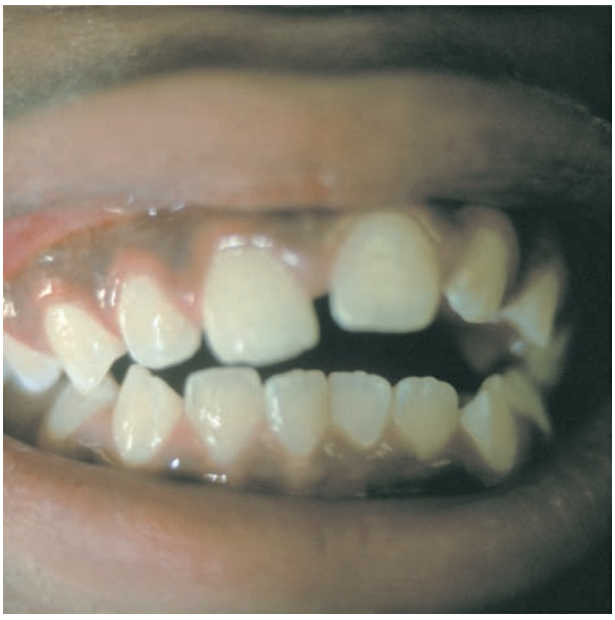
Malocclusion

Definition

Malocclusion is a misalignment in the way the upper and lower sets of teeth fit together in biting or chewing. The word malocclusion literally means "bad bite." The condition may also be referred to with such terms as irregular bite, misaligned teeth, crossbite, underbite, or overbite. American dentist and orthodontist Edward Angle (1855–1930) was the first scientist to classify malocclusion.

Demographics

Most humans have various tiny degrees of malocclusion, with most problems being handed down from generation to generation (hereditary). Their problem is not very noticeable and does not usually need to be treated. However, others have more serious forms of malocclusion; often times require orthodontic or surgical treatment.



This patient's teeth are misarranged because of excessive thumb sucking. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Orthodontia treatments usually include the use of braces and retainers. *(© Lester V. Bergman/Corbis.)*

Description

Occlusion refers to the alignment of teeth, specifically the way that the upper set of teeth fit slightly over the lower set of teeth. Malocclusion occurs when there is a misalignment of these two sets of teeth. The cause may be due to the differing sizes of the upper and lower jaws, or possibly due to the jaw in relationship to the size of the teeth. Within the problem, the teeth may appear crooked, crowded, or protruding. It may affect a person's appearance, speech, and/or ability to eat.

Three different classes of malocclusion generally occurs. They are:

- Neutrocclusion: The bite of the two sets of teeth is normal but the upper set overlap the lower teeth more than usual, which causes problems such as overcrowding of the teeth or incorrect spacing of the teeth.
- Distocclusion (retrognathism or "overbite"): The upper jaw and its teeth overlap the bottom jaw and its teeth.
- Mesiocclusio (prognathism or "underbite"): The lower jaw protrudes forward, which causes the lower jaw and its teeth to overlap the upper jaw and its teeth.

Causes and symptoms

Malocclusions are most often inherited, but may be acquired. Inherited conditions include too many or too few teeth, too much or too little space between teeth, irregular mouth and jaw size and shape, and atypical formations of the jaws and face, such as a **cleft palate**. Malocclusions may be acquired from habits like finger or thumb sucking (or pacifier use), tongue thrusting, premature loss of teeth from an accident or dental disease, and medical conditions such as enlarged tonsils and adenoids that lead to mouth breathing.

They may also occur due to incorrectly fitting **dental fillings**, appliances, retainers, and other devices worn on the teeth. Other causes include an abnormal structure to the face, **pain** or other discomfort while biting and chewing, and difficulties with speaking or breathing.

Malocclusions may be symptomless or they may produce pain from increased **stress** on the oral structures. Teeth may show abnormal signs of wear on the chewing surfaces or decay in areas of tight overlap. Chewing may be difficult.

Diagnosis

Malocclusion is most often found during a routine dental examination. A dentist will check a patient's occlusion by watching how the teeth make contact when the patient bites down normally. The dentist may ask the patient to bite down with a piece of coated paper between the upper and lower teeth; this paper

will leave colored marks at the points of contact. When malocclusion is suspected, the dentist will commonly refer the patient to an orthodontist for further diagnosis and treatment. The orthodontist will take photographs and x rays of the face and mouth for further study. To confirm the presence and extent of malocclusion, the orthodontist makes plaster, plastic, or artificial stone models of the patient's teeth from impressions. These models duplicate the fit of the teeth and are very useful in treatment planning.

Treatment

Even though most people have minor forms of malocclusion, such cases are rarely treated by a medical professional. However, when it is more serious malocclusion may be remedied by orthodontic treatment; **orthodontics** is a specialty of dentistry that manages the growth and correction of dental and facial structures. Braces are the most commonly used orthodontic appliances in the treatment of malocclusion. Such measures are used to position teeth into a more normal alignment. According to the U.S. Bureau of Labor Statistics, about 5,000 orthodontists are practicing in the United States in 2008. At any given time, approximately 4 million people in the United States are wearing braces, including about 800,000 adults.

Braces apply constant gentle force to slowly change the position of the teeth, straightening them and properly aligning them with the opposing teeth. Braces consist of brackets cemented to the surface of each tooth and wires of stainless steel or nickel titanium alloy. When the wires are threaded through the brackets, they exert pressure against the teeth, causing them to move gradually.

Invisalign® is an alternative to traditional braces and can also be used to correct malocclusion. Invisalign is a series of clear aligners that are worn to shift and straighten teeth gradually. Each aligner is custom made for the wearer and changed every two weeks to slowly shift teeth into correct alignment.

Braces are not removable for daily tooth brushing, so the patient must be especially diligent about keeping the mouth clean and removing food particles which become easily trapped, to prevent **tooth decay**. Crunchy foods should be avoided to minimize the risk of breaking the appliance. Hard fruits, vegetables, and breads must be cut into bite-sized pieces before eating. Foods that are sticky, including chewing gum, should be avoided because they may pull off the brackets or weaken the cement. Carbonated beverages may also weaken the cement, as well as contribute to tooth decay. Teeth should be brushed immediately after eating sweet foods. Special floss threaders are available to make flossing easier.

If overcrowding is creating malocclusion, one or more teeth may be extracted (surgically removed), giving the others room to move. If a tooth has not yet erupted or is prematurely lost, then the orthodontist may insert an appliance called a space maintainer to keep the other teeth from moving out of their natural position. In severe cases of malocclusion, surgery may be necessary and the patient would be referred to yet another specialist, an oral or maxillofacial surgeon.

Once the teeth have been moved into their new position, the braces are removed and a retainer is worn until the teeth stabilize in that position. Retainers do not move teeth, they only hold them in place.

Orthodontic treatment is the only effective treatment for malocclusion not requiring surgery. However, depending on the cause and severity of the condition, an orthodontist may be able to suggest other appliances as alternatives to braces.

Alternative treatment

There are some techniques of **craniosacral therapy** that can alter structure. This therapy may allow correction of some cases of malocclusion. If surgery is required, pre- and post-surgical care with homeopathic remedies, as well as vitamin and mineral supplements, can enhance recovery. Night guards are sometimes recommended to ease the strain on the jaw and to limit teeth grinding.

Prognosis

Depending on the cause and severity of the malocclusion and the appliance used in treatment, a patient may expect correction of the condition to take two or more years. Patients typically wear braces 18 to 24 months and a retainer for another year. Treatment is faster and more successful in children and teens whose teeth and bones are still developing. The length of treatment time is also affected by how well the patient follows orthodontic instructions. When malocclusion is corrected, it usually reduces the risk from tooth decay, along with helping to relieve undue pressure on the temporomandibular joint (TMJ), which can cause TMJ disorder (TMD). However, then treatment is applied to someone with malocclusion, specifically with braces, there may be some discomfort during the treatment. Irritation of the gums and mouth may result from the appliances on the teeth. Sometimes chewing or speaking may be adversely affected.

KEY TERMS

Braces—An orthodontic appliance consisting or brackets cemented to the surface of each tooth and wires of stainless steel or nickel titanium alloy. Braces are used to treat malocclusion by changing the position of the teeth.

Impression—An imprint of the upper or lower teeth made in a pliable material that sets. When this material has hardened, it may be filled with plaster, plastic, or artificial stone to make an exact model of the teeth.

Occlusion—The way the upper and lower teeth fit together in biting or chewing.

Retainer—An orthodontic appliance that is worn to stabilize teeth in a new position.

Space maintainer—An orthodontic appliance that is worn to prevent adjacent teeth from moving into the space left by an unerupted or prematurely lost tooth.

Prevention

In general, malocclusion is not preventable. It may be minimized by controlling habits such as finger or thumb sucking. An initial consultation with an orthodontist before a child is seven years old may lead to appropriate management of the growth and development of the child's dental and facial structures, circumventing many of the factors contributing to malocclusion.

Resources

BOOKS

Krishnan, Vinod, and Ze'ev Davidovitch, editors. *Biological Mechanisms of Tooth Movement*. Chichester, UK: Wiley-Blackwell, 2009.

McInerny, Thomas K, et al., editors. *American Academy of Pediatrics Textbook of Pediatric Care*. Washington, DC: American Academy of Pediatrics, 2009.

Nanda, Ravindra, and Sunil Kapila, editors. *Current Therapy in Orthodontics*. St. Louis: Mosby Elsevier, 2010.

OTHER

Malocclusion. Medline Plus, National Library of Medicine and National Institutes of Health. (February 22, 2010), www.nlm.nih.gov/medlineplus/ency/article/001058.htm. (accessed August 10, 2010).

Malocclusion and Orthodontics—Treatment Overview. WebMD. (January 22, 2009), www.webmd.com/oral-health/tc/malocclusion-and-orthodontics-treatment-overview. (accessed August 10, 2010).

ORGANIZATIONS

American Association of Oral and Maxillofacial Surgeons, 9700 West Bryn Mawr Avenue, Rosemont, IL, 60018-5701, (847) 678-6200, (800) 822-6637, (847) 678-6286, http://www.aaoms.org/.

American Association of Orthodontists, 401 North Lindbergh Boulevard, St. Louis, MO, 63141-7816, (800) 787-2444, http://www.braces.org/.

Bethany Thivierge

MALT lymphoma

Definition

MALT lymphomas are solid tumors that originate from cancerous growth of immune cells that are recruited to secretory tissue such as the gastrointestinal tract, salivary glands, lungs, and the thyroid gland.

Description

The digestive tract is generally not associated with lymphoid tissue, with the exception of small collections of lymphocytes such as Peyer's patches. A specific kind of white blood cell, B-lymphocytes, can accumulate in response to infections of the digestive tract and other secretory tissues, or as a result of autoimmune conditions such as Sjgren's syndrome. When the growth of these lymphocytes is maintained through continued infection or autoimmune disease, a malignant cell can arise and replace the normal lymphocytes. These lymphomas, derived from mucosa-associated lymphoid tissue (MALT), most commonly arise in the stomach. Their growth seems to be dependent upon continuous stimulation of the immune system by an infectious agent, such as H. pylori, or some other entity, termed an antigen, that the body recognizes as foreign. This antigen-driven growth permits these tumors to be treated by eliminating the stimulus that generated the original, normal immune response. In the stomach they are associated, in greater than 90% of all cases, with the bacteria called Helicobacter pylori (H. pylori). This bacteria is also associated with peptic stomach irritation, ulcers, and gastric **cancer**. MALT lymphomas are generally indolent, that is, they grow slowly and cause little in the way of symptoms. Those MALT lymphomas that arise in the stomach in response to H. pylori infections are generally successfully treated with **antibiotics**, which eliminate the bacteria.

Demographics

MALT lymphomas occur at a frequency of about 1.5 per 100,000 people per year in the United States and account for about 10% of all non-Hodgkin's lymphomas. The frequency varies among different populations. For example, in parts of Italy the frequency of MALT lymphomas is as high as 13 per 100,000 people per year. This can in part be attributed to different rates of infection with H. pylori. However, other hereditary, dietary, or environmental factors are almost certainly involved.

Causes and symptoms

The majority of MALT lymphomas appear to be the result of infectious agents, most commonly H. pylori in the stomach. It is not known if infectious agents also cause MALT lymphomas outside of the stomach. In some cases, such as in the thyroid, MALT lymphomas seem to arise in patients who have autoimmune diseases, which make their immune systems treat their own tissue as foreign or antigenic. It is believed that there must be additional factors, in addition to infection or autoimmunity, that influence the development of MALT lymphomas. For example, in the United States, where infections with H. pylori are quite common, less than 1 in 30,000 people who have H. pylori in their stomachs develop MALT lymphomas. In addition, individuals who develop MALT lymphomas are more likely to develop other forms of cancer. This would suggest that there might be genetic factors predisposing individuals to develop MALT lymphomas or other tumors in response to environmental or infectious agents.

In general, patients have stomach **pain**, ulcers, or other localized symptoms, but rarely do they suffer from systemic complaints such as **fatigue** or **fever**.

Diagnosis

The indolent nature of most MALT lymphomas means that the majority of patients are diagnosed at early stages with relatively nonspecific symptoms. In the case of gastric MALT lymphomas, the physician will then have a gastroenterologist perform an **endoscopy** to examine the interior of the stomach. MALT lymphomas are then recognized as areas of inflammation or ulceration within the stomach. It is unusual for masses recognizable as tumors to be seen upon examination. Definitive diagnosis of MALT lymphoma requires a biopsy, in which a bit of tissue is removed from the stomach or other involved site. Examination of this tissue by a pathologist is the first step in distinguishing among the possible diagnoses of inflammation, indolent lymphoma, or a more aggressive form of cancer, such as gastric cancer or a rapidly growing non-Hodgkin's lymphoma. The pathologist evaluates the type of lymphoid cells that are present in the biopsy to establish the nature of the lesion. In addition, it is essential that the pathologist determine whether or not the lymphoma has grown beyond the borders of the mucosa, which lines the stomach or other gland.

Treatment

The best staging system to employ for MALT lymphomas is still the subject of discussion. However, it is standard practice that patients presenting with MALT lymphomas should be evaluated in a similar manner to individuals with nodal lymphomas, the more common type of lymphoma that originates at sites within the lymphoid system. These procedures include a complete history and physical, blood tests, chest x rays, and **bone marrow biopsy**. This evaluation will permit the oncologist to determine if the disease is localized or if it has spread to other sites within the body.

In general, the prognosis for patients with MALT lymphomas is good, with overall five-year survival rates that are greater than 80%. The features that are most closely related to the outlook for newly diagnosed individual patients are: whether the primary site is in the stomach or is extra-gastric; if the disease has spread beyond the initial location; and whether the histologic evaluation of the initial tumor biopsies is consistent with a low-grade, slowly growing lesion, as compared to a high-grade lesion that is more rapidly growing. In general, the histologic grade is the most important feature, with high-grade lesions requiring the most aggressive treatment.

Treatment of MALT lymphomas differs from that of most lymphomas. In the most common type of MALT lymphomas—low-grade lesions originating in the stomach—treatment with antibiotics to eliminate H. pylori leads to complete remissions in the majority of patients. The effectiveness of this treatment is indistinguishable from surgery, **chemotherapy**, **radiation therapy**, or a combination of surgery with drugs or irradiation. Approximately one-third of patients in this group have evidence of disseminated disease, where lymphoma cells are detected at sites in addition to the gastric mucosa. The response of these patients to antibiotic treatment is not significantly different from that for individuals with localized disease. For both groups a complete remission is achieved in about 75% of patients, who remain, on average, free of disease for about 5 years.

KEY TERMS

Antigen—A foreign substance that leads to an immune response, including the production of antibodies by B cells.

Autoimmune disease—A condition in which an individual's immune system reacts to their own tissues, viewing self components as if they were foreign antigens.

Bone marrow biopsy—A procedure in which cellular material is removed from the pelvis or breastbone and examined under a microscope to look for the presence of abnormal blood cells characteristic of specific forms of leukemia and lymphoma.

Indolent lymphoma (also called low-grade)—Cancerous growths of lymphoid tissue that progress slowly to more aggressive forms of cancer.

Lymphoid tissue—Sites within the body that produce cells of the immune system, including lymph nodes, bone marrow, and the thymus.

Prognosis

Patients with MALT lymphomas arising outside of the digestive tract also have good prognoses. Effective treatment for these lymphomas has been achieved with local radiation, chemotherapy, and/or interferon. Surgery followed by chemotherapy or radiation is also effective with nongastrointestinal MALT lymphomas. Overall these patients have five-year survival rates greater than 90%.

While the outlook for patients with MALT lymphomas is good, difficulties in diagnosis and staging have left the optimal treatment a matter of continued study. This is an especially open question for those patients who fail to respond to antibiotic therapy, or whose disease recurs. It may be the case that in these patients, the MALT lymphoma may have already progressed to a point where high-grade lesions, not observed in the original biopsies, were resistant to the initial treatment. The best treatment for these patients remains to be established. In general, these patients are treated with chemotherapy in a similar manner to patients with other types of lymphoma. Given the success of antibiotics, and the good prognosis for gastric MALT lymphomas in general, no sufficient body of evidence exists to determine the best chemotherapy for patients who fail to achieve a complete and lasting remission upon initial treatment. At present, a chemotherapeutic regime designated CHOP includes the anti-cancer drugs cyclophosphamide, doxorubicin, vincristine, and prednisone. Similar drug combinations are being used for patients whose MALT lymphomas do not respond to antibiotic treatment.

Clinical trials are underway and mostly concentrate upon optimizing treatment of gastric MALT lymphomas that involve H. pylori. The aspects of treatment being addressed are the most effective antibiotics and the use of **antacids** to modulate irritation in the stomach. These protocols have been designed to follow the natural history of gastric lymphomas and to establish the biological features that predict treatment response to antibiotics and duration of remission.

Prevention

There are currently no commonly accepted means to prevent MALT lymphomas. While the H. pylori infections are associated with this and other gastric disease, the eradication of H pylori in asymptomatic individuals is not currently recommended for prevention of MALT lymphomas or gastric cancer.

Resources

OTHER

"Low-Grade Non-Hodgkin's Lymphoma: A Year 2000 Perspective." *Medscape*. June 2000. http://cme.medscape.com/viewarticle/419087_6.

Warren Maltzman, Ph.D.

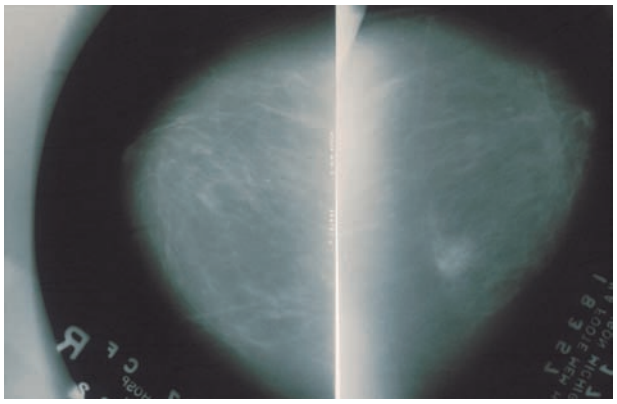
Malta fever *see* **Brucellosis**

Mammogram screening *see* **Mammography**

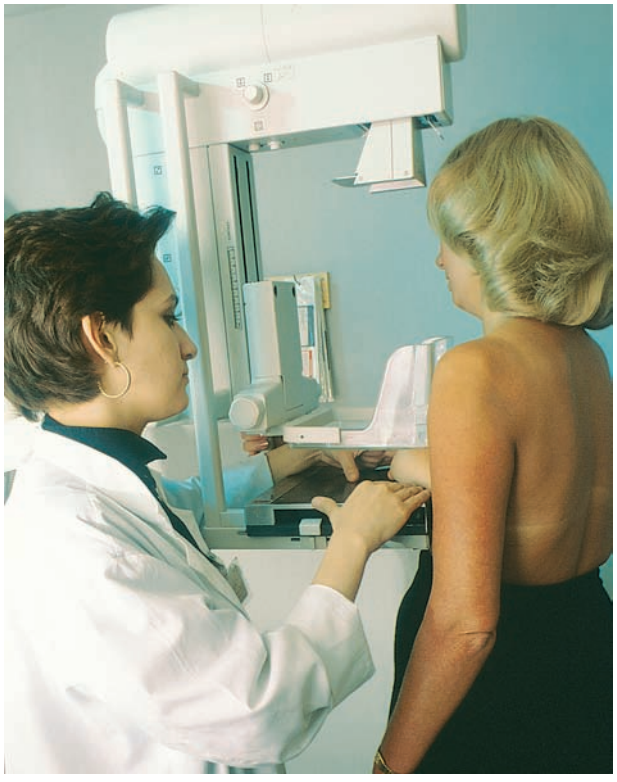
Mammography

Definition

Mammography is the study of the breast using x rays. The actual test is called a mammogram. It is an x ray of the breast that shows the fatty, fibrous, and glandular tissues. There are two types of mammograms. A screening mammogram is ordered for women who have no problems with their breasts. It consists of two x-ray views of each breast: a craniocaudal (from above) and a mediolateral oblique (from the sides). A diagnostic



Comparison of two mammograms—cancerous tissue is shown on left and normal tissue on right. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*



A person undergoing a mammography. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

mammogram is for evaluation of abnormalities in either men or women. Additional x rays from other angles, or special coned views of certain areas, are taken.

Purpose

The purpose of screening mammography is **breast cancer** detection. A screening test, by definition, is used for patients without any signs or symptoms, in order to detect disease as early as possible. Many studies have shown that having regular mammograms increases a woman's chances of finding breast **cancer** in an early stage, when it is more likely to be curable. It has been estimated that a mammogram may find a cancer as much as two or three years before it can be felt. Radiologists look specifically for the presence of microcalcifications and other abnormalities that can be associated with malignancy. New digital mammography and computer-aided reporting can automatically enhance and magnify the mammograms for easier identification of these tiny calcifications.

The American Cancer Society (ACS) guidelines recommend an annual screening mammogram for every woman of average risk beginning at age 40. In late 2009, the United States Preventive Services Task Force (USPSTF) announced a change in its guidelines for screening mammography. Although USPSTF no longer recommends routine mammograms for screening for women between the ages of 40 and 49, the American Cancer Society, after a review of both the USPSTF data and additional current research, stands by its current recommendations. According to the USPSTF, women in their forties experience false negative screening results and therefore undergo unnecessary treatment at rates high enough to make overall screening unnecessary. The American Cancer Society responded in a November 16, 2009 press release stating that the benefits of screening mammograms in women age 40 to 49 outweigh the limitations and that ultimately, mammograms save lives.

The highest risk factor for developing cancer is advancing age. Some women are at an increased risk for developing breast cancer, such as those with a positive family history of the disease. Beginning screening mammography at a younger age may be recommended for these women.

Diagnostic mammography is used to evaluate an existing problem, such as a lump, discharge from the nipple, or unusual tenderness in one area. It is also done to evaluate further abnormalities that have been seen on screening mammograms. The radiologist normally views the films immediately and may ask for additional views such as a magnification view of one specific area. Additional studies such as an ultrasound of the breast may be performed as well to determine if the lesion is cystic or solid. Breast-specific **positron emission tomography (PET)** scans as well as an MRI (**magnetic resonance imaging**) may be ordered to further evaluate a tumor, but mammography is still the first choice in detecting small tumors on a screening basis.

Description

A mammogram may be offered in a variety of settings. Hospitals, outpatient clinics, physician's offices, or other facilities may have mammography equipment. In the United States only places certified by the Food and Drug Administration (FDA) are legally permitted to perform, interpret, or develop mammograms. Mammograms are taken with dedicated machines using high frequency generators, low kvp, molybdenum targets and specialized x-ray beam filtration. Sensitive high contrast film and screen combinations along with prolonged developing enable the visualization of minute breast detail.

In addition to the usual paperwork, a woman will be asked to fill out a questionnaire asking for information on her current medical history. Beyond her personal and family history of cancer, details about menstruation, previous breast surgeries, child bearing, birth control, and **hormone replacement therapy** are recorded. Information about **breast self-examination** (BSE) and other breast health issues are usually available at no charge.

At some centers, a technologist may perform a **physical examination** of the breasts before the mammogram. Whether or not this is done, it is essential for the technologist to record any lumps, nipple discharge, breast **pain** or other concerns of the patient. All visible **scars**, **tattoos** and nipple alterations must be carefully noted as well.

Clothing from the waist up is removed, along with necklaces and dangling earrings. A hospital gown or similar covering is put on. A small self-adhesive metal marker may be placed on each nipple by the x-ray technologist. This allows the nipple to be viewed as a reference point on the film for concise tumor location and easier centering for additional views.

Patients are positioned for mammograms differently, depending on the type of mammogram being performed:

- Craniocaudal position (CC): The woman stands or sits facing the mammogram machine. One breast is exposed and raised to a level position while the height of the cassette holder is adjusted to the same level. The breast is placed mid-film with the nipple in profile and the head turned away from the side being x rayed. The shoulder is relaxed and pulled slightly backward while the breast is pulled as far forward as possible. The technologist holds the breast in place and slowly lowers the compression with a foot pedal. The breast is compressed between the film holder and a rectangle of plastic (called a paddle). The breast is compressed until the skin is taut and the breast tissue firm when touched on the lateral side. The exposure is taken immediately and the compression released. Good compression can be uncomfortable, but it is very necessary. Compression reduces the thickness of the breast, creates a uniform density and separates overlying tissues. This allows for a detailed image with a lower exposure time and decreased radiation dose to the patient. The same view is repeated on the opposite breast.
- Mediolateral oblique position (MLO): The woman is positioned with her side toward the mammography unit. The film holder is angled parallel to the pectoral muscle, anywhere from 30 to 60 degrees depending on the size and height of the patient. The taller and thinner the patient the higher the angle. The height of the machine is level with the axilla (armpit). The arm is placed at the top of the cassette holder with a corner touching the armpit. The breast is lifted forward and upward and compression is applied until the breast is held firmly in place by the paddle. The nipple should be in profile and the opposite breast held away if necessary by the patient. This procedure is repeated for the other breast. A total of four x rays, two of each breast, are taken for a screening mammogram. Additional x rays, using special paddles, different breast positions, or other techniques may be taken for a diagnostic mammogram.

The mammogram may be seen and interpreted by a radiologist right away, or it may not be reviewed until later. If there is any questionable area or abnormality, extra x rays may be recommended. These may be taken during the same appointment. More commonly, especially for screening mammograms, the woman is called back on another day for these additional films.

A screening mammogram usually takes approximately 15 to 30 minutes. A woman having a diagnostic mammogram can expect to spend up to an hour for the procedure.

The cost of mammography varies widely. Many mammography facilities accept "self referral." This means women can schedule themselves without a physician's referral. However, some insurance policies do require a doctor's prescription to ensure payment. Medicare will pay for annual screening mammograms for all women over age 39.

Preparation

The compression or squeezing of the breast necessary for a mammogram is a concern of many women. Mammograms should be scheduled when a woman's breasts are least likely to be tender. One to two weeks after the first day of the menstrual period is usually best, as the breasts may be tender during a menstrual period. Some women with sensitive breasts also find that stopping or decreasing **caffeine** intake from coffee, tea, colas, and

KEY TERMS

Breast biopsy—A procedure where suspicious tissue is removed and examined by a pathologist for cancer or other disease. The breast tissue may be obtained by open surgery, or through a needle.

Craniocaudal—Head to tail, x-ray beam directly overhead the part being examined.

Radiographically dense—An abundance of glandular tissue that results in diminished anatomic detail on the mammogram.

chocolate for a week or two before the examination decreases any discomfort. Women receiving hormone therapy may also have sensitive breasts. Over-the-counter pain relievers are recommended an hour before the mammogram appointment when pain is a significant problem.

Women should not put deodorant, powder, or lotion on their upper body on the day the mammogram is performed. Particles from these products can get on the breast or film holder and may show up as abnormalities on the mammogram. Most facilities will have special wipes available for those patients who need to wash before the mammogram.

Aftercare

No special aftercare is required.

Risks

The risk of radiation exposure from a mammogram is considered minimal and not significant. Experts are unanimous that any negligible risk is by far outweighed by the potential benefits of mammography. Patients who have **breast implants** must be x rayed with caution and compression is minimally applied so that the sac is not ruptured. Special techniques and positioning skills must be learned before a technologist can x ray a patient with breast implants.

Some breast cancers do not show up on mammograms, or "hide" in dense breast tissue. A normal (or negative) study is not a guarantee that a woman is cancer-free. The false-negative rate is estimated to be 15–20%, higher in younger women and women with dense breasts.

False positive readings are also possible. Breast biopsies may be recommended on the basis of a mammogram, and find no cancer. It is estimated that 75–80% of all breast biopsies resulted in benign (no cancer present) findings. This is considered an acceptable rate, because recommending fewer biopsies would result in too many missed cancers.

Results

A mammography report describes details about the x-ray appearance of the breasts. It also rates the mammogram according to standardized categories, as part of the Breast Imaging Reporting and Data System (BIRADS) created by the American College of Radiology (ACR). A normal mammogram may be rated as BIRADS 1 or negative, which means no abnormalities were seen. A normal mammogram may also be rated as BIRADS 2 or benign findings. This means there are one or more abnormalities but they are clearly benign (not cancerous), or variations of normal. Some kinds of calcifications, enlarged lymph nodes or obvious cysts might generate a BIRADS 2 rating.

Many mammograms are considered borderline or indeterminate in their findings. BIRADS 3 means either additional images are needed, or an abnormality is seen and is probably (but not definitely) benign. A follow-up mammogram within a short interval of six to 12 months is suggested. This helps to ensure that the abnormality is not changing, or is "stable." Only the affected side will be x rayed at this time. Some women are uncomfortable or anxious about waiting, and may want to consult with their doctor about having a biopsy. BIRADS 4 means suspicious for cancer. A biopsy is usually recommended in this case. BIRADS 5 means an abnormality is highly suggestive of cancer. A biopsy or other appropriate action should be taken.

Screening mammograms are not usually recommended for women under age 40 who have no special risk factors and a normal physical breast examination. A mammogram may be useful if a lump or other problem is discovered in a woman aged 30–40. Below age 30, breasts tend to be radiographically dense, which means the breasts contain a large amount of glandular tissue that is difficult to image in fine detail. Mammograms for this age group are controversial. An ultrasound of the breasts is usually done instead.

Patient education

The mammography technologist must be empathetic to the patient's modesty and **anxiety**. He or she must explain that compression is necessary to improve the quality of the image but does not harm the breasts. Patients may be very anxious when additional films are requested. Explaining that an extra view gives the radiologist more information will help to ease the patient's tension.

Resources

BOOKS

Centers for Disease Control and Prevention (U.S.). *Mammograms & Breast Health: An Information Guide for Women*. Atlanta: Centers for Disease Control and Prevention, 2006.

Kopans, Daniel B. *Breast Imaging*. Baltimore, MD: Lippincott Williams & Wilkins, 2007.

Suri, Jasjit S., and Rangaraj M. Rangayyan. *Recent Advances in Breast Imaging, Mammography, and Computer-Aided Diagnosis of Breast Cancer*. Bellingham, Wash: SPIE Press, 2006.

Walker, Laura Jensen. *Thanks for the Mammogram! Fighting Cancer with Faith, Hope And a Healthy Dose of Laughter*. Fleming H Revell Co, 2006.

PERIODICALS

Armstrong, K., Moye, E., Williams, S., Berlin, J.A., and E.E. Reynolds. "Screening Mammography in Women 40 to 49 Years of Age: a Systematic Review for the American College of Physicians." *Annals of Internal Medicine*. 146, (2007) 7: 516–526.

Benzel J., Laubach, P.D., Griner, E., Faria, M.F., Brunner, T.J., Johnson, J.R., and W.M. Valley. "Improving Mammography Screening." *The American Journal of Nursing*. 109, (2009) 11: 43–45.

Berg, W.A. "Benefits of Screening Mammography." *JAMA: Journal of the American Medical Association*. 303, (2010) 2: 168–169.

Hall, FM. "Computer-Aided Mammography Screening." *The New England Journal of Medicine*. 360, (2009): 8.

Mitka, Mike. "Mammography Rates Decline." *JAMA: Journal of the American Medical Association*. 297, (2007) 24: 2686.

Partridge, A.H., and E.P. Winer. "On Mammography - More Agreement Than Disagreement." *New England Journal of Medicine*. 361, (2009) 26: 2499–2500.

U.S. Preventive Services Task Force. "Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement." *Annals of Internal Medicine*. 151, (2009) 10: 716–726.

OTHER

American Cancer Society. "Mammograms and Other Breast Imaging Procedures." http://www.cancer.org/docroot/PED/content/PED_2_3X_Mammography_and_Other_Breast_Imaging_Procedures.asp(accessed February 5, 2010).

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329-4251, (800) 227–2345, http://www.cancer.org.

Susan G. Komen for the Cure, 5005 LBJ Freeway, Suite 250, Dallas, TX, 75244, (877) GO–KOMEN, (877) 465–6636, http://ww5.komen.org.

Lorraine K. Ehresman
Lee A. Shratter, M.D.
Rosalyn Carson-DeWitt, MD
Brenda W. Lerner

Manganese excess *see* **Mineral toxicity**

Mania

Definition

Mania is an abnormally elated mental state, typically characterized by feelings of euphoria, lack of inhibitions, racing thoughts, diminished need for sleep, talkativeness, risk taking, and irritability. In extreme cases, mania can induce **hallucinations** and other psychotic symptoms.

Description

Mania typically occurs as a symptom of **bipolar disorder** (a mood disorder characterized by both manic and depressive episodes). Individuals experiencing a manic episode often have feelings of self–importance, elation, talkativeness, sociability, and a desire to embark on goal–oriented activities, coupled with the less desirable characteristics of irritability, impatience, impulsiveness, hyperactivity, and a decreased need for sleep. (Hypomania is a term applied to a condition resembling mania. It is characterized by persistent or elevated expansive mood, hyperactivity, inflated self esteem, etc., but of less intensity than mania.) Severe mania may have psychotic features.

Causes and symptoms

Mania can be induced by the use or **abuse** of stimulant drugs such as **cocaine** and amphetamines. It is also the predominant feature of bipolar disorder, or manic depression, an affective mental illness that causes radical emotional changes and mood swings.

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (*DSM–IV*), the diagnostic standard for mental health professionals in the United States, describes a manic episode as an abnormally elevated mood lasting at least one week that is distinguished by at least three of the following symptoms: inflated self–esteem, decreased need for sleep, talkativeness, racing thoughts, distractibility, increase in goal–directed activity, or excessive involvement in pleasurable activities that have a high potential for painful consequences. If the mood of the patient is irritable and not elevated, four of these symptoms are required.

Diagnosis

Mania is usually diagnosed and treated by a psychiatrist and/or a psychologist in an outpatient setting. However, most severely manic patients require hospitalization. In addition to an interview, several

KEY TERMS

Bipolar disorder—Formerly called manic–depressive disorder. A mood disorder characterized alternating periods of overconfidence and activity (manic highs) and depressive lows.

Hypomania—A less severe form of elevated mood state that is a characteristic of bipolar type II disorder.

Mixed mania—A mental state in which symptoms of both depression and mania occur simultaneously.

Psychiatrist—A medical doctor who has completed specialized training in the diagnosis and treatment of mental illness. Psychiatrists can diagnose mental illnesses, provide mental health counseling, and prescribe medications.

Psychologist—A mental health professional who treats mental and behavioral disorders by support and insight to encourage healthy behavior patterns and personality growth. Psychologists also study the brain, behavior, emotions, and learning.

Psychotherapy—The treatment of mental and behavioral disorders by support and insight to encourage healthy behavior patterns and personality growth.

clinical inventories or scales may be used to assess the patient's mental status and determine the presence and severity of mania. An assessment commonly includes the Young Mania Rating Scale (YMRS). The Mini–Mental State Examination (MMSE) may also be given to screen out other illnesses such as **dementia**.

Treatment

Mania is treated primarily with drugs. The following mood–stabilizing agents are commonly prescribed to regulate manic episodes:

- Lithium (Cibalith–S, Eskalith, Lithane) is one of the oldest and most frequently prescribed drugs available for the treatment of mania. Because the drug takes four to seven days to reach a therapeutic level in the bloodstream, it is sometimes prescribed in conjunction with neuroleptics (antipsychotic drugs) and/or benzodiazepines (tranquilizers) to provide more immediate relief of mania.
- Carbamazepine (Tegretol, Atretol) is an anticonvulsant drug usually prescribed in conjunction with other mood–stabilizing agents. The drug is often used to treat bipolar patients who have not responded well to lithium therapy. As of early 1998, carbamazepine was not approved for the treatment of mania by the FDA.
- Valproate (divalproex sodium, or Depakote; valproic acid, or Depakene) is an anticonvulsant drug prescribed alone or in combination with carbamazepine and/or lithium. For patients experiencing "mixed mania," or mania with features of depression, valproate is preferred over lithium.

Clozapine (Clozaril) is an atypical antipsychotic medication used to control manic episodes in patients who have not responded to typical mood–stabilizing agents. The drug has also been a useful preventative treatment in some bipolar patients. Other new anticonvulsants (lamotrigine, gubapentin) are being investigated for treatment of mania and bipolar disorder.

Prognosis

Patients experiencing mania as a result of bipolar disorder require long–term care to prevent recurrence; bipolar disorder is a chronic condition that requires lifelong observation and treatment after diagnosis. Data show that almost 90% of patients who experience one manic episode will go on to have another.

Prevention

Mania as a result of bipolar disorder can only be prevented through ongoing pharmacologic treatment. Patient education in the form of therapy or self–help groups is crucial for training patients to recognize signs of mania and to take an active part in their treatment program. **Psychotherapy** is an important adjunctive treatment for patients with bipolar disorder.

Resources

BOOKS

Borch–Jacobsen, Mikkel. *Making Minds and Madness: From Hysteria to Depression*. New York, NY: Cambridge University Press, 2009.

Graham, George. *The Disordered Mind: An Introduction to Philosophy of Mind and Mental Illness*. New York, NY: Routledge, 2010.

North, Carol, and Sean Yutzy. *Goodwin and Guze's Psychiatric Diagnosis*. New York, NY: Oxford University Press, 2010.

Shams. *Human Relation and Personified Relational Disorders*. Raleigh, NC: lulu.com, 2009.

ORGANIZATIONS

American Academy of Child and Adolescent Psychiatry, 3615 Wisconsin Ave., NW , Washington, DC, 20016–3007, (202) 966–7300, http://www.aacap.org .

American Psychiatric Association, 1000 Wilson Blvd., Suite 1825, Arlington, VA, 22209, (703) 907–7300, apa@psych.org, http://www.psych.org/.

American Psychological Association (APA), 750 First St. NE, Washington, DC, 20002–4242, (202) 336–5500, http://www.apa.org.

National Alliance on Mental Illness (NAMI), 3803 N. Fairfax Dr., Suite 100, Arlington, VA, 22201, (703) 524–7600, (800) 950–NAMI (6264), (703) 524–9094, http://www.nami.org/Hometemplate.cfm.

National Institute of Mental Health (NIMH), 6001 Executive Blvd, Room 8184, MSC 9663, Bethesda, MD, 20892, (301) 443–4513, (866) 615–6464, (301) 443–4279, nimhinfo@nih.gov, http://www.nimh.nih.gov/index.shtml.

National Mental Health Association (NMHA), 2000 N. Beauregard St., 6th Floor, Alexandria, VA, 22311, (703) 684–7722, (800) 969–NMHA, (703) 684–5968, http://www1.nmha.org/.

Paula Anne Ford–Martin
Laura Jean Cataldo, RN, Ed.D.

Manic depression *see* **Bipolar disorder**

Manic episode *see* **Mania**

MAO inhibitors *see* **Monoamine oxidase inhibitors**

Marasmus *see* **Protein-energy malnutrition**

Marble bones *see* **Osteopetroses**

Marburg virus infection *see* **Hemorrhagic fevers**

Marfan syndrome

Definition

Marfan syndrome is an inherited disorder of the connective tissue that causes abnormalities of the patient's eyes, cardiovascular system, and musculoskeletal system. It is named for the French pediatrician, Antoine Marfan (1858-1942), who first described it in 1896. Marfan syndrome is sometimes called arachnodactyly, which means "spider-like fingers" in Greek, since one of the characteristic signs of the disease is disproportionately long fingers and toes. It is estimated that one person in every 3000-5000 has Marfan syndrome, or about 50,000 people in the United States. Marfan syndrome is one of the more common inheritable disorders.

Description

Marfan syndrome affects three major organ systems of the body: the heart and circulatory system, the bones and muscles, and the eyes. The genetic mutation responsible for Marfan was discovered in 1991. It affects the body's production of fibrillin, which is a protein that is an important part of connective tissue. Fibrillin is the primary component of the microfibrils that allow tissues to stretch repeatedly without weakening. Because the patient's fibrillin is abnormal, his or her connective tissues are looser than usual, which weakens or damages the support structures of the entire body.

The most common external signs associated with Marfan syndrome include excessively long arms and legs, with the patient's arm span being greater than his or her height. The fingers and toes may be long and slender, with loose joints that can be bent beyond their normal limits. This unusual flexibility is called hypermobility. The patient's face may also be long and narrow, and he or she may have a noticeable curvature of the spine. It is important to note, however, that Marfan patients vary widely in the external signs of their disorder and in their severity; even two patients from the same family may look quite different. Most of the external features of Marfan syndrome become more pronounced as the patient gets older, so that diagnosis of the disorder is often easier in adults than in children. In many cases, the patient may have few or very minor outward signs of the disorder, and the diagnosis may be missed until the patient develops vision problems or cardiac symptoms.

Marfan syndrome by itself does not affect a person's intelligence or ability to learn. There is, however, some clinical evidence that children with Marfan have a slightly higher rate of hyperactivity and attention-deficit disorder (ADD) than the general population. In addition, a child with undiagnosed nearsightedness related to Marfan may have difficulty seeing the blackboard or reading printed materials, and thus do poorly in school.

Marfan syndrome affects males and females equally, and appears to be distributed equally among all races and ethnic groups. The rate of mutation of the fibrillin gene, however, appears to be related to the age

of the patient's father; older fathers are more likely to have new mutations appear in chromosome 15.

Causes and symptoms

Marfan syndrome is caused by a single gene for fibrillin on chromosome 15, which is inherited in most cases from an affected parent. Between 15 and 25% of cases result from spontaneous mutations. Mutations of the fibrillin gene (FBNI) are unique to each family affected by Marfan, which makes rapid genetic diagnosis impossible, given present technology. The syndrome is an autosomal dominant disorder, which means that someone who has it has a 50% chance of passing it on to any offspring.

Another important genetic characteristic of Marfan syndrome is variable expression. This term means that the mutated fibrillin gene can produce a variety of symptoms of very different degrees of severity, even in members of the same family.

Cardiac and circulatory abnormalities

The most important complications of Marfan are those affecting the heart and major blood vessels; some are potentially life-threatening. About 90% of Marfan patients will develop cardiac complications.

- Aortic enlargement. This is the most serious potential complication of Marfan syndrome. Because of the abnormalities of the patient's fibrillin, the walls of the aorta (the large blood vessel that carries blood away from the heart) are weaker than normal and tend to stretch and bulge out of shape. This stretching increases the likelihood of an aortic dissection, which is a tear or separation between the layers of tissue that make up the aorta. An aortic dissection usually causes severe pain in the abdomen, back, or chest, depending on the section of the aorta that is affected. Rupture of the aorta is a medical emergency requiring immediate surgery and medication.
- Aortic regurgitation. A weakened and enlarged aorta may allow some blood to leak back into the heart during each heartbeat; this condition is called aortic regurgitation. Aortic regurgitation occasionally causes shortness of breath during normal activity. In serious cases, it causes the left ventricle of the heart to enlarge and may eventually lead to heart failure.
- Mitral valve prolapse. Between 75 and 85% of Marfan patients have loose or "floppy" mitral valves, which are the valves that separate the chambers of the heart. When these valves do not cover the opening between the chambers completely, the condition is called mitral valve prolapse. Complications of mitral valve prolapse include heart murmurs and arrhythmias. In rare cases, mitral valve prolapse can cause sudden death.
- Infective endocarditis. Infective endocarditis is an infection of the endothelium, the tissue that lines the heart. In patients with Marfan, it is the abnormal mitral valve that is most likely to become infected.
- Other complications. Some patients with Marfan develop cystic disease of the lungs or recurrent spontaneous pneumothorax, which is a condition in which air accumulates in the space around the lungs. Many will also eventually develop emphysema.

Musculoskeletal abnormalities

Marfan syndrome causes an increase in the length of the patient's bones, with decreased support from the ligaments that hold the bones together. As a result, the patient may develop various deformities of the skeleton or disorders related to the relative looseness of the ligaments.

Disorders of the spine

- Scoliosis. Scoliosis, or curvature of the spine, is a disorder in which the vertebrae that make up the spine twist out of line from side to side into an S-shape or a spiral. It is caused by a combination of the rapid growth of children with Marfan, and the looseness of the ligaments that help the spine to keep its shape.
- Kyphosis is an abnormal outward curvature of the spine at the back, sometimes called hunch back when it occurs in the upper back. Marfan patients may develop kyphosis either in the upper (thoracic) spine or the lower (lumbar) spine.
- Spondylolisthesis. Spondylolisthesis is the medical term for a forward slippage of one vertebra on the one below it. It produces an ache or stiffness in the lower back.
- Dural ectasia. The dura is the tough, fibrous outermost membrane covering the brain and the spinal cord. The weak dura in Marfan patients swells or bulges under the pressure of the spinal fluid. This swelling is called ectasia. In most cases, dural ectasia occurs in the lower spine, producing low back ache, a burning feeling, or numbness or weakness in the legs.

Disorders of the chest and lower body

- Pectus excavatum. Pectus excavatum is a malformation of the chest in which the patient's breastbone, or sternum, is sunken inward. It can cause difficulties in breathing, especially if the heart, spine, and lung have been affected by Marfan. It also usually causes concerns about appearance.

- Pectus carinatum. In other patients with Marfan the sternum is pushed outward and narrowed. Although pectus carinatum does not cause breathing difficulties, it can cause embarassment about appearance. A few patients with Marfan may have a pectus excavatum on one side of their chest and a pectus carinatum on the other.
- Foot disorders. Patients with Marfan are more likely to develop pes planus (flat feet) or so-called "claw" or "hammer" toes than people in the general population. They are also more likely to suffer from chronic pain in their feet.
- Protrusio acetabulae. The acetabulum is the socket of the hip joint. In patient's with Marfan, the acetabulum becomes deeper than normal during growth, for reasons that are not yet understood. Although protrusio acetabulae does not cause problems during childhood and adolescence, it can lead to a painful form of arthritis in adult life.

Disorders of the eyes and face

Although the visual problems that are related to Marfan syndrome are rarely life-threatening, they are important in that they may be the patient's first indication of the disorder. Eye disorders related to the syndrome include the following:

- Myopia (nearsightedness). Most patients with Marfan develop nearsightedness, usually in childhood.
- Ectopia lentis. Ectopia lentis is the medical term for dislocation of the lens of the eye. Between 65 and 75% of Marfan patients have dislocated lenses. This condition is an important indication for diagnosis of the syndrome because there are relatively few other disorders that produce it.
- Glaucoma. This condition is much more prevalent in patients with Marfan syndrome than in the general population.
- Cataracts. Patients with Marfan are more likely to develop cataracts, and to develop them much earlier in life, sometimes as early as 40 years of age.
- Retinal detachment. Patients with Marfan are more vulnerable to this disorder because of the weakness of their connective tissues. Untreated retinal detachment can cause blindness. The danger of retinal detachment is an important reason for patients to avoid contact sports or other activities that could cause a blow on the head or being knocked to the ground.
- Other facial problems. Patients with Marfan sometimes develop dental problems related to crowding of the teeth caused by a high-arched palate and a narrow jaw.

Other disorders

- Striae. Striae are stretch marks in the skin caused by rapid weight gain or growth; they frequently occur in pregnant women, for example. Marfan patients often develop striae over the shoulders, hips, and lower back at an early age because of rapid bone growth. Although the patient may be self-conscious about the striae, they are not a danger to health.
- Obstructive sleep apnea. Obstructive sleep apnea refers to partial obstruction of the airway during sleep, causing irregular breathing and sometimes snoring. In patients with Marfan, obstructive sleep apnea is caused by the unusual flexibility of the tissues lining the patient's airway. This disturbed breathing pattern increases the risk of aortic dissection.

Diagnosis

Presently, there is no objective diagnostic test for Marfan syndrome, in part because the disorder does not produce any measurable biochemical changes in the patient's blood or body fluids, or cellular changes that could be detected from a tissue sample. Although researchers in molecular biology are currently investigating the FBNI gene through a process called mutational analysis, it is presently not useful as a diagnostic test because there is evidence that there can be mutations in the fibrillin gene that do not produce Marfan. Similarly, there is no reliable prenatal test, although some physicians have used ultrasound to try to determine the length of fetal limbs in at-risk pregnancies.

The diagnosis is made by taking a family history and a thorough examination of the patient's eyes, heart, and bone structure. The examination should include an echocardiogram taken by a cardiologist, a slit-lamp **eye examination** by an ophthalmologist, and a work-up of the patient's spinal column by an orthopedic specialist. In terms of the cardiac examination, a standard electrocardiogram (EKG) is not sufficient for diagnosis; only the echocardiogram can detect possible enlargement of the aorta. The importance of the slit-lamp examination is that it allows the doctor to detect a dislocated lens, which is a significant indication of the syndrome.

The symptoms of Marfan syndrome in some patients resemble the symptoms of homocystinuria, which is an inherited disorder marked by extremely high levels of homocystine in the patient's blood and urine. This possibility can be excluded by a urine test.

In other cases, the diagnosis remains uncertain because of the mildness of the patient's symptoms, the absence of a family history of the syndrome, and

other variables. These borderline conditions are sometimes referred to as marfanoid syndromes.

Treatment

The treatment and management of Marfan is tailored to the specific symptoms of each patient. Some patients find that the syndrome has little impact on their overall lifestyle; others have found their lives centered on the disorder.

Cardiovascular system

After a person has been diagnosed with Marfan, he or she should be monitored with an echocardiogram every six months until it is clear that the aorta is not growing larger. After that, the patient should have an echocardiogram once a year. If the echocardiogram does not allow the physician to visualize all portions of the aorta, CT (computed tomography) or MRI (**magnetic resonance imaging**) may be used. In cases involving a possible **aortic dissection**, the patient may be given a TEE (transesophageal echocardiogram).

Medications. A Marfan patient may be given drugs called beta-blockers to slow down the rate of aortic enlargement and decrease the risk of dissection by lowering the blood pressure and decreasing the forcefulness of the heartbeat. The most commonly used beta-blockers in Marfan patients are propranolol (Inderal) and atenolol (Tenormin). Patients who are allergic to beta-blockers may be given a **calcium** blocker such as verapamil.

Because Marfan patients are at increased risk for infective **endocarditis**, they must take a prophylactic dose of an antibiotic before having dental work or minor surgery, as these procedures may allow bacteria to enter the bloodstream. Penicillin and amoxicillin are the **antibiotics** most often used.

Surgical treatment. Surgery may be necessary if the width of the patient's aorta increases rapidly or reaches a critical size (about 2 inches). The most common surgical treatment involves replacing the patient's aortic valve and several inches of the aorta itself with a composite graft, which is a prosthetic heart valve sewn into one end of a Dacron tube. This surgery has been performed widely since about 1985; most patients who have had a composite graft have not needed additional surgery.

Patients who have had a valve replaced must take an anticoagulant medication, usually warfarin (Coumadin), in order to minimize the possibility of a clot forming on the prosthetic valve.

Musculoskeletal system

Children diagnosed with Marfan should be checked for **scoliosis** by their pediatricians at each annual **physical examination**. The doctor simply asks the child to bend forward while the back is examined for changes in the curvature. In addition, the child's spine should be x rayed in order to measure the extent of scoliosis or **kyphosis**. The curve is measured in degrees by the angle between the vertebrae as seen on the x ray. Curves of 20° or less are not likely to become worse. Curves between 20 and 40 degrees are likely to increase in children or adolescents. Curves of 40 degrees or more are highly likely to worsen, even in an adult, because the spine is so badly imbalanced that the force of gravity will increase the curvature.

Scoliosis between 20 and 40 degrees in children is usually treated with a back brace. The child must wear this appliance about 23 hours a day until growth is complete. If the spinal curvature increases to 40 or 50 degrees, the patient may require surgery in order to prevent lung problems, back **pain**, and further deformity. Surgical treatment of scoliosis involves straightening the spine with metal rods and fusing the vertebrae in the straightened position.

Spondylolisthesis is treated with a brace in mild cases. If the slippage is more than 30 degree, the slipped vertebra may require surgical realignment.

Dural ectasia can be distinguished from other causes of back pain on an MRI. Mild cases are usually not treated. Medication or spinal shunting to remove some of the spinal fluid are used to treat severe cases.

Pectus excavatum and pectus carinatum can be treated by surgery. In pectus excavatum, the deformed breastbone and ribs are raised and straightened by a metal bar. After four to six months, the bar is removed in an outpatient procedure.

Protrusio acetabulae may require surgery in adult life to provide the patient with an artificial hip joint, if the arthritic pains are severe.

Pain in the feet or limbs is usually treated with a mild analgesic such as **acetaminophen**. Patients with Marfan should consider wearing shoes with low heels, special cushions, or orthotic inserts. Foot surgery is rarely necessary.

Visual and dental concerns

Patients with Marfan should have a thorough eye examination, including a slit-lamp examination, to test for dislocation of the lens as well as nearsightedness. Dislocation can be treated by a combination of

special glasses and daily use of one percent atropine sulfate ophthalmic drops, or by surgery.

Because patients with Marfan are at increased risk of glaucoma, they should have the fluid pressure inside the eye measured every year as part of an eye examination. Glaucoma can be treated with medications or with surgery.

Cataracts are treated with increasing success by implant surgery. It is important, however, to seek treatment at medical centers with eye surgeons familiar with the possible complications of **cataract surgery** in patients with Marfan syndrome.

All persons with Marfan should be taught to recognize the signs of **retinal detachment** (sudden blurring of vision in one eye becoming progressively worse without pain or redness) and to seek professional help immediately.

Children with Marfan should be evaluated by their dentist at each checkup for crowding of the teeth and possible misalignment, and referred to an orthodontist if necessary.

Athletic activities and occupational choice. People with Marfan should avoid sports or occupations that require heavy weight lifting, rough physical contact, or rapid changes in atmospheric pressure (e.g., scuba diving). Weight lifting increases blood pressure, which in turn may enlarge the aorta. Rough physical contact may cause retinal detachment. Sudden changes in air pressure may produce **pneumothorax**. Regular noncompetitive physical **exercise**, however, is beneficial for Marfan patients. Good choices include brisk walking, shooting baskets, and slow-paced tennis.

Social and lifestyle issues

SMOKING. Smoking is particularly harmful for Marfan patients because it increases their risk of **emphysema**.

PREGNANCY. Until very recently, women with Marfan were advised not to become pregnant because of the risk of aortic enlargement or dissection. The development of beta-blockers and echocardiograms, however, allows doctors now to monitor patients throughout pregnancy. It is recommended that patients have an echocardiogram during each of the three trimesters of pregnancy. Normal, vaginal delivery is not necessarily more stressful than a Caesarian section, but patients in prolonged labor may be given a Caesarian to reduce strain on the heart. A pregnant woman with Marfan should also receive **genetic counseling** regarding the 50% risk of having a child with the syndrome.

APPEARANCE AND SOCIAL CONCERNS. Children and adolescents with Marfan may benefit from supportive counseling regarding appearance, particularly if their symptoms are severe and causing them to withdraw from social activities. In addition, families may wish to seek counseling regarding the effects of the syndrome on relationships within the family. Many people respond with guilt, fear, or blame when a genetic disorder is diagnosed in the family, or they may overprotect the affected member. Support groups are often good sources of information about Marfan; they can offer helpful suggestions about living with it as well as emotional support.

KEY TERMS

Arachnodactyly—A condition characterized by abnormally long and slender fingers and toes.

Ectopia lentis—Dislocation of the lens of the eye. It is one of the most important single indicators in diagnosing Marfan syndrome.

Fibrillin—A protein that is an important part of the structure of the body's connective tissue. In Marfan's syndrome, the gene responsible for fibrillin has mutated, causing the body to produce a defective protein.

Hypermobility—Unusual flexibility of the joints, allowing them to be bent or moved beyond their normal range of motion.

Kyphosis—An abnormal outward curvature of the spine, with a hump at the upper back.

Pectus carinatum—An abnormality of the chest in which the sternum (breastbone) is pushed outward. It is sometimes called "pigeon breast."

Pectus excavatum—An abnormality of the chest in which the sternum (breastbone) sinks inward; sometimes called "funnel chest."

Scoliosis—An abnormal, side-to-side curvature of the spine.

Prognosis

The prognosis for patient's with Marfan has improved markedly in recent years. The life expectancy of people with the syndrome has increased to 72 years, up from 48 years in 1972. This dramatic improvement is attributed to new surgical techniques, improved diagnosis, and new techniques of medical treatment.

The most important single factor in improving the patient's prognosis is early diagnosis. The earlier that a patient can benefit from the new techniques and lifestyle modifications, the more likely he or she is to have a longer life expectancy.

Resources

BOOKS

Ammash, Naser, M., Thoralf M Sundt, and Heidi M Connolly. *Marfan Syndrome: Diagnosis and Management*. New York: Elsevier, 2008.

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Rebecca J. Frey, PhD

Marie-Strümpell disease *see* **Ankylosing spondylitis**

Marijuana

Definition

Marijuana *Cannabis sativa L.*, also known as hemp, is a member of the Cannabaceae family. It contains the psychoactive drug delta-9-tetrahydrocannabinol (THC).

Demographics

The whole cannabis plant, including buds, leaves, seeds, and root, have all been used throughout the long history of this controversial herb. Despite persistent legal restrictions and criminal penalties for illicit use, marijuana continues to be widely used in the United States and throughout the world, both for its mood-altering properties and its medicinal applications. According to the National Survey on drug Use and Health, in 2008, 25.8 million Americans over age 12 had used marijuana within the past year. In 2009, the World Health Organization (WHO) estimated that 147 million people or 2.5% of the world's population used marijuana.

Description

Marijuana is a somewhat weedy plant that can grow as high as 18 ft (5.4 m). The hairy leaves are arranged opposite one another on the erect and branching stem. Leaves are palmate and compound, deeply divided into five to seven narrow, toothed and pointed leaflets. Male and female flowers are small and greenish in color and grow on separate plants. Male flowers grow in the leaf axils in elongated clusters. The female flowers grow in spike-like clusters. The resinous blossoms have five sepals and five petals. The male and female blossoms can be distinguished at maturity. The male plant matures first, shedding its pollen and dying after flowering. Female plants die after dropping mature seeds.

Marijuana produces an abundance of quickly germinating seeds. This hardy annual is wind pollinated and has escaped from cultivation to grow wild along roadsides, trails, stream banks, and in wayside places throughout the world. The plant matures within three to five months after the seed has been sown.

The species *C. sativa L.* has many variations, depending on the soil, temperature, and light conditions, and the origin of the parent seed. These factors also affect the relative amounts of THC and cannabidiol, the active chemicals present in varying amounts in cannabis, and determine if the plant is primarily a fiber type or an intoxicant. Generally the species grown at higher elevations and in hotter climates exude more of resin and are more potent intoxicants.

History

Marijuana has been cultivated for thousands of years. Cannabis was first described for its therapeutic use in the first known Chinese pharmacopoeia, the *Pen Ts'ao*. (A pharmacopoeia is a book containing a list of medicinal drugs, and their descriptions of preparation and use.) Cannabis was called a "superior" herb by the Emperor Shen-Nung (2737-2697 B.C.), who is believed to have authored the work. Cannabis was recommended as a treatment for numerous common ailments.

Around that same period in Egypt, cannabis was used as a treatment for sore eyes. The herb was used in India in cultural and religious ceremonies, and recorded in Sanskrit scriptural texts around 1,400 B.C. Cannabis was considered a holy herb and was characterized as the "soother of grief," "the sky flyer," and "the poor man's heaven."

Centuries later, around 700 B.C., the Assyrian people used the herb they called *Qunnabu,* for incense. The ancient Greeks used cannabis as a remedy to treat inflammation, earache, and **edema**. Shortly after 500 B.C. the historian and geographer Herodotus recorded that the peoples known as Scythians used cannabis to produce fine linens. They called the herb *kannabis* and inhaled the "intoxicating vapor" that resulted when it

was burned. By the year 100 B.C. the Chinese were using cannabis to make paper.

Cannabis use and cultivation migrated with the movement of various traders and travelers, and knowledge of the herb's value spread throughout the Middle East, Eastern Europe, and Africa. Around 100, Dioscorides, a surgeon in the Roman Legions under the Emperor Nero, named the herb *Cannabis sativa* and recorded numerous medicinal uses. In the second century, the Chinese physician Hoa-Tho, used cannabis in surgical procedures, relying on its analgesic properties. In ancient India, around 600, Sanskrit writers recorded a recipe for "pills of gaiety," a combination of hemp and sugar. By 1150, Muslims were using cannabis fiber in Europe's first paper production. This use of cannabis as a durable and renewable source of paper fiber continued for the next 750 years.

By the 1300s, government and religious authorities, concerned about the psychoactive effects on citizens consuming the herb, began placing harsh restrictions on its use. The Emir Soudon Sheikhouni of Joneima outlawed cannabis use among the poor. He destroyed the crops and ordered that offenders' teeth be pulled out. In 1484, Pope Innocent VIII outlawed the use of hashish, a concentrated form of cannabis. Cannabis cultivation continued, however, because of its economic value as a fiber-producing plant. A little more than a century later, the English queen, Elizabeth I, issued a decree commanding that landowners holding sixty acres or more must grow hemp or pay a fine. Commerce in hemp, which was primarily valued for the strength and versatility of its fibers, was profitable and thriving. Hemp ropes and sails were crossing the sea to North America with the explorers.

By 1621, the British were growing cannabis in Virginia where cultivation of hemp was mandatory. In 1776, the Declaration of Independence was drafted on hemp paper. Both President George Washington and President Thomas Jefferson were advocates of hemp as a valuable cash crop. Jefferson urged farmers to grow the crop in lieu of tobacco. By the 1850s, hemp had become the third largest agricultural crop grown in North America. That year the United States Census recorded 8,327 hemp plantations, each with 2,000 or more acres in cultivation. However, the invention of the cotton gin was already bringing many changes, and cotton was becoming a prime and profitable textile fiber. More change came with the introduction of the sulfite and chlorine processes used to turn trees into paper. Restrictions on the personal use of cannabis as a mood-altering, psychoactive herb, were soon to follow.

Controversy

The 1856 edition of the *Encyclopedia Britannica*, in its lengthy entry on hemp, noted that the herb "produces inebriation and **delirium** of decidedly hilarious character, inducing violent laughter, jumping and dancing." This inebriating effect of marijuana use has fueled the controversy and led to restrictions that have surrounded marijuana use throughout history in many cultures and regions of the world. Cannabis use has been criminalized in some parts of the United States since 1915. Utah was the first state to criminalize it, then California and Texas. By 1923, Louisiana, Nevada, Oregon, and Washington had legal restrictions on the herb. New York prohibited cannabis use in 1927. Despite the restrictions, cannabis use was woven into the cultural and social fabric in some communities, and widespread use persisted, particularly among the Mexican, Asian, and African American populations.

In the United States in 1937, the federal government passed the Marijuana Tax Act, prohibiting the cultivation and farming of marijuana. The act prohibited industrial and medical use of marijuana and classified the flowering tops as a narcotic. Since then, restrictions on the cultivation and use of cannabis have continued. Marijuana was categorized as an illegal narcotic, in the company of **LSD**, heroin, **cocaine**, and morphine. Despite that, illegal use continued.

In a reversal of the state-by-state progression of criminalizing marijuana that led to the 1937 Marijuana Tax Act, there is a movement underway, state by state, to endorse the legalized use of medical marijuana. By 2010, 14 states in the United States had legalized medical marijuana and two other states had passed laws favorable to its medical use without actually legalizing the drug. A growing body of scientific research and many thousands of years of folk use support the importance of medical marijuana in treatment of a variety of illnesses. The economic value of hemp in the textile, paper, and cordage industries has a long history.

Controversy persists around this herb. The World Health Organization, in a 1998 study, stated that the risks from cannabis use were unlikely to seriously compare to the public health risks of the legal drugs, alcohol, and tobacco. Controversy continues on how addictive marijuana is, given the **addiction** potential of many prescription drugs used as **muscle relaxants**, hypnotics, and **analgesics**. One legitimate concern is the effect of **smoking** on the lungs. Cannabis smoke carries even more tars and other particulate matter than tobacco smoke.

KEY TERMS

Antiemetic—A drug or herbal preparation given to relieve nausea and vomiting. Marijuana has antiemetic properties.

Cannabinoids—The chemical compounds that are the active principles in marijuana.

Edema—Swelling of a body tissue due to collection of fluids.

Euphoria—An intense feeling of elation or well being. Many marijuana users experience temporary euphoria.

Glaucoma—An eye disorder caused by damage to the optic nerve resulting in vision loss. Glaucoma is usually accompanied by inflammation and increased pressure in the eye (intraocular pressure). There are several types that may develop suddenly or gradually.

Causes and Symptoms

Marijuana is ingested by smoking the dried herb, which quickly delivers the active ingredients to the blood system. It can also be added to food (often brownies) and eaten. Cannabis contains chemical compounds known as cannabinoids. Different cannabinoids seem to exert different effects on the body after ingestion. Scientific research indicates that these substances have potential therapeutic value for **pain** relief, control of **nausea and vomiting**, and appetite stimulation. The primary active agent is THC. This chemical may constitute as much as 12% of the active chemicals in the herb, and is said to be responsible for as much as 70–100% of the euphoric response, or "high," experienced when ingesting the herb. The predominance of this mental lightness or euphoria depends on the balance of other active ingredients and the freshness of the herb. THC degrades into a component known as cannabinol, or CBN. This relatively inactive chemical predominates in marijuana that has been stored too long before use. Another chemical component, cannabidiol, known as CBD, has a sedative and mildly analgesic (pain relieving) effect, and contributes to lethargy sometimes experienced by marijuana users.

Despite the fact that on the federal level marijuana use remains illegal, in the United States in the twenty-first century there is strong interest in medicinal uses of marijuana. The herb appears to have analgesic, antiemetic, anti-inflammatory, sedative, anticonvulsive, and laxative actions. Clinical studies have demonstrated its effectiveness in relieving **nausea** and **vomiting** following **chemotherapy** treatments for **cancer**. The herb has also been shown to reduce intra-ocular pressure in the eye a beneficial action in the treatment for glaucoma. However, marijuana is not more effective in lowering pressure in the eye than legal prescription drugs.

Cannabis has proven anticonvulsive action, and may be helpful in treating **epilepsy**. Marijuana also increases appetite and reduces nausea and has been used with **AIDS** patients to counter weight loss and wasting that may result from the disease. Several chemical constituents of cannabis displayed antimicrobial action and antibacterial effects in research studies. The components CBC and THC have been shown to destroy and inhibit the growth of streptococci and staphylococci bacteria. In 2007, a Harvard University study found that the active ingredient of marijuana cut lung tumor growth in mice in half.

Because marijuana use is illegal in many places and because of the conditions under which the plants are raised causes variation in the amounts of active ingredients, there is no standard dosage for medical use. In states that have legalized the use of medical marijuana, the legally permissible amounts for an individual to possess range from 1 ounce (28 g) to 24 ounces (680 g). THC extract is available legally in some countries in capsule form. In the United States this form of THC is available only for clinical experimental purposes.

The *PDR for Herbal Medicine* reports that the most common effect of marijuana use is psychotropic, as a euphoric state (pronounced gaiety, laughing fits) occurs almost immediately after smoking the herb. Long-term usage leads to a clear increase in tolerance for most of the pharmacological effects. Chronic use results in increased risk of **laryngitis**, **bronchitis**, apathy, psychic decline, and disturbances of sexual functions. In addition chronic sinus and fungal infections have been linked to chronic marijuana smoking.

Research has shown that cannabis acts to increase heartbeat by as much as 40 beats per minute. A study reported by the American Heart Association concluded that smoking marijuana can precipitate a **heart attack** in persons with pre-existing heart conditions. One hour after smoking marijuana, the likelihood of having a heart attack is 4.5 times greater than if the person had not smoked, according to the research. Marijuana also can cause a drop in blood pressure resulting in **dizziness**.

Marijuana use during **pregnancy** has been found to reduce the newborn's birth weight, a possible indication of problems. Pregnant and **breastfeeding** women should

avoid using marijuana. Other research has shown that marijuana decreases male fertility and increases the number of abnormal sperm found in semen.

An additional health concern is the effect that marijuana smoking has on the lungs. Cannabis smoke carries more tars and other particulate matter than tobacco smoke. Long-term use is also associated with an increase in respiratory diseases such as bronchitis.

Studies have shown that motor coordination and driving ability can be impaired for up to eight hours after smoking marijuana. Individuals should avoid driving and using heavy machinery for several hours after using the herb.

More seriously, marijuana has been linked to the onset or worsening of certain psychiatric conditions, including **panic disorder**, **schizophrenia**, and depersonalization disorder. Persons diagnosed with or at risk for these conditions should not use marijuana. Chronic marijuana use also interferes with the ability to organize and recall complex information.

Marijuana use may mask the perceived effects of alcohol and cocaine when the drugs are consumed together. Marijuana is said to exert a synergistic effect with other medicinal agents. When used with nitrous oxide it may enhance the nitrous oxide effect.

Marijuana use by individuals taking selective serotonin re-uptake inhibitors (SSRIs, used to treat depression) may develop manic symptoms. Use in individuals taking **tricyclic antidepressants** can produce delirium and racing heart (tachycardia).

In the United States, marijuana is considered a Class I narcotic, and federal law has restricted its use since 1937. Penalties include fines and imprisonment in some states, but the herb has been decriminalized in others. California, for example, issues cards identifying medical marijuana users and allows them to purchase the drug openly at certain clinics. As of late 2010, 14 states (Alaska, California, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington) along with the District of Columbia, had enacted laws that legalized medical marijuana. Eight states had pending legislation or ballot measures to legalize medical marijuana (Arizona, Illinois, Massachusetts, New York, North Carolina, Ohio, Pennsylvania, and South Dakota). In other countries, the legal status of and penalty for using marijuana vary widely.

Illegally purchased marijuana carries the potential to be laced with other toxins and mind-altering drugs. Since marijuana is illegal under federal law, there are no regulations or quality control to establish standardized purity of the herb.

Diagnosis

Marijuana use can be diagnosed through a urine drug-screening test. The drug is definitely detectable in urine for 1–5 days after use; however, it may be detected in the urine for as long as 21 days after use. Marijuana use is commonly looked for in pre-employment drug screening.

Treatment

Many people do not consider recreational marijuana use harmful, especially as the medical community is increasingly recognizing that the drug has medically beneficial qualities. Marijuana use often occurs in conjunction with **abuse** of alcohol and other drugs. In this situation, treatment of the other drug often takes precedence over treatment for marijuana use. **Cognitive-behavioral therapy**, in which users learn to recognize, manage and avoid situations most likely to lead to marijuana use and develop healthy ways to cope with stressful situations can be successful in stopping marijuana use in motivated individuals.

Prognosis

Marijuana use peaks during adolescence and then gradually declines, although there are still many older adults who use marijuana recreationally Although marijuana is less likely than some other drugs to lead to dependence, heavy users may experience a withdrawal syndrome characterized by **anxiety**, irritability, chills, and **muscle cramps** if they stop usage abruptly.

Prevention

Recreational marijuana use is difficult to prevent, and drug education programs have not been successful in reducing the number of people who experiment with marijuana. As medical use of marijuana becomes more common, attitudes in the United States have shifted away from punishing individuals who possess small amounts of marijuana for personal use, making prevention increasingly difficult.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Amtmann, D., P. Weydt, K. L. Johnson, et al. "Survey of Cannabis Use in Patients with Amyotrophic Lateral Sclerosis." *American Journal of Hospice and Palliative Care* 21 (March-April 2004): 95–104.

Arsenault, L., M. Cannon, J. Witton, and R. M. Murray. "Causal Association between Cannabis and Psychosis: Examination of the Evidence." *British Journal of Psychiatry* 184 (February 2004): 110–117.

Dannon, P. N., K. Lowengrub, R. Amiaz, et al. "Comorbid Cannabis Use and Panic Disorder: Short Term and Long Term Follow-Up Study." *Human Psychopharmacology* 19 (March 2004): 97–101.

Haney, M., C. L. Hart, S. K. Vosburg, et al. "Marijuana Withdrawal in Humans: Effects of Oral THC or Divalproex." *Neuropsychopharmacology* 29 (January 2004): 158–170.

Hart, S., O. O. Fischer, and A. Ullrich. "Cannabinoids Induce Cancer Cell Proliferation via Tumor Necrosis Factor Alpha-Converting Enzyme (TACE/ADAM17)-Mediated Transactivation of the Epidermal Growth Factor Receptor." *Cancer Research* 64 (March 15, 2004): 1943–1950.

Simeon, D. "Depersonalisation Disorder: A Contemporary Overview." *CNS Drugs* 18 (2004): 343–354.

OTHER

Center for Cardiovascular Education, Inc. *Smoking Marijuana Increases Heart Attack Risk*. Heart Information Network. June 14, 2000. http://www.heartinfo.org/news2000/marijuana061400.htm.

Deerman, Dixie, RN. *The Best Herb You're Not Using That Could Add Years to Your Life!* North Carolina: Community of Compassion, 2000.

Goddard, Ian Williams. *Proven: Cannabis Is Safe Medicine*. http://ccguide.org/proven.php.

Lewin, Louis. *Phantastica, Hallucinating Substances, Indian Hemp: Cannabis Indica*. http://users.lycaeum.org/~sputnik/Ludlow/Texts/phantastica.html.

Taima in Japan. *Drug War Facts: Marijuana*. http://taima.org/drugfacts/mj.htm.

ORGANIZATIONS

American Medical Marijuana Association, 17415 Ocean Drive, Fort Bragg, CA, 95437, amma@drugsense.org, http://americanmarijuana.org.

National Center for Complementary and Alternative Medicine Clearinghouse, PO Box 7923, Gaithersburg, MD, 20898, (301) 519-3153. TTY: (866) 464-3615, (888) 644-6226, (866) 464-3616, http://nccam.nih.gov.

National Clearinghouse on Alcohol and Drug Information., P. O. Box 2345, Rockville, MD, 20847, (877) SAMHSA-7; Hablamos español: (877) 767-8432; TDD: (800) 487-4889, (240) 221-4292, http://ncadi.samhsa.gov.

National Council on Alcohol and Drug Dependence, 244 East 58th Street 4th Floor, New York, NY, 10022, (212) 269-7797, 24-hour help line: (800) NCA-CALL, (212) 269-7510, national@mcadd.org, http://www.ncadd.org.

Partnership for a Drug-free America, 405 Lexington Avenue, Ste 1601, New York, NY, 10174, (212) 922-1560, (212) 922-1570, http://www.drugfree.org.

Clare Hanrahan
Rebecca J. Frey, PhD
Tish Davidson, AM

Marriage counseling

Definition

Marriage counseling is a type of **psychotherapy** for a married couple or established partners that tries to resolve problems in the relationship. Typically, two people attend counseling sessions together to discuss specific issues; however, in some cases only one partner works within the sessions. It may also be called marital therapy, couple therapy, or relationship counseling.

Before the late twentieth century, close friends, family members, or religious leaders primarily performed marriage counseling. Since then, the guidance most often comes from psychiatrists, psychologists, social workers, and marriage/family counselors. With the use of such professionals, certifications and regulations have been established to guide and control these activities. One of the most commonly accepted credentials comes from the American Association for Marriage and Family Therapy.

Purpose

Marriage counseling provides help to couples, whether they are married or not, and whether the pair are heterosexual or homosexual. It is based on research showing that individuals and their problems are best handled within the context of their relationships. Marriage counselors are trained in psychotherapy and family systems, and focus on understanding their clients' symptoms and the way their interactions contribute to problems in the relationship.

Various issues are discussed in marriage counseling. Some of the more critical issues addressed include:

- Infidelity issues
- Sexual problems
- Financial difficulties
- Physical disabilities
- Mental illnesses
- Anger management problems
- Domestic abuse
- Alcohol/substance abuse

- Communications difficulties
- Children and other family members interactions.

Description

Marriage counseling is usually a short-term therapy that may take only a few sessions to work out problems in the relationship. Longer-term counseling may also occur, with a range of sessions usually from 12 to 24 in number. Typically, marriage counselors ask questions about the couple's roles, patterns, rules, goals, and beliefs. Therapy often begins as the couple analyzes the good and bad aspects of the relationship. The marriage counselor then works with the couple to help them understand that, in most cases, both partners are contributing to problems in the relationship. When this is understood, the two can then learn to change how they interact with each other to solve problems. The partners may be encouraged to draw up a contract in which each partner describes the behavior he or she will be trying to maintain. Sometimes counseling is also provided for the entire family, not just for a couple.

Marriage is not a requirement for two people to get help from a marriage counselor. Any one person wishing to improve his or her relationships can acquire help with behavioral problems, relationship issues, or with mental or emotional disorders. Marriage counselors also offer treatment (pre-marital therapy) for couples before they get married to help them understand potential problem areas. A third type of marriage counseling involves post-marital therapy, in which divorcing couples who share children seek help in working out their differences. Couples in the midst of a divorce find that marriage therapy during separation can help them find a common ground as they negotiate interpersonal issues and child custody.

Choosing a therapist

A marriage counselor is trained to use different types of therapy in work with individuals, couples, and groups. American Association of Marriage and Family Therapy (AAMFT) training includes supervision by experienced therapists, who hold a minimum of a master's degree (including specific training in marriage and family therapy), and specific graduate training in marriage and family therapy.

When looking for a marriage counselor, a couple should find out the counselor's training and educational background, professional associations, such as the AAMFT, and state licensure, and whether the person has experience in treating particular kinds of problem. Also, questions should be asked concerning fees, insurance coverage, the average length of therapy, and so on.

Normal results

Marriage counseling helps couples learn to deal more effectively with problems, and can help prevent small problems from becoming serious. Research shows that marriage counseling, when effective, tends to improve a person's physical as well as mental health, in addition to improving the relationship.

Resources

BOOKS

Clinton, Tim, and John Trent. *The Quick-Reference Guide to Marriage and Family Counseling*. Grand Rapids, MI: Baker Books, 2009.

Davis, Rebecca L. *More Perfect Unions: The American Search for Marital Bliss*. Cambridge, MA: Harvard University Press, 2010.

Yount, David. *Making a Success of Marriage: Planning for Happily Ever After*. Lanham, MD: Rowman and Littlefield, 2010.

OTHER

Marriage Counseling. Mayo Clinic. http://www.mayoclinic.com/health/marriage-counseling/MY00839. (accessed August 10, 2010).

ORGANIZATIONS

American Association for Marriage and Family Therapy, 112 South Alfred Street, Alexandria, VA, 22314-3061, (703) 838-9808, (703) 838-9805, http://www.aamft.org/.

American Psychological Association, 750 First Street N.E., Washington, DC, 20002-4242, (202) 336-5500, (800) 374-2721, http://www.apa.org/.

Carol A. Turkington

Marshall-Marchetti-Krantz procedure

Definition

The Marshall-Marchetti-Krantz procedure surgically reinforces the bladder neck in order to prevent unintentional urine loss.

Purpose

The Marshall-Marchetti-Krantz procedure is performed to correct stress incontinence in women, a common result of **childbirth** and/or **menopause**. Incontinence also occurs when an individual involuntarily loses urine after pressure is placed on the abdomen (like during **exercise**, sexual activity, sneezing, coughing, laughing, or hugging).

KEY TERMS

Biofeedback—Biofeedback training monitors temperature and muscle contractions in the vagina to help incontinent patients control their pelvic muscles.

Bladder training—A behavioral modification program used to treat stress incontinence. Bladder training involves putting the patient on a toilet schedule, and gradually increasing the time interval between urination.

Catheter—A long, thin, flexible tube. A catheter is used to drain the bladder of urine during a Marshall-Marchetti-Krantz procedure.

Kegel exercises—Exercises that tighten the pelvic floor muscles. Kegel exercises can assist some women in controlling their stress incontinence.

Urethra—The narrow tube, leading from the bladder that drains the body's urine.

Precautions

In some women, stress incontinence may be controlled through nonsurgical means, such as:

- Kegel exercises (exercises that tighten pelvic muscles)
- Biofeedback (monitors temperature and muscle contractions in the vagina to help incontinent patients control their pelvic muscles)
- Bladder training (behavioral modification program used to treat stress incontinence)
- Medication
- Inserted incontinence devices.

Each patient should undergo a full diagnostic workup to determine the best course of treatment.

Description

The Marshall-Marchetti-Krantz procedure, also known as **retropubic suspension** or bladder neck suspension surgery, is performed by a surgeon in a hospital setting. The patient is placed under **general anesthesia**, and a long, thin, flexible tube (catheter) is inserted into the bladder through the narrow tube (urethra) that drains the body's urine. An incision is made across the abdomen, and the bladder is exposed. The bladder is separated from surrounding tissues. Stitches (sutures) are placed in these tissues near the bladder neck and urethra. The urethra is then lifted, and the sutures are attached to the pubic bone itself, or to tissue (fascia) behind the pubic bone. The sutures support the bladder neck, helping the patient gain control over urine flow.

Preparation

A complete evaluation to determine the cause of incontinence is critical to proper treatment. A thorough medical history and general **physical examination** should be performed on candidates for the Marshall-Marchetti-Krantz procedure. Diagnostic testing may include x rays, ultrasound, urine tests, and examination of the pelvis. It may also include a series of urodynamic testing exams that measure bladder pressure and capacity, and urinary flow.

Patients undergoing a Marshall-Marchetti-Krantz procedure must not eat or drink for eight hours prior to the surgery.

Aftercare

Recovery from a Marshall-Marchetti-Krantz procedure requires two to six days of hospitalization. The catheter will be removed from the patient's bladder once normal bladder function resumes. Patients are advised to refrain from heavy lifting for four to six weeks after the procedure.

Patients should contact their physician immediately if they experience **fever**, **dizziness**, or extreme **nausea**, or if their incision site becomes swollen, red, or hard.

Risks

The Marshall-Marchetti-Krantz procedure is an invasive surgical procedure and, as such, it carries risks of infection, internal bleeding, and hemorrhage. There is also a possibility of permanent damage to the bladder or urethra. The urethra may become scarred, causing a permanent narrowing, or stricture.

Normal results

Approximately 85% of women who undergo the Marshall-Marchetti-Krantz procedure are cured of their stress incontinence.

ORGANIZATIONS

American Urological Association Foundation, 1000 Corporate Blvd., Linthicum, MD, 21090, (410) 689-3700, (410) 689-3800, (866) 746-4282, auafoundation@auafoundation.org, http://www.urologyhealth.org/.

National Association for Continence, P.O. Box 1019, Charleston, SC, 29402-1019, (843) 377-0900, (843) 377-0905, (800) 252-3337, memberservices@nafc.org, http://www.nafc.org.

Paula Anne Ford-Martin

Massage therapy

Definition

Massage therapy is the scientific manipulation of the soft tissues of the body for the purpose of normalizing those tissues and consists of manual techniques that include applying fixed or movable pressure, holding, and/or causing movement of or to the body.

Purpose

Generally, massage is known to affect the circulation of blood and the flow of blood and lymph, reduce muscular tension or flaccidity, affect the nervous system through stimulation or **sedation**, and enhance tissue healing. These effects provide a number of benefits:

- reduction of muscle tension and stiffness
- relief of muscle spasms
- greater flexibility and range of motion
- increase of the ease and efficiency of movement
- relief of stress and aide of relaxation
- promotion of deeper and easier breathing
- improvement of the circulation of blood and movement of lymph
- relief of tension-related conditions, such as headaches and eyestrain
- promotion of faster healing of soft tissue injuries, such as pulled muscles and sprained ligaments, and reduction in pain and swelling related to such injuries
- reduction in the formation of excessive scar tissue following soft tissue injuries
- enhancement in the health and nourishment of skin
- improvement in posture through changing tension patterns that affect posture
- reduction in stress and an excellent stress management tool
- creation of a feeling of well-being
- reduction in levels of anxiety
- increase in awareness of the mind-body connection
- promotion of a relaxed state of mental awareness

Massage therapy also has a number of documented clinical benefits. For example, massage can reduce **anxiety**, improve pulmonary function in young **asthma** patients, reduce psycho-emotional distress in persons suffering from chronic inflammatory bowel disease, increase weight and improve motor development in premature infants, and may enhance immune system functioning. Some medical conditions that massage therapy can help are: **allergies**, anxiety and **stress**, arthritis, asthma and **bronchitis**, **carpal tunnel syndrome** and other repetitive motion injuries, chronic and temporary **pain**, circulatory problems, depression, digestive disorders, **tension headache**, **insomnia**, myofascial pain, **sports injuries**, and temporomandibular joint dysfunction.

Description

Origins

Massage therapy is one of the oldest health care practices known to history. References to massage are found in Chinese medical texts more than 4,000 years old. Massage has been advocated in Western health care practices at least since the time of Hippocrates, the "Father of Medicine." In the fourth century B.C. Hippocrates wrote, "The physician must be acquainted with many things and assuredly with rubbing" (the ancient Greek term for massage was rubbing).

The roots of modern, scientific massage therapy go back to Per Henrik Ling (1776–1839), a Swede, who developed an integrated system consisting of massage and active and passive exercises. Ling established the Royal Central Gymnastic Institute in Sweden in 1813 to teach his methods.

Modern, scientific massage therapy was introduced in the United States in the 1850s by two New York physicians, brothers George and Charles Taylor, who had studied in Sweden. The first clinics for massage therapy in the United States were opened by two Swedish physicians after the Civil War period. Doctor Baron Nils Posse operated the Posse Institute in Boston and Doctor Hartwig Nissen opened the Swedish Health Institute near the Capitol in Washington, D.C.

Although there were periods when massage fell out of favor, in the 1960s it made a comeback in a different way as a tool for relaxation, communication, and alternative healing. Today, massage is one of the most popular healing modalities. It is used by conventional, as well as alternative, medical communities and is now covered by some health insurance plans.

Massage therapy is the scientific manipulation of the soft tissues of the body for the purpose of

normalizing those tissues and consists of a group of manual techniques that include applying fixed or movable pressure, holding, and/or causing movement of or to the body. While massage therapy is applied primarily with the hands, sometimes the forearms or elbows are used. These techniques affect the muscular, skeletal, circulatory, lymphatic, nervous, and other systems of the body. The basic philosophy of massage therapy embraces the concept of *vis Medicatrix naturae*, which is aiding the ability of the body to heal itself, and is aimed at achieving or increasing health and well-being.

Touch is the fundamental medium of massage therapy. While massage can be described in terms of the type of techniques performed, touch is not used solely in a mechanistic way in massage therapy. One could look at a diagram or photo of a massage technique that depicts where to place one's hands and what direction the **stroke** should go, but this would not convey everything that is important for giving a good massage. Massage also has an artistic component.

Because massage usually involves applying touch with some degree of pressure and movement, the massage therapist must use touch with sensitivity in order to determine the optimal amount of pressure to use for each person. For example, using too much pressure may cause the body to tense up, while using too little may not have enough effect. Touch used with sensitivity also allows the massage therapist to receive useful information via his or her hands about the client's body, such as locating areas of muscle tension and other soft tissue problems. Because touch is also a form of communication, sensitive touch can convey a sense of caring—an essential element in the therapeutic relationship—to the person receiving massage.

In practice, many massage therapists use more than one technique or method in their work and sometimes combine several. Effective massage therapists ascertain each person's needs and then use the techniques that will meet those needs best.

Swedish massage uses a system of long gliding strokes, kneading, and friction techniques on the more superficial layers of muscles, generally in the direction of blood flow toward the heart, and sometimes combined with active and passive movements of the joints. It is used to promote general relaxation, improve circulation and range of motion, and relieve muscle tension. Swedish massage is the most commonly used form of massage.

Deep tissue massage is used to release chronic patterns of muscular tension using slow strokes, direct pressure, or friction directed across the grain of the muscles. It is applied with greater pressure and to deeper layers of muscle than Swedish, which is why it is called deep tissue and is effective for chronic muscular tension.

Sports massage uses techniques that are similar to Swedish and deep tissue, but are specially adapted to deal with the effects of athletic performance on the body and the needs of athletes regarding training, performing, and recovery from injury.

Neuromuscular massage is a form of deep massage that is applied to individual muscles. It is used primarily to release trigger points (intense knots of muscle tension that refer pain to other parts of the body), and also to increase blood flow. It is often used to reduce pain. Trigger point massage and myotherapy are similar forms.

Acupressure applies finger or thumb pressure to specific points located on the **acupuncture** meridians (channels of energy flow identified in Asian concepts of anatomy) in order to release blocked energy along these meridians that causes physical discomforts, and rebalance the energy flow. **Shiatsu** is a Japanese form of acupressure.

The cost of massage therapy varies according to geographic location, experience of the massage therapist, and length of the massage. In the United States, the average range is from $35-60 for a one hour session. Massage therapy sessions at a client's home or office may cost more due to travel time for the massage therapist. Most sessions are one hour. Frequency of massage sessions can vary widely. If a person is receiving massage for a specific problem, frequency can vary widely based on the condition, though it usually will be once a week. Some people incorporate massage into their regular personal health and fitness program. They will go for massage on a regular basis, varying from once a week to once a month.

The first appointment generally begins with information gathering, such as the reason for getting massage therapy, physical condition and medical history, and other areas. The client is asked to remove clothing to one's level of comfort. Undressing takes place in private, and a sheet or towel is provided for draping. The massage therapist will undrape only the part of the body being massaged. The client's modesty is respected at all times. The massage therapist may use an oil or cream, which will be absorbed into the skin in a short time.

To receive the most benefit from a massage, generally the person being massaged should give the therapist accurate health information, report discomfort of any kind (whether it is from the massage itself or due to the room temperature or any other distractions), and be as receptive and open to the process as possible.

Insurance coverage for massage therapy varies widely. There tends to be greater coverage in states that license massage therapy. In most cases, a physician's prescription for massage therapy is needed. Once massage therapy is prescribed, authorization from the insurer may be needed if coverage is not clearly spelled out in one's policy or plan.

Preparations

Going for a massage requires little in the way of preparation. Generally, one should be clean and should not eat just before a massage. One should not be under the influence of alcohol or non-medicinal drugs. Massage therapists generally work by appointment and usually will provide information about how to prepare for an appointment at the time of making the appointment.

Precautions

Massage is comparatively safe; however it is generally contraindicated, i.e., it should not be used, if a person has one of the following conditions: advanced heart diseases, **hypertension** (high blood pressure), phlebitis, thrombosis, **embolism**, kidney failure, **cancer** if massage would accelerate metastasis (i.e., spread a tumor) or damage tissue that is fragile due to **chemotherapy** or other treatment, infectious diseases, contagious skin conditions, acute inflammation, infected injuries, unhealed **fractures**, **dislocations**, **frostbite**, large hernias, torn ligaments, conditions prone to hemorrhage, and **psychosis**.

Massage should not be used locally on affected areas (i.e., avoid using massage on the specific areas of the body that are affected by the condition) for the following conditions: **rheumatoid arthritis** flare up, **eczema**, **goiter**, and open **skin lesions**. Massage may be used on the areas of the body that are not affected by these conditions.

In some cases, precautions should be taken before using massage for the following conditions: **pregnancy**, high fevers, **osteoporosis**, diabetes, recent post-operative cases in which pain and muscular splinting (i.e., tightening as a protective reaction) would be increased, apprehension, and mental conditions that may impair communication or perception. In such cases, massage may or may not be appropriate. The decision on whether to use massage must be based on whether it may cause harm. For example, if someone has osteoporosis, the concern is whether bones are strong enough to withstand the pressure applied. If one has a health condition and has any hesitation about whether massage therapy would be appropriate, a physician should be consulted.

Side effects

Massage therapy does not have side effects. Sometimes people are concerned that massage may leave them too relaxed or too mentally unfocused. To the contrary, massage tends to leave people feeling more relaxed and alert.

Research and general acceptance

Before 1939, more than 600 research studies on massage appeared in the main journals of medicine in English. However, the pace of research was slowed by medicine's disinterest in massage therapy.

Massage therapy research picked up again in the 1980s, as the growing popularity of massage paralleled the growing interest in complementary and alternative medicine. Well designed studies have documented the benefits of massage therapy for the treatment of acute and chronic pain, acute and chronic inflammation, chronic **lymphedema**, **nausea**, muscle spasm, various soft tissue dysfunctions, anxiety, depression, insomnia, and psycho-emotional stress, which may aggravate mental illness.

Premature infants treated with daily massage therapy gain more weight and have shorter hospital stays than infants who are not massaged. A study of 40 low-birth-weight babies found that the 20 massaged babies had a 47% greater weight gain per day and stayed in the hospital an average of six days less than 20 infants who did not receive massage, resulting a cost savings of approximately $3,000 per infant. Cocaine-exposed, preterm infants given massage three times daily for a 10 day period showed significant improvement. Results indicated that massaged infants had fewer postnatal complications and exhibited fewer stress behaviors during the 10 day period, had a 28% greater daily weight gain, and demonstrated more mature motor behaviors.

A study comparing 52 hospitalized depressed and adjustment disorder children and adolescents with a control group that viewed relaxation videotapes, found massage therapy subjects were less depressed and anxious, and had lower saliva cortisol levels (an indicator of less depression).

Another study showed massage therapy produced relaxation in 18 elderly subjects, demonstrated in measures such as decreased blood pressure and heart rate and increased skin temperature.

A combination of massage techniques for 52 subjects with traumatically induced spinal pain led to significant improvements in acute and chronic pain and increased muscle flexibility and tone. This study also found massage therapy to be extremely cost effective,

with cost savings ranging from 15-50%. Massage has also been shown to stimulate the body's ability to naturally control pain by stimulating the brain to produce endorphins. Fibromyalgia is an example of a condition that may be favorably affected by this effect.

A pilot study of five subjects with symptoms of tension and anxiety found a significant response to massage therapy in one or more psycho-physiological parameters of heart rate, frontalis and forearm extensor electromyograms (EMGs) and skin resistance, which demonstrate relaxation of muscle tension and reduced anxiety.

Lymph drainage massage has been shown to be more effective than mechanized methods or diuretic drugs to control lymphedema secondary to radical **mastectomy**, consequently using massage to control lymphedema would significantly lower treatment costs. A study found that massage therapy can have a powerful effect upon psycho-emotional distress in persons suffering from chronic inflammatory bowel disease. Massage therapy was effective in reducing the frequency of episodes of pain and disability in these patients.

Massage may enhance the immune system. A study suggests an increase in cytotoxic capacity associated with massage. A study of **chronic fatigue syndrome** subjects found that a group receiving massage therapy had lower depression, emotional distress, and somatic symptom scores, more hours of sleep, and lower epinephrine and cortisol levels than a control group.

ORGANIZATIONS

American Massage Therapy Association, 500 Davis Street, Suite 900, Evanston, IL, 60201-4695, (847) 864-0123, (847) 864-5196, (877) 905-2700, info@amtamassage.org, http://www.amtamassage.org/.

Elliot Greene

Mastectomy

Definition

Mastectomy is the surgical removal of the breast for the treatment or prevention of **breast cancer**.

Purpose

Mastectomy is performed as a surgical treatment for breast **cancer**. The severity of a breast cancer is evaluated according to a complex system called staging. This takes into account the size of the tumor and whether it has spread to the lymph nodes, adjacent tissues, and/or distant parts of the body. A mastectomy usually is the recommended surgery for more advanced breast cancers. Women with earlier stage breast cancers, who might also have breast-conserving surgery (**lumpectomy**), may choose to have a mastectomy. In the United States, approximately 50,000 women a year undergo mastectomy.

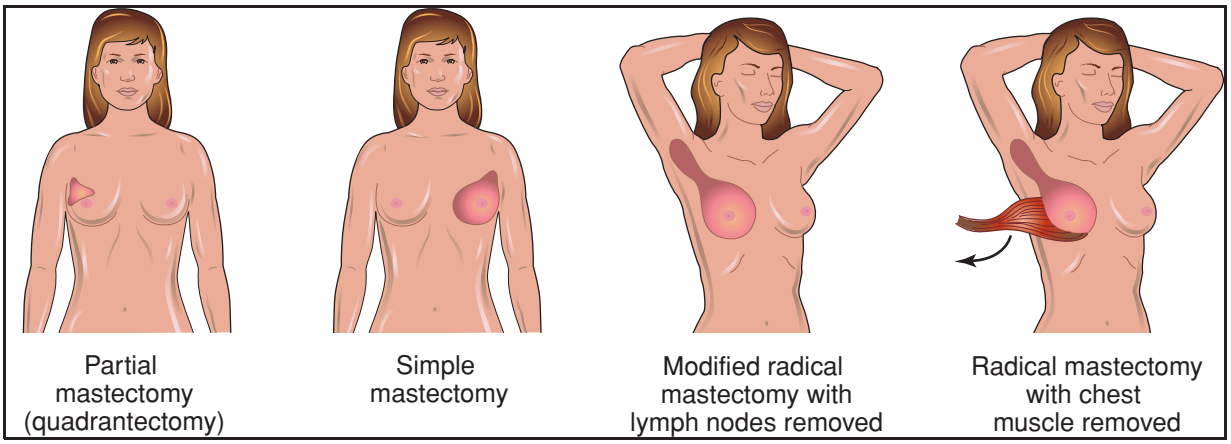
The size, location, and type of tumor are important considerations when choosing the best surgery to treat breast cancer. The size of the breast also is an important factor. A woman's psychological concerns and lifestyle choices also should be considered when making a decision.

There are many factors that may make a mastectomy the treatment of choice for a patient. Large tumors are difficult to remove with good cosmetic results. This is especially true if the woman has small breasts. Sometimes multiple areas of cancer are found in one breast, making removal of the whole breast necessary. The surgeon sometimes is unable to remove the tumor with a sufficient amount, or margin, of normal tissue surrounding it. In this situation, the entire breast needs to be removed. Recurrence of breast cancer after a lumpectomy is another indication for mastectomy.

Radiation therapy is almost always recommended following a lumpectomy. If a woman is unable to have radiation, a mastectomy is the treatment of choice. Pregnant women cannot have radiation therapy for fear of harming the fetus. A woman with certain collagen vascular diseases, such as **systemic lupus erythematosus** or **scleroderma**, would experience unacceptable scarring and damage to her connective tissue from radiation exposure. Any woman who has had therapeutic radiation to the chest area for other reasons cannot tolerate additional exposure for breast cancer therapy.

The need for radiation therapy after breast conserving surgery may make mastectomy more appealing for nonmedical reasons. Some women fear radiation and choose the more extensive surgery so radiation treatment will not be required. The commitment of time, usually five days a week for six weeks, may not be acceptable for other women. This may be due to financial, personal, or job-related factors. In geographically isolated areas, a course of radiation therapy may require lengthy travel and perhaps unacceptable amounts of time away from family or other responsibilities.

Some women choose mastectomy because they strongly fear recurrence of the breast cancer, and



There are four types of mastectomies: partial mastectomy, or lumpectomy, in which the tumor and surrounding tissue is removed; simple mastectomy, where the entire breast and some axillary lymph nodes are removed; modified radical mastectomy, in which the entire breast and all axillary lymph nodes are removed; and the radical mastectomy, where the entire breast, axillary lymph nodes, and chest muscles are removed. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

lumpectomy seems too risky. Keeping a breast that has contained cancer may feel uncomfortable for some patients. They prefer mastectomy, so the entire breast will be removed. However, studies have shown that survival rates for women choosing mastectomy and those undergoing breast-conserving surgery have been the same.

The issue of prophylactic or preventive mastectomy, or removal of the breast to prevent future breast cancer, is controversial. Women with a strong family history of breast cancer and/or who test positive for a known cancer-causing gene may choose to have both breasts removed. Patients who have had certain types of breast cancers that are more likely to recur may elect to have the unaffected breast removed. Although there is some evidence that this procedure can decrease the chances of developing breast cancer, it is not a guarantee. It is not possible to guarantee that all breast tissue has been removed. There have been cases of breast cancers occurring after both breasts have been removed.

Studies have shown that women who choose preventive mastectomy generally are satisfied with their choice, but also believe they lacked enough information before deciding, particularly about the surgery, **genetic testing**, and **breast reconstruction**. A study released in 2003 concerning women who underwent radical mastectomy of one breast and chose surgical removal of the other breast as a preventive measure found that 83% were highly satisfied with their decision.

Precautions

The decision to have mastectomy or lumpectomy should be carefully considered. It is important that the woman be fully informed of all the potential risks and benefits of each surgical treatment before making a choice.

Description

There are several types of mastectomies. The radical mastectomy, also called the Halsted mastectomy, is rarely performed today. It was developed in the late 1800s, when it was thought that more extensive surgery was most likely to cure cancer. A radical mastectomy involves removal of the breast, all surrounding lymph nodes up to the collarbone, and the underlying chest muscle. Women often were left disfigured and disabled, with a large defect in the chest wall requiring **skin grafting**, and significantly decreased arm sensation and motion. Unfortunately, and inaccurately, it still is the operation many women picture when the word mastectomy is mentioned.

Surgery that removes breast tissue, nipple, an ellipse of skin, and some axillary or underarm lymph nodes, but leaves the chest muscle intact, usually is called a modified radical mastectomy. This is the most common type of mastectomy performed today. The surgery leaves a woman with a more normal chest shape than the older radical mastectomy procedure, and a scar that is not visible in most clothing. It also allows for immediate or delayed breast reconstruction.

In a simple mastectomy, only the breast tissue, nipple, and a small piece of overlying skin are removed. If a few of the axillary lymph nodes closest to the breast also are taken out, the surgery may be called an extended simple mastectomy.

There are other variations on the term mastectomy. A skin-sparing mastectomy uses special techniques that preserve the patient's breast skin for use in reconstruction, although the nipple still is removed. Total mastectomy is a confusing expression, as it may be used to refer to a modified radical mastectomy or a simple mastectomy. In 2003, surgeons reported on a new technique that spared the nipple in many women with early stage breast cancer.

Many women choose to have breast reconstruction performed in conjunction with the mastectomy. The reconstruction can be done using a woman's own abdominal tissue, or using saline-filled artificial expanders, which leave the breast relatively flat but partially reconstructed. Additionally, there are psychological benefits to coming out of the surgery with the first step to a reconstructed breast. Immediate reconstruction will add time and cost to the mastectomy procedure, but the patient can avoid the physical impact of a later surgery.

A mastectomy typically is performed in a hospital setting, but specialized outpatient facilities sometimes are used. The surgery is done under **general anesthesia**. The type and location of the incision may vary according to plans for reconstruction or other factors, such as old **scars**. As much breast tissue as possible is removed. Approximately 10 to 20 axillary lymph nodes usually are removed. All tissue is sent to the pathology laboratory for analysis. If no immediate reconstruction is planned, surgical drains are left in place to prevent fluid accumulation. The skin is sutured and **bandages** are applied.

The surgery may take from two to five hours. Patients usually stay at least one night in the hospital, although outpatient mastectomy is increasingly performed for about 10% of all patients. Insurance usually covers the cost of mastectomy. If immediate reconstruction is performed, the length of stay, recovery period, insurance reimbursement, and fees will vary. In 1998, the Women's Health and Cancer Rights Act required insurance plans to cover the cost of breast reconstruction in conjunction with a mastectomy procedure.

Preparation

Routine preoperative preparations, such as not eating or drinking the night before surgery, typically are ordered for a mastectomy. On rare occasions, the patient also may be asked to donate blood in case a blood **transfusion** is required during surgery. The patient should advise the surgeon of any medications she is taking. Information regarding expected outcomes and potential complications also should be part of preparation for a mastectomy, as for any surgical procedure. It is especially important that women know about sensations they might experience after surgery, so they are not misinterpreted as a sign of poor wound healing or recurrent cancer.

Aftercare

In the past, women often stayed in the hospital at least several days. Now many patients go home the same day or within a day or two after their mastectomies. Visits from home care nurses can sometimes be arranged, but patients need to learn how to care for themselves before discharge from the hospital. Patients may need to learn to change bandages and/or care for the incision. The surgical drains must be attended to properly; this includes emptying the drain, measuring fluid output, moving clots through the drain, and identifying problems that need attention from the doctor or nurse. If the drain becomes blocked, fluid or blood may collect at the surgical site. Left untreated, this accumulation may cause infection and/or delayed wound healing.

After a mastectomy, activities such as driving may be restricted according to individual needs. **Pain** is usually well controlled with prescribed medication. Severe pain may be a sign of complications, and should be reported to the physician. A return visit to the surgeon is usually scheduled 7 to 10 days after the procedure.

Exercises to maintain shoulder and arm mobility may be prescribed as early as 24 hours after surgery. These are very important in restoring strength and promoting good circulation. However, intense **exercise** should be avoided for a time after surgery in order to prevent injury. The specific exercises suggested by the physician will change as healing progresses. **Physical therapy** is an integral part of care after a mastectomy, aiding in the overall recovery process.

Emotional care is another important aspect of recovery from a mastectomy. A mastectomy patient may feel a range of emotions including depression, negative self-image, grief, fear and **anxiety** about possible recurrence of the cancer, anger, or guilt. Patients are advised to seek counseling and/or support groups and to express their emotions to others, whether family, friends, or therapists. Assistance in dealing with the

KEY TERMS

Axillary—Located in or near the armpit.

Lymphedema—Swelling caused by an accumulation of fluid from faulty lymph drainage.

Mastectomy, modified radical—Total mastectomy with axillary lymph node dissection, but with preservation of the pectoral muscles.

Mastectomy, radical—Removal of the breast, pectoral muscles, axillary lymph nodes, and associated skin and subcutaneous tissue.

Mastectomy, simple—Removal of only the breast tissue, nipple and a small portion of the overlying skin

psychological effects of the breast cancer diagnosis, as well as the surgery, can be invaluable for women.

Measures to prevent injury or infection to the affected arm should be taken, especially if axillary lymph nodes were removed. There are a number of specific instructions directed toward avoiding pressure or constriction of the arm. Extra care must be exercised to avoid injury, to treat it properly if it occurs, and to seek medical attention promptly when appropriate.

Additional treatment for breast cancer may be necessary after a mastectomy. Depending on the type of tumor, lymph node status, and other factors, **chemotherapy**, radiation therapy, and/or hormone therapy may be prescribed.

Risks

Risks that are common to any surgical procedure include bleeding, infection, anesthesia reaction, or unexpected scarring. After mastectomy and axillary lymph node dissection, a number of complications are possible. A woman may experience decreased feeling in the back of her armpit or other sensations including **numbness**, **tingling**, or increased skin sensitivity. Some women report phantom breast symptoms, experiencing **itching**, aching, or other sensations in the breast that has been removed. There may be scarring around where the lymph nodes were removed, resulting in decreased arm mobility and requiring more intense physical therapy.

Approximately 10% to 20% of patients develop **lymphedema** after axillary lymph node removal. This swelling of the arm, caused by faulty lymph drainage, can range from mild to severe. It can be treated with elevation, elastic bandages, and specialized physical therapy. Lymphedema is a chronic condition that requires continuing treatment. This complication can arise at any time, even years after surgery. A new technique called sentinel lymph node mapping and biopsy often eliminates the need for removing some or all lymph nodes by testing the first lymph node for cancer.

Normal results

A mastectomy is performed as the definitive surgical treatment for breast cancer. The goal of the procedure is that the breast cancer is completely removed and does not recur.

Abnormal results

An abnormal result of a mastectomy is the incomplete removal of the breast cancer or a recurrence of the cancer. Other abnormal results include long-lasting (chronic) pain or impairment that does not improve after several months of physical therapy.

Resources

PERIODICALS

"American Women Still Having Too Many Mastectomies." *Women's Health Weekly* February 6, 2003: 10.

"Majority Satisfied with Prophylactic Mastectomy Decision." *AORN Journal* November 2003: 773.

"Studies Compare Mastectomy, Lumpectomy Survival Rates." *Clinican Reviews* January 2003: 24.

OTHER

BreastCancer.org April 15, 2001. [cited June 12, 2001]. http://www.breastcancer.org.

Living Beyond Breast Cancer April 15, 2001. [cited June 12, 2001]. http://www.lbbc.org.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

Breast Cancer Network of Strength, 135 S. LaSalle St., Suite 2000, Chicago, IL, 60603, (312) 986-8338, (312) 294-8597, (800) 221-2141, http://www.networkofstrength.org.

National Lymphedema Network, 116 New Montgomery Street, Suite 235, San Francisco, CA, 94105, (415) 908-3681, (415) 908-3813, (800) 541-3259, nln@lymphnet.org, http://www.lymphnet.org.

Ellen S. Weber, MSN
Teresa G. Odle

Mastitis

Definition

Mastitis is an inflammation within the breast tissue that is usually caused by an infection. It usually only occurs in women who are **breastfeeding** their babies; generally, during the first two months of breast-feeding an infant.

Demographics

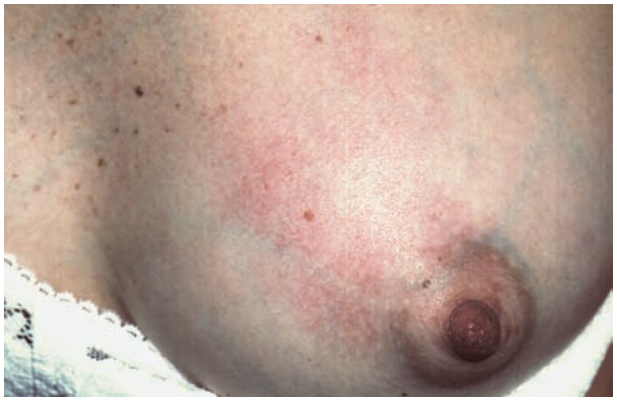
Mastitis usually occurs in lactating mothers. In some cases, it occurs as the result of inflammatory lesions on the breast of females neither pregnant nor breastfeeding. In rare cases it can occur in men.

Description

Breastfeeding is the act of allowing a baby to suckle at the breast to drink the mother's milk. In the process, unaccustomed to the vigorous pull and tug of the infant's suck, the nipples may become sore, cracked, or irritated. This creates a tiny opening in the breast, through which bacteria can enter. The presence of milk, with high sugar content, gives the bacteria an excellent source of **nutrition**. Under these conditions, the bacteria are able to multiply, until they are plentiful enough to cause an infection within the breast.

Mastitis usually begins more than two to four weeks after delivery of the baby. It is a relatively uncommon complication of breastfeeding mothers, occurring in only approximately 3% to 5% of nursing women.

Women are at increased risk from getting mastitis if one or more of the following have occurred:



Mastitis is usually caused by a bacterial infection through a nipple damaged during breastfeeding. *(Dr. P. Marazzi/SPL/Photo Researchers, Inc.)*

- Mastitis has occurred previously
- Anemia is present
- Nipples become irritated or cracked. Irritation can be caused by a nursing brassiere (bra) that is too tight
- Breast-feeding is not performed on a regular basis, or if the breasts are not completely emptied of milk during breast-feeding.

Causes and symptoms

Mastitis frequently occurs when bacteria contact a nipple on a female breast, although it can enter the breast from elsewhere. It can also occur due to improper breast-feeding techniques. The most common species of bacteria causing mastitis is called *Staphylococcus aureus*; however, it can also be caused by the species *Staphylococcus epidermidis* and certain species within the genus *Streptococci*. In 25% to 30% of people, this bacterium is present on the skin lining of normal, uninfected nostrils. It is probably this bacterium, clinging to the baby's nostrils, that is available to create infection when an opportunity (such as a crack in the nipple or a sore nipple of a nursing mother) presents itself.

Usually, only one breast is involved. An area of the affected breast becomes swollen, tender, red, hard (sometimes lumpy), itchy, and painful (often with a burning sensation). Other symptoms of mastitis include a general feeling of illness, including **fever** (with a temperature equal to or greater than 101°F [38.3°C]), **nausea**, **vomiting**, aches, shivering and chills, **fatigue**, and increased heart rate. Breast engorgement (enlarged veins and increased pressure due to excess milk production) may also occur. Advanced signs of mastitis includes swollen and tender (or painful) lymph nodes in the armpit adjacent to the infected breast and flu-like symptoms that worsen over time.

Diagnosis

Women should visit their doctor or other health care provider as soon as symptoms of mastitis appear, especially if flu-like symptoms appear, along with the presence of a reddish color on one or more of the breasts, breast **pain**, or abnormal leakage of milk from the nipples. Diagnosis by the doctor involves obtaining a sample of breast milk from the infected breast. The milk is cultured, allowing colonies of bacteria to grow. The causative bacteria then can be specially prepared for identification under a microscope. At the same time, tests can be performed to determine what type of antibiotic would be most effective against that particular bacterium. Sometimes, women and

their physicians confuse mastitis with breast engorgement, or the tenderness and redness that appear when milk builds up in the breasts. Mastitis often can be distinguished if symptoms are accompanied by fever.

Treatment

A number of **antibiotics** are used to treat mastitis, including cephalexin, amoxicillin, azithromycin, dicloxacillin, and clindamycin. Breastfeeding usually should be continued, because the rate of **abscess** formation (an abscess is a persistent pocket of pus) in the infected breast goes up steeply among women who stop breastfeeding during a bout with mastitis. Most practitioners allow women to take **acetaminophen** (such as Tylenol) or ibuprofen (such as Advil) while nursing, to relieve both fever and pain. As always, breastfeeding women need to make sure that any medication they take is also safe for the baby, since almost all drugs they take appear in the breast milk. Warm compresses applied to the affected breast can be soothing.

Prognosis

Prognosis for uncomplicated mastitis is excellent when it is treated properly with medicine. About 10% of women with mastitis will end up with an abscess within the affected breast. An abscess is a collection of pus within the breast. This complication will require a surgical procedure to drain the pus.

Prevention

The most important aspect of prevention involves good hand-washing to try to prevent the infant from acquiring the *Staphylococcus aureus* bacterium, or another species of bacteria, in the first place. Keeping the breasts, and especially the nipples, clean before breastfeeding also helps prevent infection. Preventing the breasts from becoming engorged may help prevent mastitis by preventing plugging of milk ducts. Breastfeeding often throughout the day is advised. When unable to breast-feed use a breast-pump to remove the milk. Placing warm or cold packs on the breasts can also help to relieve the pain.

To make sure all of the milk is extracted from the breast, place a warm, wet washcloth over the affected breast for about 15 to 20 minutes before breast-feeding. Such an action helps to increase the flow of milk out of the nipple during breast-feeding. Other health care practices such as getting plenty of rest, drinking sufficient fluids daily, and eating healthy, nutritious meals can also help to avoid fatigue and anemia, which also helps to prevent mastitis. Rather than stopping the act of breastfeeding suddenly it is wise to slowly reduce the amount of times breast-feeding occurs in a day over a several week period.

Resources

BOOKS

Gupta, Sunanda, Debra Holloway, and Ali Kubba, editors. *Oxford Handbook of Women's Health Nursing*. Oxford, UK: Oxford University Press, 2010.

Leifer, Gloria. *Maternity Nursing: An Introductory Text*. St. Louis: Saunders Elsevier, 2008.

London, Marcia L., et al. *Maternity and Child Nursing Care*. Upper Saddle River, NJ: Pearson Education, 2011.

OTHER

Breast Infection. Medline Plus, National Library of Medicine and National Institutes of Health. (November 11, 2009), www.nlm.nih.gov/medlineplus/ency/article/001490.htm. (accessed August 11, 2010).

Mastitis While Breast-Feeding. WebMD. (January 17, 2008), www.webmd.com/parenting/baby/tc/mastitis-while-breast-feeding-topic-overview. (accessed August 11, 2010).

ORGANIZATIONS

La Leche League International, 957 North Plum Grove Road, Schaumburg, IL, 60173, (847) 519-7730, (800) 525-3243, (847) 969-0460, http://www.llli.org/.

Rosalyn Carson-DeWitt, MD
Teresa G. Odle

Mastocytosis

Definition

Mastocytosis is a disease characterized by the presence of too many mast cells in various organs and tissues.

Description

The body has a variety of free-roaming cell populations that function as immunogenic agents. Most immunogenic cells fall into the category of white blood cells, but some remain in tissues and are not found in the blood. Mast cells are such a group.

Mast cells are found primarily in the skin and digestive system, including the liver and spleen, and produce histamine, a chemical most famous for its ability to cause **itching**. Histamine also causes acid **indigestion**, **diarrhea**, flushing, heart pounding, headaches, and can even cause the blood pressure to drop suddenly.

KEY TERMS

Nonsteroidal anti-inflammatory drugs (NSAIDs)—Aspirin, ibuprofen, naproxen, and many others.

Peptic ulcer—Ulcers in the stomach and upper duodenum (first portion of the small intestine) caused by stomach acid and a bacterium called *Helicobacter pylori*.

Mastocytosis comes in three forms. Most cases produce symptoms but do not shorten life expectancy. The three forms are:

- Mastocytoma, a benign skin tumor.
- Urticaria pigmentosa, small collections of mast cells in the skin that manifest as salmon or brown-colored patches.
- Systemic mastocytosis, the collection of mast cells in the skin, lymph nodes, liver, spleen, gastrointestinal tract, and bones.

Causes and symptoms

The cause of mastocytosis is unknown. People with systemic mastocytosis have bone and joint **pain**. Peptic ulcers are frequent because of the increased stomach acid stimulated by histamine. Many patients with systemic mastocytosis also develop urticaria pigmentosa. These **skin lesions** itch when stroked and may become fluid-filled.

Diagnosis

A biopsy of the skin patches aids diagnosis. An elevated level of histamine in the urine or blood is also indicative of mastocytosis.

Treatment

Mastocytoma usually occurs in childhood and clears-up on its own. Urticaria pigmentosa (present alone without systemic disease) also dramatically clears or improves as adolescence approaches.

Several medications are helpful in relieving symptoms of systemic mastocytosis. **Antihistamines** and drugs that reduce stomach acid are frequently needed. Headaches respond to migraine treatment. A medicine called cromolyn helps with the bowel symptoms. Several other standard and experimental medications have been used.

Prognosis

Mastocytoma and urticaria pigmentosa rarely if ever, develop into systemic mastocytosis, and both spontaneously improve over time. Systemic mastocytosis is only symptomatically treated. There is no known treatment that decreases the number of mast cells within tissue.

Resources

BOOKS

Fauci, Anthony S., et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill Professional, 2008.

J. Ricker Polsdorfer, MD

Mastoid tympanoplasty *see* **Mastoidectomy**

Mastoidectomy

Definition

Mastoidectomy is a surgical procedure to remove an infected portion of the bone behind the ear when medical treatment is not effective. This surgery is rarely needed today because of the widespread use of **antibiotics**.

Purpose

Mastoidectomy is performed to remove infected air cells within the mastoid bone caused by **mastoiditis**, ear infection, or an inflammatory disease of the middle ear (cholesteatoma). The cells are open spaces containing air that are located throughout the mastoid bone. They are connected to a cavity in the upper part of the bone, which is in turn connected to the middle ear. As a result, infections in the middle ear can sometimes spread through the mastoid bone. When antibiotics cannot clear this infection, it may be necessary to remove the infected air cells by surgery. Mastoidectomies are also performed sometimes to repair paralyzed facial nerves.

Description

Mastoidectomy is performed less often today because of the widespread use of antibiotics to treat ear infections.

There are several different types of mastoidectomy:

- Simple (or closed). The operation is performed through the ear or through a cut (incision) behind

KEY TERMS

Cholesteatoma—A rare but chronic inflammatory disease in which skin cells and debris collect in the middle ear, usually as a result of an ear infection.

Mastoid bone—The prominent bone behind the ear that projects from the temporal bone of the skull.

Mastoiditis—An inflammation of the bone behind the ear (the mastoid bone) caused by an infection spreading from the middle ear to the cavity in the mastoid bone.

the ear. The surgeon opens the mastoid bone and removes the infected air cells. The eardrum is cut (incised) to drain the middle ear. Topical antibiotics are then placed in the ear.

- Radical mastoidectomy. The eardrum and most middle ear structures are removed, but the innermost small bone (the stapes) is left behind so that a hearing aid can be used later to offset the hearing loss.
- Modified radical mastoidectomy. The eardrum and the middle ear structures are saved, which allows for better hearing than is possible after a radical operation.

The wound is then stitched up around a drainage tube, which is removed a day or two later. The procedure usually takes between two and three hours.

Preparation

The doctor will give the patient a thorough ear, nose, and throat examination as well as a detailed hearing test before surgery. Patients are given an injection before surgery to make them drowsy.

Aftercare

Painkillers are usually needed for the first day or two after the operation. The patient should drink fluids freely. After the stitches are removed, the bulky mastoid dressing can be replaced with a smaller dressing if the ear is still draining. The patient is given antibiotics for several days.

The patient should tell the doctor if any of the following symptoms occur:

- Bright red blood on the dressing.
- Stiff neck or disorientation. These may be signs of meningitis.
- Facial paralysis, drooping mouth, or problems swallowing.

Risks

Complications do not often occur, but they may include:

- Persistent ear drainage.
- Infections, including meningitis or brain abscesses.
- Hearing loss.
- Facial nerve injury. This is a rare complication.
- Temporary dizziness.
- Temporary loss of taste on the side of the tongue.

ORGANIZATIONS

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 836-4444, http://www.entnet.org.

American Hearing Research Organization, 8 South Michigan Avenue, Suite #1205, Chicago, IL, 60603-4539, (312) 726-9670, (312) 726-9695, http://www.american-hearing.org.

Better Hearing Institute, 1444 I Street, NW, Suite 700, Washington, DC, 20005, (202) 449-1100, (800) 327-9355, mail@betterhearing.org, http://www.better hearing.org/

Carol A. Turkington

Mastoiditis

Definition

Mastoiditis is an infection of the spaces within the mastoid bone (located immediately behind the outside ear) within the skull. It is usually associated with **otitis media**, an infection of the middle ear. In the most serious cases, the bone itself becomes infected.

Demographics

Mastoiditis can occur in humans at any age, and equally of males and females. However, it is more likely to occur in children, primarily in younger children from six months to about one year of age. It rarely occurs in developed countries, such as the United States. Its incidence in the United States is usually less than four out of 100,000 people (0.004%) annually.

Description

The mastoid is a part of the side (temporal bone) of the skull. It can be felt as a bony bump just behind and slightly above the level of the earlobe. The mastoid has been described as resembling a "honeycomb"

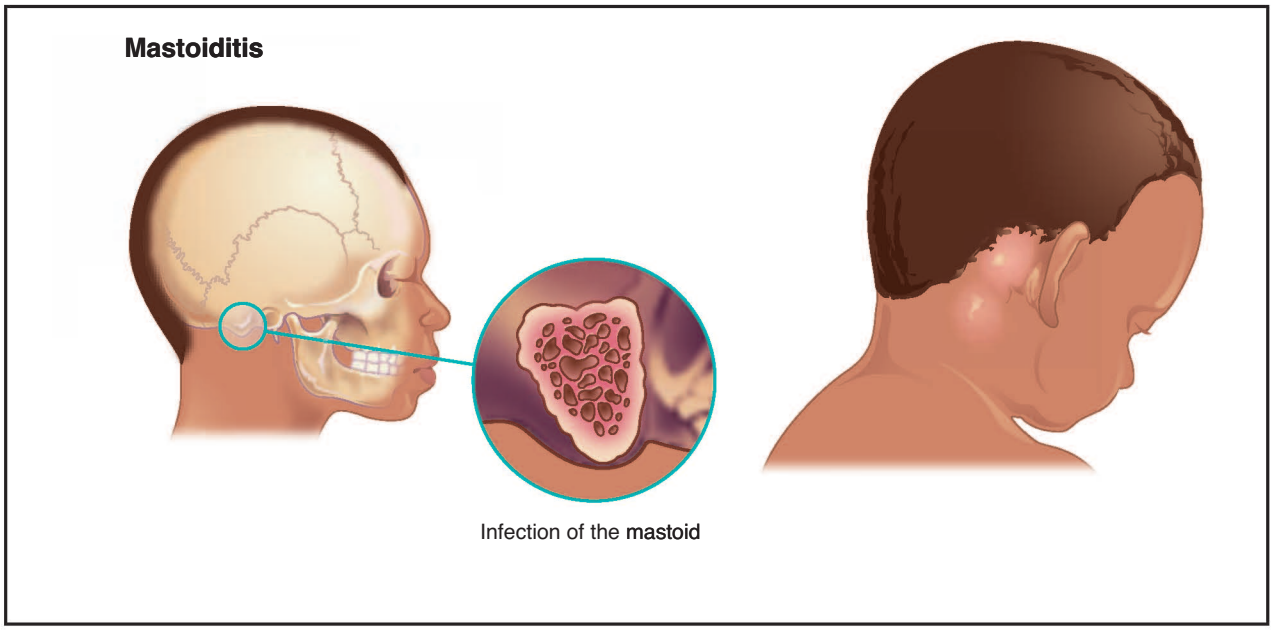


Illustration depicting infection of the mastoid (part of the temporal bone in the skull), and the appearance of the infection on the surface of the skin. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

of tiny partitioned-off airspaces. The mastoid is connected with the middle ear, so that when there is a collection of fluid in the middle ear, there is usually also a slight collection of fluid within the airspaces of the mastoid.

Mastoiditis can range from a simple case of some fluid escaping into the mastoid air cells during a middle ear infection, to a more complex infection which penetrates through to the lining of the mastoid bone, to a very severe and destructive infection of the mastoid bone itself.

Increased complications after getting mastoiditis may include:

- Paralysis of the face
- Meningitis (inflammation of the meninges)
- Hearing loss
- Infection extending throughout the body
- Vertigo (dizziness when stationary)
- Damaged or destroyed mastoid bone
- Epidural abscess

Causes and symptoms

Mastoiditis is caused by the same types of bacteria that cause middle ear infections (*Streptococcus pneumoniae* and *Haemophilus influenzae*), as well as by a variety of other bacteria (*Staphylococcus aureus*, *Pseuodomonas aeruginosa*, *Klebsiella*, ***Escherichia coli***, *Proteus*, *Prevotella*, *Fusobacterium*, *Porphyromonas*, and *Bacteroides*). Mastoiditis may occur due to the progression of an untreated, or undertreated, middle ear infection (what is called acute otitis media). The infection most often occurs in children.

Symptoms of mastoiditis may at first be the same as symptoms of an early middle ear infection. With progression, however, the swollen mastoid may push the outer ear slightly forward and away from the head. The area behind the ear will appear red and swollen, and will be very sore. **Fever** is usually present, and appears suddenly in most cases. A **headache** frequently is a symptom. There may be drainage of pus from the infected ear. In some cases, the skin over the mastoid may develop an opening through which pus drains. The reduced ability to hear may also occur. In infants, the symptoms can include irritability, **diarrhea**, fever, and poor feeding.

Diagnosis

Mastoiditis is usually suspected by a family physician or an ear, nose, and throat (ENT) specialist when a severe middle ear infection is accompanied by redness, swelling, and **pain** in the mastoid area. A **magnetic resonance imaging** (MRI) scan may be used, or a computed tomography (CT) scan may also be used; both show inflammation and fluid within the airspaces of the mastoid, as well as the erosion of the little walls of bone that should separate the air spaces. Several

KEY TERMS

Abscess—A pocket of infection, usually including a collection of pus.

Meningitis—Inflammation and infection of the tissues covering the brain and spinal cord (the meninges).

Otitis or oteitis—An infection of the middle ear; marked by an enlargement of bone, tenderness and dull aching pain.

head and skull CT scans may be requested. If fluid drains from the ear or mastoid, a culture of the drainage will allow a laboratory to indentify the causative organism. If there is no fluid available, a tiny needle can be used to obtain a sample of the fluid which has accumulated behind the eardrum.

Treatment

Identification of the causative organism guides the practitioner's choice of antibiotic. Depending on the severity of the infection, the antibiotic can be given initially through a needle in the vein (intravenously, or IV), and then (as the patient improves) by mouth. Oftentimes, long-term treatment, or repeat treatment, of **antibiotics** is necessary. The group of antibiotics called penicillin may be used unless the patient is allergic to it. In such cases, clindamycin may be used.

In the case of a very severe infection of the mastoid bone itself, with a collection of pus (**abscess**), an operation to remove the mastoid part of the temporal bone is often necessary (**mastoidectomy**). Surgery to drain the middle ear is often performed to solve the problem with the middle ear infection.

Prognosis

With early identification of mastoiditis, the prognosis is very good. Sometimes it is difficult to make sure the antibiotics reach the interior of the mastoid area. In this case, the prognosis is less positive. When symptoms are not caught early enough, however, a number of complications can occur. These include an infection of the tissues covering the brain and spinal cord (**meningitis**), a pocket of infection within the brain (abscess), or an abscess within the muscles of the neck. All of these complications have potentially more serious prognoses. With the use of antibiotics, mastoiditis has become a minor ailment, only infrequently occurring in the United States. However, before antibiotics were discovered, it could easily cause **death**. In fact, at one time mastoiditis was one of the primary causes of death among children.

Prevention

Prevention of mastoiditis involves careful and complete treatment of any middle ear infections.

Resources

BOOKS

Fisch, Ugo. *Tympanoplasty, Mastoidectomy, and Stapes Surgery*. Stuttgart, Germany: Thieme, 2008.

Nadol Jr., Joseph B., and Michael J. McKenna., editors. *Surgery of the Ear and Temporal Bone*. Philadelphia: Lippincott Williams and Wilkins, 2005.

OTHER

Ear Infections—Treatment Overview. WebMD. (February 2, 2009), http://www.webmd.com/cold-and-flu/ear-infection/ear-infections-treatment-overview. (accessed August 11, 2010).

Mastoiditis. eMedicine, WebMD. (September 28, 2009), http://emedicine.medscape.com/article/784176-overview. (accessed August 11, 2010).

Mastoiditis. MedlinePlus, National Library of Medicine and National Institutes of Health. (October 10, 2008), http://www.nlm.nih.gov/medlineplus/ency/article/001034.htm. (accessed August 11, 2010).

ORGANIZATIONS

American Academy of Otolaryngology-Head and Neck Surgery, Inc., 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 838-4444, http://www.entnet.org/.

Rosalyn Carson-DeWitt, MD

Maternal serum alpha-fetoprotein test *see* **Alpha-fetoprotein test**

Maternal to fetal infections

Definition

Maternal to fetal infections are transmitted from the mother to her fetus, either across the placenta during fetal development (prenatal) or during labor and passage through the birth canal (perinatal).

Description

Antibodies in the maternal blood prevent most infections from being transmitted to the fetus. However, some maternal to fetal infections, particularly in

the first trimester of **pregnancy**, can cause **miscarriage** or severe **birth defects**. Other infections can cause preterm labor, fetal or neonatal **death**, or serious illness in newborns. Perinatal transmissions infect the fetus after its protective membranes rupture—the water breaks—and during labor and delivery when the fetus is exposed to maternal blood. Perinatal transmission is more likely if the waters break prematurely.

Toxoplasmosis

Up to one-third of all people are infected with **toxoplasmosis**. The U.S. Centers for Disease Control and Prevention (CDC) estimate that 25-45% of women of childbearing age carry the parasite *Toxoplasma gondii* that causes toxoplasmosis. Very few infected people have symptoms and most pregnant women have antibodies that protect the fetus from infection. However, in one-third of women who are infected for the first time during pregnancy, the parasite infects the placenta and enters the fetal circulation. Congenital (present at birth) infection occurs in one out of every 800-1,400 infants born to infected mothers. The fetal infection rate is above 60% if maternal infection occurs during the third trimester, but the most severe fetal complications occur with first-trimester infection.

Viral respiratory infections

Cytomegalovirus (CMV) is the most common infection that can be transmitted to a fetus. Fifty to eighty percent of childbearing-age women have been infected by CMV prior to pregnancy. About 1-3% of women have their first or primary CMV infection during pregnancy and about one-third of these infections are transmitted to fetuses. Although most infants with congenital CMV have no problems, infection in early pregnancy can cause miscarriage or birth defects and CMV is a leading cause of congenital deafness. In later pregnancy CMV infection may cause preterm labor, **stillbirth**, or serious newborn illness. In the United States about 8,000 infants annually are born with potentially fatal CMV-related birth defects.

Fifth disease, caused by the parvovirus B19, is very common among children. About one-half of all adults are susceptible. About one-third of infants whose mothers contract fifth disease during pregnancy show signs of infection at birth. Although not usually dangerous, fifth disease contracted early in pregnancy can cause miscarriage or severe fetal anemia (low blood count) that can lead to congestive **heart failure**.

A fetus infected from its mother by *Varicella zoster* virus may develop pocks that can cause limb deformities early in development. If a woman contracts varicella (**chickenpox**) during the first 20 weeks of pregnancy, there is a 2% chance that her newborn will have varicella syndrome. The greatest risk from varicella is if the mother contracts the virus just before delivery when she has not yet produced antibodies to protect the newborn.

In the past, **rubella** was a common cause of birth defects. Routine vaccinations have made prenatal infection rare in the developed world. Rubella infection during the first 10 weeks of pregnancy may cause fetal death and more than 50% of newborns have severe birth defects. Infections contracted later in pregnancy do not cause congenital defects, although the newborn may become seriously ill and eventually develop **diabetes mellitus**.

Bacterial infections

Invasive group B streptococcal (GBS) disease is the most common cause of life-threatening infection in newborns. Up to 20% of pregnant women carry GBS in their vaginas during the last trimester, with the potential of infecting the fetus during birth. Although premature infants are more susceptible to GBS, 75% of infected infants are full-term. During the 1970s GBS emerged as the most common cause of newborn **sepsis**, or blood infection, and meningitis—infection of the fluid and lining surrounding the brain. GBS also is a frequent cause of newborn **pneumonia**. Maternal infection at conception or within the first two weeks of pregnancy may lead to hearing and vision loss and **mental retardation**. Between 1993 and 2002 congenital GBS infection in the United States decreased from 1.7 per 1,000 live births to 0.4 per 1,000 due to the use of **antibiotics** during delivery.

The food-borne bacterial infections listeriosis—caused by *Listeria monocytogenes*—and salmonellosis or food poisoning—caused by *Salmonella* bacteria—can be transmitted to a fetus. *L. monocytogenes* is ubiquitous in soil and groundwater, on plants, and in animals. Most human infections result from ingesting contaminated foods. Hormonal changes make pregnant women about 20 times more likely than other healthy adults to contract **listeriosis** and about one-third of all cases occur in pregnant women. Listeriosis can cause miscarriage, fetal or newborn death, premature delivery, or severe illness in the mother and infant.

Each year an estimated 8,000 pregnant women in the United States are infected with **syphilis** caused by

the spirochete *Treponema pallidum*. Rising rates of syphilis among pregnant women are increasing the number of infants born with congenital syphilis. Congenital syphilis is a severe, disabling, and often life-threatening disease that can cause facial deformity, blindness, and deafness.

Every year in the United States an estimated 40,000 pregnant women are infected with gonorrhea—caused by *Neisseria gonorrhoeae*—and an estimated 200,000 are infected with chlamydia—caused by *Chlamydia trachomatis*. Chlamydia can cause premature membrane rupture and labor. Both infections can cause newborn conjunctivitis—a discharge of pus from the eyes.

Sexually transmitted viral infections

Each year an estimated 8,000 pregnant American women are infected with HIV, the human **immunodeficiency** virus that causes acquired immune deficiency syndrome (**AIDS**). About 20-25% of pregnant women with untreated HIV transmit it to their fetuses. In developed countries widespread HIV testing and antiretroviral therapy have reduced maternal-fetal transmission dramatically.

Genital herpes are caused by herpes simplex virus (HSV) type-2 and, less frequently, by HSV type-1 that usually causes **cold sores**. About 25% of American adults are infected with HSV-2, affecting one in 1,800-5,000 live births. There is little risk of fetal transmission if the mother is infected before the third trimester and has no genital sores at the time of delivery. Infection during the third trimester—when the virus is likely to be active and the mother has not yet made sufficient antibodies to protect her fetus—may lead to congenital HSV infection. This can seriously damage the newborn's eyes, central nervous system, and internal organs, lead to mental retardation and, rarely, death.

Genital or venereal **warts** are caused by some types of human papillomavirus (HPV). At least 20 million Americans are infected and about 5.5 million new cases are reported annually. **Genital warts** are highly infectious and tend to grow faster during pregnancy. If vaginal warts are very large they may interfere with the infant's passage through the birth canal, necessitating a **cesarean section** (C-section).

An estimated 8,000 pregnant women are infected with **hepatitis B** in the United States every year. They are at risk for premature delivery and, if untreated, newborns may develop chronic **liver disease**.

Causes and symptoms

Toxoplasmosis

The single-celled protozoan *Toxoplasma gondii* produces eggs in cat intestines. The eggs shed in cat feces and can survive for up to 18 months in the soil. Human infection occurs from handling contaminated soil or feces or by ingesting raw or undercooked meat from infected animals.

Although the symptoms of toxoplasmosis usually are very mild or absent, infection occurring early in fetal development can cause:

- premature birth and low birth weight—under 5 lb (2.3 kg)
- slow growth
- fever
- skin rashes
- easy bruising
- anemia
- a small or large head (microcephaly or macrocephaly)
- fluid in the cavities of the brain (hydrocephaly)
- inflammation of the brain, heart, or lungs
- severe or prolonged jaundice
- an enlarged liver and spleen
- an eye inflammation called choriorectinitis, which can lead to blindness
- severe illness or death shortly after birth

Symptoms of congenital toxoplasmosis may appear months or years after birth and may include seizures or other neurological problems, **visual impairment**, **hearing loss**, or mental retardation.

Viral respiratory infections

Although most CMV-infected newborns have no symptoms, 10-15% may exhibit:

- low birth weight
- rashes
- small bruises
- jaundice
- enlarged liver and spleen
- hernias in the groin
- microcephaly or hydrocephaly
- respiratory problems
- brain damage

From 0.5-15% of CMV-infected infants develop hearing, vision, or neurological problems over several years. In addition to crossing the placenta, there is a 1% risk of perinatal CMV transmission.

Symptoms of congenital fifth disease include:

- bright red rash on the cheeks
- lacy, red rash on the neck, trunk, and legs
- joint pain
- fatigue
- malaise

Varicella syndrome in a newborn is characterized by abnormally small limbs and head, scarring of the skin, eye defects, and mental retardation.

In addition to various birth defects, newborns infected with rubella early in the pregnancy may have:

- low birth weight
- bruising
- bluish-red skin lesions
- enlarged lymph nodes
- enlarged liver and spleen
- brain inflammation
- pneumonia

Bacterial infections

Although most GBS carriers have no symptoms, GBS in pregnant women may cause bladder or urinary tract infections, infection of the womb, or stillbirth.

Pregnant women are more likely to transmit GBS to their fetuses if they:

- previously delivered a GBS-infected baby
- have a urinary tract infection caused by GBS
- carry GBS late in pregnancy
- begin labor or membrane rupture before 37 weeks of gestation
- have membrane rupture 18 hours or more before delivery
- experience fever during labor

Symptoms of congenital GBS infection include breathing difficulties, **shock**, sepsis, pneumonia, and **meningitis**.

Listeriosis may cause flu-like symptoms and the infection can be transmitted prenatally even if the mother has no symptoms.

Symptoms of salmonellosis can be severe in pregnant women and newborns and may include **diarrhea**, **fever**, abdominal cramps, and rarely, meningitis.

Syphilis can be transmitted to a fetus either prenatally or perinatally if the mother is infected during pregnancy or was inadequately treated for a past infection. In adults, syphilis usually causes genital lesions 10-90 days after exposure, with a rash developing six weeks later. Symptoms may go unnoticed. Congenital syphilis can cause premature birth or stillbirth.

A surviving newborn with untreated congenital syphilis may have no initial symptoms but may gain little weight and, during the first month of life, develop:

- rash or small fluid-filled blisters on the palms and soles of the feet
- raised bumps around the nose, mouth, and diaper region
- cracks around the mouth
- nasal discharge of mucus, pus, or blood
- enlarged lymph nodes, liver, and spleen
- bone inflammation
- rarely, meningitis

Early-stage symptoms of congenital syphilis include:

- failure to thrive
- fever
- severe congenital pneumonia
- rash and lesions around the mouth, genitalia, and anus
- bone lesions
- nose cartilage infection or saddle nose (lacking a bridge)

Symptoms of late-stage congenital syphilis include:

- copper-colored rashes on the face, palms, and soles
- scarring around earlier lesions
- gray patches on the anus or outer vagina
- notched or peg-shaped teeth
- joint swelling
- bone pain
- abnormalities in the lower leg bones
- neurological conditions
- visual loss or blindness
- hearing loss or deafness

Both **gonorrhea** and chlamydia can be transmitted perinatally. **Conjunctivitis** caused by gonorrhea usually appears two to seven days after birth. Conjunctivitis caused by chlamydia usually appears 5–12 days after birth, although sometimes it takes six weeks to develop.

Symptoms of gonorrhea in women, if present, may include:

- bleeding during vaginal intercourse
- pain or burning with urination

- yellow or bloody vaginal discharge
- pelvic inflammatory disease

Sexually transmitted viral infections

HIV can be transmitted through the placenta, during labor and delivery, and through breast milk. HIV-infected infants do not have symptoms at birth; although about 15% develop serious symptoms or die within the first year. Almost one-half die by the age of 10.

The risk of maternal HIV transmission is increased by the mother's use of illicit drugs, the amount of HIV in the mother (viral load), severe inflammation of the fetal membranes, and a prolonged period between membrane rupture and delivery.

Most women carrying HSV never have recognizable symptoms; however a first episode of genital herpes during pregnancy can be passed to the fetus and may cause premature birth. Both HSV-1 and HSV-2 can be transmitted during birth if the mother has active genital sores, causing facial or genital herpes in the newborn.

Initial symptoms of congenital herpes usually appear within four weeks of birth and may be quite mild:

- blisters on the skin
- fever
- tiredness
- loss of appetite

More serious symptoms of congenital HSV infection include:

- a skin rash with small fluid-filled blisters
- chronic or recurring eye and skin infections
- cataracts
- widespread infection affecting many organs including the lungs and liver
- a life-threatening brain infection called herpes encephalitis

Nearly 50% of women infected with HPV have no symptoms, but genital warts may appear weeks or months after infection. They can become larger during pregnancy causing difficulty with urination. Vaginal warts can reduce the elasticity of the vagina and cause obstruction during delivery. Symptoms of congenital HPV infection may include lung infection and obstructed air passages from warts inside the windpipe.

Hepatitis B can be transmitted to the fetus through the placenta, but most often it is transmitted perinatally. Since the virus is thought to pass through the umbilical cord, C-sections do not prevent transmission. Congenital hepatitis B can cause chronic liver infection, but symptoms are typically not apparent until young adulthood.

Diagnosis

Diagnosis of maternal, fetal, or congenital infection can be difficult. An obstetrician may diagnose a maternal infection based on the woman's symptoms and blood tests. Sometimes a fetal infection can be diagnosed using ultrasound. Diagnosis of congenital infections in newborns may be based on a **physical examination**, symptoms, and blood or urine tests. Ultrasound scanning may be used to image the newborn's brain and **echocardiography** may be used to diagnose heart problems.

Toxoplasmosis

Prenatal toxoplasmosis can be determined by a blood test for maternal antibodies, testing of the amniotic fluid and fetal blood, or during fetal ultrasound.

Postnatal diagnosis for congenital toxoplasmosis involves antibody tests of the cord blood and cerebrospinal fluid, an ophthalmologic and neurological examination, and a computed axial tomography (CT or CAT) scan.

A 2005 study advised that all pregnant women and newborns have blood screenings for toxoplasmosis.

Viral and bacterial infections

Blood tests can be used to diagnose listeriosis and to check for maternal antibodies against CMV or fifth disease. Ultrasound may be used for fetal fifth disease. GBS is diagnosed using bacterial cultures from blood, spinal fluid, skin, the vagina, or rectum.

Sexually transmitted infections (STIs)

The CDC recommends that all pregnant women be screened on their first prenatal visit for syphilis, gonorrhea, chlamydia, HIV, hepatitis B, and **hepatitis C**.

Infants are tested for syphilis at birth. Syphilis in an older infant may be diagnosed by a blood test, a **lumbar puncture** to look for signs of syphilis in the brain and central nervous system, an ophthalmologic examination, dark-field microscopy to visualize the spirochete, or **bone x rays**.

Maternal gonorrhea can be diagnosed by staining or culturing a cervical smear or testing for the bacterial DNA in a urine or cervical sample.

KEY TERMS

Antibody—A blood protein produced in response to a specific foreign substance including bacteria, viruses, and parasites; the antibody destroys the organism, providing protection against disease.

Cesarean section; C-section—Incision through the abdominal and uterine walls to deliver the fetus.

Conjunctivitis—An inflammation of the eye that can be caused by gonorrhea or chlamydia.

Cytomegalovirus (CMV)—A common human herpes virus that is normally not harmful but may cause severe complications if transmitted to a fetus.

Fifth disease—Erythema infectiosum; a common respiratory infection among children caused by parvovirus B19 that usually is not serious but can cause fetal complications.

Group B streptococcal (GBS) disease—A common bacterial infection that is potentially life-threatening if transmitted to a fetus during early pregnancy or birth.

Herpes simplex virus (HSV)—A very common sexually transmitted infection; type-2 HSV causes genital herpes and type-1 HSV usually causes cold sores but can cause genital herpes; congenital HSV can be transmitted to the fetus during birth if the mother has an active infection.

Human papillomavirus (HPV)—A large family of viruses, some of which cause genital warts; HPV can be transmitted to a fetus during birth.

Immune globulin—Serum containing antibodies against a specific infection.

Listeriosis—A food-borne bacterial infection caused by *Listeria monocytogenes* to which pregnant women are particularly susceptible.

Meningitis—An inflammation of the membranes covering the brain and spinal cord that can be caused by various congenital infections.

Perinatal infection—A maternal infection that is transmitted to the fetus after membrane rupture or during labor or delivery.

Placenta—The uterine organ that provides nourishment to the fetus.

Prenatal infection—A maternal infection that is transmitted to the fetus through the placenta.

Rubella—Also called German measles or three-day measles; a viral infection that causes death or severe birth defects if transmitted to the fetus during the first 10 weeks of gestation.

Salmonellosis—Food poisoning; an infection by bacteria of the genus *Salmonella* that usually causes severe diarrhea and may be transmitted to the fetus.

Sepsis—A systemic or body-wide response to infection.

Sexually transmitted infection (STI)—An infectious disease that is transmitted through sexual activity.

Ultrasound—High-frequency sound waves that are used to visualize parts of the body or a fetus in the womb.

Varicella—Chickenpox; a disease caused by the *Varicella zoster* virus—human herpes virus 3—that can cause severe birth defects if transmitted to the fetus during the first 20 weeks of pregnancy and newborn complications if it is transmitted perinatally.

Women who were not screened for HIV during pregnancy may be screened during labor or delivery with a rapid test. The most common screening for HIV tests for antibodies in the blood; however, most infants born to infected mothers test positive for 6-18 months because of the presence of maternal antibodies. An HIV blood test performed within 48 hours of birth detects only about 40% of infections, so testing is repeated at one and six months.

An HSV culture from an affected genital site—preferably on the first day of the outbreak—can test for herpes simplex. A blood test can show if a person has ever been infected with HSV and may distinguish between HSV-1 and HSV-2 and old or recently acquired infections. An examination or test can indicate whether a pregnant woman has active genital herpes near the time of delivery.

Genital warts are diagnosed visually. Vinegar may whiten infected areas to make them more visible. Cervical warts can be diagnosed by removing a piece of tissue for microscopic examination.

Treatment

Infants born with serious infections are treated in the neonatal care unit with intravenous drugs. Infants born to infected mothers may be treated with medications even if they show few or no signs of infection.

Toxoplasmosis

Maternal toxoplasmosis is treated with spiramycin during the first and early second trimesters of pregnancy. Fetal toxoplasmosis may be treated by giving the mother pyrimethamine and **sulfonamides** such as sulfadiazine during the later second and third trimesters.

Newborns with symptoms of toxoplasmosis are treated with pyrimethamine and sulfadiazine for one year; leucovorin for one year to protect the bone marrow from pyrimethamine toxicity; **corticosteroids** for heart, lung, or eye inflammations; clindamycin; and a corticosteroid to reduce the inflammation of chorioretinitis.

Viral respiratory infections

There is no effective treatment for CMV, although ganciclovir may be used to treat some symptoms.

Fetal anemia caused by fifth disease may resolve on its own. If the fetus is at risk for heart failure, a fetal blood **transfusion** may be performed. The mother also may receive medication that passes through the placenta to the fetus.

Exposure to chickenpox or rubella by a nonimmune pregnant woman may be treated with an injection of immune globulin to help prevent fetal transmission. Congenital chickenpox is treated immediately to prevent serious complications or death. There is no specific treatment for rubella infection.

Bacterial infections

Pregnant women with GBS in their urine are treated with penicillin. Most GBS-carriers are treated with intravenous antibiotics from membrane rupture through labor to prevent fetal transmission. Infants born with congenital GBS infections are treated immediately with intravenous antibiotics.

Maternal and congenital listeriosis and syphilis are treated with antibiotics.

Maternal gonorrhea may be treated with cefixime, ceftriaxone, or levofloxacin. Since women often are infected with both gonorrhea and chlamydia, a combination of antibiotics such as ceftriaxone and doxycycline or azithromycin are used to treat both infections.

An antibiotic ointment such as silver nitrate is placed under the eyelids of all newborns as preventative treatment for gonorrhea. An infant born to a gonorrhea-infected mother is treated with penicillin. Conjunctivitis caused by gonorrhea is treated with an eye ointment containing polymyxin and bacitracin, erythromycin, or tetracycline. An antibiotic such as ceftriaxone is given intravenously. Congenital chlamydia is treated with erythromycin eye ointment and oral tablets.

Viral STIs

Women who are being treated for HIV with combination drugs may stop treatment for the first trimester of pregnancy to avoid the risk of birth defects and to avoid missing doses due to **vomiting**, which can cause the growth of drug-resistant HIV strains. The side effects of the anti-retroviral drugs may worsen during pregnancy, but stopping treatment can worsen a woman's condition.

Zidovudine (ZDV, AZT, Retrovir) is the only drug that has been proven to help prevent fetal HIV infection. HIV-positive pregnant women usually take ZDV from 14-34 weeks of gestation. During delivery the mother receives ZDV intravenously. The newborn is given liquid ZDV every six hours for six weeks. A 2004 study of HIV-positive Thai women found that oral ZDV beginning at 28 weeks of gestation, with a single dose of nevirapine during labor, greatly reduces HIV transmission.

Pneumonia caused by *Pneumocystis carinii* often is the first AIDS-related illness to appear in HIV-infected infants and is a major cause of death during the first year. The CDC recommends that all babies born to HIV-infected mothers be treated with anti-pneumonia drugs beginning at 4–6 weeks and continuing until the infant is found to be HIV-negative.

Outbreaks of genital herpes just prior to delivery may be prevented by acyclovir (Zovirax), famciclovir (Famvir), or valacyclover (Valtrex). An HSV-infected newborn is treated immediately with intravenous **antiviral drugs** such as acyclovir. Eye infections are treated with trifluridine drops.

There is no cure for HPV and treatment during pregnancy often is ineffective, although it may include:

- Imiquimod cream
- 5% 5-fluorouracil cream
- trichloroacetic acid
- freezing or burning the warts with a laser
- surgical removal
- alpha interferon injected into the wart

HPV infection in newborns is treated by surgically removing the warts. If the warts obstruct breathing passages, frequent **laser surgery** is required. Interferon may be used to reduce the likelihood of recurrence.

Non-infected pregnant women may begin the hepatitis B vaccine series if they are at high-risk for infection. Infants born to mothers infected with hepatitis B are given both the first dose of hepatitis B vaccine and hepatitis B immune globulin within 12 hours of birth. The second and third doses of vaccine are given at one month and six months of age.

Prognosis

Maternal treatment with spiramycin for toxoplasmosis infection occurring within the first two weeks of pregnancy prevents transmission to the fetus. The prognosis for congenital toxoplasmosis depends on its severity.

Most infants with congenital CMV survive with treatment, but almost all are affected by its effects.

A GBS-carrier's risk of delivering an infected child decreases from one in 200 to one in 4,000 if she is treated with antibiotics. GBS-infected mothers are less likely to infect their newborns if treated with antibiotics during labor. Immediate penicillin treatment for GBS-infected newborns is very effective, but about 5% of GBS-infected newborns die.

Many fetuses infected with syphilis early in gestation are stillborn. Nearly 50% of untreated fetuses die shortly before or after birth. The fetus is at minimal risk if the mother receives adequate treatment with penicillin during pregnancy.

Pregnant women on combined antiretroviral therapy are at a 1–2% risk of transmitting HIV to the fetus. If the mother's viral load is under 1,000 and she is treated with ZDV, the risk of transmission is almost zero. Mothers with a high viral load may reduce the risk of transmission by having a C-section before labor begins and the membranes rupture. Congenital HIV infection that is treated with combination drugs, including **protease inhibitors**, may reduce the risk of death by 67%.

Women with an active HSV infection can reduce the risk of fetal transmission with a C-section. Although immediate medication for the newborn may prevent or reduce the damage from HSV, half of infants born with widespread HSV infections die and the other half may have brain damage.

Infants born to hepatitis B-infected mothers have a greater-than-95% chance of being protected against the virus if they receive the first dose of vaccine and immune globulin within 12 hours of birth.

Prevention

General advice for preventing infection during pregnancy includes:

- good hygiene—including frequent thorough hand washing and not sharing food or drinks—particularly for mothers who have or work with young children and may be at risk for CMV
- vaccinations several months before a planned pregnancy
- appropriate vaccinations after the first trimester of pregnancy
- contacting a healthcare provider immediately upon being exposed to a transmittable infection

To avoid *Taxoplasma* during pregnancy women should:

- keep cats indoors
- avoid handling cat litter without rubber gloves and wash thoroughly
- disinfect the cat box with boiling water for five minutes
- cover sandboxes
- wear gloves for gardening and wash afterward
- avoid insects that may have been exposed to cat feces
- wash after handling cats, raw meat or poultry, soil, or sand
- avoid raw or undercooked meat and poultry, unwashed fruits and vegetables, raw eggs, and unpasteurized milk
- kill *Taxoplasma* by freezing food or cooking it thoroughly

All non-immune women of childbearing age should be vaccinated against rubella and chickenpox before pregnancy. Pregnant women should be tested for immunity to rubella at their first prenatal visit.

Women should be tested for GBS between 35 and 37 weeks of pregnancy to determine whether the bacteria are likely to be present at delivery.

Since *Listeria* can grow at temperatures below 40°F (4°C), pregnant women should handle food cautiously and avoid:

- hot dogs, luncheon, and deli meats unless they are reheated to steaming
- soft cheeses
- refrigerated meat spreads
- refrigerated smoked seafood unless it is in a cooked dish
- raw unpasteurized milk

Pregnant women should use precooked or ready-to-eat perishables immediately, clean the refrigerator regularly, and keep the refrigerator at or below 40°F (4°C).

Salmonellosis may be prevented by:

- cooking all meat, poultry, seafood, and eggs thoroughly
- avoiding sushi containing raw fish
- washing raw vegetables thoroughly
- avoiding unpasteurized milk, soft cheeses, and alfalfa sprouts

STIs can be prevented by abstaining from sexual contact outside of a mutually monogamous relationship using latex **condoms** correctly and consistently, and avoiding blood-contaminated needles, razors, or other items.

Precautions for preventing fetal exposure to HIV-infected maternal blood include avoiding **amniocentesis**, fetal scalp blood sampling, and premature rupturing of the fetal membranes.

Prevention of maternal to fetal HSV transmission includes:

- abstaining from sexual activity during the last trimester of pregnancy or if there are signs of an outbreak or visible sores
- using a condom even if no symptoms are present
- postponing membrane rupture
- avoiding a fetal monitor that makes tiny punctures in the scalp
- avoiding vacuum or forceps deliveries that cause breaks in the infant's scalp

Resources

BOOKS

Bennett, Robin L. *The Practical Guide to the Genetic Family History*. Hoboken, NJ: Wiley-Blackwell, 2010.

Bruce, Debra Fulghum, Samuel Thatcher, and Britt Berg. *Making a Baby: Everything You Need to Know to Get Pregnant*. New York: Ballantine Books, 2010.

Creasy, Robert K., et al. *Creasy and Resnik's Maternal-Fetal Medicine: Principles and Practice*. 6th ed. Philadelphia: Saunders Elsevier, 2008.

Davis, Carolyn F. *100 Questions & Answers about Your Daughter's Sexual Wellness and Development*. Sudbury, MA: Jones&Bartlett Publishers, 2010.

Young, Bruce, and Amy Zavatto. *Miscarriage, Medicine & Miracles: Everything You Need to Know about Miscarriage*. Sudbury, MA: Bantam, 2009.

PERIODICALS

"Cytomegalovirus; Advances Made in Diagnosis of Maternal CMV Infection." *Women's Health Weekly* (September 2, 2004): 51.

Lallemant, M., et al. "Single-dose Prenatal Nevirapine Plus Standard Zidovudine to Prevent Mother-to-Child Transmission of HIV-1 in Thailand." *New England Journal of Medicine* 351, no. 3 (July 15, 2004): 217-28.

Montoya, J.G., and O. Liesenfeld. "Toxoplasmosis." *Lancet* 363, no. 9425 (June 12, 2004): 1965-76.

"Parasitology; Preventive Practices Eliminate the Risk for Congenital Toxoplasmosis." *Health & Medicine Week* (May 3, 2004): 715.

OTHER

"Cytomegalovirus (CMV) and Congenital CMV Infection." Centers for Disease Control and Prevention. July 28, 2010. http://www.cdc.gov/cmv/index.html (accessed October 7, 2010).

"Genital Herpes." National Institute of Allergy and Infectious Disease. April 8, 2009. http://www.niaid.nih.gov/topics/genitalherpes/pages/default.aspx (accessed October 7, 2010).

"Gonorrhea." National Institute of Allergy and Infectious Disease. September 22, 2010. http://www.niaid.nih.gov/topics/gonorrhea/pages/default.aspx (accessed October 7, 2010).

"Group B Strep Prevention (GBS, baby strep, Group B streptococcal bacteria)." Centers for Disease Control and Prevention. April 20, 2008. http://www.cdc.gov/groupbstrep/ (accessed October 7, 2010).

"Hepatitis B Guidelines for Pregnant Women." Hepatitis B Foundation. February 2007. http://www.hepb.org/pdf/pregnancy.pdf (accessed October 7, 2010).

"HIV/AIDS: Prevention of Mother-to-Infant Transmission." National Institute of Allergy and Infectious Disease. November 11, 2009. http://www.niaid.nih.gov/topics/HIVAIDS/Research/prevention/Pages/mtct.aspx (accessed October 7, 2010).

"HIV and AIDS in Pregnancy." *Professionals & Researchers.* March of Dimes. May 2009. http://www.marchofdimes.com/professionals/19695_1223.asp (accessed October 7, 2010).

"HIV and Pregnancy." *AIDSinfo*. Health Information for Patients, U.S. Department of Health and Human Services. October 2007. http://www.aidsinfo.nih.gov/contentfiles/HIVandPregnancy_FS_en.pdf (accessed October 7, 2010).

"Human Papillomavirus (HPV) and Genital Warts." National Institute of Allergy and Infectious Disease. May 12, 2010. http://www.niaid.nih.gov/topics/genitalwarts/pages/default.aspx (accessed October 7, 2010).

Protect Your Baby and Yourself from Listeriosis U.S. Department of Agriculture. April 2006. http://origin-www.fsis.usda.gov/PDF/Protect_Your_Baby.pdf (accessed October 7, 2010).

"STDs and Pregnancy—CDC Fact Sheet." Centers for Disease Control and Prevention. January 4, 2008.

http://www.cdc.gov/std/STDFact-STDs&Pregnancy. html (accessed October 7, 2010).

ORGANIZATIONS

American College of Obstetricians and Gynecologists, 409 12th St. SW, PO Box 96920, Washington, DC, 20080-6920, (202) 863-2518, http://www.acog.org.

American Social Health Association, PO Box 13827, Research Triangle Park, NC, 27709-3827, (919) 361-8400, http://www.ashastd.org.

Association of Women's Health, Obstetric and Neonatal Nurses, 2000 L Street NW, Suite 740, Washington, DC, 20036, (202) 261-2400, (800) 673-8499, http://www.awhonn.org.

Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA, 30333, (888) 232-3228, http://www.cdc.gov.

Hepatitis B Foundation, 700 East Butler Avenue, Doylestown, PA, 18901-3697, (215) 489-4900, http://www.hepb.org.

March of Dimes Birth Defects Foundation, 1275 Mamaroneck Avenue, White Plains, NY, 10605, (914) 997-4488, http://www.marchofdimes.com.

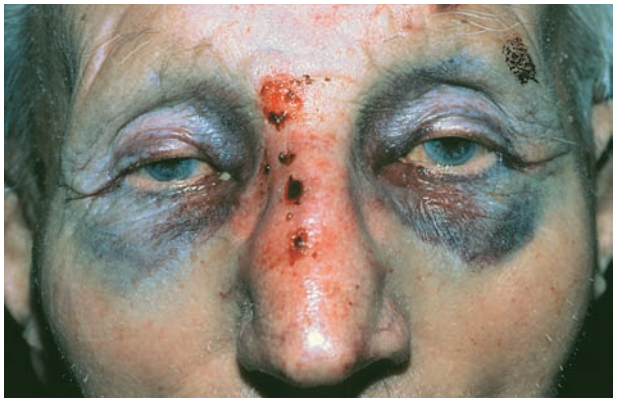
Margaret Alic, PhD
Laura Jean Cataldo, RN, EdD

Mathematics disorder *see* **Learning disorders**

Maxillofacial trauma

Definition

Maxillofacial trauma refers to any injury to the face or jaw caused by physical force, **foreign objects**, or **burns**.



Face of an elderly woman suffering from maxillofacial trauma. *(Dr. P. Marazzi/Photo Researchers, Inc.)*

Description

Maxillofacial trauma includes injuries to any of the bony or fleshy structures of the face.

Any part of the face may be affected. Teeth may be knocked out or loosened. The eyes and their muscles, nerves, and blood vessels may be injured as well as the eye socket (orbit), which can be fractured by a forceful blow. The lower jaw (mandible) may be dislocated by force. Although anchored by strong muscles for chewing, the jaw is unstable in comparison with other bones and is easily dislocated from the temporomandibular joints that attach it to the skull. A fractured nose or jaw may affect the ability to breathe or eat. Any maxillofacial trauma may also prevent the passage of air or be severe enough to cause a **concussion** or more serious brain injury.

Athletes are particularly at risk of maxillofacial injuries. Boxers suffer repeated blows to the face and occasional knockouts (traumatic brain injury). Football, basketball, hockey, and soccer players, and many other athletes are at risk for milder forms of brain injury called concussions. There are an estimated 300,000 cases every year. Overall, there are one million new traumatic brain injuries every year, causing 50,000 deaths. Of the rest, seven to nine percent are left with long–term disability.

Burns to the face are also categorized as maxillofacial trauma.

Causes and symptoms

There are no reliable statistics on the incidence of maxillofacial trauma because there are so many types, and many are not reported. Automobile accidents are a major cause of maxillofacial trauma, as is participation in sports, fights, and other violent acts. Another cause of such injuries is being hit by an object accidentally, for instance being hit by a baseball while watching a game. People most at risk are athletes, anyone who drives a vehicle or rides in one, and those who do dangerous work or engage in aggressive types of behavior.

One study reported in August 2000 that 42% of all facial **fractures** resulted from sports activity.

The major symptoms of most facial injuries are **pain**, swelling, bleeding, and bruising, although a fractured jaw also prevents the person from working his or her jaw properly, and symptoms of a fractured nose also include black eyes and possible blockage of the airway due to swelling and bleeding.

Symptoms of eye injury or orbital fracture can include blurred or double vision, decreased mobility

of the eye, and **numbness** in the area of the eye. In severe injuries there can be temporary or permanent loss of vision.

Burn symptoms are pain, redness, and possibly blisters, **fever**, and **headache**. Extensive burns can cause the victim to go into **shock**. In that situation, he or she has low blood pressure and a rapid pulse.

Symptoms of traumatic brain injury include problems with thinking, memory, and judgment as well as mood swings, and difficulty with coordination and balance. These symptoms linger for weeks or months, and in severe cases can be permanent. Double vision for months after an injury is not uncommon.

Diagnosis

Trauma is usually diagnosed in an emergency room or physician's office by **physical examination** and/or x ray. Some injuries require diagnosis by a specialist. A detailed report of how the injury occurred is also taken. In some cases, diagnosis cannot be made until swelling subsides.

Treatment

Treatment varies, depending on the type and extent of the injury.

Dislocation of the jaw can be treated by a primary care physician by exerting pressure in the proper manner. If muscle spasm prevents the jaw from moving back into alignment, a sedative is administered intravenously (IV) to relax the muscles. Afterward, the patient must avoid opening the jaw wide as he or she will be prone to repeat **dislocations**.

A jaw fracture may be minor enough to heal with simple limitation of movement and time. More serious fractures require complicated, multi–step treatment. The jaw must be surgically immobilized by a qualified oral or maxillofacial surgeon or an otolaryngologist. The jaw is properly aligned and secured with metal pins and wires. Proper alignment is necessary to ensure that the bite is correct. If the bite is off, the patient may develop a painful disorder called temporomandibular joint syndrome.

During the weeks of healing the patient is limited to a liquid diet sipped through a straw and must be careful not to choke or vomit since he or she cannot open the mouth to expel the vomitus. The surgeon will prescribe pain relievers and perhaps **muscle relaxants**. Healing time varies according to the patient's overall health, but will take at least several weeks.

Another common maxillofacial fracture is a broken nose. The bones that form the bridge of the nose may be fractured, but cartilage may also be damaged, particularly the nasal septum which divides the nose. If hit from the side, the bones and cartilage are displaced to the side, but if hit from the front, they are splayed out. Severe swelling can inhibit diagnosis and treatment. Mild trauma to the nose can sometimes heal without the person' being aware of the fracture unless there is obvious deformity. The nose will be tender for at least three weeks.

Either before the swelling begins or after it subsides, some 10 days after the injury, the doctor can assess the extent of the damage. Physical examination of the inside using a speculum and the outside, in addition to a detailed history of how the injury occurred will determine appropriate treatment. The doctor should be informed of any previous nasal fractures, nasal surgery, or chronic disease such as **osteoporosis**. Sometimes an x ray is useful, but it is not always required.

A primary care physician may treat a nasal fracture, but if there is extensive damage or the air passage is blocked, the physician will refer the patient to an otolaryngologist or a plastic surgeon for treatment. Initially the nose may be packed to control bleeding and hold the shape. It is reset under anesthesia. A protective shield or bandage may be placed over it while the fracture heals.

In the case of orbital fractures, there is great danger of permanent damage to vision. Double vision and decreased mobility of the eye are common complications. Surgical reconstruction may be required if the fracture changes the position of the eye or there is other facial deformity. Treatment requires a maxillofacial surgeon.

When the eyes have been exposed to chemicals, they must be washed out for 15 minutes with clear water. **Contact lenses** may be removed only after rinsing the eyes. The eyes should then be kept covered until the person can be evaluated by a primary care physician or ophthalmologist.

When a foreign object is lodged in the eye, the person should not rub the eye or put pressure on it, which would further injure the eyeball. The eye should be covered to protect it until medical attention can be obtained.

Several kinds of traumatic injuries can occur to the mouth. A person can suffer a laceration (cut) to the lips or tongue, or loosening of teeth, or have teeth knocked out. Such injuries often accompany a jaw fracture or other facial injury. **Wounds** to the soft

KEY TERMS

Corneal abrasion—A scratch on the surface of the eyeball.

Mandible—The lower jaw, a U–shaped bone attached to the skull at the temporomandibular joints.

Maxilla—The bone of the upper jaw, which serves as a foundation of the face and supports the orbits.

Nasal septum—The cartilage that divides the nose in half.

Orbit—The eye socket, which contains the eyeball, muscles, nerves, and blood vessels that serve the eye.

Otolaryngologist—Ear, nose, and throat specialist.

Shock—A reduction of blood flow in the body caused by loss of blood and/or fluids. Can be fatal if not treated quickly.

Temporomandibular joint (TMJ)—The mandible attaches to the temporal bone of the skull and works like a hinge.

Temporomandibular joint syndrome (TMJ syndrome)—An incorrect alignment of the lower jaw to the skull that causes the bite to be off line. It causes chronic headaches, nausea, and other symptoms.

Vermilion border—The line between the lip and the skin.

tissues of the mouth bleed freely, but the plentiful blood supply that leads to this heavy bleeding also helps healing. It is important to clean the wound thoroughly with salt water or hydrogen peroxide rinse to prevent infection. Large cuts may require sutures, and should be done by a maxillofacial surgeon for a good cosmetic result, particularly when the laceration is on the edge of the lip line (vermilion). The doctor will prescribe an antibiotic because there is normally a large amount of bacteria present in the mouth.

Any injury to the teeth should be evaluated by a dentist for treatment and prevention of infection. Implantation of a tooth is sometimes possible if it has been handled carefully and protected. The tooth should be held by the crown, not the root, and kept in milk, saline, or contact lens fluid. The patient's dentist can refer him or her to a specialist in this field.

For first degree burns, put a cold–water compress on the area or run cold water on it. Put a clean bandage on it for protection. Second and third degree burn victims must be taken to the hospital for treatment.

Fluids are replaced there through an IV. This is vital since a patient in shock will die unless lost fluids are replaced quickly. **Antibiotics** are given to combat infection since burns make the body vulnerable to infection.

Treatment for a **head injury** requires examination by a primary care physician unless symptoms point to a more serious injury. In that case, the victim must seek emergency care. A concussion is treated with rest and avoidance of contact sports. Very often athletes who have suffered a concussion are allowed to play again too soon, perhaps in the mistaken impression that the injury is not so bad if the player did not lose consciousness. Anyone who has had one concussion is at increased risk of another one.

Danger signs that the injury is more serious include worsening headaches, **vomiting**, weakness, numbness, unsteadiness, change in the appearance of the eyes, seizures, slurred speech, confusion, agitation, or the victim will not wake up. These signs require immediate transport to the hospital. A neurologist will evaluate the situation, usually with a CT scan. A stay in a **rehabilitation** facility may become necessary.

Alternative treatments

Fractures, burns, and deep lacerations require treatment by a doctor but alternative treatments can help the body withstand injury and assist the healing process. **Calcium**, **minerals**, **vitamins**, all part of a balanced and nutrient–rich diet, as well as regular **exercise**, build strong bones that can withstand force well. After an injury, **craniosacral therapy** may help healing and ease the headaches that follow a concussion or other head trauma. A physical therapist can offer ultrasound that raises temperature to ease pain, or **biofeedback** in which the patient learns how to tense and relax muscles to relieve pain. **Hydrotherapy** may ease the **stress** of recovering from trauma. Chinese medicine seeks to reconnect the chi along the body's meridians and thus aid healing. Homeopathic physicians may prescribe natural medicines such as Arnica or Symphytum to enhance healing.

Prognosis

When appropriate treatment is obtained quickly after an injury, the prognosis can be excellent. However, if the victim of trauma has osteoporosis or a

debilitating chronic disease, healing is more problematic. Healing also depends upon the extent of the injury. An automobile accident or a gunshot wound, for example, can cause severe facial trauma that may require multiple surgical procedures and a considerable amount of time to heal. Burns and lacerations cause scarring that might be improved by **plastic surgery**.

Prevention

Safety equipment is vital to preventing maxillofacial trauma from automobile accidents and sports. Here is a partial list of equipment people should always use:

- seat belts
- automobile air bags
- approved child safety seats
- helmets for riding motorcycles or bicycles, skateboarding, snowboarding, and other sports
- safety glasses for the job, yard work, sports
- other approved safety equipment for sports, such as mouthguards, masks, and goggles

Resources

BOOKS

Bluhm, Carla, and Nathan Clendenin. *Someone Else's Face in the Mirror: Identity and the New Science of Face Transplants*. Santa Barbara, CA: Praeger, 2009.

PERIODICALS

Perkins, Stephen W. "The Incidence of Sports-Related Facial Trauma in Children." *Ear, Nose and Throat Journal* 79 (August 2000): 632–638.

Roberts, Graham. "Dental Emergencies (ABC of Oral Health)." *British Medical Journal* 321(7260) (September 2, 2000): 559–62.

ORGANIZATIONS

American Association of Oral and Maxillofacial Surgeons (AAOMS), 9700 W. Bryn Mawr Ave., Rosemont, IL, 60018, (847) 678–6200, http://www.aaoms.org.

Brain Injury Association, Inc., 105 N. Alfred St., Alexandria, VA, 22314, (703) 236–6000, http://www.biausa.org.

Barbara J. Mitchell
Laura Jean Cataldo, RN, Ed.D.

MCS syndrome *see* **Multiple chemical sensitivity**

MD *see* **Muscular dystrophy**

Measles

Definition

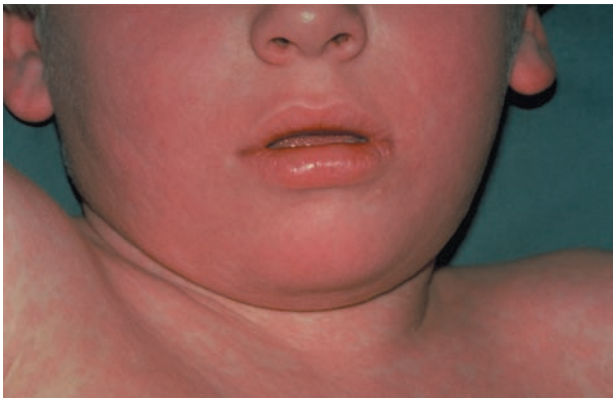
Measles is an infection caused by a virus, which causes an illness displaying a characteristic skin rash known as an exanthem. Measles is also sometimes called rubeola, 5-day measles, or hard measles.

Description

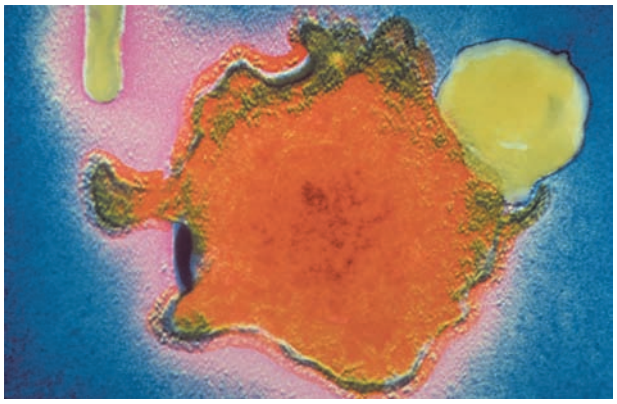
Measles infections appear all over the world. Prior to the current effective immunization program, large-scale measles outbreaks occurred on a two to three-year cycle, usually in the winter and spring. Smaller outbreaks occurred during the off-years. Babies up to about eight months of age are usually protected from contracting measles, due to immune cells they receive from their mothers in the uterus. Once someone has had measles infection, he or she can never get it again.

Causes and symptoms

Measles is caused by a type of virus called a paramyxovirus. It is an extremely contagious infection, spread through the tiny droplets that may spray into the air when an individual carrying the virus sneezes or coughs. About 85% of those people exposed to the virus will become infected with it. About 95% of those people infected with the virus will develop the illness called measles. Once someone is infected with the virus, it takes about 7–18 days before he or she actually becomes ill. The most contagious time period is the three to five days before symptoms begin through about four days after the characteristic measles rash has begun to appear.



Measles on child's face. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*



A transmission electron microscopy (TEM) image of a single measles virion. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

The first signs of measles infection are **fever**, extremely runny nose, red, runny eyes, and a **cough**. A few days later, a rash appears in the mouth, particularly on the mucous membrane which lines the cheeks. This rash consists of tiny white dots (like grains of salt or sand) on a reddish bump. These are called Koplik's spots, and are unique to measles infection. The throat becomes red, swollen, and sore.

A couple of days after the appearance of the Koplik's spots, the measles rash begins. It appears in a characteristic progression, from the head, face, and neck, to the trunk, then abdomen, and next out along the arms and legs. The rash starts out as flat, red patches, but eventually develops some bumps. The rash may be somewhat itchy. When the rash begins to appear, the fever usually climbs higher, sometimes reaching as high as 105°F (40.5°C). There may be **nausea**, **vomiting**, **diarrhea**, and multiple swollen lymph nodes. The cough is usually more problematic at this point, and the patient feels awful. The rash usually lasts about five days. As it fades, it turns a brownish color, and eventually the affected skin becomes dry and flaky.

Many patients (about 5–15%) develop other complications. Bacterial infections, such as ear infections, sinus infections, and **pneumonia** are common, especially in children. Other viral infections may also strike the patient, including **croup**, **bronchitis**, **laryngitis**, or viral pneumonia. Inflammation of the liver, appendix, intestine, or lymph nodes within the abdomen may cause other complications. Rarely, inflammations of the heart or kidneys, a drop in **platelet count** (causing episodes of difficult-to-control bleeding), or reactivation of an old **tuberculosis** infection can occur.

An extremely serious complication of measles infection is swelling of the brain. Called **encephalitis**, this can occur up to several weeks after the basic measles symptoms have resolved. About one out of every thousand patients develops this complication, and about 10-15% of these patients die. Symptoms include fever, **headache**, sleepiness, seizures, and **coma**. Long-term problems following recovery from measles encephalitis may include seizures and **mental retardation**.

A very rare complication of measles can occur up to 10 years following the initial infection. Called **subacute sclerosing panencephalitis**, this is a slowly progressing, smoldering swelling and destruction of the entire brain. It is most common among people who had measles infection prior to the age of two years. Symptoms include changes in personality, decreased intelligence with accompanying school problems, decreased coordination, involuntary jerks and movements of the body. The disease progresses so that the individual becomes increasingly dependent, ultimately becoming bedridden and unaware of his or her surroundings. Blindness may develop, and the temperature may spike (rise rapidly) and fall unpredictably as the brain structures responsible for temperature regulation are affected. **Death** is inevitable.

Measles during **pregnancy** is a serious disease, leading to increased risk of a **miscarriage** or **stillbirth**. In addition, the mother's illness may progress to pneumonia.

Diagnosis

Measles infection is almost always diagnosed based on its characteristic symptoms, including Koplik's spots, and a rash which spreads from central body structures out toward the arms and legs. If there is any doubt as to the diagnosis, then a specimen of body fluids (mucus, urine) can be collected and combined with fluorescent-tagged measles virus antibodies. Antibodies are produced by the body's immune cells that can recognize and bind to markers (antigens) on the outside of specific organisms, in this case the measles virus. Once the fluorescent antibodies have attached themselves to the measles antigens in the specimen, the specimen can be viewed under a special microscope to verify the presence of measles virus.

Treatment

There are no treatments available to stop measles infection. Treatment is primarily aimed at helping the patient to be as comfortable as possible, and watching

KEY TERMS

Antibodies—Cells made by the immune system which have the ability to recognize foreign invaders (bacteria, viruses), and thus stimulate the immune system to kill them.

Antigens—Markers on the outside of such organisms as bacteria and viruses, which allow antibodies to recognize foreign invaders.

Encephalitis—Swelling, inflammation of the brain.

Exanthem (plural, exanthems or exanthemata)—A skin eruption regarded as a characteristic sign of such diseases as measles, German measles, and scarlet fever.

Koplik's spots—Tiny spots occurring inside the mouth, especially on the inside of the cheek. These spots consist of minuscule white dots (like grains of salt or sand) set onto a reddened bump. Unique to measles.

carefully so that **antibiotics** can be started promptly if a bacterial infection develops. Fever and discomfort can be treated with **acetaminophen**. Children with measles should never be given **aspirin**, as this has caused the fatal disease **Reye's syndrome** in the past. A cool-mist vaporizer may help decrease the cough. Patients should be given a lot of liquids to drink, in order to avoid **dehydration** from the fever.

Some studies have shown that children with measles encephalitis benefit from relatively large doses of vitamin A.

Alternative treatment

Botanical immune enhancement (with **echinacea**, for example) can assist the body in working through this viral infection. Homeopathic support also can be effective throughout the course of the illness. Some specific alternative treatments to soothe patients with measles include the Chinese herbs bupleurum (*Bupleurum chinense*) and peppermint (*Mentha piperita*), as well as a preparation made from empty cicada (*Cryptotympana atrata*) shells. The itchiness of the rash can be relieved with witch hazel (*Hamamelis virginiana*), chickweed (*Stellaria media*), or oatmeal baths. The eyes can be soothed with an eyewash made from the herb eyebright (*Euphrasia officinalis*). Practitioners of **ayurvedic medicine** recommend ginger or clove tea.

Prognosis

The prognosis for an otherwise healthy, well-nourished child who contracts measles is usually quite good. In developing countries, however, death rates may reach 15–25%. Adolescents and adults usually have a more difficult course. Women who contract the disease while pregnant may give birth to a baby with hearing impairment. Although only 1 in 1,000 patients with measles will develop encephalitis, 10–15% of those who do will die, and about another 25% will be left with permanent brain damage.

Prevention

Measles is a highly preventable infection. A very effective vaccine exists, made of live measles viruses which have been treated so that they cannot cause actual infection. The important markers on the viruses are intact, however, which causes an individual's immune system to react. Immune cells called antibodies are produced, which in the event of a future infection with measles virus will quickly recognize the organism, and kill it off. Measles vaccines are usually given at about 15 months of age; because prior to that age, the baby's immune system is not mature enough to initiate a reaction strong enough to insure long-term protection from the virus. A repeat injection should be given at about 10 or 11 years of age. Outbreaks on college campuses have occurred among unimmunized or incorrectly immunized students.

Measles vaccine should not be given to a pregnant woman, however, in spite of the seriousness of gestational measles. The reason for not giving this particular vaccine during pregnancy is the risk of transmitting measles to the unborn child.

Surprisingly, new cases of measles began being reported in some countries—including Great Britain—in 2001 because of parents' fears about vaccine safety. The combined vaccine for measles, **mumps**, and **rubella** (MMR) was claimed to cause **autism** or bowel disorders in some children. However, the World Health Organization (WHO) says there is no scientific merit to these claims. The United Nations expressed concern that unwarranted fear of the vaccine would begin spreading the disease in developing countries, and ultimately in developed countries as well. Parents in Britain began demanding the measles vaccine as a separate dose and scientists were exploring that option as an alternative to the combined MMR vaccine. Unfortunately, several children died during an outbreak of measles in Dublin because they had not received the vaccine. Child mortality due to measles is considered

largely preventable, and making the MMR vaccine widely available in developing countries is part of WHO's strategy to reduce child mortality by two-thirds by the year 2015.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Chiba, M. E., M. Saito, N. Suzuki, et al. "Measles Infection in Pregnancy." *Journal of Infection* 47 (July 2003): 40–44.

Jones, G., R. W. Steketee, R. E. Black, et al. "How Many Child Deaths Can We Prevent This Year?" *Lancet* 362 (July 5, 2003): 65–71.

McBrien, J., J. Murphy, D. Gill, et al. "Measles Outbreak in Dublin, 2000." *Pediatric Infectious Disease Journal* 22 (July 2003): 580–584.

"Measles—United States, 2000. (From the Centers for Disease Control and Prevention)." *Journal of the American Medical Association* 287, no. 9 (March 6, 2002): 1105–1112.

Scott, L. A., and M. S. Stone. "Viral Exanthems." *Dermatology Online Journal* 9 (August 2003): 4.

Sur, D. K., D. H. Wallis, and T. X. O'Connell. "Vaccinations in Pregnancy." *American Family Physician* 68 (July 15, 2003): 299–304.

"WHO: Vaccine Fears Could Lead to Unnecessary Deaths." *Medical Letter on the CDC & FDA* March 17, 2002: 11.

ORGANIZATIONS

American Academy of Pediatrics (AAP), 141 Northwest Point Boulevard, Elk Grove Village, IL, 60007-1098, (847) 434-4000, (847) 424-8000, kidsdocs@aap.org, http://www.aap.org.

Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

Rosalyn Carson-DeWitt, MD
Rebecca J. Frey, PhD

Mebendazole *see* **Antihelminthic drugs**

Mechanical debridement *see* **Debridement**

Mechanical ventilation *see* **Inhalation therapies**

Meckel's diverticulum

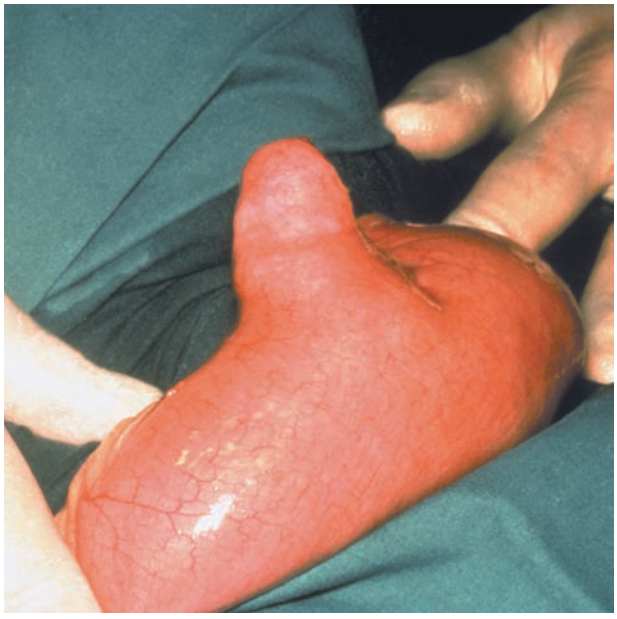
Definition

Meckel's diverticulum is a congenital pouch (diverticulum) approximately two inches in length and located at the lower (distal) end of the small intestine. It was named for Johann F. Meckel, a German anatomist who first described the structure.

Description

The diverticulum is most easily described as a blind pouch that is a remnant of the omphalomesenteric duct or yolk sac that nourished the early embryo. It contains all layers of the intestine and may have ectopic tissue present from either the pancreas or stomach.

The rule of 2s is the classical description. It is located about 2 ft from the end of the small intestine, is often about 2 in in length, occurs in about 2% of the population, is twice as common in males as females, and can contain two types of ectopic tissue—stomach or pancreas. Many who have a Meckel's diverticulum never have trouble but those that do present in the first two decades of life and often in the first two years.



A close-up image of a patient's small intestine with a protruding sac. This condition, called Meckel's diverticulum, is a congenital abnormality occurring in 2% of the population, usually males. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

KEY TERMS

Appendectomy—The procedure to surgically remove an appendix.

Appendicitis—Inflammation of the appendix.

Appendix—A portion of intestine attached to the cecum.

Cecum—The first part of the large bowel.

Congenital—Refers to a disorder which is present at birth.

Distal—Away from the point of origin.

Ectopic—Tissue found in an abnormal location.

Intussusception—One piece of bowel inside another, causing obstruction.

Isotope—Any of two or more species of atoms of a chemical element with the same atomic number and nearly identical chemical behavior but with differing atomic mass and physical properties.

Peptic ulcer—A wound in the bowel that can be caused by stomach acid or a bacterium called *Helicobacter pylori*.

Volvulus—A twisted loop of bowel, causing obstruction.

There are three major complications that may result from the development of Meckel's diverticulum. The most common problem is inflammation or infection that mimics **appendicitis**. This diagnosis is defined at the time of surgery for suspected appendicitis. Bleeding caused by ectopic stomach tissue that results in a bleeding ulcer is the second most frequent problem. Bleeding may be brisk or massive. The third potential complication is obstruction due to **intussusception**, or a twist around a persistent connection to the abdominal wall. This problem presents as a small bowel obstruction, however, the true cause is identified at the time of surgical exploration.

Meckel's diverticulum is a developmental defect that is present in about 2% of people, but does not always cause symptoms. Meckel's diverticula (plural of diverticulum) are found twice as frequently in men as in women. Complications occur three to five times more frequently in males.

Causes and symptoms

Meckel's diverticulum is not hereditary. It is a vestigial remnant of the omphalomesenteric duct, an embryonic structure that becomes the intestine. As such, there is no genetic defect or abnormality.

Symptoms usually occur in children under 10 years of age. There may be bleeding from the rectum, **pain** and **vomiting**, or simply tiredness and weakness from unnoticed blood loss. It is common for a Meckel's diverticulum to be mistaken for the much more common disease appendicitis. If there is obstruction, the abdomen will distend and there will be cramping pain and **vomiting**.

Diagnosis

The situation may be so acute that surgery is needed on an emergency basis. This is often the case with bowel obstruction. With heavy bleeding or severe pain, whatever the cause, surgery is required. The finer points of diagnosis can be accomplished when the abdomen is open for inspection during a surgical procedure. This situation is called an acute abdomen.

If there is more time (not an emergency situation), the best way to diagnose Meckel's diverticulum is with a nuclear scan. A radioactive isotope injected into the bloodstream will accumulate at sites of bleeding or in stomach tissue. If a piece of stomach tissue or a pool of blood shows up in the lower intestine, Meckel's diverticulum is indicated.

Treatment

A Meckel's diverticulum that is causing discomfort, bleeding, or obstruction must be surgically removed. This procedure is very similar to an **appendectomy**.

Prognosis

The outcome after surgery is usually excellent. The source of bleeding, pain, or obstruction is removed so the symptoms also disappear. A Meckel's diverticulum will not return.

Resources

BOOKS

Hebden, John, Mark Donnelly, and Mark Rickets. *Gastrointestinal Problems: Your Questions Answered*. Edinburgh; New York: Churchill Livingston, 2006.

Hodgson, H. J. F., Claire Cousins, and Ralph Boulton. *A Color Handbook of Gastroenterology*. New York: Thieme Medical Publishers, 2010.
Yamada, Tadataka, ed. *Handbook of Gastroenterology*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2005.

OTHER

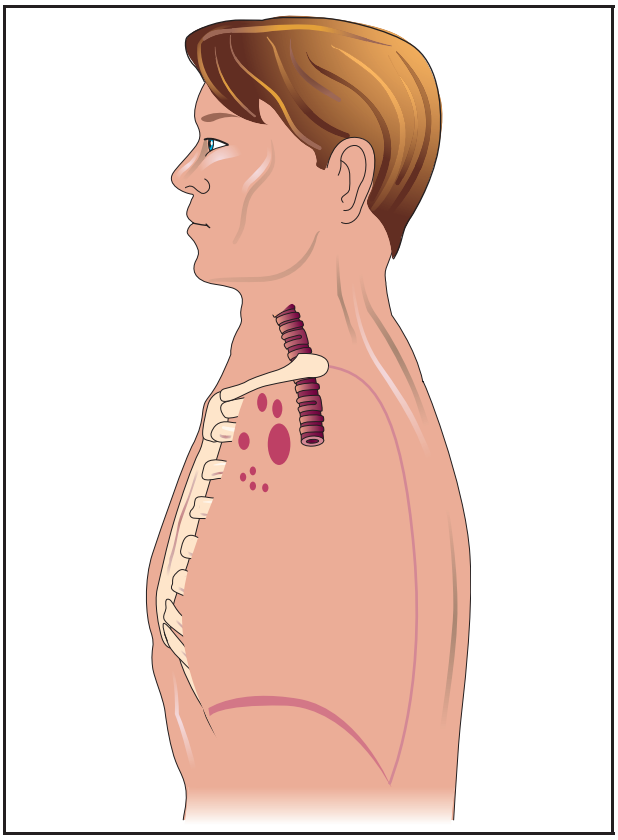
American Academy of Family Physicians. http://www.aafp.org/afp/20000215/1037.html.
"Meckel's Diverticulum." *Merck Manual*. http://www.merck.com/pubs/mmanual/section19/chapter268/268d.htm.

ORGANIZATIONS

American Academy of Family Physicians (AAFP), 11400 Tomahawk Creek Parkway, Leawood, KS, 66211-2680, (913) 906-6000, (913) 906-6075, (800) 271-2237, http://www.aafp.org/.
American Academy of Pediatrics (AAP), 141 Northwest Point Boulevard, Elk Grove Village, IL, 60007-1098, (847) 434-4000, (847) 424-8000, kidsdocs@aap.org, http://www.aap.org.
American College of Gastroenterology, P. O. Box 342260, Bethesda, MD, 20827-2260, (301) 263-9000, http://www.acg.gi.org.
American College of Surgeons, 633 North St. Clair St., Chicago, IL, 60611-3211, (212) 202-5000, (312) 202-5001, (800) 621-4111, postmaster@facs.org, http://www.facs.org.
American Medical Association, 515 N. State St., Chicago, IL, 60654, (800) 621-8335, http://www.ama-assn.org/.

L. Fleming Fallon, Jr., MD, DrPH

Median nerve entrapment *see* **Carpal tunnel syndrome**



Mediastinoscopy is a surgical procedure used to detect or stage lymphoma or lung cancer. In this procedure, the surgeon makes an incision below the neck and inserts a mediastinoscope (a narrow, hollow tube with an attached light) through it to reach the area behind the breastbone. The surgeon can then insert tools through the scope to collect tissue for laboratory analysis. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

Mediastinoscopy

Definition

Mediastinoscopy is a surgical procedure that allows physicians to view areas of the mediastinum, the cavity behind the breastbone that lies between the lungs. The organs in the mediastinum include the heart and its vessels, the lymph nodes, trachea, esophagus, and thymus.

Mediastinoscopy is most commonly used to detect or stage **cancer**. It is also ordered to detect infection, and to confirm diagnosis of certain conditions and diseases of the respiratory organs. The procedure involves insertion of an endotracheal (within the trachea) tube, followed by a small incision in the chest. A mediastinoscope is inserted through the incision. The purpose of this equipment is to allow the physician to directly see the organs inside the mediastinum, and to collect tissue samples for laboratory study.

Purpose

Mediastinoscopy is often the diagnostic method of choice for detecting lymphoma, including Hodgkin's disease. The diagnosis of **sarcoidosis** (a chronic lung disease) and the staging of lung cancer can also be accomplished through mediastinoscopy. Lung cancer staging involves the placement of the cancer's progression into stages, or levels. These stages help a physician study cancer and provide consistent definition levels of cancer and corresponding treatments. The lymph nodes in the mediastinum are likely to show if lung cancer has spread beyond the lungs. Mediastinoscopy allows a physician to observe and extract a sample from the nodes for further study. Involvement

of these lymph nodes indicates diagnosis and stages of lung cancer.

Mediastinoscopy may also be ordered to verify a diagnosis that was not clearly confirmed by other methods, such as certain radiographic and laboratory studies. Mediastinoscopy may also aid in certain surgical biopsies of nodes or cancerous tissue in the mediastinum. In fact, the surgeon may immediately perform a surgical procedure if a malignant tumor is confirmed while the patient is undergoing mediastinoscopy, thus combining the diagnostic exam and surgical procedure into one operation when possible.

Although still performed in 2001, advancements in computed tomography (CT) and **magnetic resonance imaging** (MRI) techniques, as well as the new developments in ultrasonography, have led to a decline in the use of mediastinoscopy. In addition, better results of fine-needle aspiration (drawing out fluid by suction) and core-needle biopsy (using a needle to obtain a small tissue sample) investigations, along with new techniques in **thoracoscopy** (examination of the thoracic cavity with a lighted instrument called a thoracoscope) offer additional options in examining mediastinal masses. Mediastinoscopy may be required, however, when these other methods cannot be used or when the results they provide are inconclusive.

Precautions

Because mediastinoscopy is a surgical procedure, it should only be performed when the benefits of the exam's findings outweigh the risks of surgery and anesthesia. Patients who previously had mediastinoscopy should not receive it again if there is scarring present from the first exam.

Several other medical conditions, such as impaired cerebral circulation, obstruction or distortion of the upper airway, or thoracic **aortic aneurysm** (abnormal dilation of the thoracic aorta) may also preclude mediastinoscopy. Anatomic structures that can be compressed by the mediastinoscope may complicate these pre-existing medical conditions.

Description

Mediastinoscopy is usually performed in a hospital under **general anesthesia**. An endotracheal tube is inserted first, after **local anesthesia** is applied to the throat. Once the patient is under general anesthesia, a small incision is made usually just below the neck or at the notch at the top of the breastbone. The surgeon may clear a path and feel the patient's lymph nodes first to evaluate any abnormalities within the nodes. Next, the physician will insert the mediastinoscope through the incision. The scope is a narrow, hollow tube with an attached light that allows the surgeon to see inside the area. The surgeon can insert tools through the hollow tube to help perform biopsies. A sample of tissue from the lymph nodes or a mass can be extracted and sent for study under a microscope or on to a laboratory for further testing.

In some cases, analysis of the tissue sample which shows malignancy will suggest the need for immediate surgery while the patient is already prepared and under anesthesia. In other cases, the surgeon will complete the visual study and tissue extraction and stitch the small incision closed. The patient will remain in the surgery recovery area until it is determined that the effects of anesthesia have lessened and it is safe for the patient to leave the area. The entire procedure should take about an hour, not counting preparation and recovery time. Studies have shown that mediastinoscopy is a safe, thorough, and cost-effective diagnostic tool with less risk than some other procedures.

Preparation

Patients are asked to sign a consent form after having reviewed the risks of mediastinoscopy and known risks or reactions to anesthesia. The physician will normally instruct the patient to fast from midnight before the test until after the procedure is completed. A physician may also prescribe a sedative the night before the exam and before the procedure. Often a local anesthetic will be applied to the throat to prevent discomfort during placement of the endotracheal tube.

Aftercare

Following mediastinoscopy, patients will be carefully monitored to watch for changes in vital signs or indications of complications of the procedure or the anesthesia. A patient may have a **sore throat** from the endotracheal tube, temporary chest **pain**, and soreness or tenderness at the site of incision.

Risks

Complications from the actual mediastinoscopy procedure are relatively rare—the overall complication rate in various studies has been 1.3–3.0%. However, the following complications, in decreasing order of frequency, have been reported:

- hemorrhage
- pneumothorax (air in the pleural space)
- recurrent laryngeal nerve injury, causing hoarseness
- infection

KEY TERMS

Endotracheal—Placed within the trachea, also known as the windpipe.

Hodgkin's disease—A malignancy of lymphoid tissue found in the lymph nodes, spleen, liver, and bone marrow.

Lymph nodes—Small round structures located throughout the body; contain cells that fight infections.

Pleural space—Space between the layers of the pleura (membrane lining the lungs and thorax).

Sarcoidosis—A chronic disease characterized by nodules in the lungs, skin, lymph nodes, and bones; however, any tissue or organ in the body may be affected.

Thymus—An unpaired organ in the mediastinal cavity that is important in the body's immune response.

- tumor implantation in the wound
- phrenic nerve injury (injury to a thoracic nerve)
- esophageal injury
- chylothorax (chyle—a milky lymphatic fluid—in the pleural space)
- air embolism (air bubble)
- transient hemiparesis (paralysis on one side of the body)

The usual risks associated with general anesthesia also apply to this procedure.

Normal results

In the majority of procedures performed to diagnose cancer, a normal result involves evidence of small, smooth, normal-appearing lymph nodes and no abnormal tissue, growths, or signs of infection. In the case of lung cancer staging, results are related to the severity and progression of the cancer.

Abnormal results

Abnormal findings may indicate lung cancer, **tuberculosis**, the spread of disease from one body part to another, sarcoidosis (a disease that causes nodules, usually affecting the lungs), lymphoma (abnormalities in the lymph tissues), and Hodgkin's disease.

Resources

BOOKS

Fischbach, Frances Talaska, and Marshall Barnett Dunning. *A Manual of Laboratory and Diagnostic Tests*. 8th ed. Philadelphia: Wolters Kluwer Heath/Lippincott Williams & Wilkins, 2009.

Pagana, Kathleen Deska, and Timothy J. Pagana. *Mosby's Manual of Diagnostic and Laboratory Tests*. 4th ed. St. Louis: Mosby, 2009.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800) 227-2345, http://www.cancer.org.

American Lung Association, 1301 Pennsylvania Ave. NW, Suite 800, Washington, DC, 20001, (202) 758-3355, (202) 452-1805, (800) 548-8252, info@lungusa.org, http://www.lungusa.org/.

Lung Cancer Alliance, 888 16th St, NW, Suite 140, Washington, DC, 20006, (202) 463-2080, (800) 298-2436, info@ lunjgcanceralliance.org, http://www.lungcanceralliance.org.

Teresa Odle

Medical marijuana *see* **Marijuana**

Meditation

Definition

Meditation is a practice of concentrated focus upon a sound, object, visualization, the breath, movement, or attention itself in order to increase awareness of the present moment, reduce **stress**, promote relaxation, and enhance personal and spiritual growth.

Purpose

Meditation benefits people with or without acute medical illness or stress. People who meditate regularly have been shown to feel less **anxiety** and depression. They also report that they experience more enjoyment and appreciation of life and that their relationships with others are improved. Meditation produces a state of deep relaxation and a sense of balance or equanimity. According to Michael J. Baime, "Meditation cultivates an emotional stability that allows the meditator to experience intense emotions fully while simultaneously maintaining perspective on them." Out of this experience of emotional stability, one may gain greater insight and understanding about one's thoughts, feelings, and actions. This insight in turn offers the possibility to feel more confident and in control of life. Meditation facilitates a greater sense of calmness, empathy, and acceptance of self and others.

Meditation can be used with other forms of medical treatment and is an important complementary

Two people engaged in meditation. *(iofoto/Shutterstock.com.)*

therapy for both the treatment and prevention of many stress-related conditions. Regular meditation can reduce the number of symptoms experienced by patients with a wide range of illnesses and disorders. Based upon clinical evidence as well as theoretical understanding, meditation is considered to be one of the better therapies for **panic disorder**, **generalized anxiety disorder**, substance dependence and **abuse**, ulcers, **colitis**, chronic **pain**, **psoriasis**, and dysthymic disorder. It is considered to be a valuable adjunctive therapy for moderate **hypertension** (high blood pressure), prevention of cardiac arrest (**heart attack**), prevention of **atherosclerosis** (hardening of arteries), arthritis (including fibromyalgia), **cancer**, **insomnia**, migraine, and prevention of **stroke**. Meditation may also be a valuable complementary therapy for **allergies** and **asthma** because of the role stress plays in these conditions. Meditative practices have been reported to improve function or reduce symptoms in patients with some neurological disorders as well. These include people with Parkinson's disease, people who experience **fatigue** with **multiple sclerosis**, and people with **epilepsy** who are resistant to standard treatment.

Overall, a 1995 report to the National Institutes of Health on alternative medicine concluded that, "More than 30 years of research, as well as the experience of a large and growing number of individuals and health care providers, suggests that meditation and similar forms of relaxation can lead to better health, higher quality of life, and lowered health care costs. . ."

Description

Origins

Meditation techniques have been practiced for millennia. Originally, they were intended to develop spiritual understanding, awareness, and direct experience of ultimate reality. The many different religious traditions in the world have given rise to a rich variety of meditative practices. These include the contemplative practices of Christian religious orders, the Buddhist practice of sitting meditation, and the whirling movements of the Sufi dervishes. Although meditation is an important spiritual practice in many religious and spiritual traditions, it can be practiced by anyone regardless of their religious or cultural background to relieve stress and pain.

As Western medical practitioners begin to understand the mind's role in health and disease, there has been more interest in the use of meditation in medicine. Meditative practices are increasingly offered in medical clinics and hospitals as a tool for improving health and quality of life. Meditation has been used as the primary therapy for treating certain diseases; as an additional therapy in a comprehensive treatment plan; and as a means of improving the quality of life of people with debilitating, chronic, or terminal illnesses.

Sitting meditation is generally done in an upright seated position, either in a chair or cross-legged on a cushion on the floor. The spine is straight yet relaxed. Sometimes the eyes are closed. Other times the eyes are open and gazing softly into the distance or at an object. Depending on the type of meditation, the meditator may be concentrating on the sensation of the movement of the breath, counting the breath, silently repeating a sound, chanting, visualizing an image, focusing awareness on the center of the body, opening to all sensory experiences including thoughts, or performing stylized ritual movements with the hands.

Movement meditation can be spontaneous and free-form or involve highly structured, choreographed, repetitive patterns. Movement meditation is particularly helpful for those people who find it difficult to remain still.

Generally speaking, there are two main types of meditation. These types are concentration meditation and mindfulness meditation. Concentration meditation practices involve focusing attention on a single object. Objects of meditation can include the breath, an inner or external image, a movement pattern (as in **tai chi** or **yoga**), or a sound, word, or phrase that is repeated silently (mantra). The purpose of concentrative practices is to learn to focus one's attention or develop concentration. When thoughts or emotions

MAHARISHI MAHESH YOGI (1911–2008)

(Bernard Gotfryd/Premium Archive/Getty Images.)

Maharishi Mahesh Yogi was one of the most recognized spiritual leaders of the world. Almost single-handedly, the Maharishi (meaning great sage) brought Eastern culture into Western consciousness. He emerged in the late 1950s in London and the United States as a missionary in the cause of Hinduism, the philosophy of which is called Vedanta—a belief that "holds that God is to be found in every creature and object, that the purpose of human life is to realize the godliness in oneself and that religious truths are universal."

By 1967, the Maharishi became a leader among flower-children and an anti-drug advocate. The Maharishi's sudden popularity was helped along by such early fans as the Beatles, Mia Farrow, and Shirley MacLaine. These people, and many others, practiced Transcendental Meditation (TM), a Hindu-influenced procedure that endures in the United States to this day.

When the 1960s drew to a close, the Maharishi began to fade from public view. The guru still had enough followers, though, to people the Maharishi International University, founded in 1971. One of the main draws of Maharishi International University was the study of TM-Sidha, an exotic form of Transcendental Meditation. Sidhas believe that group meditation can elicit the maharishi effect—a force strong enough to conjure world peace.

In 1990, the Maharishi relocated his headquarters from Seelisberg, Switzerland to a former Franciscan monastery in Vlodrop, Netherlands, where he continued his work in TM and tried to affect change in the world with peace. He died in 2008. More information about TM and the history of it's credited founder can be found on http://www.tm.org/

arise, the meditator gently directs the mind back to the original object of concentration.

Mindfulness meditation practices involve becoming aware of the entire field of attention. The meditator is instructed to be aware of all thoughts, feelings, perceptions or sensations as they arise in each moment. Mindfulness meditation practices are enhanced by the meditator's ability to focus and quiet the mind. Many meditation practices are a blend of these two forms.

The study and application of meditation to health care has focused on three specific approaches: 1. transcendental meditation (TM); 2. The "relaxation response," a general approach to meditation developed by Dr. Herbert Benson; and 3. mindfulness meditation, specifically the program of mindfulness-based **stress reduction** (MBSR) developed by Jon Kabat-Zinn.

Transcendental meditation

TM has its origins in the Vedic tradition of India and was introduced to the West by Maharishi Mahesh Yogi. TM has been taught to somewhere between two and four million people. It is one of the most widely practiced forms of meditation in the West. TM has been studied many times; these studies have produced much of the information about the physiology of meditation. In TM, the meditator sits with closed eyes and concentrates on a single syllable or word (mantra) for 20 minutes at a time, twice a day. When thoughts or feelings arise, the attention is brought back to the mantra. According to Charles Alexander, an important TM researcher, "During TM, ordinary waking mental activity is said to settle down, until even the subtlest thought is transcended and a completely unified wholeness of awareness...is experienced. In this silent, self-referential state of pure wakefulness, consciousness is fully awake to itself alone. . . ." TM supporters believe that TM practices are more beneficial than other meditation practices.

The relaxation response

The relaxation response involves a similar form of mental focusing. Dr. Herbert Benson, one of the first Western doctors to conduct research on the effects of

meditation, developed this approach after observing the profound health benefits of a state of bodily calm he calls "the relaxation response." In order to elicit this response in the body, he teaches patients to focus upon the repetition of a word, sound, prayer, phrase, or movement activity (including swimming, jogging, yoga, and even knitting) for 10–20 minutes at a time, twice a day. Patients are also taught not to pay attention to distracting thoughts and to return their focus to the original repetition. The choice of the focused repetition is up to the individual. Instead of Sanskrit terms, the meditator can choose what is personally meaningful, such as a phrase from a Christian or Jewish prayer.

Mindfulness meditation

Mindfulness meditation comes out of traditional Buddhist meditation practices. Psychologist Jon Kabat-Zinn has been instrumental in bringing this form of meditation into medical settings. In formal mindfulness practice, the meditator sits with eyes closed, focusing the attention on the sensations and movement of the breath for approximately 45–60 minutes at a time, at least once a day. Informal mindfulness practice involves bringing awareness to every activity in daily life. Wandering thoughts or distracting feelings are simply noticed without resisting or reacting to them. The essence of mindfulness meditation is not what one focuses on but rather the quality of awareness the meditator brings to each moment. According to Kabat-Zinn, "It is this investigative, discerning observation of whatever comes up in the present moment that is the hallmark of mindfulness and differentiates it most from other forms of meditation. The goal of mindfulness is for you to be more aware, more in touch with life and whatever is happening in your own body and mind at the time it is happening—that is, the present moment." The MBSR program consists of a series of classes involving meditation, movement, and group process. There are over 240 MBSR programs offered in health care settings around the world.

Meditation is not considered a medical procedure or intervention by most insurers. Many patients pay for meditation training themselves. Frequently, religious groups or meditation centers offer meditation instruction free of charge or for a nominal donation. Hospitals may offer MBSR classes at a reduced rate for their patients and a slightly higher rate for the general public.

Precautions

Meditation appears to be safe for most people. There are, however, case reports and studies noting some adverse effects. Thirty-three to 50% of the people participating in long silent meditation retreats (two weeks to three months) reported increased tension, anxiety, confusion, and depression. On the other hand, most of these same people also reported very positive effects from their meditation practice. Kabat-Zinn notes that these studies fail to differentiate between serious psychiatric disturbances and normal emotional mood swings. These studies do suggest, however, that meditation may not be recommended for people with psychotic disorders, severe depression, and other severe **personality disorders** unless they are also receiving psychological or medical treatment.

KEY TERMS

Dervish—A member of the Sufi order. Their practice of meditation involves whirling ecstatic dance.

Mantra—A sacred word or formula repeated over and over to concentrate the mind.

Transcendental meditation (TM)—A meditation technique based on Hindu practices that involves the repetition of a mantra.

Side effects

There are no reported side effects from meditation except for positive benefits.

Research and general acceptance

The scientific study of the physiological effects of meditation began in the early 1960s. These studies prove that meditation affects metabolism, the endocrine system, the central nervous system, and the autonomic nervous system. In one study, three advanced practitioners of Tibetan Buddhist meditation practices demonstrated the ability to increase "inner heat" as much as 61%. During a different meditative practice they were able to dramatically slow down the rate at which their bodies consumed oxygen. Preliminary research shows that mindfulness meditation is associated with increased levels of melatonin. These findings suggest a potential role for meditation in the treatment and prevention of breast and prostrate cancer.

Despite the inherent difficulties in designing research studies, there is a large amount of evidence of the medical benefits of meditation. Meditation is particularly effective as a treatment for chronic pain. Studies have shown meditation reduces symptoms of pain and pain-related drug use. In a four-year follow-up study, the majority of patients in a MBSR program

reported "moderate to great improvement" in pain as a result of participation in the program.

Meditation has long been recommended as a treatment for high blood pressure; however, there is a debate over the amount of benefit that meditation offers. Although most studies show a reduction in blood pressure with meditation, medication is still more effective at lowering high blood pressure.

Meditation may also be an effective treatment for **coronary artery disease**. A study of 21 patients practicing TM for eight months showed increases in their amount of **exercise** tolerance, amount of workload, and a delay in the onset of ST-segment depression. Meditation is also an important part of Dean Ornish's program, which has been proven to reverse coronary artery disease.

Research also suggests that meditation is effective in the treatment of chemical dependency. Gelderloos and others reviewed 24 studies and reported that all of them showed that TM is helpful in programs to stop **smoking** and also in programs for drug and alcohol abuse.

Studies also imply that meditation is helpful in reducing symptoms of anxiety and in treating anxiety-related disorders. Furthermore, a study in 1998 of 37 psoriasis patients showed that those practicing mindfulness meditation had more rapid clearing of their skin condition, with standard UV light treatment, than the control subjects. Another study found that meditation decreased the symptoms of fibromyalgia; over half of the patients reported significant improvement. Meditation was one of several stress management techniques used in a small study of HIV-positive men. The study showed improvements in the T-cell counts of the men, as well as in several psychological measures of well-being.

Resources

BOOKS

Ernst, Edzard, Max H. Pittler, and Barbara Wider, eds. *The Desktop Guide to Complementary and Alternative Medicine: An Evidence–Based Approach*. 2nd ed. St. Louis: Mosby, 2006.

Freeman, Lyn W. *Mosby's Complementary & Alternative Medicine: A Research–Based Approach*. 3rd ed. St. Louis: Mosby, 2008.

ORGANIZATIONS

Benson-Henry Institute for Mind-Body Medicine, 151 Merrimac Street, 4th Floor, Boston, MA, 02114, (617) 643-6090, (617) 643-6077, mindbody@partners.org, http://www.massgeneral.org.

Insight Meditation Society, 1230 Pleasant St., Barre, MA, 01005, (973) 355-4378, rc@dharma.org, http://www.dharma.org/.

Linda Chrisman

Mediterranean diet

Definition

The Mediterranean diet is better described as a nutritional model or pattern of food consumption rather than a diet in the usual sense of the word. To begin with, there is more than one Mediterranean diet, if the phrase is understood to refer to the traditional foods and eating patterns found in the countries bordering the Mediterranean Sea. Francesco Visioli, a researcher who has edited two books on the subject, prefers the term "Mediterranean diets" in the plural to reflect the fact that "the populations in the Mediterranean area have different cultures, religions, economic prosperity, and [levels of] education, and all these factors have some influence on dietary habits and health." For example, Visioli notes that alcohol intake is very low in the Maghreb (coastal northwestern Africa) because most inhabitants of the region are Muslim, and consequently cereal grains figure more prominently in their diet than in most other Mediterranean countries. In addition, the differences among the various forms of the Mediterranean diet are important in understanding some of the research studies that have been done on it, as will be described more fully below.

Origins

The origins of the pattern of food consumption found in Mediterranean countries go back several millennia into history; descriptions of meals in ancient Greek and Roman literature would not be out of place in contemporary Mediterranean diet cookbooks. The first description of the traditional Mediterranean diet as it was followed in the mid-twentieth century, however, was not in a cookbook; it was in a research study funded by the Rockefeller Foundation and published in 1953. The author was Leland Allbaugh, who carried out a study of the island of Crete as an underdeveloped area. Allbaugh noted the heavy use of olive oil, whole-grain foods, fruits, fish, and vegetables in cooking as well as the geography and other features of the island.

The Cretan version of the Mediterranean diet became the focus of medical research on the Mediterranean diet following the publication of Ancel Keys's Seven Country Study in 1980. Keys (1904–2004) was a professor of physiology at the University of Minnesota who had a varied background in biology and biochemistry before turning to **nutrition** almost by accident. Hired by the Army in 1941 to develop portable rations for troops in combat, Keys was responsible for creating what the Army then called K rations.

Mediterranean diet

Frequency	Food	Tips
Monthly	Red meats	No more than a few times month
Weekly	Sweets	Opt instead for naturally sweet fresh fruit
	Eggs	Less than 4 per week, including those in processed foods
	Poultry	A few times a week. Take the skin off and choose white meat to lower fat intake
	Fish	A few times a week
Daily	Cheese and yogurt	Cheese and yogurt are good sources of calcium. Choose low-fat varieties
	Olive oil	The beneficial health effects of olive oil are due to its high content of monounsaturated fats and antioxidants. Olive oil is high in calories, consume in moderation to reduce calorie intake
	Fruits	At least a serving at every meal. A serving of fruit is a healthy option for snacks
	Vegetables	At least a serving at every meal. Choose a variety of colors
	Beans, legumes, nuts	Beans are a healthy source of protein, and are loaded with soluble fiber, which has been shown to lower blood cholesterol levels by five percent or more. Most nuts contain monounsaturated (heart-healthy) fat. A handful of nuts is a healthy option for snacks
	Whole grains, including breads, pasta, rice, couscous, and polenta	A grain is considered whole when all three parts—bran, germ and endosperm—are present. Substitute whole wheat for white bread, brown rice for white rice and whole-wheat flour when baking. Mix pasta, rice, couscous, polenta and potatoes with vegetables and legumes
	Water	At least 6 glasses daily
	Wine (in moderation)	The U.S. Department of Agriculture defines moderation as no more than a five-ounce glass of wine daily for women and up to 2 glasses (10 ounces) daily for men
	Physical activity	Thirty minutes of cardiovascular activity a day is recommended to get in shape, burn calories and boost the metabolism

Mediterranean diet tips, based on the Mediterranean diet pyramid. *(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)*

His next wartime project was a **starvation** experiment, which he conducted in order to determine the food needs of starving civilians in war-torn Europe. American soldiers who were trying to feed refugees in the newly liberated countries found that there was no reliable medical information about treating starvation victims. Keys recruited 36 healthy male volunteers in 1944 who were conscientious objectors, most of them from the historic peace churches. For five months the subjects were given half the normal calorie requirement of an adult male and asked to **exercise** regularly on a treadmill. The average weight loss was 25% of body weight. Three months after the experiment ended, Keys found that none of the subjects had regained their weight or physical capacity. He learned that renutrition following starvation requires several months of above-average calorie intake, that vitamin supplements are needed, and that the proportion of protein in the diet must be increased. He wrote a booklet with this information for use by relief agencies after the war ended.

In the process of studying the effects of starvation in European men who survived the war, however, Keys noticed that the rate of heart attacks among them dropped markedly as food supplies decreased. He wondered whether dietary factors might be involved in heart disease. A study of Minnesota businessmen and professors in the mid-1950s showed him that the fat content of food—particularly the saturated fats found in the meat and dairy products consumed in large amounts by Midwesterners—was indeed a factor. After that experiment, Keys began to think in terms of diet as preventive medicine. He first encountered Mediterranean **diets** during visits to Italy and Spain to conduct research for the World Health Organization. His studies of food consumption patterns in those countries eventually led to the Seven Countries Study, which was a systematic comparison of diet, risk factors for heart disease, and disease experience in men between the ages of 40 and 59 in eighteen rural areas of Japan, Finland, Greece, Italy, the former Yugoslavia, the Netherlands, and the United States from 1958 to 1970. (Women were not included as subjects because of the rarity of heart attacks among them at that time and because the physical examinations were fairly invasive). In addition to asking the subjects to keep records of their food intake, the researchers performed chemical analyses of the foods the subjects ate. It was found that the men living on the island of Crete—the location of Leland Allbaugh's 1953 study—had the lowest rate of heart attacks of any group of subjects in the study.

Subsequent studies of Mediterranean diets have been conducted in subjects who have already suffered heart attacks and in women subjects. One consistent

finding of recent research, however, is that subjects are less healthy in the early twenty-first century than the participants of the late 1950s because the traditional diets of the Mediterranean region have been increasingly abandoned in favor of fast foods and higher consumption of fatty meat products and sweets, as well as other staples of American and Northern European diets that are high in trans-fatty acids. In addition, changing agricultural practices around the Mediterranean have resulted in poultry and meat with higher fat content than was the case in the 1960s. As a result of concern about these trends, an association for the advancement of the Mediterranean diet was formed in Spain in 1995 and later funded the Foundation for the Advancement of the Mediterranean Diet, which is presently headquartered in Barcelona. The Foundation's objectives include publication and dissemination of scientific findings about the diet and the promotion of its healthful use among different population groups.

Description

Typical Mediterranean diet

In general, Mediterranean diets have five major characteristics:

- High levels of fruits and vegetables, breads and other cereals, potatoes, beans, nuts, and seeds.
- Olive oil as the principal or only source of fat in the diet.
- Moderate amounts of dairy products, fish, and poultry; little use of red meat.
- Eggs used no more than 4 times weekly.
- Wine consumed in moderate amounts—two glasses per day for men, one glass for women.

Since wine and olive oil are obtained from their respective plant sources by physical (crushing or pressing) rather than chemical processes, their nutrients retain all the properties of their sources. Wine contains polyphenols, which are powerful **antioxidants** and also have a relaxing effect on blood vessels, thus lowering blood pressure.

The Mediterranean Diet Pyramid is an illustrated version of this typical dietary pattern. The base of the pyramid is labeled "Daily Physical Activity," with four layers of foods consumed on a daily basis above it. Fish, poultry, eggs, and sweets are in the next section of the pyramid—foods that may be eaten weekly. At the very top of the pyramid is red meat, to be eaten no more than once a month. The pyramid may be found online at http://www.mediterraneandietinfo.com/Mediterranean-Food-Pyramid.htm and several other nutrition websites.

The Cretan diet

The Cretan version of the Mediterranean diet as it was used on the island in the 1960s was distinctive in several respects because it contained:

- A higher proportion of total calories from fat (40%), almost all of it from olive oil. It was low in animal fats (butter was rarely eaten) and saturated fats.
- A relatively low level of carbohydrate intake (45% of daily calories), with most of the carbohydrates coming from fruits (2 to 3 per day) and vegetables (2 to 3 cups per day)—many of them foods with a low glycemic index. Vegetables are an integral part of meals in the Cretan diet—they are not considered side dishes.
- Generous portions of whole-grain bread (8 slices per day). The bread was made from slowly fermented dough, however, and had a lower glycemic index than most contemporary breads.
- Moderate intake of fish (about 40 grams per day), which, however, is rich in omega-3 fatty acids.
- A higher intake of meat than in most versions of the Mediterranean diet, mostly as lamb, chicken, or pork.
- High intake of alpha-linolenic acid (ALA; an omega-3 fatty acid thought to lower the risk of heart disease) from nuts (particularly walnuts), seeds, wild greens (particularly purslane [*Portulaca oleracea*]), and legumes. Lamb is also a good source of ALA.

Online versions of the Mediterranean diet

Two of the diets available through eDiets.com as of early 2007 are Mediterranean-type diets, the New Mediterranean Diet and the Sonoma Diet. Both plans are recipe-based, are customized to incorporate foods that the dieter enjoys, and provide personalized weekly meal plans. The New Mediterranean Diet costs $4.49 per week, with a minimum enrollment of 12 weeks, or $53.88 for the three-month trial period. The Sonoma Diet, which is an adaptation of the traditional Mediterranean diet to foods more commonly available in the United States, costs $5 per week for a minimum enrollment period of five weeks. The Sonoma Diet comes with a portion guide and wine guide as well as a customized weekly meal plan.

Function

The function of Mediterranean diets as used in the United States and Western Europe is primarily preventive health care and only secondarily as a means to weight loss. There are several books available with weight-loss regimens based on Mediterranean diets, as well as cookbooks with recipes from a variety of Mediterranean countries.

Benefits

Preventive health care

Most of the scientific research that has been done on Mediterranean diets concerns their role in preventing or lowering the risk of various diseases.

HEART DISEASE. Mediterranean diets became popular in the 1980s largely because of their association with lowered risk of heart attacks and **stroke**, particularly in men, following the publication of the Seven Countries study. Mediterranean diets are thought to protect against heart disease because of their high levels of **omega-3 fatty acids** even though blood cholesterol levels are not lowered.

ALZHEIMER'S DISEASE. A study published in *Annals of Neurology* in 2006 reported that subjects in a group of 2000 participants averaging 76 years of age who followed a Mediterranean-type diet closely were less likely to develop Alzheimer's than those who did not. Further study is needed, however, to discover whether factors other than diet may have affected the outcome.

ASTHMA AND ALLERGIES. A group of researchers in Crete reported in 2007 that the low rate of **wheezing** and **allergic rhinitis** (runny nose) on the island may be related to the traditional Cretan diet. Children who had a high consumption of nuts, grapes, oranges, apples, and tomatoes (the main local products) were less likely to suffer from **asthma** or nasal **allergies**. Children who ate large amounts of margarine, however, were more likely to develop these conditions.

METABOLIC SYNDROME. Research conducted at a clinic in Naples, Italy, suggests that Mediterranean diets lower the risk of developing or reversing the effects of metabolic syndrome, a condition associated with **insulin resistance** and an increased risk of heart disease and type 2 diabetes. The results from this clinic were corroborated by a study done at Tufts University in Massachusetts, which found that the symptoms of metabolic syndrome were reduced even in patients who did not lose weight on the diet.

Weight loss

Some population studies carried out in Mediterranean countries (particularly Italy and Spain) have found that close adherence to a traditional Mediterranean diet is associated with lower weight and a lower body mass index. Although there are relatively few studies of Mediterranean diets as weight-reduction regimens, a research team at the Harvard School of Public Health reported in 2007 that a Mediterranean-style diet is an effective approach to weight loss for many people. A major reason for its effectiveness is the wide variety of enjoyable foods permitted on the diet combined with a rich tradition of ethnic recipes making use of these foods—which makes it easier and more pleasant for people to stay on the diet for long periods of time.

Precautions

People who are making any major change in their dietary pattern in general should always consult their physician first. In addition, people who are taking **monoamine oxidase inhibitors** (MAOIs) for the treatment of depression should check with their doctor, as these drugs interact with a chemical called tyramine to cause sudden increases in blood pressure. Tyramine is found in red wines, particularly aged wines like Chianti, and in aged cheeses.

People using a Mediterranean diet for weight reduction should watch portion size and monitor their consumption of olive oil, cheese, and yogurt, which are high in calories. Dieters may wish to consider switching to low-fat cheeses and yogurts.

Because olive oil is a staple of Mediterranean diets, consumers should purchase it from reliable sources. The safety of olive oil is not ordinarily a concern in North America; however, samples of olive oils sold in Europe and North Africa are sometimes found to be contaminated by mycotoxins (toxins produced by molds and fungi that grow on olives and other fruits). Some mycotoxins do not have any known effects on humans, but aflatoxin, which has been found in olive oil, is a powerful carcinogen and has been implicated in **liver cancer**.

Risks

There are no major risks associated with following a traditional Mediterranean diet for people who have consulted a physician beforehand if they intend to use the diet as a weight-loss regimen. Health crises caused by food interactions with MAOIs are uncommon but can be fatal (about 90 deaths over a 40-year period).

The risk of **cancer** or any other disease from aflatoxin-contaminated olive oil is minimal in the United States and Canada.

Research and general acceptance

Mediterranean diets have been the subject of more medical research since the 1960s than any other regional or ethnic diet. Interest in Mediterranean diets has been high because nutritional research in general has moved away from curing deficiency diseases in the direction of preventive health care.

The Seven Countries Study

The results from the Seven Countries study were published in book form in 1980. The research teams found that Japanese and Greek men had far lower rates of cardiovascular disease than men from the other five other countries, with the Greek subjects from the island of Crete having the lowest rate of all. Although the study and thirty years of follow-up reports showed that the relationship among heart disease, body mass, weight, and **obesity** is complex, the Seven Countries research also showed that the type of fat in the diet is more important than the amount, and that the use of monounsaturated fats—particularly olive oil—is correlated with a lower risk of **heart attack** and stroke. The twenty-year follow-up report indicated that 81% of the difference in coronary deaths among the seven countries could be explained by differences in the average intake of saturated fatty acids.

A detailed description of the Seven Countries study, the research that preceded it, and an overview of its findings can be found online on the website of the University of Minnesota School of Public Health, Division of Epidemiology and Community Health, at http://www.epi.umn.edu/about/7countries/index.shtm.

The Lyon Diet Heart Study

The Lyon Diet Heart Study was the first clinical trial to demonstrate the beneficial effects of a Mediterranean-type diet. Begun in 1995, it was a major investigation of the effectiveness of a modified Cretan diet in preventing recurrent heart attacks. The subjects were a group of 605 Frenchmen under 70 years of age who had been treated in the previous 6 months for a heart attack. They were recruited from several hospitals in the area of Lyon, a city in east-central France. Half the subjects were given an hour-long educational introduction to a modified version of the Cretan diet (canola oil was substituted for olive oil) and advised to follow this Mediterranean-style diet. The other half (the control group) were given a prudent diet recommended by the American Heart Association (AHA). At the end of 4 years, overall **death** rates were 56% lower in the group that followed the modified Cretan diet.

Ongoing research

Mediterranean diets continue to be fruitful subjects for medical investigators, partly because the countries where they originated are changing so rapidly, and partly because discussion continues as to which of the components of these diets is the most important in disease prevention. Although olive oil has been the focus of many studies, recent research done in Greece seems to indicate that the combination of the various foods and food groups in Mediterranean diets is what makes them so healthful, rather than any one specific component. This position is sometimes called the whole-diet approach.

In addition, other researchers are studying lifestyle factors other than food that may well contribute to the beneficial effects of Mediterranean cooking. These include a generally more relaxed attitude toward life; higher levels of physical activity (made possible in part by the warm sunny climate of the region); and the **fasting** practices of Greek Orthodox Christians, which lower fat intake and restrict the believer to a vegetarian diet for about 110 days out of every year.

Resources

BOOKS

Keys, Ancel B., with Christ Aravanis. *Seven Countries: A Multivariate Analysis of Death and Coronary Heart Disease*. Cambridge, MA: Harvard University Press, 1980.

Keys, Ancel B., and Margaret Keys. *How to Eat Well and Stay Well the Mediterranean Way*. Garden City, NY: Doubleday, 1975.

Keys, Margaret, and Ancel B. Keys. *The Benevolent Bean*. New York: Noonday Press, 1972.

Parker, Steven Paul, MD. *The Advanced Mediterranean Diet: Lose Weight, Feel Better, Live Longer*. Mesa, AZ: Vanguard Press, 2007.

Simopoulos, Artemis P., and Francesco Visioli, eds. *Mediterranean Diets*. New York: Karger, 2000.

Simopoulos, Artemis P., and Francesco Visioli. *More on Mediterranean Diets*. New York: Karger, 2007.

COOKBOOKS

Gutterson, Connie. *The Sonoma Diet Cookbook*. Des Moines, IA: Meredith Books, 2006.

Jenkins, Nancy Harmon. *The Mediterranean Diet Cookbook: A Delicious Alternative for Lifelong Health*. New York: Bantam Books, 1994.

Seaver, Jeannette. *My New Mediterranean Cookbook: Eat Better, Live Longer by Following the Mediterranean Diet*. New York: Arcade Publishing, 2004.

PERIODICALS

Carollo, C., R. L. Presti, and G. Caimi. "Wine, Diet, and Arterial Hypertension." *Angiology* 58 (February-March 2007): 92–96.

Chatzi, L., G. Apostolaki, I. Bibakis, et al. "Protective Effect of Fruits, Vegetables, and the Mediterranean Diet on Asthma and Allergies among Children in Crete." *Thorax*, April 5, 2007.

Dalziel, K., L. Segal, and M. de Lorgeril. "A Mediterranean Diet Is Cost-Effective in Patients with Previous Myocardial Infarction." *Journal of Nutrition* 136 (July 2006): 1879–1885.

de Lorgeril, M., and P. Salen. "The Mediterranean Diet in Secondary Prevention of Coronary Heart Disease." *Clinical and Investigative Medicine* 29 (June 2006): 154–158.

de Lorgeril, M., P. Salen, J. L. Martin, et al. "Mediterranean Diet, Traditional Risk Factors, and the Rate of Cardiovascular Complications after Myocardial Infarction: Final Report of the Lyon Diet Heart Study." *Circulation* 99 (February 16, 1999): 779–785.

Ferracane, R., A. Tafuri, A. Logieco, et al. "Simultaneous Determination of Aflatoxin B_1 and Ochratoxin A and Their Natural Occurrence in Mediterranean Virgin Olive Oil." *Food Additives and Contaminants* 24 (February 2007): 173–180.

Hoffman, William. "Meet Monsieur Cholesterol." *University of Minnesota Update*, Winter 1979. Available online at http://mbbnet.umn.edu/hoff/hoff_ak.html (accessed April 8, 2007). Interesting and readable biographical profile of Ancel Keys and his interest in Mediterranean diets.

Keys, Ancel, PhD, Henry L. Taylor, PhD, Henry Blackburn, MD, et al. "Coronary Heart Disease among Minnesota Business and Professional Men Followed Fifteen Years." *Circulation* 28 (September 1963): 381–395.

Malik, V. S., and F. B. Hu. "Popular Weight-Loss Diets: From Evidence to Practice." *Nature Clinical Practice; Cardiovascular Medicine* 4 (January 2007): 34–41.

Meydani, M. "A Mediterranean-Style Diet and Metabolic Syndrome." *Nutrition Reviews* 63 (September 2005): 312–314.

Panagiotakis, D.B., C. Pitsavos, F. Arvaniti, and C. Stefanidis. "Adherence to the Mediterranean Food Pattern Predicts the Prevalence of Hypertension, Hypercholesterolemia, Diabetes and Obesity among Healthy Adults; the Accuracy of the MedDiet Score." *Preventive Medicine*, December 30, 2006.

Sarri, K. O., M. K. Linardakis, F. N. Bervanaki, et al. "Greek Orthodox Fasting Rituals: A Hidden Characteristic of the Mediterranean Diet of Crete." *British Journal of Nutrition* 92 (August 2004): 277–284.

Scarmeas, N., Y. Stern, M.X. Tang, et al. "Mediterranean Diet and Risk for Alzheimer's Disease." *Annals of Neurology* 59 (June 2006): 912–921.

Schroder, H., J. Marrugat, J. Vila, et al. "Adherence to the Traditional Mediterranean Diet Is Inversely Associated with Body Mass Index and Obesity in a Spanish Population." *Journal of Nutrition* 134 (December 2004): 3355–3361.

Trichopoulou, A., and E. Critselis. "Mediterranean Diet and Longevity." *European Journal of Cancer Prevention* 13 (October 2004): 453–456.

OTHER

American Heart Association (AHA). *Lyon Diet Heart Study*. Available online at http://www.americanheart.org/presenter.jhtml?identifier=4655 (accessed April 10, 2007).

American Heart Association (AHA). *Mediterranean Diet*. Available online at http://www.americanheart.org/presenter.jhtml?identifier=4644 (accessed April 10, 2007).

European Food Information Council (EUFIC). "Secrets of . . . the Mediterranean Diet." *Food Today* 43 (May 2004). Available online at http://www.eufic.org/article/en/page/FTARCHIVE/artid/mediterranean-diet/?lowres=1ndash (accessed April 9, 2007).

Mayo Clinic staff. *Mediterranean Diet: Can It Prevent Alzheimer's?* Available online at http://www.mayoclinic.com/health/mediterranean-diet/AN01475 (posted November 21, 2006; accessed April 9, 2007).

Mayo Clinic staff. *Mediterranean Diet for Heart Health*. Available online at http://www.mayoclinic.com/health/mediterranean-diet/CL00011 (posted June 21, 2006; accessed April 7, 2007).

Mediterranean Diet Info. *Mediterranean Diet Food Pyramid*. Available online at http://www.mediterraneandietinfo.com/Mediterranean-Food-Pyramid.htm (accessed April 9, 2007).

Visioli, Francesco, PhD. "Mediterranean Diets." *Linus Pauling Institute Newsletter*, Fall/Winter 2000. Available online at http://lpi.oregonstate.edu/f-w00/mediterr.html (accessed April 9, 2007).

ORGANIZATIONS

American Heart Association (AHA).National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, http://www.americanheart.org.

Fundacin Dieta Mediterrnea, http://www.dietamediterranea.com.

Linus Pauling Institute (LPI). Oregon State University, 571 Weniger Hall, Corvallis, OR, 97331-6512, (541) 737-5075, http://lpi.oregonstate.edu/index.html.

University of Minnesota School of Public Health, Division of Epidemiology and Community Health (EpiCH), West Bank Office Building,1300 South Second Street, Suite 300, Minneapolis, MN, 55454-1015, (612) 624-1818, http://www.epi.umn.edu/about/7countries/index.shtm.

Rebecca J. Frey, Ph.D.

Medullary sponge kidney

Definition

Medullary sponge kidney is a congenital defect of the kidneys where the kidneys fill with pools of urine.

Demographics

One in every 100 to 200 people have some form of this disease.

KEY TERMS

Congenital—Present at birth.

Intravenous pyelogram—X rays of the upper urinary system using a contrast agent that is excreted by the kidneys into the urine.

Thiazide diuretic—A particular class of medication that encourages urine production.

Ureter—A tube that carries urine from the kidney to the bladder.

Description

The kidneys filter urine from the blood and direct it down tiny collecting tubes toward the ureters (ducts that carry urine from the kidney to the bladder). These tiny tubes gradually join together until they reach the renal pelvis, where the ureters begin. As the tubes join, they are supposed to get progressively bigger as they get fewer in number. In medullary sponge kidney, the tubes are irregular in diameter, forming pools of urine along the way. These pools encourage stone formation and infection.

Causes and symptoms

Although some cases of this disorder seem to be inherited, usually the cause is not known.

The symptoms associated with medullary sponge kidney are those related to infection and stone passage. Infection causes **fever**; back and flank **pain**; cloudy, frequent, and burning urine; and general discomfort. Stones cause pain in the flank or groin as they pass. They usually cause some bleeding. The bleeding may not be visible in the urine, but it is apparent under a microscope.

Diagnosis

Recurring kidney infections, bleeding, or stones will prompt x rays of the kidneys. The appearance of medullary sponge kidney on an intravenous pyelogram (x rays of the upper urinary system) is characteristic.

Treatment

Many people never have trouble with this disorder. For those that do, infections and stones require periodic treatment. Infections should be treated with **antibiotics** early in order to prevent kidney damage. Stones may need to be surgically removed. Often, removal can be accomplished without an incision but rather by reaching up with instruments through the lower urinary tract to grab the stones. This procedure is called a ureteroscopy. There is also a method of stone treatment called extracorporeal shock wave **lithotripsy** (ESWL). A special machine delivers a focused blast of shock waves that breaks stones into sand so that they will pass out naturally. It is considered reasonably safe and usually effective.

Prognosis

Ignoring symptoms can result in progressive damage to the kidneys and ultimate kidney failure, but attentive early treatment will preserve kidney function.

Prevention

Diligent monitoring for infection at regular intervals and at the first symptom will give the best long-term results. By drinking extra liquids, most stones can be prevented. The most common kind of stones, **calcium** stones, can be deterred by regularly taking a medication (thiazide diuretic) that encourages urine production.

Resources

BOOKS

Bennett, Robin L. *The Practical Guide to the Genetic Family History*. 2nd ed. New York, NY: Wiley-Blackwell, 2010.

Clatworthy, Menna. *Nephrology: Clinical Cases Uncovered*. New York, NY: Wiley-Blackwell, 2010.

O'Callaghan, Chris. *The Renal System at a Glance*. 3rd ed. New York, NY: Wiley-Blackwell, 2009.

Rodman, John S., et al. *No More Kidney Stones*. Hoboken, NJ: Wiley, 2007.

Stam, Lawrence, E. *100 Questions & Answers about Kidney Dialysis*. Sudbury, MA: Jones and Bartlett Publishers, 2009.

ORGANIZATIONS

American Association of Kidney Patients, 3505 E. Frontage Rd., Suite 315, Tampa, FL, 33607, (800) 749-2257, info@aakp.org, http://www.aakp.org.

American Kidney Fund (AKF), 6110 Executive Boulevard, Suite 1010, Rockville, MD, 20852, (800) 638-8299, http://www.kidneyfund.org.

National Kidney Foundation, 30 East 33rd St., New York, NY, 10016, (800) 622-9010, http://www.kidney.org.

National Kidney and Urologic Disease Information Clearinghouse, 3 Information Way, Bethesda, MD, 20892, (800) 891-5390, nkudic@info.niddk.nih.gov, http://kidney.niddk.nih.gov.

Paula Ford-Martin
J. Ricker Polsdorfer, MD
Laura Jean Cataldo, RN, EdD

Medulloblastoma *see* **Brain tumor**
Mefloquine *see* **Antimalarial drugs**
Megalencephaly *see* **Congenital brain defects**
Melanoma *see* **Malignant melanoma**

KEY TERMS

Osteomyelitis—An inflammation of bone or bone marrow, often caused by bacterial infections. Chronic melioidosis may cause osteomyelitis.

Septicemia—Bacterial infection of the bloodstream. One form of melioidosis is an acute septicemic infection.

Melioidosis

Definition

Melioidosis is an **infectious disease** of humans and animals caused by a gram-negative bacillus found in soil and water. It has both acute and chronic forms.

Description

Melioidosis, which is sometimes called *Pseudomonas pseudomallei* infection, is endemic (occurring naturally and consistently) in Southeast Asia, Australia, and parts of Africa. It was rare in the United States prior to recent immigration from Southeast Asia. Melioidosis is presently a public health concern because it is most common in **AIDS** patients and intravenous drug users.

Causes and symptoms

Melioidosis is caused by *Pseudomonas pseudomallei,* a bacillus that can cause disease in sheep, goats, pigs, horses, and other animals, as well as in humans. The organism enters the body through skin abrasions, **burns**, or **wounds** infected by contaminated soil; inhalation of dust; or by eating food contaminated with *P. pseudomallei*. Person-to-person transmission is unusual. Drug addicts acquire the disease from shared needles. The incubation period is two to three days.

Chronic melioidosis is characterized by **osteomyelitis** (inflammation of the bone) and pus-filled abscesses in the skin, lungs, or other organs. Acute melioidosis takes one of three forms: a localized skin infection that may spread to nearby lymph nodes; an infection of the lungs associated with high **fever** (102°F/38.9°C), **headache**, chest **pain**, and coughing; and septicemia (blood poisoning) characterized by disorientation, difficulty breathing, severe headache, and an eruption of pimples on the head or trunk. The third form is most common among drug addicts and may be rapidly fatal.

Diagnosis

Melioidosis is usually suspected based on the patient's history, especially travel, occupational exposure to infected animals, or a history of intravenous drug. Diagnosis must then be confirmed through laboratory tests. *P. pseudomallei* can be cultured from samples of the patient's sputum, blood, or tissue fluid from abscesses. Blood tests, including complement fixation (CF) tests and hemagglutination tests, also help to confirm the diagnosis. In acute infections, chest x rays and **liver function tests** are usually abnormal.

Treatment

Patients with mild or moderate infections are given a course of trimethoprim-sulfamethoxazole (TMP/SMX) and ceftazidime by mouth. Patients with acute melioidosis are given a lengthy course of ceftazidime followed by TMP/SMX. In patients with acute septicemia, a combination of **antibiotics** is administered intravenously, usually tetracycline, chloramphenicol, and TMP/SMX.

Prognosis

The mortality rate in acute cases of pulmonary melioidosis is about 10%; the mortality rate for the septicemic form is significantly higher (slightly above 50%). The prognosis for recovery from mild infections is excellent.

Prevention

There is no form of immunization for melioidosis. Prevention requires prompt cleansing of scrapes, burns, or other open wounds in areas where the disease is common and avoidance of needle sharing among drug addicts.

Resources

BOOKS

Fauci, Anthony S., et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill Professional, 2008.

Rebecca J. Frey, PhD

Membranous glomerulopathy *see* **Nephrotic syndrome**

Memory loss

Definition

Memory loss is the inability to recall past events or knowledge. It is also called forgetfulness, **amnesia**, impaired memory, and loss of memory. Forgetfulness is generally mild and is experienced by almost everyone during life. Amnesia is total loss of memories, such as name and personal history.

General description

Mild memory loss, such as the inability to recall someone's name or where an item was last placed (such as keys or eyeglasses), occurs in adults of all ages. It usually becomes more frequent as a person ages. Mild memory loss is referred to as forgetfulness. Mild cognitive impairment (MCI) or impaired memory is considered a transitional state between normal forgetfulness and severe memory loss. At least one cognitive (thinking) function, usually memory, is below normal or declining. When memory is affected, the condition is called amnesic MCI. Although some people with MCI remain stable or even improve, studies show that the majority, especially those with amnesic MCI, eventually develop **dementia**.

Severe memory loss is memory impairment to such a degree that it affects a person's ability to do everyday activities, such as driving, handling finances, or shopping. Severe memory loss includes dementia and Alzheimer's disease.

There is a big difference between mild and severe forgetfulness. Mild forgetfulness is more common as people age. It may take longer for older people to learn new things, remember familiar names or words, or where they last placed commonly used objects. These are usually signs of mild forgetfulness and not serious memory loss problems. The most common types of severe memory loss are dementia and Alzheimer's disease.

Dementia

Dementia is a descriptive term for a collection of symptoms caused by a number of disorders affecting the brain. People with dementia have significantly impaired intellectual functioning that interferes with normal activities and relationships. They lose their ability to solve problems and maintain emotional control, and they may experience personality changes and behavioral problems, such as agitation, **delusions**, and **hallucinations**. While memory loss is a common symptom of dementia, memory loss by itself does not mean that a person has dementia.

Dementia is a condition almost always associated with the elderly. Doctors diagnose dementia only if two or more brain functions—such as memory and language skills—are significantly impaired without loss of consciousness. There are different types of dementia, including Alzheimer's disease (AD), Pick disease, frontal lobe dementia, multi-infarct dementia, and dementia caused by an **infectious disease**, usually human **immunodeficiency** virus (HIV). AD is the most common type of dementia.

Alzheimer's disease

Alzheimer's disease (AD) is an illness of the brain and is a type of dementia. AD causes changes in the

Possible causes of reversible memory loss

- **Alcoholism:** Abuse of alcohol can severely impair a person's mental abilities and may cause memory loss by interacting with medications.
- **Depression or other mental health disorder:** Stress, anxiety, or depression can trigger temporary memory loss, especially in older people. When the stress is diminished, the symptoms disappear.
- **Medications:** Single medications or certain drug interactions may produce side effects or symptoms that mimic Alzheimer's disease. Specific medications include pain relievers, blood pressure medications, and sedatives.
- **Minor head trauma or injuries:** Falls or other head injuries may cause a loss of consciousness, with the victim having no recollection of the incident. Patients should see a doctor if they find an unexplained lump on the head or feel mentally fuzzy after even a minor fall.
- **Vitamin B-12 deficiency:** Vitamin B-12 helps to maintain healthy nerve and red blood cells. A deficiency, particularly common in older adults, may result in memory loss.

SOURCE: Mayo Clinic, "Memory loss: When to seek help." Available online at: http://www.mayoclinic.com/health/memory-loss/HQ00094 (accessed August 16, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

brain tissue, including abnormal clumps (amyloid plaques) and tangled bundles of fibers (neurofibrillary tangles). Excessive amounts of these plaques and tangles in the brain are considered signs of AD. Onset of AD usually begins after age 60 and nearly half of people age 85 and older may be affected. Although it is not a normal part of **aging**, AD is a disorder that, with almost no exceptions, affects older people and progresses as the person ages. There is no cure and only limited treatments are available.

The cause of AD is unknown but it is suspected to be caused by multiple factors. In addition to formation of amyloid plaques and neurofibrillary tangles, researchers have found other brain changes in people with AD. Nerve cells die in areas of the brain that are vital to memory and other mental abilities, and connections between nerve cells are disrupted. There are lower levels of some of the chemicals in the brain that carry messages back and forth between nerve cells. AD may impair thinking and memory by disrupting these messages.

Genetics also plays a role in disease development. AD is a genetic disease, meaning it is inherited and may affect several members in a family. The extent genetic factors play in developing AD remains unclear. Some studies indicate more than half of people with AD inherited it in their genetic profile. Other studies indicate only 25% of AD cases are inherited. Non-inherited AD is referred to as sporadic Alzheimer's disease. As of 2007, researchers had discovered three genes that can cause early-onset AD when mutated, and two genes that increase the risk for late-onset AD (one of which is the SORL 1 gene).

AD often starts slowly. People with AD often blame their forgetfulness on old age. Over time, their memory problems worsen and they lose the ability to drive a car, cook a meal, or even read a newspaper. They may get lost easily and find even simple things confusing. Some people become worried, angry, or violent. At some point, people with advanced AD may need someone to take care of all their needs, including feeding, bathing, and grooming, either at home or in a nursing home.

Demographics

No statistics are kept on mild memory loss since it is considered a minor inconvenience that nearly everyone experiences, especially as they grow older. The same is true for MCI, since there is no medical consensus on its definition. Accurate figures are also difficult to obtain because not everyone with a decline of memory shows symptoms.

As of 2007, the U. S. Congress' Office of Technology Assessment estimated that up to 6.8 million people in the United States had dementia, and at least 1.8 million of those were severely affected. Studies have found that almost half of all people age 85 and older have some form of dementia. Dementia usually begins after age 60, and the risk increases with age. At least 5% of men and women ages 65–74 have dementia.

The Alzheimer's Association estimates 5.1 million Americans have AD. By 2050 the number could rise to 13.2 million, according to the American Health Assistance Foundation (AHAF). The exact number is difficult to determine since AD is often misdiagnosed as another condition or is not diagnosed until the disease is in its later stages. The AHAF reports that approximately 65,800 people die from complication related to AD, and 350,000 new cases of AD are diagnosed each year in the United States. Worldwide, AHAF estimates 26 million people have AD as of 2007 and projects that number will increase to 106 million by 2050.

Causes and symptoms

Causes of memory loss besides the normal forgetfulness associated with aging include:

- side effects of medication
- dementia, Alzheimer's disease, and other degenerative nerve disorders of the brain
- trauma or injury to the head
- seizures
- alcoholism and drug abuse
- stroke
- brain tumors or infection
- herpes encephalitis
- depression

All forms of dementia result from the **death** of nerve cells and/or the loss of communication among these cells.

Diagnosis

Mild memory loss

Without using formal tests it may be possible to get an idea of cognitive function by discussing current events with the patient. A physician may ask the person if they read the newspapers or watch the news on television. If so, the physician questions the patient about a recent news event. If the person is interested in sports or a particular sports team, questions related to the sport or team should be asked that any fan would know, such as the name of the team's manager or head coach, or the names and positions of top players.

Dementia and AD

Doctors use a number of methods to diagnose dementia and AD. Unfortunately, a definitive diagnosis of AD cannot be confirmed unless an **autopsy** is performed after death. Diagnosis before death is based upon observational findings of unexplained, slowly progressive dementia and brain-imaging studies that show a reduction in the size of the brain. Brain-imaging (neuroimaging) refers to the use of **positron emission tomography (PET)**, **magnetic resonance imaging** (MRI), or computed topography (CT) scans. These are special types of pictures that allow the brain or other internal body structures to be visualized.

Tests that measure memory, language skills, math skills, and other abilities related to mental functioning are also used to help the physician accurately diagnose a patient's condition. For example, people with dementia or AD often show changes in executive functions (such as problem-solving), memory, and the ability to perform once-automatic tasks. Diagnosis is established after first excluding other possible causes for dementia or AD. It is important that any treatable conditions, such as depression, normal pressure **hydrocephalus**, or vitamin B_{12} deficiency, which cause similar symptoms are ruled out. Early, accurate diagnosis of dementia and AD is important for patients and their families because it allows early treatment of symptoms. For people with AD or other progressive dementias, early diagnosis may allow them to plan for the future while they can still help to make decisions. These patients also may benefit from drug treatment.

Treatment

The clinical effectiveness of treating mild memory impairment where no specific medical cause has been identified, has yet to be fully tested. It is believed that these individuals might represent patients who are just beginning to develop AD and might benefit more from available treatments for AD than those patients with dementia. Besides drugs, other ways to improve memory in older adults is to learn a new skill, such as using the internet; use memory tools such as appointment calendars, to-do lists, and reminder notes; getting adequate sleep; exercising regularly; eating a healthy diet; and restricting alcohol consumption.

There is no cure for dementia and there are no treatments that reverse or halt disease progression for most of the dementias. Patients can benefit to some extent from treatment with available medications and other measures, such as cognitive training. Many people with dementia, particularly those in the early stages, may benefit from practicing tasks designed to improve performance in specific aspects of cognitive functioning. For example, people can sometimes be taught to use memory aids, such as mnemonics, computerized recall devices, or note taking. Behavior modification—rewarding appropriate or positive behavior and ignoring inappropriate behavior—also may help control unacceptable or dangerous behaviors associated with dementia.

There is no cure for AD. However, medicines that treat the symptoms of AD are available and work best for patients in the early stage of the disease. Some medicines keep memory loss and other symptoms from getting worse for a time. Other medicines work to help people with AD sleep better or feel less worried and depressed. These medicines do not directly treat the disease, but they do help patients feel more comfortable in their surroundings.

As of 2008, there were five oral drugs approved by the U.S. Food and Drug Administration (FDA) to control the symptoms of AD and slow its progression. Four of these drugs, called cholinesterase inhibitors, slow the metabolic breakdown of acetylcholine, an important brain chemical involved in nerve cell communication. These drugs make more of this chemical available for communication between cells, which in turn slows the progression of cognitive impairment. Cholinesterase inhibitors can be effective for patients with mild to moderate symptoms of AD. These four drugs are tacrine (Cognex), donepezil (Aricept), rivastigmine (Exelon), and galantamine (Razadyne). In 2006, the FDA approved the use of donepezil to treat severe symptoms of AD and in 2007, approved rivastigmine in a patch form that delivers the drug through the skin. The fifth drug, memantine (Namenda), is approved to treat moderate to severe AD. Adverse side effects of all five drugs include **nausea**, **dizziness**, **headache**, and **fatigue**. Some of these drugs also are used to treat non-AD types of dementia.

Nutrition/Dietetic concerns

Several studies have found that high fat and high calorie **diets** may increase the risk of developing AD and other types of progressive dementia. Other risk factors for dementia and AD include alcohol, salt, and refined carbohydrates. It is recommended that patients with dementia avoid environmental toxins, such as tobacco smoke.

The incidence of AD in European and North American countries has been shown to be reduced with fish consumption. Researchers speculate that **Omega-3 fatty acids** in fish may delay the onset of

KEY TERMS

Amnesic—Relating to amnesia, the loss of memory.

Amyloid plaque—A waxy, translucent substance composed of complex protein fibers and polysaccharides that forms in body tissues in some degenerative diseases, such as Alzheimer's disease.

Antioxidant—A substance that inhibits the destructive effects of oxidation in the body.

Computed tomography (CT) scan—A diagnostic radiological scan in which cross-sectional images of the body are formed and shown on a computer screen.

Delusion—A persistent false belief held in the face of strong contradictory evidence.

Dementia—A usually progressive deterioration of intellectual functions, such as memory, that can occur while other brain functions such as those controlling movement and the senses are retained.

Genetic disease—A disease that is inherited from one or both parents.

Hydrocephalus—An increase of cerebrospinal fluid around the brain, resulting in an enlarged head.

Magnetic resonance imaging (MRI)—An imaging technique that uses electromagnetic radiation to obtain images of the body's soft tissues.

Parkinson's disease—A progressive nervous disorder marked by symptoms of trembling hands, lifeless face, monotone voice, and a slow shuffling walk.

Positron emission tomography (PET)—A method of medical imaging capable of displaying the metabolic activity of organs in the body that is useful in investigating brain disorders.

Tomography—A technique of using ultrasound, gamma rays, or x rays to produce a focused image of the structures across a specific depth within the body, while blurring details at other depths.

AD. Anti-inflammatory agents, such as **antioxidants**, have shown some effectiveness in treating dementia. A diet that includes antioxidants such as vitamin C, vitamin E, selenium, green tea, and **ginkgo biloba** extract, may be beneficial. Ginkgo biloba, in addition to its antioxidant properties, increases blood and oxygen flow to the brain, thereby boosting brain function.

Therapy

For mild memory loss, therapy may include activities such as playing cards, board games, and word games like crossword puzzles and anagrams. Reading books, magazines, or newspapers regularly, and then discussing them with friends, relatives, or caregivers also aids memory retention.

There are no specific therapies associated with dementia or AD. A patient with these disorders is encouraged to **exercise** as much as their symptoms or physical limitations allow. Daily supervised walks are a good general exercise for people with severe memory impairment. Physicians recommend that people with dementia or AD try to live as normal a life as possible. This includes maintaining contact with and visiting friends and relatives, and maintaining their usual daily routines. Caregivers can assist with these recommendations.

Prognosis

Only about 15% of people with mild memory loss progress to dementia or AD. The other 85% continues to live a relatively normal life with memory loss causing only minimal interference in their daily lives. Patients with dementia or AD typically survive 8–10 years after diagnosis. Death is most frequently related to **malnutrition**, secondary infection (infection that is not the initial medical problem, such as **pneumonia**) or heart disease. Malnutrition is a state in which not enough calories are taken in to support the normal functions of the human body. Malnourished people are also more prone to infections. There is no evidence that links AD to heart disease, but the rate for both increases as people age.

Prevention

Restricting alcohol intake to one or two drinks a day or less, not **smoking**, eating a healthy diet, and exercising both mentally and physically on a regular basis can prevent or delay the onset of mild memory loss. Higher education achievement seems to reduce risk, but this may be related to people of higher education remaining more mentally active in retirement.

As of early 2008, there was no known way to prevent dementia or AD. A number of studies in laboratory mice indicate that a Mediterranean-style diet low in sugar and saturated animal fat, and high in

fruits, vegetables, and whole-grains may reduce the risk of developing abnormal memory loss, including dementia. Several studies also suggest that a glass of red wine once a day may provide protection against memory loss.

Research has revealed a number of other factors that may prevent or delay the onset of memory loss some people. For example, studies have shown that people with diabetes who maintain tight control over glucose (sugar) levels in their blood tend to score better on tests of cognitive function than those with poorly controlled diabetes. Several studies also suggest that people who engage in intellectually stimulating activities, such as social interactions, chess, crossword puzzles, and playing a musical instrument significantly lower their risk of developing forms of dementia. Mental activities may stimulate the brain in a way that increases a person's cognitive reserve—the ability to cope with or compensate for the pathologic changes associated with dementia.

Care giver concerns

Caring for a person with severe memory loss at home is a difficult task and can become overwhelming. Each day brings new challenges as the caregiver copes with changing levels of ability and new patterns of behavior. Caregivers themselves often are at increased risk for depression and illness, especially if they do not receive adequate support from family, friends, and the community. A major struggle caregivers face is dealing with the difficult behaviors of the person they are caring for. Basic activities of daily living such as dressing, bathing, and eating often become difficult to manage for both the person with severe memory loss and the caregiver. Having a plan for getting through the day can help caregivers cope.

Each person with severe memory loss is unique and responds differently. Caregivers should remain calm and offer reassurance to the person in their care. Community organizations are often available to provide assistance and support groups for caregivers can provide a place to express their feelings and help anticipate future challenges. The person with severe memory loss must be monitored closely when they are unable to determine their own care. Caregivers should learn to recognize signs that the memory loss is getting progressively worse.

Resources

BOOKS

Einberger, Kristin, and Janelle Sellick. *Strengthen Your Mind: Activities for People with Early Memory Loss*. Baltimore: Health Professions Press, 2006.

Lear, Martha. *Where Did I Leave My Glasses? The What, When, and Why of Normal Memory Loss*. New York: Wellness Central, 2008.

Mace, Nancy L., and Peter V. Rabins. *The 36-Hour Day: A Family Guide to Caring for People with Alzheimer Disease, Other Dementias, and Memory Loss in Later Life*. Baltimore: Johns Hopkins University Press, 2006.

Pearce, Nancy. *Inside Alzheimer's: How to Hear and Honor Connections with a Person Who Has Dementia*. Taylors, SC: Forrason Press, 2007.

PERIODICALS

Christensen, Daniel D., and Peter Lin. "Practical Treatment Strategies for Patients with Alzheimer's Disease." *Journal of Family Practice* 17, no. 7 (December 2007).

Cowper, Anne. "Memory Loss." *Australian Journal of Medical Herbalism* Fall 2006: 119–120.

Halvorson, Ryan. "Regular Exercise Decreases Memory Loss." *IDEA Fitness Journal* July-August 2007: 19.

Harris, Phyllis Braudy, and John Keady. "Wisdom, Resilience and Successful Aging: Changing Public Discourses on Living with Dementia." *Dementia* 7, no. 1 (February 2008): 5–8.

Mahendra, Nidhi, and Allegra Apple. "Human Memory Systems: A Framework for Understanding Dementia." *ASHA Leader* 12, no. 16 (November 27, 2007): 8–12.

Pomerantz, Jay M. "Pharmacological Approaches to Alzheimer's Disease." *Drug Benefit Trends* December 1, 2007: 495.

OTHER

"Coping with Memory Loss." *Consumer Health Information*. May 3, 2007 [cited April 13, 2008]. U.S. Food and Drug Administration. http://www.fda.gov/consumer/features/memoryloss0507.html.

"Eldercare Search." *Eldercare Locator*. [Cited April 13, 2008]. Department of Health and Human Services. http://www.eldercare.gov/Eldercare/Public/Home.asp.

"Memory Self-Tests." *Memory Loss and the Brain*. 2004 [cited April 13, 2008]. The Memory Disorder Project at Rutgers University. http://www.memorylossonline.com/learning_memory/mem_games/memorygames1.html.

ORGANIZATIONS

Alzheimer's Association, 225 N. Michigan Ave., 17th Floor, Chicago, IL, 60601-7633, (312) 335-8700, (800) 272-3900, (866) 699-1246, info@alz.org, http://www.alz.org.

Alzheimer's Australia, P.O. Box 4019, HawkerACT, Australia, 2614, 612 6254 4233, (800) 100-500 (Australia only), http://www.alzheimers.org.au.

Alzheimer's Disease Education and Referral Center, P.O. Box 8250, Silver Spring, MD, 20907-8250, (800) 438-4380, (301) 495-3334, adear@nia.nih.gov, http://www.nia.nih.gov/alzheimers.

Alzheimer's Foundation of America, 322 8th Ave., 6th Floor, New York, NY, 10001, (866) 232-8484, (646) 638-1546, info@alzfdn.org, http://www.alzfdn.org.

American Geriatrics Society, Empire State Building, 350 Fifth Ave., Suite 801, New York, NY, 10118, (212) 308-1414, (212) 832-8646, info@americangeriatrics.org, http://www.americangeriatrics.org.

American Health Assistance Foundation, 22512 Gateway Center Dr., Clarkburg, MD, 20871, (301) 948-3244, (800) 437-2423, (301) 258-9454, iquiroz@ahaf.org, http://www.ahaf.org.

Association for Frontotemporal Dementias, 1616 Walnut St., Suite 1100, Philadelphia, PA, 19103, (267) 514-7221, (866) 507-7222, info@ftd-picks.org, http://www.ftd-picks.org.

European Alzheimer's Disease Consortium, Dept. of Internal Medicine and Clinical Gerontology, Toulouse University Hospital, 170 Avenue de Casselardit, Toulouse, France, 31300, 33-5-6177-7649, 33-5-6149-7109, reynish.e@chu-toulouse.fr, http://www.eadc.alz.heimer-europe.org.

Ken R. Wells

Memory loss *see* **Amnesia**

Ménière's disease

Definition

Ménière's disease is a condition characterized by recurrent vertigo (**dizziness**), **hearing loss**, and **tinnitus** (a roaring, buzzing or ringing sound in the ears).

Description

Ménière's disease was named for the French physician Prosper Ménière, who first described the illness in 1861. It is an abnormality within the inner ear. A fluid called endolymph moves in the membranous labyrinth or semicircular canals within the bony labyrinth inside the inner ear. When the head or body moves, the endolymph moves, causing nerve receptors in the membranous labyrinth to send signals to the brain about the body's motion. A change in the volume of the endolymph fluid, or swelling or rupture of the membranous labyrinth, is thought to result in Ménière's disease symptoms.

Causes and symptoms

Causes

The cause of Ménière's disease is unknown; however, scientists are studying several possible causes, including noise pollution, viral infections, or alterations in the patterns of blood flow in the structures of the inner ear. Since Ménière's disease sometimes runs in families, researchers are also looking into genetic factors as possible causes of the disorder.

One area of research that shows promise is the possible relationship between Ménière's disease and **migraine headache**. Dr. Ménière himself suggested the possibility of a link, but early studies yielded conflicting results. A rigorous German study published in late 2002 reported that the lifetime prevalence of migraine was 56% in patients diagnosed with Ménière's disease as compared to 25% for controls. The researchers noted that further work is necessary to determine the exact nature of the relationship between the two disorders.

A study published in late 2002 reported that there is a significant increase in the number of CD4 cells in the blood of patients having an acute attack of Ménière's disease. CD4 cells are a subtype of T cells, which are produced in the thymus gland and regulate the immune system's response to infected or malignant cells. Further research is needed to clarify the role of these cells in Ménière's disease.

Another possible factor in the development of Ménière's disease is the loss of myelin from the cells surrounding the vestibular nerve fibers. Myelin is a whitish fatty material in the cell membrane of the Schwann cells that form a sheath around certain nerve cells. It acts like an electrical insulator. A team of researchers at the University of Virginia reported in 2002 that the vestibular nerve cells in patients with unilateral Ménière's disease are demyelinated; that is, they have lost their protective "insulation." The researchers are investigating the possibility that a viral disease or disorder of the immune system is responsible for the demyelination of the vestibular nerve cells.

Symptoms

The symptoms of Ménière's disease are associated with a change in fluid volume within the labyrinth of the inner ear. Symptoms include severe dizziness or vertigo, tinnitus, hearing loss, and the sensation of **pain** or pressure in the affected ear. Symptoms appear suddenly, last up to several hours, and can occur as often as daily to as infrequently as once a year. A typical attack includes vertigo, tinnitus, and hearing loss; however, some individuals with Ménière's disease may experience a single symptom, like an occasional bout of slight dizziness or periodic, intense ringing in the ear. Attacks of severe vertigo can force the sufferer to have to sit or lie down, and may be accompanied by **headache**, **nausea**, **vomiting**, or **diarrhea**. Hearing

tends to recover between attacks, but becomes progressively worse over time.

Ménière's disease usually starts between the ages of 20 and 50 years; however, it is not uncommon for elderly people to develop the disease without a previous history of symptoms. Ménière's disease affects men and women in equal numbers. In most patients only one ear is affected but in about 15% both ears are involved.

Diagnosis

An estimated 3–5 million people in the United States have Ménière's disease, and almost 100,000 new cases are diagnosed each year. Diagnosis is based on medical history, **physical examination**, hearing and **balance tests**, and medical imaging with **magnetic resonance imaging** (MRI).

Several types of tests may be used to diagnose the disease and to evaluation the extent of hearing loss. In patients with Ménière's disease, audiometric tests (hearing tests) usually indicate a sensory type of hearing loss in the affected ear. Speech discrimination or the ability to distinguish between words that sound alike is often diminished. In about 50% of patients, the balance function is reduced in the affected ear. An electronystagnograph (ENG) may be used to evaluate balance. Since the eyes and ears work together through the nervous system to coordinate balance, measurement of eye movements can be used to test the balance system. For this test, the patient is seated in a darkened room and recording electrodes, similar to those used with a heart monitor, are placed near the eyes. Warm and cool water or air are gently introduced into the each ear canal and eye movements are recorded.

Another test that may be used is an electrocochleograph (EcoG), which can measure increased inner ear fluid pressure.

Treatment

There is no cure for Ménière's disease, but medication, surgery, and dietary and behavioral changes, can help control or improve the symptoms.

Medications

Symptoms of Ménière's disease may be treated with a variety of oral medicine or through injections. **Antihistamines**, like diphenhydramine, meclizine, and cyclizine can be prescribed to sedate the vestibular system. A barbiturate medication like pentobarbital may be used to completely sedate the patient and relieve the vertigo. Anticholinergic drugs, like atropine or scopolamine, can help minimize **nausea and vomiting**. Diazepam has been found to be particularly effective for relief of vertigo and nausea in Ménière's disease. There have been some reports of successful control of vertigo after **antibiotics** (gentamicin or streptomycin) or a steroid medication (dexamethasone) are injected directly into the inner ear. Some researchers have found that gentamicin is effective in relieving tinnitus as well as vertigo.

A newer medication that appears to be effective in treating the vertigo associated with Ménière's disease is flunarizine, which is sold under the trade name Sibelium. Flunarizine is a **calcium** channel blocker and anticonvulsant that is presently used to treat Parkinson's disease, migraine headache, and other circulatory disorders that affect the brain.

Surgical procedures

Surgical procedures may be recommended if the vertigo attacks are frequent, severe, or disabling and cannot be controlled by other treatments. The most common surgical treatment is insertion of a small tube or shunt to drain some of the fluid from the canal. This treatment usually preserves hearing and controls vertigo in about one-half to two-thirds of cases, but it is not a permanent cure in all patients.

The vestibular nerve leads from the inner ear to the brain and is responsible for conducting nerve impulses related to balance. A vestibular neurectomy is a procedure where this nerve is cut so the distorted impulses causing dizziness no longer reach the brain. This procedure permanently cures the majority of patients and hearing is preserved in most cases. There is a slight risk that hearing or facial muscle control will be affected.

A labyrinthectomy is a surgical procedure in which the balance and hearing mechanism in the inner ear are destroyed on one side. This procedure is considered when the patient has poor hearing in the affected ear. Labyrinthectomy results in the highest rates of control of vertigo attacks, however, it also causes complete deafness in the affected ear.

Alternative treatment

Changes in diet and behavior are sometimes recommended. Eliminating **caffeine**, alcohol, and salt may relieve the frequency and intensity of attacks in some people with Ménière's disease. Reducing **stress** levels and eliminating tobacco use may also help.

Acupuncture is an alternative treatment that has been shown to help patients with Ménière's disease. The World Health Organization (WHO) lists Ménière's disease as one of 104 conditions that can be treated effectively with acupuncture.

KEY TERMS

Myelin—A whitish fatty substance that acts like an electrical insulator around certain nerves in the peripheral nervous system. It is thought that the loss of the myelin surrounding the vestibular nerves may influence the development of Ménière's disease.

T cell—A type of white blood cell produced in the thymus gland that regulates the immune system's response to diseased or malignant cells. It is possible that a subcategory of T cells known as CD4 cells plays a role in Ménière's disease.

Tinnitus—A roaring, buzzing or ringing sound in the ears.

Transcutaneous electrical nerve stimulation (TENS)—A treatment in which a mild electrical current is passed through electrodes on the skin to stimulate nerves and block pain signals.

Vertigo—The medical term for dizziness or a spinning sensation.

Prognosis

Ménière's disease is a complex and unpredictable condition for which there is no cure. The vertigo associated with the disease can generally be managed or eliminated with medications and surgery. Hearing tends to become worse over time, and some of the surgical procedures recommended, in fact, cause deafness.

Prevention

Since the cause of Ménière's disease is unknown, there are no current strategies for its prevention. Research continues on the environmental and biological factors that may cause Ménière's disease or induce an attack, as well as on the physiological components of the fluid and labyrinth system involved in hearing and balance. Preventive strategies and more effective treatment should become evident once these mechanisms are better understood.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Ruckenstein, Michael J. *Ménière's Disease: Evidence and Outcomes*. San Diego: Plural, 2010.

PERIODICALS

Ballester, M., P. Liard, D. Vibert, and R. Hausler. "Ménière's Disease in the Elderly." *Otology and Neurotology* 23 (January 2002): 73–78.

Corvera, J., G. Corvera-Behar, V. Lapilover, and A. Ysunza. "Objective Evaluation of the Effect of Flunarizine on Vestibular Neuritis." *Otology and Neurotology* 23 (November 2002): 933–937.

Friberg, U., and H. Rask-Andersen. "Vascular Occlusion in the Endolymphatic Sac in Ménière's Disease." *Annals of Otology, Rhinology, and Laryngology* 111 (March 2002): 237–245.

Fung, K., Y. Xie, S. F. Hall, et al. "Genetic Basis of Familial Ménière's Disease." *Journal of Otolaryngology* 31 (February 2002): 1–4.

Ghosh, S., A. K. Gupta, and S. S. Mann. "Can Electrocochleography in Ménière's Disease Be Noninvasive?" *Journal of Otolaryngology* 31 (December 2002): 371–375.

Mamikoglu, B., R. J. Wiet, T. Hain, and I. J. Check. "Increased CD4+ T cells During Acute Attack of Ménière's Disease." *Acta Otolaryngologica* 122 (December 2002): 857–860.

Radtke, A., T. Lempert, M. A. Gresty, et al. "Migraine and Ménière's Disease: Is There a Link?" *Neurology* 59 (December 10, 2002): 1700–1704.

Spencer, R. F., A. Sismanis, J. K. Kilpatrick, and W. T. Shaia. "Demyelination of Vestibular Nerve Axons in Unilateral Ménière's Disease." *Ear, Nose and Throat Journal* 81 (November 2002): 785–789.

Yetiser, S., and M. Kertmen. "Intratympanic Gentamicin in Ménière's Disease: The Impact on Tinnitus." *International Journal of Audiology* 41 (September 2002): 363–370.

ORGANIZATIONS

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 836-4444, http://www.entnet.org.

EAR Foundation of Arizona, 668 North 44th Street, Suite 300, Phoenix, AZ, 85008, (602) 685-1050, (602) 239-5117, melissa@earfoundationaz.com, http://www.earfoundationaz.com.

Vestibular Disorders Association (VEDA), P.O. Box 4467, Portland, OR, 97208-4467, (503) 229-8064, (800) 837-8428, http://www.vestibular.org.

Altha Roberts Edgren
Rebecca J. Frey, PhD

Meningioma *see* **Brain tumor**

Meningitis

Definition

Meningitis is a potentially fatal inflammation of the meninges, the membranes that encase the brain and spinal cord. Meningitis is most commonly caused

HATTIE ALEXANDER (1901–1968)

(© Betmann/Corbis.)

Hattie Alexander, a dedicated pediatrician, medical educator, and researcher in microbiology, won international recognition for deriving a serum to combat influenzal meningitis, a common disease that previously had been nearly always fatal to infants and young children. Alexander subsequently investigated microbiological genetics and the processes whereby bacteria, through genetic mutation, acquire resistance to antibiotics. In 1964, as president of the American Pediatric Society, she became one of the first women to head a national medical association.

As an intern at the Harriet Lane Home of Johns Hopkins Hospital from 1930 to 1931, Alexander became interested in influenzal meningitis. The source of the disease was *Hemophilus influenzae*, a bacteria that causes inflammation of the meninges, the membranes surrounding the brain and spinal cord. In 1931, Alexander began a second internship at the Babies Hospital of the Columbia-Presbyterian Medical Center in New York City. There, she witnessed first-hand the futility of medical efforts to save babies who had contracted influenzal meningitis.

Alexander's early research focused on deriving a serum (the liquid component of blood, in which antibodies are contained) that would be effective against influenzal meningitis. Serums derived from animals that have been exposed to a specific disease-producing bacterium often contain antibodies against the disease and can be developed for use in immunizing humans against it. Alexander knew that the Rockefeller Institute in New York City, however, had been able to prepare a rabbit serum for the treatment of pneumonia, another bacterial disease. Alexander therefore experimented with rabbit serums, and by 1939 was able to announce the development of a rabbit serum effective in curing infants of influenzal meningitis.

In the early 1940s, Alexander experimented with the use of drugs in combination with rabbit serum in the treatment of influenzal meningitis. Within the next two years, she saw infant deaths due to the disease drop by eighty percent.

by viruses, but also may be caused by a bacterial, or less commonly, a fungal infection. Non-infective causes of meningitis include certain drug **allergies**, some cancers, and **systemic lupus erythematosus** (SLE). Inflammation causes swelling of the brain. As the brain swells, fragile brain tissues are pressed against the skull. Brain cells in these areas can become damaged and eventually die.

Demographics

According to the Centers for Disease Control and Prevention (CDC), there are about 1.5 cases of bacterial meningitis for every 100,000 persons in the United States each year. The introduction of Hib vaccine against *Haemophilus influenzae* in 1990 has changed the demographics of bacterial meningitis in North America, shifting the median age of this type of meningitis from less than 2 years of age to 39 years. In addition, in the 2000s, there was an increase in cases among adults over age 60.

People of any race can get meningitis; however, African Americans are more likely to get meningitis than either Caucasian or Hispanic Americans. Infant males in the United States are three times more likely to develop meningitis than infant females; the rates are similar for both genders in adults.

The rates of meningitis in developing countries are thought to be at least 10 times as high as those in the United States and Canada. The lack of vaccines in these countries is the major factor in the difference. Periodic epidemics occur in sub-Saharan Africa and parts of India.

Description

Doctors sometimes divide cases of meningitis into three categories according to the speed of symptom

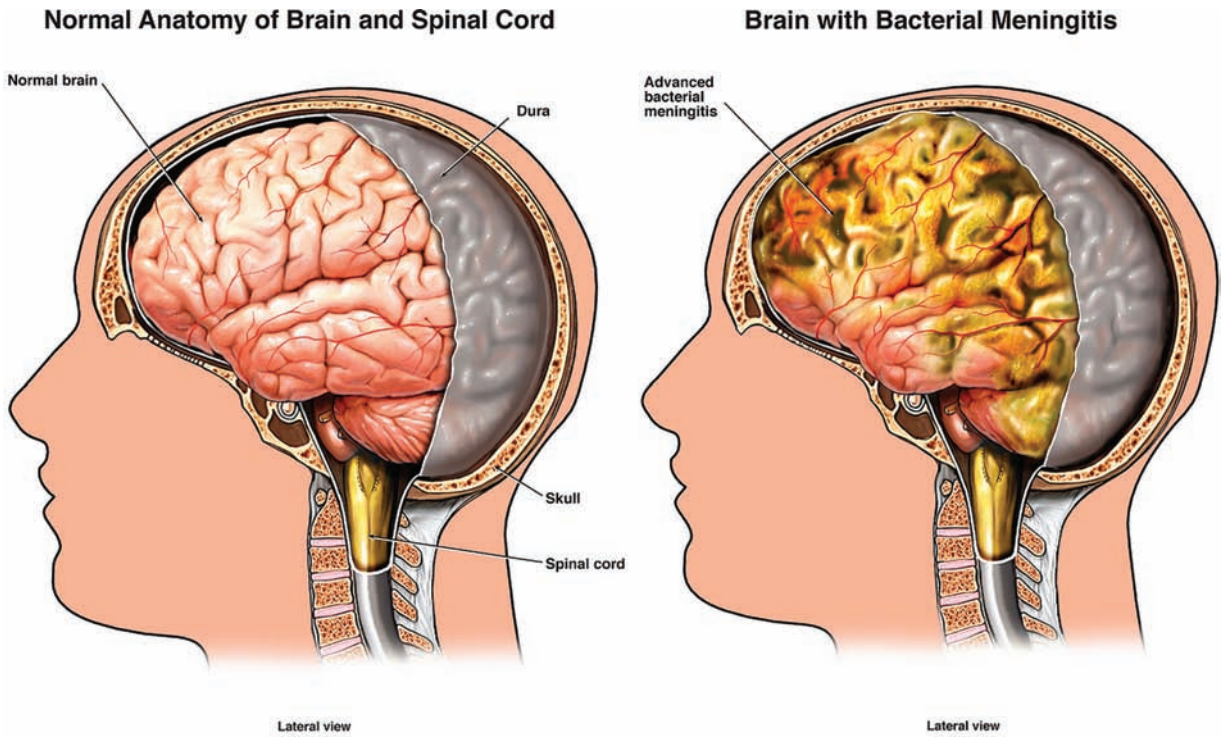


Illustration of bacterial meningitis in an adult. *(© PHOTOTAKE Inc./Alamy.)*

development. Acute meningitis develops in less than 24 hours and is caused by one of several species of bacteria; it is considered a medical emergency. Subacute meningitis takes between 1 and 7 days for symptoms to appear; it may be caused by bacteria or viruses. Chronic meningitis develops over a period of more than a week and may result from an infection or a noninfectious cause.

Structure of the brain

In order to understand why meningitis can be so dangerous, it is important to have a basic understanding of the anatomy of the brain. The meninges are three separate membranes, layered together, which encase the brain and spinal cord:

- The dura mater is the toughest, outermost layer, and is closely attached to the inside of the skull.
- The middle layer, the arachnoid mater, is important because of its involvement in the normal flow of the cerebrospinal fluid (CSF), a lubricating and nutritive fluid that bathes both the brain and the spinal cord.
- The innermost layer, the pia mater, helps direct blood vessels into the brain.
- The space between the arachnoid mater and the pia mater contains CSF, which helps insulate the brain from trauma. Many blood vessels, as well as peripheral and cranial nerves, pass through this space.

CSF, produced in specialized chambers deep inside the brain, flows over the surface of the brain and spinal cord. This fluid serves to cushion these relatively delicate structures, as well as supplying important nutrients for brain cells. CSF is reabsorbed by blood vessels located within the meninges. A careful balance between CSF production and reabsorption is important to avoid the accumulation of too much CSF.

Because the brain is enclosed in the hard, bony case of the skull, any disease that produces swelling will be damaging to the brain. The skull cannot expand at all, so when the swollen brain tissue pushes up against the skull's hard bone, the brain tissue becomes damaged and the blood supply is compromised, and this tissue may ultimately die. Furthermore, swelling on the right side of the brain will not only cause pressure and damage to that side of the brain, but by taking up precious space within the tight confines of the skull, the left side of the brain will also be pushed up against the hard surface of the skull, causing damage to the left side of the brain, as well.

Types of meningitis

Viral meningitis, which is also called aseptic meningitis, is the most common type of meningitis. It is a

less severe infection than bacterial meningitis, is rarely fatal, and may not require any specific treatment. Viral meningitis is caused by one or more enteroviruses, which are viruses that normally live in the digestive tract. Viral meningitis usually develops in the late summer and early fall, and is most likely to affect children and adults under age 30. Most viral infections occur in children under the age of 5. Enteroviruses are present in saliva, throat mucus, and feces; they can be transmitted through direct contact with an infected person or an infected object or surface. Viral meningitis can also be caused by the viruses that cause **chickenpox**, **mumps**, HIV infection, **West Nile virus** infection, and **genital herpes**.

Bacterial meningitis is a medical emergency and has a high mortality rate if untreated. The origin of a bacterial infection leading to meningitis varies according to an individual's age, habits, geographical location, and health status. In newborns, the most common agents of meningitis are those contracted from the mother during labor and delivery, including the bacteria Group B streptococci, ***Escherichia coli***, and *Listeria monocytogenes*. Older children are more frequently infected by *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae* bacteria, while adults are infected by *S. pneumoniae* and *N. meningitidis*. Persons who have had pneumococcal meningitis may be left with lifelong damage to their nervous system that includes deafness and brain damage. *N. meningitidis* is highly contagious and can cause epidemics. Epidemics of meningitis most often occur under crowded conditions, such as day care centers, college residence halls, or military barracks. Meningococcal meningitis has a mortality rate of 10–15 %.

Meningitis caused by fungi is rare in the general population but is a fairly common opportunistic infection in patients with HIV infection.

Risk factors

Risk factors for meningitis include:

- age. Since the introduction of childhood vaccines, bacterial meningitis is now more common in young adults.
- group living situations. These may include military bases, college dormitories, and child care centers.
- having a weakened immune system. People with AIDS or diabetes are at increased risk of meningitis.
- working with animals. Farmers and others who work with animals have an increased risk of *Listeria* infections.
- pregnancy.
- spleen removal. People who have had their spleen (a part of the immune system) removed have weaker immune systems.
- gender. Among newborns, boys are 3 times more likely than girls to get meningitis.
- lifestyle. Unsafe sexual practices and having a large number of sexual partners increases the risk of viral meningitis.

Causes and symptoms

Meningitis occurs when disease organisms that have entered the body and multiplied in the nose, mouth, and throat get into the bloodstream and are carried to the brain and the meninges. In a few cases meningitis can develop when the bacteria gain entrance to the body through a surgical incision or an injury to the head or neck. A few cases of meningitis result from inflammatory diseases like lupus or certain cancers.

Organisms causing meningitis

About 90% of cases of viral meningitis is caused by viruses from the enterovirus family. Viruses from this family also cause viral **gastritis** (stomach flu). However, viruses that cause mumps, **measles**, and **polio** can also cause viral meningitis. Although these diseases are uncommon in developed countries, they are still prevalent in the developing world and may be of concern to travelers.

Bacterial meningitis is caused primarily by four types of bacteria.

- *Streptococcus pneumoniae*. This is also called pneumococcal meningitis. This bacterium also causes pneumonia, ear, and sinus infections. It is a leading cause of bacterial meningitis in young children.
- *Neisseria meningitidis*. Also called meningococcal meningitis, this bacterium is highly contagious and is often responsible for outbreaks of meningitis among young adults.
- *Haemophilus influenzae*. Routine childhood vaccinations against Haemophilus bacteria have been available since the 1990s and in the developed world have substantially reduced this cause of meningitis.
- *Listeria monocytogenes*. Pregnant women and older adults are at higher risk than other groups for contracting listeria meningitis. Listeria can cross the placenta and kill a developing fetus.

Methods of disease transmission

Bacterial meningitis can be passed from person to person through coughing, sneezing, or kissing, but the

disease does not spread as easily as the **common cold**. Once in the body, the bacteria are carried to the brain through the blood. However, in some cases, a person may have another type of infection (for instance, infection of the lungs, throat, or tissues of the heart) caused by an organism that can also cause meningitis. If this initial infection is not properly treated, the organism will continue to multiply, find its way into the blood stream, and be delivered in sufficient quantities to invade past the blood-brain barrier. Direct spread occurs when an organism spreads to the meninges from infected tissue next to or very near the meninges. This can occur, for example, with a severe and poorly treated ear or sinus infection. Insect and pet **bites** can also deliver disease organisms directly into the bloodstream.

Patients who experience skull **fractures** have abnormal openings to the sinuses, nasal passages, and middle ears. Organisms that usually live in the human respiratory system without causing disease can pass through openings caused by such fractures, reach the meninges, and cause infection. Similarly, patients who undergo surgical procedures or who have had foreign bodies surgically placed within their skulls (such as tubes to drain abnormal amounts of accumulated CSF) have an increased risk of meningitis.

Disease organisms can also reach the meninges via an uncommon method called intraneural spread. Intraneural spread involves an organism invading the body at a considerable distance away from the head, spreading along a nerve, and using that nerve as a pathway into the skull, where the organism can multiply and cause meningitis. Herpes simplex virus is known to use this type of spread, as is the **rabies** virus.

Symptoms

The most important symptoms used to diagnose meningitis are a high **fever**, stiff neck, and severe **headache**, which may come on in less than a day after infection. Other symptoms in adults may include:

- nausea and vomiting.
- extreme sensitivity to light (photophobia).
- confusion and difficulty concentrating.
- seizures.
- loss of appetite.
- drowsiness or difficulty waking up.
- skin rash (more common with meningococcal meningitis).

Infants and small children may have somewhat different symptoms:

- bulging of the soft spot (fontanelle) at the top of an infant's skull.
- constant crying.
- poor feeding.
- unusual sleepiness.
- stiffness in the baby's body as well as neck.

It is important to note that very young infants may not show the classic signs of meningitis. Early in infancy, a baby's immune system is not yet developed enough to mount a fever in response to infection, so fever may be absent. In some infants with meningitis, seizures are the only identifiable symptom. Similarly, debilitated elderly people may not have fever or other clearly identifiable symptoms of meningitis.

Diagnosis

Diagnosis of the cause of meningitis is essential to proper treatment, as the **antibiotics** used to treat bacterial meningitis are not useful in treating viral meningitis. A patient who has acute bacterial meningitis will usually have treatment started as soon as the doctor obtains a sample of cerebrospinal fluid for testing. The CSF is obtained by performing a **lumbar puncture**, also known as a spinal tap. This is a procedure in which a needle is inserted into an area in the lower back where the doctor can easily obtain a sample of cerebrospinal fluid.

Examination

An examination of a patient with suspected meningitis will include a recent history of the patient's activities to indicate possible exposure to disease agents, such as recent travel, contact with infected persons, or contact with animals or insects. The season of the year may be an important diagnostic clue; **enterovirus infections** are more common in North America in late summer and early fall, while insect-borne infections are more common in late spring and summer. The doctor will also perform a neurological examination, which includes testing of the patient's hearing and speech, vision, coordination and balance, reflexes, mental status, and recent changes in mood or behavior. In addition, certain manipulations of the patient's head (lowering the head, chin toward chest, for example) are difficult to perform and painful for a person with meningitis.

A patient with subacute meningitis may be given an examination to check for an ear, throat, or sinus infection. In addition to moving the patient's head, the doctor may also perform two other maneuvers to see whether the patient's meninges are inflamed. In one test, the doctor raises the patient's leg at the hip to a

KEY TERMS

Arachnoid mater—The middle layer of the meninges.

Aseptic meningitis—A term that is sometimes used for meningitis that is not caused by bacteria.

Blood-brain barrier—An arrangement of cells within the blood vessels of the brain that prevents the passage of toxic substances, including infectious agents, from the blood and into the brain. It also makes it difficult for certain medications to pass into brain tissue.

Cerebrospinal fluid (CSF)—Fluid made in chambers within the brain which then flows over the surface of the brain and spinal cord. CSF provides nutrition to cells of the nervous system, as well as providing a cushion for the structures of the central nervous system.

Dura mater—The outermost layer of the meninges.

Enteroviruses—A family of viruses that normally live in the digestive tract.

Hydrocephalus—Abnormal accumulation of cerebrospinal fluid within the cavities inside the brain.

Lumbar puncture (LP)—A medical test in which a very narrow needle is inserted into a specific space between the vertebrae of the lower back in order to obtain a sample of CSF for examination. It is also known as a spinal tap.

Meninges (singular, meninx)—The membranes that cover the brain and spinal cord.

Opportunistic infection—An infection caused by an organism that does not cause disease in a person with a healthy immune system.

Photophobia—Abnormal sensitivity to light.

Pia mater—The innermost layer of the meninges.

Systemic lupus erythematosus (SLE)—A chronic, inflammatory, autoimmune disorder in which the individual's immune system attacks, injures, and destroys the body's own organs and tissues. It may affect many organ systems including the skin, joints, lungs, heart, and kidneys.

right angle from the examining table and tries to straighten the lower leg. If the leg cannot be straightened or if the patient experiences neck **pain**, he or she most likely has meningitis. The other maneuver involves bending the patient's neck forward as they lie on the table. If the knees and hips flex upward, the patient probably has meningitis.

Tests

If a sample of CSF is taken, it is sent to a laboratory for analysis. The CSF is then examined under a microscope to look for bacteria or fungi. Normal CSF contains set percentages of glucose and protein. These percentages will vary with bacterial, viral, or other causes of meningitis. For example, bacterial meningitis causes a smaller than normal percentage of glucose to be present in CSF, as the bacteria are essentially "eating" the host's glucose, and using it for their own **nutrition** and energy production. Normal CSF should contain no infection-fighting cells (white blood cells), so the presence of white blood cells in CSF is another indication of meningitis. Some of the withdrawn CSF is also put into special lab dishes to allow growth of the suspected infecting organism, which can then be identified more easily.

Identification of the specific bacterium can take as long as a week; meanwhile, the doctor can begin to treat the patient with a broad-spectrum antibiotic until the test results come back. In some cases the doctor will swab the patient's throat to obtain a sample of mucus and saliva for culture. The sample can be sent to a local or state laboratory or to the CDC for analysis. Throat cultures usually take between 2 and 3 days to yield results.

In March 2007 the Food and Drug Administration (FDA) approved a rapid CSF test that identifies virus particles in CSF called the Xpert EV test. Using a sample of CSF, this test can accurately identify about 90% of viral meningitis cases in less than three hours. Since bacterial meningitis is often fatal, if no virus is found in the CSF, the disease is treated as if it is caused by bacteria until proven otherwise. This test allows doctors to distinguish fairly quickly between viral and bacterial meningitis and avoid giving unnecessary antibiotics to patients with viral meningitis.

The doctor may also order such imaging tests as a computed tomography (CT) scan or **magnetic resonance imaging** (MRI). A CT scan may detect signs of inflammation of the meninges. Imaging tests can also be used to rule out head trauma, **stroke**, tumors, and **blood clots** in the brain.

Treatment

Traditional

Meningitis is a medical emergency. Individuals with the symptoms of meningitis must get to a hospital

as quickly as possible, particularly if the symptoms have developed in less than one day. People who are acutely ill and are taken to a hospital are usually treated within 30 minutes of their arrival, as emergency room doctors assume that the patient has bacterial meningitis and do not want to delay treatment until the specific organism is identified. A sample of cerebrospinal fluid is taken by a spinal tap for analysis; then the patient is given intravenous penicillin or another broad-spectrum antibiotic, intravenous fluids, and pure oxygen to assist breathing. The patient may also need to be treated for seizures, or to have fluid drained from the sinuses or from the space between the meninges and the brain. After the specific bacterium has been identified, the doctor can adjust the type and dosage of the antibiotics given to the patient. People with bacterial meningitis may need additional treatment for **shock**, seizures, **dehydration**, and brain swelling. Serious cases of bacterial meningitis may require treatment in an intensive care unit (ICU) and **life support**.

Viral meningitis cannot be treated with antibiotics. Patients are usually advised to stay home and rest in bed for a few weeks. They can take over-the-counter pain relievers for muscle aches and pains and to bring down fever. If the viral meningitis is caused by the herpes virus, the doctor may also prescribe acyclovir or gancyclovir, **antiviral drugs** used to treat herpes.

Drugs

Bacterial meningitis is usually treated with a combination of intravenous antibiotics. The specific combination depends on the patient's age and immune status; however, most antibiotic combinations consist of ampicillin (Marcillin, Omnipen) plus cefotaxime (Claforan) or ceftriaxone (Rocephin) plus vancomycin (Vancocin). Treatment is given for 7–10 days for less severe infections to 14–21 days for severe infections. In some cases the patient may also be given **steroids**, most commonly dexamethasone, to reduce inflammation caused by the bacteria.

Alternative

Because meningitis is a potentially deadly condition, traditional medical doctors should be contacted immediately for diagnosis and treatment. Alternative treatments should be used only to support the recovery process following appropriate antibiotic treatments, or used concurrently with antibiotic treatments.

Alternative therapies, such as homeopathy, **traditional Chinese medicine**, and Western herbal medicine may help patients regain their health and build up their immune systems. The recovering individual, under the direction of a professional alternative therapist, may opt to include mushrooms into his or her diet to stimulate immune function. The patient should contact an experienced herbalist or homeopathic practitioner for specific remedies.

Prognosis

The patient's prognosis depends on the type of meningitis that they have as well as their overall health. Patients who experience only headache, fever, and stiff neck may recover in 2–4 weeks. Patients with bacterial meningitis typically show some relief within 48 to 72 hours following initial treatment; however, they are more likely to experience complications caused by the disease. Acute bacterial meningitis has a mortality rate of 10–15 percent even with treatment. The reported mortality rates for each specific organism are 19–26% for *S. pneumoniae* meningitis, 3–6% for *H. influenzae* meningitis, 3–13% for *N. meningitidis* meningitis, and 15–29% for *L. monocytogenes* meningitis. Pneumococcal meningitis may have a mortality rate as high as 21 percent. Of the patients who survive bacterial meningitis, between 10 and 20 percent will suffer such complications as blindness, **hydrocephalus**, **hearing loss**, **learning disorders**, or even **paralysis**. Scarring of the meninges may result in obstruction of the normal flow of CSF, causing abnormal accumulation of CSF. This may be a chronic problem for some people, requiring the installation of shunt tubes to drain the accumulation on a regular basis.

Viral meningitis is usually a much milder disease than bacterial meningitis. Patients receiving treatment for viral meningitis and **encephalitis** usually see some relief in 24–48 hours. Some patients may need to be hospitalized for supportive care for a week or so, but most can recover at home within two to four weeks. Complications are rare with viral meningitis; the mortality rate is less than 1%.

Prevention

As of 2010, several vaccines can be used to prevent meningitis. As has already been mentioned, the rates of *Haemophilus influenzae* meningitis among young children dropped dramatically after the Hib vaccine was added to childhood immunization schedules in the 1990s. Other vaccines have been developed to protect adults as well as children from pneumococcal and meningococcal meningitis. There is one type of pneumococcal vaccine known as PCV7, recommended for children between 2 and 5 years of age who are at high risk of infection.

A different vaccine known as PPV is recommended for adults at risk of pneumococcal meningitis: those over 65, those with weakened immune systems, those with diabetes or heart disease, and those whose spleen was removed. The vaccine that protects against the meningococcus is known as Menactra or MCV4. It is recommended for all children at 11–12 and for college students who were not vaccinated at that age. MCV4 can also be used to protect people exposed to meningitis during an outbreak or who must travel to countries with high rates of meningococcal meningitis. Adults over 55 should be immunized with a similar vaccine called MPSV4, a meningococcal polysaccharide vaccine known as Menomune.

Other preventive measures that people can take include:

- Keeping the immune system strong by getting enough sleep, exercising regularly, and eating a healthy diet.
- Washing the hands regularly, particularly when living in a dormitory or similar shared housing situation.
- Avoiding sharing glasses, drinking cups, food utensils, and similar items with others who may be infected or exposed to infection.
- Covering the mouth or nose before sneezing or coughing.
- Taking any antibiotics that may be prescribed during a meningitis outbreak in one's school or workplace.
- Asking the doctor about vaccination against meningitis before traveling abroad.

Resources

BOOKS

Goldman, Lee, and Dennis Ausiello., eds. *Cecil Textbook of Medicine*, 23rd ed. Philadelphia Saunders Elsevier, 2008.

Goldsmith, Connie. *Meningitis*. Minneapolis, MN: Twenty-First Century Books, 2008.

Klosterman, Lorrie. *Meningitis*. New York: Marshall Cavendish Benchmark, 2007.

PERIODICALS

Black, S. "Pneumococcal Vaccine Reduces the Rates of Pneumococcal Meningitis in Children." *Journal of Pediatrics* 155 (July 2009): 149–50.

Jolobe, O. M. "We Ought to Perform Blood Cultures on Admission in All Cases of Suspected Meningitis." *Journal of the American Geriatrics Society* 57 (June 2009): 1131–2.

Kim, K. S. "Treatment Strategies for Central Nervous System Infections." *Expert Opinion on Pharmacotherapy* 10 (June 2009): 1307–17.

Pelton, S. I., and G. P. Gilmet. "Expanding Prevention of Invasive Meningococcal Disease." *Expert Review of Vaccines* 8 (June 2009): 717–27.

Verma, R., and M. C. Fisher. "Bacterial Meningitis Vaccines: Not Just for Kids." *Current Infectious Disease Reports* 11 (July 2009): 302–08.

OTHER

Meningitis. Mayo Foundation for Education and Research. August 8, 2008. http://www.mayoclinic.com/health/meningitis/DS00118

Meningitis. MedlinePlus. April 5, 2010. http://www.nlm.nih.gov/medlineplus/meningitis.html

Meningitis and Encephalitis Fact Sheet. National Institute of Neurological Disorders and Stroke (NINDS). December 18, 2009. http://www.ninds.nih.gov/disorders/encephalitis_meningitis/encephalitis_meningitis.htm

Meningitis: Questions and Answers. United States Centers for Disease Control and Prevention. February 23, 2010. http://www.cdc.gov/meningitis/about/faq.html

ORGANIZATIONS

Immunization Action Coalition (IAC), 1573 Selby Avenue, Suite 234, Saint Paul, MN, 55104, (651)647-9009, (651)647-9131, admin@immunize.org, http://www.immunize.org.

Infectious Diseases Society of America (IDSA), 1300 Wilson Boulevard, Suite 300, Arlington, VA, 22209, (703) 299-0200, (703) 299-0204, info@idsociety.org, http://www.idsociety.org.

Meningitis Research Foundation, Midland Way, ThornburyBristol, United Kingdom, BS25 2BS, 01454 281811, 01454 281094, info@meningitis.org, http://www.meningitis.org.

National Institute of Allergy and Infectious Diseases Office of Communications and Government Relations, 6610 Rockledge Drive, MSC 6612, Bethesda, MD, 20892-6612, (301) 496-5717, (866) 284-4107 or TDD: (800)877-8339 (for hearing impaired), (301) 402-3573, http://www3.niaid.nih.gov.

National Institute of Neurological Disorders and Stroke (NINDS), P.O. Box 5801, Bethesda, MD, 20828, (301) 496-5751. TTY: (301) 468-5981, (800) 352-9424, http://www.ninds.nih.gov.

United States Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (404) 639-3534, 800-CDC-INFO (800-232-4636). TTY: (888) 232-6348, inquiry@cdc.gov, http://www.cdc.gov.

World Health Organization (WHO), Avenue Appia 20, 1211 Geneva 27, Switzerland, + 41 22 791 21 11, + 41 22 791 31 11, info@who.int, http://www.who.int/en.

Helen Colby, MS
Tish Davidson, A.M.

Meningocele *see* **Spina bifida**

Meningococcemia

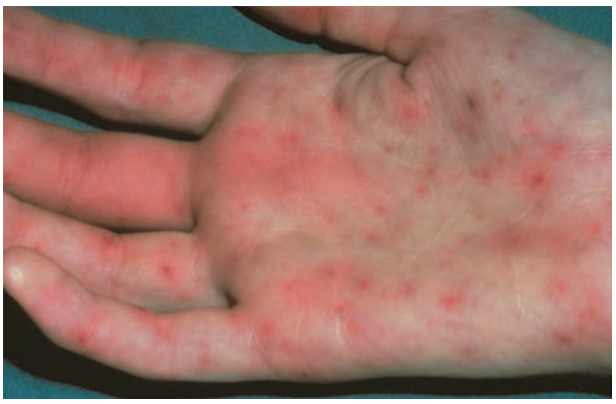
Definition

Meningococcemia is the presence of meningococcus in the bloodstream. Meningococcus, a bacteria formally called *Neisseria meningitidis*, can be one of the most dramatic and rapidly fatal of all infectious diseases.

Causes and symptoms

Meningococcemia, a relatively uncommon infection, occurs most commonly in children and young adults. In susceptible people, it may cause a very severe illness that can produce **death** within hours. The bacteria, which can spread from person to person, usually first causes a colonization in the upper airway, but without symptoms. From there, it can penetrate into the bloodstream to the central nervous system and cause **meningitis** or develop into a full-blown bloodstream infection (meningococcemia). Fortunately in most colonized people, this does not happen and the result of this colonization is long-lasting immunity against the particular strain.

After colonization is established, symptoms can develop within one day to one to two weeks. After a short period of time (one hour up to one to two days) when the patient complains of **fever** and muscle aches, more severe symptoms can develop. Unfortunately during this early stage, a doctor cannot tell this illness from any other illness, such as a viral infection like **influenza**. Unless the case is occurring in a person known to have been exposed to or in the midst of an epidemic of meningococcal disease, there may be no specific symptoms or signs found that help the doctor diagnose the problem. Rarely, a low-grade bloodstream infection called chronic meningococcemia can occur.



A close-up image of a person's hand with meningococcemia. This disease is caused by the presence of meningococcus (*Neisseria meningitidis*) in the bloodstream. The organism can cause multiple illnesses and can damage small blood vessels. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

After this initial period, the patient will often complain of continued fever, shaking chills, overwhelming weakness, and even a feeling of impending doom. The organism is multiplying in the bloodstream, unchecked by the immune system. The severity of the illness and its dire complications are caused by the damage the organism does to the small blood vessel walls. This damage is called a **vasculitis**, an inflammation of a blood vessel. Damage to the small vessels causes them to become leaky. The first signs of the infection's severity are small bleeding spots seen on the skin (petechiae). A doctor should always suspect meningococcemia when he/she finds an acutely ill patient with fever, chills, and petechiae.

Quickly (within hours), the blood vessel damage increases and large bleeding areas on the skin (purpura) are seen. The same changes are taking place in the affected person's internal organs. The blood pressure is often low and there may be signs of bleeding from other organs (like coughing up blood, nose bleeds, blood in the urine). The organism not only damages the blood vessels by causing them to leak, but also causes clotting inside the vessels. If this clotting occurs in the larger arteries, it results in major tissue damage. Essentially, large areas of skin, muscle, and internal organs die from lack of blood and oxygen. Even if the disease is quickly diagnosed and treated, the patient has a high risk of dying.

Diagnosis

The diagnosis of meningococcemia can be made by the growth of the organism from blood cultures. Treatment should begin when the diagnosis is suspected and should not be delayed waiting for positive cultures. Obtaining fluid from a petechial spot and staining it in the laboratory can assist in quickly seeing the organism.

Treatment

Immediate treatment of a suspected case of meningococcemia begins with **antibiotics** that work against the organism. Possible choices include penicillin G, ceftriaxone (Rocephin), cefotaxime (Claforan), or trimethoprim/sulfamethoxazole (Bactrim, Septra). If the patient is diagnosed in a doctor's office, antibiotics should be given immediately if possible, even before transfer to the hospital and even if cultures cannot be obtained before treatment. It is most likely

KEY TERMS

Blood culture—A procedure where blood is collected from a vein and is placed in a small bottle that contains a special liquid; the liquid will make any organisms that are present in the blood sample grow. These organisms can then be grown and identified in the laboratory so that the proper antibiotic can be given to the patient.

Colonization—The presence of bacteria on a body surface (like on the skin, mouth, intestines or airway) without causing disease in the person.

Complement—One of several proteins in the blood that acts with other proteins to assist in killing bacteria.

Meningitis—Inflammation of the membranes of the brain or spinal cord.

that the speed of initial treatment will affect the ultimate outcome.

Prognosis

As many as 15-20% of patients with meningococcemia will die as a result of the acute infection. A significant percentage of the survivors will have tissue damage that requires surgical treatment. This treatment may consist of skin grafts, or even partial or full amputations of an arm or leg. Certain people with immune system defects (particularly those with defects in the complement system) may have recurrent episodes of meningococcemia. These patients, however, seem to have a less serious outcome.

Prevention

Although a vaccine is available for meningococcus, it is still difficult at this time to produce a vaccine for the type B organism, the most common one in the United States. Because of this and the short time that the vaccine seems to offer protection, the product has not been routinely used in the United States. It can be used for travelers going to areas where meningococcal disease is more common or is epidemic. Recently, the vaccine has been suggested for use in incoming college freshman, particularly those living in dormitories. These students appear to have a somewhat higher risk of meningococcal infections.

It is, however, recommended that all people take certain antibiotics if they have had contact (like at home or in a daycare) with a person who has meningococcal infection. The most common antibiotics given are rifampin (Rifadin) or ciprofloxacin (Cipro). These medicines are usually taken by mouth twice a day for two days. This treatment will decrease the risk of infection in these people who have been exposed. However, the overall risk to people who have been exposed, even without antibiotic use, is probably no more than 1-2%.

ORGANIZATIONS

University of Maryland Medical System, 22 S. Greene Street, Baltimore, MD 21201. TDD: (401) 328-9600 or (800) 492-5538, http://www.umm.edu/ency/article/001349.htm.

Larry I. Lutwick, MD

Meningomyelocele *see* **Spina bifida**
Menkes' syndrome *see* **Mineral deficiency**

Menopause

Definition

Menopause represents the irreversible end of ovulation and menstruation. Technically menopause refers to the final menstrual period after which a woman can no longer conceive children. Nevertheless, menopause is not an abrupt event, but a gradual process that involves many physical and hormonal changes before fertility ceases. Menopause is not a disease that needs to be treated, but a natural result of **aging**. However, the changes that occur during the time surrounding menopause can cause symptoms of widely varying severity that a women may wish to treat. Women have many options for managing these symptoms.

Description

Perimenopause is the time surrounding menopause. It can last for several years, and many women have irregular periods and other changes during this time. Although it is not easy to pinpoint when menopause begins, doctors agree that it is complete when a woman has not had a menstrual period for a full year.

There is no method to determine when the ovaries will begin to scale back, but a woman can get a general idea of when she will experience menopause based on her family history, body type, and lifestyle. A woman is likely to enter menopause at about the same age as her mother and sisters. Women who are smokers are more likely to begin menopause earlier than

nonsmokers. Women who began menstruating early will not necessarily stop having periods early. Eight out of every 100 women stop menstruating before age 40. At the other end of the spectrum, five out of every 100 continue to have periods until they are almost 60. The average age of menopause is 51.

Causes & symptoms

Once a woman enters **puberty**, her body releases one of the more than 400,000 eggs (ova) that are stored in her ovaries, about every 28 days in response to the interaction of several hormones. Blood supply to the womb (uterus) increases, and the lining of the uterus thickens in anticipation of receiving a fertilized egg. If the egg is not fertilized, the level of progesterone, the hormone mainly responsible for this uterine thickening, drops, and the uterine lining is sloughed off along with some blood. This menstrual flow is visible evidence ovulation has occurred.

By the time a woman reaches her late 30s or 40s, her ovaries begin to produce less of the female hormones estrogen and progesterone and to release eggs less regularly. As the levels of hormones fluctuate, the menstrual cycle begins to change. Some women may have longer periods with heavy flow followed by shorter cycles and very little bleeding. Others will begin to miss periods entirely. These irregular menstrual cycles make it more difficult for a woman to become pregnant. The gradual decline of estrogen also causes a wide variety of changes in tissues that respond to estrogen including the vagina, vulva, uterus, bladder, urethra, breasts, bones, heart, blood vessels, brain, skin, hair, and mucous membranes. Less immediately, the long-term lack of estrogen can make a woman more vulnerable to **osteoporosis**.

The most common symptom of perimenopause include:

- changes in the menstrual cycle
- hot flashes
- night sweats
- insomnia
- mood swings and increased irritability
- memory or concentration problems
- vaginal dryness
- heavy bleeding
- fatigue
- depression
- changes in the thickness and texture of hair
- headaches
- heart palpitations
- sexual disinterest
- urinary changes
- weight gain

Diagnosis

The clearest indication of menopause is the absence of a period for one full year. If it has been at least three months since a woman's last period, a follicle-stimulating hormone (FSH) test might be helpful in determining whether menopause has occurred. FSH levels rise steadily as a woman ages. The FSH test alone cannot be used as proof that a woman has entered early menopause. A better measure of menopause is to determine the levels of FSH, estrogen, progesterone, testosterone, and related hormones at mid-cycle. These tests are not routinely performed as most women can recognize the symptoms of perimenopause and menopause. They can, however, be helpful diagnostic tests in younger women who are showing symptoms of perimenopause.

Treatment

Decisions about if and how to treat symptoms associated with perimenopause should be made by a woman and her health care provider after taking into consideration her medical history and current research findings. Some women report success in using natural remedies to treat the unpleasant symptoms of menopause, although alternative therapies have only received significant attention in the United States in the last decade or so. Debate continues until scientific studies can prove these treatments' effectiveness on menopausal symptoms.

For women nearing menopause, alternative medical practitioners and traditional healthcare professionals generally recommend a diet high in fresh fruits, fresh vegetables, whole grains, nuts, seeds, and fresh vegetable juices and low in sugary treats and fats, especially animal fats. Calorie and portion control becomes more important as metabolism slows. Because a decrease in estrogen accelerates bone loss, women should make sure they get enough **calcium**. Most often a calcium supplement is recommended in addition to dairy products that provide calcium. Women generally need less iron after menopause because they no longer bleed monthly.

Herbs

Herbs have been used to relieve menopausal symptoms for centuries. In reasonable quantities, many herbs are relatively safe. Often adverse reactions to herbs come not from the herbs themselves, but from contaminants. Because the United States Food and

Drug Administration (FDA) does not regulate herbal products as strictly as pharmaceutical medicines, contamination, mislabeling, or accidental overdose is possible. Herbs should be purchased from a recognized company or through a qualified herbal practitioner. Herbal practitioners recommend a dose based on a woman's history, body size, lifestyle, diet, and reported symptoms. Women who choose to take herbs for menopausal symptoms should learn as much as possible about herbs and work with a qualified practitioner such as an herbalist, a traditional Chinese doctor, or a naturopathic physician.

The following list of herbs include those that herbalists recommend to treat menopausal symptoms:

- black cohosh (*Cimicifuga racemosa*): hot flashes and other menstrual complaints
- black currant (*Ribes migrum*): breast tenderness
- chaste tree/chasteberry (*Vitex agnus-castus*): hot flashes, excessive menstrual bleeding, moodiness
- chickweed (*Stellaria media*): hot flashes
- evening primrose oil (*Oenothera biennis*): mood swings, irritability, breast tenderness
- fennel (*Foeniculum vulgare*): hot flashes, digestive gas, bloating
- flaxseed (*Linum usitatissimum*): excessive menstrual bleeding, breast tenderness, and other symptoms, including dry skin and vaginal dryness
- ginkgo (*Ginkgo biloba*): memory problems
- ginseng (*Panax ginseng*): hot flashes, fatigue, vaginal thinning
- hawthorn (*Crataegus laevigata*): memory problems, fuzzy thinking
- horsetail (*Equisetum arvense*): osteoporosis
- lady's mantle (*Alchemilla vulgaris*): excessive menstrual bleeding
- Licorice (*Glycyrrhiza glabra*) root: general menopausal symptoms
- Mexican wild yam (*Dioscorea villosa*) root: vaginal dryness, hot flashes, general menopause symptoms
- motherwort (*Leonurus cardiaca*): night sweats, hot flashes
- oat straw (*Avena sativa*): mood swings, anxiety
- passionflower (*Passiflora incarnata*): insomnia, pain
- raspberry leaf (*Rubus idaeus*): normalizes hormonal system
- sage (*Salvia officinalis*): mood swings, headaches, night sweats
- skullcap (*Scutellaria lateriflora*): insomnia
- sesame oil (*Sesamum orientale*): vaginal dryness (applied topically)
- valerian (*Valeriana officinalis*): insomnia
- violet (*Viola odorata*): hot flashes.

Natural estrogens (phytoestrogens)

Phytoestrogens are estrogen compounds found in plants. Proponents of plant estrogens (including soy products) believe that plant estrogens are better than synthetic estrogens, but science has not yet proved this. The results of small preliminary trials suggest that the estrogen compounds in soy products (soy is very high in plant estrogens) can relieve the severity of hot flashes and lower cholesterol. In one study at Bowman-Gray Medical School in North Carolina, women were able to ease their menopausal symptoms such as hot flashes by eating a large amount of fruits, vegetables, and whole grains, together with 4 oz of tofu four times a week. However, no one has shown that plant estrogens can provide these benefits without causing the same negative side effects as estrogen replacement therapy. In addition, it is difficult to judge how much estrogen is in various plant products as there is no requirement for standardization. Many women believe that natural or plant-based means harmless. In large doses, phytoestrogens can promote the abnormal growth of cells in the uterine lining. Unopposed estrogen of any type can lead to an increased risk of **cancer**.

Several studies have shown that a black cohosh extract (Remifemin) relieved menopausal symptoms as well as or better than estrogen and that it showed the greatest promise among alternative treatments. In a 2007 study conducted at the University of Pennsylvania and published in *International Journal of Cancer*, Remifemin was also shown to reduce the risk of **breast cancer**. The United States Office of Dietary Supplements considers the evidence from studies of black cohosh promising but cautions that the long-term safety of this herb has not been established and recommends that if women choose to use black cohosh extract, they do so for no more than six months.

Flaxseeds also are a good source of phytoestrogens. Other sources include red clover leaf, licorice, wild yam, chickpeas, pinto beans, lima beans, and pomegranates. In 2003, red clover leaf was thought to offer relief for hot flashes, but in two short clinical trials, it failed to demonstrate hot flash relief.

Homeopathy

Women interested in homeopathic remedies for menopausal symptoms should consult a homeopathic physician. The following homeopathic remedies are

often recommended to alleviate specific groups of symptoms:

- lachesis: hot flashes, irritability, talkativeness, tightness around abdomen, dizziness, fainting
- sepia: bleeding between periods, chilliness, tearfulness, withdrawal from loved ones, sinking feeling in stomach
- pulsatilla: tearfulness, thirstless, feels better with others, avoids heat, hot flashes, varicose veins, hemorrhoids
- sulfur: philosophical personality, feeling hot, itching and burning of vagina and rectum
- lycopodium: low self esteem, bloated after eating, infrequent menstruation, low blood sugar, weak digestion, belching
- *Argentum nitricum:* gas, indigestion, craving for sweets and chocolate, panic attacks, fear of crossing bridges
- Magnesium phosphoricum: severe cramping
- transitional formula: hot flashes, night sweats, insomnia, skin-crawling sensation
- women's formula: perimenopause, PMS, irregular cycles, infertility, absent or excessive bleeding, menopausal discomfort
- vital formula: anxiety, headaches, palpitations, PMS, mood swings

Yoga

Many women find that **yoga** can ease menopausal symptoms. Yoga focuses on helping women unite the mind, body, and spirit to create balance. Because yoga has been shown to balance the endocrine system, some experts believe it may affect hormone-related problems. Studies have found that yoga can reduce **stress**, improve mood, boost a sluggish metabolism, and slow the heart rate. Specific yoga positions deal with particular problems, such as hot flashes, mood swings, vaginal and urinary problems, and other pains.

Exercise

Exercise helps ease hot flashes by lowering the amount of circulating FSH and by raising endorphin levels (which drop during a hot flash). Even exercising 20 minutes three times a week can significantly reduce hot flashes. Weight bearing exercises help to prevent osteoporosis. Regular exercise also provides many health benefits unrelated to menopause.

Acupuncture

This ancient Asian art involves placing very thin needles into different parts of the body to stimulate the system and unblock energy. It is usually painless and has been used for many menopausal symptoms including **insomnia**, hot flashes, and irregular periods. Practitioners believe that **acupuncture** can facilitate the opening of blocked energy channels, allowing the life force energy (chi) to flow freely. This allows the menopausal woman to keep her energy moving. Blocked energy usually increases the symptoms of menopause.

Acupressure and massage

Therapeutic massage involving **acupressure** can bring relief from a wide range of menopause symptoms by placing finger pressure at the same meridian points on the body that are used in acupuncture. There are more than 80 different types of massage, including foot **reflexology**, **Shiatsu** massage, and Swedish massage, but they all are based on the idea that boosting the circulation of blood and lymph benefits health. Breast massage (rubbing castor oil or olive oil on the breasts for five minutes three times a week) is claimed to help balance hormone levels, help the uterus contract during menstruation, and prevents cramping pains.

Biofeedback

Some women have been able to control hot flashes through **biofeedback**, a painless technique that helps a person train her mind to control her body. A biofeedback machine provides information about body processes (such as heart rate) as the woman relaxes her body. Using this technique, it is possible to control the body's temperature, heart rate, and breathing.

Other treatments

Therapeutic touch, an energy-based practice, may relieve menopausal symptoms. Cold compresses on the face and neck can ease hot flashes. Sound or **music therapy** may relieve stress and other menopausal symptoms. Prayer or **meditation** can help improve coping ability.

Dietary supplements

Women should discuss the use of dietary supplements with their health care provider. Some supplements interfere with the action of traditional pharmaceuticals and herbal remedies. Other supplements are harmful in large quantities. Supplementation with calcium, vitamin D, vitamin K, boron, manganese, magnesium, and phosphorous may aid in preventing osteoporosis. Vitamin E supplementation may reduce hot flashes and risk of heart disease.

KEY TERMS

Endometrium—The lining of the uterus that is shed with each menstrual period.

Estrogen—Female hormone produced by the ovaries and released by the follicles as they mature. Responsible for female sexual characteristics, estrogen stimulates and triggers a response from at least 300 tissues, and may help some types of breast cancer to grow. After menopause, the production of the hormone gradually stops.

Follicle-stimulating hormone (FSH)—The pituitary hormone that stimulates the ovary to mature egg capsules (follicles). It is linked with rising estrogen production throughout the cycle. An elevated FSH (above 40) indicates menopause.

Hormone—A chemical messenger secreted by a gland that is released into the blood, and that travels to distant cells where it exerts an effect.

Hormone replacement therapy (HRT)—The use of estrogen and progesterone to replace hormones that the ovary no longer supplies. HRT is no longer used as long-term therapy for postmenopausal women.

Hot flash—A wave of heat that is one of the most common perimenopausal symptoms, triggered by the hypothalamus' response to estrogen withdrawal.

Hysterectomy—Surgical removal of the uterus.

Ovary—One of the two almond-shaped glands in the female reproductive system responsible for producing eggs and the hormones estrogen and progesterone.

Phytoestrogen—An estrogen-like substance produced by plants.

Placebo—A pill or liquid given during the study of a drug or dietary supplement that contains no medication or active ingredient. Usually study participants do not know if they are receiving a pill containing the drug or an identical-appearing placebo.

Progesterone—The hormone that is produced by the ovary after ovulation to prepare the uterine lining for a fertilized egg.

Testosterone—Male hormone produced by the testes and (in small amounts) in the ovaries. Testosterone is responsible for some masculine secondary sex characteristics such as growth of body hair and deepening voice.

Uterus—The female reproductive organ that contains and nourishes a fetus from implantation until birth. Also known as the womb.

Allopathic treatment

When a woman enters menopause, her levels of estrogen drop and symptoms, such as hot flashes and vaginal dryness, begin. Before 2002, many physicians treated these symptoms with **hormone replacement therapy** (HRT). HRT treats these symptoms by increasing estrogen and progesterone levels enough to suppress symptoms. However, in the summer of 2002, preliminary results from a large Women's Health Initiative study were released that showed HRT could have significantly harmful effects (harmful enough that the study was stopped early). The study found that a combination of estrogen and progestin (a form of progesterone) HRT caused the following when compared to a placebo (no hormones):

- increased risk of heart attack, stroke, and blood clots
- increased risk of invasive breast cancer
- increased risk of dementia
- decreased risk of colorectal cancer
- decreased risk of bone fractures

Treatment with estrogen alone produced the following results:

- no change in the risk of heart attacks
- increased risk of stroke and blood clots
- unclear changes in the risk of breast cancer
- no change in the risk of colorectal cancer
- decreased risk of bone fractures
- no data available on changes in risk of dementia

At the time the results of the Women's Health Initiative became available, about 9 million American women were using HRT. Most physicians now no longer routinely recommend HRT to treat menopausal symptoms. Nevertheless, under certain circumstances when symptoms associated with menopause are so severe as to interfere with activities of daily life, a short course of HRT may be prescribed. Some doctors believe that short-term use of estrogen for those women with severe symptoms of hot flashes or night sweats is a sensible choice as long as they do not have a history of breast cancer. However, other doctors believe that in almost all cases the risks of HRT

outweigh the benefits. The decision should be made by a woman and her doctor after taking into consideration her medical history and situation. Women who choose to take hormones should have an annual mammogram, breast exam, and **pelvic exam** and should report any unusual vaginal bleeding or spotting (a sign of possible uterine cancer).

Postmenopausal treatment for osteoporosis

Raloxifene (Evista, Keoxifene) is a drug that is used to treat osteoporosis (bone loss) in postmenopausal women. It does not increase the risk breast cancer, although it may increase breast tenderness. It may also worsen hot flashes and cause uterine bleeding. It is not a treatment for symptoms associated with menopause. Several other drugs are also available to help reduce the risk of **fractures** in postmenopausal women with osteoporosis. In 2002, the FDA approved teriparatide (Forteo) for the treatment of osteoporosis. Ibandronate (Boniva) and alendronate (Fosamax) are also used to treat osteoporosis in postmenopausal women.

Testosterone replacement

The ovaries also produce a small amount of male hormones (about 300 micrograms), which decrease slightly as a woman enters menopause. Most women never need testosterone replacement. Testosterone can improve the libido, and decrease **anxiety** and depression. Adding testosterone is especially beneficial to women who have had hysterectomies. Testosterone also eases breast tenderness and helps prevent bone loss. Side effects include mild **acne** and some facial hair growth.

Expected results

Menopause is a natural condition of aging. Some women experience no problems associated with menopause, while others notice significant unpleasant symptoms. Results of allopathic and alternative treatments vary from one woman to another.

Prevention

Because menopause is a natural part of the aging process it cannot be prevented, however, some of the symptoms can be relieved by the treatments listed above.

Resources

BOOKS

Boston Women's Health Book Collective. *Our Bodies, Ourselves: Menopause*. New York: Simon & Schuster, 2006.

Jones, Marcia L., et al. *Menopause for Dummies,* 2nd ed. Indianapolis, IN: Wiley Pub., 2007.

Lee, John R. and Virginia Hopkins. *What Your Doctor May Not Tell You about Menopause: The Breakthrough Book on Natural Hormone Balance*. New York: Warner Books, 2004.

Manson, JoAnn E. and Shari Bassuk. *Hot Flashes, Hormones, & Your Health*. New York: McGraw-Hill, 2007.

Northrup, Christiane. *The Wisdom of Menopause: Creating Physical and Emotional Health and Healing During the Change,* rev. ed. New York: Bantam Books, 2006.

Wingert, Pat and Barbara Kantrowitz. *Is It Hot in Here? Or Is It Me?: The Complete Guide to Menopause*. New York: Workman Pub., 2006.

OTHER

"Hormone Therapy News." April 3, 2007 [cited October 30, 2009]. *National Women's Health Network*. http://www.nwhn.org/newsletter/article.cfm?content_id=112

"Menopause" *Federation of Feminist Women's Health Centers*. October 5, 2007 [cited October 30, 2009]. http://www.fwhc.org/menopause/index.htm

"Menopause Infocenter" *Holistic Online*. [cited October 30, 2009]. http://www.holisticonline.com/remedies/hrt/hrt_home.htm

"Menopause Online" *Menopause Online*. [cited October 30, 2009]. http://www.menopause-online.com

ORGANIZATIONS

American Holistic Medical Association., PO Box 2016, Edmonds, WA, 98020, (425) 967-0737., http://www.holisticmedicine.org.

American Menopause Foundation, Inc., Empire State Bldg., 350 Fifth Ave., Ste. 2822, New York, NY, 10118, (212) 714- 2398., http://www.americanmenopause.org.

Federation of Feminist Women's Health Centers., 14220 Interurban Ave South #140, Seattle, WA, 98168, http://www.fwhc.org/menopause.

National Women's Health Network., 514 10th Street NW, Suite 400, Washington, DC, 20004, (202) 628-7814, http://www.nwhn.org.

North American Menopause Society., PO Box 94527, Cleveland, OH, 44101, (216) 844-8748., http://www.menopause.org.

Belinda Rowland
Laura Jean Cataldo, RN, Ed.D.

Menorrhagia *see* **Dysfunctional uterine bleeding**

Men's health

Definition

Men's health is concerned with identifying, preventing, and treating conditions that are most common or specific to men.

Purpose

Men live on average seven years less than women; life expectancy in the United States is 72 years for men and 79 years for women. The reasons for this discrepancy are not completely understood. Men may have some genetic predisposition for lower life expectancy, as women tend to outlive men in most areas throughout the world. But men also have different lifestyle patterns that increase the wear and tear on their bodies. Studies have shown that men tend to drink and smoke more than women, men obtain medical care less frequently than women, and men generally have more stressful habits. It is clear to health professionals that men can benefit from increased knowledge of male medical issues and by understanding how lifestyle choices impact health.

According to the Centers for Disease Control (CDC), the ten leading causes of **death** for men in the United States are:

1. heart disease
2. cancer
3. stroke
4. accidents
5. lung disease (including emphysema and chronic bronchitis)
6. pneumonia
7. diabetes
8. suicide
9. liver disease
10. homicides

Men can experience conditions as diverse as **sexually transmitted diseases** (STDs), mental illness, arthritis, urinary tract infections, athletic injuries, hair and skin problems, and digestive disorders. The field of men's health strives to reduce the risks and incidence of men's conditions by researching preventive practices, designing testing procedures for early detection, and recommending specialized courses of treatment.

Description

Prevention

Preventive practices for men's health emphasize diet, **exercise** and **stress** management, as well as elimination of risky behaviors such as **smoking** and excessive drinking. Four of the leading causes of death for American men are related to diet—heart disease, **cancer**, **stroke**, and diabetes. In addition, men are more likely than women to have diet-related conditions including high cholesterol, high blood pressure, and **obesity**, all of which increase the risk of certain diseases and premature death.

For American men, dietary problems are usually not the result of getting too little nourishment but of eating too much fat, sugar, and overall calories. The dietary change most likely to improve the health of males is reduced intake of fats, particularly cholesterol and saturated fats. Cholesterol and saturated fats are found mainly in meat and dairy products. Calories from fat should amount to no more than 30% of total daily calories. Eating adequate protein is generally not a problem for American men, so replacing some dairy and meat consumption with high fiber vegetable proteins such as beans and soy would be beneficial. Complex carbohydrates should provide the bulk of daily calories, such as those from whole grains and legumes, while sugar intake such as in soft drinks, desserts, and processed foods should be significantly reduced. Increasing dietary fiber is recommended by eating plenty of fresh fruits, vegetables, whole grains, and legumes. Other principles of a healthy diet are avoiding artificial and processed foods, eating food that is as fresh and natural as possible, drinking plenty of water, and avoiding hydrogenated or partially hydrogenated oils, which contain unhealthy substances called trans-fatty acids. Overeating should be avoided as should snacking between meals. Alcohol intake should be limited to one or two glasses per day.

Exercise

The health of men has been affected as work patterns have shifted. Physical labor has been replaced by machines and office work. Studies have estimated that more than 30% of Americans are now obese, which means that nearly one out of three people is significantly overweight. Obesity poses many risks including increased chance of heart disease, diabetes, and some cancers. Effective exercise programs help men control weight, reduce stress, increase energy levels, improve self-esteem, reduce **pain** and injuries, and improve sleep. Exercise programs should emphasize flexibility and stretching as well as plenty of aerobic

activities, such as running and swimming. These activities exercise the heart and lungs and burn excess calories. Men may also choose anaerobic activities such as weight training to add muscles and increase strength. Routines should begin with warm-ups to reduce the chances of injuries and end with cool-down exercises to speed recovery.

Stress reduction

Stress is a silent killer; chronic (long-term) stress is a risk factor in many of the major diseases affecting men's mortality rates. Prolonged stress may cause ulcers, **sleep disorders**, addictions, depression, **anxiety**, and other conditions. Reduction of stress may require changes in both activities and attitudes. Exercise is recommended, as is reducing dependence on alcohol and nicotine. Men with extreme job-related stress may choose to spend more time with their families or in enjoyable activities. Men with stress levels that lead to destructive behaviors may need to pursue **psychotherapy** or significant lifestyle changes. **Nutrition**, social support, and healthy sleep patterns also reduce stress.

Alternative therapies may help with **stress reduction**. Their use has been adopted by many leading health centers. **Biofeedback** utilizes machines that monitor users' stress levels, helping people learn to control them. **Meditation** and other mind/body techniques are taught to enable the relaxation response, which has the opposite effects of stress in the body.

Testing

Routine physical examinations performed by physicians are recommended every three years for men in their twenties and thirties, every two years for men in their forties, and every year for men over 50. Physicians may order several screening tests depending on the age and condition of the patient. Blood tests screen for diabetes, high cholesterol, cancer, infections, and HIV. The prostate-specific antigen (PSA) test is a blood screen for **prostate cancer**. The digital rectal exam is used to manually check the prostate gland for enlargement or irregularities. Urine tests check for infections, kidney problems, and diabetes. The **fecal occult blood test** examines the stool for indications of ulcers or cancer. A **sigmoidoscopy** checks the health of the rectum and lower colon. Electrocardiograms (ECGs) check the status of the heart. Older men should consult an ophthalmologist (eye specialist) every two years for vision and glaucoma testing.

Men may perform self-tests as preventative measures. During a skin cancer self-exam, the entire skin is checked closely for irregular or changing **moles**, lesions, or blemishes, usually red, white or blue in color. Abnormal findings should be reported to a physician. Like some forms of skin cancer, **testicular cancer** tends to spread rapidly and early detection is crucial. The testicular self-exam is best performed in the shower or bath, because warm water relaxes the scrotum. The testicles are gently rolled and massaged between the fingers and thumb to feel for bumps, swelling, tenderness, or irregularities. Some self-test kits are available in pharmacies, including kits for blood pressure, high cholesterol, colorectal cancer, and blood glucose (diabetes). These do not take the place of proper medical care, and physicians should be consulted before their use.

Heart disease

Heart disease is the major cause of death among men. It claims nearly 500,000 lives each year in the United States and is more likely in men than women. Heart disease can take several forms but the most prevalent is coronary heart disease, in which the blood vessels that supply the heart with oxygen become blocked and the heart muscle becomes increasingly stressed. Arteriosclerosis, a major factor, is the hardening of arteries due to the accumulation of fatty materials. **Hypertension**, or high blood pressure, also poses major risks for both heart disease and stroke. **Angina** pectoris is the chest pain associated with the early stages of heart disease; it affects more than three million American men. When the blockage of blood supply to the heart becomes severe, a myocardial infarction (**heart attack**) may occur, which can be fatal.

The main symptom of angina pectoris is sharp pain on the left side of the chest that may radiate throughout the upper body. Other symptoms include **shortness of breath**, **dizziness**, **fatigue**, and swelling in the legs and ankles. Angina may be triggered by physical or emotional stress and lasts up to 30 minutes. Heart attacks have similar symptoms but with longer and more intense pain in the chest and upper body and may be accompanied by cold sweats and **vomiting**.

The American Heart Association lists the main risk factors for heart disease as being male, old age, having family history of the disease, smoking, high **cholesterol, high** blood pressure, diabetes, **alcoholism**, obesity, physical inactivity, and stress. Lifestyle habits such as diet, exercise and stress control play major roles in the development and prevention of heart disease in men.

Osteoporosis

Osteoporosis is a disease characterized by a decrease in bone mass and density. Often thought of as disease more prevalent in women, more than two million men have the disease. It develops about 10 to 15 years later in life in men than in women and risk of **fractures** from the disease can be greater in men. Men can decrease their risk by increasing **calcium** and vitamin D.

Cancer

The American Cancer Society (ACS) estimates that more than 1.5 million cases of cancer were reported in 2010, not including the nearly 2 million cases of skin cancers. Men have a slightly higher risk for cancer than women. The World Health Organization (WHO) estimates that the number of cancer cases in most countries will double in the next 25 years, while men's prostate cancer is expected to go up 40% worldwide. The most common cancers in men are skin, prostate, lung, colorectal (colon and rectum), lymphoma (lymph glands), oral (mouth and throat), and testicular cancer. The ACS lists seven warning signs of cancer:

- unusual bleeding or discharge
- changes in bowel or bladder patterns
- persistent sores
- lumps or irregularities on the body
- difficulty swallowing or indigestion
- changes in warts or moles
- persistent cough or hoarseness in the throat

Although the causes of cancer are incompletely understood, there are several risk factors that increase its chances: family history of cancer, smoking, poor diet (high in fat, low in fiber), excessive alcohol consumption, skin damage from sunlight, and exposure to radiation, chemicals, and environmental pollutants.

The prostate gland is a walnut-sized organ in the male reproductive system, located near the rectum below the bladder. The ACS reported that nearly 217,000 new cases of prostate cancer would be diagnosed in 2010, causing more than 32,000 deaths, making prostate cancer the second most fatal cancer for men behind lung cancer. Worldwide studies have shown that about 12% of men in Western countries get prostate cancer, while 50% have enlarged prostates. Benign prostatic hyperplasia (BPH) is the enlargement of the prostate gland, called benign when it is non-cancerous although growth can be rapid.

With early detection, 98% of men with prostate cancer survive for five years. Symptoms of prostate cancer include difficulty in stopping or starting urination, frequent nighttime urination (nocturia), weak urine flow, and blood in the urine or semen.

Testicular cancer is most common in men between the ages of 15 and 34. The ACS estimated that there would be about 8,100 new cases of testicular cancer in 2005 in the United States. Cigarette smoking increases the risk of testicular cancer but quitting smoking does not reduce the risk.

Stroke

Strokes occur when the blood supply to the brain is interrupted and brain function becomes impaired due to lack of oxygen. Ischemic strokes occur due to blood vessels becoming blocked while hemorrhagic strokes are the result of broken blood vessels in or near the brain. Ischemic strokes account for about 80% of all strokes. The American Heart Association estimates that more than 600,000 Americans have strokes each year, with men having a 20% higher risk of stroke than women, although more women die from strokes. Other risk factors are hypertension (high blood pressure), previous heart attacks, age, family history, high cholesterol, smoking, obesity, alcoholism, and physical inactivity. African Americans have 60% greater chances for strokes than whites.

Symptoms of strokes include sudden weakness or **numbness**, blurring or loss of vision, difficulty speaking or understanding, sudden severe **headache**, and dizziness or falling. Stroke victims should receive immediate emergency care.

Diabetes mellitus

Carbohydrate intolerance—the inability to properly metabolize sugars—is known as **diabetes mellitus**, often just shortened to diabetes. The pancreas makes insulin, a hormone responsible for a cell's uptake of glucose (sugar) from blood for energy. People who have diabetes do not make enough insulin, or else the body cannot use what is made. Treatment includes achieving a healthy weight, engaging in exercise, and prescription medication. Sometimes people are able to cure their diabetes with diet and weight loss.

A proper diet for people with diabetes is comparable to what the average healthy person should already be eating. Basic tenets include: eat three meals daily, incorporate healthful snacks, focus on foods high in fiber, combine protein and carbohydrates with moderate amounts of unsaturated fat, and avoid sugar-sweetened beverages to reduce overall caloric intake.

Male urinary tract problems

The urinary system includes the kidneys and bladder, the ureters between the kidneys and bladder, and the urethra, the tube through which urine flows from the bladder. Symptoms of urinary tract problems include frequent urination, excessive urination at night, painful or burning urination, weak urination, blood in the urine, or incontinence (involuntary loss of urine). **Urethritis** is infection of the urethra, which is a major symptom of sexually transmitted diseases (STDs). **Kidney stones** (nephrolithiasis) are the most common urinary tract problems, accounting for nearly one out of every 100 hospital admissions in the United States. Eighty percent of kidney stone patients are men. About 12% of American men develop kidney stones during their lifetimes. Kidney stones cause extreme pain when they move from the kidneys into the ureters. Ten percent of kidney stone cases require surgery. The best prevention for kidney stones is drinking plenty of fluids daily.

The male reproductive system

The male reproductive system includes the penis, testicles, scrotum, prostate, and other organs. Problems include **orchitis**, or infection of the testicles, and hydrocele, the buildup of fluid on the testicles. **Epididymitis** is inflammation of the tube that transports sperm from the testicles, and can cause severe pain, swelling, and **fever**. A varicocele is a group of **varicose veins** in the scrotum that can cause swelling and damage sperm. **Peyronie's disease** is the abnormal curvature of the penis caused by accumulated scar tissue. **Testicular torsion** is considered a medical emergency, when a testicle becomes twisted and blood supply is cut off. This condition can lead to permanent damage if not treated quickly. It is most common in males between the ages of 12 and 18. **Prostatitis** is infection or inflammation of the prostate gland.

Sexually transmitted diseases include **genital warts**, chlamydia, **gonorrhea**, **syphilis**, **genital herpes**, hepatitis, and HIV (human **immunodeficiency** virus). HIV is the leading cause of death for American men between the ages of 25 and 45. Symptoms of STDs include discharge of fluid from the penis; painful urination; sores, lesions, **itching**, or **rashes** in the genital area; and swelling of the lymph nodes in the groin.

Prevention of STDs begins with safe sexual behavior: wearing **condoms**, limiting the number of sexual partners, not mixing sexual encounters with alcohol, and avoiding sexual contact with infected people, prostitutes, and intravenous drug users. Men who engage in risky behaviors should have frequent HIV tests and medical examinations.

Male sexual health

Erectile dysfunction (ED), also called **impotence**, is a man's inability to maintain an erection for sexual intercourse. It affects nearly one in every 10 American men. Incidence of ED increases with age, but the problem can occur at any age. Up to 80% of ED is caused by physical problems, while 20% of cases are psychogenic, or psychological in origin. Causes of ED include hormonal problems, injuries, nerve damage, diseases, infections, diabetes, stress, depression, anxiety, drug **abuse**, and interactions with prescription drugs. ED may be the first indication of circulation problems due to diabetes, high blood pressure, or **coronary artery disease**.

A self-test men can perform to determine whether ED is physical or psychological is the stamp test, or nocturnal penile tumescence test. Physically healthy men experience several prolonged erections during sleep. The stamp test is done by attaching a strip of stamps around the penis before bedtime; if the stamps are torn in the morning, it generally indicates that nocturnal (nightly) erections have occurred and thus ED is not physiological. Men with ED should see a urologist for further diagnosis and discussion of the several treatment options available including drugs, hormone injections, and surgical repair or implants. Several new prescription drugs have become available in recent years.

Infertility occurs when men lack an adequate supply of sperm to cause **pregnancy**. As many as 15% of American couples, or more than five million Americans, are affected by infertility in one or both partners. A WHO project found that in about 20% of infertile couples, the problem was due to the man, while in another 27% of couples both partners had infertility problems. Injuries, **birth defects**, infections, environmental pollutants, chronic stress, drug abuse, and hormonal problems may account for male infertility, while one in four cases has no apparent cause and is termed idiopathic infertility. Declining sperm counts have been observed in industrialized countries, and possible explanations for this decrease are as diverse as increased environmental pollutants to the use of plastic diapers, which a German study claims damages infant testicles by keeping in excess heat. Male infertility can be diagnosed by sperm analysis, blood tests, radiographic scans of the testicles, and other tests.

Other types of **sexual dysfunction** include **premature ejaculation**, in which men cannot sustain

intercourse long enough to bring their partners to climax, and retarded ejaculation (also called male orgasmic disorder) when male orgasm becomes difficult. Some men have periods of inadequate sexual desire (**hypoactive sexual desire disorder**), while sexual aversion disorder (SAD) is fear and repulsion of sexual activity. **Dyspareunia** is painful intercourse, and should be reported to physicians as it may indicate STDs or infections. In addition to medical care, sexual dysfunction may be treated by **sex therapy** or psychotherapy depending on its causes.

Vasectomies, a form of male birth control, are surgical operations that sever the tubes that transport sperm from the testicles. Vasectomies can be reversed but 10% of men become infertile due to the surgery. **Circumcision** is the surgical removal of the foreskin of the penis, for religious and medical reasons, performed on 60% of newborn males in the United States. Increasing controversy surrounds this procedure. Advocates of circumcision claim it prevents infections (called **balanitis**) on the head of the penis and reduces chances of **penile cancer**. Opponents of circumcision claim that the outdated procedure affords no medical benefits, causes unnecessary pain for infants, and that the lack of a foreskin may reduce sexual pleasure and performance.

Men's emotional health

Depression is a mood disorder marked by sadness, emotional pain, and the inability to feel pleasure. At least 10% of men will experience an episode of major depression at least once in their lives. Men with depression are five times more likely to commit **suicide**, a major cause of mortality in men. Men are half as likely as women to seek psychological help. Men may experience depression and emotional problems between the ages of 50 and 65, called the midlife crisis, as men face the major transition into retirement and older age.

Panic attacks have symptoms of overwhelming fear, chest pain, shortness of breath, numbness, and increased heart rate. Men may mistake them as heart attacks. Men also are plagued by addictions to nicotine, alcohol, and other drugs, which are often the unhealthy escape routes from deeper emotional issues. Studies have estimated that as many as one-third of Americans have sleep disorders, which may be psychological in origin and related to anxiety, stress, and lifestyle.

Mental illness can be particularly difficult for men because in our society men are taught to withhold rather than express emotions and feelings. Emotional problems can be strong signals for men to communicate and confront deeper issues. Help can be found from physicians, psychotherapists, and spiritual or religious counselors.

KEY TERMS

Emphysema—Disease of severe lung deterioration and impairment.

Obesity—Condition defined as being overweight by 30% of normal limits.

Sigmoidoscopy—Test procedure using an optical instrument to view the internal rectum and colon.

Urologist—Physician specializing in male reproductive and urinary systems.

Resources

PERIODICALS

"Cigarette Smoking Influences Testicular Cancer Risk." *Medical Devices & Surgical Technology Week* March 28, 2004: 218.

"Men's Health: Erectile Dysfunction." *Medical Update* January 2004: 2.

"Osteoporosis Develops Later in Men, Hits Harder." *Internal Medicine News* March 15, 2004: 30.

OTHER

A Man's Life Online Magazine. http://www.manslife.com.

The Prostate Cancer Infolink. http://www.comed.com/prostate.

ORGANIZATIONS

American Foundation for Urologic Disease, 1128 N. Charles St., Baltimore, MD, 21201, (401) 468-1800, http://www.afud.org.

American Urological Association Foundation, 1000 Corporate Blvd., Linthicum, MD, 21090, (410) 689-3700, (410) 689-3800, (866) 746-4282, auafoundation@auafoundation.org, http://www.urologyhealth.org/.

The Center for Holistic Urology, Columbia University Medical Center. Atchley Pavilion 11th Floor, 161 Ft. Washington Ave., New York, NY, 10032, (212) 305-0114, http://www.holisticurology.columbia.edu.

Douglas Dupler, MA
Teresa G. Odle
Laura Jean Cataldo, RN, EdD

Menstrual disorders

Definition

A menstrual disorder is a physical or emotional problem that interferes with the normal menstrual cycle, causing **pain**, unusually heavy or light bleeding, delayed menarche, or missed periods.

Description

A woman of childbearing age should menstruate every 28 days or so unless she is pregnant or moving into **menopause**. Numerous things can go wrong with the normal menstrual cycle, some the result of physical causes, others emotional. These include **amenorrhea**, or the cessation of menstruation, menorrhagia, or heavy bleeding, and **dysmenorrhea**, or severe menstrual cramps. Nearly every woman will experience one or more of these menstrual irregularities at some time in her life.

Amenorrhea

There are two types of amenorrhea: primary and secondary. Overall, they affect 2–5% of childbearing women, a number that is considerably higher among female athletes (possibly as high as 66%).

Primary amenorrhea occurs when a girl at least 16 years old is not menstruating. Young girls may not have regular periods for their first year or two, or their periods may be very light, a condition known as **oligomenorrhea**. A light flow is nothing to worry about. But if the period has not begun at all by age 16, there may be something wrong. Amenorrhea is most common in girls who are severely underweight and/or **exercise** intensely, both of which affect the amount of body fat necessary to trigger the release of hormones that, in turn, begin **puberty**.

Secondary amenorrhea occurs in women of childbearing age after a period of normal menstruation and is diagnosed when menstruation has stopped for three months. It can occur in women of any age.

Dysmenorrhea

Characterized by menstrual cramps or painful periods, dysmenorrhea, which comes from the Greek words for "painful flow," affects nearly every woman at some point in her life. It is the most common reproductive problem in women, resulting in numerous days absent from school, work, and other activities. There are two types: primary and secondary.

Primary, or normal cramps, affects up to 90% of all women, usually occurring in women about three years after they start menstruating and continuing through their mid-twenties or until they have a child. About 10% of women who have this type of dysmenorrhea cannot work, attend school, or participate in their normal activities. It may be accompanied by backache, **dizziness**, **headache**, **nausea**, **vomiting**, **diarrhea**, and tenseness. The symptoms typically start a day or two before menstruation, usually ending when menstruation actually begins.

Secondary dysmenorrhea has an underlying physical cause and primarily affects older women, although it may also occur immediately after a woman begins menstruation.

Menorrhagia

Menorrhagia, or heavy bleeding, most commonly occurs in the years just before menopause or just after women start menstruating. It occurs in 15–20% of American women.

Premenstrual dysphoric disorder (PMDD)

The fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*, or DSM-IV, lists **premenstrual dysphoric disorder** (PMDD) in an appendix of criteria sets for further study. To meet full criteria for PMDD, a patient must have at least five out of 11 emotional or physical symptoms during the week preceding the menses for most menstrual cycles over the previous 12 months. Although the DSM-IV definition of PMDD as a mental disorder is controversial because of fear that it could be used to justify prejudice or job discrimination against women, there is evidence that a significant proportion of premenopausal women experience emotional distress or impairment in job functioning in the week before their menstrual period. One group of researchers estimates that 3–8% of women of childbearing age meet the strict DSM-IV criteria for PMDD, with another 13–18% having symptoms severe enough to interfere with their normal activities.

Causes and symptoms

Amenorrhea

The only symptom of primary amenorrhea is delayed menstruation. In addition to low body weight or excessive exercise, other causes of primary amenorrhea include Turner's syndrome, a birth defect related to the reproductive system, or ovarian problems. In 2003, a group of researchers reported on a new genetic mutation associated with primary amenorrhea. In

KEY TERMS

Adenomyosis—Uterine thickening caused when endometrial tissue, which normally lines the uterus, extends outward into the fibrous and muscular tissue of the uterus.

Cervical polyps—Growths originating from the surface of the cervix or endocervical canal. These small, fragile growths hang from a stalk and protrude through the cervical opening (the os).

Cushing's syndrome—A group of conditions caused by increased production of cortisol hormones or by the administration of glucocorticoid hormones (cortisone-like hormones).

Endometriosis—A condition in which the tissue that normally lines the uterus (endometrium) grows in other areas of the body, causing pain, irregular bleeding, and frequently, infertility.

Fibroids—Benign tumors of muscle and connective tissue that develop within or are attached to the uterine wall.

Hyperthyroidism—An imbalance in metabolism that occurs from overproduction of thyroid hormone.

Inflammatory bowel disease—A chronic inflammatory disease that can affect any part of the gastrointestinal tract but most commonly affects the ileum.

Lupus (systemic lupus erythematosus or SLE)—A chronic inflammatory autoimmune disorder that may affect many organ systems including the skin, joints, and internal organs.

Menarche—The first menstrual period or the establishment of the menstrual function.

Osteopenia—Reduction in bone mass, usually caused by a lowered rate of formation of new bone that is insufficient to keep up with the rate of bone destruction. Osteopenia often occurs together with amenorrhea and eating disorders in female athletes. It can lead to premature osteoporosis if left untreated.

Pelvic inflammatory disease (PID)—A general term referring to infection involving the lining of the uterus, the Fallopian tubes, or the ovaries.

Turner's syndrome—A disorder in women caused by an inherited chromosomal defect. This disorder inhibits sexual development and causes infertility. A symptom is absence of menstruation.

secondary amenorrhea, the primary symptom is the ceasing of menstruation for at least three months. Causes include **pregnancy** or **breastfeeding**, sudden weight loss or gain, intense exercise, **stress**, endocrine disorders affecting the thyroid, pituitary, or adrenal glands, including **Cushing's syndrome** and **hyperthyroidism**, and problems with or surgery on the ovaries, including removal of the ovaries, cysts or ovarian tumors.

Amenorrhea in athletes or dancers is frequently associated with two other disorders—osteopenia, or reduced bone mass, and **eating disorders**. This combination is sometimes called the female athlete triad. Osteopenia is of concern because it can lead to premature **osteoporosis**.

Dysmenorrhea

Primary dysmenorrhea is related to the production of prostaglandins, natural chemicals the body makes that cause an inflammatory reaction. They also cause the muscles of the uterus to contract, thus helping the uterus shed the lining built up during the first part of a woman's cycle. Women with severe menstrual pain have higher levels of prostaglandin in their menstrual blood than women who do not have such pain. In some women, prostaglandins can cause some of the smooth muscles in the gastrointestinal tract to contract, resulting in the nausea, **vomiting**, and diarrhea some women experience. Prostaglandins also cause the arteries and veins to expand, so that blood collects in them rather than flowing freely through them, causing pain and heaviness. Yet another reason for severe cramps, particularly in women who have not yet had a baby, is that the flow of the blood and clots through the tiny cervical opening is painful. After a woman has a baby, however, the cervix opening is larger.

Secondary dysmenorrhea is more serious and is related to some underlying cause. The pain may feel like regular menstrual cramps, but may last longer than normal and occur throughout the month. It may be stronger on one side of the body than the other. Possible causes include:

- a tipped uterus
- endometriosis, a condition in which the same type of tissue found in the lining of the uterus occurs outside the uterus, usually elsewhere in the pelvic cavity

- adenomyosis, a condition in which the endometrial lining grows into the muscle of the uterus
- fibroids
- pelvic inflammatory disease (PID)
- an IUD
- a uterine, ovarian, bowel, or bladder tumor
- uterine polyps
- inflammatory bowel disease
- scarring or adhesions from earlier surgery

Menorrhagia

Heavy bleeding during menstruation is usually related to a hormonal imbalance, although other causes include fibroids, cervical or endometrial polyps, the autoimmune disease lupus, **pelvic inflammatory disease** (PID), blood platelet disorder, a hereditary blood factor deficiency, or, possibly, some reproductive cancers. Thus, menorrhagia is actually a symptom of an underlying condition rather than a disease itself. It may also be related to the use of an **IUD**.

Women with menorrhagia experience not only significant inconvenience, but may feel very tired due to the loss of iron-rich blood. It is usually diagnosed when a woman soaks through a tampon or pad every hour for several hours or has a period lasting more than seven days. Clots are not related to menorrhagia, although women with heavy cycles may pass clots. They are typically a normal part of menstruation, more common when a woman has been sitting or in a stationary position for a while.

Diagnosis

Women should seek care from a gynecologist, family practitioner, or internist for menstrual irregularities. Depending on the problem, various tests and procedures will be performed, but the one common to any menstrual problem is a **pelvic exam**. This should be scheduled when women are not menstruating, simply for convenience.

Examination

Male doctors typically have a female nurse or assistant in the room. The examination begins by checking the external genitalia for any sores or irregularities. Then the doctor inserts a speculum (a metal duckbill-shaped device that holds open the vagina) into the vagina and peers throughout the opening to evaluate the health of the cervix (opening of the uterus), and inside the vagina, looking for growths or any other abnormalities.

The doctor also manually examines the woman, inserting two fingers into the vagina while pressing on the abdomen, again feeling for any lumps or other abnormalities, checking the size and shape of the reproductive organs, and watching for any signs of infection, such as tenderness or pain. The exam is typically covered by insurance and takes about ten minutes.

Tests

Several different tests may be done for menstrual irregularities. Blood, stool, and urine tests may be conducted to check for levels of various hormones, blood cells, and other chemicals. In the absence of menses, a pregnancy test can be done to test for the presence of certain hormones that indicate a pregnancy has occurred.

An ultrasound, typically performed by a trained ultrasound technologist, involves using sound waves to get an image of the reproductive system. It is used to look for fibroids and other ovarian abnormalities that may cause heavy bleeding or cramps. Typically, the technologist smears a jelly over the woman's stomach, then places a probe on her stomach and watches the images appear on a computer screen. It is painless. Women may be asked not to urinate for several hours prior to the test, as a full bladder makes it easier to see the other internal organs. The test takes about 20 minutes.

An **endometrial biopsy** is used to check the health of uterine tissue in women who have unusually heavy bleeding. This test should be performed by the physician. Women should take a pain reliever such as ibuprofen or naproxen prior to the procedure, as there may be some cramping. The woman lies back on the table with her feet in stirrups and the doctor inserts a speculum, then opens the cervix slightly with an instrument called a tenaculum. Then the doctor slides a small, hollow catheter into the uterus and sucks out a small piece of tissue from the uterine lining. The tissue is examined for any abnormalities in a laboratory. The test takes about 30 minutes and is typically covered by insurance. Some bleeding may result afterward.

Procedures

Dilatation and curettage (D&C) is a very common minor surgical procedure in which the cervix is opened and the lining of the uterus is scraped for a tissue sample. This procedure is performed for the purpose of diagnosis as well as treatment for problems such as cervical polyps or **endometriosis**. It is also performed after a **miscarriage** or abortion.

Laparascopy and **hysteroscopy** are surgical procedures in which a small camera is inserted into the woman to view the inside of the pelvis, abdomen, or uterus.

Treatment

Amenorrhea

For primary amenorrhea with no underlying problem, no treatment is necessary, and a wait-and-see approach is often adopted. If women have genetic or hormonal abnormalities, amenorrhea is often treated with **oral contraceptives** that contain combinations of estrogen and progestin. Side effects include bloating, weight gain, and **acne**, although some birth control pills actually improve acne. Progestins, or synthetic progesterone, are also used alone to "jump start" a woman's period. They include medroxyprogesterone (Provera, Amen, **Depo-Provera**), norethindrone acetate (Aygestin, Norlutate), and norgestrel (Ovrel). If the amenorrhea is due to a physical problem, such as a closed vagina, surgery may be required.

With secondary amenorrhea, treatment depends on the cause. Hormonal imbalances are treated with supplemental hormones. Tumors or cysts may require surgery. **Obesity** may require a diet and exercise regimen, while amenorrhea resulting from too much dieting or exercise necessitates lifestyle changes.

Dysmenorrhea

Primary dysmenorrhea is typically treated with nonsteroidal anti-inflammatory medications like ibuprofen and naproxen, which studies show help 64–100% of women. Birth control pills relieve pain and symptoms in about 90% of women by suppressing ovulation and reducing the amount of menstrual blood. It may take up to three cycles before a woman feels relief. Heat from a heating pad or hot bath, can also help relieve pain.

Treatment for secondary dysmenorrhea depends on the underlying cause of the condition.

Menorrhagia

If there are no other problems, and the bleeding is due to hormonal imbalances, birth control pills are often prescribed to bring the bleeding under control and regulate menstruation. Such medications as ibuprofen and naproxen can also help reduce the bleeding and any cramping associated with it. In severe cases, doctors may recommend removing the uterus during a **hysterectomy**, or performing some form of endometrial ablation, which removes the lining of the uterus. These procedures are typically only offered to women who have completed their families. A recent British study reported that many women prefer endometrial ablation to hysterectomy because it is less invasive and safer. In 2009, the FDA approved the intrauterine hormonal device, Mirena, for use in women experiencing heavy bleeding.

Premenstrual dysphoric disorder (PMDD)

Medications that have been reported to be effective in treating PMDD include the **tricyclic antidepressants** and the **selective serotonin reuptake inhibitors** (SSRIs). Effective treatments other than medications include cognitive behavioral therapy (CBT), aerobic exercise, and dietary supplements containing **calcium**, magnesium, and vitamin B_6.

Alternative treatment

Amenorrhea

There are several herbal remedies that can bring on menstruation, including: black cohosh, cramp bark, chasteberry, celery, turmeric, and marsh mallow. Numerous relaxation techniques, such as **meditation**, deep breathing, and **yoga** can help reduce stress and its effects on menstruation.

Dysmenorrhea

Alternative treatments used to help relieve menstrual pain include:

- Transcutaneous electrical nerve stimulation (TENS). Several studies found relieved pain in 42–60% of participants, working faster than naproxen in one study.
- Acupuncture: One study of 43 patients followed for a year found that 90% of those who had acupuncture once a week for three menstrual cycles had less pain, and 43% used less pain medication.
- Omega-3 fatty acids: Often sold as fish oil supplements, they are a known anti-inflammatory, working against the effects of prostaglandins. Studies found that women with low amounts of omega-3 fatty acids in their diets were more likely to have menstrual cramps; those who took supplements had less pain.
- Vitamin B_1: One large study found that symptoms disappeared in 87% of women who took 100 mg a day for 90 days.
- Magnesium supplements: One study of 30 women who took 4.5 mg of oral magnesium three times daily for part of the month decreased their symptoms up to 84%.

Menorrhagia

Herbs used to treat menorrhagia include yarrow, nettles, and shepherd's purse, as well as agrimony (particularly used in Chinese medicine), ladies mantle,

vervain, and red raspberry, which are thought to strengthen the uterus. Vitex is another herb recommended for a variety of menstrual disorders ranging from menorrhagia to **premenstrual syndrome** (PMS). Women may want to discuss with their doctor about taking an iron supplement to replace the iron lost during the heavy bleeding. Helpful **vitamins** include vitamin A, because women with heavy bleeding typically have lower levels of vitamins A, K (aids in clotting), and C and bioflavinoids, which help strengthen veins and capillaries. Zinc may also help.

Prognosis

The prognosis for all menstrual irregularities is good once treatment is initiated.

Prevention

Amenorrhea

Simply following a healthy exercise and nutritional program can help prevent amenorrhea, as can reducing stress and learning relaxation techniques. Avoiding excessive alcohol intake and quitting **smoking** may prevent missed periods.

Dysmenorrhea

Prevention includes taking certain dietary supplements and vitamins. Exercise may also help.

Menorrhagia

There is little women can do to prevent this menstrual irregularity other than discovering the root cause.

Resources

BOOKS

Davis, Carolyn F. *100 Questions & Answers about Your Daughter's Sexual Wellness and Development*. Sudbury, MA: Jones & Bartlett Publishers, 2010.

Nelson, Miriam, and Jennifer Ackerman. *The Strong Women's Guide to Total Health*. New York: Rodale Books, 2010.

Rosenfeld, Jo Ann, ed. *Handbook of Women's Health*. 2nd ed. New York: Cambridge University Press, 2009.

Stein, Elissa, and Susan Kim. *Flow: The Cultural Story of Menstruation*. New York: St. Martin's Griffin, 2009.

Thacker, Holly. *The Cleveland Clinic Guide to Menopause*. New York: Kaplan Publishing, 2009.

PERIODICALS

Aegerter, C., D. Friess, and L. Alberio. "Menorrhagia Caused by Severe Hereditary Factor VII Deficiency. Case 1." *Hämostaseologie* 23 (August 2003): 99–102.

Donaldson, M. L. "The Female Athlete Triad. A Growing Health Concern." *Orthopedic Nursing* 22 (September-October 2003): 322–324.

Halbreich, U., J. Borenstein, T. Pearlstein, and L. S. Kahn. "The Prevalence, Impairment, Impact, and Burden of Premenstrual Dysphoric Disorder (PMS/PMDD)." *Psychoneuroendocrinology* 28, Supplement 3 (August 2003): 1–23.

Meduri, G., et al. "Delayed Puberty and Primary Amenorrhea Associated with a Novel Mutation of the Human Follicle-Stimulating Hormone Receptor: Clinical, Histological, and Molecular Studies." *Journal of Clinical Endocrinology and Metabolism* 88 (August 2003): 3491–3498.

Paddison, K. "Menorrhagia: Endometrial Ablation or Hysterectomy?" *Nursing Standard* 18, no. 1 (September 17, 2003): 33–37.

Rapkin, A. "A Review of Treatment of Premenstrual Syndrome and Premenstrual Dysphoric Disorder." *Psychoneuroendocrinology* 28, Supplement 3 (August 2003): 39–53.

"Research Eyes IUS Use for Menstrual Bleeding." *Contraceptive Technology Update* Supplement 3 (June 2004): 67–69.

ORGANIZATIONS

American Congress of Obstetricians and Gynecologists (ACOG), PO Box 96920, Washington, DC, 20090-6920, (202) 638-5577, http://www.acog.org.

American Psychiatric Association (APA), 1000 Wilson Boulevard, Suite 1825, Arlington, VA, 22209, (888) 357-7924, http://www.psych.org.

Healthy Women, 157 Broad Street, Suite 106, Red Bank, NJ, 07701, (877) 986-9472, http://www.healthywomen.org.

Society for Women's Health Research, 1025 Conneticut Ave. NW, Suite 701, Washington, DC, 20036, (202) 223-8224, info@swhr.org, http://www.womenshealthresearch.org.

Rebecca J. Frey, PhD
Debra Gordon
Teresa G. Odle
Laura Jean Cataldo, RN, EdD

Menstrual pain *see* **Dysmenorrhea**

Mental retardation

Definition

Mental retardation is a developmental disability that first appears in children under the age of 18. It is defined as an intellectual functioning level (as measured by standard tests for intelligence quotient) that is

well below average and significant limitations in daily living skills (adaptive functioning).

Description

Mental retardation occurs in 2.5–3% of the general population. About 6–7.5 million mentally retarded individuals live in the United States alone. Mental retardation begins in childhood or adolescence before the age of 18. In most cases, it persists throughout adulthood. A diagnosis of mental retardation is made if an individual has an intellectual functioning level well below average and significant limitations in two or more adaptive skill areas. Intellectual functioning level is defined by standardized tests that measure the ability to reason in terms of mental age (intelligence quotient or IQ). Mental retardation is defined as IQ score below 70–75. Adaptive skills are the skills needed for daily life. Such skills include the ability to produce and understand language (communication); home-living skills; use of community resources; health, safety, leisure, self-care, and social skills; self-direction; functional academic skills (reading, writing, and arithmetic); and work skills.

In general, mentally retarded children reach developmental milestones such as walking and talking much later than the general population. Symptoms of mental retardation may appear at birth or later in childhood. Time of onset depends on the suspected cause of the disability. Some cases of mild mental retardation are not diagnosed before the child enters preschool. These children typically have difficulties with social, communication, and functional academic skills. Children who have a neurological disorder or illness such as **encephalitis** or **meningitis** may suddenly show signs of cognitive impairment and adaptive difficulties.

Mental retardation varies in severity. *The Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition (*DSM-IV*) is the diagnostic standard for mental healthcare professionals in the United States. The *DSM-IV* classifies four different degrees of mental retardation: *mild, moderate, severe*, and *profound.* These categories are based on the functioning level of the individual.

Mild mental retardation

Approximately 85% of the mentally retarded population is in the mildly retarded category. Their IQ score ranges from 50–75, and they can often acquire academic skills up to the 6th grade level. They can become fairly self-sufficient and in some cases live independently, with community and social support.

Moderate mental retardation

About 10% of the mentally retarded population is considered moderately retarded. Moderately retarded individuals have IQ scores ranging from 35–55. They can carry out work and self-care tasks with moderate supervision. They typically acquire communication skills in childhood and are able to live and function successfully within the community in a supervised environment such as a group home.

Severe mental retardation

About 3–4% of the mentally retarded population is severely retarded. Severely retarded individuals have IQ scores of 20–40. They may master very basic self-care skills and some communication skills. Many severely retarded individuals are able to live in a group home.

Profound mental retardation

Only 1–2% of the mentally retarded population is classified as profoundly retarded. Profoundly retarded individuals have IQ scores under 20–25. They may be able to develop basic self-care and communication skills with appropriate support and training. Their retardation is often caused by an accompanying neurological disorder. The profoundly retarded need a high level of structure and supervision.

The American Association on Mental Retardation (AAMR) has developed another widely accepted diagnostic classification system for mental retardation. The AAMR classification system focuses on the capabilities of the retarded individual rather than on the limitations. The categories describe the level of support required. They are: *intermittent support, limited support, extensive support*, and *pervasive support*. To some extent, the AAMR classification mirrors the *DSM-IV* classification. Intermittent support, for example, is support needed only occasionally, perhaps during times of **stress** or crisis. It is the type of support typically required for most mildly retarded individuals. At the other end of the spectrum, pervasive support, or life-long, daily support for most adaptive areas, would be required for profoundly retarded individuals.

Causes and symptoms

Low IQ scores and limitations in adaptive skills are the hallmarks of mental retardation. Aggression, self-injury, and **mood disorders** are sometimes associated with the disability. The severity of the symptoms and the age at which they first appear depend on the cause. Children who are mentally retarded reach developmental milestones significantly later than expected, if at all. If retardation is caused by chromosomal or other

genetic disorders, it is often apparent from infancy. If retardation is caused by childhood illnesses or injuries, learning and adaptive skills that were once easy may suddenly become difficult or impossible to master.

In about 35% of cases, the cause of mental retardation cannot be found. Biological and environmental factors that can cause mental retardation include:

Genetics

About 5% of mental retardation is caused by hereditary factors. Mental retardation may be caused by an inherited abnormality of the genes, such as **fragile X syndrome**. Fragile X, a defect in the chromosome that determines sex, is the most common inherited cause of mental retardation. Single gene defects such as **phenylketonuria** (PKU) and other inborn errors of metabolism may also cause mental retardation if they are not found and treated early. An accident or mutation in genetic development may also cause retardation. Examples of such accidents are development of an extra chromosome 18 (trisomy 18) and **Down syndrome**. Down syndrome, also called mongolism or trisomy 21, is caused by an abnormality in the development of chromosome 21. It is the most common genetic cause of mental retardation.

Prenatal illnesses and issues

Fetal alcohol syndrome affects one in 600 children in the United States. It is caused by excessive alcohol intake in the first twelve weeks (trimester) of **pregnancy**. Some studies have shown that even moderate alcohol use during pregnancy may cause learning disabilities in children. Drug **abuse** and cigarette **smoking** during pregnancy have also been linked to mental retardation.

Maternal infections and illnesses such as glandular disorders, **rubella**, **toxoplasmosis**, and **cytomegalovirus infection** may cause mental retardation. When the mother has high blood pressure (**hypertension**) or blood poisoning (toxemia), the flow of oxygen to the fetus may be reduced, causing brain damage and mental retardation.

Birth defects that cause physical deformities of the head, brain, and central nervous system frequently cause mental retardation. Neural tube defect, for example, is a birth defect in which the neural tube that forms the spinal cord does not close completely. This defect may cause children to develop an accumulation of cerebrospinal fluid on the brain (**hydrocephalus**). Hydrocephalus can cause learning impairment by putting pressure on the brain.

Childhood illnesses and injuries

Hyperthyroidism, **whooping cough**, **chickenpox**, **measles**, and Hib disease (a bacterial infection) may cause mental retardation if they are not treated adequately. An infection of the membrane covering the brain (meningitis) or an inflammation of the brain itself (encephalitis) cause swelling that in turn may cause brain damage and mental retardation. Traumatic brain injury caused by a blow or a violent shake to the head may also cause brain damage and mental retardation in children.

Environmental factors

Ignored or neglected infants who are not provided the mental and physical stimulation required for normal development may suffer irreversible learning impairments. Children who live in poverty and suffer from **malnutrition**, unhealthy living conditions, and improper or inadequate medical care are at a higher risk. Exposure to lead can also cause mental retardation. Many children have developed **lead poisoning** by eating the flaking lead-based paint often found in older buildings.

Diagnosis

If mental retardation is suspected, a comprehensive **physical examination** and medical history should be done immediately to discover any organic cause of symptoms. Conditions such as hyperthyroidism and PKU are treatable. If these conditions are discovered early, the progression of retardation can be stopped and, in some cases, partially reversed. If a neurological cause such as brain injury is suspected, the child may be referred to a neurologist or neuropsychologist for testing.

A complete medical, family, social, and educational history is compiled from existing medical and school records (if applicable) and from interviews with parents. Children are given intelligence tests to measure their learning abilities and intellectual functioning. Such tests include the Stanford-Binet Intelligence Scale, the Wechsler Intelligence Scales, the Wechsler Preschool and Primary Scale of Intelligence, and the Kaufmann Assessment Battery for Children. For infants, the Bayley Scales of Infant Development may be used to assess motor, language, and problem-solving skills. Interviews with parents or other caregivers are used to assess the child's daily living, muscle control, communication, and social skills. The Woodcock-Johnson Scales of Independent Behavior and the Vineland Adaptive Behavior Scale (VABS) are frequently used to test these skills.

KEY TERMS

Amniocentesis—A test usually done between 16 and 20 weeks of pregnancy to detect any abnormalities in the development of the fetus. A small amount of the fluid surrounding the fetus (amniotic fluid) is drawn out through a needle inserted into the mother's womb. Laboratory analysis of this fluid can detect various genetic defects, such as Down syndrome, or neural tube defects.

Developmental delay—The failure to meet certain developmental milestones, such as sitting, walking, and talking, at the average age. Developmental delay may indicate a problem in development of the central nervous system.

Down syndrome—A disorder caused by an abnormality at the 21st chromosome. One symptom of Down syndrome is mental retardation.

Extensive support—Ongoing daily support required to assist an individual in a specific adaptive area, such as daily help with preparing meals.

Hib disease—An infection caused by *Haemophilus influenza* type b (Hib). This disease mainly affects children under the age of five. In that age group, it is the leading cause of bacterial meningitis, pneumonia, joint and bone infections, and throat inflammations.

Inborn error of metabolism—A rare enzyme deficiency; children with inborn errors of metabolism do not have certain enzymes that the body requires to maintain organ functions. Inborn errors of metabolism can cause brain damage and mental retardation if left untreated. Phenylketonuria is an inborn error of metabolism.

Limited support—A predetermined period of assistance required to deal with a specific event, such as training for a new job.

Phenylketonuria (PKU)—An inborn error in metabolism that prevents the body from using phenylalanine, an amino acid necessary for normal growth and development.

Trisomy—An abnormality in chromosomal development. Chromosomes are the structures within a cell that carry its genetic information. They are organized in pairs. Humans have 23 pairs of chromosomes. In a trisomy syndrome, an extra chromosome is present so that the individual has three of a particular chromosome instead of the normal pair. An extra chromosome 18 (trisomy 18) causes mental retardation.

Ultrasonography—A process that uses the reflection of high-frequency sound waves to make an image of structures deep within the body. Ultrasonography is routinely used to detect fetal abnormalities.

Treatment

Federal legislation entitles mentally retarded children to free testing and appropriate, individualized education and skills training within the school system from ages 3–21. For children under the age of three, many states have established early intervention programs that assess, recommend, and begin treatment programs. Many day schools are available to help train retarded children in basic skills such as bathing and feeding themselves. Extracurricular activities and social programs are also important in helping retarded children and adolescents gain self-esteem.

Training in independent living and job skills is often begun in early adulthood. The level of training depends on the degree of retardation. Mildly retarded individuals can often acquire the skills needed to live independently and hold an outside job. Moderate to profoundly retarded individuals usually require supervised community living.

Family therapy can help relatives of the mentally retarded develop coping skills. It can also help parents deal with feelings of guilt or anger. A supportive, warm home environment is essential to help the mentally retarded reach their full potential.

Prognosis

Individuals with mild to moderate mental retardation are frequently able to achieve some self-sufficiency and to lead happy and fulfilling lives. To reach these goals, they need appropriate and consistent educational, community, social, family, and vocational supports. The outlook is less promising for those with severe to profound retardation. Studies have shown that these individuals have a shortened life expectancy. The diseases that are usually associated with severe retardation may cause the shorter life span. People with Down syndrome will develop the brain changes that characterize **Alzheimer's disease** in later life and may develop the clinical symptoms of this disease as well.

Prevention

Immunization against diseases such as measles and Hib prevents many of the illnesses that can cause mental retardation. In addition, all children should undergo routine developmental screening as part of their pediatric care. Screening is particularly critical for those children who may be neglected or undernourished or may live in disease-producing conditions. Newborn screening and immediate treatment for PKU and hyperthyroidism can usually catch these disorders early enough to prevent retardation.

Good prenatal care can also help prevent retardation. Pregnant women should be educated about the risks of drinking and the need to maintain good **nutrition** during pregnancy. Tests such as **amniocentesis** and ultrasonography can determine whether a fetus is developing normally in the womb.

Resources

OTHER

Americans with Disabilities Act (ADA) Page. http://www.usdoj.gov/crt/ada/adahom1.htm.

ORGANIZATIONS

American Association on Intellectual and Developmental Disabilities, 501 3rd Street, NW Suite 200, Washington, DC, 20001, (202) 387-1968, (202) 387-2193, (800) 424-3688, http://www.aamr.org.

The Arc, 1660 L Street, NW, Suite 301, Washington, DC, 20036, (202) 534-3700, (202) 534-3731, (800) 433-5255, info@thearc.org, http://www.thearc.org.

Paula Anne Ford-Martin

Mental status examination

Definition

A mental status examination (MSE) is an assessment of a patient's level of cognitive (knowledge-related) ability, appearance, emotional mood, and speech and thought patterns at the time of evaluation. It is one part of a full neurologic (nervous system) examination and includes the examiner's observations about the patient's attitude and cooperativeness as well as the patient's answers to specific questions. The most commonly used test of cognitive functioning per se is the so-called Folstein Mini-Mental Status Examination (MMSE), developed in 1975.

Purpose

The purpose of a mental status examination is to assess the presence and extent of a person's mental impairment. The cognitive functions that are measured during the MSE include the person's sense of time, place, and personal identity; memory; speech; general intellectual level; mathematical ability; insight or judgment; and reasoning or problem-solving ability. Complete MSEs are most commonly given to elderly people and to other patients being evaluated for **dementia** (including AIDS-related dementia). Dementia is an overall decline in a person's intellectual function—including difficulties with language, simple calculations, planning or decision-making, and motor (muscular movement) skills as well as loss of memory. The MSE is an important part of the differential diagnosis of dementia and other psychiatric symptoms or disorders. The MSE results may suggest specific areas for further testing or specific types of required tests. A mental status examination can also be given repeatedly to monitor or document changes in a patient's condition.

Precautions

The MSE cannot be given to a patient who cannot pay attention to the examiner, for example as a result of being in a **coma** or unconscious; or is completely unable to speak (aphasic); or is not fluent in the language of the examiner.

Description

The MMSE of Folstein evaluates five areas of mental status, namely, orientation, registration, attention and calculation, recall, and language. A complete MSE is more comprehensive and evaluates the following ten areas of functioning:

- Appearance. The examiner notes the person's age, race, sex, civil status, and overall appearance. These features are significant because poor personal hygiene or grooming may reflect a loss of interest in self-care or physical inability to bathe or dress oneself.
- Movement and behavior. The examiner observes the person's gait (manner of walking), posture, coordination, eye contact, facial expressions, and similar behaviors. Problems with walking or coordination may reflect a disorder of the central nervous system.
- Affect. Affect refers to a person's outwardly observable emotional reactions. It may include either a lack of emotional response to an event or an overreaction.
- Mood. Mood refers to the underlying emotional "atmosphere" or tone of the person's answers.

- Speech. The examiner evaluates the volume of the person's voice, the rate or speed of speech, the length of answers to questions, the appropriateness and clarity of the answers, and similar characteristics.
- Thought content. The examiner assesses what the patient is saying for indications of hallucinations, delusions, obsessions, symptoms of dissociation, or thoughts of suicide. Dissociation refers to the splitting-off of certain memories or mental processes from conscious awareness. Dissociative symptoms include feelings of unreality, depersonalization, and confusion about one's identity.
- Thought process. Thought process refers to the logical connections between thoughts and their relevance to the main thread of conversation. Irrelevant detail, repeated words and phrases, interrupted thinking (thought blocking), and loose, illogical connections between thoughts, may be signs of a thought disorder.
- Cognition. Cognition refers to the act or condition of knowing. The evaluation assesses the person's orientation (ability to locate himself or herself) with regard to time, place, and personal identity; long- and short-term memory; ability to perform simple arithmetic (counting backward by threes or sevens); general intellectual level or fund of knowledge (identifying the last five presidents, or similar questions); ability to think abstractly (explaining a proverb); ability to name specified objects and read or write complete sentences; ability to understand and perform a task (showing the examiner how to comb one's hair or throw a ball); ability to draw a simple map or copy a design or geometrical figure; ability to distinguish between right and left.
- Judgment. The examiner asks the person what he or she would do about a commonsense problem, such as running out of a prescription medication.
- Insight. Insight refers to a person's ability to recognize a problem and understand its nature and severity.

The length of time required for a mental status examination depends on the patient's condition. It may take as little as five minutes to examine a healthy person. Patients with speech problems or intellectual impairments, dementia, or other organic brain disorders may require fifteen or twenty minutes. The examiner may choose to spend more time on certain portions of the MSE and less time on others, depending on the patient's condition and answers.

Preparation

Preparation for a mental status examination includes a careful medical and psychiatric history of the patient. The history helps the examiner to interpret the patient's appearance and answers with greater accuracy, because some physical illnesses may produce psychiatric symptoms or require medications that influence the patient's mood or attentiveness. The psychiatric history should include a family history as well as the patient's personal history of development, behavior patterns, and previous treatment for mental disorders (if any). Symptoms of dissociation, for example, often point to a history of childhood **abuse**, **rape**, or other severe emotional traumas in adult life. The examiner should also include information about the patient's occupation, level of education, marital status, and right- or left-handedness. Information about occupation and education helps in evaluating the patient's use of language, extent of **memory loss**, reasoning ability, and similar functions. Handedness is important in determining which half of the patient's brain is involved in writing, picking up a pencil, or other similar tasks that he or she may be asked to perform during the examination.

Aftercare

Depending on the examiner's specific observations, the patient may be given additional tests for follow-up. These tests might include blood or urine samples to test for drug or alcohol abuse, anemia, diabetes, disorders of the liver or kidneys, vitamin or thyroid deficiencies, medication side effects, or **syphilis** and **AIDS**. Brain imaging (CT, MRI, or **PET** scans) may be used to look for signs of seizures, strokes, head trauma, brain tumors, or other evidence of damage to specific parts of the brain. A spinal tap may be performed if the doctor thinks the patient may have an infection of the central nervous system.

Normal results

Normal results for a mental status examination depend to some extent on the patient's history, level of education, and recent life events. For example, a depressed mood is appropriate in the context of a recent **death** or other sad event in the patient's family but inappropriate in the context of a recent pay raise. Speech patterns are often influenced by racial or ethnic background as well as by occupation or schooling. In general, however, the absence of obvious **delusions**, **hallucinations**, or thought disorders together with the presence of insight, good judgment, and socially appropriate appearance and behavior are considered normal results. A normal numerical score for the MMSE is between 28 and 30.

Abnormal results

Abnormal results for a mental status examination include:

KEY TERMS

Aphasia—The loss of the ability to speak, or to understand written or spoken language. A person who cannot speak or understand language is said to be aphasic.

Cognition—The act or process of knowing or perceiving.

Coma—A state of prolonged unconsciousness in which a person cannot respond to spoken commands or mildly painful physical stimuli.

Delusion—A belief that is resistant to reason or contrary to actual fact. Common delusions include delusions of persecution, delusions about one's importance (sometimes called delusions of grandeur), or delusions of being controlled by others.

Dementia—A decline in a person's level of intellectual functioning. Dementia includes memory loss as well as difficulties with language, simple calculations, planning or decision-making, and motor (muscular movement) skills.

Dissociation—The splitting off of certain mental processes from conscious awareness. Specific symptoms of dissociation include feelings of unreality, depersonalization, and confusion about one's identity.

Hallucination—A sensory experience, usually involving either sight or hearing, of something that does not exist outside the mind.

Illusion—A false visual perception of an object that others perceive correctly. A common example is the number of sightings of "UFOs" that turn out to be airplanes or weather balloons.

Obsession—Domination of thoughts or feelings by a persistent idea, desire, or image.

Organic brain disorder—An organic brain disorder refers to impaired brain function due to damage or deterioration of brain tissue.

- Any evidence of organic brain damage.
- Evidence of thought disorders.
- A mood or affect that is clearly inappropriate to its context.
- Thoughts of suicide.
- Disturbed speech patterns.
- Dissociative symptoms.
- Delusions or hallucinations.

A score below 27 on the MMSE usually indicates an organic brain disorder.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

McPhee, Stephen, and Maxine Papadakis. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw-Hill Medical, 2009.

Rebecca J. Frey, PhD

Mercury poisoning

Definition

Mercury **poisoning** is exposure to harmful amounts of the toxic element, usually by breathing mercury vapors or ingesting compounds containing mercury. Mercury poisoning can permanently damage the nervous system and immune system, as well as the brain, lungs, kidneys, heart, and liver. High–level exposure can be fatal. Developing fetuses are particularly sensitive to mercury poisoning.

Demographics

The prevalence of mercury poisoning in American children is hotly debated, but is generally considered to be rare. Fish and shellfish contaminated with methylmercury are the major sources of mercury poisoning in the United States and around the world. A 2009 study by the U.S. Centers for Disease Control and Prevention (CDC) on the exposure of children to elemental mercury found that the largest releases exposing the most children were caused by children stealing mercury from a school or industrial site. The vast majority of elemental exposures:

- were minimal or nontoxic
- occurred in homes or schools
- involved broken thermometers

Description

Mercury (Hg) is a naturally occurring element in air, water, and soil. There are three forms of mercury that pose different potential health hazards:

- Elemental or metallic mercury, also called quicksilver, is a shiny, silvery metal that is a liquid at room

Safe tuna consumption

If you weigh:	Don't eat more than one can of tuna every: White Albacore	Chunk light
20 lbs	10 weeks	3 weeks
30 lbs	6 weeks	2 weeks
40 lbs	5 weeks	11 days
50 lbs	4 weeks	9 days
60 lbs	3 weeks	7 days
70 lbs	3 weeks	6 days
80 lbs	2 weeks	6 days
90 lbs	2 weeks	5 days
100 lbs	2 weeks	5 days
110 lbs	12 days	4 days
120 lbs	11 days	4 days
130 lbs	10 days	4 days
140 lbs	10 days	3 days
150+ lbs	9 days	3 days

SOURCE: Food and Drug Administration test results for mercury and fish, and the Environmental Protection Agency's determination of safe levels of mercury. Accessed from the Natural Resources Defense Council's "Eating Tuna Safely," available online at: http://www.nrdc.org/health/effects/mercury/tuna.asp (September 20, 2010).

Safe tuna consumption by weight, based on mercury levels. *(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)*

temperature, but is easily vaporized to a colorless, odorless gas that can be inhaled. Elemental mercury is released into the air by natural processes such as volcanic activity and by various industrial processes, especially coal–burning power plants. It is extremely poisonous and 79–80% of inhaled mercury vapor is absorbed by the lungs. In the past, mercury vapors poisoned hat makers—hence the Mad Hatter of *Alice in Wonderland*. Elemental mercury is used in thermometers, compact fluorescent light bulbs (CFLs), electrical switches, and older–type dental fillings.

- Inorganic mercury compounds include mercuric oxide (HgO) and mercuric salts, such as mercuric chloride ($HgCl_2$). These compounds are usually white powders or crystals. Inorganic mercury is used in many industries and can be found in some skin ointments and creams, disinfectants, fungicides, folk medicines, red cinnabar pigment, and button batteries that power small electronics.
- Organic mercury compounds are carbon–containing substances, such as methylmercury, ethylmercury, and phenylmercury. Bacteria in soil and water convert inorganic mercury in the environment into methylmercury, which accumulates in fish. Larger and older fish generally have the highest levels of methylmercury. In some parts of the world, organic mercury is used as an antifungal agent in seed grain fed to animals. It is also found in older antiseptics and in some medical preservatives, including trace amounts of thimerosal in some childhood vaccines.

Because the body cannot easily rid itself of mercury, repeated exposure result in its build up in tissues. Elemental mercury vapor and methylmercury are the most dangerous forms because they readily reach the brain. Most humans have trace amounts of methylmercury in their bodies. Methylmercury crosses the placenta to the developing fetus, whose red blood cells can have mercury concentrations that are 30% higher than those of the mother. It also passes to the newborn child through breast milk. Fetuses, infants, and young children are significantly more sensitive to the effects of mercury than adults. During the 1950s, large amounts of organic mercury were dumped in Japan's Minamata Bay, killing some 1,000 people and causing severe nervous system damage in unborn children. Thus mercury poisoning is sometimes called fetal Minamata Bay disease. Mercury poisonings have also occurred from eating meat from animals fed contaminated grain.

Risk factors

The major risk factor for mercury poisoning in children is the consumption of large amounts of contaminated fish and shellfish. Children who play with found or spilled mercury are also at risk.

Causes and symptoms

The most common cause of mercury poisoning is eating fish and shellfish contaminated with high levels of methylmercury. Less common causes of mercury poisoning include:

- inhalation of vapors from spills, breakage of mercury–containing devices, off–gassing from polyurethane flooring containing a mercury catalyst, or mercury accumulation in poorly ventilated buildings
- breathing contaminated air from incinerators or industry
- inadequate remediation of toxic sites
- mercury used in cultural rituals or ceremonies
- mercury tracked home from workplaces
- mercury–based amalgams in dental fillings
- swallowing or inhaling mercury–containing batteries or their components
- direct skin contact with the element or its compounds

The same level of mercury vapor can result in higher mercury concentrations in children than in adults, because children have larger lung surface

Mercury levels in fish

Least mercury

Anchovies
Butterfish
Catfish
Clam
Crab (Domestic)
Crawfish/Crayfish
Croaker (Atlantic)
Flounder
Haddock (Atlantic)
Hake
Herring
Mackerel (N. Atlantic, Chub)
Mullet
Oyster
Perch (Ocean)
Plaice
Pollock
Salmon (Canned)
Salmon (Fresh)
Sardine
Scallop
Shad (American)
Shrimp
Sole (Pacific)
Squid (Calamari)
Tilapia
Trout (Freshwater)
Whitefish
Whiting

Moderate mercury

Bass (Striped, Black)
Carp
Cod (Alaskan)
Croaker (White Pacific)
Halibut (Atlantic)
Halibut (Pacific)
Jacksmelt (Silverside)
Lobster
Mahi Mahi
Monkfish
Perch (Freshwater)
Sablefish
Skate
Snapper
Tuna (Canned chunk light)
Tuna (Skipjack)
Weakfish (Sea Trout)

High mercury

Bluefish
Grouper
Mackerel (Spanish, Gulf)
Sea bass (Chilean)
Tuna (Canned Albacore)
Tuna (Yellowfin)

Highest mercury

Mackerel (King)
Marlin
Orange roughy
Shark
Swordfish
Tilefish
Tuna (Bigeye, Ahi)

Least mercury: Less than 0.09 parts per million (ppm)
Moderate mercury: 0.09–0.29 ppm; safe to eat six or less servings each month
High mercury: 0.3–0.49 ppm, safe to eat three or less servings each month
Highest mercury: More than 0.5 ppm; avoid eating

SOURCE: Food and Drug Administration test results for mercury and fish, and the Environmental Protection Agency's determination of safe levels of mercury. Accessed from the Natural Resources Defense Council's "Consumer Guide to Mercury in Fish," available online at: http://www.nrdc.org/health/effects/mercury/guide.asp (September 20, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

areas for their body weight. Furthermore, since mercury vapors are more dense than air, there are higher levels closer to the ground where children breathe in the vapors. Although elemental mercury vapor is only slowly absorbed through the skin, it can irritate the skin and eyes and cause **contact dermatitis**. Touching or swallowing elemental liquid mercury is usually not harmful because it rolls off the skin and very little is absorbed by the gastrointestinal tract.

The effects of mercury exposure depend on a variety of factors including the:

- form of mercury
- dose
- route of exposure—inhaled, ingested, or skin contact
- child's age, with fetuses and very young children being most susceptible
- child's health

Symptoms of elemental mercury poisoning appear within a few hours of exposure to high levels of vapor. Smaller amounts inhaled daily cause symptoms that develop over time. Symptoms can include:

- a metallic taste
- swollen, bleeding gums
- skin rashes
- eye irritation
- respiratory symptoms, especially in children, including severe coughing, shortness of breath, or difficulty breathing
- gastrointestinal symptoms, including nausea, vomiting, and diarrhea
- fever and chills
- high blood pressure or heart rate
- headaches
- neuromuscular symptoms, such as weakness, twitching, tremors, muscle atrophy, and impaired nerve responses
- emotional effects, such as mood swings, irritability, nervousness, or excessive shyness
- insomnia
- disturbed sensations
- cognitive impairment
- with high exposure, kidney impairment, respiratory failure, and death

Unlike elemental mercury, inorganic and organic mercury are absorbed through the intestinal tract, although a swallowed battery may pass harmlessly through a child. Symptoms of inorganic mercury poisoning include:

- skin rashes and dermatitis
- metallic taste
- drooling
- mouth lesions, severe mouth pain, and throat swelling
- severe abdominal pain
- vomiting
- bloody diarrhea
- decreased or absent urination
- severe breathing difficulty
- muscle weakness

- mood swings
- memory loss
- mental disturbances
- shock
- kidney failure
- death

Methylmercury can interfere with the neurological development of fetuses, infants, and children, causing:

- cerebral palsy
- brain damage and mental retardation
- language deficits
- attention deficits
- poor coordination
- growth retardation
- blindness
- seizures
- microcephaly (small head)

Symptoms of organic mercury poisoning most often develop over years or decades and include:

- "pins and needles" in the hands and feet and around the mouth
- numbness or pain on the skin
- poor coordination
- tremors
- muscle weakness
- impaired vision or blindness
- impaired speech and hearing
- impaired memory
- seizures and death with high–level exposure

KEY TERMS

Button batteries—Tiny, round batteries containing mercuric chloride that power items such as watches, hearing aids, calculators, cameras, and penlights.

Cerebral palsy—Brain damage before, during, or just after birth that results in lack of muscle coordination and problems with speech.

Chelators—Various compounds that bind to metals such as mercury.

Contact dermatitis—Skin inflammation from contact with an allergen or other irritating substance.

Elemental mercury; Hg—Metallic mercury; quicksilver; a heavy, silvery, poisonous metallic element that is a liquid at room temperature but vaporizes readily.

Inorganic mercury—Inorganic compounds such as mercuric oxide (HgO) and mercuric chloride ($HgCl_2$).

Mercuric chloride; mercury(II) chloride; $HgCl_2$—A poisonous crystalline form of inorganic mercury that is used as a disinfectant and fungicide.

Methylmercury—Any of various toxic compounds containing the organic grouping CH_3Hg. These compounds occur as industrial byproducts and pesticide residues, accumulate in fish and other organisms, especially those high on the food chain, and are rapidly absorbed through the human intestine to cause neurological disorders such as Minamata disease.

Organic mercury—Poisonous compounds containing mercury and carbon, such as methylmercury, ethylmercury, and phenylmercury.

Thimerosal—A crystalline organic mercury compound used as an antifungal and antibacterial agent and present in very small amounts in some vaccines.

Diagnosis

Examination

The child's vital signs—including temperature, pulse, breathing rate, and blood pressure—will be monitored. Important diagnostic information includes:

- the type and amount of exposure
- the time and duration of exposure
- the name of the product and its ingredients and strength

Tests

Blood or urine samples can be tested for exposure to elemental and inorganic mercury. Exposure to methylmercury is measured in whole blood or scalp hair. Mercury levels are often expressed as parts per million (ppm). For example, 1 ppm mercury in hair is equal to 1 milligram (mg) per kilogram (kg) of hair. The average mercury level in the hair of unaffected people is 2 ppm. Blood and urine tests may also be used to detect kidney damage from mercury poisoning.

Procedures

- For swallowed inorganic mercury, an endoscope—a flexible instrument with a camera—may be inserted through the throat to look for burns in the esophagus or stomach.

- X rays are taken immediately to locate swallowed batteries and monitor their passing through the gastrointestinal tract.
- X rays may be taken to diagnose lung or kidney damage.

Treatment

Traditional

Although inhaled elemental mercury poisoning can be difficult to treat, possibilities include:

- humidified oxygen or air
- a breathing tube inserted in the lungs
- suctioning mercury out of the lungs

Inorganic mercury poisoning is treated with supportive measures, including possibly intravenous fluids and electrolytes.

- Swallowed mercuric oxide may be treated by gastric lavage, in which a tube is inserted through the mouth to wash out the stomach.
- Swallowed mercuric chloride may be treated by making the child vomit.
- Endoscopy may be used to remove a swallowed battery from the esophagus or stomach.
- An inhaled battery is removed immediately from the larynx with a laryngoscope or from the lungs with a bronchoscope or by surgery.

Treatment for methylmercury poisoning depends on the severity and is similar to treatments for **cerebral palsy**. It may include fluids and electrolytes and **kidney dialysis**.

Drugs

Chelators—drugs that bind mercury and other heavy metals—may be required for weeks or months to remove mercury from the blood and protect the kidneys and brain. Other medications to treat mercury poisoning include:

- activated charcoal to absorb swallowed mercury in the stomach
- drugs to induce vomiting for mercuric chloride poisoning
- laxatives for mercuric oxide or mercuric chloride poisoning
- medications to treat symptoms

Alternative

There are various alternative types of **chelation therapy**. These include bentonite clay baths and combinations of herbs, amino acids, and other **nutritional supplements**.

Home remedies

Mercury poisoning should be treated by immediately removing the child from the source of exposure, if possible. The U.S. National Poison Control Center should be called for instructions: (800) 222–1222.

Prognosis

- A single low–level exposure to elemental mercury does not usually require treatment and is unlikely to have long–term effects.
- Untreated mercury poisoning can eventually cause pain, muscle weakness, vision loss, paralysis, or death.
- Severe elemental mercury poisoning can cause long–term damage to the lungs, kidneys, and central nervous system, including brain damage. Very large exposures are usually fatal.
- Swallowed batteries usually pass through the gastrointestinal tract without causing serious damage; however the prognosis depends on the type of battery and how quickly the condition is treated.
- Severe inorganic mercury poisoning can cause massive blood and fluid loss, kidney failure, and probable death.
- Mercuric chloride is very toxic and even small swallowed doses can cause kidney failure and death. The prognosis depends on the amount of mercury, the symptoms within the first 10–15 minutes, and how quickly the poisoning is treated. Poisoning that occurs slowly over time may result in permanent brain damage.
- Mercuric oxide poisoning also can lead to organ failure and death.
- Damage from methylmercury is irreversible, although the symptoms do not usually worsen without additional exposure. Chronic brain damage from organic mercury poisoning is hard to treat and some children never recover. Methylmercury poisoning may also increase the risk for heart attacks.
- Both mercuric chloride and methylmercury are considered possible carcinogens.

Prevention

The U.S. Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) recommend that young children and women who are pregnant, may become pregnant, or are nursing:

- not eat swordfish, shark, king mackerel, or tilefish, all of which have high mercury levels
- eat up to 12 ounces (340 grams or two average portions) per week of a variety of low–mercury fish and shellfish, such as shrimp, canned light tuna, salmon, pollock, catfish, fish sticks, or fast–food fish
- eat no more than six ounces (170 grams) per week of albacore ("white") tuna steak, which has higher levels of mercury
- check local advisories for fish caught by family and friends in local waters
- eat no more than six ounces (170 grams) per week of noncommercially caught fish from local waters if no advisories are available, and eat no other fish during the week
- feed young children smaller portions of fish

Other preventions for mercury poisoning include:

- teaching children never to touch mercury or any shiny, silver liquid
- carefully handling and properly disposing of mercury–containing products such as thermometers and fluorescent light bulbs
- following established procedures for mercury spills
- never vacuuming up spilled mercury, since this causes vaporization
- keeping children and pregnant women away from areas where liquid mercury is used
- contacting local health departments for large mercury spills

Resources

BOOKS

Groth, Edward. *Over the Limit: Eating Too Much High–Mercury Fish*. Montpelier, VT: Mercury Policy Project, 2008.

PERIODICALS

Brennan, Richard J. "Nightmare of Mercury Poisoning Returns." *Toronto Star* (April 6, 2010): A1.

Daley, Beth. "Mercury Leaks Found as New Bulbs Break; Energy Benefits of Fluorescents May Outweigh Risk." *Boston Globe* (February 26, 2008): B2.

Haggart, Kelly. "Mercury Research Bears Fruit in the Amazon." *Women & Environments International* no. 76/77 (Fall 2008): 5–8.

Philibert, Aline, Maryse Bouchard, and Donna Mergler. "Neuropsychiatric Symptoms, Omega–3, and Mercury Exposure in Freshwater Fish–Eaters." *Archives of Environmental & Occupational Health* 63(3) (Fall 2008): 143–53.

OTHER

Agency for Toxic Substances and Disease Registry. "ToxFAQs for Mercury." ToxFAQs. (February 18, 2010). http://www.atsdr.cdc.gov/tfacts46.html (accessed September 27, 2010).

Besser, Richard E. "Children's Exposure to Elemental Mercury: A National Review of Exposure Events." Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention, Mercury Workgroup. (February 2009). http://www.atsdr.cdc.gov/mercury/docs/MercuryRTCFinal2013345.pdf (accessed September 27, 2010).

"Mercury." MedlinePlus. (July 6, 2010). http://www.nlm.nih.gov/medlineplus/mercury.html (accessed September 27, 2010).

"Mercury." National Toxicology Program Center for the Evaluation of Risks to Human Reproduction. (July 9, 2010). http://cerhr.niehs.nih.gov/common/mercury.html (accessed September 27, 2010).

"Mercury." U.S. Environmental Protection Agency. (June 25, 2010). http://www.epa.gov/mercury/index.html (accessed September 27, 2010).

"Mercury and Your Health." Agency for Toxic Substances and Disease Registry. (January 22, 2010). http://www.atsdr.cdc.gov/mercury (accessed September 27, 2010).

U.S. Food and Drug Administration. U.S. Environmental Protection Agency. "What You Need to Know about Mercury in Fish and Shellfish." U.S. Food and Drug Administration. http://www.fda.gov/downloads/Food/ResourcesForYou/Consumers/UCM182158.pdf (accessed September 27, 2010).

ORGANIZATIONS

Agency for Toxic Substances and Disease Registry (ATSDR), 4770 Buford Hwy. NE, Atlanta, GA, 30341, (888) 422–8737; (800) 232–4636, (770) 488–4178, cdcinfo@cdc.gov, http://www.atsdr.cdc.gov.

National Institute of Neurological Disorders and Stroke (NINDS), NIH Neurological Institute, PO Box 5801, Bethesda, MD, 20824, (301) 496–5751, (800) 352–9424, http://www.ninds.nih.gov/index.htm.

U.S. Environmental Protection Agency (EPA), Ariel Rios Building, 1200 Pennsylvania Ave. NW, Washington, DC, 20460, http://www.epa.gov.

U.S. Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD, 20993–0002, (888) INFO–FDA, http://www.fda.gov.

Margaret Alic, PhD

Mesothelioma

Definition

Mesothelioma, also called malignant mesothelioma, is an uncommon disease that causes **cancer** cells to form within the lining of the chest, abdomen, or around the heart. Its primary cause is believed to be

exposure to asbestos. Malignant mesothelioma is also known as asbestos cancer or simply "meso."

Demographics

Mesothelioma remains relatively uncommon in the United States, with approximately 2,500–3,000 new cases reported annually. The incidence rates are much higher in Western Europe (over 5,000 cases reported annually). These numbers are expected to climb over the next 20 years because symptoms do not appear until 30–50 years after asbestos exposure. Older males (median age 60 at diagnosis) are three to five times more likely to develop mesothelioma than females. This is most like because males predominance in those professions with an increased risk of asbestos exposure.

Description

Mesothelioma causes cancerous cells to develop in the body's mesothelium, where they can spread to and damage vital organs and tissue. These malignant cells can also metastasize (spread) to other sites in the body. Mesothelioma is very difficult to diagnose and responds poorly to most treatment modalities, resulting in a poor prognosis.

The disease derives its name from the mesothelium, a sac-like membrane that protects most of the body's internal organs. The mesothelium is divided into two distinct protective layers of cells: the visceral layer directly surrounding the organ and the parietal layer, a sac around the body cavity. By releasing a lubricating fluid, the mesothelium allows the organs to move more freely within the body cavity. (e.g., in the contraction and expansion of the lungs). The mesothelium also is referred to according to where it is located in the body: pleura (chest), peritoneum (abdomen), and pericardium (heart).

Over two-thirds of all mesothelioma cases begin in the pleura region. Pleural mesothelioma spreads through the chest cavity, occasionally developing in the lungs as well. The disease most commonly causes an excess build-up of fluid inside the chest cavity (**pleural effusion**). This excess fluid increases pressure on the lungs and restricts breathing. In addition, malignant cells can cause the pleural lining to thicken and restrict the breathing space even further.

Peritoneal mesothelioma is the second most common form of the disease, accounting for less than 30% of all cases. Malignant cells form in the peritoneum, affecting the abdomen, bowel, liver, and spleen. Similar to pleural mesothelioma, the peritoneal mesothelioma causes a build up of excess fluid in the abdominal cavity. Normal functions such as digestion can be hindered by the obstruction of organ movement.

Very rare forms of mesothelioma occur in the pericardium, as well as the mesothelium of the male and female reproductive organs. Cystic mesothelioma of the peritoneum, another rare form of the disease, occurs predominantly in women and is more benign in nature.

Malignant mesothelioma takes the form of one of three cell-types: epithelioid (50% to 70% of cases), sarcomatous (7% to 20% of cases), and biphasic/mixed (20% to 35% of cases). Of these cell-types, epithelioid mesothelioma carries the most favorable prognosis, followed by biphasic, and finally sarcomatous (very aggressive).

Causes and symptoms

Causes

Approximately 80% of all mesothelioma patients have a history of asbestos exposure. The majority of these patients were employed in an industry that involved the use of asbestos in some fashion. In addition to occupational exposure, household exposure of family members is not uncommon. An exposed individual can carry the asbestos particles on their clothing, skin, and in their hair when they return home, resulting in paraoccupational exposure. Even brief exposure to asbestos, as little as one to two months, can result in long-term consequences. Although the dangers of asbestos have been known for decades, the long latency period of mesothelioma (30–40 years) means that majority of patients were exposed as far back as the 1950s. Estimates suggest that up to eight million Americans have already been exposed. Workers who, in particular, show a higher incidence of asbestos exposure include:

- insulators (asbestos workers)
- boilermakers
- shipfitters
- steel workers
- maintenance workers
- plumbers
- brake mechanics

Exposure to asbestos most often causes the lose of one copy of chromosome 22. Other changes also appear in tumor suppressor genes. These genes regulate the growth and division of cells. In cancer, the regulatory mechanism malfunctions and cells grow wildly and form tumors.

Symptoms

Mesothelioma is very aggressive once it takes hold. However, its initial symptoms are generally non-specific in nature and/or mimic other conditions, such as persistent **pneumonia** or gastronomical disorders. Some patients will exhibit no symptoms at all. As such, proper evaluation and diagnosis are commonly delayed.

Patients with pleural mesothelioma most commonly exhibit signs of dyspnea, pleural effusions, and/or chest **pain**. The majority of pleural effusion symptoms will appear in the right lung (60% of the time). Patients also may have persistent **cough**, weight loss, weakness, **fever**, and difficulty swallowing (dysphagia).

Patients with peritoneal mesothelioma most commonly show signs of pain and/or swelling in the abdomen from fluid retention or tumor growth. Weight loss, **nausea**, bowel obstruction, anemia, fever, and swelling in the legs and/or feet are also known symptoms.

Diagnosis

Examination

Only a physician can properly diagnose mesothelioma. A review of the patient's medical history, including any past exposure to asbestos, should be conducted for any patient displaying dyspnea, chest pain, fluid build-up, or pain and/or swelling in the abdomen. This review may be followed with a complete **physical examination** that should involve the use of imaging techniques. X rays, computed tomography (CT) scans, and magnetic resonance (MRI) scans of the chest and/or abdomen, as well as lung function tests, provide the doctor with critical diagnostic information. Although **positron emission tomography** scans are expensive and may not be covered under most insurance, this diagnostic tool has proven very useful in determining tumor sites and staging of the disease.

Procedures

If indicated, the doctor may wish to internally examine the patient's chest and/or abdominal cavity. These diagnostic procedures, known as **thoracoscopy** (chest) and peritoneoscopy (abdomen), usually are conducted in a hospital setting. Both procedures involve a fiber-optic imaging tool being inserted into the patient through an incision. These endoscopic tools provide the doctor with a closer look at the body cavity and any abnormal tissue or fluid build-up found therein. Excess fluid can be suctioned out through a needle or tube in a process known as **thoracentesis** (for the chest) or **paracentesis** (for the abdomen). Additionally, the doctor may perform a biopsy of any abnormal tissue they discover during this time. Pathological examination of abnormal tissue, as well as fluid, remains the only effective method of confirming the diagnosis of mesothelioma. Biopsy will also assist the doctor in properly staging the disease's progression.

Cancer staging

Once a confirmation of malignant mesothelioma has been established, the doctor will conduct further tests to determine the extent to which the primary disease has spread. This diagnostic process is known as staging. Malignant pleural mesothelioma of can be broken into four stages:

- Localized Malignant Mesothelioma (Stage 1)—Cancer is present in the right or left pleura. May involve the lung, the pericardium, or diaphragm on that side.
- Advanced Malignant Mesothelioma (Stage 2)—Cancer has spread beyond the right or left pleura to lymph nodes on that side. May involve the lung, the pericardium, or diaphragm on that side.
- Advanced Malignant Mesothelioma (Stage 3)—Cancer has spread into the chest wall, diaphragm, ribs, heart, esophagus, or through the abdominal lining. Nearby lymph nodes may or may not be involved.
- Advanced Malignant Mesothelioma (Stage 4)—Cancer shows evidence of metastasis or spread through the bloodstream to distant organs and/or tissues.

Recurrent malignant mesothelioma may also develop, where the cancer returns in its original location or elsewhere in the body even after treatment.

Treatment

There are three traditional treatment modalities for mesothelioma: surgery, **radiation therapy**, and **chemotherapy**. The location and the stage of the disease, as well as the patient's age and health status, will determine which treatment is most appropriate. Modalities can be combined if indicated. Indeed, the multimodality approach appears to provide the most positive results for treating mesothelioma.

Surgery, the most common treatment, involves the removal of the tumor. In the early stages of mesothelioma, this usually involves removal of a section of the mesothelium and surrounding tissue, but may require removing part of the diaphragm as well. For more advanced stages of the disease, removing the entire lung (a procedure known as **pneumonectomy**) may be the only option.

Radiation therapy, also known as radiotherapy, destroys and shrinks the cancer cells through various

types of radiation. Both external (from a machine) and internal (such direct application of as radioisotopes) radiation therapies can be used to treat malignant mesothelioma.

Finally, chemotherapy, a systemic treatment modality, uses **anticancer drugs** to destroy the cancerous cells throughout the body. The majority of drugs used to treat mesothelioma are delivered intravenously. The effectiveness of intracavitary chemotherapy, the process of directly injecting the drugs into the chest or abdominal cavity, is being studied.

Pain and other symptoms caused by fluid build-up around the chest and/or abdomen can be treated by draining excess fluid through a needle or tube. These procedures are known as thoracentesis (chest) and paracentesis (abdomen). Drugs, radiotherapy, and surgery can also relieve or prevent further fluid accumulation.

Physicians are currently studying other treatment modalities, such as immunotherapy, **gene therapy**, and intraoperative **photodynamic therapy**. Individuals with mesothelioma who wish to participate in a clinical trial of an experimental therapy can find a list of clinical trials at http://clinicaltrials.gov. There is no cost to the patient to participate in a clinical trial.

Alternative and Complementary treatment

Nutritional issues are common in patients with cancer. The cancer causes some problems with diet and **nutrition**, while others are related to treatment or medication side effects. Maintaining adequate food intake and balanced nutrition in patients with lung cancer is important. A dietitian who specializes in cancer patients can suggest ways to maintain nutrition during treatment.

Although alternative practitioners may offer remedies for "curing" cancer, there is no known way to rid the body of cancer cells. Turning to unproven alternative remedies may be tempting as health declines, but this is unlikely to be helpful and may interfere with beneficial traditional therapy. Responsible alternative medicine practitioners view cancer as a holistic problem and strive to strengthen and support the physical, mental, and spiritual aspects of patients. Alternative practices that support psychological and spiritual health often prove beneficial to improving the quality of life of the individual with cancer. Techniques to reduce **stress**, such as **acupuncture**, **aromatherapy**, massage, and **reflexology**, can provide addition benefit to the patient's sense of well-being.

Palliative care

Because mesothelioma is an aggressive cancer with a poor prognosis, **palliative care** may be the preferred or only option available to patients. This is particularly true for the advanced stages of the disease. By treating the symptoms rather than the disease itself, the goal of this approach is to improve quality of life rather than to extend life. Palliative care aims to relieve the patient's discomfort caused by dyspnea and pain. Chemotherapy, radiation, and/or surgical treatment as needed to control symptoms, in combination with effective management of pain and respiratory function, should form the basis of proper palliative care of patients with mesothelioma.

KEY TERMS

Asbestos—A naturally occurring mineral, utilized worldwide for its durability and heat resistant qualities. Extremely fibrous in nature, asbestos particles can easily enter the respiratory system and damage sensitive tissue. This damage can result in asbestosis, mesothelioma, and lung cancer.

Dyspnea—A difficulty in breathing or shortness of breath, typically associated with some form of heart or lung disease. Also known as air hunger.

Mesothelium—A membrane/sac that protects the body's major internal organs and allows them freedom of movement (for example, lung contractions). The mesothelium is comprised of several regions, including the abdominal cavity (peritoneum), the chest cavity (pleura), and pericardium (heart).

Palliative—Treatment and care whose goal is to relieve pain and improve quality of life when a cure is not possible.

Pleural effusion—An abnormal accumulation of fluid in the pleura, a fibrous membrane that lines the inside of the chest cavity and protects the lungs. This accumulation can cause shortness of breath, cough, and chest pain.

Prognosis

The stage, location, and cell-type is involved, as well as the patient's age and health status affect life expectancy. Even with aggressive treatment, the prognosis for mesothelioma patients is poor. Overall survival rate from time of diagnosis is about one year. Pleural mesothelioma offers a median survival time of approximately 16–17 months after initial symptoms. Prognosis for peritoneal mesothelioma is poorer and has a median survival time of only ten months after initial symptoms. The more advanced stages of

mesothelioma may offer as little as four or five months of survival time.

The survival time for patients with localized mesothelioma can be extended several months with aggressive therapy, with roughly 20% of patients surviving past the five-year mark. Therapy programs recently developed at leading cancer centers have extended this survival time even further. In 2010, the five-year survival rate for patients with mesothelioma was 10%. Low as this number is, it represents an improvement over earlier survival times.

Prevention

Avoiding asbestos exposure or taking protective measures if exposure is unavoidable is the best way to prevent mesothelioma. Unfortunately, because of the significant delay between exposure and onset (30–50 years), it is probably too late to prevent the development of mesothelioma for most patients. Not **smoking** may slow the disease's progression and/or prevent other further complications associated with asbestos exposure.

Resources

BOOKS

Pass, Harvey I. *100 Questions & Answers about Mesothelioma,* 2nd ed. Sudbury, MA: Jones and Bartlett Publishers, 2010.

OTHER

Malignant Mesothelioma. National Cancer Institute. August 19, 2009. http://www.cancer.gov/cancertopics/pdq/treatment/malignantmesothelioma/patient.

Mesothelioma. MedlinePlus. January 11, 2010. http://www.nlm.nih.gov/medlineplus/mesothelioma.html.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd., NE, Atlanta, GA, 30329, (404) 320-3333, (800) ACS-2345, http://www.cancer.org.

Mesothelioma Applied Research Foundation, PO Box 91840, Santa Barbara, CA, 93190-1840, (805) 563-8400, (805) 563-8411, http://www.curemeso.org/site/c.kkLUJ7MPKtH/b.3076109/k.FF9C/Mesothelioma_Applied_Research_Foundation.htm.

National Cancer Institute Public Inquires Office., 6116 Executive Boulevard, Room 3036A, Bethesda, MD, 20892-8322, (800) 4-CANCER. TTY (800) 332-8615, http://www.cancer.gov.

Jason Fryer
Tish Davidson, AM

Metabolic acidosis

Definition

Metabolic acidosis is a pH imbalance in which the body has accumulated too much acid and does not have enough bicarbonate to effectively neutralize the effects of the acid.

Description

Metabolic acidosis, as a disruption of the body's acid/base balance, can be a mild symptom brought on by a lack of insulin, a **starvation** diet, or a gastrointestinal disorder like **vomiting** and **diarrhea**. Metabolic acidosis can indicate a more serious problem with a major organ like the liver, heart, or kidneys. It can also be one of the first signs of **drug overdose** or **poisoning**.

Causes and symptoms

Metabolic acidosis occurs when the body has more acid than base in it. Chemists use the term "pH" to describe how acidic or basic a substance is. Based on a scale of 14, a pH of 7.0 is neutral. A pH below 7.0 is an acid; the lower the number, the stronger the acid. A pH above 7.0 is a base; the higher the number, the stronger the base. Blood pH is slightly basic (alkaline), with a normal range of 7.36-7.44.

Acid is a natural by-product of the breakdown of fats and other processes in the body; however, in some conditions, the body does not have enough bicarbonate, an acid neutralizer, to balance the acids produced. This can occur when the body uses fats for energy instead of carbohydrates. Conditions where metabolic acidosis can occur include chronic **alcoholism**, **malnutrition**, and **diabetic ketoacidosis**. Consuming a diet low in carbohydrates and high in fats can also produce metabolic acidosis. The disorder may also be a symptom of another condition like kidney failure, liver failure, or severe diarrhea. The build up of lactic acid in the blood due to such conditions as **heart failure**, **shock**, or **cancer**, induces metabolic acidosis. Some poisonings and overdoses (**aspirin**, methanol, or ethylene glycol) also produce symptoms of metabolic acidosis.

In mild cases of metabolic acidosis, symptoms include **headache**, lack of energy, and sleepiness. Breathing may become fast and shallow. **Nausea**, **vomiting**, diarrhea, **dehydration**, and loss of appetite are also associated with metabolic acidosis. Diabetic patients with symptoms of metabolic acidosis may also have breath that smells fruity. The patient may lose consciousness or become disoriented. Severe cases can produce **coma** and **death**.

KEY TERMS

Diabetic ketoacidosis—A condition caused by low insulin levels where the amount of sugar and ketones in the blood is high.

pH—A measurement of the acidity or alkalinity of a solution based on the amount of hydrogen ions available. Based on a scale of 14, a pH of 7.0 is neutral. A pH below 7.0 is an acid; the lower the number, the stronger the acid. A pH above 7.0 is a base; the higher the number, the stronger the base. Blood pH is slightly alkaline (basic) with a normal range of 7.36-7.44.

Diagnosis

Metabolic acidosis is suspected based on symptoms, but is usually confirmed by laboratory tests on blood and urine samples. Blood pH below 7.35 confirms the condition. Levels of other blood components, including potassium, glucose, ketones, or lactic acid, may also be above normal ranges. The level of bicarbonate in the blood will be low, usually less than 22 mEq/L. Urine pH may fall below 4.5 in metabolic acidosis.

Treatment

Treatment focuses first on correcting the acid imbalance. Usually, **sodium** bicarbonate and fluids will be injected into the blood through a vein. An intravenous line may be started to administer fluids and allow for the quick injection of other drugs that may be needed. If the patient is diabetic, insulin may be administered. Drugs to regulate blood pressure or heart rate, to prevent seizures, or to control **nausea and vomiting** might be given. Vital signs like pulse, respiration, blood pressure, and body temperature will be monitored. The underlying cause of the metabolic acidosis must also be diagnosed and corrected.

Prognosis

If the metabolic acidosis is recognized and treated promptly, the patient may have no long-term complications, however, the underlying condition that caused the acidosis needs to be corrected or managed. Severe metabolic acidosis that is left untreated will lead to coma and death.

Prevention

Diabetic patients need to routinely test their urine for sugar and acetone, strictly follow their appropriate diet, and take any medications or insulin to prevent metabolic acidosis. Patients receiving **tube feedings** or intravenous feedings must be monitored to prevent dehydration or the accumulation of ketones or lactic acid.

Resources

BOOKS

Schrier, Robert W. *Renal and Electrolyte Disorders*. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2010.

Altha Roberts Edgren

Metabolic alkalosis

Definition

Metabolic alkalosis is a pH imbalance in which the body has accumulated too much of an alkaline substance, such as bicarbonate, and does not have enough acid to effectively neutralize the effects of the alkali.

Description

Metabolic alkalosis, as a disturbance of the body's acid/base balance, can be a mild condition, brought on by **vomiting**, the use of **steroids** or diuretic drugs, or the overuse of **antacids** or **laxatives**. Metabolic alkalosis can also indicate a more serious problem with a major organ such as the kidneys.

Causes and symptoms

Metabolic alkalosis occurs when the body has more base than acid in the system. Chemists use the term "pH" to decribe how acidic or alkaline (also called basic) a substance is. Based on a scale of 14, a pH of 7.0 is neutral. A pH below 7.0 is an acid; the lower the number, the stronger the acid. A pH above 7.0 is alkaline; the higher the number, the stronger the alkali. Blood pH is slightly alkaline, with a normal range of 7.36-7.44. Conditions that lead to a reduced amount of fluid in the body, like **vomiting** or excessive urination due to use of diuretic drugs, change the balance of fluids and salts. The blood levels of potassium and **sodium** can decrease dramatically, causing symptoms of metabolic alkalosis.

In cases of metabolic alkalosis, slowed breathing may be an initial symptom. The patient may have episodes of apnea (not breathing) that may go on 15 seconds or longer. **Cyanosis**, a bluish or purplish discoloration of the skin, may also develop as a sign of

KEY TERMS

pH—A measurement of the acidity or alkalinity of a solution based on the amount of hydrogen ions available. Based on a scale of 14, a pH of 7.0 is neutral. A pH below 7.0 is an acid; the lower the number, the stronger the acid. A pH above 7.0 is a base; the higher the number, the stronger the base. Blood pH is slightly alkaline (basic) with a normal range of 7.36-7.44.

inadequate oxygen intake. **Nausea**, vomiting, and **diarrhea** may also occur. Other symptoms can include irritability, twitching, confusion, and picking at bedclothes. Rapid heart rate, irregular heart beats, and a drop in blood pressure are also symptoms. Severe cases can lead to convulsions and **coma**.

Diagnosis

Metabolic alkalosis may be suspected based on symptoms, but often may not be noticeable. The condition is usually confirmed by laboratory tests on blood and urine samples. Blood pH above 7.45 confirms the condition. Levels of other blood components, including salts like potassium, sodium, and chloride, fall below normal ranges. The level of bicarbonate in the blood will be high, usually greater than 29 mEq/L. Urine pH may rise to about 7.0 in metabolic alkalosis.

Treatment

Treatment focuses first on correcting the imbalance. An intravenous line may be started to administer fluids (generally normal saline, a salt water solution) and allow for the quick injection of other drugs that may be needed. Potassium chloride will be administered. Drugs to regulate blood pressure or heart rate, or to control **nausea and vomiting** might be given. Vital signs like pulse, respiration, blood pressure, and body temperature will be monitored. The underlying cause of the metabolic alkalosis must also be diagnosed and corrected.

Prognosis

If metabolic alkalosis is recognized and treated promptly, the patient may have no long-term complications; however, the underlying condition that caused the alkalosis needs to be corrected or managed. Severe metabolic alkalosis that is left untreated will lead to convulsions, **heart failure**, and coma.

Prevention

Patients receiving **tube feedings** or intravenous feedings must be monitored to prevent an imbalance of fluids and salts, particularly potassium, sodium, and chloride. Overuse of some drugs, including **diuretics**, laxatives, and antacids, should be avoided.

Resources

BOOKS

Cecil, Russell L., Lee Goldman, and D. A. Audiello. *Cecil Medicine*. 23rd ed, Philadelphia: Saunders Elsevier, 2008.

Fauci, Anthony S., et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill Professional, 2008.

McPhee, Stephen, and Maxine Papadakis. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw-Hill Medical, 2009.

Schrier, Robert W. *Renal and Electrolyte Disorders*. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2010.

Altha Roberts Edgren

Metabolic encephalopahty *see* **Delirium**

Methadone

Definition

Methadone is a powerful narcotic drug in the same class as heroin. This class is known as the opioids.

Purpose

Methadone, formerly known as dolophine, is a psycho-active drug, meaning that it affects the mind or behavior. It belongs to the class of opioids, drugs that share some of the analgesic properties, and mimic the action of some of the body's naturally occurring chemicals called peptides, such as endorphins and enkephalines.

Methadone is used to relieve chronic **pain** in **cancer** patients and as a maintenance drug to control withdrawal symptoms in people undergoing treatment for opiate **addiction**.

In opiate addiction treatment, methadone blocks the opioid receptors of the brain that bind opiates such as heroin. The blocking of these receptors leads to two major effects:

- because these chemical receptors remain blocked by methadone for up to 24 hours, even if a person addicted to heroin takes heroin after the administration of methadone, this person is not likely to feel the same effects of the heroin as he or she previously felt;
- because the action of methadone is associated with slower and less intense withdrawal symptoms than those of heroin, the patient can experience milder opiate effects while the addiction is being treated and avoid the unpleasant withdrawal symptoms associated with heroin.

Methadone has also been shown to reduce cravings for heroin while not altering a person's mood.

Precautions

Methadone magnifies the effects of alcohol and other **central nervous system depressants**, such as **antihistamines**, cold medicines, sedatives, tranquilizers, other prescription and over-the-counter (OTC) pain medications, **barbiturates**, seizure medications, **muscle relaxants**, and certain anesthetics including some dental anesthetics. Alcohol and other central nervous system depressants should not be taken or consumed while methadone is being taken.

Methadone is a powerful narcotic. It can cause some people to feel drowsy, dizzy, or light-headed. People taking methadone should not drive a car or operate machinery.

Intentional or accidental overdose of methadone can lead to unconsciousness, **coma**, or **death**. The signs of methadone overdose include confusion, difficulty speaking, seizures, severe nervousness or restlessness, severe **dizziness**, severe drowsiness, and/or slow or troubled breathing. These symptoms are increased by alcohol or other central nervous system (CNS) depressants. Anyone who feels that he or she, or someone else, may have overdosed on methadone, or a combination of methadone and other central nervous system depressants, should seek emergency medical attention for that person at once.

Description

A typical adult dosage for methadone is 5–20 mg as an oral solution, 2.5–10 mg as an oral tablet or injection, every four to eight hours as necessary for pain. When used for **detoxification**, methadone is initially given in a dose of 15–100 mg per day as an oral solution. This dose is then decreased until the patient no longer requires the medication. The injection form of methadone is only used for detoxification in patients who are unable to take the medication by mouth.

Preparation

No preparation is generally necessary prior to the intake of methadone as a pain reliever. In cases of maintenance treatments, it is important to be sure that the patient is not currently intoxicated by alcohol, heroin, other opioids, or taking other central nervous system depressants.

Aftercare

Patients receiving methadone should be monitored for adverse reactions to this drug, and/or possible accidental overdose.

Risks

Methadone can interfere with or exacerbate certain medical conditions. For these reasons, it is important that the prescribing physician be informed of any current case, or history of:

- alcohol abuse
- brain disease or head injury
- colitis
- drug dependency, particularly of narcotics
- emotional problems
- emphysema, asthma, or other chronic lung disease
- enlarged prostate
- gallstones or gallbladder disease
- heart disease
- kidney disease
- liver disease
- problems with urination
- seizures
- underactive thyroid

Side effects

The most common side effects of methadone include:

- constipation
- dizziness
- drowsiness
- itching
- nausea
- urine retention
- vomiting

Less common side effects of methadone include:

- abnormally fast or slow heartbeat
- blurred or double vision
- cold, clammy skin

KEY TERMS

Analgesic—Any agent that relieves pain.

Central nervous system (CNS) depressant—Any drug that tends to reduce the activity of the central nervous system. The major drug categories included in this classification are: alcohol, anesthetics, anti-anxiety medications, antihistamines, antipsychotics, hypnotics, narcotics, sedatives, and tranquilizers.

Endorphins—Any of several opiate peptides naturally produced in the brain that bind to certain neuron receptors and have the effect of relieving pain.

Enkephalines—Peptide produced by the body that have analgesic properties.

Morphine—Morphine is the naturally occurring opioid in the opium poppy, *Papaver somniferum*. It is a powerful narcotic analgesic, and its primary clinical use is in the management of moderately severe to severe pain. After heroin, morphine has the greatest potential for addiction of all narcotic analgesics.

Narcotic—Any drug that produces insensibility or stupor and/or generally causes effects similar to those caused by morphine.

Opiate—Any narcotic analgesic derived from a natural source, such as morphine from the opium poppy.

Opioid receptors—Receptors located in the brain and various organs that bind opiates or opioid substances.

Opioids—One of the major classes of semi or fully synthetic psycho-active drugs that includes methadone.

Psychoactive drugs—Any drug that affects the mind or behavior. There are five main classes of psychoactive drugs: opiates and opioids (e.g. heroin and methadone); stimulants (e.g. cocaine, nicotine), depressants (e.g. tranquilizers, antipsychotics, alcohol), hallucinogens (e.g. LSD), and marijuana and hashish.

Receptor—A molecular structure on the surface that selectively binds a specific substance resulting in a specific physiological effect.

- depression or other mood changes
- dry mouth
- fainting
- hallucinations
- hives
- loss of appetite
- nightmares or unusual dreams
- pinpoint pupils of the eyes
- redness or flushing of the face
- restlessness
- rigid muscles
- ringing or buzzing in the ears
- seizure
- severe drowsiness
- skin reaction at the site of injection
- stomach cramps or pain
- sweating
- trouble sleeping (insomnia)
- yellowing of the skin or whites of the eyes

Normal results

Normal results after the administration of methadone to treat chronic pain is the alleviation of that patient's pain, at least to the point where the pain is bearable.

Normal results of methadone treatment to control heroin addiction, is that the patient reduces heroin intake almost immediately upon starting methadone treatments, followed by complete abstinence, usually within two weeks after starting treatment.

ORGANIZATIONS

National Alliance for Medication Assisted Recovery, 435 Second Avenue, New York, NY, 10010, nama.info@methadone.org, http://www.methadone.org.

National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD, 20847-2345, (877) 726-4727, http://store.samhsa.gov/.

Paul A. Johnson, Ed.M.

Methamphetamine

Definition

Methamphetamine, or meth, is an addictive central nervous system (CNS) stimulant with limited medical value. The United States Drug Enforcement Administration (DEA) lists methamphetamine as a Schedule II drug, which means it has high **abuse**

Methamphetamine

Short-term effects:

- Increased alertness
- Rapid and irregular heartbeat
- Rise in blood pressure and body temperature

Long-term effects:

- Anxiety and feelings of confusion
- Dental problems
- Increased risk of contracting diseases such as HIV/AIDS and hepatitis
- Insomnia
- Mood disturbances
- Violent behavior

In 2008, 850,000 Americans aged 12 and older had abused methamphetamine at least once in the past year, 11% of whom were younger than 18.

SOURCE: National Institutes of Health, National Institute on Drug Abuse, "Methamphetamine." Available online at: http://www.drugabuse.gov/drugpages/methamphetamine.html; also Substance Abuse and Mental Health Services Administration, *Results from the 2008 National Survey on Drug Use and Health: National Findings*. Available online at: http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.cfm (accessed August 19, 2010).

Consequences of methamphetamine abuse. *(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)*

potential and must be prescribed by a prescription that cannot be refilled.

Demographics

The national Monitoring the Future survey of 2008 found that in 2007 about 1.3 million Americans had used methamphetamine, a decrease from 1.9 million in 2006. This survey found that 2.3% of eighth graders, 2.4% of 10th graders, and 2.8% of twelfth graders had tried methamphetamine at some time in their lives.

In the United States, methamphetamine use peaks in white men 30–40 years old; however, according the Monitoring the Future survey, the average age of first use in 2007 was 19.1 years. In the United States, Methamphetamine use is highest in western states. Internationally, methamphetamine use is highest in Eastern Europe and Southeast Asia.

Description

Methamphetamine was first synthesized in Japan in 1919 and was used as a drug therapy in **asthma** inhalers in the 1930s. Amphetamines of all kinds were used during World War II by both sides to increase the alertness and prolong wakefulness of soldiers. After the war, the government developed stricter regulations for the manufacture and use of amphetamines, but they remained popular among people who wanted to stay awake for long periods (e.g., students, long-haul truckers) and were commonly used by people who wanted to lose weight. In 1970, more restrictions were put on methamphetamine, so that today it is a Schedule II drug. Despite this, methamphetamine remains a popular drug of abuse.

Methamphetamine is produced illegally in many countries, including the United States, and can be synthesized with readily available materials. The drug's misuse is deemed to be a major societal problem. Methamphetamine is addictive. It goes by the street names of ice, crystal, crystal meth, speed, crank, and glass.

Methamphetamine is similar to other CNS stimulants, such as amphetamine (its parent drug), methylphenidate, and **cocaine**, in that it stimulates dopamine reward pathways in the brain. Consistent with its stimulant profile, methamphetamine causes increased activity and talkativeness, decreased appetite and **fatigue**, and a general sense of well being. Compared to amphetamine, methamphetamine is more potent and longer lasting, and it has more harmful effects on the brain. In animals, a single high dose of methamphetamine has been shown to damage nerve terminals in the dopamine-containing regions of the brain.

Methamphetamine is a white, odorless, bitter-tasting crystalline powder that easily dissolves in water or alcohol. Misuse occurs in many forms, as methamphetamine can be smoked, snorted, injected, or taken orally. When smoked or injected, methamphetamine enters the brain very rapidly and immediately produces an intense but short-lived rush that many abusers find extremely pleasurable. Snorting or oral ingestion produces euphoria—a feeling of being high—within minutes. As with other abused stimulants, methamphetamine is most often used in a binge-and-crash pattern. A "run" of repeated doses may be continued over the course of days (binge) before stopping (crash). Exhaustion occurs with repeated use of methamphetamine, involving intense fatigue and need for sleep after the stimulation phase.

Approved medical indications for the drug are the sleep disorder **narcolepsy**, **attention deficit hyperactivity disorder (ADHD)**, and extreme **obesity**, but in each case methamphetamine is a second-line drug at best and is used only after other, less harmful drugs have failed.

The prescription drug (brand name Desoxyn) comes in the form of a small white tablet, which is orally ingested. Dosing begins at 5 mg once or twice a day and is increased weekly until the lowest effective dose is attained. Desoxyn should not be taken with

KEY TERMS

Central nervous system (CNS)—Part of the nervous system consisting of the brain, cranial nerves and spinal cord. The brain is the center of higher processes, such as thought and emotion and is responsible for the coordination and control of bodily activities and the interpretation of information from the senses. The cranial nerves and spinal cord link the brain to the peripheral nervous system, that is the nerves present in the rest of body.

Dopamine—A neurochemical made in the brain that is involved in many brain activities, including movement and emotion.

Hallucination—A false or distorted perception of objects, sounds, or events that seems real. Hallucinations usually result from drugs or mental disorders.

Psychosis—A serious mental disorder characterized by defective or lost contact with reality often with hallucinations or delusions.

other stimulants (including **caffeine** and **decongestants**) or **antidepressant drugs** (especially **monoamine oxidase inhibitors** [MAOs], but also **tricyclic antidepressants**). Desoxyn should not be taken by patients with glaucoma, cardiovascular disease (including **hypertension** and arteriosclerosis), or **hyperthyroidism**.

Causes and Symptoms

Short-term effects of methamphetamine relate to its stimulation of the brain and the cardiovascular system. Euphoria and rush, alertness, increased physical activity, and decreased sleep and appetite occur from an increase in available dopamine in the brain. Any or all of these effects can lead to compulsive use of the drug that characterizes **addiction**. In addition, methamphetamine causes rapid heart beat (tachycardia), increased respiration, and increased blood pressure (hypertension), and with very high doses, increased body temperature (hyperthermia) and convulsions can occur.

Chronic use of methamphetamine can result in two hallmark features of addiction: tolerance and dependence. Tolerance to the euphoric effects in particular can prompt abusers to take higher or more frequent doses of the drug. Withdrawal symptoms in chronic users include depression, **anxiety**, fatigue, and an intense craving for the drug. Users who inject methamphetamine risk contracting life-threatening viruses such as HIV and hepatitis through the use of dirty needles.

With repeated use, methamphetamine can cause anxiety, **insomnia**, mood disturbances, confusion, **hallucinations**, **psychosis**, and violent behavior. Psychotic features sometimes emerge, such as **paranoia**, hallucinations, and **delusions**, and can last well after methamphetamine use has stopped. **Stroke** and weight loss are other long-term effects.

Diagnosis

Methamphetamine use may be suspected by the symptoms described above and confirmed with a urine drug screening test

Treatment

For acute intoxication accompanied by psychosis, patients may be calmed by reassurance and a quiet setting, but sometimes **antipsychotic drugs** or sedatives are administered. Substances that prevent absorption from the gastrointestinal tract (e.g., **activated charcoal**) may be used if the drug was taken orally. Additional care is given as needed (e.g., keeping the airways open, treatment of seizures.) Individual with methamphetamine intoxication may be violent, agitated, and a danger to themselves and others.

The most effective treatment for methamphetamine addiction is cognitive-behavioral intervention such as counseling but may also include family education, drug testing, and group support in a twelve-step program. The goal of these modalities is to modify the patient's thinking, expectancies, and behaviors to increase coping skills in the face of life's stressors. Contingent management is a promising behavioral intervention, where incentives are provided in exchange for staying clean and for participating in treatment. Residential programs/therapeutic communities may be helpful, particularly in more severe cases.

Antidepressant drugs such as bupropion (Wellbutrin) can be a useful treatment aid, but as of 2010, there are no FDA-approved medications specifically for the treat stimulant addiction.

Prognosis

Addiction is a complex disorder, and prospects for individual addicts vary widely. Chronic methamphetamine use causes changes in brain and mental function While some effects are reversible, others are very long lasting and perhaps permanent. Methamphetamine is addictive. Relapses are common, and cravings may continue for a long time after drug use has stopped.

Prevention

Teenagers are a target group for prevention strategies as adolescence and young adulthood are associated with exposure to and an inclination to experiment with drugs. Drug education and prevention programs should begin a early, and parents and teachers should be alert to the possibility of methamphetamine abuse.

Resources

BOOKS

Lee, Steven J. *Overcoming Crystal Meth Addiction: An Essential Guide to Getting Clean*. New York: Marlowe & Co., 2006.

Weisheit, Ralph A. and William White. *Methamphetamine: Its History, Pharmacology, and Treatment*. Center City, MN: Hazelden, 2009.

OTHER

Derlet, Robert W., Timothy E. Albertson and John J. Richards. Toxicity, Methamphetamine December 4, 2009. http://emedicine.medscape.com/article/820918-overview

Methamphetamine. MedlinePlus December 15, 2009. http://www.nlm.nih.gov/medlineplus/methamphetamine.html

Methamphetamine Abuse and Addiction. National Institute on Drug Abuse July 2009. http://www.nida.nih.gov/ResearchReports/methamph/methamph.html

NIDA InfoFacts: Methamphetamine. National Institute on Drug Abuse July 2009. http://www.drugabuse.gov/infofacts/methamphetamine.html

Warning Signs: Is Your Child Using Meth? Partnership for a Drug-Free America undated [accessed March 2, 2010]. http://www.drugfree.org/Portal/DrugIssue/MethResources/is_my_child.html

ORGANIZATIONS

National Clearinghouse on Alcohol and Drug Information, P. O. Box 2345, Rockville, MD, 20847, (877) SAMHSA-7; Hablamos español: (877) 767-8432; TDD: (800) 487-4889, (240) 221-4292, http://ncadi.samhsa.gov.

National Council on Alcohol and Drug Dependence, 244 East 58th Street 4th Floor, New York, NY, 10022, (212) 269-7797, 24-hour help line: (800) NCA-CALL, (212) 269-7510, national@mcadd.org, http://www.ncadd.org.

Partnership for a Drug-free America, 405 Lexington Avenue, Ste 1601, New York, NY, 10174, (212) 922-1560, (212) 922-1570, http://www.drugfree.org.

Jill U. Adams
Tish Davidson, AM

Methemoglobinemia

Definition

When excessive hemoglobin in the blood is converted to another chemical that cannot deliver oxygen to tissues, called methemoglobin.

Description

The molecule hemoglobin in the blood is responsible for binding oxygen to give to the body. When hemoglobin is oxidized to methemoglobin its structure changes and it is no longer able to bind oxygen. Hemoglobin is constantly under oxidizing stresses: however, normally less than 1% of a person's hemoglobin is in the methemoglobin state. This is due to the body's systems that reduce methemoglobin back to hemoglobin. Infants have a higher risk of acquiring methemoglobinemia because infant hemoglobin is more prone to be oxidized to methemoglobin.

Causes and symptoms

Methemoglobinemia can either be congenital or acquired.

There are two causes of the congenital form. One cause is a defect in the body's systems to reduce methemoglobin to hemoglobin. The other cause is a mutant form of hemoglobin called hemoglobin M that cannot bind to oxygen. Both of these forms are typically benign.

Acquired methemoglobinemia is caused by an external source, usually a drug or medication. Some of these medications include benzocaine, lidocaine and prilocaine. These medications can inhibit the body's systems of reducing methemoglobin to hemoglobin resulting in methemoglobinemia.

With a methemoglobin level of 3-15% skin can turn to a pale gray or blue (**cyanosis**). With levels above 25% the following symptoms may be present:

- Cyanosis unaffected by oxygen administration
- Blood that is dark or chocolate in color that will not change to red in the presence of oxygen
- Headache
- Weakness
- Confusion
- Chest pain

When methemoglobin levels are above 70% **death** may result if not treated immediately.

KEY TERMS

Cyanosis—When the body does not receive enough oxygen.

Oxidation—When a chemical element or compound loses an electron.

Reduction—When a chemical element or compound gains an electron.

Diagnosis

Diagnosis is based on the symptoms and history. If these are indicative of methemoglobinemia blood tests are performed to confirm the presence and level of methemoglobin.

Treatment

For acquired methemoglobinemia the typical treatment is with methylene blue. This is administered with an IV over a five-minute period and results are typically seen within 20 minutes. Methylene blue reduces methemoglobin back to hemoglobin.

Though congenital methemoglobinemia is usually benign, the form due to a defective reducing system can be treated with ascorbic acid (vitamin C) taken daily. The other congenital form due to hemoglobin M has no treatment as of late.

Alternative treatment

There are not any known alternative treatments for methemoglobinemia. Methylene blue, or a similar treatment, is needed to reduce methemoglobin to hemoglobin.

Prognosis

If found early, acquired methemoglobinemia can be easily treated with no side effects. After treatment with methylene blue the patient can expect a full recovery.

Congenital methemoglobinemia is typically benign and should be observed. If methemoglobinemia symptoms occur the person should be taken to the hospital for treatment.

Prevention

If a person gets methemoglobinemia from a certain medication that medication should be avoided at all costs in the future. For people with congenital methemoglobinemia medications or other things that are known to oxidize hemoglobin should be avoided.

Resources

BOOKS

Surhone, Lambert M., Mariam T. Tennoe, and Susan F. Henssonow, eds. *Methemoglobinemia*. Seattle: Betascript, 2010.

OTHER

eMedicine. Website. 2001. http://www.emedicine.com.

Thomas Scott Eagan
Ronald Watson, PhD

Methylphenidate *see* **Central nervous system stimulants**

Metoprolol *see* **Beta blockers**

Metronidazole *see* **Antiprotozoal drugs**

Micronaz *see* **Antifungal drugs, topical**

Microphthalmia and anophthalmia

Definition

Anophthalmia is the complete absence of an eye. Microphthalmia is an eye that is abnormally small.

Description

Anophthalmia is caused by a defect in embryonic development. The total absence of an eye is extremely rare and often a clinical sign associated with a broad range of genetic disorders or, more commonly, a sporadic mutation. Sporadic transmission occurs in the affected individual due to a genetic abnormality. It is not passed on from the parents, but usually due to a combination of environmental and genetic influences. More commonly anophthalmia clinically presents as a small cyst. The defect, which causes anophthalmia, is an absence of the optic vesicle, a structure important for eye development. The genetic abnormality usually occurs during weeks one to three after conception. It is estimated that the incidence of microphthalmia occurs 0.22 times per 1,000 live births. Anophthalmia can occur during adult life but not associated with a genetic cause.

Microphthalmia refers to an abnormally small eye. This clinical sign is often associated with autosomal dominant or recessively transmitted genetic disorders. Most disorders dominantly inherited with microphthalmia are associated with some visual capabilities

in infancy and early childhood. Microphthalmia may be isolated (the only presenting sign) or associated with a range of ocular or systemic abnormalities. Isolated cases of microphthalmia may be sporadic or inherited. There is a variable degree of **visual impairment**. Microphthalmia occurs due to autosomal recessive transmission and is part of a syndrome associated with abnormalities in the retina or systemic lesions. Microphthalmia results from a developmental defect after formation of the optic vesicle. The developmental abnormality causes the optic vesicle to fold inwards, resulting in the formation of a cyst. The cyst will progressively swell from birth, and it may be situated along the optic nerve. The cyst may also be situated along other important eye structures.

Causes and symptoms

Microphthalmia and anophthalmia can be caused by sporadic or genetic mutations. Anophthalmia is characterized by a total absence of an eye. Anophthalmia in an adult is usually caused by trauma, infection, tumor, or advanced eye disease.

Diagnosis

Microscope examination confirms the diagnosis of true anophthalmia. The clinician examines a piece of tissue taken from the eye and notes eviscerated tissue. For microphthalmia the confirmation can be established by eye measurements. Eyes that have an axial length of <21 mm in an adult or <19 mm in a one-year-old child are described as having microphthalmia.

Treatment

Large cysts causing microphthalmia should be aspirated or removed surgically. There is no known cure for anophthalmia or microphthalmia. For anophthalmia a prosthetic eye can be fitted which may involve surgery. Treatment for microphthalmia depends on the complexity of eye involvement.

Prognosis

For anophthalmia, prosthetic eyes should be seen by a specialist two to three times per year to assess fit, mobility, and smoothness. They are usually well tolerated and have good appearance and mobility. The clinical course for microphthalmia depends on the extent of smallness, but usually patients progress favorably without major treatment. Since the smallness is distinctly noticeable, there may be individual cosmetic considerations.

KEY TERMS

Axial—A straight line passing through a spherical body between its two poles and about which the body may revolve.

Eviserated—Removal of eye contents.

Prostheses—A synthetic object that resembles a missing anatomical part.

Retina—A major portion of the eye responsible for reception of visual light rays.

Prevention

There is no known prevention for either, since these clinical signs are commonly associated with genetic inheritance.

Resources

BOOKS

Yanoff, Myron, et al, eds. *Ophthalmology*. 3rd ed. Edinburgh: Mosby International, 2009.

ORGANIZATIONS

American Society of Human Genetics, 9650 Rockville Pike, Bethesda, MD, 20814-3998, (301) 634-7300, (301) 634-7079, http://www.ashg.org/.

Laith Farid Gulli, M.D.

Middle ear infection *see* **Otitis media**

Mifeprex *see* **Mifepristone**

Mifepristone

Definition

Mifepristone, mifeprex, RU 486, is a drug used to produce medical abortion within 49 days of the last menstrual period.

Purpose

This medication is primarily used for ending pregnancies within 19 days after the last menstrual period.

Description

Mifepristone blocks progesterone, the hormone necessary for maintaining **pregnancy**, causing the uterus to shed its lining and producing menstrual-like bleeding.

Three doctor or clinic visits are required for medical termination of pregnancy. Following a medical history, **physical examination**, and confirmation of pregnancy, 600mg of mifepristone, three 200mg tablets, are given as a single dose. Two days later, on day three, if termination of pregnancy cannot be confirmed, 400mcg of misoprostol, two 200mcg tablets, are given at one time. Additional medication, like ibuprofen, may be needed to relieve abdominal **pain** and cramping. On day 14, if termination cannot be confirmed, **dilatation and curettage** or suction evacuation of the uterine cavity is done, usually under **local anesthesia**. Depending on the amount of vaginal bleeding, a **hemoglobin test** may be needed.

Contraindications to medical termination of pregnancy

- Women who are more than seven weeks pregnant, 49 days since their last menstrual period, should not take mifepristone.
- Women who have an IUD, intrauterine device, for contraception.
- Women who take long-term corticosteroids or have chronic adrenal failure.
- Women with bleeding disorders or who take blood thinning medications like warfarin or aspirin.
- Women with suspected ectopic pregnancy
- Women who do not have adequate access to emergency medical services
- Women who cannot or will not adhere to the three visit protocol for medical termination of pregnancy.

Aftercare

There may be heavy bleeding and abdominal cramping when early pregnancies are interrupted with mifepristone and misoprostol.

Until vaginal bleeding has essentially stopped, sexual intercourse increases the risk of infection.

It may take days or weeks for women to stabilize their hormonal balances after medical abortion. Some women experience mood swings, **anxiety**, the blues or even depression. Though these symptoms subside over time, counseling or support groups may be helpful.

Complications of medical abortion

Uterine infection, with **fever** and abdominal pain and tenderness, is the most serious complication of medical abortion.

Anemia from heavy or prolonged vaginal bleeding can be a serious complication.

KEY TERMS

Dilatation and curettage (D and C)—A surgical procedure where the cervix is dilated and an instrument is introduced to scrape tissue from the walls of the uterus to complete termination of pregnancy.

Misprostol—A drug used in combination with mifepristone to cause uterine contractions that expel the contents of the uterus.

Other common side effects include: **fatigue**, headaches, **dizziness**, anxiety, **nausea**, **vomiting**, **diarrhea**, and low-back pain.

Normal results

Most women feel better within two weeks. Bleeding and spotting usually stop within 16 days, but may last up to a month.

Abnormal results

In some cases, mifepristone does not completely terminate pregnancy. When that happens, surgical termination like **dilatation and curettage** (D and C) or suction of the uterine cavity is required. Five to eight percent of women taking mifepristone require a surgical termination of pregnancy, according to the FDA. During a D and C, usually done under local anesthesia at a hospital or clinic, the cervix is dilated and an instrument is used to scrape residual tissue away from the walls of the uterus. This generally stops heavy bleeding.

Resources

PERIODICALS

"Abortion Pills Account for 5% of U.S. Abortions." *Medical Letter on the CDC and FDA* February 9, 2003: 7.

OTHER

"Mifeprex (mifepristone) Information." http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111323.htm.

James Waun, MD, RPh

Migraine headache

Definition

Migraine is a type of **headache** marked by severe head **pain** lasting several hours or more.

Description

Migraine is an intense and often debilitating type of headache. The term *migraine* is derived from the Greek word *hemikrania*, meaning "half the head," because the classic migraine headache affects only one side of the person's head. Migraines affect as many as 24 million people in the United States, and are responsible for billions of dollars in lost work, poor job performance, and direct medical costs. Approximately 18% of women and 6% of men experience at least one migraine attack per year. Currently, one American in 11 now suffers from migraines, more than three times as many are women, with most of them being between the ages of 30 and 49. Migraines often begin in adolescence, and are rare after age 60.

Two types of migraine are recognized. Eighty percent of migraine sufferers experience "migraine without aura" (common migraine). In "migraine with aura," or classic migraine, the pain is preceded or accompanied by visual or other sensory disturbances, including **hallucinations**, partial obstruction of the visual field, **numbness** or **tingling**, or a feeling of heaviness. Symptoms are often most prominent on one side of the head or body, and may begin as early as 72 hours before the onset of pain.

People who experience migraines overwhelmingly describe them as intensely painful with an onset often characterized by an "aura," which is a sensory warning described as seeing flashes of light, or spots, or feeling a tingling in limbs. Migraines can be extremely incapacitating and can last for hours or even days. For instance, "status migrainosus" is a severe migraine that can last 72 hours or longer and often results in hospitalization. For many sufferers, migraine is associated with other illnesses such as depression, **anxiety**, **stroke**, **irritable bowel syndrome**, **epilepsy**, and **hypertension**.

Demographics

The World Health Organization (WHO) considers migraines to be one of the most debilitating diseases in the world. In the United States, some 17% of women and 6% of men have experienced a migraine. According to the National Headache Foundation, an estimated 28 million Americans have migraine headaches. A 2005 survey, sponsored by the National Headache Foundation, reported that 90% of people with migraines could not function normally on the day of a migraine attack, 80% experienced abnormal sensitivity to light and noise, 75% experienced **nausea and vomiting**, 30% required bed rest, and 25% missed at least 1 day of work due to migraine in past 3 months. In Canada, more than 3 million people suffer from migraine headaches. Women tend to develop migraines three times more often than men. Migraine headaches start in childhood or adolescence and continue throughout adult life.

Causes

The cause of migraines is presently unknown. They are believed to be sparked by spasms in the cerebral arteries which constrict or widen abnormally as a result of serotonin imbalance. Although the precise cause is still being researched, migraine-triggering factors have been documented. For example, women often report that their migraine occurs during or right before the onset of their menstrual cycle. Other triggers include:

- stress
- lack of sleep
- changes in weather
- use of contraceptives
- use of hormone replacement therapies
- environmental chemicals
- liver problems
- dental infections
- some foods including cured meats, red wine, onion, freshly baked yeast products, eggs, alcohol, nuts, and aged cheese
- medical conditions
- medications

The most widely accepted hypothesis of migraine suggests that a migraine attack is precipitated when pain-sensing nerve cells in the brain (called nociceptors) release chemicals called neuropeptides. At least one of the neurotransmitters, substance P, increases the pain sensitivity of nearby nociceptors. This process is called sensitization.

Other neuropeptides act on the smooth muscle surrounding cranial blood vessels. This smooth muscle regulates blood flow in the brain by relaxing or contracting, thus dilating (enlarging) or constricting the enclosed blood vessels. At the onset of a migraine headache, neuropeptides are thought to cause muscle relaxation, allowing vessel dilation and increased blood flow. Other neuropeptides increase the leakiness of cranial vessels, allowing fluid leak, and promote inflammation and tissue swelling. The pain of migraine is thought to result from this combination of increased pain sensitivity, tissue and vessel swelling, and inflammation. The aura seen during a migraine may be related to constriction in the blood vessels that dilate in the headache phase.

Migraines commonly develop in three distinct stages:

- The aura phase: This stage marks the onset of migraine and commonly lasts from 15 to 30 minutes with symptoms that may involve visual disturbances, numbness, dizziness, ringing in the ear, weakness on one side of the body, and sensitivity to light, smells, and noises.
- The headache phase: This phase is characterized by an excruciating headache that may last from hours to days with symptoms such as nausea, sensitivity to light, diarrhea, vomiting, excessive perspiration and chills. It often occurs only on one side of the head.
- The post–headache phase: After the headache has subsided, the skull often remains very tender and the person feels totally exhausted.

Genetics

Susceptibility to some types of migraine is inherited. A child of a migraine sufferer has as much as a 50% chance of developing migraines. If both parents are affected, the chance rises to 70%. In 2002, a team of Australian researchers identified a region on human chromosome 1 that influences susceptibility to migraine. It is likely that more than one gene is involved in the inherited forms of the disorder. Many cases of migraine, however, have no obvious familial basis. It is likely that the genes that are involved set the stage for migraine, and that full development requires environmental influences, as well.

Two groups of Italian researchers have recently identified two loci on human chromosomes 1 and 14 respectively that are linked to migraine headaches. The locus on chromosome 1q23 has been linked to familial hemiplegic migraine type 2, while the locus on chromosome 14q21 is associated with migraine without aura.

Triggers

A wide variety of foods, drugs, environmental cues, and personal events are known to trigger migraines. It is not known how most triggers set off the events of migraine, nor why individual migraine sufferers are affected by particular triggers but not others.

Common food triggers include:

- alcohol
- caffeine products, as well as caffeine withdrawal
- chocolate
- foods with an extremely high sugar content
- dairy products
- fermented or pickled foods
- citrus fruits
- nuts
- processed foods, especially those containing nitrites, sulfites, or monosodium glutamate (MSG)

Environmental and event-related triggers include:

- stress or time pressure
- menstrual periods, menopause
- sleep changes or disturbances, including oversleeping
- prolonged overexertion or uncomfortable posture
- hunger or fasting
- odors, smoke, or perfume
- strong glare or flashing lights

Drugs that may trigger migraine include:

- oral contraceptives
- estrogen replacement therapy
- Theophylline
- Reserpine
- Nifedipine
- Indomethicin
- Cimetidine
- overuse of decongestants
- analgesic overuse
- benzodiazepine withdrawal

Symptoms

Migraine without aura may be preceded by elevations in mood or energy level for up to 24 hours before the attack. Other pre-migraine symptoms may include **fatigue**, depression, and excessive yawning.

Aura most often begins with shimmering, jagged arcs of white or colored light progressing over the visual field in the course of 10–20 minutes. This may be preceded or replaced by dark areas or other visual disturbances. **Numbness and tingling** are common, especially of the face and hands. These sensations may spread, and may be accompanied by a sensation of weakness or heaviness in the affected limb.

Migraine pain is often present only on one side of the head, although it may involve both, or switch sides during attacks. The pain is usually throbbing, and may range from mild to incapacitating. It is often accompanied by **nausea** or **vomiting**, painful sensitivity to light and sound, and intolerance of food or odors. Blurred vision is also common.

The pain tends to intensify over the first 30 minutes to several hours, and may last from several hours to a day, or longer. Afterward, the affected person is usually weary, and sensitive to sudden head movements.

Diagnosis

Diagnosis is commonly established on the basis of the patient's medical history and a physical exam. The following tests may also be prescribed to rule out other possible causes of headache:

- Computerized tomography (CT) scan: A CT scan uses computer-directed x rays that provide a view of the brain to identify possible conditions that may also cause headache, such as tumors, infections, and other medical problems.
- Magnetic resonance imaging (MRI): This imaging technique uses radio waves and a powerful magnet to produce very detailed views of the brain and its blood vessels. It may also help diagnose tumors, strokes, aneurysms, and other brain abnormalities.
- Spinal tap: In this procedure, a thin needle is inserted between two vertebrae in the lower back to extract a sample of cerebrospinal fluid for laboratory analysis. It may eliminate other diseases such as meningitis that also cause intense headaches.

Treatment

At the onset of symptoms, the migraine sufferer should seek out a quiet, dark room and attempt to sleep. Placing a cold, damp cloth or a cold pack on the forehead may help. Additionally, tying a headband tightly around the head can relieve migraines.

Migraine headaches are often linked with **food allergies** or intolerances. Identification and elimination of the offending food or foods can decrease the frequency of migraines and/or alleviate these headaches altogether.

Magnesium and **calcium** have been shown to be of benefit to migraine sufferers, as these **minerals** maintain healthy blood vessels. Pantothenic acid is also considered helpful, as it helps the body produce serotonin.

Allopathic treatments

Nonsteroidal anti-inflammatory drugs (NSAIDs) **acetaminophen** (Tylenol), ibuprofen (Motrin), and naproxen (Aleve) are helpful for early and mild headache. Excedrin Migraine is a combination product that is indicated for migraine headache.

More severe or unresponsive attacks may be treated with ergotamine (botulinum toxin), dihydroergotamine, sumatriptan (Imitrex), beta-blockers and calcium channel-blockers, antiseizure drugs, antidepressants (SSRIs), meperidine, or metoclopramide. Some of these drugs are also available as nasal sprays, intramuscular injections, or rectal suppositories when **vomiting** prevents taking the drug by mouth.

Sumatriptan and other triptan drugs (zolmitriptan, rizatriptan, naratriptan, almotriptan, and frovatriptan) should not be taken by people with any kind of **vascular disease** because they cause coronary artery narrowing. Otherwise these drugs have been shown to be very safe.

Continued use of some **antimigraine drugs** can lead to "rebound headache," marked by frequent or chronic headaches, especially in the early morning hours. Rebound headache can be avoided by using antimigraine drugs under a doctor's supervision, with the minimum dose necessary to treat symptoms. Tizanidine (Zanaflex) has been reported to be effective in treating rebound headaches when taken together with an NSAID.

Treatment of migraine presents special problems in the elderly. The presence of other diseases may prevent the use of some medications. Another concern is that older patients are more likely than younger ones to experience adverse side effects. Older migraine patients accordingly require cautious treatment that takes into account possible pharmacological interactions associated with their greater use of drugs for other medical conditions. Paracetamol (acetaminophen) is considered the safest medication for symptomatic treatment of migraine in the elderly.

Alternative treatment

Alternative treatments for migraine include:

- Acupressure. Pressing on the Gates of Consciousness (GB 20) points can relieve migraine.
- Acupuncture. A National Institutes of Health (NIH) panel concluded that acupuncture may be a useful treatment for headache.
- Aromatherapy. The essential oil rosemary eases migraine pain.
- Autogenic training. Autogenic training is a form of self-hypnosis developed in Germany in the 1930s that has been shown in several studies to relieve the pain of migraine.
- Cognitive behavior therapy.
- Herbals. Valerian (*Valeriana officinalis*), passionflower (*Passiflora incarnata*), feverfew (*Chrysanthemum parthenium*), ginger, ginkgo (*Ginkgo biloba*), goldenseal (*Hydrastis canadensis*), hawthorn (*Crataegus oxyacantha*), linden, wood betony (*Stachys officinalis*), skullcap (*Scutellaria lateriflora*), or cramp bark (*Viburnum opulus*) may relieve migraines.
- Hydrotherapy. Contrast showers, in which a short hot shower is followed by a longer cold shower, may

KEY TERMS

Aura—A group of visual or other sensations that precedes the onset of a migraine attack.

Autogenic training—A form of self-hypnosis developed in Germany that appears to be beneficial to migraine sufferers.

Coenzyme Q_{10}—A substance used by cells in the human body to produce energy for cell maintenance and growth. It is being studied as a possible preventive for migraine headaches.

Nociceptor—A specialized type of nerve cell that senses pain.

Transcutaneous electrical nerve stimulation (TENS)—A treatment in which a mild electrical current is passed through electrodes on the skin to stimulate nerves and block pain signals.

halt an oncoming migraine. A hot enema can temporarily relieve migraine pain.

- Naturopathy. Migraine headaches are one of the most common reasons for consulting naturopathic practitioners. Naturopaths typically treat migraine with a combination of nutritional therapy and mind/body techniques.
- Relaxation techniques. Meditation, yoga, hypnosis, visualization, breathing exercises, or progressive muscular relaxation may halt the progression of a migraine.
- Supplements. Clinical studies have shown that vitamin B_2 (riboflavin), magnesium, 5-HTP, or melatonin can reduce the severity of migraines.
- Transcutaneous electrical nerve stimulation (TENS).

Prognosis

Most people can control migraines through recognizing and avoiding triggers, and by using effective treatments. Some people with severe migraines do not respond to preventive or drug therapy. Migraines usually wane in intensity by age 60 and beyond.

Taking a combination of medications when migraine attacks occur brings some amount of relief to most people and allows them to limit the disabling effects of these headaches. Some researchers believe that women after **menopause** may experience fewer migraines due to the decline in estrogen levels.

Prevention

Migraine sufferers are encouraged to keep track of their personal triggering factors since avoiding them can decrease the occurrence of migraine attacks. For some people, it may mean avoiding certain foods associated with previous migraine headaches, for others it may mean the avoidance of stressful situations. **Stress** management therapies, such as relaxation and **biofeedback**, may also reduce the occurrence and intensity of migraine headaches.

One substance that is being studied as a possible migraine preventive is coenzyme Q_{10}, a compound used by cells to produce energy needed for cell growth and maintenance. Coenzyme Q_{10} has been studied as a possible complementary treatment for **cancer**. Its use in preventing migraines is encouraging and merits further study.

Lifestyle changes can help prevent migraine. Besides avoiding triggers, regular aerobic **exercise** has been shown to help reduce stress. Women who have identified estrogen as a trigger may select to avoid this type of medication or consult with their physician to modify dosage.

A study published in early 2003 reported that three drugs currently used to treat disorders of muscle tone are being explored as possible preventive treatments for migraine. They are botulinum toxin type A (Botox), baclofen (Lioresal), and tizanidine (Zanaflex). Early results of open trials of these medications are positive.

Anti-epileptic drugs, which are also known as anticonvulsants, are also being studied as possible migraine preventives. Sodium valproate (Epilim) is the only drug approved by the Food and Drug Administration (FDA) for prevention of migraine. Such newer anticonvulsants as gabapentin (Neurontin) and topiramate (Topamax) are presently being evaluated as migraine preventives.

A natural preparation made from butterbur root (*Petasites hybridus*) has been sold in Germany since the 1970s as a migraine preventive under the trade name Petadolex. Petadolex has been available in the United States since December 1998 and has passed several clinical safety and postmarketing surveillance trials.

Other possible preventive measures include: eating at regular times, not skipping meals, reducing the use of **caffeine** and pain-relievers, restricting physical exertion (especially on hot days), and keeping regular sleep hours, but not oversleeping.

Resources

BOOKS

Delaune, Valerie. *Trigger Point Therapy for Headaches & Migraines: Your Self–Treatment Workbook for Pain Relief*. Ypsilanti, MI: New Harbinger Publications, 2008.

Diamond, Seymour, and Merle Lea Diamond. *A Patient's Guide to Headache and Migraine*. 2nd ed. Newtown, PA: Handbooks in Health Care, 2009.

Foster, Carol A. *Migraine: Your Questions Answered*. New York, NY: DK Publishing, 2007.

Marcus, Dawn A. *10 Simple Solutions to Migraines: Recognize Triggers, Control Symptoms, And Reclaim Your Life*. Ypsilanti, MI: New Harbinger Publications, 2006.

Mauskop, Alex.*Migraine and Headache*. New York: Oxford University Press, 2009.

Pelletier, Kenneth R., MD. *The Best Alternative Medicine*, Part II, "CAM Therapies for Specific Conditions: Headaches." New York: Simon & Schuster, 2007.

Quinn, V. R. *Check–Up Chart Migraine Journal & Workbook*. Zebulon, NC: Concise Concepts, 2004.

Robert, Teri. *Living Well with Migraine Disease and Headaches: What Your Doctor Doesn't Tell You...That You Need to Know*. New York, NY: Harper Collins Publishers, 2005.

Young, William B., and Stephen D. Silberstein. *Migraine and Other Headaches*. New York, NY: Demos Medical Publishing, 2004.

PERIODICALS

Corbo, J. "The Role of Anticonvulsants in Preventive Migraine Therapy." *Current Pain and Headache Reports* 7 (February 2003): 63–66.

Danesch, U., and R. Rittinghausen. "Safety of a Patented Special Butterbur Root Extract for Migraine Prevention." *Headache* 43 (January 2003): 76–78.

Freitag, F. G. "Preventative Treatment for Migraine and Tension-Type Headaches : Do Drugs Having Effects on Muscle Spasm and Tone Have a Role?" *CNS Drugs* 17 (2003): 373–381.

Haan, J., et al. "Migraine in the Elderly: A Review." *Cephalagia* 27, no. 2 (February 2007): 97–106.

Lipton, R. B., A. I. Scher, T. J. Steiner, et al. "Patterns of Health Care Utilization for Migraine in England and in the United States." *Neurology* 60 (February 11, 2003): 441–448.

Marconi, R., M. De Fusco, P. Aridon, et al. "Familial Hemiplegic Migraine Type 2 Is Linked to 0.9Mb Region on Chromosome 1q23" *Annals of Neurology* 53 (March 2003): 376–381.

Martins, K. M., at al. "Migraine in the Elderly: A Comparison with Migraine in Young Adults." *Headache* 46, no. 2 (February 2006): 312–316.

Sarchielli, P., et al. "Practical Considerations for the Treatment of Elderly Patients with Migraine." *Drugs and Aging* 23, no. 6 (2006): 461–489.

Soragna, D., A. Vettori, G. Carraro, et al. "A Locus for Migraine without Aura Maps on Chromosome 14q21.2-q22.3." *American Journal of Human Genetics* 72 (January 2003): 161–167.

Tepper, S. J., and D. Millson. "Safety Profile of the Triptans." *Expert Opinion on Drug Safety* 2 (March 2003): 123–132.

OTHER

Commonly Used Acute Migraine Treatments. American Headaches Society, Information Sheet. http://www.achenet.org/education/patients/CommonlyUsedAcuteMigraineTreatments.asp

Migraine. Mayo Clinic, Information Page. http://www.mayo clinic.com/print/migraine-headache/DS00120/DSECTION = all&METHOD = print

Migraine. NINDS Information Page. http://www.ninds.nih.gov/disorders/migraine/migraine.htm

Migraine Headaches: Ways to Deal with the Pain. American Academy of Family Physicians, FamilyDoctor.org Information. http://familydoctor.org/online/famdocen/home/common/brain/disorders/127.printerview.html

Trigger Avoidance Information. American Headache Society, Information Page. http://www.achenet.org/tools/TriggerAvoidanceInformation.asp

ORGANIZATIONS

American Headache Society (AHS), 19 Mantua Road, Mount Royal, NJ, 08061, (856)423 0258, (856)423-0082, http://www.achenet.org.

American Pain Foundation, 201 North Charles St., Suite 710, Baltimore, MD, 21201-4111, (888)615-PAIN, info@ painfoundation.org, http://www.painfoundation.org.

National Institute of Neurological Disorders and Stroke (NINDS), P.O. Box 5801, Bethesda, MD, 20824, (301) 496-5751, (800) 352-9424, http://www.ninds.nih.gov.

Rebecca J. Frey, Ph.D.
Monique Laberge, Ph.D.
Belinda Rowland
Laura Jean Cataldo, RN, Ed.D.

Miliaria *see* **Prickly heat**

Mineral deficiency

Definition

The term mineral deficiency means a condition in which the concentration of any one of the **minerals** essential to human health is abnormally low in the body. In some cases, an abnormally low mineral concentration is defined as that which leads to an impairment in a function dependent on the mineral. In other cases, the convention may be to define an abnormally low mineral concentration as a level lower than that found in a specific healthy population.

The mineral nutrients are defined as all inorganic substances that are required for life. As far as human **nutrition** is concerned, the inorganic nutrients include

water, **sodium**, potassium, chloride, **calcium**, phosphate, sulfate, magnesium, iron, copper, zinc, manganese, iodine, selenium, and molybdenum. Although these substances are all elements, they are never consumed in that form in the diet. Instead, they are consumed in the form of compounds, such as sulfates and iodides.

There is some evidence that other inorganic nutrients, such as chromium and boron, play a part in human health, but their role is not well established. Fluoride has been proven to increase the strength of bones and teeth, but there is little or no reason to believe that it is needed for human life.

The mineral content of the body may be measured by testing samples of blood plasma, red blood cells, or urine. In the case of calcium and phosphate deficiency, the diagnosis may also involve taking x rays of the skeleton. In the case of iodine deficiency, the diagnosis may include examining the patient's neck with the eyes and hands. In the case of iron deficiency, the diagnosis may include the performance of a stair–stepping test by the patient. Since all minerals serve strikingly different functions in the body, tests for the corresponding deficiency are markedly different from each other.

Description

Laboratory studies with animals have revealed that severe deficiencies in any one of the inorganic nutrients can result in very specific symptoms, and finally in **death**, due to the failure of functions associated with that nutrient. In humans, deficiency in one nutrient may occur less often than deficiency in several nutrients. A patient suffering from **malnutrition** tends to be deficient in a variety of nutrients. In the United States, malnutrition is most often found among severe alcoholics. In part, this is because alcohol consumption may supply half of the energy requirement, resulting in a mineral and vitamin intake of half the expected level. Deficiencies in one nutrient do occur, for example, in human populations living in iodine–poor regions of the world, and in iron deficient persons who lose excess iron by abnormal bleeding.

Inorganic nutrients have a great variety of functions in the body. Water, sodium, and potassium deficiencies are most closely associated with abnormal nerve action and cardiac **arrhythmias**. Deficiencies in these nutrients tend to result not from a lack of content in the diet, but from excessive losses due to severe **diarrhea** and other causes. Iodine deficiency is a global public health problem. It occurs in parts of the world with iodine–deficient soils, and results in **goiter**, which involves a relatively harmless swelling of the neck, and cretinism, a severe birth defect. The only use of iodine in the body is for making thyroid hormone. However, since thyroid hormone has a variety of roles in development of the embryo, iodine deficiency during **pregnancy** results in a number of **birth defects**.

Calcium deficiency due to lack of dietary calcium occurs only rarely. However, calcium deficiency due to **vitamin D deficiency** can be found among certain populations. Vitamin D is required for the efficient absorption of calcium from the diet, and hence vitamin D deficiency in growing infants and children can result in calcium deficiency.

Dietary phosphate deficiency is rare because phosphate is plentiful in plant and animal foods, but also because phosphate is efficiently absorbed from the diet into the body. Iron deficiency causes anemia (lack of red blood cells), which results in tiredness and **shortness of breath**.

Dietary deficiencies in the remaining inorganic nutrients tend to be rare. Magnesium deficiency is uncommon, but when it occurs it tends to occur in chronic alcoholics, in persons taking diuretic drugs, and in those suffering from severe and prolonged diarrhea. Magnesium deficiency tends to occur with the same conditions that provoke deficiencies in sodium and potassium. Zinc deficiency is rare, but it has been found in impoverished populations in the Middle East, who rely on unleavened whole wheat bread as a major food source. Copper deficiency is also rare, but dramatic and health–threatening changes in copper metabolism occur in two genetic diseases, Wilson's disease and Menkes' disease.

Selenium deficiency may occur in regions of the world where soils are poor in selenium. Low–selenium soils can produce foods that are also low in selenium. Premature infants may also be at risk for selenium deficiency. Manganese deficiency is very rare. Experimental studies with humans fed a manganese deficient diet have revealed that the deficiency produces a scaly, red rash on the skin of the upper torso. Molybdenum deficiency has probably never occurred, but indirect evidence suggests that if molybdenum deficiency could occur, it would result in **mental retardation** and death.

Causes and symptoms

Sodium deficiency (**hyponatremia**) and water deficiency are the most serious and widespread deficiencies in the world. These deficiencies tend to arise from excessive losses from the body, as during prolonged and severe diarrhea or **vomiting**. Diarrheal diseases are a major world health problem, and are responsible for about a quarter of the 10 million infant

deaths that occur each year. Nearly all of these deaths occur in impoverished parts of Africa and Asia, where they result from contamination of the water supply by animal and human feces.

The main concern in treating diarrheal diseases is **dehydration**, that is, the losses of sodium and water which deplete the fluids of the circulatory system (the heart, veins, arteries, and capillaries). Severe losses of the fluids of the circulatory system result in **shock**. Shock nearly always occurs when dehydration is severe enough to produce a 10% reduction in body weight. Shock, which is defined as inadequate supply of blood to the various tissues of the body, results in a lack of oxygen to all cells of the body. Although diarrheal fluids contain a number of electrolytes, the main concern in avoiding shock is the replacement of sodium and water.

Sodium deficiency and potassium deficiency also frequently result during treatment with drugs called **diuretics**. Diuretics cause loss of sodium from the body. These drugs are used to treat high blood pressure (**hypertension**), where the resulting decline in blood pressure reduces the risk for cardiovascular disease. However, diuretics can lead to sodium deficiency, resulting in low plasma sodium levels. A side effect of some diuretics is excessive loss of potassium, and low plasma potassium (**hypokalemia**) may result.

Iodine deficiency tends to occur in regions of the world where the soil is poor in iodine. Where soil used in agriculture is poor in iodine, foods grown in the soil will also be low in iodine. An iodine intake of 0.10–0.15 mg/day is considered to be nutritionally adequate, while iodine deficiency occurs at levels of less than 0.05 mg/day. Goiter, an enlargement of the thyroid gland (located in the neck), results from iodine deficiency. Goiter continues to be a problem in eastern Europe, parts of India and South America, and in Southeast Asia. Goiter has been eradicated in the United States because of the fortification of foods with iodine. Iodine deficiency during pregnancy results in cretinism in the newborn. Cretinism involves mental retardation, a large tongue, and sometimes deafness, muteness, and lameness.

Iron deficiency occurs due to periods of dietary deficiency, rapid growth, and excessive loss of the body's iron. Human milk and cow milk both contains low levels of iron. Infants are at risk for acquiring iron deficiency because their rapid rate of growth depends on a corresponding increased supply of dietary iron, for use in making blood and muscles. Human milk is a better source of iron than cow milk, since about half of the iron in human breast milk is absorbed by the infant's digestive tract. In contrast, only 10% of the iron in cow milk is absorbed by the infant. Surveys of lower–income families in the United States have revealed that about six percent of infants are anemic indicating a deficiency of iron in their **diets**. Blood loss that occurs with menstruation in women, as well as with a variety of causes of intestinal bleeding is a major cause of iron deficiency. The symptoms of iron deficiency are generally limited to anemia, and the resulting tiredness, weakness, and a reduced ability to perform physical work.

Calcium and phosphate are closely related nutrients. About 99% of the calcium and 85% of the phosphate in the body occur in the skeleton, where they exist as crystals of solid calcium phosphate. Both of these nutrients occur in a great variety of foods. Milk, eggs, and green, leafy vegetables are rich in calcium and phosphate. Whole cow milk, for example, contains about 1.2 g calcium and 0.95 g phosphorus per kg of food. Broccoli contains 1.0 g calcium and 0.67 g phosphorus per kg food. Eggs supply about one third of the calcium and phosphate of the overall population of the United States. Dietary deficiencies in calcium (**hypocalcemia**) or phosphate are extremely rare throughout the world. Vitamin D deficiency can be found among young infants, the elderly, and others who may be shielded from sunshine for prolonged periods of time. Vitamin D deficiency impairs the absorption of calcium from the diet, and in this way can provoke calcium deficiency even when the diet contains adequate calcium.

Zinc deficiency has been found among peasant populations in rural areas of the Middle East. Unleavened whole wheat bread can account for 75% of the energy intake in these areas. This diet, which does not contain meat, does contain zinc, but it also contains phytic acid at a level of about three grams per day. Phytic acid, which occurs naturally in wheat, inhibits zinc absorption. The yeast used to leaven bread produces enzymes that inactivate the phytic acid. Unleavened bread does not contain yeast, and therefore, contains intact phytic acid. The symptoms of zinc deficiency include lack of sexual maturation, lack of pubic hair, and small stature. The amount of phytic acid in a typical American diet cannot provoke zinc deficiency.

Zinc deficiency is relatively uncommon in the United States, but it may occur in adults with **alcoholism** or intestinal malabsorption problems. Low plasma zinc has been found in patients with alcoholic **cirrhosis**, **Crohn's disease**, and **celiac disease**. Experimental studies with humans have shown that the signs of zinc deficiency are detectable after two to five weeks of consumption of the zinc–free diet. The signs include a

rash and diarrhea. The rash occurs on the face, groin, hands, and feet. These symptoms can easily be reversed by administering zinc. An emerging concern is that increased calcium intake can interfere with zinc absorption or retention. Hence, there is some interest in the question as to whether persons taking calcium to prevent **osteoporosis** should also take zinc supplements.

Severe alterations in copper metabolism occur in two genetic diseases, Wilson's disease and Menkes' disease. Both of these diseases are rare and occur in about one in 100,000 births. Both diseases involve mutations in copper transport proteins, that is, in special channels that allow the passage of copper ions through cell membranes. Menkes' disease is a genetic disease involving mental retardation and death before the age of three years. The disease also results in steely or kinky hair. The hair is tangled, grayish, and easily broken. Menkes' disease involves a decrease in copper levels in serum, the liver, and brain, and increases in copper in cells of the intestines and kidney.

Selenium deficiency may occur in premature infants, since this population naturally tends to have low levels of plasma selenium. Full term infants have plasma selenium levels of about 0.001–0.002 mM, while premature infants may have levels about one third this amount. Whether these lower levels result in adverse consequences is not clear. Selenium deficiency occurs in regions of the world containing low–selenium soils. These regions include Keshan Province in China, New Zealand, and Finland. In Keshan Province, a disease (Keshan disease) occurs which results in deterioration of regions of the heart and the development of fibers in these regions. Keshan disease, which may be fatal, is thought to result from a combination of selenium deficiency and a virus.

Diagnosis

The diagnosis of deficiencies in water, sodium, potassium, iron, calcium, and phosphate involves chemical testing of the blood plasma, urine, and red blood cells.

Iodine deficiency can be diagnosed by measuring the concentration of iodine in the urine. A urinary level greater than 0.05 mg iodine per gram creatinine means adequate iodine status. Levels under 0.025 mg iodine/g creatinine indicate a serious risk.

Normal blood serum magnesium levels are 1.2–2.0 mM. Magnesium deficiency results in hypomagnesemia, which is defined as serum magnesium levels below 0.8 mM. Magnesium levels below 0.5 mM provoke a decline in serum calcium levels. Hypomagnesemia can also result in low serum potassium. Some of the symptoms of hypomagnesemia, which include twitching and convulsions, actually result from the hypocalcemia. Other symptoms of hypomagnesemia, such as cardiac arrhythmias, result from low potassium levels.

There is no reliable test for zinc deficiency. When humans eat diets containing normal levels of zinc (16 mg/day), the level of urinary zinc is about 0.45 mg/day, while humans consuming low–zinc diets (0.3 mg/day) may have urinary levels of about 0.150 mg/day. Plasma zinc levels tend to be maintained during a dietary deficiency in zinc. Plasma and urinary zinc levels can be influenced by a variety of factors, and for this reason cannot provide a clear picture of zinc status.

Selenium deficiency may be diagnosed by measuring the selenium in plasma or red blood cells, where the normal values are 70 ng/mL and 90 ng/mL, respectively. There is also some interest in measuring the activity of an enzyme in blood platelets, in order to assess selenium status. This enzyme is glutathione peroxidase. Platelets are small cells of the bloodstream which are used mainly to allow the clotting of blood after an injury.

Treatment

The treatment of deficiencies in sodium, potassium, calcium, phosphate, and iron usually involves intravenous injections of the deficient mineral.

Iodine deficiency can be easily prevented and treated by fortifying foods with iodine. Table salt is fortified with 100 mg potassium iodide per kg sodium chloride. Goiter was once common in the United States in areas from Washington State to the Great Lakes region, but this problem has been eliminated by the use of iodized salt. Public health programs in impoverished countries have involved injections of synthetic oils containing iodine. Goiter is reversible but, cretinism is not.

Magnesium deficiency can be treated with a magnesium–rich diet. If magnesium deficiency is due to a prolonged period of depletion, treatment may include injections of magnesium sulfate (2.0 mL of 50% $MgSO_4$). Where magnesium deficiency is severe enough to provoke convulsions, magnesium needs to be administered by injections or infusions. For infusion, 500 mL of a 1% solution (1 gram/100 mL) of magnesium sulfate is gradually introduced into a vein over the course of about five hours.

Zinc deficiency and copper deficiency are quite rare, but when they are detected or suspected, they can be treated by consuming zinc or copper, on a daily basis, at levels defined by the RDA.

KEY TERMS

Recommended Dietary Allowance—The Recommended Dietary Allowances (RDAs) are quantities of nutrients that are required each day to maintain human health. RDAs are established by the Food and Nutrition Board of the National Academy of Sciences and may be revised every few years. A separate RDA value exists for each nutrient.

Selenium deficiency in adults can be treated by eating 100 mg selenium per day for a week, where the selenium is supplied as selenomethionine. The incidence of Keshan disease in China has been reduced by supplementing children's diets with 1.0 mg sodium selenite per week.

Prognosis

In iodine deficiency, the prognosis for treating goiter is excellent; however cretinism cannot be reversed. The effects of iron deficiency are not life–threatening and can be easily treated. The prognosis for treating magnesium deficiency is excellent. The symptoms may be relieved promptly or, at most, within two days of starting treatment. In cases of zinc deficiency in Iran and other parts of the Middle East, supplementation of the diets of affected young adults with zinc has been found to provoke the growth of pubic hair and enlargement of genitalia to a normal size within a few months.

Prevention

In a healthy population, all mineral deficiencies can be prevented by the consumption of inorganic nutrients at levels defined by the Recommended Dietary Allowances (RDA). Where a balanced diet is not available, government programs for treating individuals, or for fortifying the food supply, may be used. Government sponsored programs for the prevention of iron deficiency and iodine deficiency are widespread throughout the world. Selenium treatment programs have been used in parts of the world where selenium deficiency exists. Attention to potassium status, and to the prevention of potassium deficiency, is an issue mainly in patients taking diuretic drugs. In many cases of mineral deficiency, the deficiency occurs because of disease, and individual medical attention, rather than preventative measures, is used. The prevention of calcium deficiency is generally not an issue or concern, however calcium supplements are widely used with the hope of preventing osteoporosis. The prevention of deficiencies in magnesium, zinc, copper, manganese, or molybdenum are not major health issues in the United States. Ensuring an adequate intake of these minerals, by eating a balanced diet or by taking mineral supplements, is the best way to prevent deficiencies.

Resources

BOOKS

Bender, David A. *A Dictionary of Food and Nutrition*. New York, NY: Oxford University Press, 2009.

Minich, Deanna M. *Quantum Supplements: A Total Health and Wellness Makeover with Vitamins, Minerals, and Herbs*. San Francisco, CA: Conari Press, 2010.

Sharon, Michael. *Nutrient A–Z: A User's Guide to Foods, Herbs, Vitamins, Minerals & Supplements,* 4th ed. New York, NY: Carlton Publishing Group, 2009.

ORGANIZATIONS

American Dietetic Association, 120 South Riverside Plaza, Suite 2000, Chicago, IL, 60606–6995, (800) 877–1600, http://www.eatright.org.

Food and Nutrition Information Center, National Agricultural Library, United States Department of Agriculture, 10301 Baltimore Ave., Room 105, Beltsville, MD, 20705, (301) 504–5414, http://fnic.nal.usda.gov.

Linus Pauling Institute. Oregon State University, 571 Weniger Hall, Corvallis, OR, 97331–6512, (541) 717–5075, (541) 737–5077, http://lpi.oregonstate.edu.

Office of Dietary Supplements, National Institutes of Health., 6100 Executive Blvd., Room 3B01, MSC 7517, Bethesda, MD, 20892–7517, (301) 435–2920, http://ods.od.nih.gov.

Tom Brody, Ph.D.
Laura Jean Cataldo, RN, Ed.D.

Mineral excess *see* **Mineral toxicity**

Mineral toxicity

Definition

The term mineral toxicity means a condition in which the concentration in the body of any one of a variety of **minerals** is abnormally high, and in which there is an adverse effect on health.

Description

In general, mineral toxicity results when there is an accidental consumption of too much of any mineral, as with drinking ocean water (**sodium** toxicity) or with overexposure to industrial pollutants, household

chemicals, or certain drugs. Mineral toxicity may also apply to toxicity that can be the result of certain diseases or injuries. For example, **hemochromatosis** leads to iron toxicity; Wilson's disease results in copper toxicity; severe trauma can lead to **hyperkalemia** (potassium toxicity).

The mineral nutrients are defined as all the inorganic substances that are required for life. As far as human **nutrition** is concerned, the inorganic nutrients include water, sodium, potassium, chloride, **calcium**, phosphate, sulfate, magnesium, iron, copper, zinc, manganese, iodine, selenium, and molybdenum.

The mineral content of the body may be measured by testing samples of blood plasma, red blood cells, and urine.

Causes and symptoms

An increase in the concentrations of sodium in the bloodstream can be toxic. The normal concentration of sodium in blood plasma is 136–145 mM, while levels over 152 mM can result in seizures and **death**. Increased plasma sodium, which is called **hypernatremia**, causes various cells of the body, including those of the brain, to shrink. Shrinkage of brain cells results in confusion, **coma**, **paralysis** of the lung muscles, and death. Death has occurred in situations in which table salt (sodium chloride) was accidently used, instead of sugar, for feeding infants. Death due to sodium toxicity has also resulted when baking soda (sodium bicarbonate) was used during attempted therapy of excessive **diarrhea** or **vomiting**. Although a variety of processed foods contain high levels of sodium chloride, the levels used are not enough to result in sodium toxicity.

The normal level of potassium in the bloodstream is in the range of 3.5–5.0 mM, while levels of 6.3–8.0 mM (severe hyperkalemia) result in cardiac **arrhythmias** or even death due to cardiac arrest. Potassium is potentially quite toxic; however toxicity or death due to potassium **poisoning** is usually prevented because of the **vomiting** reflex. Consumption of food results in mild increases in the concentration of potassium in the bloodstream, but levels of potassium do not become toxic because of the uptake of potassium by various cells of the body, as well as by the action of the kidneys transferring the potassium ions from the blood to the urine. The body's regulatory mechanisms can easily be overwhelmed, however, when potassium chloride is injected intravenously, as high doses of injected potassium can easily result in death.

Iodine toxicity can result from an intake of 2.0 mg of iodide per day. Ttoxicity results in impairment of the creation of thyroid hormone, resulting in lower levels of thyroid hormone in the bloodstream. The thyroid gland enlarges, as a consequence, and a **goiter** develops. This enlargement is also called **hyperthyroidism**. Goiter is usually caused by iodine deficiency. In addition to goiter, iodine toxicity produces ulcers on the skin. This condition has been called "kelp acne," because of its association with eating kelp, an ocean plant, which contains high levels of iodine. Iodine toxicity occurs in Japan, where large amounts of seaweed are consumed.

Iron toxicity is not uncommon, due to the wide availability of iron pills. A lethal dose of iron is in the range of 200–250 mg iron/kg body weight. Hence, a child who accidently eats 20 or more iron tablets may die as a result of iron toxicity. Within six hours of ingestion, iron toxicity can result in vomiting, diarrhea, abdominal **pain**, seizures, and possibly coma. A latent period, during which symptoms appear to improve, may occur, but that period is followed by **shock**, low blood glucose, liver damage, convulsions, and death, occurring 12–48 hours after toxic levels of iron are ingested.

Nitrite poisoning should be considered along with iron toxicity, since nitrite produces its toxic effect by reacting with the iron component of hemoglobin. Hemoglobin is an iron–containing protein found in red blood cells. This protein is responsible for the transport of nearly all of the oxygen, acquired from the lungs, to various tissues and organs of the body. Hemoglobin accounts for the red color of red blood cells. A very small fraction of hemoglobin spontaneously oxidizes per day, producing a protein of a slightly different structure, called methemoglobin. Normally, the amount of methemoglobin constitutes less than one percent of total hemoglobin. Methemoglobin can accumulate in the blood as a result of nitrite poisoning. Infants are especially susceptible to poisoning by nitrite.

Nitrate, which is naturally present in green leafy vegetables and in the water supply is rapidly converted to nitrite by naturally occurring bacteria residing on our tongue, as well as in the intestines, and then absorbed into the bloodstream. The amount of nitrate that is supplied by leafy vegetables and in drinking water is generally about 100–170 mg/day. The amount of nitrite supplied by a typical diet is much less, that is, than 0.1 mg nitrite/day. Poisoning by nitrite, or nitrate after its conversion to nitrite, results in the inability of hemoglobin to carry oxygen throughout the body. This condition is manifested by the blue color of skin. Adverse symptoms occur when over 30% of hemoglobin has been converted to methemoglobin, and these symptoms include cardiac arrhythmias, **headache**, **nausea and vomiting**, and in severe cases, seizures.

Calcium and phosphate are closely related nutrients. Calcium toxicity is rare, but overconsumption of calcium supplements may lead to deposits of calcium phosphate in the soft tissues of the body. Phosphate toxicity can occur with overuse of **laxatives** or **enemas** that contain phosphate. Severe phosphate toxicity can result in **hypocalcemia**, and in various symptoms resulting from low plasma calcium levels. Moderate phosphate toxicity, occurring over a period of months, can result in the deposit of calcium phosphate crystals in various tissues of the body.

Zinc toxicity is rare, but it can occur in metal workers who are exposed to fumes containing zinc. Excessive dietary supplements of zinc can result in **nausea**, vomiting, and diarrhea. Chronic intake of excessive zinc supplements can result in copper deficiency, as zinc inhibits the absorption of copper.

Severe alterations in copper metabolism occur in two genetic diseases, Wilson's disease and Menkes' disease. Both of these diseases are rare and occur in about one in 100,000 births. Both diseases involve mutations in the proteins that transport copper, that is, in special channels that allow the passage of copper ions through cell membranes. Wilson's disease tends to occur in teenagers and in young adults, and then remain for the lifetime. Copper accumulates in the liver, kidney, and brain, resulting in damage to the liver and nervous system. Wilson's disease can be successfully controlled by lifelong treatment with d–penicillamine. Treatment also involves avoiding foods that are high in copper, such as liver, nuts, chocolate, and mollusks. After an initial period of treatment with penicillamine, Wilson's disease may be treated with zinc (150 mg oral Zn/day). The zinc inhibits the absorption of dietary copper.

Selenium toxicity occurs in regions of the world, including some parts of China, where soils contain high levels of selenium. A daily intake of 0.75–5.0 mg selenium may occur in these regions, due to the presence of selenium in foods and water. Early signs of selenium toxicity include nausea, weakness, and diarrhea. With continued intake of selenium, changes in fingernails and hair loss results, and damage to the nervous system occurs. The breath may acquire a garlic odor, as a result of the increased production of dimethylselenide in the body, and its release via the lungs.

Manganese toxicity occurs in miners in manganese mines, where men breath air containing dust bearing manganese at a concentration of 5–250 mg/cubic meter. Manganese toxicity in miners has been documented in Chile, India, Japan, Mexico, and elsewhere. Symptoms of manganese poisoning typically occur within several months or years of exposure. These symptoms include a mental disorder resembling **schizophrenia**, as well as hyperirritability, violent acts, **hallucinations**, and difficulty in walking.

KEY TERMS

Recommended Dietary Allowance—The Recommended Dietary Allowances (RDAs) are quantities of nutrients that are required each day to maintain human health. RDAs are established by the Food and Nutrition Board of the National Academy of Sciences and may be revised every few years. A separate RDA value exists for each nutrient.

Diagnosis

The initial diagnosis of mineral toxicity involves questioning the patient in order to determine any unusual aspects of the diet, unusual intake of drugs and chemicals, and possible occupational exposure. Diagnosis of mineral toxicities also involves measuring the metal concentration in the plasma or urine. Concentrations that are above the normal range can confirm the initial, suspected diagnosis.

Treatment

Iron toxicity is treated by efforts to remove remaining iron from the stomach, by use of a solution of five percent sodium bicarbonate. Where plasma iron levels are above 0.35 mg/dL, the patient is treated with deferoxamine. Treatment of manganese toxicity involves removal of the patient from the high manganese environment, as well as lifelong doses of the drug L–dopa. The treatment is only partially successful. Treatment of nitrite or nitrate toxicity involves inhalation of 100% oxygen for several hours. If oxygen treatment is not effective, then methylene blue may be injected, as a 1.0% solution, in a dose of 1.0 mg methylene blue/kg body weight.

Prognosis

The prognosis for treating toxicity due to sodium, potassium, calcium, and phosphate is usually excellent. Toxicity due to the deposit of calcium phosphate crystals is not usually reversible. The prognosis for treating iodine toxicity is excellent. For any mineral overdose that causes coma or seizures, the prognosis for recovery is often poor, and death results in a small fraction of patients. For any mineral toxicity that causes nerve damage, the prognosis is often fair to poor.

Prevention

When mineral toxicity results from the excessive consumption of mineral supplements, toxicity can be prevented by not using supplements. In the case of manganese, toxicity can be prevented by avoiding work in manganese mines. In the case of iodine, toxicity can be prevented by avoiding overconsumption of seaweed or kelp. In the case of selenium toxicity that arises due to high–selenium soils, toxicity can be prevented by relying on food and water acquired from a low–selenium region.

Resources

BOOKS

Bender, David A. *A Dictionary of Food and Nutrition*. New York, NY: Oxford University Press, 2009.

Minich, Deanna M., *Quantum Supplements: A Total Health and Wellness Makeover with Vitamins, Minerals, and Herbs*. San Francisco, CA: Conari Press, 2010.

Sharon, Michael. *Nutrient A–Z: A User's Guide to Foods, Herbs, Vitamins, Minerals & Supplements,* 4th ed. New York, NY: Carlton Publishing Group, 2009.

ORGANIZATIONS

American Dietetic Association, 120 South Riverside Plaza, Suite 2000, Chicago, IL, 60606–6995, (800) 877–1600, http://www.eatright.org.

Food and Nutrition Information Center, National Agricultural Library, United States Department of Agriculture, 10301 Baltimore Ave., Room 105, Beltsville, MD, 20705, (301) 504–5414, http:fnic.nal.usda.gov.

Linus Pauling Institute. Oregon State University, 571 Weniger Hall, Corvallis, OR, 97331–6512, (541) 717–5075, (541) 737–5077, http://lpi.oregonstate.edu.

Office of Dietary Supplements, National Institutes of Health, 6100 Executive Blvd., Room 3B01, MSC 7517, Bethesda, MD, 20892–7517, (301) 435–2920, http://ods.od.nih.gov.

Tom Brody, Ph.D.
Laura Jean Cataldo, RN, Ed.D.

Minerals

Definition

The minerals (inorganic nutrients) that are relevant to human **nutrition** include water, **sodium**, potassium, chloride, **calcium**, phosphate, sulfate, magnesium, iron, copper, zinc, manganese, iodine, selenium, and molybdenum. Cobalt is a required mineral for human health, but it is supplied by vitamin B_{12}. Cobalt appears to have no other function, aside from being part of this vitamin. There is some evidence that chromium, boron, and other inorganic elements play some part in human nutrition, but the evidence is indirect and not yet convincing. Fluoride seems not to be required for human life, but its presence in the diet contributes to long term dental health. Some of the minerals do not occur as single atoms, but occur as molecules. These include water, phosphate, sulfate, and selenite (a form of selenium). Sulfate contains an atom of sulfur. We do not need to eat sulfate, since the body can acquire all the sulfate it needs from protein.

The statement that various minerals, or inorganic nutrients, are required for life means that their continued supply in the diet is needed for growth, maintenance of body weight in adulthood, and for reproduction. The amount of each mineral that is needed to support growth during infancy and childhood, to maintain body weight and health, and to facilitate **pregnancy** and **lactation**, are listed in a table called the Recommended Dietary Allowances (RDA). This table was compiled by the Food and Nutrition Board, a committee that serves the United States government. All of the values listed in the RDA indicate the daily amounts that are expected to maintain health throughout most of the general population. The actual levels of each inorganic nutrient required by any given individual is likely to be less than that stated by the RDA. The RDAs are all based on studies that provided the exact, minimal requirement of each mineral needed to maintain health. However, the RDA values are actually greater than the minimal requirement, as determined by studies on small groups of healthy human subjects, in order to accomodate the variability expected among the general population.

The RDAs for adult males are 800 mg of calcium, 800 mg of phosphorus, 350 mg of magnesium, 10 mg of iron, 15 mg of zinc, 0.15 mg of iodine, and 0.07 mg of selenium. The RDA for sodium is expressed as a range (0.5-2.4 g/day). The minimal requirement for chloride is about 0.75 g/day, and the minimal requirement for potassium is 1.6-2.0 g/day, though RDA values have not been set for these nutrients. The RDAs for several other minerals has not been determined, and here the estimated safe and adequate daily dietary intake has been listed by the Food and Nutrition Board. These values are listed for copper (1.5-3.0 mg), manganese (2-5 mg), fluoride (1.5-4.0 mg), molybdenum (0.075-0.25 mg), and chromium (0.05-0.2 mg). In noting the appearance of chromium in this list, one should note that the function of chromium is essentially unknown, and evidence for its necessity exists only for animals, and not for human beings. In considering the amount of any mineral used for treating **mineral deficiency**, one should compare the recommended level with the RDA

for that mineral. Treatment at a level that is one tenth of the RDA might not be expected to be adequate, while treatment at levels ranging from 10-1,000 times the RDA might be expected to exert a toxic effect, depending on the mineral. In this way, one can judge whether any claim of action, for a specific mineral treatment, is likely to be adequate or appropriate.

Purpose

People are treated with minerals for several reasons. The primary reason is to relieve a mineral deficiency, when a deficiency has been detected. Chemical tests suitable for the detection of all mineral deficiencies are available. The diagnosis of the deficiency is often aided by tests that do not involve chemical reactions, such as the **hematocrit** test for the red blood cell content in blood for iron deficiency, the visual examination of the neck for iodine deficiency, or the examination of bones by densitometry for calcium deficiency. Mineral treatment is conducted after a test and diagnosis for iron-deficiency anemia, in the case of iron, and after a test and diagnosis for hypomagnesemia, in the case of magnesium, to give two examples.

A second general reason for mineral treatment is to prevent the development of a possible or expected deficiency. Here, minerals are administered when tests for possible mineral deficiency are not given. Examples include the practice of giving young infants iron supplements, and of the food industry's practice of supplementing infant formulas with iron. The purpose here is to reduce the risk for **iron deficiency anemia**. Another example is the practice of many women of taking calcium supplements, with the hope of reducing the risk of **osteoporosis**.

Most minerals are commercially available at supermarkets, drug stores, and specialty stores. There is reason to believe that the purchase and consumption of most of these minerals is beneficial to health for some, but not all, of the minerals. Potassium supplements are useful for reducing blood pressure, in cases of persons with high blood pressure. The effect of potassium varies from person to person. The consumption of calcium supplements is likely to have some effect on reducing the risk for osteoporosis. The consumption of selenium supplements is expected to be of value only for residents of Keshan Province, China, because of the established association of selenium deficiency in this region with "Keshan disease."

Precautions

During emergency treatment of sodium deficiency (**hyponatremia**), potassium deficiency (**hypokalemia**), and calcium deficiency (**hypocalcemia**) with intravenous injections, extreme caution must be taken to avoid producing toxic levels of each of these minerals (**hypernatremia**, **hyperkalemia**, and **hypercalcemia**), as **mineral toxicity** can be life-threatening in some instances. The latter three conditions can be life threatening. Selenium is distinguished among most of the nutrients in that dietary intakes at levels only ten times that of the RDA can be toxic. Hence, one must guard against any overdose of selenium. Calcium and zinc supplements, when taken orally, are distinguished among most of the other minerals in that their toxicity is relatively uncommon.

Description

Minerals are used in treatments by three methods, namely, by replacing a poor diet with a diet that supplies the RDA, by consuming oral supplements, or by injections or infusions. Injections are especially useful for infants, for mentally disabled persons, or where the physician wants to be totally sure of compliance. Infusions, as well as injections, are essential for medical emergencies, as during mineral deficiency situations like hyponatremia, hypokalemia, hypocalcemia, and hypomagnesemia. Oral mineral supplements are especially useful for mentally alert persons who otherwise cannot or will not consume food that is a good mineral source, such as meat. For example, a vegetarian who will not consume meat may be encouraged to consume oral supplements of iron, as well as supplements of vitamin B_{12}.

Iron treatment is used for young infants, given as supplements of 7 mg of iron per day to prevent anemia. Iron is also supplied to infants via the food industry's practice of including iron at 12 mg/L in cow milk-based infant formulas, as well as adding powdered iron at levels of 50 mg iron per 100 g dry infant cereal.

Calcium supplements, along with estrogen and calcitonin therapy, are commonly used in the prevention and treatment of osteoporosis. Estrogen and calcitonin are naturally occurring hormones. Bone loss occurs with **diets** supplying under 400 mg Ca/day. Bone loss can be minimized with the consumption of the RDA for calcium. There is some thought that all postmenopausal women should consume 1,000–1,500 mg of calcium per day. These levels are higher than the RDA. There is some evidence that such supplementation can reduce bone losses in some bones, such as the elbow (ulna), but not in other bones. Calcium absorption by the intestines decreases with **aging**, especially after the age of 70. The regulatory mechanisms of the intestines that allow absorption of adequate calcium

(500 mg Ca/day or less) may be impaired in the elderly. Because of these changes, there is much interest in increasing the RDA for calcium for older women.

Fluoride has been proven to reduce the rate of **tooth decay**. When fluoride occurs in the diet, it is incorporated into the structure of the teeth, and other bones. The optimal range of fluoride in drinking water is 0.7-1.2 mg/L. This level results in a reduction in the rate of tooth decay by about 50%. The American Dental Association recommends that persons living in areas lacking fluoridated water take fluoride supplements. The recommendation is 0.25 mg F/day from the ages of 0-2 years, 0.5 mg F/day for 2-3 years, and 1.0 mg F/day for ages 3-13 years.

Magnesium is often used to treat a dangerous condition, called **eclampsia**, that occasionally occurs during pregnancy. In this case, magnesium is used as a drug, and not to relieve a deficiency. High blood pressure is a fairly common disorder during pregnancy, affecting 1-5% of pregnant mothers. **Hypertension** during pregnancy can result in increased release of protein in the urine. In pregnancy, the combination of hypertension with increased urinary protein is called **preeclampsia**. Preeclampsia is a concern during pregnancies as it may lead to eclampsia. Eclampsia involves convulsions and possibly **death** to the mother. Magnesium sulfate is the drug of choice for preventing the convulsions of eclampsia.

Treatment with cobalt, in the form of vitamin B_{12}, is used for relieving the symptoms of **pernicious anemia**. Pernicious anemia is a relatively common disease which tends to occur in persons older than 40 years. Free cobalt is never used for the treatment of any disease.

Preparation

Evaluation of a patient's mineral levels requires a blood sample, and the preparation of plasma or serum from the blood sample. An overnight fast is usually recommended as preparation prior to drawing the blood and chemical analysis. The reason for this is that any mineral present in the food consumed at breakfast may artificially boost the plasma mineral content beyond the normal **fasting** level, and thereby mask a mineral deficiency. In some cases, red blood cells are used for the mineral status assay.

Aftercare

The healthcare provider assesses the patient's response to mineral treatment. A positive response confirms that the diagnosis was correct. Lack of response indicates that the diagnosis was incorrect, that the patient had failed to take the mineral supplement, or that a higher dose of mineral was needed. The response to mineral treatment can be monitored by chemical tests, by an examination of red blood cells or white blood cells, or by physiological tests, depending on the exact mineral deficiency.

Risks

There are few risks associated with mineral treatment. In treating emergency cases of hyponatremia, hypokalemia, or hypocalcemia by intravenous injections, there exists a very real risk that giving too much sodium, potassium, or calcium, can result in hypernatremia, hyperkalemia, or hypercalcemia, respectively. Risk for toxicity is rare where treatment is by dietary means. This is because the intestines act as a barrier, and absorption of any mineral supplement is gradual. The gradual passage of any mineral through the intestines, especially when the mineral supplement is taken with food, allows the various organs of the body to acquire the mineral. Gradual passage of the mineral into the bloodstream also allows the kidneys to excrete the mineral in the urine, should levels of the mineral rise to toxic levels in the blood.

Resources

BOOKS

Dutrow, Barbara and Klein, Cornelis. *Manual of Mineral Science, 23rd Edition* Wiley, 2007.

Tom Brody, PhD
Karl Finley

Minnesota multiphasic personality inventory (MMPI-2)

Definition

The Minnesota Multiphasic Personality Inventory (MMPI-2; MMPI-A) is a written psychological assessment, or test, used to diagnose mental disorders.

Purpose

The MMPI is used to screen for personality and **psychosocial disorders** in adults and adolescents. It is also frequently administered as part of a neuropsychological test battery to evaluate cognitive functioning.

KEY TERMS

Neuropsychological testing—Tests used to evaluate patients who have experienced a traumatic brain injury, brain damage, or organic neurological problems (e.g., dementia). It may also be used to evaluate the progress of a patient who has undergone treatment or rehabilitation for a neurological injury or illness.

Norms—Normative or mean score for a particular age group.

Psychopathology—A mental disorder or illness, such as schizophrenia, personality disorder, or major depressive disorder.

Standardization—The process of determining established norms and procedures for a test to act as a standard reference point for future test results.

Precautions

The MMPI should be administered, scored, and interpreted by a clinical professional trained in its use, preferably a psychologist or psychiatrist. The MMPI is only one element of psychological assessment, and should never be used alone as the sole basis for a diagnosis. A detailed history of the test subject and a review of psychological, medical, educational, or other relevant records are required to lay the groundwork for interpreting the results of any psychological measurement.

Cultural and language differences in the test subject may affect test performance and may result in inaccurate MMPI results. The test administrator should be informed before psychological testing begins if the test taker is not fluent in English and/or has a unique cultural background.

Description

The original MMPI was developed at the University of Minnesota and introduced in 1942. The current standardized version for adults 18 and over, the MMPI-2, was released in 1989, with a subsequent revision of certain test elements in early 2001. The MMPI-2 has 567 items, or questions, and takes approximately 60 to 90 minutes to complete. There is a short form of the test that is comprised of the first 370 items on the long-form MMPI-2. There is also a version of the inventory for adolescents age 14 to 18, the MMPI-A.

The questions asked on the MMPI are designed to evaluate the thoughts, emotions, attitudes, and behavioral traits that comprise personality. The results of the test reflect an individual's personality strengths and weaknesses, and may identify certain disturbances of personality (psychopathologies) or mental deficits caused by neurological problems.

There are six validity scales and ten basic clinical or personality scales scored in the MMPI-2, and a number of supplementary scales and subscales that may be used with the test. The validity scales are used to determine whether the test results are actually valid (i.e., if the test-taker was truthful, answered cooperatively and not randomly) and to assess the test-taker's response style (i.e., cooperative, defensive). Each clinical scale uses a set or subset of MMPI-2 questions to evaluate a specific personality trait. The MMPI should always be administered in a controlled environment by a psychologist or other qualified mental health professional trained in its use.

Preparation

The administrator should provide the test subject with information on the nature of the test and its intended use, complete standardized instructions to taking the MMPI (including any time limits, and information on the confidentiality of the results).

Normal results

The MMPI should be scored and interpreted by a trained professional. When interpreting test results for test subjects, the test administrator will review what the test evaluates, its precision in evaluation and any margins of error involved in scoring, and what the individual scores mean in the context of overall norms for the test and the background of the test subject.

Resources

BOOKS

Graham, John R. *MMPI–2: Assessing Personality and Psychopathology*. 4th ed. New York: Oxford University Press, 2006.

ORGANIZATIONS

ERIC Clearinghouse on Assessment and Evaluation, 1131 Shriver Laboratory (Bldg 075), University of Maryland, College Park, MD, 20742, (800) 464-3742, feedback3@ericae.net, http://www.ericae.net.

Paula Anne Ford-Martin

Minor tranquilizers *see* **Antianxiety drugs**

Minority health

Definition

Minority health addresses the special medical and/or health needs associated with specific ethnic and racial groups—those that are included in the minority populations within the United States.

Demographics

Some of the specific ethnic and racial groups in the United States that are included within minority populations, as stated by the Office of Minority Health (part of the U.S. Department of Health and Human Services), include Native Americans and Alaska Natives, Asian Americans, Blacks/African Americans, Hispanics/Latinos, Native Hawaiians, and other Pacific Islanders.

Description

The United States, as well as many other countries, experiences cultural diversity. This poses specific health issues that are specific to ethnic groups. Additionally, the propensity for certain diseases or illnesses is of concern in certain minority groups. These specific health issues include infant mortality rates, **cancer**, cardiovascular disease, diabetes, HIV (human **immunodeficiency** virus) infection, and immunizations.

Infant mortality rates

Infant mortality rates (IMRs) in the United States and in all countries worldwide are an accurate indicator of health status. They provide information concerning programs about **pregnancy** education and counseling, technological advances, and procedures and aftercare. IMRs vary among racial groups. The IMR in the United States, in 2010, is estimated to be 6.22 per 1,000 live births, according to the Central Intelligence Agency. Males have an IMR of 6.9, while females have 5.51.

African Americans had an IMR of 13.6 per 1,000 live births, approximately 2.5 times higher than Caucasians. The IMRs among American Native Indian groups varies greatly, with some communities possessing IMRs about two times more than national rates. Overall Native Americans had an IMR of 8.1. Additionally Hispanic Americans IMRs (7.6 per 1,000 live births, overall) are also diverse for separate groups, since the IMRs for example among Puerto Rican Americans is higher (8.3 per 1,000 live births) while with Mexican Americans it is lower (5.5 per 1,000 live births). Asian- and Pacific Islander Americans came in at 4.9, Central Americans and South-Americans at 4.7, and Cuban Americans at 4.4 per 1,000 live births. (Statistics for the various minority groups were provided by the U.S. Centers for Disease Control and Prevention.)

Cancer

Cancer is a serious national, worldwide, and minority health concern. In 2008, the number of non-institutionalized adults who had ever been diagnosed with cancer in the United States stood at 17.9 million, or about 7.9% of the adult population. It is the second cause of **death** in the United States, claiming over half a million lives each year (approximately 565,000 in 2008, according to the American Cancer Society). Approximately 50% of persons who develop cancer will die from it.

There is great disparity among the cancer rates in minority groups. Across genders, cancer death rates for African Americans are 35% higher when compared to statistics for Caucasian Americans. The death rates for **prostate cancer** (two times more) and lung cancer (27 times more) are disproportionately higher when compared to Caucasians. In addition, Hispanic men and women have higher incidence and mortality rates for stomach and **liver cancer** than non-Hispanics.

Additionally, Alaskan native men and women have a greater propensity for cancers in the rectum and colon than do Caucasians. Native American/Alaska Native men are more at risk for liver and **stomach cancer**, when compared to non-Hispanic white men. Asian American men are more prone to stomach cancer than are non-Hispanic white men. At the same time, Asian and Pacific Islander American women will develop stomach cancer more often than non-Hispanic American white women.

There are also gender differences among ethnic groups and specific cancers. Lung cancers in African American and Hawaiian men are higher when compared with Caucasian males. Vietnamese females who live in the United States have five times more new cases of **cervical cancer** when compared to Caucasian women. Hispanic females also have a greater incidence of cervical cancer than Caucasian females, and they are more likely to have **kidney cancer** when compared to non-Hispanic white women.

Cardiovascular disease

Cardiovascular disease is responsible for the leading cause of disability and death rates about equal to death from all other diseases combined. Cardiovascular disease can affect the patient's lifestyle and function in

addition to having an impact on family members. The financial costs are very high. Among ethnic and racial groups, cardiovascular disease is the leading cause of death. African Americans are more likely to have high blood pressure than other ethnic groups in the United States. However, African Americans and non-Hispanic white Americans have similar rates of heart disease. Unfortunately, African American males are three times more likely to die from heart disease than are white males.

Stroke is the leading cause of cardiovascular related death, which occurs in higher numbers for Asian American males when compared to Caucasian men. Mexican American men and women and African-American males have a higher incidence of **hypertension**. African American women have higher rates of being overweight, which is a major risk factor of cardiovascular disease. Mexican Americans, African Americans, Native Hawaiian/Pacific Islanders, and Native Americans/Alaskan Natives also have higher rates of **obesity** than do other groups.

Diabetes

Diabetes—a serious health problem in Americans and ethnic groups—is the seventh leading cause of death in the United States. About 40% of all American adults have pre-diabetes. Racial and ethnic minorities are especially at risk for diabetes. The prevalence of diabetes in African Americans is about twice than for Caucasians, according to the Office of Mental Health. The elderly within the African American population is especially at risk for diabetes, even more so for women over the age of 65 years. Diabetes is also common in older Hispanics. Native Americans and Alaska Natives have approximately double the risk for diabetes than do non-Hispanic whites.

HIV

HIV infection/AIDS (acquired immune deficiency syndrome) is the most common cause of death for all persons age 25 to 44 years old. Ethnic groups account for about 25% of the United States population and nearly two-thirds of all recently diagnosed **AIDS** cases, according to the Office of Minority Health. In addition, about 75% of all babies born with HIV/AIDS is a member of one of the minority groups in the United States. Besides an increase of sexual transmission of HIV/AIDS within the minority communities, there is also an increase in HIV among ethnic groups related to intravenous drug usage. Specifically, African Americans, both men and women, are more likely to die from AIDS than are non-Hispanic white men.

Immunizations

The gap among immunization, the reduction of preventable disease by **vaccination**, between minority groups and whites has narrowed over the past years. However, there are still smaller percentages of minority adults being immunized when compared to white adults. Overall, immunization rates among all groups are much higher than compared to adults. In 2008, the Office of Minority Health reported that 70% of older non-Hispanic whites received the **influenza** (flu) vaccination, while only 51% of older African Americans and 56% of Hispanics received the vaccine.

Tuberculosis is a disease that is controlled by immunizations. However, Asian and Pacific Islander Americans were 23 times more at risk for contracting tuberculosis (TB) than were non-Hispanic whites. **Hepatitis B** is another disease controlled with vaccines. Even though rates of hepatitis B continue to decline in the United States in the twenty-first century, its rate is twice as high for non-Hispanic blacks when compared to non-Hispanic whites. The Office of Minority Health also reports that, in 2008, older Asian Americans and Hispanic Americans (those over 65 years of age) were less likely to have received a **pneumonia** vaccine as compared to older non-Hispanic whites.

The Office of Minority Health and Health Disparities (OMHHD) stated that, in 2000, children living below the poverty level in the United States had lower immunization levels overall than did those above the poverty level. Disparities still exist, in 2010, concerning immunization rates among racial and ethnic groups in the United States. During the 2010s, the OMHHD hopes to be able to achieve and maintain a 90% rate of childhood immunization and to achieve a 60% rate in flu and pneumonia vaccinations in the United States. Such rates would help to eliminate disparities among minority groups within regards to immunizations.

Causes and symptoms

IMRs are correlated with prenatal care. Women who receive adequate prenatal care tend to have better pregnancy outcomes when compared to little or no care. Women who receive inadequate prenatal care also have increased chances of delivering a very low birth weight (VLBW) infant, which is linked to risk of early death.

Cancer is related to several preventable lifestyle choices. Tobacco use, diet, and exposure to the Sun (skin cancer) can be prevented by lifestyle modifications. Additionally many cancers can occur due to lack of interest and/or lack of availability for screening and educational programs.

DR. ANTONIA NOVELLO (1944–)

(Terry Ashe/Getty Images.)

Born Antonia Coello was born in Fajardo, Puerto Rico, on August 23, 1944, the oldest of three children. At eight years old, she suffered two blows that she would carry all of her life. Her father, Antonio Coello, died, leaving her mother, Ana Delia Flores Coello, to raise her children alone until she later remarried Ramon Flores, an electrician. Novello was also diagnosed with a chronic condition called congenital megacolon, an illness in which her colon was overly large and not functioning properly, which required regular hospitalization. Although an operation would have helped Novello, it was not performed until she was 18 years old, and even after the surgery, complications followed her for years. Because of her childhood illness, Novello grew up wanting to be a doctor.

On October 17, 1989, President George Bush officially nominated Novello for Surgeon General. The fourteenth United States Surgeon General, Novello, sworn in on March 9, 1990, remarked that "the American dream is well and alive. . .today the West Side Story comes to the West Wing." Novello was the first woman and the first Hispanic to be appointed Surgeon General of the United States. Noted for her philosophy of "good science, good sense" and for her approachability, Novello was dedicated to the prevention of AIDS, substance abuse, and smoking, as well as to the education of the American public. Her special concerns were for women, children, and hispanics—populations often overlooked by public health services.

After serving as Surgeon General, Dr. Novello was a special representative to United Nations Children's Fund from 1993 to 1996, where she expanded her efforts to address the health and nutritional needs of women, children, and adolescents, to a global scale. From 1996 to 1999 she was visiting professor of health policy and management at Johns Hopkins School of Health and Hygiene, where she advised on health services for poor communities. To mark the fiftieth anniversary of the Universal Declaration of Human Rights in 1998, Novello organized an unprecedented meeting between Surgeon General David Satcher and seven others who had held the office. In 1999, Governor George Pataki nominated her to be commissioner of health for the state of New York, a move that drew cries of betrayal from the abortion rights movement over her opposition to abortion. At the time, Mr. Pataki called her a trailblazer in addressing children's health issues who could help lead the state's effort to save money by moving recipients of Medicaid, the health care program for the poor, into managed care.

Novello served as commissioner until 2006. On May 12, 2009 in New York, she was charged in a 20 count indictment with theft of government services, defrauding the government and filing a false instrument. On June 26, 2009, in a plea deal with prosecutors, she pleaded guilty to one charge of filing a false document involving a worker's duties.

Cardiovascular diseases are higher among persons with high blood cholesterol and high blood pressure. Certain lifestyle choices may increase the chance for heart disease includes lack of **exercise**, overweight, and cigarette **smoking**. Cardiovascular disease is responsible for over 50% of the deaths in persons with diabetes.

HIV occurs at a higher frequency among homosexuals (the number of African American males who have AIDS through sex with men has increased). Additionally unprotected sexual intercourse and sharing used needles for IV drug injection are strongly correlated with infection.

Vaccinations are an effective method of preventing certain disease such as **polio**, **tetanus**, pertussis, **diphtheria**, influenza, hepatitis b, and pneumococcal infections. Approximately 90% of influenza related mortality is associated with persons aged 65 and older. This is mostly due to neglect of vaccinations. About 45,000 adults each year die of diseases related to hepatitis B, pneumococcal, and influenza infections.

Diagnosis

The diagnosis of VLBW is by weight. Infants who weigh 1,500 grams (1.5 kilograms, or 3.3 pounds) at

KEY TERMS

Prevalence—Number of existing cases relative to time.

Propensity—A greater risk for developing a disease.

birth are at high risk for death. For cancer, the diagnosis can be made through screening procedures such as **mammography** (for **breast cancer**), PAP smear (PAP is short for papanicolau, which is used to identify cervical cancer), and lifestyle modifications such as avoidance of ultraviolet rays from the Sun (and artificially produced radiation, such as from **tanning** beds), cigarette smoking, balanced **diets**, and adequate **nutrition**. Other specific screening tests (PSA, prostate surface antigen) are helpful for diagnosing prostate cancer.

Cardiovascular diseases can be detected by medical check-ups. Blood pressure and cholesterol levels can be measured. Obesity can be diagnosed by assessing a person's weight relative to their height (what is called BMI, or body mass index). Diabetes and its complications can be detected by blood tests, in-depth eye examinations, and studies that assess the flow of blood through blood vessels in legs. HIV can be detected through a careful history/physical examination and analysis of blood using a special test called a western blot. Infections caused by lack of immunizations can either be detected by careful **physical examination** and culturing the specific microorganism in the laboratory.

Treatment

Treatment is directed at the primary causes(s) that minorities have increased chances of developing disease(s). Cancer may require treatment utilizing surgery, radiotherapy, or **chemotherapy**. Cardiovascular diseases may require surgical procedures for establishing a diagnosis and initiating treatment. Depending on the extent of disease, cardiovascular management can become complicated requiring medications and daily lifestyle modifications. Treatment usually includes medications, dietary modifications, and—if complications arise—specific interventions tailored to alleviating the problem. HIV can be treated with specific medications and more often than not with symptomatic treatment as reported complications arise. Diseases caused by lack of immunizations are treated based on the primary disease. The best method of treatment is through prevention and generating public awareness through educational awareness.

Alternative treatment

Alternative therapies do exist, but more research is needed to substantiate present data. The diseases that relate to minority health are best treated with nationally accepted standards of care.

Prognosis

Generally the prognosis is related to the diagnosis, patients state of health, age, and if there is another disease or complication in addition to the presenting problem. The course for IMRs is related to educational programs and prenatal care, which includes medical and psychological treatments. The prognosis for chronic diseases such as cardiovascular problems, high blood pressure, cancer, and diabetes is variable. These diseases are not cured and control is achieved by standardized treatment options. Eventually complications, even with treatment can potentially occur. For HIV the clinical course at present is death even though this process may take years. Educational programs with an emphasis on disease prevention can potentially improve outcomes concerning pediatric and geriatric diseases.

Prevention

Prevention is accomplished best through educational programs specific to target populations. IMRs can be prevented by increasing awareness, interest, and accessibility for prenatal care that address a comprehensive approach for the needs of each patient. Regular physicals and special screening tests ca potentially prevent certain cancers in high-risk groups. Educational programs concerning lifestyle modifications, diet, exercise, and testing may prevent the development of cardiovascular disease and diabetes. Educational programs assemble to illicit IV drug abusers and persons who engage in unprotected sexual intercourse may decrease the incidence of HIV infection.

All adults in the United States should be proactive, making sure to get information on those preventable diseases they are at most risk for acquiring and for which vaccines are available. Parents and other caregivers should make sure that their children have been fully vaccinated by the age of two years. Sons and daughters of **aging** parents should assure that their parents are receiving the necessary vaccines, such as pneumococcal vaccines (for pneumonia), which will help them stay healthy and minimize their risks of premature death.

The importance of diagnosing, treating, and preventing minority health programs over the next decade will become increasingly important. The U.S.

Census Bureau estimates that by 2100, only about 40% of the U.S. population will consist of non-Hispanic whites. As minority groups grow faster in the future, their health will become a larger factor in the overall health of all Americans. Hopefully, the disparities in health issue with minorities, when compared to whites, will dissipate, especially with regards to preventable diseases, disabilities, and mortality.

Resources

BOOKS

Gilman, Sander L. *Diseases and Diagnoses: The Second Age of Biology*. New Brunswick, NJ: Transaction, 2010.

Hofrichter, Richard, and Rajiv Bhatia, editors. *Tackling Health Inequities Through Public Health Practice: Theory to Action*. Oxford, UK: Oxford University Press, 2010.

Liburd, Leandris C., editor. *Diabetes and Health Disparities: Community-based Approaches for Racial and Ethnic Populations*. New York: Springer, 2010.

OTHER

Cancer. Centers for Disease Control and Prevention. (April 15, 2010), http://www.cdc.gov/nchs/fastats/cancer.htm (accessed September 16, 2010).

Cancer Death Rate down but 565, 650 Seen in 2008. Reuters. (February 20, 2008), http://www.reuters.com/article/idUSN1926392720080220 (accessed September 16, 2010).

Country Comparison: Infant mortality rate. Central Intelligence Agency. (September 2010), https://www.cia.gov/library/publications/the-world-factbook/rankorder/2091rank.html (accessed September 16, 2010).

Eliminate Disparities in Adult and Child Immunization Rates. Office of Minority Health and Health Disparities, Centers for Disease Control and Prevention. (June 5, 2007), http://www.cdc.gov/omhd/amh/factsheets/immunization.htm (accessed September 16, 2010).

Immunizations Data/Statistics. Office of Minority Health, Department of Health and Human Services. (April 20, 2010), http://minorityhealth.hhs.gov/templates/browse.aspx?lvl=3&lvlid=60 (accessed September 16, 2010).

Minority Health. Wychoff Heights Medical Center. http://www.wyckoffhospital.org/body.cfm?id=587 (accessed September 16, 2010).

Recent Trends in Infant Mortality in the United States. Centers for Disease Control and Prevention. (October 2008), http://www.cdc.gov/nchs/data/databriefs/db09.htm (accessed September 16, 2010).

ORGANIZATIONS

Office of Minority Health, Post Office Box 37337, Washington, DC, 20013-7337, (800) 444-6472, http://minorityhealth.hhs.gov/.

Office of Minority Health and Health Disparities, 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, http://www.cdc.gov/omhd/.

Minoxidil

Definition

Minoxidil is a drug that is available in two forms: as a solution or foam, Rogaine, applied topically to the scalp to promote hair growth, and as tablets, Loniten, to treat high blood pressure.

Purpose

Hair growth and the reversal of male pattern baldness was a side effect noted when Loniten was used to treat high blood pressure. How it stimulates hair growth is not known.

Rogaine solution and foam, in 2% and 5% concentrations, are available in the U.S. without a prescription.

Rogaine is more likely to be effective in men and women under age 40. It must be used daily for up to three months before hair growth become noticeable. Once daily use is stopped, hair loss begins again. Rogaine is more likely to be effective in men and women under age 40.

Minoxidil does not work for everyone. Forty-eight percent of men who use it for one year can expect to see moderate to dense regrowth of hair; thirty-six percent minimal regrowth, and sixteen percent no regrowth.

Women and men respond similarly to topical minoxidil.

Minoxidil tablets, orally, is only used for treating severe high blood pressure and has serious has side effects that generally require using additional medications.

Precautions

It is important to carefully follow the package directions for the amount to use (dose) and proper application and handling of minoxidil solution or foam.

Minoxidil should not be used 24 hours before or after applying hair treatments such as coloring, permanent or relaxer. Before applying these treatments, the hair should be thoroughly washed and dried.

After applying minoxidil, hands should be thoroughly washed.

To reduce the risk of absorption through the skin, Minoxidil should be used only on small areas of the scalp.

People with sunburns and/or chronic skin or scalp **rashes** or conditions may absorb minoxidil into their bodies and run a greater risk of side effects.

People who have had unusual or allergic skin reactions to dyes and preservatives may be at greater risk for allergic reactions to minoxidil foam or solution.

People who use cortisone creams or ointments, petroleum jelly (Vaseline), or tretinoin (Retin-A) on their scalps risk absorbing more minoxidil into their bodies and experiencing side effects.

Minoxidil enters breast milk and is not recommended for use in nursing mothers.

Preparation

Before applying topical minoxidil, the hair and scalp should be clean and dry.

Aftercare

Immediately after applying minoxidil, hands and other areas of the body that may have come into contact with the drug, where hair growth is not desired, should be washed.

Do not wash hair for four hours after applying minoxidil.

Topical minoxidil should be allowed to air-dry for two to four hours before clothing is pulled on or off over the head, a hat is worn, or the person using it goes to bed. Minoxidil may stain clothing, hats, or bed linens.

Do not use a blow dryer or other hair-drying method. People using minoxidil should not shampoo, wash, or rinse their hair for at least 4 hours after minoxidil is applied.

Risks

More common side effects from using topical minoxidil include **itching**, burning, redness, and tenderness over hair roots in treated areas. These usually go away within a couple of weeks.

Unwanted hair growth may occur adjacent to treated areas or in areas where the medicine has been inadvertently transferred.

Side effects that may occur if topically minoxidil is absorbed into the body include:

- changes in vision, most commonly blurred vision
- chest pain
- dizziness
- rapid or irregular pulse
- very low blood pressure
- fast or irregular heartbeat
- flushing of the skin
- headache
- lightheadedness
- numbness or tingling in the hands, feet, or face
- rapid weight gain
- swelling of the hands, feet, lower legs, or face

Normal results

When new growth begins, the first hairs may be soft and barely visible. For some, this is the extent of the effectiveness of this medication. For others, the down-like hair develops into hair of the same color and thickness as the other hairs on their heads.

Minoxidil is a treatment, not a cure, for hair loss. Once a person stops using it, the re-grown hair will be lost within 90 days.

Resources

OTHER

"Minoxidil (topical route)." Mayo Clinic online. http://www.mayoclinic.com/health/drug-information/DR601937 (accessed July 30, 2009).

James Waun, MD, RPh

Miscarriage

Definition

Miscarriage means loss of an embryo or fetus before the 20th week of **pregnancy**. Most miscarriages occur during the first 14 weeks of pregnancy. The medical term for miscarriage is spontaneous abortion.

Description

Miscarriages are very common. Approximately 20% of pregnancies (one in five) end in miscarriage. The most common cause is a genetic abnormality of the fetus. Not all women realize that they are miscarrying and others may not seek medical care when it occurs.

A miscarriage is often a traumatic event for both partners, and can cause feelings similar to the loss of a child or other member of the family. Fortunately, 90% of women who have had one miscarriage subsequently have a normal pregnancy and healthy baby; 60% are able to have a healthy baby after two miscarriages. Even a woman who has had three miscarriages in a

row still has more than a 50% chance of having a successful pregnancy the fourth time.

Causes and symptoms

There are many reasons why a woman's pregnancy ends in miscarriage. Often the cause is not clear. However, more than half the miscarriages that occur in the first eight weeks of pregnancy involve serious chromosomal abnormalities or **birth defects** that would make it impossible for the baby to survive. These are different from inherited genetic diseases. They probably occur during development of the specific egg or sperm, and therefore are not likely to occur again.

In about 17% of cases, miscarriage is caused by an abnormal hormonal imbalance that interferes with the ability of the uterus to support the growing embryo. This is known as luteal phase defect. In another 10% of cases, there is a problem with the structure of the uterus or cervix. This can especially occur in women whose mothers used diethylstilbestrol (DES) when pregnant with them.

The risk of miscarriage is increased by:

- Smoking (up to a 50% increased risk)
- Infection
- Exposure to toxins (such as arsenic, lead, formaldehyde, benzene, and ethylene oxide)
- Multiple pregnancy
- Poorly controlled diabetes.

The most common symptom of miscarriage is bleeding from the vagina, which may be light or heavy. However, bleeding during early pregnancy is common and is not always serious. Many women have slight vaginal bleeding after the egg implants in the uterus (about 7-10 days after conception), which can be mistaken for a threatened miscarriage. A few women bleed at the time of their monthly periods through the pregnancy. However, any bleeding in the first three months of pregnancy (first trimester) is considered a threat of miscarriage.

Women should not ignore vaginal bleeding during early pregnancy. In addition to signaling a threatened miscarriage, it could also indicate a potentially life-threatening condition known as **ectopic pregnancy**. In an ectopic pregnancy, the fetus implants at a site other than the inside of the uterus. Most often this occurs in the fallopian tube.

Cramping is another common sign of a possible miscarriage. The cramping occurs because the uterus attempts to push out the pregnancy tissue. If a pregnant woman experiences both bleeding and cramping the possibility of miscarriage is more likely than if only one of these symptoms is present.

If a woman experiences any sign of impending miscarriage, she should be examined by a practitioner. The doctor or nurse will perform a **pelvic exam** to check if the cervix is closed as it should be. If the cervix is open, miscarriage is inevitable and nothing can preserve the pregnancy. Symptoms of an inevitable miscarriage may include dull relentless or sharp intermittent **pain** in the lower abdomen or back. Bleeding may be heavy. Clotted material and tissue (the placenta and embryo) may pass from the vagina.

A situation in which only some of the products in the uterus have been expelled is called an incomplete miscarriage. Pain and bleeding may continue and become severe. An incomplete miscarriage requires medical attention.

A "missed abortion" occurs when the fetus has died but neither the fetus nor placenta is expelled. There may not be any bleeding or pain, but the symptoms of pregnancy will disappear. The physician may suspect a missed abortion if the uterus does not continue to grow. The physician will diagnose a missed abortion with an ultrasound examination.

A woman should contact her doctor if she experiences any of the following:

- Any bleeding during pregnancy.
- Pain or cramps during pregnancy.
- Passing of tissue.
- Fever and chills during or after miscarriage.

Diagnosis

If a woman experiences any sign of impending miscarriage she should see a doctor or nurse for a pelvic examination to check if the cervix is closed, as it should be. If the cervix is open, miscarriage is inevitable.

An ultrasound examination can confirm a missed abortion if the uterus has shrunk and the patient has had continual spotting with no other symptoms.

Treatment

Threatened miscarriage

For women who experience bleeding and cramping, bed rest is often ordered until symptoms disappear. Women should not have sex until the outcome of the threatened miscarriage is determined. If bleeding and cramping are severe, women should drink fluids only.

KEY TERMS

Diethylstilbestrol (DES)—This is a synthetic estrogen drug that is used to treat a number of hormonal conditions. However, it causes problems in developing fetuses and should not be taken during pregnancy. From about 1938 to 1971, DES was given to pregnant women because it was thought to prevent miscarriage. Children of women who took the drug during pregnancy are at risk for certain health problems.

Dilatation and curettage (D&C)—A procedure in which the neck of the womb (cervix) is expanded and the lining of the uterus is scraped to remove pregnancy tissue or abnormal tissue.

Embryo—An unborn child in the first eight weeks after conception. After the eighth week until birth, the baby is called a fetus.

Miscarriage

Although it may be psychologically difficult, if a woman has a miscarriage at home she should try to collect any material she passes in a clean container for analysis in a laboratory. This may help determine why the miscarriage occurred.

An incomplete miscarriage or missed abortion may require the removal of the fetus and placenta by a D&C (**dilatation and curettage**). In this procedure the contents of the uterus are scraped out. It is performed in the doctor's office or hospital.

After miscarriage, a doctor may prescribe rest or **antibiotics** for infection. There will be some bleeding from the vagina for several days to two weeks after miscarriage. To give the cervix time to close and avoid possible infection, women should not use tampons or have sex for at least two weeks. Couples should wait for one to three normal menstrual cycles before trying to get pregnant again.

Prognosis

A miscarriage that is properly treated is not life-threatening, and usually does not affect a woman's ability to deliver a healthy baby in the future.

Feelings of grief and loss after a miscarriage are common. In fact, some women who experience a miscarriage suffer from major depression during the six months after the loss. This is especially true for women who don't have any children or who have had depression in the past. The emotional crisis can be similar to that of a woman whose baby has died after birth.

Prevention

The majority of miscarriages cannot be prevented because they are caused by severe genetic problems determined at conception. Some doctors advise women who have a threatened miscarriage to rest in bed for a day and avoid sex for a few weeks after the bleeding stops. Other experts believe that a healthy woman (especially early in the pregnancy) should continue normal activities instead of protecting a pregnancy that may end in miscarriage later on, causing even more profound distress.

If miscarriage was caused by a hormonal imbalance (luteal phase defect), this can be treated with a hormone called progesterone to help prevent subsequent miscarriages. If structural problems have led to repeated miscarriage, there are some possible procedures to treat these problems. Other possible ways to prevent miscarriage are to treat genital infections, eat a well-balanced diet, and refrain from **smoking** and using recreational drugs.

ORGANIZATIONS

American College of Obstetricians and Gynecologists (ACOG), PO Box 96920, Washington, DC, 20090-6920, (202) 638-5577, http://www.acog.org.

Hygeia Foundation, 264 Amity Road Suite 211, Woodbridge, CT, 06525, (800) 893-9198, info@hygeiafoundation.org, http://www.hygeiafoundation.org.

Carol A. Turkington

Mitral incompetence *see* **Mitral valve insufficiency**

Mitral regurgitation *see* **Mitral valve insufficiency**

Mitral stenosis *see* **Mitral valve stenosis**

Mitral valve insufficiency

Definition

Mitral valve insufficiency is a term used when the valve between the upper left chamber of the heart (atrium) and the lower left chamber (ventricle) does not close well enough to prevent back flow of blood when the ventricle contracts. Mitral valve insufficiency

is also known as mitral valve regurgitation or mitral valve incompetence.

Description

Normally, blood enters the left atrium of the heart from the lungs and is pumped through the mitral valve into the left ventricle. The left ventricle contracts to pump the blood forward into the aorta. The aorta is a large artery that sends oxygenated blood through the circulatory system to all of the tissues in the body. If the mitral valve is leaky due to mitral valve insufficiency, it allows some blood to get pushed back into the atrium. This extra blood creates an increase in pressure in the atrium, which then increases blood pressure in the vessels that bring the blood from the lungs to the heart. Increased pressure in these vessels can result in increased fluid buildup in the lungs.

Causes and symptoms

In the past, **rheumatic fever** was the most common cause of mitral valve insufficiency. However, the increased use of **antibiotics** for **strep throat** has made rheumatic **fever** rare in developed countries. In these countries, mitral valve insufficiency caused by rheumatic fever is seen mostly in the elderly. In countries with less developed health care, rheumatic fever is still common and is often a cause of mitral valve insufficiency.

Heart attacks that damage the structures that support the mitral valve are a common cause of mitral valve insufficiency. Myxomatous degeneration can cause a "floppy" mitral valve that leaks. In other cases, the valve simply deteriorates with age and becomes less efficient.

People with mitral valve insufficiency may not have any symptoms at all. It is often discovered during a doctor's visit when the doctor listens to the heart sounds.

Both the left atrium and left ventricle tend to get a little bigger when the mitral valve does not work properly. The ventricle has to pump more blood so it gets bigger to increase the force of each beat. The atrium gets bigger to hold the extra blood. An enlarged ventricle can cause **palpitations**. An enlarged atrium can develop an erratic rhythm (**atrial fibrillation**), which reduces its efficiency and can lead to **blood clots** forming in the atrium.

Diagnosis

When the doctor listens to the heart sounds, mitral valve insufficiency is generally recognized by the sound the blood makes as it leaks backward. It sounds like a regurgitant murmur. The next step is generally a **chest x ray** and an electrocardiogram (ECG) to see if the heart is enlarged. The most definitive noninvasive test is **echocardiography**, a test that uses sound waves to make an image of the heart. This test gives a picture of the valve in action and shows the severity of the problem.

KEY TERMS

Aorta—A large artery beginning at the base of the left ventricle.

Atrium—One of the two upper chambers of the heart.

Rheumatic fever—An illness that sometimes follows a streptococcal infection of the throat.

Ventricle—One of the two lower chambers of the heart.

Treatment

A severely impaired valve needs to be repaired or replaced. Either option will require surgery. Repairing the valve can fix the problem completely or reduce it enough to make it bearable and prevent damage to the heart. Valves can be replaced with either a mechanical valve or one that is partly mechanical and partly from a pig's heart.

Mechanical valves are effective but can increase the incidence of blood clots. To prevent blood clots from forming, the patient will need to take drugs that prevent abnormal blood clotting (anticoagulants). The valves made partly from a pigs heart do not have as great a risk of blood clots but don't last as long as fully mechanical valves. If a valve wears out, it must be replaced again.

Damaged heart valves are easily infected. Anytime a procedure is contemplated that might allow infectious organisms to enter the blood, the person with mitral valve insufficiency should take antibiotics to prevent possible infection.

Prognosis

The diagnostic, medical and surgical procedures available to the person with mitral valve insufficiency are all likely to produce good results.

Prevention

The only possible way to prevent mitral valve insufficiency is to prevent rheumatic fever. This can be done by evaluating sore throats for the presence of

the bacteria that causes strep throat. Strep throat is easily treated with antibiotics.

Resources

OTHER

The Merck Page. http://www.merck.com.

ORGANIZATIONS

American Heart Association National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, Review. personal.info@heart.org.

Dorothy Elinor Stonely

Mitral valve prolapse

Definition

Mitral valve prolapse (MVP) is a ballooning of the support structures of the mitral heart valve into the left upper collection chamber of the heart.

Description

Other names for MVP include floppy valve and Barlow's syndrome. The mitral valve is located on the left side of the heart between the top chamber (left atrium) and the bottom chamber (left ventricle). The valve opens and closes according to the heartbeat and the pressure that is exerted upon it from the blood in both chambers.

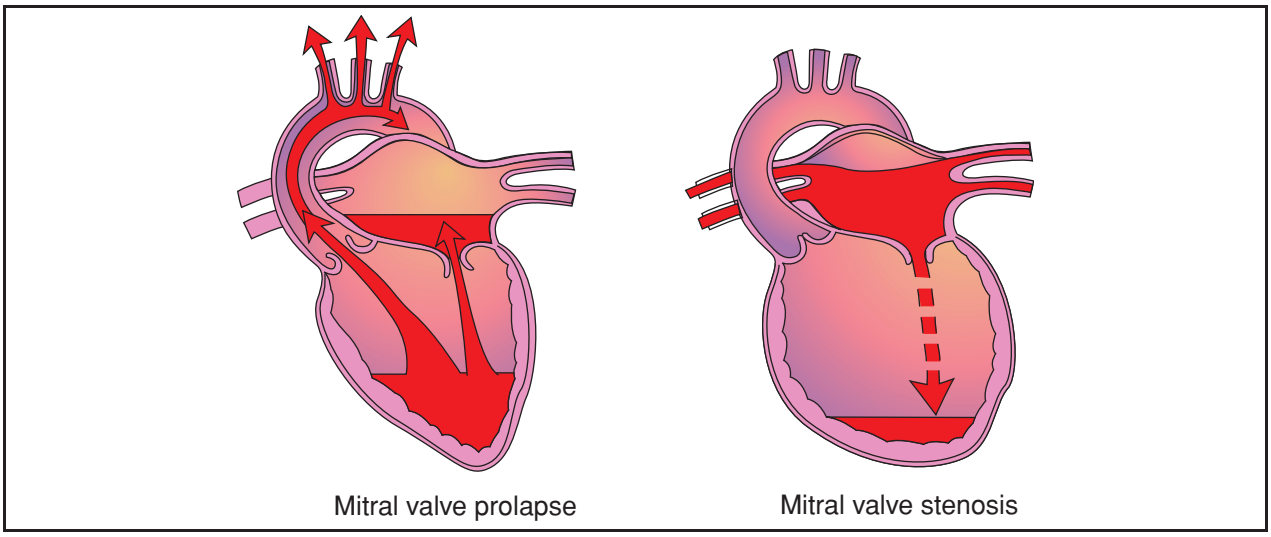
The valve has supporting structures that attach to the heart muscle to help it open and close properly. When these structures weaken or lengthen abnormally, the valve may balloon into the left atrium. Sometimes this can cause the mitral valve to leak blood backward.

This condition may be inherited and occurs in approximately 10% of the population. It affects more women than men and often peaks after the age of 40.

Causes and symptoms

MVP may occur due to rheumatic heart disease but is usually found in healthy people. Changes that occur in the valve are caused by rapid multiplication of cells in the middle layer that presses on the outer layer. The outer layer weakens, causing a prolapse of the valve toward the left atrium.

Most persons do not have symptoms. Those that do may experience sharp, left-sided chest **pain**. Some complain of **fatigue**, or a pounding feeling in the chest. Others can have an irregular heart beat and even pass out. Some persons may experience difficulty breathing, ankle swelling and fluid in the lungs. Other symptoms may include **anxiety**, headaches, morning tiredness and constantly cold hands and feet. **Death** from this condition is rare.



Mitral valve prolapse occurs when the mitral valve does not open and close properly. When this happens, the valve may balloon into the left atrium of the heart, causing the mitral valve to leak blood backward. Mitral valve stenosis refers to the narrowing of the mitral valve, in which the flow of blood from the atrium to the ventricle becomes restricted. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

KEY TERMS

Heart murmur—Sound during the heartbeat caused by a heart valve that does not close properly.

Rheumatic heart disease—A condition caused by a streptococcus infection which can result in permanent heart damage.

Diagnosis

The diagnosis of MVP is based on symptoms and physical exam. During the exam, the physician may hear a click and/or heart murmur with a stethoscope.

The best diagnostic test for MVP is the echocardiogram. The test reflects sound waves through the chest wall to give two-dimensional color flow pictures of the heart, its size, position, motion, chambers, and valves. Unfortunately, during the early 1980s, this diagnosis was often made excessively from faulty echocardiographic criteria prevalent at that time.

Any person with symptoms or family history of MVP should consider having an echocardiogram. The test takes 15-20 minutes and is done in doctor's offices and hospitals. It is performed by trained technicians and is read by cardiologists. Family physicians, internists, cardiologists, and nurse practitioners can treat MVP. Echocardiograms are recommended periodically depending on the extent of valve leakage.

Treatment

Persons who experience certain types of an irregular heartbeat with MVP should be treated. Propranolol (Inderal) or other **beta blockers** or **digoxin** (Lanoxin) are often helpful. Persons who develop moderate to severe symptoms with a leaky mitral valve may require repair or replacement of the mitral valve with an artificial heart valve. Persons with MVP and a leaky valve need to protect themselves from heart or heart valve infections. **Antibiotics** should be taken before any surgical, dental or oral procedures according to the American Heart Association recommendations.

Other treatments include drinking lots of fluids during strenuous activity and hot weather. Water pills, **caffeine** and donating blood may aggravate the symptoms of MVP.

Prognosis

MVP is usually not a serious condition. However, dangerous, untreated irregular heartbeats may rarely cause sudden death. These persons should be carefully monitored.

Resources

PERIODICALS

McGrath, Dicey. "Mitral Valve Prolapse." *American Journal of Nursing* May 1997: 40-41.

Lisa Papp, RN

Mitral valve stenosis

Definition

The term stenosis means an abnormal narrowing of an opening. Mitral valve stenosis refers to a condition in the heart in which one of the valve openings has become narrow and restricts the flow of blood from the upper left chamber (left atrium) to the lower left chamber (left ventricle).

Description

In the heart, the valve that regulates the flow of blood between the left atrium and the left ventricle is called the mitral valve. If the mitral valve is abnormally narrow, due to disease or birth defect, blood flow from the atrium to the ventricle is restricted. This restricted flow leads to an increase in the pressure of blood in the left atrium. Over a period of time, this back pressure causes fluid to leak into the lungs. It can also lead to an abnormal heart rhythm (**atrial fibrillation**), which further decreases the efficiency of the pumping action of the heart.

Causes and symptoms

Mitral valve stenosis is almost always caused by **rheumatic fever**. As a result of rheumatic **fever**, the leaflets that form the opening of the valve are partially fused together. Mitral valve stenosis can also be present at birth. Babies born with this problem usually require surgery if they are to survive. Sometimes, growths or tumors can block the mitral valve, mimicking mitral valve stenosis.

If the restriction is severe, the increased blood pressure can lead to **heart failure**. The first symptoms of heart failure, which are **fatigue** and **shortness of breath**, usually appear only during physical activity. As the condition gets worse, symptoms may also be felt even during rest. A person may also develop a deep red coloring in the cheeks.

KEY TERMS

Atrium—One of the two upper chambers of the heart.

Beta blocker—A drug that can be used to reduce blood pressure.

Rheumatic fever—An illness which sometimes follows a streptococcal infection of the throat.

Ventricle—One of the two lower chambers of the heart.

Diagnosis

Mitral valve stenosis is usually detected by a physician listening to heart sounds. Normal heart valves open silently to permit the flow of blood. A stenotic valve makes a snapping sound followed by a "rumbling" murmur. The condition can be confirmed with a **chest x ray** and an electrocardiogram, both of which will show an enlarged atrium. **Echocardiography**, which produces images of the heart's structure, is also helpful in making the diagnosis. If surgery is necessary, **cardiac catheterization** may be done to fully evaluate the heart before the operation.

Treatment

Drug therapy may help to slow the heart rate, strengthen the heart beat, and control abnormal heart rhythm. Drugs such as **beta blockers**, **calcium channel blockers**, and **digoxin** may be prescribed. A drug that prevents abnormal blood clotting (anticoagulant) called warfarin (Coumadin) may be recommended. If drug therapy does not produce satisfactory results, valve repair or replacement may be necessary.

Repair can be accomplished in two ways. In the first method, **balloon valvuloplasty**, the doctor will try to stretch the valve opening by threading a thin tube (catheter) with a balloon tip through a vein and into the heart. Once the catheter is positioned in the valve, the balloon is inflated, separating the fused areas. The second method involves opening the heart and surgically separating the fused areas.

If the valve is damaged beyond repair, it can be replaced with a mechanical valve or one that is partly mechanical and partly made from a pig's heart.

Prognosis

Procedures available to treat mitral valve stenosis, whether medical or surgical, all produce effective results.

Prevention

The only possible way to prevent mitral valve stenosis is to prevent rheumatic fever. This can be done by evaluating sore throats for the presence of the bacteria that causes **strep throat**. Strep throat is easily treated with **antibiotics**.

Resources

OTHER

The Merck Page. http://www.merck.com.

ORGANIZATIONS

American Heart Association National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, Review. personal.info@heart.org.

Dorothy Elinor Stonely

Molar pregnancy *see* **Hydatidiform mole**

Moles

Definition

A mole (nevus) is a pigmented (colored) spot on the outer layer of the skin (epidermis).

Description

Moles can be round, oval, flat, or raised. They can occur singly or in clusters on any part of the body. Most moles are brown, but colors can range from pinkish flesh tones to yellow, dark blue, or black.

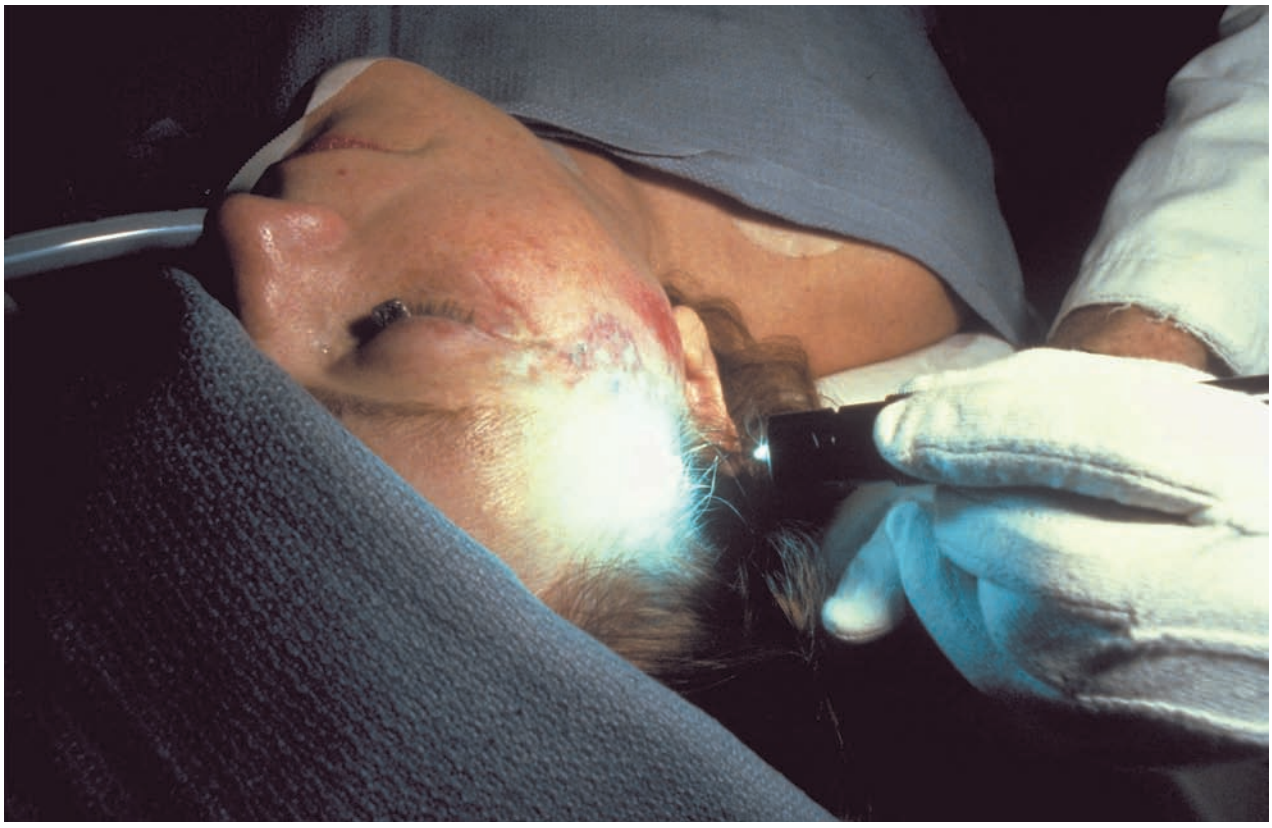
Demographics

Everyone has at least a few moles. They generally appear by the time a person is 20 and resemble freckles at first. A mole's color and shape don't usually change. Changes in hormone levels that occur during **puberty** and **pregnancy** can make moles larger and darker. New moles may also appear during this period.

A mole usually lasts about 50 years before beginning to fade. Some moles disappear completely, and some never lighten at all. Some moles develop stalks that raise them above the skin's surface; these moles eventually drop off.

Types of moles

About 1–3% of all babies have one or more moles when they are born. Moles that are present at birth are called congenital nevi.



Woman's birthmark being removed by laser. *(Alexander Tsiaras/Photo Researchers, Inc.)*

Other types of moles include:

- Junctional moles, which are usually brown and may be flat or slightly raised.
- Compound moles, which are slightly raised, range in color from tan to dark brown, and involve pigment-producing cells (melanocytes) in both the upper and lower layers of the skin (epidermis and dermis).
- Dermal moles, which range from flesh-color to brown, are elevated, most common on the upper body, and may contain hairs.
- Sebaceous moles, which are produced by overactive oil glands and are yellow and rough-textured.
- Blue moles, which are slightly raised, colored by pigment deep within the skin, and most common on the head, neck, and arms of women.

Most moles are benign, but atypical moles (dysplastic nevi) may develop into **malignant melanoma**, a potentially fatal form of skin **cancer**. Atypical moles are usually hereditary. Most are bigger than a pencil eraser, and the shape and pigmentation are irregular.

Congenital nevi are more apt to become cancerous than moles that develop after birth, especially if they are more than eight inches in diameter. Lentigo maligna (melanotic freckle of Hutchinson), most common on the face and after the age of 50, first appears as a flat spot containing two or more shades of tan. It gradually becomes larger and darker. One in three of these moles develop into a form of skin cancer known as lentigo maligna melanoma.

Causes and symptoms

The cause of moles is unknown, although atypical moles seem to run in families and result from exposure to sunlight.

In the past several years, researchers have identified two genes known as CDKN2A and CDK4 that govern susceptibility to melanoma in humans. Most experts, however, think that these susceptibility genes are not sufficient by themselves to account for moles becoming cancerous but are influenced by a combination of other inherited traits and environmental factors.

Diagnosis

Only a small percentage of moles require medical attention. A mole that has the following symptoms

should be evaluated by a dermatologist (a physician spealizing in skin diseases).

- Appears after the age of 20
- Bleeds
- Itches
- Looks unusual or changes in any way.

A doctor who suspects skin cancer will remove all or part of the mole for microscopic examination. This procedure, which is usually performed in a doctor's office, is simple, relatively painless, and does not take more than a few minutes. It does leave a scar.

The doctor may also use a dermatoscope to examine the mole prior to removal. The dermatoscope, which can be used to distinguish between benign moles and melanomas, is an instrument that resembles an ophthalmoscope. An immersion oil is first applied to the mole to make the outer layers of skin transparent.

A combination of high-frequency ultrasound and color Doppler studies has also been shown to have a high degree of accuracy in distinguishing between melanomas and benign moles.

Treatment

If laboratory analysis confirms that a mole is cancerous, the dermatologist will remove the rest of the mole. Patients should realize that slicing off a section of a malignant mole will not cause the cancer to spread.

Removing a mole for cosmetic reasons involves numbing the area and using scissors or a scalpel to remove the elevated portion. The patient is left with a flat mole the same color as the original growth. Cutting out parts of the mole above and beneath the surface of the skin can leave a scar more noticeable than the mole.

Cryotherapy may also be used to remove moles. In cryotherapy, the physician uses an extremely cold liquid to freeze and destroy the skin growth.

Scissors or a razor can be used to temporarily remove hair from a mole. Permanent hair removal, however, requires electrolysis or surgical removal of the mole.

Prognosis

Moles are rarely cancerous and, once removed, unlikely to recur. A dermatologist should be consulted if a mole reappears after being removed.

Prevention

Wearing a sunscreen and limiting sun exposure may prevent some moles. Anyone who has moles should examine them every month and see a dermatologist if changes in size, shape, color, or texture occur or if new moles appear.

KEY TERMS

Dermatology—The branch of medicine that studies and treats disorders of the skin.

Malignant melanoma—A potentially fatal form of skin cancer that develops from melanocytes, which are skin cells containing melanin.

Melanin—A dark insoluble pigment found in humans in the skin, hair, choroid layer of the eye, and a part of the brain called the substantia nigra.

Nevus (plural, nevi)—The medical term for any anomaly of the skin that is present at birth, including moles and birthmarks.

A team of researchers at Duke University reported in 2003 that topical application of a combination of 15% vitamin C and 1% vitamin E over a four-day period offered significant protection against **sunburn**. The researchers suggest that this combination may protect skin against **aging** caused by sunlight as well.

Anyone with a family history of melanoma should see a dermatologist for an annual skin examination. Everyone should know the ABCDEs of melanoma:

- A: Asymmetry, which occurs when the two halves of the mole are not identical
- B: Borders that are irregular or indistinct
- C: Color that varies in a single mole
- D: Diameter, which should be no larger than a pencil eraser (about 6 mm)
- E: Elevated above the surrounding tissue.

A mole with any of these characteristics should be evaluated by a dermatologist.

Advances in photographic technique have now made it easier to track the development of moles with the help of whole-body photographs. A growing number of hospitals are offering these photographs as part of outpatient mole-monitoring services.

Resources

BOOKS

Beers, Mark H., MD, and Robert Berkow, MD, editors. "Dermatologic Disorders: Malignant Tumors." Section 10, Chapter 126. In *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2004.

Grichnik JM, et al. Benign Neoplasias and Hyperplasias of Melanocytes. In: Wolff K, et al. *Fitzpatrick's Dermatology in General Medicine, 7th ed.* New York, N.Y.: McGraw-Hill Medical, 2008.

PERIODICALS

Abbasi NR, et al. Early diagnosis of cutaneous melanoma: Revisiting the ABCD criteria. *Journal of the American Medical Association* 2004:292;2771.

ORGANIZATIONS

American Academy of Dermatology, 930 N. Meacham Road, P.O. Box 4014, Schaumburg, IL, 60168-4014, (847) 330-0230, (847) 330-0050, www.aad.org.

American Cancer Society, 250 Williams Street, Atlanta, GA, 30303, (404) 320-3333.

National Cancer Institute (NCI), 6116 Executive Boulevard, MSC8332, Suite 3036A, Bethesda, MD, 20892-8322, (800) 821-CANCER, www.nci.nih.gov.

Nevus Outreach, Inc., 1601 Madison Blvd., Bartesville, OK, 74006, (877) 426-3887, www.nevus.org.

Maureen Haggerty
Rebecca J. Frey, PhD
Karl Finley

Molybdenum excess *see* **Mineral toxicity**
Mometasone *see* **Corticosteroids**
Moncytic ehrlichiosis *see* **Ehrlichiosis**
Mongolism *see* **Down syndrome**
Moniliasis *see* **Candidiasis**

Monkeypox

Definition

Monkeypox is an **infectious disease** caused by an orthopoxvirus. Orthopoxviruses are a genus of viruses that include the disease agents that cause human **smallpox**, cowpox, and camelpox as well as monkeypox. Monkeypox, which was first identified in humans in an outbreak in Africa in 1970, usually produces a less severe illness with fewer fatalities than smallpox. However, its symptoms are similar: **fever**, pus-filled blisters all over the body, and respiratory problems.

Monkeypox is classified as a **zoonosis**, which means that it is a disease of animals that can be transmitted to humans under natural conditions. The first cases of monkeypox reported in humans involved contact between humans and animals in the African rain forest. The outbreak that made headlines in the United States in June 2003, however, involved animals purchased as pets from pet stores. In nature, monkeypox has been found in monkeys, chimpanzees, rabbits, prairie dogs, Gambian rats, ground squirrels, and mice. It is not known as of late 2003 whether other wild or domestic animals can contract monkeypox.

Description

Prior to 2003, most monkeypox cases were diagnosed in remote areas of central and west Africa. Between February 1996 and October 1997, however, there were 511 suspected cases of monkeypox in the Democratic Republic of the Congo (DRC, formerly Zaire). This outbreak, the largest ever, raised fears that the virus had mutated and become more infectious.

In late 1997, the U.S. Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) announced that this relatively large outbreak was likely due to human behavior, rather than virus mutation. During the outbreak, the DRC was embroiled in civil war. Food shortages increased reliance on hunting and raised chances that people would come into contact with infected animals.

The 2003 outbreak in the United States, which was the first confirmed instance of community-acquired monkeypox in North America, came to the attention of the CDC in early June, when a laboratory in Wisconsin identified the monkeypox virus in samples taken from the skin of an infected patient and lymph node tissue from the patient's pet prairie dog. By the end of June, cases of monkeypox in humans had been identified in six Midwestern states (Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin). The patients acquired the virus from infected prairie dogs purchased as pets, which in turn were infected through contact with animals imported from Africa that were sold in the same pet stores.

Monkeypox is less severe than smallpox and can sometimes be confused with **chickenpox**. It seems partly preventable with smallpox **vaccination**, but vaccination programs were discontinued in the late 1970s. (Barring samples stored in laboratories, smallpox has been eradicated.) People under the age of 16—those born after smallpox vaccination ended—seem the most susceptible to monkeypox. During the 1996-97 outbreak, approximately 85% of the cases were in this age group.

Although the monkeypox virus is related to the smallpox virus, experts do not think (as of late 2003) that it is likely to be cultivated as an agent of bioterrorism. Monkeypox is much less easily transmitted person-to-person than smallpox and has a much lower fatality rate.

Causes and symptoms

The monkeypox virus is transmitted to humans through an infected animal's blood, body sores, or bite; or through handling an infected animal's bedding or cage. Initial symptoms of monkeypox in humans include fever, a bodywide rash (exanthem) of pus-filled blisters, and flu-like muscle aches and **fatigue**. These symptoms can be accompanied by **diarrhea**, swollen lymph nodes, a **sore throat**, and mouth sores. In some cases, a victim may experience trouble breathing. Symptoms are at their worst for 3–7 days, after which the fever lessens and blisters begin to form crusts.

The symptoms of monkeypox in pet rabbits, rats, or mice include inflammation of the eyes, a nasal discharge, fever, loss of appetite, a skin rash, and tiredness. Pet monkeys typically develop a rash with pus-filled lesions on the palms of the hands, trunk, and tail. They may also have mouth ulcers.

Diagnosis

Since the symptoms of monkeypox resemble other diseases caused by orthopox viruses, definitive diagnosis may require laboratory testing to uncover the virus or evidence (from antibodies in the blood) that it is present. Laboratory techniques that can be used to identify the monkeypox virus include electron microscopy, polymerase chain reaction (PCR), immunohistochemistry, and ELISA testing.

Treatment

Like most viruses, monkeypox cannot be resolved with medication. The only treatment option is symptomatic—that is, patients are made as comfortable as possible. In March 1998, the U.S. Army Medical Research Institute for Infectious Diseases reported that an antiviral drug called cidofovir may combat monkeypox infection. Additional studies report that cidofovir appears to be safe and effective as a treatment for monkeypox in humans.The drug has worked successfully in primates, but further research is needed to determine its effectiveness in humans.

Prognosis

Children are more likely to contract the disease and have the highest **death** rate. Monkeypox is not as lethal as smallpox, but the death rate among young children may reach 2–10%. In some cases, hospitalization is required. Recovery is good among survivors, although some scarring may result from the blisters.

KEY TERMS

Antiviral—Refers to a drug that can destroy viruses and help treat illnesses caused by them.

Bioterrorism—The intentional use of disease-causing microbes or other biologic agents to intimidate or terrorize a civilian population for political or military reasons.

Mutation—A change in an organism's genetic code that causes it to develop new characteristics.

Orthopoxvirus—The genus of viruses that includes monkeypox, smallpox, cowpox, and camelpox.

Symptomatic—Refers to treatment that addresses the symptoms of an illness, but not its underlying cause.

Zoonosis (plural, zoonoses)—Any disease of animals that can be transmitted to humans under natural conditions. Monkeypox is a zoonosis.

Prevention

Monkeypox is one of the diseases that physicians, veterinarians, and public health officials are required by law to report to the CDC.

Although smallpox vaccination offers some protection against monkeypox, experts do not generally recommend getting a smallpox vaccination simply to guard against monkeypox if one has not been exposed to it. However, the CDC recommends as of June 2003 that anyone who has had close contact with humans or animals infected with monkeypox, or has helped to care for them, should be vaccinated against smallpox. The vaccination can be administered as late as 14 days after exposure to the virus. In addition, veterinarians or public health personnel conducting field investigations should be vaccinated before any exposure to monkeypox.

As of late 2003, no cases of monkeypox were identified in cats or dogs belonging to people infected by the June outbreak. The American Veterinary Medicine Association (AVMA) recommends, however, that cats, dogs, or other mammals that have been in contact with an animal known to have monkeypox should be kept in quarantine for 30 days from the date of exposure.

People who have a pet with symptoms of monkeypox should *not* take it to an animal shelter or release it into the wild. They should isolate it from humans and other animals, and take it to a veterinarian in a closed, chew-proof container with air holes.

On June 11, 2003, the CDC and the Food and Drug Administration (FDA) issued a joint order prohibiting

the importation of rats and other rodents from Africa. In addition, the agencies banned the sale and distribution of prairie dogs and six species of African rodents in the United States.

Resources

PERIODICALS

Altman, Larry K., MD, and Jodi Wilgoren. "20 Cases of Disease Related to Smallpox Detected in the U.S." *New York Times* June 9, 2003.

Centers for Disease Control and Prevention. "Multistate Outbreak of Monkeypox—Illinois, Indiana, and Wisconsin, 2003." *Morbidity and Mortality Weekly Report* 52 (June 13, 2003): 537–540.

Centers for Disease Control and Prevention. "Update: Multistate Outbreak of Monkeypox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003." *Morbidity and Mortality Weekly Report* 52 (June 20, 2003): 561–564.

Centers for Disease Control and Prevention. "Update: Multistate Outbreak of Monkeypox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003." *Morbidity and Mortality Weekly Report* 52 (June 27, 2003): 589–590.

Rosen, T., and J. Jablon. "Infectious Threats from Exotic Pets: Dermatological Implications." *Dermatologic Clinics* 21 (April 2003): 229–236.

Smee, D. F., K. W. Bailey, and R. W. Sidwell. "Comparative Effects of Cidofovir and Cyclic HPMPC on Lethal Cowpox and Vaccinia Virus Respiratory Infections in Mice." *Chemotherapy* 49 (June 2003): 126–131.

OTHER

American Veterinary Medical Association (AVMA). "Foreign Animal Disease Alert: Investigation Uncovers First Outbreak of Monkeypox Infection in the Western Hemisphere," June 23, 2003. http://www.avma.org/pubhlth/monkeypox/default.asp.

American Veterinary Medical Association (AVMA). *Monkeypox Backgrounder*. Schaumburg, IL: AVMA, June 2003.

Centers for Disease Control and Prevention (CDC). *Fact Sheet: Basic Information About Monkeypox*. Atlanta, GA: CDC, June 2003.

ORGANIZATIONS

American Veterinary Medical Association (AVMA), 1931 North Meacham Road, Suite 100, Schaumburg, IL, 60173-4360, (847) 925-1329, (800) 248-2862, http://www.avma.org/.

Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

Julia Barrett
Rebecca J. Frey, PhD

Monoamine oxidase inhibitors

Definition

Monoamine oxidase inhibitors (MAOI) are medicines used to treat severe mental depression.

Purpose

Like other **antidepressant drugs**, MAOI help reduce the sadness, hopelessness, apathy and lack of interest in life that are typical of depression. In use since the 1950s, these drugs are associated with greater risks of interactions with foods and other drugs than other types of antidepressants, and are generally reserved for cases where other drugs are not effective.

Description

MAOI work by correcting chemical imbalances in the brain. Normally, chemicals, called neurotransmitters, carry signals between brain cells. Some neurotransmitters, such as serotonin and norepinephrine, play important roles in controlling mood. MAOI are believed to block or reduce the breakdown of serotonin and norepinephrine, prolonging and increasing their effects.

MAOI are available only with a physician's prescription. Examples include isocarboxazid (Marplan), phenelzine (Nardil), tranylcypromine (Parnate), available as tablets; and selegiline (Emsam), available as a skin patch.

Recommended dosage

Dosage depends on the type of MAOI prescribed, the type of depression treated, and characteristics of individual patients. Prescribers or pharmacists can advise on correct dosage and use.

Always take MAOI exactly as directed. These drugs may take up to several weeks to be effective. Do not stop taking them suddenly, as withdrawal symptoms may occur. Prescribers should advise and monitor reducing or discontinuing these drugs.

MAOI may be taken with or without food, or on an empty stomach. Some foods and beverages must be avoided while taking these drugs.

Precautions

All types of antidepressant medications increase the risk of **suicide** in children, adolescents, and young adults.

These drugs may worsen **psychosis**, and should not be used alone to treat **bipolar disorder**.

Diabetics using insulin may experience more low blood sugars when they take MAOI

MAOI may cause serious and possibly life-threatening high blood pressure within several hours after eating certain foods like aged cheeses, smoked or pickled meats, chocolate, foods containing monosodium glutamate (MSG), or drinking red wine or caffeinated beverages. Before started on these drugs, a full list of foods and beverages to be avoided should be obtained from a physician or pharmacist.

The effects and interactions of these drugs with food, beverages and other drugs may continue for up to two weeks after they are discontinued.

MAOI should be discontinued at least two weeks before anesthesia or elective surgery, or dental procedures where local anesthetics containing epinephrine might be used.

These drugs may produce dangerously high blood pressure in people who take **central nervous system stimulants** to treat **attention deficit hyperactivity disorder (ADHD)**.

When taken with **central nervous system depressants**, like cyclobenzaprine (Flexeril), meperidine (Demerol), bupropion (Wellbutrin), and buspirone (Buspar), **delirium**, excitement, **coma**, seizures, or high **fever** may occur.

At least five weeks should elapse after discontinuing **selective serotonin reuptake inhibitors** (SSRIs), like Prozac, before beginning treatment with MAOI.

Anyone who is taking MAOIs should not use medicines that have not been approved or prescribed by physicians familiar with these drugs. This includes over-the-counter medicines like sleep aids; colds, coughs, hay fever, or **asthma** medications, including nose drops or sprays containing neosynephrine or pseudoephedrine; medicines to increase alertness or keep from falling asleep, like NoDoz; and appetite control products.

MAOI may cause blurred vision or make people feel drowsy, dizzy or lightheaded. Anyone taking these drugs should not drive, use machines or do other potentially dangerous activities until they are familiar with the drugs's effects.

The elderly may be more sensitive to the effects of MAOI.

Special conditions

People with certain medical conditions or who are taking certain other medicines can have problems if they take MAOI. Before taking these drugs, be sure to let your physician know about any of these conditions:

ALLERGIES. Anyone who has had unusual reactions to MAOI in the past should let his or her physician know before taking them again. Physicians should be told about **allergies** to foods, dyes, preservatives, or other substances.

PREGNANCY. MAOI may increase the risks of **birth defects** or problems in newborns. Women who are, or may become, pregnant should discuss these issues with their physicians before taking a MAOI.

BREASTFEEDING. MAOI pass into breast milk and are not recommended for nursing mothers unless the expected benefits outweigh the risks.

DIABETES. Diabetics using insulin and/or oral drugs to control blood sugar should be aware that MAOI increase sensitivity to these drugs.

ANGINA. People with **angina** (chest **pain**) may feel more energetic while taking MAOI and should be careful not to overexert themselves.

OTHER MEDICAL CONDITIONS. Before using MAOI, people with any of these medical problems should make sure their physicians are aware of their conditions:

- Alcohol abuse
- High blood pressure
- Recent heart attack or stroke
- Heart or blood vessel disease
- Liver disease
- Kidney disease
- Frequent or severe headaches
- Epilepsy
- Parkinson's disease
- Current or past mental illness
- Asthma or bronchitis
- Overactive thyroid
- Pheochromocytoma (a tumor of the adrenal gland).

USE OF CERTAIN MEDICINES. Taking MAOI with certain other drugs may affect the way the drugs work and increase the risk of side/adverse effects.

Side effects

The most common side effects include **dizziness**, lightheadedness, drowsiness, weakness, blurred vision, shakiness or trembling, restlessness, sleep problems or twitching during sleep, weight gain, decreased sexual ability, difficulty with urination, and **headache**. These problems usually go away as the body adjusts to the drug and do not require medical treatment unless they interfere with normal activities.

KEY TERMS

Anxiety—Apprehension in response to real or imagined stress, danger, or dreaded situations. Physical symptoms like rapid pulse, sweating, trembling, fatigue, and weakness may accompany anxiety.

Central nervous system—The brain and spinal cord.

Depression—A mental condition where people feel extremely sad and lose interest in life. People with depression may also have sleep problems and loss of appetite and may have trouble concentrating and carrying out everyday activities.

Neurotransmitters—Chemicals that carry impulses, messages, between nerve cells.

Phobia—Intense, illogical fear of specific things like heights, crowds or open spaces.

Withdrawal symptoms—Physical and/or mental symptoms that occur when people stop using drugs to which they have become physically or psychologically dependent.

Serious side/averse effects may occur. If any of the following occur seek emergency medical attention:

- Severe chest pain
- Severe headache
- Stiff, sore neck
- Enlarged pupils
- Hypersensitivity to light
- Rapid or slow heartbeat
- Sweating, with or without fever or cold, clammy skin
- Nausea and vomiting.

Other side effects may occur. Anyone who has unusual or troublesome symptoms while taking MAOI should contact their physician.

Interactions

MAOI interact with many other medicines, changing the effects of one or both drugs and changing the risks of side/adverse effects. *People taking MAOI must check with their physicians before taking other prescription or nonprescription (over-the-counter) medicines.*

Drugs that interact with MAO inhibitors include:

- Central nervous system (CNS) depressants, stimulants, over the counter medicines for allergies, colds, hay fever, sleep and asthma; sedatives; tranquilizers; prescription pain medicines; muscle relaxants; antiseizure medicines; barbiturates; and anesthetics
- Medicine for high blood pressure
- Other antidepressants, including tricyclic antidepressants (such as Tofranil and Norpramin), antidepressants that raise serotonin levels (such as Prozac and Zoloft), and bupropion (Wellbutrin)
- Insulin and diabetes medicines taken by mouth
- Water pills (diuretics)

The list above does not include every drug that may interact with MAOI. Check with a physician or pharmacist before combining MAOI with any other prescription or nonprescription (over-the-counter) medicine.

Nancy Ross-Flanigan

Mononucleosis *see* **Infectious mononucleosis**

Montezuma's revenge *see* **Traveler's diarrhea**

Mood disorders

Definition

Mood disorders are mental disorders characterized by periods of depression, sometimes alternating with periods of elevated mood.

Description

While many people go through sad or elated moods from time to time, people with mood disorders suffer from severe or prolonged mood states that disrupt their daily functioning. Among the general mood disorders classified in the fourth edition (1994) of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM–IV*) are major depressive disorder, **bipolar disorder**, and dysthymia.

In classifying and diagnosing mood disorders, doctors determine if the mood disorder is unipolar or bipolar. When only one extreme in mood (the depressed state) is experienced, this type of depression is called unipolar. Major depression refers to a single severe period of depression, marked by negative or hopeless thoughts and physical symptoms like **fatigue**. In major depressive disorder, some patients have isolated episodes of depression. Between these episodes, the patient does not feel depressed or have other symptoms

associated with depression. Other patients have more frequent episodes.

Bipolar depression or bipolar disorder (sometimes called manic depression) refers to a condition in which people experience two extremes in mood. They alternate between depression (the "low" mood) and **mania** or hypomania (the "high" mood). These patients go from depression to a frenzied, abnormal elevation in mood. Mania and hypomania are similar, but mania is usually more severe and debilitating to the patient.

Dysthymia is a recurrent or lengthy depression that may last a lifetime. It is similar to major depressive disorder, but dysthymia is chronic, long–lasting, persistent, and mild. Patients may have symptoms that are not as severe as major depression, but the symptoms last for many years. It seems that a mild form of the depression is always present. In some cases, people also may experience a major depressive episode in addition to their dysthymia, a condition sometimes referred to as a "double depression."

Causes and symptoms

Mood disorders tend to run in families. These disorders are associated with imbalances in certain chemicals that carry signals between brain cells (neurotransmitters). These chemicals include serotonin, norepinephrine, and dopamine. Women are more vulnerable to unipolar depression than are men. Major life stressors (such as divorce, serious financial problems, and **death** of a family member) often provoke the symptoms of depression in susceptible people.

Major depression is more serious than just feeling "sad" or "blue." The symptoms of major depression may include:

- Loss of appetite
- A change in sleep patterns, such as not sleeping (insomnia) or sleeping too much
- Feelings of worthlessness, hopelessness, or inappropriate guilt
- Fatigue
- Difficulty in concentrating or making decisions
- Overwhelming and intense feelings of sadness or grief
- Disturbed thinking.
- The person may also have physical symptoms such as stomachaches or headaches

Bipolar disorder includes mania or hypomania. Mania is an abnormal elevation in mood. The person may be excessively cheerful, have grandiose ideas, and may sleep less. He or she may talk nonstop for hours, have unending enthusiasm, and demonstrate poor judgement. Sometimes the elevation in mood is marked by irritability and hostility rather than cheerfulness. While the person may at first seem normal with an increase in energy, others who know the person well see a marked difference in behavior. The patient may seem to be in a frenzy and often will make poor, bizarre, or dangerous choices in his/her personal and professional lives. Hypomania is not as severe as mania and does not cause the level of impairment in work and social activities that mania can.

Diagnosis

Doctors diagnose mood disorders based on the patient's description of the symptoms as well as the patient's family history. The length of time the patient has had symptoms also is important. Generally patients are diagnosed with dysthymia if they feel depressed more days than not for at least two years. The depression is mild but long lasting. In major depressive disorder, the patient is depressed almost all day nearly every day of the week for at least two weeks. The depression is severe. Sometimes laboratory tests are performed to rule out other causes for the symptoms (such as thyroid disease). The diagnosis may be confirmed when a patient responds well to medication.

Treatment

The most effective treatment for mood disorders is a combination of medication and **psychotherapy**. Individuals may have better results if they also participate in family-focused therapy. The four different classes of drugs used in mood disorders are:

- Heterocyclic antidepressants (HCAs), such as amitriptyline (Elavil)
- Selective serotonin reuptake inhibitors (SSRI inhibitors), such as fluoxetine (Prozac), paroxetine (Paxil), and sertraline (Zoloft)
- Monoamine oxidase inhibitors (MAOI inhibitors), such as phenelzine sulfate (Nardil) and tranylcypromine sulfate (Parnate)
- Mood stabilizers, such as lithium carbonate (Eskalith) and valproate, often used in people with bipolar mood disorders.

A number of psychotherapy approaches are useful as well. Interpersonal psychotherapy helps the patient recognize the interaction between the mood disorder and interpersonal relationships. Cognitive–behavioral therapy explores how the patient's view of the world may be affecting his or her mood and outlook.

When depression fails to respond to treatment or when there is a high risk of **suicide**, **electroconvulsive**

KEY TERMS

Cognitive therapy—Psychotherapy technique designed to help people change their attitudes, perceptions, and patterns of thinking.

Electroconvulsive therapy (ECT)—Therapy for mood disorders that involves passing electrical current through the brain in order to create a brief convulsion.

Neurotransmitter—A chemical that aids or alters the transmission of impulses between the points that connect nerves.

Serotonin—A chemical messenger in the brain thought to play a role in mood regulation.

therapy (ECT) sometimes is used. ECT is believed to affect neurotransmitters as medications do. Patients are anesthetized and given **muscle relaxants** to minimize discomfort. Then low–level electric current is passed through the brain to cause a brief convulsion. The most common side effect of ECT is mild, short–term **memory loss**.

Alternative treatment

There are many alternative therapies that may help in the treatment of mood disorders, including **acupuncture**, botanical medicine, homeopathy, **aromatherapy**, constitutional **hydrotherapy**, and **light therapy**. The therapy used is an individual choice. Short–term clinical studies have shown that the herb **St. John's wort** (*Hypericum perforatum*) can effectively treat some types of depression. Though it appears very safe, the herb may have some side effects and its long–term effectiveness has not been proven. It has not been tested in patients with bipolar disorder. Despite uncertainty concerning its effectiveness, a 2003 report said acceptance of the treatment continues to increase. A poll showed that about 41% of 15,000 science professionals in 62 countries said they would use St. John's wort for mild to moderate depression. Although St. John's wort appears to be a safe alternative to conventional antidepressants, care should be taken, as the herb can interfere with the actions of some pharmaceuticals. The usual dose is 300 mg three times daily. St. John's wort and **antidepressant drugs** should not be taken simultaneously, so patients should tell their doctor if they are taking St. John's wort.

Prognosis

Most cases of mood disorders can be successfully managed if properly diagnosed and treated.

Prevention

People can take steps to improve mild depression and keep it from becoming worse. They can learn **stress** management (such as relaxation training or breathing exercises), **exercise** regularly, and avoid drugs or alcohol.

Resources

BOOKS

Baldwin, Robert. *Depression in Later Life*. New York, NY: Oxford University Press, 2010.

Graham, George. *The Disordered Mind: An Introduction to Philosophy of Mind and Mental Illness*. New York, NY: Routledge, 2010.

Miklowitz, David J. *Bipolar Disorder: A Family–Focused Treatment Approach,* 2nd ed. New York, NY: Guilford Press, 2010.

North, Carol, and Sean Yutzy. *Goodwin and Guze's Psychiatric Diagnosis*. New York, NY: Oxford University Press, 2010.

O'Connor, Richard. *Undoing Depression: What Therapy Doesn't Teach You and Medication Can't Give You,* 2nd ed. New York, NY: Little, Brown and Company, 2010.

Shams, K. *Human Relations and Personified Relational Disorders*. Raleigh, NC: lulu.com, 2009.

Smith, Hilary. *Welcome to the Jungle: Everything You Ever Wanted to Know about Bipolar but Were Too Freaked Out to Ask*. San Francisco, CA: Conari Press, 2010.

Wootton, Tom, et al. *Bipolar in Order: Looking at Depression, Mania, Hallucination, and Delusion from the Other Side*. Tiburon, CA: Bipolar Advantage Publishers, 2010.

PERIODICALS

"Family-Focused Therapy May Reduce Relapse Rate." *Health & Medicine Week* September 29, 2003: 70.

"St. John's Wort Healing Reputation Upheld." *Nutraceuticals International*. September 2003.

ORGANIZATIONS

American Psychiatric Association, 1000 Wilson Blvd., Suite 1825, Arlington, VA, 22209, (703) 907–7300, apa@psych.org, http://www.psych.org/.

American Psychological Association (APA), 750 First St. NE, Washington, DC, 20002–4242, (202) 336–5700, http://www.apa.org.

Anxiety Disorders Association of America., 8730 Georgia Ave., Suite 600, Silver Spring, MD, 20910, (240) 485–1001, http://www.adaa.org.

Depression and Bipolar Support Alliance (DBSA), 730 N. Franklin St., Suite 501, Chicago, IL, 60610, (800) 826–3632, http://www.dbsalliance.org.

National Alliance on Mental Illness (NAMI), Colonial Place Three, 2107 Wilson Blvd., Suite 300, Arlington, VA, 22201, (703) 524–7600, (800) 950–NAMI (6264), (703) 524–9094, http://www.nami.org/Hometemplate.cfm.

National Institute of Mental Health (NIMH), 6001 Executive Blvd, Room 8184, MSC 9663, Bethesda, MD,

20892, (301) 443–4513, (866) 615–6464, (301) 443–4279, nimhinfo@nih.gov, http://www.nimh.nih.gov/index.shtml.

National Mental Health Association (NMHA), 2000 N. Beauregard St., 6th Floor, Alexandria, VA, 22311, (703) 684–7722, (800) 969–NMHA, (703) 684–5968, http://www1.nmha.org/.

Robert Scott Dinsmoor
Teresa G. Odle
Laura Jean Cataldo, RN, Ed.D.

Morning after pill *see* **Mifepristone**

Motion sickness

Definition

Motion sickness is the uncomfortable **dizziness**, **nausea**, and **vomiting** that people experience when their sense of balance and equilibrium is disturbed by constant motion. Riding in a car, aboard a ship or boat, or riding on a swing all cause stimulation of the vestibular system and visual stimulation that often leads to discomfort. While motion sickness can be bothersome, it is not a serious illness, and can be prevented.

Demographics

Motion sickness is a common problem, with nearly 80% of the general population suffering from it at one time or another in their lives. People with migraine headaches or Ménière's syndrome, however, are more likely than others to have recurrent episodes of motion sickness. Researchers at the Naval Medical Center in San Diego, California, reported in 2003 that 70% of research subjects with severe motion sickness had abnormalities of the vestibular system; these abnormalities are often found in patients diagnosed with migraines or **Ménière's disease**.

While motion sickness may occur at any age, it is more common in children over the age of two, with the majority outgrowing this susceptibility.

Description

When looking at the causes of motion sickness, it is helpful to understand the role of the sensory organs. The sensory organs control a body's sense of balance by telling the brain what direction the body is pointing, the direction it is moving, and if it is standing still or turning. These messages are relayed by the inner ears (or labyrinth); the eyes; skin pressure receptors, such as in those in the feet; muscle and joint sensory receptors, which track what body parts are moving; and the central nervous system (the brain and spinal cord), which is responsible for processing all incoming sensory information.

Motion sickness and its symptoms arise when conflicting messages are sent to the central nervous system. An example of this phenomenon occurs while reading a book in the back seat of a moving car. The inner ears and skin receptors sense the motion, but the eyes register only the stationary pages of the book. This conflicting information may cause the usual motion sickness symptoms of dizziness, **nausea and vomiting**.

Causes and symptoms

While all five of the body's sensory organs contribute to motion sickness, excess stimulation to the vestibular system within the inner ear (the body's "balance center") has been shown to be one of the primary reasons for this condition. Balance problems, or vertigo, are caused by a conflict between what is seen and how the inner ear perceives it, leading to confusion in the brain. This confusion may result in higher heart rates, rapid breathing, nausea and sweating, along with dizziness and **vomiting**.

Pure optokinetic motion sickness is caused solely by visual stimuli, or what is seen. The optokinetic system is the reflex that allows the eyes to move when an object moves. Many people suffer when the object they view is rotating or swaying, even if they are standing still.

Additional factors that may contribute to the occurrence of motion sickness include:

- Poor ventilation.
- Anxiety or fear. Both have been found to lower a person's threshold for experiencing motion sickness symptoms.
- Food. It is recommended that a heavy meal of spicy and greasy foods be avoided before and during a trip.
- Alcohol. A drink is often thought to help calm the nerves, but in this case it could upset the stomach further. A hangover prior to the next morning's trip may also lead to motion sickness.
- Genetic factors. Research suggests that some people inherit a predisposition to motion sickness. This predisposition is more marked in some ethnic groups than in others. One study published in 2002 found that persons of Chinese or Japanese ancestry are significantly more vulnerable to motion sickness than persons of British ancestry.

KEY TERMS

Acupressure—Often described as acupuncture without needles, acupressure is a traditional Chinese medical technique based on the theory of *qi* (life energy) flowing in energy meridians or channels in the body. Applying pressure with the thumb and fingers to acupressure points is thought to relieve specific conditions and promote overall balance and health.

Acupuncture—Based on the same traditional Chinese medical foundation as acupressure, acupuncture uses sterile needles inserted at specific points to treat certain conditions or relieve pain.

Neurological system—The tissue that initiates and transmits nerve impulses, including the brain, spinal cord, and nerves.

Optokinetic—A reflex that causes a person's eyes to move when his or her field of vision moves.

Vertigo—The sensation of moving around in space, or objects moving around a person. It is a disturbance of equilibrium.

Vestibular system—The brain and parts of the inner ear that work together to detect movement and position.

- Pregnancy. Susceptibility in women to vomiting during pregnancy appears to be related to motion sickness, although the precise connections are not yet well understood.

Often viewed as a minor annoyance, some travelers are temporarily immobilized by motion sickness, and a few continue to feel its effects for hours and even days after a trip (the "mal d'embarquement" syndrome).

Diagnosis

Most cases of motion sickness are mild and self–treatable disorders. If symptoms such as dizziness become chronic, a doctor may be able to help alleviate the discomfort by looking further into a patient's general health. Questions regarding medications, head injuries, recent infections, and other questions about the ear and neurological system will be asked. An examination of the ears, nose, and throat, as well as tests of nerve and balance function, may also be completed.

Severe cases of motion sickness symptoms, and those that become progressively worse, may require additional, specific tests. Diagnosis in these situations deserves the attention and care of a doctor with specialized skills in diseases of the ear, nose, throat, equilibrium, and neurological system.

Treatment

There are a variety of medications to help ease the symptoms of motion sickness, and most of these are available without a prescription. Known as over-the-counter (OTC) medications, these products should be taken 30–60 minutes before traveling in order to prevent motion sickness symptoms, as well as during an extended trip.

Drugs

The following OTC drugs consist of ingredients that have been considered safe and effective for the treatment of motion sickness by the Food and Drug Administration (FDA):

- Marezine (and others). Includes the active ingredient cyclizine and is not for use in children under age six.
- Benadryl (and others). Includes the active ingredient diphenhydramine and is not for use in children under age six.
- Dramamine (and others). Includes the active ingredient dimenhydrinate and is not for use in children under age two.
- Bonine (and others). Includes the active ingredient meclizine and is not for use in children under age 12.

Each of the active ingredients listed above are **antihistamines** whose main side effect is drowsiness. Caution should be used when driving a vehicle or operating machinery, and alcohol should be avoided when taking any drug for motion sickness. Large doses of OTC drugs for motion sickness may also cause **dry mouth** and occasional blurred vision.

The side effects of antihistamine antiemetics indicate that they should not be used by members of flight crews responsible for the control of aircraft or for other tasks that require sustained attention and alertness.

The FDA recommends that people with **emphysema**, chronic **bronchitis**, glaucoma, or difficulty urinating due to an **enlarged prostate** not use OTC drugs for motion sickness unless directed by their doctor.

Longer trips may require a prescription medication called scopolamine (Transderm Scop). Formerly used in the transdermal skin patch (now discontinued), travelers must now ask their doctor to prescribe it in the form of a gel. In gel form, scopolamine is most effective when smeared on the arm or neck and covered with a bandage.

PATRICIA SUZANNE COWINGS (1948–)

Patricia Suzanne Cowings was born on December 15, 1948, in New York City. She was one of four children born to Sadie and Albert Cowings, a grocery store owner. Cowings showed interest in science by the time she was eleven years old. She enrolled in the State University of New York at Stony Brook, earning her bachelor's degree with honors in 1970. She began her graduate work at the University of California at Davis where she was awarded both her master's and her doctoral degrees in 1973. Cowings also received an associateship from the National Research Council that same year, which allowed her to complete two years of research at NASA's Ames Research Center. She has held a position as a researcher with Ames since 1977, and is currently the principal investigator of Psychophysiological Research Laboratories at NASA Ames Research Center (ARC), as well as a professor of psychiatry at the University of California, Los Angeles.

Cowings's work at Ames' Psychophysiological Research Laboratory led to major breakthroughs for astronauts. Her pioneering experiments with biofeedback as a method to control bodily functions has proven very effective for astronaut crews who experience "zero-gravity sickness syndrome." Her program was finally used during the 1992 *Endeavour* space flight. Presently, Cowings is researching exercises that will allow astronauts to maintain muscle strength while in zero gravity. She has published numerous papers with her colleague and husband, William B. Toscano. In addition, she has written articles including *The Relationship of Motion Sickness Susceptibility to Learned Autonomic Control for Symptom Suppression* (1982), *Autogenic-Feedback Training as a Preventive Method for Space Adaptation Syndrome* (1985), and *Autogenic-Feedback Training: A Preventive Method for Motion and Space Sickness* (1990).

Another prescription drug that is sometimes given for motion sickness is ondansetron (Zofran), which was originally developed to treat nausea associated with **cancer chemotherapy**. Unlike cyclizine, ondansetron appears to be safe for use in children under the age of six.

One newer class of anti–emetic drugs include compounds known as neurokinin–1 (substance P) antagonists. The neurokinins are usually prescribed for the control of nausea before surgery and following cancer chemotherapy, as well as preventing nausea in persons who have previously experienced severe motion sickness. The first of these new antiemetic drugs was known as aprepitant, and is sold under the trade name Emend.

Alternative treatment

Alternative treatments for motion sickness have become widely accepted as a standard means of care. Ginger (*Zingiber officinale*) in its various forms is often used to calm the stomach, and it is now known that the oils it contains (gingerols and shogaols) appear to relax the intestinal tract in addition to mildly depressing the central nervous system. Some of the most effective forms of ginger include the powdered, encapsulated form; ginger tea prepared from sliced ginger root; or candied pieces. All forms of ginger should be taken on an empty stomach.

Placing manual pressure on the Neiguan or Pericardium–6 **acupuncture** point (located about three finger–widths above the wrist on the inner arm), either by acupuncture, **acupressure**, or a mild, electrical pulse, has shown to be effective against the symptoms of motion sickness. Elastic wristbands sold at most drugstores are also used as a source of relief due to the pressure it places in this area. Pressing the small indentation (just below the earlobes in the indentations behind the jawbone) may also help in the functioning of the ear's balancing mechanism.

There are several homeopathic remedies that work specifically for motion sickness. They include *Cocculus*, *Petroleum*, and *Tabacum*. Alternative treatments should be used with care, as the benefits of many such treatments have not been confirmed by scientific research.

The National Aeronautics and Space Administration (NASA) has developed an additional treatment for motion sickness that has shown benefit for both military pilots and astronauts. NASA's autogenic feedback training exercises encourage pilots to reduce motion sickness symptoms by controlling their own responses to the sensations of flight using **biofeedback** and self–suggestion exercises. After one six–hour training session, eighty percent of pilot volunteers who had previously experienced symptoms of motion sickness reported increased motion sickness tolerance. With more study, NASA anticipates that the program could provide similar benefit to persons experiencing motion sickness, extreme **fatigue**, jet–lag, **insomnia**, and high **stress** work environments.

Prognosis

While there is no cure for motion sickness, its symptoms can be controlled or even prevented. Most people respond successfully to the variety of treatments available, or avoid the unpleasant symptoms through prevention methods.

Prevention

Because motion sickness is easier to prevent than treat once it has begun, the best treatment is prevention. The following steps may help deter the unpleasant symptoms of motion sickness before they occur:

- Avoid reading while traveling, and do not sit in a backward facing seat.
- Always ride where the eyes may see the same motion that the body and inner ears feel. Safe positions include the front seat of the car while looking at distant scenery; the deck of a ship where the horizon can be seen; and sitting by the window of an airplane. The least motion on an airplane is in a seat over the wings.
- Maintain a fairly straight–ahead view.
- Eat a light meal before traveling, or if already nauseated, avoid food altogether.
- Avoid watching or talking to another traveler who is having motion sickness.
- Take motion sickness medicine at least 30–60 minutes before travel begins, or as recommended by a physician.
- Learn to live with the condition. Even those who frequently endure motion sickness can learn to travel by anticipating the conditions of their next trip. Research also suggests that increased exposure to the stimulation that causes motion sickness may help decrease its symptoms on future trips.

Resources

BOOKS

Moelleken, B.R.W. "Medical Effects of Air Travel and Selection of Patients for Air Travel Section of Disorders Due to Physical Agents." In S.J. McPhee, et al., editors. *Current Medical Diagnosis and Treatment,* 47th ed., 1356–57. New York: McGraw-Hill, 2008.

PERIODICALS

Chepyala, P., and K.W. Olden. "Nausea and Vomiting." *Current Treatment Options in Gastroenterology*. 11(2) (March 2008): 135–44.

Villard, S.J., M.B. Flanagan, G.M. Albanese, and T.A. Stoffregen. "Postural Instability and Motion Sickness in a Virtual Moving Room." *Human Factors* 50(2) (April 2008): 332–45.

OTHER

Carroll, Dale. "Motion Sickness." Traveler's Health–Yellow Book. U.S. Centers for Disease Control and Prevention (CDC).http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter–2/motion– sickness.asp x (accessed on September 13, 2010).

NASA Ames Research Center. "Autogenic Feedback Training Exercise (AFTE) in High–Stress Environments." National Aeronautics and Space Administration. http://humansystems.arc.nasa.gov/groups/psychophysio/factsheets/Cow ings_AFTE.pdf (accessed September 13, 2010).

ORGANIZATIONS

Vestibular Disorders Association, PO Box 13305, Portland, Oregon, 97213, (800) 837–8428, (503) 229–8064, copyeditor@vestibular.org, http://www.vestibular.org/index.php.

Beth A. Kapes
Rebecca J. Frey, PhD
Karl Finley

Mountain sickness *see* **Altitude sickness**
Mouth cancer *see* **Head and neck cancer**

Movement disorders

Definition

Movement disorders are a group of diseases and syndromes affecting the ability to produce and control movement.

Description

Although it seems simple and effortless, normal movement in fact requires an astonishingly complex system of control. Disruption of any portion of this system can cause a person to produce movements that are too weak, too forceful, too uncoordinated, or too poorly controlled for the task at hand. Unwanted movements may occur at rest. Intentional movement may become impossible. Such conditions are called movement disorders.

Abnormal movements themselves are symptoms of underlying disorders. In some cases, the abnormal movements are the only symptoms. Disorders causing abnormal movements include:

- Parkinson's disease
- Parkinsonism caused by drugs or poisons
- Parkinson–plus syndromes (progressive supranuclear palsy, multiple system atrophy, and cortical–basal ganglionic degeneration)
- Huntington's disease
- Wilson's disease
- Inherited ataxias (Friedreich's ataxia, Machado–Joseph disease, and spinocerebellar ataxias)
- Tourette syndrome and other tic disorders
- Essential tremor
- Restless leg syndrome

- Dystonia
- Stroke
- Cerebral palsy
- Encephalopathies
- Intoxication
- Poisoning by carbon monoxide, cyanide, methanol, or manganese.

Causes and symptoms

Causes

Movement is produced and coordinated by several interacting brain centers, including the motor cortex, the cerebellum, and a group of structures in the inner portions of the brain called the basal ganglia. Sensory information provides critical input on the current position and velocity of body parts, and spinal nerve cells (neurons) help prevent opposing muscle groups from contracting at the same time.

To understand how movement disorders occur, it is helpful to consider a normal voluntary movement, such as reaching to touch a nearby object with the right index finger. To accomplish the desired movement, the arm must be lifted and extended. The hand must be held out to align with the forearm, and the forefinger must be extended while the other fingers remain flexed.

THE MOTOR CORTEX. Voluntary motor commands begin in the motor cortex located on the outer, wrinkled surface of the brain. Movement of the right arm is begun by the left motor cortex, which generates a large volley of signals to the involved muscles. These electrical signals pass along upper motor neurons through the midbrain to the spinal cord. Within the spinal cord, they connect to lower motor neurons, which convey the signals out of the spinal cord to the surface of the muscles involved. Electrical stimulation of the muscles causes contraction, and the force of contraction pulling on the skeleton causes movement of the arm, hand, and fingers.

Damage to or **death** of any of the neurons along this path causes weakness or **paralysis** of the affected muscles.

ANTAGONISTIC MUSCLE PAIRS. This picture of movement is too simple, however. One important refinement to it comes from considering the role of opposing, or antagonistic, muscle pairs. Contraction of the biceps muscle, located on the top of the upper arm, pulls on the forearm to flex the elbow and bend the arm. Contraction of the triceps, located on the opposite side, extends the elbow and straightens the arm. Within the spine, these muscles are normally wired so that willed (voluntary) contraction of one is automatically accompanied by blocking of the other. In other words, the command to contract the biceps provokes another command within the spine to prevent contraction of the triceps. In this way, these antagonist muscles are kept from resisting one another. Spinal cord or brain injury can damage this control system and cause involuntary simultaneous contraction and spasticity, an increase in resistance to movement during motion.

THE CEREBELLUM. Once the movement of the arm is initiated, sensory information is needed to guide the finger to its precise destination. In addition to sight, the most important source of information comes from the "position sense" provided by the many sensory neurons located within the limbs (proprioception). Proprioception is the response allows a person to touch the nose with the finger even with the eyes closed. The balance organs in the ears provide important information about posture. Both postural and proprioceptive information are processed by a structure at the rear of the brain called the cerebellum. The cerebellum sends out electrical signals to modify movements as they progress, "sculpting" the barrage of voluntary commands into a tightly controlled, constantly evolving pattern. Cerebellar disorders cause inability to control the force, fine positioning, and speed of movements (ataxia). Disorders of the cerebellum may also impair the ability to judge distance so that a person under- or overreaches the target (dysmetria). Tremor during voluntary movements can also result from cerebellar damage.

THE BASAL GANGLIA. Both the cerebellum and the motor cortex send information to a set of structures deep within the brain that help control involuntary components of movement (basal ganglia). The basal ganglia send output messages to the motor cortex, helping to initiate movements, regulate repetitive or patterned movements, and control muscle tone.

Circuits within the basal ganglia are complex. Within this structure, some groups of cells begin the action of other basal ganglia components and some groups of cells block the action. These complicated feedback circuits are not entirely understood. Disruptions of these circuits are known to cause several distinct movement disorders. A portion of the basal ganglia called the substantia nigra sends electrical signals that block output from another structure called the subthalamic nucleus. The subthalamic nucleus sends signals to the globus pallidus, which in turn blocks the thalamic nuclei. Finally, the thalamic nuclei send signals to the motor cortex. The substantia nigra, then, begins movement and the globus pallidus blocks it.

This complicated circuit can be disrupted at several points. For instance, loss of substantia nigra cells,

as in Parkinson's disease, increases blocking of the thalamic nuclei, preventing them from sending signals to the motor cortex. The result is a loss of movement (motor activity), a characteristic of Parkinson's.

In contrast, cell loss in early Huntington's disease decreases blocking of signals from the thalamic nuclei, causing more cortex stimulation and stronger but uncontrolled movements.

Disruptions in other portions of the basal ganglia are thought to cause tics, **tremors**, dystonia, and a variety of other movement disorders, although the exact mechanisms are not well understood.

Some movement disorders, including Huntington's disease and inherited ataxias, are caused by inherited genetic defects. Some disease that cause sustained muscle contraction limited to a particular muscle group (focal dystonia) are inherited, but others are caused by trauma. The cause of most cases of Parkinson's disease is unknown, although genes have been found for some familial forms.

Symptoms

Abnormal movements are broadly classified as either hyperkinetic—too much movement—and hypokinetic—too little movement. Hyperkinetic movements include:

- Dystonia. Sustained muscle contractions, often causing twisting or repetitive movements and abnormal postures. Dystonia may be limited to one area (focal) or may affect the whole body (general). Focal dystonias may affect the neck (cervical dystonia or torticollis), the face (one–sided or hemifacial spasm, contraction of the eyelid or blepharospasm, contraction of the mouth and jaw or oromandibular dystonia, simultaneous spasm of the chin and eyelid or Meige syndrome), the vocal cords (laryngeal dystonia), or the arms and legs (writer's cramp, occupational cramps). Dystonia may be painful as well as incapacitating.
- Tremor. Uncontrollable (involuntary) shaking of a body part. Tremor may occur only when muscles are relaxed or it may occur only during an action or holding an active posture.
- Tics. Involuntary, rapid, nonrhythmic movement or sound. Tics can be controlled briefly.
- Myoclonus. A sudden, shock–like muscle contraction. Myoclonic jerks may occur singly or repetitively. Unlike tics, myoclonus cannot be controlled even briefly.
- Chorea. Rapid, nonrhythmic, usually jerky movements, most often in the arms and legs.
- Ballism. Like chorea, but the movements are much larger, more explosive and involve more of the arm or leg. This condition, also called ballismus, can occur on both sides of the body or on one side only (hemiballismus).
- Akathisia. Restlessness and a desire to move to relieve uncomfortable sensations. Sensations may include a feeling of crawling, itching, stretching, or creeping, usually in the legs.
- Athetosis. Slow, writhing, continuous, uncontrollable movement of the arms and legs.

Hypokinetic movements include:

- Bradykinesia. Slowness of movement.
- Freezing. Inability to begin a movement or involuntary stopping of a movement before it is completed.
- Rigidity. An increase in muscle tension when an arm or leg is moved by an outside force.
- Postural instability. Loss of ability to maintain upright posture caused by slow or absent righting reflexes.

Diagnosis

Diagnosis of movement disorders requires a careful medical history and a thorough physical and neurological examination. Brain imaging studies are usually performed. Imaging techniques include computed tomography scan (CT scan), **positron emission tomography (PET)**, or **magnetic resonance imaging** (MRI) scans. Routine blood and urine analyses are performed. A **lumbar puncture** (spinal tap) may be necessary. Video recording of the abnormal movement is often used to analyze movement patterns and to track progress of the disorder and its treatment. **Genetic testing** is available for some forms of movement disorders.

Treatment

Treatment of a movement disorder begins with determining its cause. Physical and **occupational therapy** may help make up for lost control and strength. Drug therapy can help compensate for some imbalances of the basal ganglionic circuit. For instance, levodopa (L–dopa) or related compounds can substitute for lost dopamine–producing cells in Parkinson's disease. Conversely, blocking normal dopamine action is a possible treatment in some hyperkinetic disorders, including tics. Oral medications can also help reduce overall muscle tone. Local injections of botulinum toxin can selectively weaken overactive muscles in dystonia and spasticity. Destruction of peripheral nerves through injection of phenol can reduce spasticity. All of these treatments may have some side effects.

KEY TERMS

Botulinum toxin—Any of a group of potent bacterial toxins or poisons produced by different strains of the bacterium *Clostridium botulinum*. The toxins cause muscle paralysis, and thus force the relaxation of a muscle in spasm.

Cerebral palsy—A movement disorder caused by a permanent brain defect or injury present at birth or shortly after. It is frequently associated with premature birth. Cerebral palsy is not progressive.

Computed tomography (CT)—An imaging technique in which cross–sectional x rays of the body are compiled to create a three–dimensional image of the body's internal structures.

Encephalopathy—An abnormality in the structure or function of tissues of the brain.

Essential tremor—An uncontrollable (involuntary) shaking of the hands, head, and face. Also called familial tremor because it is sometimes inherited, it can begin in the teens or in middle age. The exact cause is not known.

Fetal tissue transplantation—A method of treating Parkinson's and other neurological diseases by grafting brain cells from human fetuses onto the basal ganglia. Human adults cannot grow new brain cells but developing fetuses can. Grafting fetal tissue stimulates the growth of new brain cells in affected adult brains.

Hereditary ataxia—One of a group of hereditary degenerative diseases of the spinal cord or cerebellum. These diseases cause tremor, spasm, and wasting of muscle.

Huntington's disease—A rare hereditary condition that causes progressive chorea (jerky muscle movements) and mental deterioration that ends in dementia. Huntington's symptoms usually appear in patients in their 40s. There is no effective treatment.

Levodopa (L–dopa)—A substance used in the treatment of Parkinson's disease. Levodopa can cross the blood–brain barrier that protects the brain. Once in the brain, it is converted to dopamine and thus can replace the dopamine lost in Parkinson's disease.

Magnetic resonance imaging (MRI)—An imaging technique that uses a large circular magnet and radio waves to generate signals from atoms in the body. These signals are used to construct images of internal structures.

Parkinson's disease—A slowly progressive disease that destroys nerve cells in the basal ganglia and thus causes loss of dopamine, a chemical that aids in transmission of nerve signals (neurotransmitter). Parkinson's is characterized by shaking in resting muscles, a stooping posture, slurred speech, muscular stiffness, and weakness.

Positron emission tomography (PET)—A diagnostic technique in which computer–assisted x rays are used to track a radioactive substance inside a patient's body. PET can be used to study the biochemical activity of the brain.

Progressive supranuclear palsy—A rare disease that gradually destroys nerve cells in the parts of the brain that control eye movements, breathing, and muscle coordination. The loss of nerve cells causes palsy, or paralysis, that slowly gets worse as the disease progresses. The palsy affects ability to move the eyes, relax the muscles, and control balance.

Restless legs syndrome—A condition that causes an annoying feeling of tiredness, uneasiness, and itching deep within the muscle of the leg. It is accompanied by twitching and sometimes pain. The only relief is in walking or moving the legs.

Tourette syndrome—An abnormal condition that causes uncontrollable facial grimaces and tics and arm and shoulder movements. Tourette syndrome is perhaps best known for uncontrollable vocal tics that include grunts, shouts, and use of obscene language (coprolalia).

Wilson's disease—An inborn defect of copper metabolism in which free copper may be deposited in a variety of areas of the body. Deposits in the brain can cause tremor and other symptoms of Parkinson's disease.

Surgical destruction or inactivation of basal ganglionic circuits has proven effective for Parkinson's disease and is being tested for other movement disorders. Transplantation of fetal cells into the basal ganglia has produced mixed results in Parkinson's disease.

Alternative treatment

There are several alternative therapies that can be useful when treating movement disorders. The progress made will depend on the individual and his/her

condition. Among the therapies that may be helpful are **acupuncture**, homeopathy, touch therapies, postural alignment therapies, and **biofeedback**.

Prognosis

The prognosis for a patient with a movement disorder depends on the specific disorder.

Prevention

Prevention depends on the specific disorder.

Resources

BOOKS

Chaudhuri, Ray, K., and William Ondo. *Movement Disorders in Clinical Practice*. New York, NY: Springer, 2010.

Newell, Lori A. *The Book of Exercise and Yoga for Those with Parkinson's Disease: Using Movement and Meditation to Manage Symptoms*. Charleston, SC: CreateSpace, 2010.

Truong, Daniel D., Mayank Pathak, and Karen Frei. *Living Well with Dystonia: A Patient Guide*. New York, NY: Demos Health, 2010.

Wyborny, Sheila. *Tourette Syndrome*. San Diego, CA, 2010.

ORGANIZATIONS

American Academy of Neurology , 1080 Montreal Ave., Saint Paul, MN, 55116, (800) 879–1960, http://www.aan.com.

American Academy of Physical Medicine and Rehabilitation , 9700 West Bryn Mawr Ave., Suite 200, Rosemont, IL, 60018–5701, 847–737–6000, http://www.aapmr.org.

American Physical Therapy Association, 1111 North Fairfax St., Alexandria, VA, 22314–1488, (703) 684–APTA (2782). TDD: (703) 683–6748, (800) 999–APTA (2782), http://www.apta.org.

The Movement Disorder Society , 555 East Wells St., Suite 1100 , Milwaukee, WI, 53202–3823 , (414) 276–2145, http://www.movementdisorders.org/.

Worldwide Education and Awareness for Movement Disorders, One Gustave L. Levy Pl., PO Box 1052, New York, NY, 10029, (800) 437–6683, http://www.wemove.org.

Richard Robinson
Laura Jean Cataldo, RN, Ed.D.

Movement therapy

Definition

Movement therapy refers to a broad range of Eastern and Western movement approaches used to promote physical, mental, emotional, and spiritual well-being.

Purpose

The physical benefits of movement therapy include greater ease and range of movement, increased balance, strength and flexibility, improved muscle tone and coordination, joint resiliency, cardiovascular conditioning, enhanced athletic performance, stimulation of circulation, prevention of injuries, greater longevity, **pain** relief, and relief of rheumatic, neurological, spinal, **stress**, and respiratory disorders. Movement therapy can also be used as a **meditation** practice to quiet the mind, foster self-knowledge, and increase awareness. In addition, movement therapy is beneficial in alleviating emotional distress that is expressed through the body. These conditions include **eating disorders**, excessive clinging, and **anxiety** attacks. Since movements are related to thoughts and feelings, movement therapy can also bring about changes in attitude and emotions. People report an increase in self-esteem and self-image. Communication skills can be enhanced and tolerance of others increased. The physical openness facilitated by movement therapy leads to greater emotional openness and creativity.

Description

Origins

Movement is fundamental to human life. In fact movement is life. Contemporary physics tells us that the universe and everything in it is in constant motion. We can move our body and at the most basic level our body is movement. According to the somatic educator Thomas Hanna, "The living body is a moving body—indeed, it is a constantly moving body." The poet and philosopher Alan Watts eloquently states a similar view, "A living body is not a fixed thing but a flowing event, like a flame or a whirlpool." Centuries earlier, the great Western philosopher Socrates understood what modern physics has proven, "The universe is motion and nothing else."

Since the beginning of time, indigenous societies around the world have used movement and dance for individual and community healing. Movement and song were used for personal healing, to create community, to ensure successful crops, and to promote fertility. Movement is still an essential part of many healing traditions and practices throughout the world.

Western movement therapies generally developed out of the realm of dance. Many of these movement approaches were created by former dancers or choreographers who were searching for a way to prevent injury, attempting to recover from an injury, or who were curious about the effects of new ways of moving.

Some movement therapies arose out of the fields of **physical therapy**, psychology, and bodywork. Other movement therapies were developed as way to treat an incurable disease or condition.

Eastern movement therapies, such as **yoga**, **qigong**, and t'ai chi began as a spiritual or self-defense practices and evolved into healing therapies. In China, for example, Taoist monks learned to use specific breathing and movement patterns in order to promote mental clarity, physical strength, and support their practice of meditation. These practices, later known as qigong and t'ai chi eventually became recognized as ways to increase health and prolong life.

There are countless approaches to movement therapy. Some approaches emphasize awareness and attention to inner sensations. Other approaches use movement as a form of **psychotherapy**, expressing and working through deep emotional issues. Some approaches emphasize alignment with gravity and specific movement sequences, while other approaches encourage spontaneous movement. Some approaches are primarily concerned with increasing the ease and efficiency of bodily movement. Other approaches address the reality of the body "as movement" instead of the body as only something that runs or walks through space.

The term movement therapy is often associated with dance therapy. Some dance therapists work privately with people who are interested in personal growth. Others work in mental health settings with autistic, brain injured and learning disabled children, the elderly, and disabled adults.

Laban movement analysis (LMA), formerly known as Effort-Shape is a comprehensive system for discriminating, describing, analyzing, and categorizing movements. LMA can be applied to dance, athletic coaching, fitness, acting, psychotherapy, and a variety of other professions. Certified movement analysts can "observe recurring patterns, note movement preferences, asses physical blocks and dysfunctional movement patterns, and the suggest new movement patterns." As a student of Rudolf Laban, Irmgard Bartenieff developed his form of movement analysis into a system of body training or reeducation called Bartenieff fundamentals (BF). The basic premise of this work is that once the student experiences a physical foundation, emotional, and intellectual expression become richer. BF uses specific exercises that are practiced on the floor, sitting, or standing to engage the deeper muscles of the body and enable a greater range of movement.

Authentic movement (AM) is based upon Mary Starks Whitehouse's understanding of dance, movement, and depth psychology. There is no movement instruction in AM, simply a mover and a witness. The mover waits and listens for an impulse to move and then follows or "moves with" the spontaneous movements that arise. These movements may or may not be visible to the witness. The movements may be in response to an emotion, a dream, a thought, pain, joy, or whatever is being experienced in the moment. The witness serves as a compassionate, non judgmental mirror and brings a "special quality of attention or presence." At the end of the session the mover and witness speak about their experiences together. AM is a powerful approach for self development and awareness and provides access to preverbal memories, creative ideas, and unconscious movement patterns that limit growth.

Gabrielle Roth (5 Rhythms movement) and Anna Halprin have both developed dynamic movement practices that emphasize personal growth, awareness, expression, and community. Although fundamentally different forms, each of these movement/dance approaches recognize and encourage our inherent desire for movement.

Several forms of movement therapy grew out of specific bodywork modalities. **Rolfing** movement integration (RMI) and Rolfing rhythms are movement forms which reinforce and help to integrate the structural body changes brought about by the hands-on work of Rolfing (structural integration). RMI uses a combination of touch and verbal directions to help develop greater awareness of one's vertical alignment and habitual movement patterns. RMI teacher Mary Bond says, "The premise of Rolfing Movement Integration... is that you can restore your structure to balance by changing the movement habits that perpetuate imbalance." Rolfing rhythms is a series of lively exercises designed to encourage awareness of the Rolfing principles of ease, length, balance, and harmony with gravity.

The movement education component of **Aston-Patterning** bodywork is called neurokinetics. This movement therapy teaches ways of moving with greater ease throughout every day activities. These movement patterns can also be used to release tension in the body. Aston fitness is an **exercise** program which includes warm-up techniques, exercises to increase muscle tone and stability, stretching, and cardiovascular fitness.

Rosen method movement (an adjunct to Rosen method bodywork) consists of simple fun movement exercises done to music in a group setting. Through gentle swinging, bouncing, and stretching every joint in the body experiences a full range of movement. The movements help to increase balance and rhythm and create more space for effortless breathing.

The movement form of **Trager psychophysical integration** bodywork, Mentastics, consists of fun, easy swinging, shaking, and stretching movements.

These movements, developed by Dr. Milton Trager, create an experience of lightness and freedom in the body, allowing for greater ease in movement. Trager also worked successfully with **polio** patients.

Awareness through movement, the movement therapy form of the **Feldenkrais method**, consists of specific structured movement experiences taught as a group lesson. These lessons reeducate the brain without tiring the muscles. Most lessons are done lying down on the floor or sitting. Moshe Feldenkrais designed the lessons to "improve ability ... turn the impossible into the possible, the difficult into the easy, and the easy into the pleasant."

Ideokinesis is another movement approach emphasizing neuromuscular reeducation. Lulu Sweigart based her work on the pioneering approach of her teacher Mabel Elsworth Todd. Ideokinesis uses imagery to train the nervous system to stimulate the right muscles for the intended movement. If one continues to give the nervous system a clear mental picture of the movement intended, it will automatically select the best way to perform the movement. For example, to enhance balance in standing, Sweigart taught people to visualize "lines of movement" traveling through their bodies. Sweigart did not train teachers in ideokinesis but some individuals use ideokinetic imagery in the process of teaching movement.

The Mensendieck system of functional movement techniques is both corrective and preventative. Bess Mensendieck, a medical doctor, developed a series of exercises to reshape, rebuild, and revitalize the body. A student of this approach learns to use the conscious will to relax muscles and releases tension. There are more than 200 exercises that emphasize correct and graceful body movement through everyday activities. Unlike other movement therapy approaches this work is done undressed or in a bikini bottom, in front of mirrors. This allows the student to observe and feel where a movement originates. Success has been reported with many conditions including Parkinson's disease, muscle and joint injuries, and repetitive strain injuries.

The **Alexander technique** is another functional approach to movement therapy. In this approach a teacher gently uses hands and verbal directions to subtly guide the student through movements such as sitting, standing up, bending and walking. The Alexander technique emphasizes balance in the neck-head relationship. A teacher lightly steers the students head into the proper balance on the tip of the spine while the student is moving in ordinary ways. The student learns to respond to movement demands with the whole body, in a light integrated way. This approach to movement is particularly popular with actors and other performers.

Pilates or physical mind method is also popular with actors, dancers, athletes, and a broad range of other people. Pilates consists of over 500 exercises done on the floor or primarily with customized exercise equipment. The exercises combine sensory awareness and physical training. Students learn to move from a stable, central core. The exercises promote strength, flexibility, and balance. Pilates training is increasingly available in sports medicine clinics, fitness centers, dance schools, spas, and physical therapy offices.

Many approaches to movement therapy emphasize awareness of internal sensations. Charlotte Selver, a student of somatic pioneer Elsa Gindler, calls her style of teaching sensory awareness (SA). This approach has influenced the thinking of many innovators, including Fritz Perls, who developed **gestalt therapy**. Rather than suggesting a series of structured movements, visualizations, or body positions, in SA the teacher outlines experiments in which one can become aware of the sensations involved in any movement. A teacher might ask the student to feel the movement of her breathing while running, sitting, picking up a book, etc. This close attunement to inner sensory experience encourages an experience of body-mind unity in which breathing becomes less restricted and posture, coordination, flexibility, and balance are improved. There may also be the experience of increased energy and aliveness.

Gerda Alexander Eutony (GAE) is another movement therapy approach that is based upon internal awareness. Through GAE one becomes a master of self-sensing and knowing which includes becoming sensitive to the external environment, as well. For example, while lying on the floor sensing the breath, skin or form of the body, one also senses the connection with the ground. GAE is taught in group classes or private lessons which also include hands-on therapy. In 1987, after two years of observation in clinics throughout the world, GAE became the first mind-body discipline accepted by the World Health Organization (WHO) as an alternative health-care technique.

Kinetic awareness developed by dancer-choreographer Elaine Summers, emphasizes emotional and physical inquiry. Privately or in a group, a teacher sets up situations for the student to explore the possible causes of pain and movement restrictions within the body. Rubber balls of various sizes are used as props to focus attention inward, support the body in a stretched position and massage a specific area of the body. The work helps one to deal with chronic pain, move easily again after injuries and increase energy, flexibility, coordination, and comfort.

Body-mind centering (BMC) was developed by Bonnie Bainbridge Cohen and is a comprehensive educational and therapeutic approach to movement. BMC practitioners use movement, touch, **guided imagery**, developmental repatterning, dialogue, music, large balls, and other props in an individual session to meet the needs of each person. BMC encourages people to develop a sensate awareness and experience of the ligaments, nerves, muscles, skin, fluids, organs, glands, fat, and fascia that make up one's body. It has been effective in preventing and rehabilitating from chronic injuries and in improving neuromuscular response in children with **cerebral palsy** and other neurological disorders.

Continuum movement has also been shown to be effective in treating neurological disorders including spinal chord injury. Developed by Emilie Conrad and Susan Harper, continuum movement is an inquiry into the creative flux of our body and all of life. Sound, breath, subtle and dynamic movements are explored that stimulate the brain and increase resonance with the fluid world of movement. The emphasis is upon unpredictable, spontaneous or spiral movements rather than a linear movement pattern. According to Conrad, "Awareness changes how we physically move. As we become more fluid and resilient so do the mental, emotional, and spiritual movements of our lives."

Eastern movement therapies such as yoga, t'ai chi, and qigong are also effective in healing and preventing a wide range of physical disorders, encouraging emotional stability, and enhancing spiritual awareness. There are a number of different approaches to yoga. Some emphasize the development of physical strength, flexibility, and alignment. Other forms of yoga emphasize inner awareness, opening, and meditation.

Precautions

People with acute injuries and chronic physical and mental conditions need to be careful when choosing a form of movement therapy. It is best to consult with a knowledgeable physician, physical therapist, or mental health therapist.

A special form of movement therapy known as constraint-induced movement therapy, or CIMT, is being used as of the early 2000s to rehabilitate the upper limbs of patients who have suffered a **stroke**, traumatic brain injury, or damage to the spinal cord. In CIMT, the arm that has been less affected by the injury is constrained by a sling for 90% of the patient's waking hours for a period of two weeks. The sling forces the patient to use the weaker arm more often; in addition, a physical therapist works with the patient to practice repetitive motions with the weaker arm. CIMT also appears to be useful in treating children with muscular weakness on one side of the body caused by cerebral palsy.

Research and general acceptance

Although research has documented the beneficial effects of dance therapy, qigong, t'ai chi, yoga, Alexander technique, awareness through movement (Feldenkrais), and Rolfing, other forms of movement therapy have not been as thoroughly researched.

CIMT has become widely accepted in **rehabilitation** medicine since its introduction in the mid-1990s, although some doctors still consider it experimental. Further research in CIMT is being carried out by the National Institute of Neurological Disorders and Stroke (NINDS), one of the National Institutes of Health.

Resources

BOOKS

Payne, Helen. *Dance Movement Therapy: Theory, Research and Practice*. London; New York: Routledge, 2006.

PERIODICALS

Bunch, W. "Dancing through the Pain. Physician Executive Launches New Business to Treat Patients with Chronic Pain." *Physician Executive* 30 (January-February 2004): 30–33.

Mark, V. W., and E. Taub. "Constraint-Induced Movement Therapy for Chronic Stroke Hemiparesis and Other Disabilities." *Restorative Neurology and Neuroscience* 22 (March 2004): 317–336.

Page, S. J., S. Sisto, P. Levine, and R. E. McGrath. "Efficacy of Modified Constraint-Induced Movement Therapy in Chronic Stroke: A Single-Blinded Randomized Controlled Trial." *Archives of Physical Medicine and Rehabilitation* 85 (January 2004): 14–18.

Taub, E., S. L. Ramey, S. DeLuca, and K. Echols. "Efficacy of Constraint-Induced Movement Therapy for Children with Cerebral Palsy with Asymmetric Motor Impairment." *Pediatrics* 113 (February 2004): 305–312.

ORGANIZATIONS

National Institute of Neurological Disorders and Stroke (NINDS), NIH Neurological Institute, P. O. Box 5801, Bethesda, MD, 20824, (301) 496-5751, (800) 352-9424, http://www.ninds.nih.gov/.

Linda Chrisman
Rebecca J. Frey, PhD

Mpell disease *see* **Ankylosing spondylitis**
MR *see* **Magnetic resonance imaging**
MRI *see* **Magnetic resonance imaging**

MRSA infections

Definition

Methicillin–resistant *Staphylococcus aureus* (MRSA) infections are caused by a strain of staphylococcus bacterium that often does not respond to most classes of **antibiotics**.

Description

MRSA belongs to the emerging category of multidrug–resistant organisms (MDROs). These organisms are mostly disease–causing (pathogenic) bacteria that are resistant to one or more classes of antimicrobial agents. Methicillin is an antibiotic that has been used successfully to treat infections caused by *Staphylococcus aureus*, commonly known as "staph" infections. Staph bacteria are found on the skin and in the nose of approximately 33% of the general population. These staph bacteria are generally harmless unless they enter the body through a cut or other wound. If this happens, they often only cause minor skin infections in healthy people, or infections easily treated with antibiotics. Over the years however, the staph bacterium has mutated into MRSA, a strain that is resistant to methicillin and other antibiotics such as oxacillin, penicillin, and amoxicillin, meaning that these antibiotics are unable to clear the infections. MRSA infections have become a serious health issue, because they have a higher rate of fatalities.

There are two types of MRSA infections. The first is called "Healthcare–associated MRSA" (HA–MRSA) and it affects persons and patients admitted to hospitals and healthcare facilities such as nursing homes and dialysis centers. The second type is called "Community–associated MRSA" (CA–MRSA) and affects people who have not been hospitalized or had a medical procedure during the year before onset of infection. Individuals commonly affected by CA–MRSA include people involved in close–contact sports and activities, such as football players and wrestlers.

Demographics

MRSA was first isolated in the United States in 1968. By the early 1990s, MRSA accounted for 20%–25% of staph infections in hospitalized patients. In 2005, MRSA caused more than 94,000 life–threatening infections and approximately 18,650 deaths in the United States, most of them associated with hospitals, according to a Centers for Disease Control (CDC) report. The study found that about 85% of all invasive MRSA infections were associated with health care settings, of which two–thirds occurred in people who were hospitalized, underwent a medical procedure, or resided in a long–term care facility within the previous year. In contrast, about 15% of reported cases were considered to be CA–MRSA infections, meaning that MRSA infection occurred in people without documented exposures to healthcare. The infection rates were highest among people 65 years of age or older. African Americans were affected at twice the rate of whites, which could be due their higher rates of chronic illness.

Causes and symptoms

MRSA infections are caused by methicillin–resistant *Staphylococcus aureus*. The spread of MRSA infections however, is a consequence of:

- Unnecessary antibiotic use. MRSA infections are linked to years of unnecessary antibiotic use. Antibiotics are commonly prescribed for colds, flu, and other viral infections that do not respond to these drugs, as well as for simple bacterial infections that should normally clear on their own. Unfortunately, antibiotics promote the emergence of drug–resistant bacteria because they can't destroy all bacteria. Some bacteria survive treatment with one antibiotic and learn to resist by mutating. Often, a mutation against one antibiotic is often successful against other antibiotics.
- Presence of antibiotics in the food chain. In the Unites States, antibiotics are routinely given to cows, beef cattle, pigs, and chickens with the consequence that people often take them unknowingly in their food, as in milk or meats. Antibiotics can also find their way into drinking water systems when the runoff from animal feedlots contaminates streams and groundwater.
- Poor hygiene. The main mode of HA–MRSA transmission to other patients is through human hands, especially those of healthcare workers and patients sharing facilities. Hands may become contaminated with MRSA bacteria by contact with infected patients or with environmental surfaces in close proximity to the patient. The bacteria can then spread when a healthcare worker or patient touches other patients.

Symptoms of MRSA infections are variable. Skin infections usually cause pimples or **boils** that can be swollen, painful, and drain pus. They can quickly turn into deep, painful abscesses and can cause potentially life–threatening infections in bones, joints, surgical **wounds**, the bloodstream, heart valves, and lungs. Symptoms of serious MRSA infection may include:

- Rash
- Shortness of breath
- Fever, chills
- Chest pain
- Muscle aches
- Headache

Diagnosis

MRSA is diagnosed by testing a tissue sample or nasal secretions for signs of staph bacteria. The sample is sent to a lab where it is incubated in a dish of nutrients that promote the growth of staph colonies which can then be identified.

In January 2008, the U.S. Food and Drug Administration (FDA) cleared for marketing the first rapid blood test for MRSA. It is called the "BD GeneOhm StaphSR Assay" and it uses molecular methods to identify whether a blood sample contains genetic material from the MRSA bacterium or the more common, less dangerous staph bacterium that can still be treated with methicillin. Rather than waiting more than two days for test results, health care personnel are now able to identify the source of a staph infection in only two hours, allowing for more effective treatment.

Treatment

Options for treating patients with MRSA infections are often extremely limited. Both HA and CA–MRSA still respond to certain antibiotics. In hospitals and care facilities, treatment generally relies on the antibiotic vancomycin. For serious infections, this antibiotic is administered intravenously, often for several weeks. CA–MRSA may be treated with vancomycin or other antibiotics that have proved effective against particular strains. However, vancomycin is also growing resistant with some hospitals reporting vancomycin–resistant *Staphylococcus aureus* (VRSA) infections. There are a limited number of antibiotics available to treat infections caused by VRSA and there is growing concern in the medical community that we will eventually run out of antibiotic–based treatment options, because *Staphylococcus aureus* seems to be mutating as fast as antibiotics are being developed. Increasingly, physicians are selecting to surgically drain abscesses caused by MRSA rather than prescribe antibiotics. For mild to moderate MRSA skin infections, incision and drainage by a healthcare provider has become the first–line treatment.

Alternative treatment

There are no alternatives to using antibiotics that are efficient or treatments that avoid them, such as **abscess** drainage.

Prognosis

The prognosis for MRSA infections varies with the type and severity of the infection, and the general health condition of the person who has the infection. MRSA **pneumonia** and blood poisoning have high documented **death** rates. Mild CA–MRSA infections that are appropriately treated result in recovery in almost all cases.

Prevention

In the United States, national efforts are underway to raise public awareness about MRSA and to encourage preventive measures such as washing hands and general clean hygiene. As a general rule, people should:

- Wash hands frequently with soap and water. Hands should be scrubbed briskly for 15 seconds, then dried with a disposable towel, also used to turn off the faucet in a public setting.
- Carry small bottles of alcohol–based hand sanitizer for use when there is no access to soap and water.
- Avoid sharing personal items such as towels, sheets, razors, clothing, and athletic equipment.
- Keep cuts and wounds clean and covered with sterile, dry bandages until they are closed and healed.
- Avoid contact with other people's wounds.
- Wash towels and bed linens in a washing machine using the hot water setting preferably with bleach and dry in a hot dryer.
- In case of skin infection, ask the care provider for a MRSA test, so as to avoid being prescribed drugs that are not effective.
- If prescribed an antibiotic course, it should be completed, even if the infection seems to be clearing.

In a health care clinic or hospital setting, people and patients can ask caregivers to:

- Wash their hands or use an alcohol–based hand sanitizer before being touched or examined.
- Wash their own hands frequently with soap and water.
- Ensure that intravenous tubes and catheters are inserted under sterile conditions.

However, it is now recognized that measures limited to hand washing will not prevent the spread of

KEY TERMS

Abscess—Localized collection of pus in any part of the body that is surrounded by swelling.

Antibiotic—A drug used to treat infections caused by bacteria and other microorganisms.

Antibiotic–resistant—Microorganisms that continue to multiply although exposed to antibiotics.

Antimicrobial agent—A substance that kills microorganisms such as bacteria or mold, or stops them from growing and causing disease.

Bacterium—A single–celled microorganism that can be seen only through a microscope. Many bacteria cause disease.

Boil—A collection of pus localized deep in the skin.

Immune system—The integrated body system of organs, tissues, cells, and cell products such as antibodies that protects the body from foreign organisms or substances.

Multidrug–resistant organisms (MDROs)—Bacteria that are resistant to one or more classes of antimicrobial agents and usually are resistant to all but one or two commercially available antimicrobial agents.

Mutation—A change in hereditary material of an organism that can improve its chance of surviving and passing the beneficial change on to its offspring.

Pathogen—A disease–causing microorganism.

Pus—A generally viscous, yellowish–white fluid formed in infected tissue, consisting of white blood cells, cellular debris, and dead tissue.

MRSA and other MDROs. Health care facilities are now developing strategies to counter the spread of HA–MRSA. One proposed strategy that may control the spread of infection includes active surveillance for the detection of MRSA in patients admitted to intensive care units and other high–risk care areas. Another approach would be to screen all patients admitted to a health care facility.

Other strategies involve the reengineering of health care settings. For example, a recent clinical trial sponsored by the Canadian Institutes of Health Research (CIHR) is studying how engineering controls affect the acquisition and transmission of pathogenic organisms in a hospital environment. The trial involves a group of patients admitted to a hospital ward with novel **infection control** design features such as abundance of sinks, predominance of private rooms, absence of shared bathrooms/curtains, etc. compared to a group of patients admitted to a conventional ward. The study, started in 2008, aims to compare MRSA (and other MDRO) infection rates in both groups to identify which design factors are most important in pathogen transmission. In the United States, the Healthcare Infection Control Practices Advisory Committee reports that successful control of MDROs has been documented in the United States and abroad using a variety of combined interventions such as:

- Maintaining staffing levels appropriate in health care facilities for the required level of care.
- Providing the necessary number and appropriate placement of hand–washing sinks and alcohol–containing hand rub dispensers in the facility.
- Health care provider education to improve understanding of the MDRO problem.
- Surveillance control programs to detect newly emerging pathogens.
- Increased cleaning and disinfection of frequently touched surfaces (e.g., bedrails, charts, bedside commodes, doorknobs) in hospital settings.

Resources

BOOKS

Callahan, Gerald N. *Infection: The Uninvited Universe*. New York: St. Martin's Press, 2006.

Chang, Hernan R. *MRSA and Staphylococcal Infections*. Morrisville: Lulu Publishing, 2006.

Salyers, Abigail A., and Dixie D. Whitt. *Revenge of the Microbes: How Bacterial Resistance is Undermining the Antibiotic Miracle*. Washington: ASM Press, 2005.

PERIODICALS

Fergie, J., Purcell, K. "The epidemic of methicillin–resistant Staphylococcus aureus colonization and infection in children: effects on the community, health systems, and physician practices." *Pediatrics Annals* 36, no. 7 (July 2007): 404–412.

Kuehn, B. M. "Antibiotic–resistant 'superbugs' may be transmitted from animals to humans." *Journal of the American Medical Association* 298, no. 18 (November 2007): 2125–2126.

Rim, J. Y., Bacon, A. E. "Prevalence of community–acquired methicillin–resistant Staphylococcus aureus colonization in a random sample of healthy individuals." *Infection Control and Hospital Epidemiology* 28, no. 9 (September 2007): 1044–1046.

Shams, W. E. "Methicillin–resistant Staphylococcus aureus: an established pathogen with emerging infections." *South Medical Journal* 100, no. 5 (May 2007): 464–465.

Spurgeon, D. "Prevalence of MRSA in US hospitals hits new high." *BMJ* 335, no. 7627 (November 2007): 961.

Williams, N. "Growing threat of superbugs." *Current Biology* 17, no. 14 (July 2007): R525–R526.

OTHER

Community–Associated MRSA Information for the Public Webpage, Centers for Disease Control and Prevention (February 3, 2005) http://cdc.gov/ncidod/dhqp/ar_mrsa_ca_public.html

"FDA Clears First Quick Test for Drug–Resistant Staph Infections." *FDA News* January 2, 2008 (January 16, 2008) http://www.fda.gov/bbs/topics/NEWS/2007/NEW01768.html

"Gay Men More Likely to Contract 'Superbug'." *Health Day* January 15, 2008 (January 16, 2008) http://abcnews.go.com/Health/Healthday/story?id=4510066

"Key to MRSA Virulence in Community Discovered." *Health Day* November 12, 2007 (January 16, 2008) http://www.nlm.nih.gov/medlineplus/news/fullstory_57479.html

MRSA in Healthcare Settings Webpage, CDC (October 3, 2007) http://www.cdc.gov/ncidod/dhqp/ar_mrsa_spotlight_2006.html

MSRA Infection Webpage, Mayo Clinic (November 9, 2007) http://www.mayoclinic.com/health/mrsa/DS00735

MSRA Infection Webpage, Medline Plus (December 21, 2007) http://www.nlm.nih.gov/medlineplus/ency/article/007261.htm

ORGANIZATIONS

Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

National Institute of Allergies and Infectious Diseases, 6610 Rockledge Drive, MSC 6612, Bethesda, MD, 20892-6612, (301) 496-5717, (301) 402-3573, (866) 284-4107, ocpostoffice@niaid.nih.gov, http://www.niaid.nih.gov.

Monique Laberge, PhD

MS *see* **Multiple sclerosis**

M's disease *see* **Waldenström's macroglobulinemia**

Mucopolysaccharidoses

Definition

Mucopolysaccharidosis (MPS) is a general term for a number of inherited diseases that are caused by the accumulation of mucopolysaccharides, resulting in problems with an individual's development. With each condition, mucopolysaccharides accumulate in the cells and tissues of the body because of a deficiency of a specific enzyme. The specific enzyme that is deficient or absent is what distinguishes one type of MPS from another. However, before these enzymes were identified, the MPS disorders were diagnosed by the signs and symptoms that an individual expressed. The discovery of these enzymes resulted in a reclassification of some of the MPS disorders. These conditions are often referred to as MPS I, MPS II, MPS III, MPS IV, MPS VI, MPS VII, and MPS IX. However, these conditions are also referred to by their original names, which are Hurler, Hurler-Scheie, Scheie (all MPS I), Hunter (MPS II), Sanfilippo (MPS III), Morquio (MPS IV), Maroteaux-Lamy (MPS VI), Sly (MPS VII), and Hyaluronidase deficiency (MPS IX).

Description

Mucopolysaccharides are long chains of sugar molecules that are essential for building the bones, cartilage, skin, tendons, and other tissues in the body. Normally, the human body continuously breaks down and builds mucopolysaccharides. Another name for mucopolysaccharides is glycosaminoglycans (GAGs). There are many different types of GAGs and specific GAGs are unable to be broken down in each of the MPS conditions. There are several enzymes involved in breaking down each GAG and a deficiency or absence of any of the essential enzymes can cause the GAG to not be broken down completely and result in its accumulation in the tissues and organs in the body. In some MPS conditions, in addition to the GAG being stored in the body, some of the incompletely broken down GAGs can leave the body via the urine. When too much GAG is stored, organs and tissues can be damaged or not function properly.

Genetic profile

Except for MPS II, the MPS conditions are inherited in an autosomal recessive manner. MPS conditions occur when both of an individual's genes that produce the specific enzyme contain a mutation, causing them to not work properly. When both genes do not work properly, either none or a reduced amount of the enzyme is produced. An individual with an autosomal

recessive condition inherits one of those non-working genes from each parent. These parents are called "carriers" of the condition. When two people are known carriers for an autosomal recessive condition, they have a 25% chance with each **pregnancy** to have a child affected with the disease. Some individuals with MPS do have children of their own. Children of parents who have an autosomal recessive condition are all carriers of that condition. These children are not at risk to develop the condition unless the other parent is a carrier or affected with the same autosomal recessive condition.

Unlike the other MPS conditions, MPS II is inherited in an X-linked recessive manner. This means that the gene causing the condition is located on the X chromosome, one of the two sex chromosomes. Since a male has only one X chromosome, he will have the disease if the X chromosome inherited from his mother carries the defective gene. Females, because they have two X chromosomes, are called "carriers" of the condition if only one of their X chromosomes has the gene that causes the condition, while the other X chromosome does not.

Causes and symptoms

Each type of MPS is caused by a deficiency of one of the enzymes involved in breaking down GAGs. It is the accumulation of the GAGs in the tissues and organs in the body that cause the wide array of symptoms characteristic of the MPS conditions. The accumulating material is stored in cellular structures called lysosomes, and these disorders are also known as lysosomal storage diseases.

MPS I

MPS I is caused by a deficiency of the enzyme alpha-L-iduronidase. Three conditions, Hurler, Hurler-Scheie, and Scheie syndromes, all are caused by a deficiency of this enzyme. Initially, these three conditions were felt to be separate because each were associated with different physical symptoms and prognoses. However, once the underlying cause of these conditions was identified, it was realized that these three conditions were all variants of the same disorder. The gene involved with MPS I is located on chromosome 4p16.3.

MPS I H (HURLER SYNDROME). It has been estimated that approximately one baby in 100,000 will be born with Hurler syndrome. Individuals with Hurler syndrome tend to have the most severe form of MPS I. Symptoms of Hurler syndrome are often evident within the first year or two after birth. Often these infants begin to develop as expected, but then reach a point where they begin to lose the skills that they have learned. Many of these infants may initially grow faster than expected, but their growth slows and typically stops by age three. Facial features also begin to appear "coarse." They develop a short nose, flatter face, thicker skin, and a protruding tongue. Additionally, their heads become larger and they develop more hair on their bodies with the hair becoming coarser. Their bones are also affected, with these children usually developing joint **contractures** (stiff joints), **kyphosis** (a specific type of curve to the spine), and broad hands with short fingers. Many of these children experience breathing difficulties, and respiratory infections are common. Other common problems include heart valve dysfunction, thickening of the heart muscle (**cardiomyopathy**), enlarged spleen and liver, clouding of the cornea, **hearing loss**, and **carpal tunnel syndrome**. These children typically do not live past age 12.

MPS I H/S (HURLER-SCHEIE SYNDROME). Hurler-Scheie syndrome is felt to be the intermediate form of MPS I, meaning that the symptoms are not as severe as those in individuals who have MPS I H but not as mild as those in MPS I S. Approximately one baby in 115,000 will be born with Hurler-Scheie syndrome. These individuals tend to be shorter than expected, and they can have normal intelligence, however, some individuals with MPS I H/S will experience learning difficulties. These individuals may develop some of the same physical features as those with Hurler syndrome, but usually they are not as severe. The prognosis for children with MPS I H/S is variable with some individuals dying during childhood, while others living to adulthood.

MPS I S (SCHEIE SYNDROME). Scheie syndrome is considered the mild form of MPS I. It is estimated that approximately one baby in 500,000 will be born with Scheie syndrome. Individuals with MPS I S usually have normal intelligence, but there have been some reports of individuals with MPS I S developing psychiatric problems. Common physical problems include corneal clouding, heart abnormalities, and orthopedic difficulties involving their hands and back. Individuals with MPS I S do not develop the facial features seen with MPS I H and usually these individuals have a normal life span.

MPS II (Hunter syndrome)

Hunter syndrome is caused by a deficiency of the enzyme iduronate-2-sulphatase. All individuals with Hunter syndrome are male, because the gene that causes the condition is located on the X chromosome, specifically Xq28. Like many MPS conditions, Hunter syndrome is divided into two groups, mild and severe. It has been estimated that approximately 1 in 110,000 males are born with Hunter syndrome, with the severe

form being three times more common than the mild form. The severe form is felt to be associated with progressive **mental retardation** and physical disability, with most individuals dying before age 15. In the milder form, most of these individuals live to adulthood and have normal intelligence or only mild mental impairments. Males with the mild form of Hunter syndrome develop physical differences similar to the males with the severe form, but not as quickly. Men with mild Hunter syndrome can have a normal life span and some have had children. Most males with Hunter syndrome develop joint stiffness, chronic **diarrhea**, enlarged liver and spleen, heart valve problems, hearing loss, kyphosis, and tend to be shorter than expected. These symptoms tend to progress at a different rate depending on if an individual has the mild or severe form of MPS II.

MPS III (Sanfilippo syndrome)

MPS III, like the other MPS conditions, was initially diagnosed by the individual having certain physical characteristics. It was later discovered that the physical symptoms associated with Sanfilippo syndrome could be caused by a deficiency in one of four enzymes. Each type of MPS III is now subdivided into four groups, labeled A-D, based on the specific enzyme that is deficient. All four of these enzymes are involved in breaking down the same GAG, heparan sulfate. Heparan sulfate is mainly found in the central nervous system and accumulates in the brain when it cannot be broken down because one of those four enzymes are deficient or missing.

MPS III is a variable condition with symptoms beginning to appear between ages two and six years of age. Because of the accumulation of heparan sulfate in the central nervous system, the central nervous system is severely affected. In MPS III, signs that the central nervous system is degenerating usually are evident in most individuals between ages six and 10. Many children with MPS III will develop seizures, sleeplessness, thicker skin, joint contractures, enlarged tongues, cardiomyopathy, behavior problems, and mental retardation. The life expectancy in MPS III is also variable. On average, individuals with MPS III live until they are teenagers, with some living longer and others not that long.

MPS IIIA (SANFILIPPO SYNDROME TYPE A). MPS IIIA is caused by a deficiency of the enzyme heparan N-sulfatase. Type IIIA is felt to be the most severe of the four types, in which symptoms appear and **death** occurs at an earlier age. A study in British Columbia estimated that one in 324,617 live births are born with MPS IIIA. MPS IIIA is the most common of the four types in Northwestern Europe. The gene that causes MPS IIIA is located on the long arm of chromosome 17 (location 17q25).

MPS IIIB (SANFILIPPO SYNDROME TYPE B). MPS IIIB is due to a deficiency in N-acetyl-alpha-D-glucosaminidase (NAG). This type of MPS III is not felt to be as severe as Type IIIA and the characteristics vary. Type IIIB is the most common of the four in southeastern Europe. The gene associated with MPS IIIB is also located on the long arm of chromosome 17 (location 17q21).

MPS IIIC (SANFILIPPO SYNDROME TYPE C). A deficiency in the enzyme acetyl-CoA-alpha-glucosaminide acetyltransferase causes MPS IIIC. This is considered a rare form of MPS III. The gene involved in MPS IIIC is believed to be located on chromosome 14.

MPS IIID (SANFILIPPO SYNDROME TYPE D). MPS IIID is caused by a deficiency in the enzyme N-acetylglucosamine-6-sulfatase. This form of MPS III is also rare. The gene involved in MPS IIID is located on the long arm of chromosome 12 (location 12q14).

MPS IV (Morquio syndrome)

As with several of the MPS disorders, Morquio syndrome was diagnosed by the presence of particular signs and symptoms. However, it is now known that the deficiency of two different enzymes can cause the characteristics of MPS IV. These two types of MPS IV are called MPS IV A and MPS IV B. MPS IV is also variable in its severity. The intelligence of individuals with MPS IV is often completely normal. In individuals with a severe form, skeletal abnormalities can be extreme and include dwarfism, kyphosis (backward-curved spine), prominent breastbone, flat feet, and knock-knees. One of the earliest symptoms seen in this condition usually is a difference in the way the child walks. In individuals with a mild form of MPS IV, limb stiffness, and joint **pain** are the primary symptoms. MPS IV is one of the rarest MPS disorders, with approximately one baby in 300,000 born with this condition.

MPS IV A (MORQUIO SYNDROME TYPE A). MPS IV A is the "classic" or the severe form of the condition and is caused by a deficiency in the enzyme galactosamine-6-sulphatase. The gene involved with MPS IV A is located on the long arm of chromosome 16 (location 16q24.3).

MPS IV B (MORQUIO SYNDROME TYPE B). MPS IV B is considered the milder form of the condition. The enzyme, beta-galactosidase, is deficient in MPS IV B. The location of the gene that produces beta-galactosidase is located on the short arm of chromosome 3 (location 3p21).

KEY TERMS

Cardiomyopathy—A thickening of the heart muscle.

Enzyme—A protein that catalyzes a biochemical reaction or change without changing its own structure or function.

Joint contractures—Stiffness of the joints that prevents full extension.

Kyphosis—An abnormal outward curvature of the spine, with a hump at the upper back.

Lysosome—Membrane-enclosed compartment in cells, containing many hydrolytic enzymes; where large molecules and cellular components are broken down.

Mucopolysaccharide—A complex molecule made of smaller sugar molecules strung together to form a chain. Found in mucous secretions and intercellular spaces.

Recessive gene—A type of gene that is not expressed as a trait unless inherited by both parents.

X-linked gene—A gene carried on the X chromosome, one of the two sex chromosomes.

MPS VI (Maroteaux-Lamy syndrome)

MPS VI, which is another rare form of MPS, is caused by a deficiency of the enzyme N-acetylglucosamine-4-sulphatase. This condition is also variable; individuals may have a mild or severe form of the condition. Typically, the nervous system or intelligence of an individual with MPS VI is not affected. Individuals with a more severe form of MPS VI can have airway obstruction, develop **hydrocephalus** (extra fluid accumulating in the brain) and have bone changes. Additionally, individuals with a severe form of MPS VI are more likely to die while in their teens. With a milder form of the condition, individuals tend to be shorter than expected for their age, develop corneal clouding, and live longer. The gene involved in MPS VI is believed to be located on the long arm of chromosome 5 (approximate location 5q11-13).

MPS VII (Sly syndrome)

MPS VII is an extremely rare form of MPS and is caused by a deficiency of the enzyme beta-glucuronidase. It is also highly variable, but symptoms are generally similar to those seen in individuals with Hurler syndrome. The gene that causes MPS VII is located on the long arm of chromosome 7 (location 7q21).

MPS IX (Hyaluronidase deficiency)

MPS IX is a condition that was first described in 1996 and has been grouped with the other MPS conditions by some researchers. MPS IX is caused by the deficiency of the enzyme hyaluronidase. In the few individuals described with this condition, the symptoms are variable, but some develop soft-tissue masses (growths under the skin). Also, these individuals are shorter than expected for their age. The gene involved in MPS IX is believed to be located on the short arm of chromosome 3 (possibly 3p21.3-21.2)

Many individuals with an MPS condition have problems with airway constriction. This constriction may be so serious as to create significant difficulties in administering **general anesthesia**. Therefore, it is recommended that surgical procedures be performed under **local anesthesia** whenever possible.

Diagnosis

While a diagnosis for each type of MPS can be made on the basis of the physical signs described above, several of the conditions have similar features. Therefore, enzyme analysis is used to determine the specific MPS disorder. Enzyme analysis usually cannot accurately determine if an individual is a carrier for a MPS condition. This is because the enzyme levels in individuals who are not carriers overlaps the enzyme levels seen in those individuals who are carrier for a MPS. With many of the MPS conditions, several mutations have been found in each gene involved that can cause symptoms of each condition. If the specific mutation is known in a family, DNA analysis may be possible.

Once a couple has had a child with an MPS condition, prenatal diagnosis is available to them to help determine if a fetus is affected with the same MPS as their other child. This can be accomplished through testing samples using procedures such as an **amniocentesis** or **chorionic villus sampling** (CVS). Each of these procedures has its own risks, benefits, and limitations.

Treatment

There is no cure for mucopolysaccharidosis. There are several types of experimental therapies that are being investigated. Typically, treatment

involves trying to relieve some of the symptoms. For MPS I and VI, **bone marrow transplantation** has been attempted as a treatment option. In those conditions, bone marrow transplantation has sometimes been found to help slow down the progression or reverse some of symptoms of the disorder in some children. The benefits of a bone marrow transplantation are more likely to be noticed when performed on children under two years of age. However it is not certain that a bone marrow transplant can prevent further damage to certain organs and tissues, including the brain. Furthermore, bone marrow transplantation is not felt to be helpful in some MPS disorders and there are risks, benefits, and limitations with this procedure. In 2000, ten individuals with MPS I received recombinant human alpha-L-iduronidase every week for one year. Those individuals showed an improvement with some of their symptoms. Additionally, there is ongoing research involving gene replacement therapy (the insertion of normal copies of a gene into the cells of patients whose gene copies are defective).

Prevention

No specific preventive measures are available for genetic diseases of this type. For some of the MPS diseases, biochemical tests are available that will identify healthy individuals who are carriers of the defective gene, allowing them to make informed reproductive decisions. There is also the availability of prenatal diagnosis for all MPS disease to detect affected fetuses.

Resources

PERIODICALS

Kakkis, E. D., et al. "Enzyme-Replacement Therapy in Mucopolysaccharidosis I." *The New England Journal of Medicine* 344 (2001): 182–188.

OTHER

National Library of Medicine. National Institutes of Health. http://www.nlm.nih.gov/.

"NINDS Mucopolysaccharidoses Information Page." The National Institute of Neurological Disorders and Stroke. National Institutes of Health. http://www.ninds.nih.gov/health_and_medical/disorders/mucopolysaccharidoses.htm.

Online Mendelian Inheritance in Man (OMIM). National Center for Biotechnology Information. http://www.ncbi.nlm.nih.gov/Omim/.

ORGANIZATIONS

Canadian Society for Mucopolysaccharide and Related Diseases, PO Box 30034, North Vancouver, Canada British Columbia, V7H 2Y8, (604) 924-5130, (604) 924-5131, (800) 667-1846, info@mpssociety.ca, http://www.mpssociety.ca.

National Endocrine and Metabolic Diseases Information Service, 6 Information Way, Bethesda, MD, 20892-3569, (703) 738-4829, (888) 828-0904, endoandmeta@info.niddk.nih.gov, http://endocrine.niddk.nih.gov.

The National Information Centre for Inherited Metabolic Diseases, The Quadrangle, Crewe Hall, Weston Rd., Cheshire, England, CW1-6UR, 440 (845) 241-2172, (800) 652-3181, fam.svcs@climb.org.uk, http://www.climb.org.uk.

National MPS Society, PO Box 14686 , Durham, NC, 27709-4686, (877) 677-1001, (919) 806-2055, info@mps society.org, http://www.mpssociety.org.

National Organization for Rare Disorders, P.O. Box 8923, New Fairfield, CT, 06812-8923, (800) 999-6673, http://www.rarediseases.org.

Society for Mucopolysaccharide Diseases, MPS House, Repton Place, White Lion Road, Amersham, Buckinghamshire, UK, HP7 9LP, 440 (845) 389-9901, mps@mpssociety.co.uk, http://www.mpssociety.co.uk.

Zain Hansen MPS Foundation, 23400 Henderson Rd, Covelo, CA, 95428

Sharon A. Aufox, MS, CGC

Mucormycosis

Definition

Mucormycosis is a rare but often fatal disease caused by certain fungi. It is sometimes called zygomycosis or phycomycosis. Mucormycosis is an opportunistic infection that typically develops in patients with weakened immune systems, diabetes, kidney failure, organ transplants, or **chemotherapy** for **cancer**. It may also develop in patients receiving an iron chelating drug called desferrioxamine (Desferal) as treatment for acute iron **poisoning**.

Description

In the United States, mucormycosis is most likely to develop in the patient's nasal area or in the lungs; however, it may also develop on the skin or in the digestive tract. Gastrointestinal disease usually develops only in severely malnourished patients. Cutaneous mucormycosis is most likely to develop under occlusive surgical **dressings**. Occlusive dressings are intended to keep air out of incisions or other **wounds**, but they also trap body heat and moisture.

The incidence of the disease is difficult to evaluate because it is very rare; however, the rate seems to be increasing. One American cancer center reported in

2000 that mucormycosis was found in 0.7% of patients at **autopsy** and in 20 patients per 100,000 admissions to the center. The most recent mortality statistics from the Centers for Disease Control and Prevention (CDC) indicate that a total of 22 Americans died from mucormycosis in 2001—1 from pulmonary mucormycosis, 5 from rhinocerebral mucormycosis, 2 from disseminated mucormycosis, and 14 from unspecified forms of the disease.

As far as is known, mucormycosis affects members of either sex and all races equally, although the pulmonary form of the disease is somewhat more common in men than in women. Mucormycosis may develop in patients in any age group, including newborns.

Rhinocerebral mucormycosis

Rhinocerebral mucormycosis is an infection of the nose, eyes, and brain. The fungus destroys the tissue of the nasal passages, sinuses, or hard palate, producing a black or pus-filled discharge and visible patches of dying tissue. The patient will typically have **fever**, **pain**, and forward bulging of the eyes (proptosis). The fungus then invades the tissues around the eye socket and eventually the brain. At that point the patient may have convulsions or **paralysis** on one side of the body.

Pulmonary mucormycosis

Most patients with the pulmonary form of the disease are being treated for leukemia. The fungus enters the patient's lungs, where it eventually invades a major blood vessel, causing the patient to **cough** up blood or hemorrhage into the lungs.

Gastrointestinal mucormycosis

Gastrointestinal mucormycosis has been reported in premature or low-birth-weight infants as well as malnourished adults. It may lead to intestinal perforation and other complications requiring immediate surgery. A Spanish hospital reported in 2004 on an outbreak of gastrointestinal mucormycosis that affected five patients in an ICU over a 14-week period. Two of the patients died. The outbreak was eventually traced to a supply of wooden tongue depressors that had been contaminated by two species of *Rhizopus* fungi.

Causes and symptoms

Mucormycosis is caused by fungi of several different species, including *Mucor*, *Rhizopus*, *Absidia*, and *Rhizomucor*. When these organisms gain access to the mucous membranes of the patient's nose or lungs, they multiply rapidly and invade the nearby blood vessels. The fungi destroy soft tissue and bone, as well as the walls of blood vessels.

The early symptoms of rhinocerebral mucormycosis include fever, sinus pain, **headache**, and **cellulitis**. As the fungus reaches the eye tissues, the patient develops dilated pupils, drooping eyelids, a bulging eye, and eventually hemorrhage of the blood vessels in the brain, causing convulsions, partial paralysis, and **death**.

The symptoms of pulmonary mucormycosis include fever and difficulty breathing, with eventual bleeding from the lungs.

The symptoms of gastrointestinal mucormycosis are not unique to the disease, which may complicate diagnosis. Patients typically complain of pressure or pain in the abdomen, **nausea**, and **vomiting**.

Diagnosis

Diagnosis is usually based on a combination of the patient's medical history and a visual examination of the nose, throat, and eyes. The doctor will take a tissue sample for biopsy, or a PAS, potassium hydroxide (KOH), or Calcofluor stain in order to make a tentative diagnosis. Confirmation requires a laboratory culture.

Imaging studies are not needed to make the diagnosis. If the patient has mucormycosis, however, **magnetic resonance imaging** (MRI) and **computed tomography scans** (CT scans) will usually show the destruction of soft tissue or bone in patients with advanced disease. Chest x rays will sometimes show a cavity in the lung or an area filled with tissue fluid if the patient has pulmonary mucormycosis.

Treatment

Treatment is usually begun without waiting for laboratory reports because of the rapid spread and high mortality rate of the disease. Therapy includes intravenous amphotericin B (Fungizone); surgical removal of infected tissue; and careful monitoring of the disorder or condition that is responsible for the patient's vulnerability. Most patients who survive require a 4–6-week course of treatment.

Follow-up care includes educating patients about the signs of recurrent mucormycosis—particularly facial swelling and a black discharge from the nose—and telling them to see a doctor at once if they notice these symptoms.

Patients who survive rhinocerebral mucormycosis are often left with severe facial disfigurement and usually require **plastic surgery** to restore their appearance.

KEY TERMS

Amphotericin B—An antibiotic used to treat mucormycosis and other severe fungal infections.

Opportunistic infection—An infection that develops only when a person's immune system is weakened.

Orbit—The bony cavity or socket surrounding the eye.

Zygomycosis—Another term for mucormycosis. The fungi that cause mucormycosis belong to a group called Zygomycetes.

Prognosis

The prognosis for recovery from mucormycosis is poor. The mortality rate is 30%–50% of patients with the rhinocerebral form, and even higher for patients with pulmonary mucormycosis. The disease is almost 100% fatal for patients with **AIDS**.

Prevention

Prevention depends on protecting high-risk patients from contact with sugary foods, decaying plants, moldy bread, manure, and other breeding grounds for fungi. In addition, health care professionals treating hospital inpatients should be careful to change occlusive dressings frequently and check the underlying skin for any signs of possible fungal infection.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Maravi-Poma, E., J. L. Rodriguez-Tudela, J. G. de Jalon, et al. "Outbreak of Gastric Mucormycosis Associated with the Use of Wooden Tongue Depressors in Critically Ill Patients." *Intensive Care Medicine* 30 (April 2004): 724–728.

Numa, W. A., Jr, P. K. Foster, J. Wachholz, et al. "Cutaneous Mucormycosis of the Head and Neck with Parotid Gland Involvement: First Report of a Case." *Ear, Nose, and Throat Journal* 83 (April 2004): 282–286.

Siu, K. L., and W. H. Lee. "A Rare Cause of Intestinal Perforation in an Extreme Low Birth Weight Infant—Gastrointestinal Mucormycosis: A Case Report." *Journal of Perinatology* 24 (May 2004): 319–321.

Wolf, O., Z. Gil, L. Leider-Trejo, et al. "Tracheal Mucormycosis Presented as an Intraluminal Soft Tissue Mass." *Head and Neck* 26 (June 2004): 541–543.

ORGANIZATIONS

Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

Rebecca J. Frey, PhD

Mucoviscidosis *see* **Cystic fibrosis**

MUGA scan *see* **Multiple-gated acquisition (MUGA) scan**

Multiple chemical sensitivity

Definition

Multiple chemical sensitivity—also known as MCS syndrome, environmental illness, idiopathic environmental intolerance, chemical **AIDS**, total allergy syndrome, or simply MCS—is a disorder in which a person develops symptoms from exposure to chemicals in the environment. With each incidence of exposure, lower levels of the chemical will trigger a reaction and the person becomes increasingly vulnerable to reactions triggered by other chemicals.

Medical experts disagree on the cause of the syndrome, and as to whether MCS is a clinically recognized illness. In a 1992 position statement that remains unchanged today, the American Medical Association's Council on Scientific Affairs does not recognize MCS as a clinical condition due to a lack of accepted diagnostic criteria and controlled studies on the disorder. Many researchers in Europe as well as the United States regard MCS as a contemporary version of neurasthenia, a concept first introduced by a physician named George Miller Beard in 1869.

Demographics

Because MCS is difficult to diagnose, estimates vary as to what percentage of the population develops MCS. However, most MCS patients are female. The median age of MCS patients is 40 years old, and most experienced symptoms before they were 30 years old. There is also a large percentage of Persian Gulf War veterans who have reported symptoms of chemical sensitivity since their return from the Gulf in the early 1990s.

KEY TERMS

Capsaicin—An alkaloid found in hot peppers that is used in an inhalation test to identify patients with MCS.

Degas—To release and vent gases. New building materials often give off gases and odors and the air should be well circulated to remove them.

Neurasthenia—A term coined in the late nineteenth century to refer to a condition of chronic mental and physical weakness and fatigue. Some researchers regard MCS as a twentieth-century version of neurasthenia.

Sick building syndrome—An illness related to MCS in which a person develops symptoms in response to chronic exposure to airborne environmental chemicals found in a tightly sealed building.

Description

Multiple chemical sensitivity typically begins with one high-dose exposure to a chemical, but it may also develop with long-term exposure to a low level of a chemical. Chemicals most often connected with MCS include: formaldehyde; pesticides; solvents; petrochemical fuels such as diesel, gasoline, and kerosene; waxes, detergents, and cleaning products; latex; tobacco smoke; perfumes and fragrances; and artificial colors, flavors, and preservatives. People who develop MCS are commonly exposed in one of the following situations: on the job as an industrial worker; residing or working in a poorly ventilated building; or living in conditions of high air or water pollution. Others may be exposed in unique incidents.

Causes and symptoms

Chemical exposure is often a result of indoor air pollution. Buildings that are tightly sealed for energy conservation may cause a related illness called sick building syndrome, in which people develop symptoms from chronic exposure to airborne environmental chemicals such as formaldehyde from the furniture, carpet glues, and latex caulking. A person moving into a newly constructed building, which has not had time to degas, may experience the initial high-dose exposure that leads to MCS.

As of 2010, the specific biochemical and physiological mechanisms in humans that lead to MCS are not well understood, however, studies suggest that MCS is the end result of four different mechanisms of sensitization acting to reinforce one another. Further research is required to test this hypothesis.

The symptoms of MCS vary from person to person and are not chemical-specific. Symptoms are not limited to one physiological system, but primarily affect the respiratory and nervous systems. Symptoms commonly reported are **headache**, **fatigue**, weakness, difficulty concentrating, short-term **memory loss**, **dizziness**, irritability and depression, **itching**, **numbness**, burning sensation, congestion, **sore throat**, hoarseness, **shortness of breath**, **cough**, and stomach pains.

One commonly reported symptom of MCS is a heightened sensitivity to odors, including a stronger emotional reaction to them. A Japanese study published in late 2002 reported that patients diagnosed with MCS can identify common odors as accurately as most people, but regard a greater number of them as unpleasant.

One test that has been devised to evaluate patients with MCS is the capsaicin inhalation test. Capsaicin is an alkaloid found in hot peppers that is sometimes used in topical creams and rubs for the treatment of arthritis. When inhaled, capsaicin causes coughing in healthy persons as well as those with **allergies** that affect the airway; however, persons with MCS cough more deeply and frequently than control subjects when given a dose of capsaicin. Although the test is not diagnostic in the strict sense, it has been shown to be an effective way of identifying patients with MCS.

Diagnosis

Multiple chemical sensitivity is a twentieth-century disorder, becoming more prevalent as more human-made chemicals are introduced into the environment in greater quantities. It is especially difficult to diagnose because it presents no consistent or measurable set of symptoms and has no single diagnostic test or marker. For example, a 2002 study of **PET** scans of MCS patients found no significant functional changes in the patients' brain tissues. Physicians are often either unaware of MCS as a condition, or refuse to accept that MCS exists. They may be unable to diagnose it, or may misdiagnose it as another degenerative disease, or may label it as a psychosomatic illness (a physical illness that is caused by emotional problems). Their lack of understanding generates frustration, **anxiety**, and distrust in patients already struggling with MCS. However, a new specialty of medicine is evolving to address MCS and related illnesses: occupational and environmental medicine. A physician looking for MCS will take a complete patient history and try to identify chemical exposures.

Some MCS patients may be helped by a psychologic evaluation, particularly if they show signs of panic attacks or other **anxiety disorders**. It is known that many patients with MCS suffer from comorbid depression and anxiety. In addition, MCS patients appear to have high rates of **mood disorders** compared to **asthma** patients as well as normal test subjects.

Treatment

While doctors may recommend **antihistamines**, **analgesics**, and other medications to combat the symptoms, the most effective treatment is to avoid those chemicals which trigger the symptoms. This becomes increasingly difficult as the number of offending chemicals increases, and people with MCS often remain at home where they are able to control the chemicals in their environment. This isolation often limits their abilities to work and socialize, so supportive counseling may also be appropriate.

Alternative treatment

Some MCS patients find relief with **detoxification** programs of **exercise** and sweating, and chelation of heavy metals. Others support their health with nutritional regimens and immunotherapy vaccines. Some undergo food-allergy testing and testing for accumulated pesticides in the body to learn more about their condition and what chemicals to avoid. Homeopathy and **acupuncture** can give added support to any treatment program for MCS patients. Botanical medicine can help to support the liver and other involved organs.

Prognosis

Once MCS sets in, sensitivity continues to increase and a person's health continues to deteriorate. Strictly avoiding exposure to triggering chemicals for a year or more may improve health.

Prevention

Multiple chemical sensitivity is difficult to prevent because even at high-dose exposures, different people react differently. Ensuring adequate ventilation in situations with potential for acute high-dose or chronic low-dose chemical exposure, as well as wearing the proper protective equipment in industrial situations, will minimize the risk.

Resources

BOOKS

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed., revised. Washington, DC: American Psychiatric Association, 2000.

Matthews, Bonnye L. *Defining Multiple Chemical Sensitivity* McFarland, 2007.

PERIODICALS

Das-Munshi, G. J. Rubin, S. Wessely, Multiple Chemical Sensitivities: A Systematic Review of Provocation Studies, *Journal of Allergy and Clinical Immunology,* 118 (2006): 1257-1264.

Ternesten-Hasseus, E., M. Bende, and E. Millqvist. "Increased Capsaicin Cough Sensitivity in Patients with Multiple Chemical Sensitivity." *Journal of Occupational and Environmental Medicine* 44 (November 2002): 1012–1017.

ORGANIZATIONS

American Academy of Environmental Medicine, P.O. Box CN 1001-8001, New Hope, PA, 18938, (215) 862-4544

American College of Occupational and Environmental Medicine (ACOEM), 1114 North Arlington Heights Road, Arlington Heights, IL, 60004, (847) 818-1800, www.acoem.org.

Bethany Thivierge
Rebecca J. Frey, PhD
Karl Finley

Multiple-gated acquisition (MUGA) scan

Definition

The multiple-gated acquisition (MUGA) scan is a non-invasive nuclear test that uses a radioactive isotope called technetium to evaluate the functioning of the heart's ventricles.

Purpose

The MUGA scan is performed to determine if the heart's left and right ventricles are functioning properly and to diagnose abnormalities in the heart wall. It can be ordered in the following patients:

- With known or suspected coronary artery disease, to diagnose the disease and predict outcomes
- With lesions in their heart valves
- Who have recently had a heart attack, to assess damage to heart tissue and predict the likelihood of future cardiac events

KEY TERMS

Ejection fraction—The fraction of all blood in the ventricle that is ejected at each heartbeat. One of the main advantages of the MUGA scan is its ability to measure ejection fraction, one of the most important measures of the heart's performance.

Electrocardiogram—A test in which electronic sensors called electrodes are placed on the body to record the heart's electrical activities.

Heart attack—A cardiac emergency that occurs when a clot blocks blood flow in one or more of the heart's arteries. Oxygen supply to the heart muscle is cut off, resulting in the death of heart tissue in the affected area.

Ischemia—A decreased supply of oxygenated blood to a body part or organ, often marked by pain and organ dysfunction, as in ischemic heart disease.

Non-invasive—A procedure that does not penetrate the body.

Radioactive isotope—One of two or more atoms with the same number of protons but a different number of neutrons with a nuclear composition. In nuclear scanning, radioactive isotopes are used as a diagnostic agent.

Technetium—A radioactive isotope frequently used in radionuclide scanning of the heart and other organs. It is produced during nuclear fission reactions.

Ventricles—The heart's lower chambers are called the left and right ventricles. They send blood to the lungs and throughout the body. The MUGA scan is performed to evaluate the ventricles.

- With congestive heart failure
- Who have undergone percutaneous transluminal coronary angioplasty, coronary artery bypass graft surgery, or medical therapy, to assess the efficacy of the treatment
- With low cardiac output after open-heart surgery
- Who are undergoing chemotherapy

Precautions

Pregnant women and those who are **breastfeeding** should not be exposed to technetium.

Description

The MUGA scan measures the heart's function and the flow of blood through it. The strongest chamber in the heart is the left ventricle, which serves as the main pump of blood through the body. The left ventricular is assessed by measuring the amount of blood pumped with each heartbeat (the ejection fraction), ventricle filling, and the blood flow into the pumping chamber. A normal ejection fraction is 50% or more. The heart's ejection fraction is one of the most important measures of its performance. The right ventricle's ability to pump blood to the lungs is also assessed, and any abnormalities in the heart wall are identified. The MUGA scan is the most accurate, non-invasive test available to assess the heart's ventricles.

MUGA is a nuclear heart scan, which means that it involves the use of a radioactive isotope that targets the heart and a radionuclide detector that traces the absorption of the radioactive isotope. The isotope is injected into a vein and absorbed by healthy tissue at a known rate during a certain time period. The radionuclide detector, in this case a gamma scintillation camera, picks up the gamma rays emitted by the isotope.

During the MUGA scan, electrodes are placed on the patient's body so that an electrocardiogram (ECG) can be conducted. The imaging equipment and computer are synchronized with the ECG so that images of the heart can be recorded without motion or blur. Then a small amount of a mildly radioactive isotope called technetium Tc99m stannous pyrophosphate, usually called technetium, is injected, usually into an arm vein. While the patient lies motionless on the test table, a gamma scintillation camera follows the movement of the technetium through the blood circulating in the heart. The camera, which looks like an x-ray machine and is suspended above the table, moves back and forth over the patient. It displays multiple images of the heart in motion and records them on a computer for later analysis.

The MUGA scan is usually performed in a hospital's nuclear medicine department, but it can also be performed in an outpatient facility or at the patient's bedside if equipment is available. The scan is done immediately after injection of the technetium and usually takes about 30 minutes to one hour. It is also called multigated graft acquisition, multigated acquisition scan, cardiac blood-pool imaging, and equilibrium radionuclide **angiography**. Test results can be

affected by patient movement during the test, electrocardiogram abnormalities, an irregular heartbeat, or long-acting nitrates.

The MUGA scan can be done with the patient at rest or exercising (called a **stress** MUGA). The stress MUGA is often performed in patients who have or are suspected of having **coronary artery disease**. The resting MUGA is compared to the stress MUGA and changes in the heart's pumping performance are analyzed. In some cases, the rest MUGA is compared to a nitroglycerin MUGA, in which a strong heart drug called nitroglycerin is administered to the patient before the scan. For the nitroglycerin MUGA, a cardiologist should be present.

The MUGA scan is not dangerous. The technetium is completely gone from the body within a few days of the test. The scan itself exposes the patient to about the same amount of radiation as a **chest x ray**. The patient can resume normal activities immediately after the test.

Normal results

If the patient's heart is normal, the technetium will appear to be evenly distributed in the scans. In a stress MUGA, patients with normal hearts will exhibit an increase in ejection fraction or no change.

Abnormal results

An uneven distribution of technetium in the heart indicates that the patient has coronary artery disease, a **cardiomyopathy**, or blood shunting within the heart. Abnormalities in a resting MUGA usually indicate a **heart attack**, while those that occur during **exercise** usually indicate **ischemia**. In a stress MUGA, patients with coronary artery disease may exhibit a decrease in ejection fraction.

ORGANIZATIONS

American Heart Association National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, Review.personal.info@heart.org.

Texas Heart Institute. Heart Information Service, MC 3-116, PO Box 20345, Houston, TX, 77225, (832) 355-4011, (800) 292-2221, http://www.texasheart.org.

Lori De Milto

Multiple endocrine adenomatosis *see* **Multiple endocrine neoplasia syndromes**

Multiple endocrine neoplasia syndromes

Definition

The multiple endocrine neoplasia (MEN) syndromes are three related disorders affecting the thyroid and other hormonal (endocrine) glands of the body. MEN has previously been known as familial endocrine adenomatosis.

Description

The three forms of MEN are MEN1 (Wermer's syndrome), MEN2A (Sipple syndrome), and MEN2B (previously known as MEN3). Each is an autosomal dominant genetic condition which predisposes to hyperplasia (excessive growth of cells) and tumor formation in a number of endocrine glands.

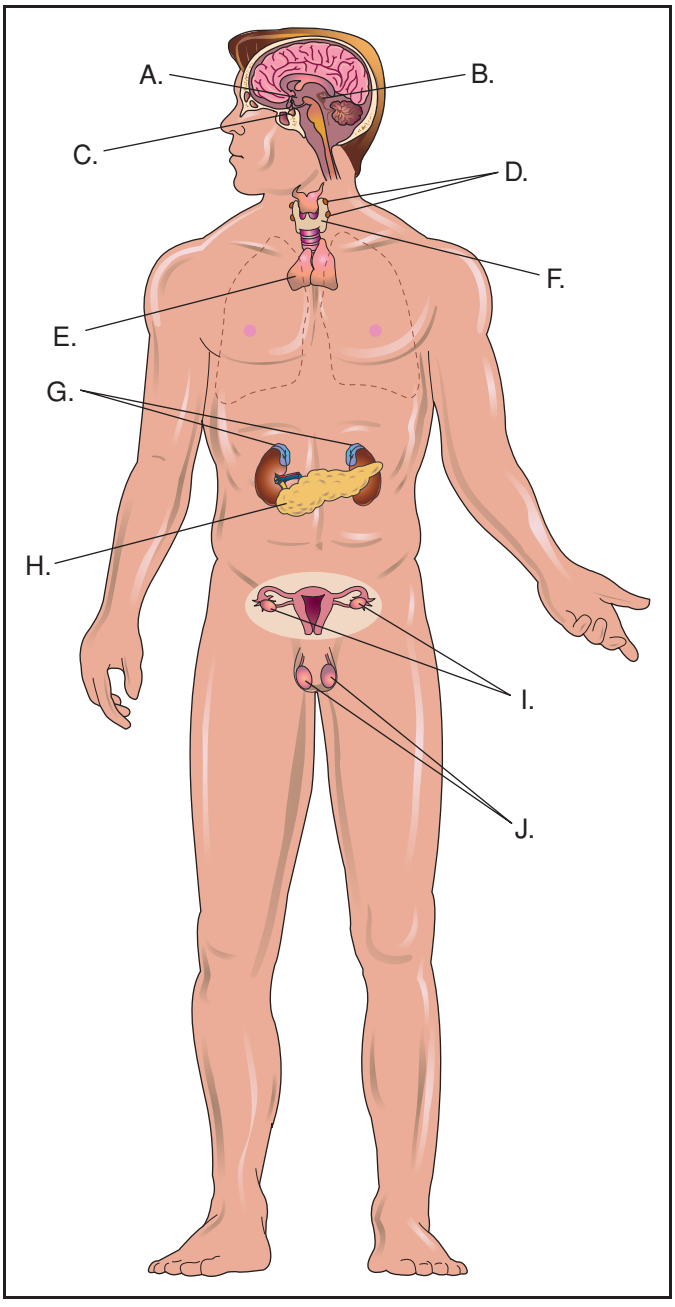
Causes and symptoms

MEN1 patients experience hyperplasia or tumors of several endocrine glands, including the parathyroids, the pancreas, and the pituitary. The most frequent symptom of MEN1 is **hyperparathyroidism**. Overgrowth of the parathyroid glands leads to over secretion of parathyroid hormone, which leads to elevated blood **calcium** levels, **kidney stones**, weakened bones, and nervous system depression. Almost all MEN1 patients show parathyroid symptoms by age 40.

Tumors of the pancreas known as gastrinomas are also common in MEN1. Excessive secretion of gastrin (a hormone secreted into the stomach to aid in digestion) by these tumors can cause upper gastrointestinal ulcers. The anterior pituitary and the adrenal glands can also be affected. Unlike MEN2, the thyroid gland is rarely involved in MEN1 symptoms.

Patients with MEN2A and MEN2B experience two main symptoms, medullary **thyroid cancer** (MTC) and a tumor of the adrenal gland medulla known as **pheochromocytoma**. MTC is a slow—growing **cancer**, but one that can be cured in less than 50% of cases. Pheochromocytoma is usually a benign tumor that causes excessive secretion of adrenal hormones, which, in turn, can cause life—threatening **hypertension** and cardiac arrhythmia.

The two forms of MEN2 are distinguished by additional symptoms. MEN2A patients have a predisposition to increase in size (hypertrophy) and to develop tumors of the parathyroid gland. Although similar to MEN1, less than 20% of MEN2A patients show parathyroid involvement.



The human endocrine system: A. Hypothalamus. B. Pineal. C. Pituitary. D. Parathyroid. E. Thymus. F. Thyroid. G. Adrenals. H. Pancreas. I. Ovaries (female). J. Testes (male). *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

MEN2B patients show a variety of additional conditions: a characteristic facial appearance with swollen lips; tumors of the mucous membranes of the eye, mouth, tongue, and nasal cavity; enlarged colon; and skeletal abnormalities. Symptoms develop early in life (often under five years of age) in cases of MEN2B and the tumors are more aggressive. MEN2B is about ten—fold less common than MEN2A.

MEN1 is caused by mutation at the PYGM gene. PYGM is one of a group of genes known as tumor suppressor genes. A patient who inherits one defective copy of a tumor suppressor gene from either parent has a strong predisposition to the disease because of the high probability of incurring a second mutation in at least one dividing cell. That cell no longer possesses even one normal copy of the gene. When both copies are defective, tumor suppression fails and tumors develop.

Both types of MEN2 are caused by mutations in another gene, known as RET. A mutation in only one copy of the RET gene is sufficient to cause disease. A number of different mutations can lead to MEN2A, but only one specific genetic alteration leads to MEN2B.

For all types of MEN, the children of an affected individual have a 50% chance of inheriting the defective gene.

Diagnosis

Classical diagnosis of MEN is based on clinical features and on testing for elevated hormone levels. For MEN1, the relevant hormone is parathyroid hormone. For both types of MEN2, the greatest concern is development of medullary thyroid cancer. MTC can be detected by measuring levels of the thyroid hormone, calcitonin. Numerous other hormone levels can be measured to assess the involvement of the various other endocrine glands.

Diagnosis of MEN2B can be made by **physical examination** alone. However, MEN2A shows no distinct physical features and must be identified by measuring hormone levels or by finding endocrine tumors.

Since 1994, genetic screening using DNA technology has been available for both MEN1 and MEN2. This new methodology allows diagnosis prior to the onset of symptoms.

In the past, there was no way of definitively identifying which children had inherited the defective gene. As a result, all children had to be considered at risk. In the case of MEN2A and MEN2B, children would undergo frequent calcitonin testing. Molecular techniques now allow a positive distinction to be made between children who are and are not actually at risk.

Children who are identified as carriers of the RET gene can be offered total **thyroidectomy** on a preventative (prophylactic) basis to prevent the development of MTC.

KEY TERMS

Endocrine—A term used to describe the glands that produce hormones in the body.

Hyperplasia—An overgrowth of normal cells within an organ or tissue.

Medullary thyroid cancer (MTC)—A slow-growing tumor associated with MEN.

Neoplasm—An abnormal formation of tissue; for example, a tumor.

Pheochromocytoma—A tumor of the medullary of the adrenal gland.

Treatment

No comprehensive treatment is available for genetic conditions such as MEN. However, some of the consequences of MEN can be symptomatically treated.

Pheochromocytoma in both types of MEN 2 can be cured by surgical removal of this slow growing tumor.

Treatment of MTC is by surgical removal of the thyroid, although doctors may disagree at what stage to remove the thyroid. After thyroidectomy, the patient will receive normal levels of thyroid hormone orally or by injection.

Even when surgery is performed early, metastatic spread of the cancer may have already occurred. Since this cancer is slow growing, metastasis may not be obvious. Metastasis is very serious in MTC because **chemotherapy** and **radiation therapy** are not effective in controlling its spread.

Prognosis

Diagnosed early, the prognosis for the MEN diseases is reasonably good, even for MEN2B, the most dangerous of the three forms. Even in the absence of treatment, a few individuals with MEN2A mutations will never show any symptoms at all. Analysis of at—risk family members using molecular genetic techniques will lead to earlier treatment and improved outcomes.

Prevention

One of the most serious consequences of MEN is MTC, which can be prevented by thyroidectomy. There is no preventive measure to block the occurrence of genetic mutations such as those that cause MEN.

Resources

BOOKS

Bennett, Robin L. *The Practical Guide to the Genetic Family History,* 2nd ed. New York, NY: Wiley—Blackwell, 2010.

Books LLC. *Parathyroid Disorders: Hyperparathyroidism, Parathyroid Gland, Hypoparathyroidism, Parathyroid Disease, Secondary Hyperparathyroidism*. Bel Air, CA: Books LLC, 2010.

Harrow, Benjamin. *Glands in Health and Disease (1922)*. Charleston, SC: CreateSpace, 2010.

Opie, Eugene Lindsay. *Disease of the Pancreas: Its Cause and Nature*. Charleston, SC: BiblioBazaar, 2009.

Van Nostrand, Douglas, et al. *Thyroid Cancer: A Guide for Patients,* 2nd ed. Pasadena, MD: Keystone Press, 2010.

ORGANIZATIONS

Canadian MEN Society, PO Box 100, Meola, Saskatchewan, S0M 1XO, (306) 892–2080

National Institutes of Health (NIH), 9000 Rockville Pike, Bethesda, MD, 20892, (301) 496-4000, http://www.nih.gov/index.html.

National Library of Medicine, 8600 Rockville Pike, Bethesda, MD, 20894, http://www.nlm.nih.gov/medlineplus/medlineplus.html.

National Organization for Rare Diseases, PO Box 8923, Fairfield, CT, 06812, (213) 745–6518, http://www.rarediseases.org.

Victor Leipzig, Ph.D.
Laura Jean Cataldo, RN, Ed.D.

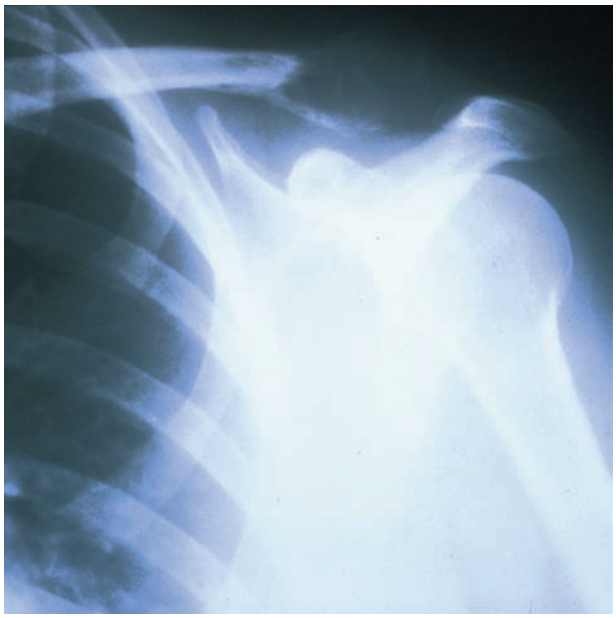
Multiple myeloma

Definition

Multiple myeloma is a **cancer** in which antibody-producing plasma cells grow in an uncontrolled and invasive (malignant) manner.

Description

Multiple myeloma, also known as plasma cell myeloma, is the second-most common cancer of the blood. It is the most common type of plasma cell neoplasm. Multiple myeloma accounts for approximately 1% of all cancers and 2% of all deaths from cancer. Multiple myeloma is a disease in which malignant plasma cells spread through the bone marrow and hard outer portions of the large bones of the body. These myeloma cells may form tumors called plasmacytomas. Eventually, multiple soft spots or holes, called osteolytic lesions, form in the bones.



This x ray of the patient's left clavicle indicates an occurrence of myelomas in the bone. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Bone marrow is the spongy tissue within the bones. The breastbone, spine, ribs, skull, pelvic bones, and the long bone of the thigh all are particularly rich in marrow. Bone marrow is a very active tissue that is responsible for producing the cells that circulate in the blood. These include the red blood cells that carry oxygen, the white blood cells that develop into immune system cells, and platelets, which cause blood to clot.

Plasma cells and immunoglobulins

Plasma cells develop from B-lymphocytes or B-cells, a type of white blood cell. B-cells, like all blood cells, develop from unspecialized stem cells in the bone marrow. Each B-cell carries a specific antibody that recognizes a specific foreign substance called an antigen. Antibodies are large proteins called immunoglobulins (Igs), which recognize and destroy foreign substances and organisms such as bacteria. When a B-cell encounters its antigen, it begins to divide rapidly to form mature plasma cells. These plasma cells are all identical (monoclonal). They produce large amounts of identical antibody that are specific for the antigen.

Malignant plasma cells

Multiple myeloma begins when the genetic material (DNA) is damaged during the development of a stem cell into a B-cell in the bone marrow. This causes the cell to develop into an abnormal or malignant plasmablast, a developmentally early form of plasma cell. Plasmablasts produce adhesive molecules that allow them to bond to the inside of the bone marrow. A growth factor, called interleukin-6, promotes uncontrolled growth of these myeloma cells in the bone marrow and prevents their natural **death**. Whereas normal bone marrow contains less than 5% plasma cells, bone marrow of an individual with multiple myeloma contains over 10% plasma cells.

In most cases of multiple myeloma, the malignant plasma cells all make an identical Ig. Igs are made up of four protein chains that are bonded together. Two of the chains are light and two are heavy. There are five classes of heavy chains, corresponding to five types of Igs with different immune system functions. The Igs from myeloma cells are nonfunctional and are called paraproteins. All of the paraproteins from any one individual are monoclonal (identical) because the myeloma cells are identical clones of a single plasma cell. Thus, the paraprotein is a monoclonal protein or M-protein. The M-proteins crowd out the functional Igs and other components of the immune system. They also cause functional antibodies, which are produced by normal plasma cells, to rapidly break down. Thus, multiple myeloma depresses the immune system.

In about 75% of multiple myeloma cases, the malignant plasma cells also produce monoclonal light chains, or incomplete Igs. These are called Bence-Jones proteins and are secreted in the urine. Approximately 1% of multiple myelomas are called nonsecretors because they do not produce any abnormal Ig.

Osteolytic lesions

About 70% of individuals with multiple myeloma have soft spots or lesions in their bones. These lesions can vary from quite small to grapefruit-size. In part, these lesions occur because the malignant plasma cells rapidly outgrow the normal bone-forming cells. In addition, malignant myeloma cells produce factors that affect cells called osteoclasts. These are the cells that normally destroy old bone, so that new bone can be produced by cells called osteoblasts. The myeloma cell factors increase both the activation and the growth of osteoclasts. As the osteoclasts multiply and migrate, they destroy healthy bone and create lesions. **Osteoporosis**, or widespread bone weakness, may develop.

There are more than 40,000 multiple myeloma patients in the United States. The American Cancer Society predicts an additional 14,400 new cases in 2001. About 11,200 Americans will die of the disease

in 2001. Multiple myeloma is one of the leading causes of cancer deaths among African Americans.

In Western industrialized countries, approximately four people in 100,000 develop multiple myeloma. The incidence of multiple myeloma among African Americans is 9.5 per 100,000, about twice that of Caucasians. Asians have a much lower incidence of the disease. In China, for example, the incidence of multiple myeloma is only one in 100,000. The offspring and siblings of individuals with multiple myeloma are at a slightly increased risk for the disease.

At diagnosis, the average age of a multiple myeloma patient is 68 to 70. Although the average age at onset is decreasing, most multiple myelomas still occur in people over 40. This cancer is somewhat more prevalent in men than in women.

Causes and symptoms

Associations

The cause of multiple myeloma has not been determined. However, a number of possible associations have been identified:

- decreased immune system function; the immune systems of older individuals may be less efficient at detecting and destroying cancer cells
- genetic (hereditary) factors, suggested by the increased incidence in some ethnic groups and among family members
- occupational factors, suggested by the increased incidence among agricultural, petroleum, wood, and leather workers, and cosmetologists
- long-term exposure to herbicides, pesticides, petroleum products, heavy metals, plastics, and dusts such as asbestos
- radiation exposure, as among Japanese atomic bomb survivors, nuclear weapons workers, and medical personnel such as radiologists
- Kaposi's sarcoma-associated herpes virus (also called human herpes virus-8 or HHV-8), found in the blood and bone marrow cells of many multiple myeloma patients

Early symptoms

The accumulation of malignant plasma cells can result in tiny cracks or **fractures** in bones. Malignant plasma cells in the bone marrow can suppress the formation of red and white blood cells and platelets. About 80% of individuals with multiple myeloma are anemic due to low red blood cell formation. Low white blood cell formation results in increased susceptibility to infection, since new, functional antibodies are not produced. In addition, normal circulating antibodies are rapidly destroyed. Low platelet formation can result in poor blood clotting. It is rare, however, that insufficient white blood cell and platelet formations are presenting signs of multiple myeloma.

These factors cause the early symptoms of multiple myeloma:

- pain in the lower back or ribs
- fatigue and paleness due to anemia (low red blood cell count)
- frequent and recurring infections, including bacterial pneumonia, urinary-tract and kidney infections, and shingles
- bleeding

Bone destruction

Bone **pain**, particularly in the backbone, hips, and skull, is often the first symptom of multiple myeloma. As malignant plasma cells increase in the bone marrow, replacing normal marrow, they exert pressure on the bone. As overly active osteoclasts (large cells responsible for the breakdown of bone) remove bone tissue, the bone becomes soft. Fracture and spinal cord compression may occur.

Plasmacytomas (malignant tumors of plasma cells) may weaken bones, causing fractures. Fractured bones or weak or collapsed spinal bones, in turn, may place unusual pressure on nearby nerves, resulting in nerve pain, burning, or **numbness** and muscle weakness. Proteins produced by myeloma cells also may damage nerves.

Calcium from the destroyed bone enters the blood and urine, causing **hypercalcemia**, a medical condition in which abnormally high concentrations of calcium compounds exist in the bloodstream. High calcium affects nerve cell and kidney function. The symptoms of hypercalcemia include:

- weakness and fatigue
- depression
- mental confusion
- constipation
- increased thirst
- icreased urination
- nausea and vomiting
- kidney pain
- kidney failure

Hypercalcemia affects about one-third of multiple myeloma patients.

Serum proteins

The accumulation of M-proteins in the serum (the liquid portion of the blood) may cause additional complications, such as hyperviscosity syndrome, or thickening of the blood (though rare in multiple myeloma patients). Symptoms of hyperviscosity include:

- fatigue
- headaches
- shortness of breath
- mental confusion
- chest pain
- kidney damage and failure
- vision problems
- Raynaud's phenomenon

Poor blood circulation, or Raynaud's phenomenon, can affect any part of the body, but particularly the fingers, toes, nose, and ears.

Cryoglobulinemia occurs when the protein in the blood forms particles under cold conditions. These particles can block small blood vessels and cause pain and numbness in the toes, fingers, and other extremities during cold weather.

Amyloidosis is a rare complication of multiple myeloma. It usually occurs in individuals whose plasma cells produce only Ig light chains. These Bence-Jones proteins combine with other serum proteins to form amyloid protein. This starchy substance can invade tissues, organs, and blood vessels. In particular, amyloid proteins can accumulate in the kidneys, where they block the tiny tubules that are the kidney's filtering system. Indicators of amyloidosis include:

- carpal tunnel syndrome
- kidney failure
- liver failure
- heart failure

Diagnosis

Blood and urine tests

Often, the original diagnosis of multiple myeloma is made from routine blood tests that are performed for other reasons. Blood tests may indicate:

- anemia
- abnormal red blood cells
- high serum protein levels
- how levels of normal antibody
- high calcium levels
- high blood urea nitrogen (BUN) levels
- high creatinine levels

Urea and creatinine normally are excreted in the urine. High levels of urea and creatinine in the blood indicate that the kidneys are not functioning properly to eliminate these substances.

Protein electrophoresis is a laboratory technique that uses an electrical current to separate the different proteins in the blood and urine on the basis of size and charge. Since all of the multiple myeloma M-proteins in the blood and urine are identical, electrophoresis of blood and urine from a patient with multiple myeloma shows a large M-protein spike, corresponding to the high concentration of monoclonal Ig. Electrophoresis of the urine also can detect Bence-Jones proteins.

Bones

A **bone marrow aspiration** utilizes a very thin, long needle to remove a sample of marrow from the hip bone. Alternatively, a **bone marrow biopsy** with a larger needle removes solid marrow tissue. The marrow is examined under the microscope for plasma cells and tumors. If 10% to 30% of the cells are plasma cells, multiple myeloma is the usual diagnosis.

X rays are used to detect osteoporosis, osteolytic lesions, and fractures. Computer-assisted tomography (CAT or CT) scans can detect lesions in both bone and soft tissue. **Magnetic resonance imaging** (MRI) may give a more detailed image of a certain bone or a region of the body.

Treatment

Related disorders

Monoclonal gammopathy of undetermined significance (MGUS) is a common condition in which a monoclonal Ig is detectable. However, there are no tumors or other symptoms of multiple myeloma. MGUS occurs in about 1% of the general population and in about 3% of those over age 70. Over a period of years, about 16% to 20% of those with MGUS will develop multiple myeloma or a related cancer called malignant lymphoma.

Occasionally, only a single plasmacytoma develops, either in the bone marrow (isolated plasmacytoma of the bone) or other tissues or organs (extramedullary plasmacytoma). Some individuals with solitary plasmacytoma may develop multiple myeloma.

Clinical stages

The Durie-Salmon system is used to stage multiple myeloma. Stage I multiple myeloma requires all of the following (1 gram = approx. 0.02 pints, 1 deciliter = approx. 0.33 ounces):

- hemoglobin (the oxygen-transporting molecule of red blood cells) above 10 grams/deciliter (g/dl)
- serum calcium below 12 mg/dl
- normal bone structure or only isolated plasmacytoma
- low M-protein, based on established guideline levels of Ig protein chains

Approximately 5% of multiple myeloma cases are not progressing at diagnosis, and may not progress for months or years. This is called smoldering myeloma. These patients have stage I blood chemistry but no symptoms.

Stage II multiple myeloma fits neither stage I nor stage III. Stage III multiple myeloma meets one or more the following criteria:

- hemoglobin below 8.5 g/dl
- serum calcium above 12 mg/dl
- advanced bone lesions
- high M-protein

Each stage is subclassified as A or B, based on serum creatinine indicators of normal or abnormal kidney function. Most patients have stage III multiple myeloma at diagnosis.

Prognostic indicators

Prognostic indicators for multiple myeloma may be used instead of, or in addition to, the staging system described above. Prognostic indicators are laboratory tests that help to define the stage of the disease at diagnosis, and its progression during treatment. These indicators are:

- plasmablastic multiple myeloma (presence of plasmablasts, the precursor malignant plasma cells)
- plasma cell labeling index (the percentage of plasma cells that are actively dividing)
- beta 2-microglobulin, a protein secreted by B-cells that correlates with the myeloma cell mass (also indicates kidney damage)

Since multiple myeloma often progresses slowly, and since the treatments can be toxic, the disease may not be treated until M-protein levels in the blood are quite high. In particular, MGUS and smoldering myeloma may be followed closely but not treated. Solitary plasmacytomas are treated with radiation and/or surgery and followed closely with examinations and laboratory tests.

Chemotherapy

Chemotherapy, or treatment with anti-cancer drugs, is used for multiple myeloma. MP, a combination of the drugs melphalan and prednisone, is the standard treatment. Usually, the drugs are taken by mouth every 3 to 4 weeks for 6 to 9 months or longer, until the M-protein levels in the blood stop decreasing. MP usually results in a 50% reduction in M-protein.

Dexamethasone, a corticosteroid, sometimes is used to treat the elderly or those in poor health. It can drop the M-protein levels by 40% in untreated individuals and by 20% to 40% in patients who have not responded to previous treatment. Other chemotherapy drugs, including cyclophosphamide, carmustine, doxorubicin, vincristine, and chlorambucil, may be used as well.

Multiple myeloma usually recurs within a year after the end of chemotherapy. Although the chemotherapy can be repeated after each recurrence, it is progressively less responsive to treatment.

Side effects of chemotherapy may include:

- anemia
- hair loss
- nausea
- vomiting
- diarrhea
- mood swings
- swelling
- acne

These side effects disappear after treatment is discontinued.

Other drug treatments

Bisphosphonates are drugs that inhibit the activity of osteoclasts. These drugs can slow the progression of bone disease, reduce pain, and help prevent bone fractures. Different types of bisphosphonates inhibit osteoclasts in different ways. They also reduce the production of interleukin-6 by bone marrow cells. Laboratory studies suggest that bisphosphonates may kill or inhibit the growth of multiple myeloma cells. Pamidronate is the most common bisphosphonate for treating multiple myeloma.

The drug thalidomide appears to have several anti-myeloma activities. Thalidomide affects the immune system in various ways and it appears to inhibit myeloma cells, both directly and indirectly. It also inhibits the growth of new blood vessels that are needed by tumors. However, if thalidomide is taken during **pregnancy**, it an cause severe **birth defects** or death of the fetus.

The drug allopurinol may be used to reduce high blood levels of uric acid that result from kidney

KEY TERMS

Amyloidosis—A complication of multiple myeloma in which amyloid protein accumulates in the kidneys and other organs, tissues, and blood vessels.

Anemia—Any condition in which the red blood cell count is below normal.

Antibody—Immunoglobulin produced by immune system cells that recognizes and binds to a specific foreign substance (antigen).

Antigen—Foreign substance that is recognized by a specific antibody.

B-cell (B-lymphocyte)—Type of white blood cell that produces antibodies.

Bence-Jones protein—Light chain of an immunoglobulin that is overproduced in multiple myeloma and is excreted in the urine.

Beta 2-microglobulin—Protein produced by B-cells; high concentrations in the blood are indicative of multiple myeloma.

Cryoglobulinemia—Condition in which protein in the blood forms particles in the cold, blocking blood vessels, leading to pain and numbness of the extremities.

Electrophoresis—Use of an electrical field to separate proteins in a mixture (such as blood or urine), on the basis of the size and electrical charge of the proteins.

Hemoglobin—Protein in red blood cells that carries oxygen.

Hypercalcemia—Abnormally high levels of calcium in the blood.

Hyperviscosity—Thick, viscous blood, caused by the accumulation of large proteins, such as immunoglobulins, in the serum.

Immunoglobulin (Ig)—Antibody; large protein produced by B-cells that recognizes and binds to a specific antigen.

M-protein—Monoclonal or myeloma protein; paraprotein; abnormal antibody found in large amounts in the blood and urine of individuals with multiple myeloma.

Malignant—A characteristic of cancer cells that grow uncontrollably and invade other tissues.

Monoclonal—Identical cells or proteins; cells (clones) derived from a single, genetically distinct cell, or proteins produced by these cells.

Monoclonal gammopathy of undetermined significance (MGUS)—Common condition in which M-protein is present, but there are no tumors or other symptoms of disease.

Neoplasm—Tumor made up of cancer cells.

Osteoblast—Bone-forming cell.

Osteoclast—Cell that absorbs bone.

Osteolytic lesion—Soft spot or hole in bone caused by cancer cells.

Osteoporosis—Condition in which the bones become weak and porous, due to loss of calcium and destruction of cells.

Paraprotein—M-protein; abnormal immunoglobulin produced in multiple myeloma.

Plasma cell—Type of white blood cell that produces antibodies; derived from an antigen-specific B-cell.

Platelet—Cell that is involved in blood clotting.

Stem cell—Undifferentiated cell that retains the ability to develop into any one of numerous cell types.

dysfunction. **Diuretics** can improve kidney function. Infections require prompt treatment with **antibiotics**.

BONE AND PERIPHERAL BLOOD STEM CELL TRANSPLANTATION. Bone marrow or peripheral blood stem cell transplantations (PBSCT) are used to replace the stem cells of the bone marrow following high-dosage chemotherapy. Chemotherapy destroys the bone marrow stem cells that are necessary to produce new blood cells. In an autologous transplant, the patient's bone marrow stem cells or peripheral blood stem cells (immature bone marrow cells found in the blood) are collected, treated with drugs to kill any myeloma cells, and frozen prior to chemotherapy. Growth factors are used to increase the number of peripheral stem cells prior to collection. A procedure called apheresis is used to collect the peripheral stem cells. Following high-dosage chemotherapy, the stem cells are reinjected into the individual. In an allogeneic transplant, the donor stem cells come from a genetically related individual such as a sibling.

Other treatments

Blood transfusions may be required to treat severe anemia.

Plasmapheresis, or plasma exchange **transfusion**, may be used to thin the blood to treat hyperviscosity syndrome. In this treatment, blood is removed and passed through a machine that separates the plasma,

containing the M-protein, from the red and white blood cells and platelets. The blood cells are transfused back into the patient, along with a plasma substitute or donated plasma.

Multiple myeloma may be treated with high-energy x rays directed at a specific region of the body. **Radiation therapy** is used for treating bone pain.

Alternative treatment

Interferon alpha, an immune-defense protein that is produced by some white blood cells and bone marrow cells, can slow the growth of myeloma cells. It usually is given to patients following chemotherapy, to prolong their remission. However, interferon may have toxic effects in older individuals with multiple myeloma.

Once multiple myeloma is in remission, calcium and vitamin D supplements can improve bone density. It is important not to take these supplements when the myeloma is active. Individuals with multiple myeloma must drink large amounts of fluid to counter the effects of hyperviscous blood.

Prognosis

The prognosis for individuals with MGUS or solitary plasmacytoma is very good. Most do not develop multiple myeloma. However, approximately 15% of all patients with multiple myeloma die within three months of diagnosis. About 60% respond to treatment and live for an average of two and a half to three years following diagnosis. Approximately 23% of patients die of other illnesses associated with advanced age.

The prognosis for a given individual may be based on the prognostic indicators described above. The median survival for those without plasmablasts, and with a low plasma cell labeling index (PCLI) and low beta 2-microglobulin, is 5.5 years. The median survival for patients with plasmablastic multiple myeloma, or with a high PCLI (1% or greater) and high beta 2-microglobulin (4 or higher), is 1.9 and 2.4 years, respectively. Many multiple myeloma patients are missing part or all of chromosome 13. The deletion of this chromosome, along with high beta 2-microglobulin, leads to a poor prognosis.

With treatment, multiple myeloma may go into complete remission. This is defined as:

- M-protein absent from the blood and urine
- myeloma cells not detectable in the bone marrow
- no clinical symptoms
- negative laboratory tests

However, with very sensitive testing, a few myeloma cells are usually detectable and eventually lead to a recurrence of the disease, in the bone or elsewhere in the body.

Prevention

There are no clearly established risk factors for multiple myeloma and it is possible that a combination of factors interact to cause the disease. Thus, there is no method for preventing multiple myeloma.

Resources

BOOKS

Heller, Robert J. *Multiple Myeloma: The Plain English Handbook for Patients and Care Givers*. Marietta, GA : Wollaston Press, 2006.

OTHER

"About Myeloma." *Multiple Myeloma Research Foundation*. April 16, 2001. [cited June 15,2001]. http://www.multiplemyeloma.org/aboutmyeloma.html.

Complementary and Alternative Therapies for Leukemia, Lymphoma, Hodgkin's Disease and Myeloma. The Leukemia and Lymphoma Society. March 27, 2001. [cited June 15, 2001]. http://www.leukemia-lymphoma.org.

Facts and Statistics About Leukemia, Lymphoma, Hodgkin's Disease and Myeloma. The Leukemia and Lymphoma Society. March 15, 2001. [cited Mar27, 2001]. http://www.leukemia-lymphoma.org.

"Multiple Myeloma and Other Plasma Cell Neoplasms." *CancerNet* National Cancer Institute. March 2001. [cited April 16, 2001]. http://cancernet.nci.nih.gov.

"Multiple Myeloma." *Cancer Resource Center*. American Cancer Society. April 16, 2001. [cited June 15, 2001]. http://www.cancer.org/Cancer/MultipleMyeloma/DetailedGuide/index.

ORGANIZATIONS

Multiple Myeloma Research Foundation, 383 Main Avenue 5th Floor, Norwalk, CT, 06851, (203) 229-0464, (203) 229-0572, info@themmrf.org, http://www.themmrf.org.

Margaret Alic, Ph.D.

Multiple personality disorder

Definition

Multiple personality disorder, or MPD, is a mental disturbance classified as one of the **dissociative disorders** in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM–IV*). It

has been renamed dissociative identity disorder (DID). MPD or DID is defined as a condition in which "two or more distinct identities or personality states" alternate in controlling the patient's consciousness and behavior. Note: "Split personality" is not an accurate term for DID and should not be used as a synonym for **schizophrenia**.

Description

The precise nature of DID (MPD) as well as its relationship to other mental disorders is still a subject of debate. Some researchers think that DID may be a relatively recent development in western society. It may be a culture–specific syndrome found in western society, caused primarily by both childhood **abuse** and unspecified long–term societal changes. Unlike depression or **anxiety disorders**, which have been recognized, in some form, for centuries, the earliest cases of persons reporting DID symptoms were not recorded until the 1790s. Most were considered medical oddities or curiosities until the late 1970s, when increasing numbers of cases were reported in the United States. Psychiatrists are still debating whether DID was previously misdiagnosed and underreported, or whether it is currently overdiagnosed. Because childhood trauma is a factor in the development of DID, some doctors think it may be a variation of **post–traumatic stress disorder** (PTSD). DID and PTSD are conditions in which dissociation is a prominent mechanism. The female to male ratio for DID is about 9:1, but the reasons for the gender imbalance are unclear. Some experts have attributed the imbalance in reported cases to higher rates of abuse of female children, and some to the possibility that males with DID are underreported because they might be in prison for violent crimes.

The most distinctive feature of DID is the formation and emergence of alternate personality states, or "alters." Patients with DID experience their alters as distinctive individuals possessing different names, histories, and personality traits. It is not unusual for DID patients to have alters of different genders, sexual orientations, ages, or nationalities. Some patients have been reported with alters that are not even human; alters have been animals, or even aliens from outer space. The average DID patient has between two and 10 alters, but some have been reported with over one hundred.

Causes and symptoms

The severe dissociation that characterizes patients with DID is currently understood to result from a set of causes:

- An innate ability to dissociate easily
- Repeated episodes of severe physical or sexual abuse in childhood
- The lack of a supportive or comforting person to counteract abusive relative(s)
- The influence of other relatives with dissociative symptoms or disorders

The relationship of dissociative disorders to childhood abuse has led to intense controversy and lawsuits concerning the accuracy of childhood memories. The brain's storage, retrieval, and interpretation of childhood memories are still not fully understood.

The major dissociative symptoms experienced by DID patients are **amnesia**, depersonalization, derealization, and identity disturbances.

Amnesia

Amnesia in DID is marked by gaps in patients' memory for long periods of their past, in some cases, their entire childhood. Most DID patients have amnesia, or "lost time," for periods when another personality is "out." They may report finding items in their house that they can not remember having purchased, finding notes written in different handwriting, or other evidence of unexplained activity.

Depersonalization

Depersonalization is a dissociative symptom in which the patient feels that his or her body is unreal, is changing, or is dissolving. Some DID patients experience depersonalization as feeling to be outside of their body, or as watching a movie of themselves.

Derealization

Derealization is a dissociative symptom in which the patient perceives the external environment as unreal. Patients may see walls, buildings, or other objects as changing in shape, size, or color. DID patients may fail to recognize relatives or close friends.

Identity disturbances

Identity disturbances in DID result from the patient's having split off entire personality traits or characteristics as well as memories. When a stressful or traumatic experience triggers the reemergence of these dissociated parts, the patient switches—usually within seconds—into an alternate personality. Some patients have histories of erratic performance in school or in their jobs caused by the emergence of alternate personalities during examinations or other

stressful situations. Patients vary with regard to their alters' awareness of one another.

Diagnosis

The diagnosis of DID is complex and some physicians believe it is often missed, while others feel it is overdiagnosed. Patients have been known to have been treated under a variety of other psychiatric diagnoses for a long time before being re–diagnosed with DID. The average DID patient is in the mental health care system for six to seven years before being diagnosed as a person with DID. Many DID patients are misdiagnosed as depressed because the primary or "core" personality is subdued and withdrawn, particularly in female patients. However, some core personalities, or alters, may genuinely be depressed, and may benefit from antidepressant medications. One reason misdiagnoses are common is that DID patients may truly meet the criteria for **panic disorder** or somatization disorder.

Misdiagnoses include schizophrenia, **borderline personality disorder**, and, as noted, somatization disorder and panic disorder. DID patients are often frightened by their dissociative experiences, which can include losing awareness of hours or even days of time, meeting people who claim to know them by another name, or feeling "out of body." Persons with the disorder may go to emergency rooms or clinics because they fear they are going insane.

When a doctor is evaluating a patient for DID, he or she will first rule out physical conditions that sometimes produce amnesia, depersonalization, or derealization. These conditions include head injuries; brain disease, especially seizure disorders; side effects from medications; **substance abuse** or intoxication; AIDS–dementia complex; or recent periods of extreme physical **stress** and sleeplessness. In some cases, the doctor may give the patient an electroencephalograph (EEG) to exclude **epilepsy** or other seizure disorders. The physician also must consider whether the patient is **malingering** and/or offering fictitious complaints.

If the patient appears to be physically normal, the doctor will next rule out psychotic disturbances, including schizophrenia. Many patients with DID are misdiagnosed as schizophrenic because they may "hear" their alters "talking" inside their heads. If the doctor suspects DID, he or she can use a screening test called the Dissociative Experiences Scale (DES). If the patient has a high score on this test, he or she can be evaluated further with the Dissociative Disorders Interview Schedule (DDIS) or the Structured Clinical Interview for *DSM–IV* Dissociative Disorders (SCID–D). The doctor may also use the Hypnotic Induction Profile (HIP) or a similar test of the patient's hypnotizability.

Treatment

Treatment of DID may last for five to seven years in adults and usually requires several different treatment methods.

Psychotherapy

Ideally, patients with DID should be treated by a therapist with specialized training in dissociation. This specialized training is important because the patient's personality switches can be confusing or startling. In addition, many patients with DID have hostile or suicidal alter personalities. Most therapists who treat DID patients have rules or contracts for treatment that include such issues as the patient's responsibility for his or her safety. **Psychotherapy** for DID patients typically has several stages: an initial phase for uncovering and "mapping" the patient's alters; a phase of treating the traumatic memories and "fusing" the alters; and a phase of consolidating the patient's newly integrated personality.

Most therapists who treat multiples, or DID patients, recommend further treatment after personality integration, on the grounds that the patient has not learned the social skills that most people acquire in adolescence and early adult life. In addition, **family therapy** is often recommended to help the patient's family understand DID and the changes that occur during personality reintegration.

Many DID patients are helped by group as well as individual treatment, provided that the group is limited to people with dissociative disorders. DID patients sometimes have setbacks in mixed therapy groups because other patients are bothered or frightened by their personality switches.

Medications

Some doctors will prescribe tranquilizers or antidepressants for DID patients because their alter personalities may have **anxiety** or **mood disorders**. However, other therapists who treat DID patients prefer to keep medications to a minimum because these patients can easily become psychologically dependent on drugs. In addition, many DID patients have at least one alter who abuses drugs or alcohol, substances which are dangerous in combination with most tranquilizers.

KEY TERMS

Alter—An alternate or secondary personality in a patient with DID.

Amnesia—A general medical term for loss of memory that is not due to ordinary forgetfulness. Amnesia can be caused by head injuries, brain disease, or epilepsy as well as by dissociation.

Depersonalization—A dissociative symptom in which the patient feels that his or her body is unreal, is changing, or is dissolving.

Derealization—A dissociative symptom in which the external environment is perceived as unreal.

Dissociation—A psychological mechanism that allows the mind to split off traumatic memories or disturbing ideas from conscious awareness.

Dissociative identity disorder (DID)—Term that replaced Multiple Personality Disorder (MPD). A condition in which two or more distinctive identities or personality states alternate in controlling a person's consciousness and behavior.

Hypnosis—An induced trance state used to treat the amnesia and identity disturbances that occur in dissociative identity disorder (DID).

Multiple personality disorder (MPD)—The former, though often still used, term for dissociative identity disorder (DID).

Primary personality—The core personality of an DID patient. In women, the primary personality is often timid and passive, and may be diagnosed as depressed.

Psychotherapy—The treatment of mental and behavioral disorders by support and insight to encourage healthy behavior patterns and personality growth.

Trauma—A disastrous or life–threatening event that can cause severe emotional distress. DID is associated with trauma in a person's early life or adult experience.

Hypnosis

While not always necessary, hypnosis is a standard method of treatment for DID patients. Hypnosis may help patients recover repressed ideas and memories. Further, hypnosis can also be used to control problematic behaviors that many DID patients exhibit, such as **self–mutilation**, or **eating disorders** like **bulimia nervosa**. In the later stages of treatment, the therapist may use hypnosis to "fuse" the alters as part of the patient's personality integration process.

Alternative treatment

Alternative treatments that help to relax the body are often recommended for DID patients as an adjunct to psychotherapy and/or medication. These treatments include **hydrotherapy**, botanical medicine (primarily herbs that help the nervous system), therapeutic massage, and **yoga**. Homeopathic treatment can also be effective for some people. **Art therapy** and the keeping of journals are often recommended as ways that patients can integrate their past into their present life. **Meditation** is usually discouraged until the patient's personality has been reintegrated.

Prognosis

Some therapists believe that the prognosis for recovery is excellent for children and good for most adults. Although treatment takes several years, it is often ultimately effective. As a general rule, the earlier the patient is diagnosed and properly treated, the better the prognosis.

Prevention

Prevention of DID requires intervention in abusive families and treating children with dissociative symptoms as early as possible.

Resources

BOOKS

Courtois, Christine A., and Julian D. Ford., editors. *Treating Complex Traumatic Stress Disorders: An Evidence–Based Guide*. New York, NY: The Guilford Press, 2009.

Graham, George. *The Disordered Mind: An Introduction to Philosophy of Mind and Mental Illness*. New York, NY: Routledge, 2010.

North, Carol, and Sean Yutzy. *Goodwin and Guze's Psychiatric Diagnosis*. New York, NY: Oxford University Press, 2010.

Shams, K. *Human Relation and Personified Relational Disorders*. Raleigh, NC: lulu.com, 2009.

ORGANIZATIONS

American Academy of Child and Adolescent Psychiatry, 3615 Wisconsin Ave., NW , Washington, DC, 20016–3007, (202) 966–7300, http://www.aacap.org.

American Psychiatric Association, 1000 Wilson Blvd., Suite 1825, Arlington, VA, 22209, (703) 907–7300, apa@psych.org, http://www.psych.org/.

American Psychological Association (APA), 750 First St. NE, Washington, DC, 20002–4242, (202) 336–5700, http://www.apa.org.

National Alliance on Mental Illness (NAMI), 3803 N. Fairfax Dr., Suite 100, Arlington, VA, 22201, (703) 524–7600, (800) 950–NAMI (6264), (703) 524–9094, http://www.nami.org/Hometemplate.cfm.

National Institute of Mental Health (NIMH), 6001 Executive Blvd., Room 8184, MSC 9663, Bethesda, MD, 20892, (301) 443–4513, (866) 615–6464, (301) 443–4279, nimhinfo@nih.gov, http://www.nimh.nih.gov/index.shtml.

National Mental Health Association (NMHA), 2000 N. Beauregard St., 6th Floor, Alexandria, VA, 22311, (703) 684–7722, (800) 969–NMHA, (703) 684–5968, http://www1.nmha.org/.

Rebecca J. Frey, Ph.D.
Laura Jean Cataldo, RN, Ed.D.

Multiple pregnancy

Definition

A multiple **pregnancy** is a pregnancy in which more than one fetus develops in the uterus at the same time.

Demographics

Multiple pregnancies occur in 1–2% of all pregnancies. The rate of twinning (the bearing of twins) is believed to be underestimated, as twin pregnancies with a singleton birth (an offspring born singly) are usually not recorded as twins.

Multiple births are more likely to occur in women who become pregnant after the age of 35. This is because hormonal changes in the body that occur as the woman ages increase the chance of more than one egg to being released at a time. Treatment for **infertility** also increases the chance of having a multiple pregnancy.

According to the United States Centers for Disease Control and Prevention (CDC) in 2006 there were 137,085 sets of twins born in the United States, 6,118 sets of triplets, 355 sets of quadruplets, and 67 instances of quintuplets or higher order births. That is a rate of twins of 32.1 per 1,000 live births and a rate of triplets or higher order births of 153.3 per 100,000 live births.

Description

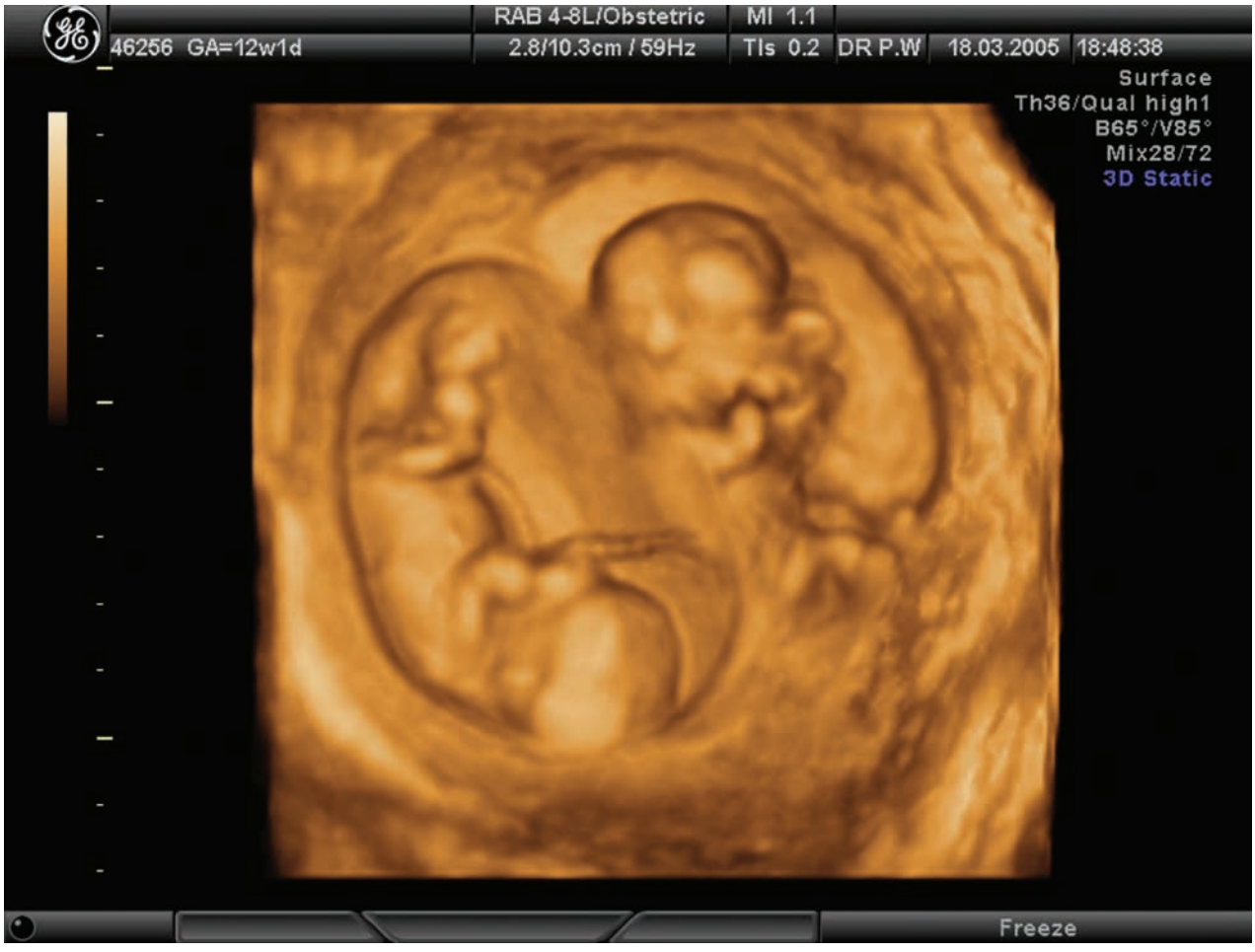
A multiple pregnancy may be the result of the natural process of twinning, or it may be the result of the woman having taken fertility drugs. Because of the increase in artificial reproductive technology (ART), the incidence of multiple pregnancies has increased. The CDC reports that since 1980 the number of twins has risen by 52% and the number of triplets and high order multiples (more than three) has increased by 404%. An older maternal age and the use of fertility techniques are seen as the two major factors in these increases. While singletons have a 10% risk of being born preterm, multiple births have a 57% chance of being born prematurely. Premature birth places a newborn at higher risk for morbidity and mortality.

There are two categories of twins: monozygotic (identical twins) and dizygotic (fraternal twins). Monozygotic twins are twins that have developed from a single fertilized ovum (egg) that splits during embryonic development. These twins have the same genetic makeup and are always the same sex. They may be surrounded by one chorion (the outer embryonic membrane of the developing fetus), or may each have their own chorion. They may be surrounded by one amniotic sac (innermost of the membranes surrounding the embryo) or may each have their own amniotic sac. They may share a placenta or may each have their own placenta. These different possibilities depend on the time of the embryonic development at which the division took place. About 2–5% of monozygotic twins will share one amniotic sac. This rare occurrence puts the twins at risk for umbilical cord entanglement, cessation of blood flow, and **death**. Double survival of monoamniotic twins is rare.

Dizygotic twins develop from two fertilized ova. Their genetic makeup is different, and they are no more similar as any two siblings in a family. They may be the same or different sex. Each has its own chorion, amniotic sac, and placenta. While each twin has its own placenta, the placental implantations may be close enough that they fuse into one.

Multiple pregnancies of three or more fetuses may be the result of a single fertilized egg that splits, of multiple egg fertilizations, or a combination of the two processes.

Twins may not grow at the same rate. A 25% or more disparity in their growth is referred to as discordance, which occurs in about 10% of twin pregnancies. An extreme case of discordance occurs in the condition called twin-to-twin **transfusion**, also known as twin **oligohydramniospolyhydramnios** sequence. In



A 3D ultrasound image of twin fetuses. *(© Medical-on-Line/Alamy.)*

this situation, one twin becomes the donor twin (receives too little blood from vessels in the fetuses' shared placenta that connect their blood circulations) and the other twin is the recipient (receives too much blood). The donor twin becomes small, pale, hypotensive, and anemic, with very little amniotic fluid. The recipient twin is large, polycythemic, hypertensive, with an excess of amniotic fluid. Both are at risk for **heart failure** and death.

Causes and symptoms

In a woman's menstrual cycle, one egg, or ovum, is normally released every month. If more than one egg is released, it is possible for each egg to be fertilized separately by different sperm cells. Fertility drugs encourage the release of more than one egg during the monthly menstrual cycle. In the case of monozygotic twins, only one egg was released and fertilized; but after fertilization it split, and separate fetuses developed. If the split is not complete, conjoined twins develop. Conjoined twins share certain body parts and organs. They may be referred to as Siamese twins. The chance of multiple pregnancy increases with an increase in maternal age. Genetics and racial background also play a role.

Diagnosis

A multiple pregnancy is suspected if the woman's uterus is growing too quickly for the gestational age, with excessive maternal weight gain, elevated levels of alpha-fetoprotein (a fetal protein that increases in the mother's blood during pregnancy) levels, unexplained severe maternal anemia, or with the auscultation (listening to sound to aid in diagnosis and treatment) of more than one fetal heartbeat. If undiagnosed at the time of quickening, the mother may feel movement in different parts of the uterus at the same time. Ultrasound can confirm the presence of a multiple pregnancy. Once the multiple pregnancy is confirmed,

ultrasonography may be used to check fetal growth over time, and the presence of any anomalies.

While a mother carrying a singleton may have one ultrasound done during the pregnancy, the mother of a multiple pregnancy is much more likely to have several ultrasounds done. The experience, skill, and ability of the ultrasound technician to provide a calm environment can be a great help to the mother and her partner. The nurse working in a high-risk obstetric practice can provide a great deal of teaching both to inform the mother about what to expect and to decrease **anxiety** through knowledge.

A condition referred to as vanishing twin syndrome occurs in up to 50% of twin pregnancies diagnosed very early by ultrasound. This syndrome occurs when a twin pregnancy was diagnosed, but later one twin is found to have disappeared. It is not clear what causes this syndrome. In these cases, there may have been early pregnancy vaginal bleeding and a lower human chorionic gonadotropin (hCG; a type of hormone) level than would be expected. The placenta often shows a whitish area and the remnant of a gestational sac. The mother and surviving twin (born singly) are generally both healthy.

Treatment

The diagnosis of a multiple pregnancy will result in it being treated as a **high-risk pregnancy** because of associated maternal and fetal risks. In a triplet pregnancy the mother may be offered the choice of selective reduction to twins. However, the literature is unclear as to the overall value of reduction from three to two fetuses. In high order multiples, to decrease the risk of very early preterm birth and potential loss of fetal viability, selective reduction may take place. In selective reduction, high order multiples are reduced to triplets or twins. The procedure is usually completed before the end of the third month of gestation and involves a chemical injection into one or more developing embryos. A fetus that shows chromosomal damage is usually targeted first. While this process increases the chances of the viability of the remaining fetuses, it carries a significant emotional burden for the parents. It also raises ethical issues concerning the "right-to-life" of a fetus. Efforts are being made in the field of ART to prevent the development of high order multiples in order to avoid this situation as much as possible.

Prognosis

Prognosis for a multiple pregnancy depends on many factors. The higher the number of fetuses, the greater the risks. A twin pregnancy carries significantly more risks than a singleton pregnancy. The risks for triplets are similar to that of twins. The risks increase significantly with multiples of four or higher. Twins have a ten-fold risk of perinatal mortality over singletons.

While many multiple pregnancies have an excellent outcome, multiple pregnancy is still considered a high-risk pregnancy. The average gestation for a singleton is 38 to 42 weeks. For twins gestation averages 37 weeks; for triplets, 33 weeks; and for quadruplets, 31 weeks. The mother carrying a multiple pregnancy has an increased risk of:

- premature birth
- pregnancy-related hypertension and preeclampsia
- hydramnios (excess amniotic fluid)

LOUIS GERALD KEITH (1935–)

Louis Gerald Keith and his twin brother, Donald, were born on April 24, 1935, to Russian immigrants. Although the boys received much attention due to their status as twins, their parents encouraged them to pursue their own goals, and at age twelve, Louis decided he wanted to become a doctor. After completing his bachelor of science degree at the University of Illinois, Keith entered the Chicago Medical school, graduating with his degree in 1960. He joined the U.S. Public Health Service and was stationed in Puerto Rico after completing his residency and internship at Cook County Hospital. Keith returned to Chicago after receiving his certification in obstetrics and gynecology in 1967 and worked as a professor and a physician.

Keith began his research on twins when a friend's twin brother died of lymphoma. The fact that Keith was a twin made his research more personally fulfilling and worthwhile to him. Keith and Donald founded the Center for the Study of Multiple Birth in 1977 located in Chicago. The center, a non-profit facility, was the first multiple birth research organization in the United States. Keith has delivered many speeches and has published various study results. In addition to books and scientific articles written individually and cooperatively, he was co-author of *Multiple Pregnancy: Epidemiology, Gestation and Prenatal Outcome* (1996) with his brother Donald, and others. He was previously the chief obstetrician at the Prentice Women's Hospital and Maternity Center in Chicago, and is currently Professor of Obstetrics and Gynecology and Director of the Section of Undergraduate Education and Medical Student Affairs at Northwestern University Medical School in Chicago.

- placenta previa (placenta covering the mouth of the womb-cervix)
- folic acid and iron deficiency
- gestational diabetes
- urinary tract infection
- placental abruption after the vaginal delivery of the first twin (separation of the placenta from the uterus before the baby is born)
- uterine atony (failure of the uterus to contract after birth) and postpartal hemorrhage due to exaggerated stretching of the uterus
- fatigue and backache
- cesarean delivery

The risks to fetuses in a multiple pregnancy are greater than that for a singleton and include:

- premature birth (Preterm labor for twins is seven to ten times more likely than for singletons and is a significant factor in perinatal morbidity and mortality.)
- intrauterine growth restriction
- congenital anomalies
- cerebral palsy with increased risk often due to preterm delivery
- discordance; more common with triplets than with twins
- dead fetus syndrome
- combined pregnancy, in which one twin develops in the uterus while the other is ectopic (other than in the uterus, such as the fallopian tube or peritoneal cavity)
- delayed delivery of second twin
- placental abruption

Prevention

Twinning is a naturally occurring phenomenon and cannot be completely prevented. It occurs more often in older mothers. Multiple births due to ART are a concern because a multiple pregnancy represents a complication of pregnancy. Efforts within the ART community are being made to minimize the incidence of high order multiples. Efforts to prevent or minimize maternal and fetal complications will result in closer monitoring. More frequent ultrasounds, biophysical profile, and/or nonstress tests may be ordered. Cervical length and change may be monitored as an indicator of preterm delivery. If both twins are vertex and vaginal delivery is attempted, both fetal heart rates will be monitored. Cesarean deliveries of twins are more common than for singletons. This is especially true in high order multiples. The overall cesarean delivery rate tends to be about 75%.

KEY TERMS

Chorion—The outer embryonic membrane of the developing fetus that gives rise to the placenta. Inside the chorion is the amniotic sac or sacs, inside of which are the fetuses.

Morbidity—Morbidity refers to an illness or disease condition. In statistics it refers to the rate at which a disease occurs.

Mortality—Mortality means death. In statistics it refers to the rate at which death occurs in a population for a particular disease condition.

Singleton—A singleton is a fetus that develops alone in the uterus.

Resources

BOOKS

Fierro, Pamela. *Twins, Triplets, and More: Lifesaving Techniques and Advice for Surviving Life with Multiples.* Avon, MA: Adams Media, 2009.

Gromada, Karen Kerkhoff. *Mothering Multiples: Breastfeeding & Caring for Twins or More,* 3rd rev. ed. Schaumburg, IL: La Leche League International, 2007.

Scalise, Dagmara. *Twin Sense: A Sanity-Saving Guide to Raising Twins–From Pregnancy Through the First Year.* New York: AMACOM, 2009.

PERIODICALS

Goodnight, William and Roger Newman. "Optimal Nutrition for Improved Twin Pregnancy Outcome." *Obstetrics & Gynecology,* (November 2009), 114(5), 1121-34.

Melamid, Nir, Yariv Yogev, and Marek Glezerman. "Effect of Fetal Sex on Pregnancy Outcome in Twin Pregnancies." *Obstetrics & Gynecology,* (November 2009), 114(5), 1085-92.

ORGANIZATIONS

American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, IL, 60007-1098, (847)434-4000, (847)434-8000, http://www.aap.org.

Center for the Study of Multiple Birth, 33 East Superior Street, Suite 464, Chicago, IL, 60611, (312)695-1677, (312)908-8777, www.multiplebirth.com.

National Organization of Mothers of Twins Clubs, 2000 Mallory Lane, Suite 130-600, Franklin, TN, 37067, (248) 231-4480, info@nomotc.org, www.nomotc.org.

Esther Csapo Rastegari, R.N., B.S.N., Ed.M.
Tish Davidson, A.M.

Multiple sclerosis

Definition

Multiple sclerosis (MS) is a chronic autoimmune disorder affecting movement, sensation, and bodily functions. It is caused by destruction of the myelin insulation covering nerve fibers (neurons) in the central nervous system (brain and spinal cord).

Demographics

In 2008, multiple sclerosis affected about 400,000 people in the United States, with 10,000 new cases being diagnosed each year. Worldwide, MS affects between 1.5 and 2.5 million people. Most people have their first symptoms between the ages of 20 and 40; symptoms rarely begin before age 15 or after age 60. Women are almost twice as likely to get MS as men, especially in their early years. People of northern European ancestry are more likely to be affected than people of other racial backgrounds, and MS rates are higher in the United States, Canada, and Northern Europe than other parts of the world. The disorder is unknown among certain native peoples such as the Inuit (native people of the Arctic) and Maori (Native people of New Zealand).

Description

Multiple sclerosis is a slowly progressive disease of the central nervous system (CNS), which is comprised of the brain and spinal cord. In 1868, French physician Jean-Martin Charcot (1825-1893) provided the first detailed clinical description of the disease. Today researchers know that MS is an autoimmune disorder that causes the destruction of myelin, the insulating material that surrounds nerve fibers (neurons). Myelin helps electrical signals pass quickly and smoothly between the brain and the rest of the body. When the myelin layer is destroyed, nerve messages are sent more slowly and less efficiently. Patches of scar tissue, called plaques, form over the affected areas, further disrupting nerve communication. The symptoms of MS occur when the brain and spinal cord nerves no longer communicate properly with other parts of the body. MS causes a wide variety of symptoms and can affect vision, balance, strength, sensation, coordination, and bodily functions.

Risk factors

The risk of developing MS is slightly higher if another family member is affected, suggesting the influence of genetic factors. If one person in a family has MS, then that person's close family relatives (parents, children, siblings) have about a 5% greater chance of developing MS than people who do not have family members with the disorder. In addition, the higher prevalence of MS among people of northern European background suggests some genetic susceptibility.

Causes and symptoms

Causes

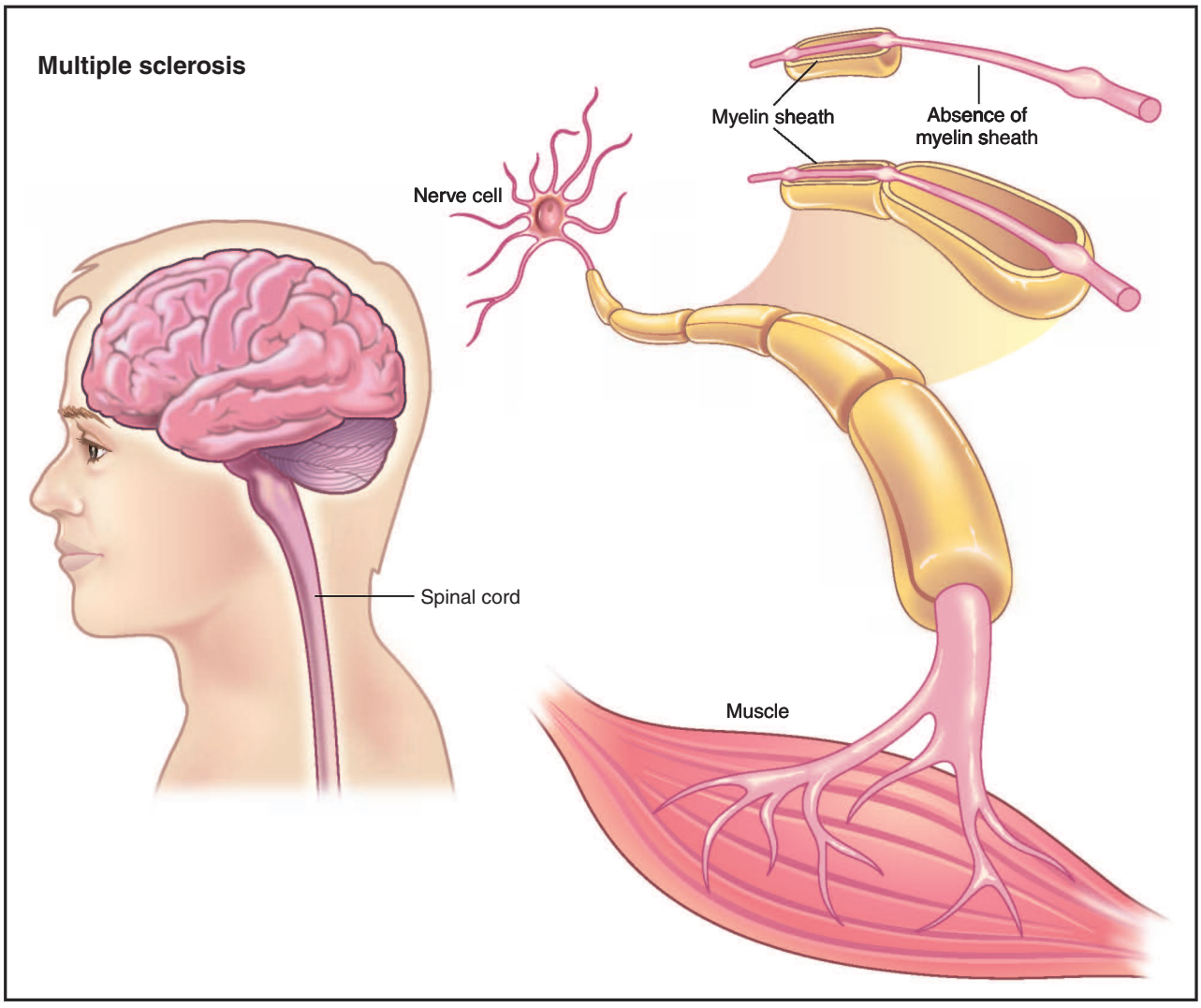
Multiple sclerosis is an autoimmune disorder, meaning it is caused by the body's own immune system. For unknown reasons, immune cells attack and destroy the myelin sheath that insulates neurons in the brain and spinal cord. This myelin sheath speeds transmission of nerve impulses and prevents electrical activity in one cell from short-circuiting to another cell. Disruption of communication between the brain and other parts of the body prevents normal passage of sensations and control messages, leading to the symptoms of MS. The demyelinated areas appear as plaques, small round areas of gray neuron without the white myelin covering. The progression of symptoms in MS is correlated with development of new plaques in the portion of the brain or spinal cord controlling the affected areas. Because there appears to be no pattern in the appearance of new plaques, the progression of MS can be unpredictable.

Despite considerable research, the trigger for this autoimmune destruction is still unknown. At various times, evidence has pointed to genes, environmental factors, viruses, or a combination of these.

The fact that the risk of developing MS is slightly higher if another family member is affected, suggests that there is a genetic susceptibility to the disease.

The role of an environmental factor is suggested by studies of the effect of migration on the risk of developing MS. Age plays an important role in determining this change in risk—young people in low-risk groups who move into countries with higher MS rates display the risk rates of their new surroundings, while older migrants retain the risk rate of their original home country. One interpretation of these studies is that an environmental factor, either protective or harmful, is acquired in early life; the risk of disorder later in life reflects the effects of the early environment.

These same data can be used to support the involvement of a slow-acting virus, one that is acquired early in live but begins its destructive effects much later.



Multiple sclerosis (MS) is an autoimmune disease in which immune cells attack and destroy the myelin sheath, which stimulates neurons in the brain and spinal cord. When the myelin is destroyed, nerve messages are sent more slowly and less efficiently. Scar tissue then forms over the affected areas, disrupting nerve communication. MS symptoms occur when the brain and spinal cord nerves cease to communicate properly with other parts of the body. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

Slow viruses are known to cause other disorders, including **AIDS**. In addition, viruses have been implicated in other **autoimmune disorders**. Many claims have been made for the role of viruses, slow or otherwise, as the trigger for MS, but as of 2009 no strong candidate has emerged.

How a virus could trigger the autoimmune reaction is also unclear. There are two main models of virally induced autoimmunity. The first suggests the immune system is actually attacking a virus (one too well-hidden for detection in the laboratory), and the myelin damage is an unintentional consequence of fighting the infection. The second model suggests the immune system mistakes myelin for a viral protein, one it encountered during a prior infection. Primed for the attack, it destroys myelin because it resembles the previously recognized viral invader.

Either of these models allows a role for genetic factors, since certain genes can increase the likelihood of autoimmunity, and it seems likely that more than one gene is involved in a person's susceptibility to MS. Environmental factors as well might change the sensitivity of the immune system or interact with myelin to provide the trigger for the secondary immune

response. Possible environmental triggers that have been invoked in MS include viral infection, trauma, electrical injury, and chemical exposure, although controlled studies do not support a causative role.

Symptoms

MS is a diverse disease. No two affected persons are the same and each will experience different combinations of symptoms with differing severity. The symptoms of multiple sclerosis may occur in one of three patterns:

- The most common pattern is the relapsing-remitting pattern, in which there are clearly defined symptomatic attacks lasting 24 hours or more, followed by complete or almost complete improvement. The period between attacks may be a year or more at the beginning of the disorder, but may shrink to several months later on. About three-quarters of all people diagnosed with MS have this version of the disorder. This pattern is especially common in younger people who develop MS.
- In the primary progressive pattern, the disorder progresses without remission or with only occasional plateaus or slight improvements. This pattern is more common in older people. About 10% of people with the disorder have this pattern.
- In the secondary progressive pattern, the person with MS begins with relapses and remissions, followed by more steady progression of symptoms. In some people, what begins as a relapsing-remitting pattern develops into a secondary progressive pattern.

Between 10–20% of people have a benign type of MS, meaning their symptoms progress very little over the course of their lives.

Because plaques may form in any part of the central nervous system, the symptoms of MS vary widely from person-to-person and from stage-to-stage of the disorder. Initial symptoms often include:

- muscle weakness, causing difficulty walking
- loss of coordination or balance
- numbness, "pins and needles," (paresthesias) or other abnormal sensations
- visual disturbances, including blurred or double vision.

later symptoms may include:

- Fatigue
- muscle spasticity and stiffness
- tremors
- paralysis
- pain
- vertigo
- speech or swallowing difficulty
- loss of bowel and bladder control
- incontinence, constipation
- sexual dysfunction
- cognitive changes.

Weakness in one or both legs is common, and may be the first symptom noticed by a person with MS. Muscle spasticity, where muscles are excessive and continuously contracted, is also common and may be more disabling than weakness.

Double vision or eye tremor (**nystagmus**) may result from involvement of the nerve pathways controlling movement of the eye muscles. Visual disturbances result from involvement of the optic nerves (**optic neuritis**) and may include development of blind spots in one or both eyes, changes in color vision, or blindness. Optic neuritis usually involves only one eye at a time and is often associated with movement of the effected eye.

More than half of all people affected by MS have **pain** during the course of their disorder, and many experience chronic pain, including pain from spasticity. Acute pain occurs in about 10% of cases. This pain may be a sharp, stabbing pain especially in the face, neck, or down the back. Facial **numbness** and weakness are also common.

Cognitive changes, including memory disturbances, depression, and personality changes, are found in people affected by MS, although it is not entirely clear whether these changes are due primarily to the disorder or to the psychological reaction to it. Depression may be severe enough to require treatment in up to 25% of those with MS. A smaller number of people experience disorder-related euphoria, or abnormally elevated mood, usually after a long disorder duration and in combination with other psychological changes.

Symptoms of MS may be worsened by heat or increased body temperature, including **fever**, intense physical activity, or exposure to sun, hot baths, or showers.

Diagnosis

There is no single test that confirms the diagnosis of multiple sclerosis, and there are a number of other disorders with similar symptoms. While one person's diagnosis may be immediately suggested by symptoms and history, another's may not be confirmed without multiple tests and prolonged observation. The distribution of symptoms is important: MS affects multiple areas of the body over time. The pattern of symptoms is also critical, especially as evidence of the relapsing-

KEY TERMS

Clinical trial—All new drugs undergo clinical trials before approval. Clinical trials are carefully conducted tests in which effectiveness and side effects are studied, with the placebo effect eliminated.

Evoked potentials—Tests that measure the brain's electrical response to stimulation of sensory organs (eyes or ears) or peripheral nerves (skin). These tests may help confirm the diagnosis of multiple sclerosis.

Myelin—A layer of insulation that surrounds the nerve fibers in the brain and spinal cord.

Plaque—Patches of scar tissue that form where the layer of myelin covering the nerve fibers is destroyed by the multiple sclerosis disorder process.

Primary progressive—A pattern of symptoms of multiple sclerosis in which the disorder progresses without remission, or with occasional plateaus or slight improvements.

Relapsing-remitting—A pattern of symptoms of multiple sclerosis in which symptomatic attacks occur that last 24 hours or more, followed by complete or almost complete improvement.

Secondary progressive—A pattern of symptoms of multiple sclerosis in which there are relapses and remissions, followed by more steady progression of symptoms.

remitting pattern, so a detailed medical history is one of the most important parts of the diagnostic process. A thorough search to exclude other causes of a patient's symptoms is especially important if the following features are present: 1) family history of neurologic disorder, 2) symptoms and findings attributable to a single anatomic location, 3) persistent back pain, 4) age of onset over 60 or under 15 years of age, or 5) progressively worsening disorder.

Tests

In addition to the medical history and a standard **neurological exam**, several lab tests are used to help confirm or rule out a diagnosis of MS:

- Magnetic resonance imaging (MRI) can reveal plaques on the brain and spinal cord. Gadolinium enhancement can distinguish between old and new plaques, allowing a correlation of new plaques with new symptoms. Plaques may be seen in several other disorders as well, including encephalomyelitis, neurosarcoidosis, and cerebral lupus. Plaques on MRI may be difficult to distinguish from small strokes, areas of decreased blood flow, or changes seen with trauma or normal aging.
- A lumbar puncture, or spinal tap, is done to measure levels of immune system proteins, which are usually elevated in the cerebrospinal fluid of a person with MS. This test may not be necessary if other tests are diagnostic.
- Evoked potential tests are electrical tests of conduction speed in the nerves that can reveal reduced speeds consistent with the damage caused by plaques. These tests may be done with small electrical charges applied to the skin (somatosensory evoked potential), with light patterns flashed on the eyes (visual evoked potential), or with sounds presented to the ears (auditory evoked potential).

The clinician making the diagnosis, usually a neurologist, may classify the disorder as "definite MS," meaning the symptoms and test results all point toward MS as the cause. "Probable MS" and "possible MS" reflect less certainty and may require more time to pass to observe the progression of the disorder and the distribution of symptoms.

Treatment

As of 2009, there was no cure for MS. Nevertheless, several drugs may slow progression of the disorder and moderate some symptoms in many patients, especially if started early.

MS causes a wide variety of symptoms, and the treatments for these are equally diverse. Most symptoms can be treated and complications avoided with good care and attention from medical professionals. Good health and **nutrition** remain important preventive measures. **Vaccination** against **influenza** can prevent respiratory complications. Preventing complications such as **pneumonia**, **bedsores**, injuries from falls, or urinary infection requires attention to the primary problems that may cause them. Shortened life spans with MS are almost always due to complications rather than primary symptoms themselves.

Drugs

Drug treatment of MS must be individualized. Not all drugs are appropriate for all patients. In the United States as of 2009, MS was most often treated with four drugs known as the ABCR drugs. These drugs are

interferon beta-1a (Avonex), interferon beta-1b (Betaseron and Rebif) and glatiramer acetate (Copaxone). These drugs, on average, reduce relapses in the relapsing-remitting form of MS by about one-third. Different measurements from tests of each have demonstrated other benefits as well: Avonex may slow the progress of physical impairment, Betaseron and Rebif may reduce the severity of symptoms, and Copaxone may decrease disability. All four drugs are administered by injection, some into muscle (IM), and some under the skin (SC). Some controversy exists on the most effective dose and the frequency with which these drugs should be administered.

Although the ABCR drugs reduce relapses and may keep patients in relatively good health for the short-term, their long-term success has not been proven and they do not work well for patients who have reached a steadily progressive stage of MS. Individuals with progressive forms of MS may be treated with mitoxantrone (Novantrone), cyclophosphamide (Cytoxan, Neosar), azathioprine (Imuran), or methotrexate (Rheumatrex). All these drugs suppress the immune system. None is ideal, and all have potentially serious side effects. Corticosteroid drugs such as methylprednisolone (Medrol) also may be used to reduce inflammation. Long-term use of **corticosteroids** also causes serious side effects.

Training in bowel and bladder care may be needed to prevent or compensate for incontinence. If the urge to urinate becomes great before the bladder is full, some drugs may be helpful, including propantheline bromide (Probanthine), oxybutynin chloride (Ditropan), or imipramine (Tofranil). Baclofen (Lioresal) may relax the sphincter muscle, allowing full emptying. Intermittent catheterization is effective in controlling bladder dysfunction. In this technique, a catheter is used to periodically empty the bladder.

Spasticity can be treated with oral medications, including baclofen and diazepam (Valium), or by injection with botulinum toxin (Botox). Spasticity relief may also bring relief from chronic pain. More acute types of pain may respond to carbamazepine (Tegretol) or diphenylhydantoin (Dilantin). **Low back pain** is common from increased use of the back muscles to compensate for weakened legs. **Physical therapy** and over-the-counter pain relievers may help.

Fatigue may be partially avoidable with changes in the daily routine to allow more frequent rests. Amantadine (Symmetrel) and Modafinil (Provigil), although not specifically approved for use with MS, are often used to treat fatigue and improve alertness. Pemoline (Cylert), a drug formerly used to treat fatigue in MS patients, was withdrawn from sale in the United States in October 2005 because of potentially fatal liver complications. Visual disturbances often respond to corticosteroids. Other symptoms that may be treated with drugs include seizures, vertigo, and tremor.

Clinical trials of new drugs and drug combinations to treat MS are ongoing. Individuals with MS who wish to participate in the trial of an experimental therapy can find a list of clinical trials currently enrolling volunteers at http://clinicaltrials.gov. There is no cost to the patient to participate in a clinical trial.

Rehabilitative therapy

Physical therapy helps the person with MS to strengthen and retrain affected muscles, maintain range of motion, prevent muscle stiffening, learn to use assistive devices such as canes and walkers, and to learn safer and more energy-efficient ways of moving, sitting, and transferring. **Exercise** and stretching programs are usually designed by the physical therapist and taught to the patient and caregivers for use at home. Exercise is an important part of maintaining function for the person with MS. Swimming is often recommended, not only for its low-impact workout, but also because it allows strenuous activity without overheating.

Occupational therapy helps the person with MS adapt to her environment and adapt the environment to her. The occupational therapist suggests alternate strategies and assistive devices for activities of daily living, such as dressing, feeding, and washing, and evaluates the home and work environment for safety and efficiency improvements that may be made.

Alternative

Bee venom has been suggested as a treatment for MS, but no studies or objective reports support this claim.

In several studies, **marijuana** has been shown to have variable effects on the symptoms of MS. Improvements have been documented for tremor, pain, and spasticity, and worsening for posture and balance. Side effects have included weakness, **dizziness**, relaxation, and incoordination, as well as euphoria.

Some studies support the value of high doses of **vitamins**, **minerals**, and other dietary supplements for controlling disorder progression or improving symptoms. Alpha-linoleic and linoleic acids, as well as selenium and vitamin E, have shown effectiveness in the treatment of MS. Selenium and vitamin E act as **antioxidants**. In addition, a diet low in saturated fats, maintained over a long period, may retard the disorder process.

Studies have also shown that t'ai chi can be an effective therapy for MS because it works to improve balance and increase strength.

There are conflicting views about the herb **Echinacea** and its benefit to MS. Some alternative practitioners recommend Echinacea for people with MS. However, Echinacea appears to stimulate different parts of the immune system, particularly immune cells known as macrophages. In MS these cells are very active already and further stimulation could worsen the disorder.

Prognosis

It is difficult to predict how multiple sclerosis will progress in any one person. Most people with MS will be able to continue to walk and function at their work for many years after their diagnosis. The factors associated with the mildest course of MS are being female, having the relapsing-remitting form, having the first symptoms at a younger age, having longer periods of remission between relapses, and initial symptoms of decreased sensation or vision rather than of weakness or incoordination.

Fewer than 5% of people with MS have a severe progressive form, leading to **death** from complications within five years. At the other extreme, 10–20% have a benign form, with a very slow or no progression of their symptoms. Studies have shown that about seven out of 10 people with MS are still alive 25 years after their diagnosis, compared to about nine out of 10 people of similar age without disorder. On average, MS shortens the lives of affected women by about six years, and men by 11 years. **Suicide** is a significant cause of death in MS, especially in younger patients. Suicide is completed 7.5 times more often in patients with MS than in those without the disorder.

The degree of disability a person experiences five years after onset is, on average, about three-quarters of the expected disability at 10–15 years. A benign course for the first five years usually indicates the disorder will not cause marked disability.

Prevention

There is no known way to prevent multiple sclerosis. Until the cause of the disorder is discovered, this is unlikely to change. Good nutrition, adequate rest, avoidance of **stress**, heat, and extreme physical exertion, and good bladder hygiene may improve quality of life and reduce symptoms.

Resources

BOOKS

Blackstone, Margaret. *The First Year: Multiple Sclerosis: An Essential Guide for the Newly Diagnosed*. New York: Marlowe, 2007.

OTHER

"Multiple Sclerosis." MedlinePlus. September 14, 2009 [September 22, 2009]. http://www.nlm.nih.gov/medlineplus/multiplesclerosis.html

"So You Have Multiple Sclerosis... What's Next?" Accelerated Cure Project for Multiple Sclerosis December 2005 [September 22, 2009]. http://www.acceleratedcure.org/downloads/bcp-ms-whatsnext.pdf

ORGANIZATIONS

Multiple Sclerosis Foundation (MSF), 6350 North Andrews Avenue, Fort Lauderdale, FL, 33309-2130, (954) 776-6805, (888) MS-FOCUS, (954) 351-0630, support@msfocus.org, http://www.msfacts.org.

National Institute of Neurological Disorders and Stroke (NINDS), P.O. Box 5801, Bethesda, MD, 20828, (301) 496-5751. TTY: (301) 468-5981, (800) 352-9424, http://www.ninds.nih.gov.

National Multiple Sclerosis Society, 733 Third Avenue, New York, NY, 10017, (800) 344-4867, http://www.nmss.org.

Genevieve T. Slomski, Ph.D.
Tish Davidson, A.M.

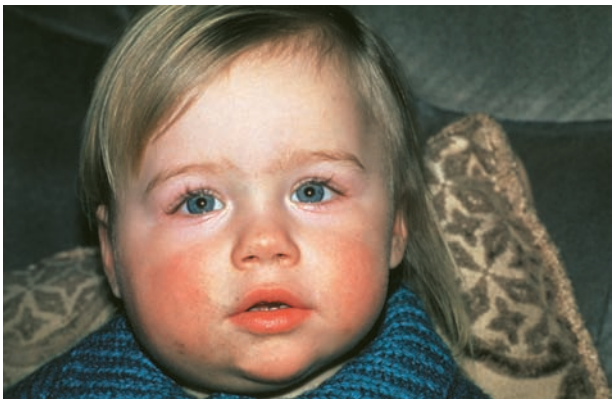
Mumps

Definition

Mumps is a relatively mild short-term viral infection of the salivary glands that usually occurs during childhood. Typically, mumps is characterized by a painful swelling of both cheek areas, although the person could have swelling on one side or no perceivable swelling at all. The salivary glands are also called the parotid glands, therefore, mumps is sometimes referred to as an inflammation of the parotid glands (epidemic parotitis). The word mumps comes from an old English dialect, meaning lumps or bumps within the cheeks.

Description

Mumps is a very contagious infection that spreads easily in such highly populated areas as day care centers and schools. Although not as contagious as **measles** or **chickenpox**, mumps was once quite common. Prior to the release of a mumps vaccine in the United States in 1967, approximately 92% of all children had



A young child with mumps. *(SPL/Photo Researchers, Inc.)*

been exposed to mumps by the age of 15. In these pre-vaccine years, most children contracted mumps between the ages of four and seven. Mumps epidemics came in two to five year cycles. The greatest mumps epidemic was in 1941 when approximately 250 cases were reported for every 100,000 people. In 1968, the year after the live mumps vaccine was released, only 76 cases were reported for every 100,000 people. By 1985, less than 3,000 cases of mumps were reported throughout the entire United States, which works out to about 1 case per 100,000 people. The reason for the decline in mumps was the increased usage of the mumps vaccine. However, 1987 noted a five-fold increase in the incidence of the disease because of the reluctance of some states to adopt comprehensive school immunization laws. Since then, state-enforced school entry requirements have achieved student immunization rates of nearly 100% in kindergarten and first grade. In 1996, the Centers for Disease Control and Prevention (CDC) reported only 751 cases of mumps nationwide, or, in other words, about one case for every five million people.

Causes and symptoms

The paramyxovirus that causes mumps is harbored in the saliva and is spread by sneezing, coughing, and other direct contact with another person's infected saliva. Once the person is exposed to the virus, symptoms generally occur in 14-24 days. Initial symptoms include chills, **headache**, loss of appetite, and a lack of energy. However, an infected person may not experience these initial symptoms. Swelling of the salivary glands in the face (parotitis) generally occurs within 12-24 hours of the above symptoms. Accompanying the **swollen glands** is **pain** on chewing or swallowing, especially with acidic beverages, such as lemonade. A **fever** as high as 104°F (40°C) is also common. Swelling of the glands reaches a maximum on about the second day and usually disappears by the seventh day. Once a person has contracted mumps, they become immune to the disease, despite how mild or severe their symptoms may have been.

While the majority of cases of mumps are uncomplicated and pass without incident, some complications can occur. Complications are, however, more noticeable in adults who get the infection. In 15% of cases, the covering of the brain and spinal cord becomes inflamed (**meningitis**). Symptoms of meningitis usually develop within four or five days after the first signs of mumps. These symptoms include a stiff neck, headache, **vomiting**, and a lack of energy. Mumps meningitis is usually resolved within seven days, and damage to the brain is exceedingly rare.

The mumps infection can spread into the brain causing inflammation of the brain (**encephalitis**). Symptoms of mumps encephalitis include the inability to feel pain, seizures, and high fever. Encephalitis can occur during the parotitis stage or one to two weeks later. Recovery from mumps encephalitis is usually complete, although complications, such as seizure disorders, have been noted. Only about 1 in 100 with mumps encephalitis dies from the complication.

About one-quarter of all post-pubertal males who contract mumps can develop a swelling of the scrotum (**orchitis**) about seven days after the parotitis stage. Symptoms include marked swelling of one or both testicles, severe pain, fever, **nausea**, and headache. Pain and swelling usually subside after five to seven days, although the testicles can remain tender for weeks.

Girls occasionally suffer an inflammation of the ovaries, or oophoritis, as a complication of mumps, but this condition is far less painful than orchitis in boys.

As of late 2002, some researchers in Europe are studying the possibility that mumps increases a person's risk of developing inflammatory bowel disease (IBD) in later life. This hypothesis will require further research, as present findings are inconclusive.

Diagnosis

When mumps reaches epidemic proportions, diagnosis is relatively easy on the basis of the physical symptoms. The doctor will take the child's temperature, gently palpate (touch) the skin over the parotid glands, and look inside the child's mouth. If the child has mumps, the openings to the ducts inside the mouth will be slightly inflamed and have a "pouty" appearance. With so many people vaccinated today, a case of

KEY TERMS

Asymptomatic—Persons who carry a disease and may be capable of transmitting the disease but who do not exhibit symptoms of the disease are said to be asymptomatic.

Autism—A severe developmental disorder that usually begins before three years of age and affects a child's social as well as intellectual development. Some researchers theorized that immunization with the MMR vaccine was a risk factor for autism.

Encephalitis—Inflammation of the brain.

Epidemic parotitis—The medical name for mumps.

Immunoglobulin G (IgG)—A group of antibodies against certain viral infections that circulate in the bloodstream. One type of IgG is specific against the mumps paramyxovirus.

Meningitis—Inflammation of the membranes covering the brain and spinal cord.

Orchitis—Inflammation or swelling of the scrotal sac containing the testicles.

Paramyxovirus—A genus of viruses that includes the causative agent of mumps.

Parotitis—Inflammation and swelling of the salivary glands.

mumps must be properly diagnosed in the event the salivary glands are swollen for reasons other than viral infection. For example, in persons with poor **oral hygiene**, the salivary glands can be infected with bacteria. In these cases, **antibiotics** are necessary. Also in rare cases, the salivary glands can become blocked, develop tumors, or swell due to the use of certain drugs, such as iodine. A test can be performed to determine whether the person with swelling of the salivary glands actually has the mumps virus.

As of late 2002, researchers in London have reported the development of a bioassay for measuring mumps-specific IgG. This test would allow a doctor to check whether an individual patient is immune to mumps, and allow researchers to measure the susceptibility of a local population to mumps in areas with low rates of **vaccination**.

Treatment

When mumps does occurs, the illness is usually allowed to run its course. The symptoms, however, are treatable. Because of difficulty swallowing, the most important challenge is to keep the patient fed and hydrated. The individual should be provided a soft diet, consisting of cooked cereals, mashed potatoes, broth-based soups, prepared baby foods, or foods put through a home food processor. **Aspirin**, **acetaminophen**, or ibuprofen can relieve some of the pain due to swelling, headache, and fever. Avoid fruit juices and other acidic foods or beverages that can irritate the salivary glands. Avoid dairy products that can be hard to digest. In the event of complications, a physician should be contacted at once. For example, if orchitis occurs, a physician should be called. Also, supporting the scrotum in a cotton bed on an adhesive-tape bridge between the thighs can minimize tension. Ice packs are also helpful.

Alternative treatment

Acupressure can be used effectively to relieve pain caused by swollen glands. The patient can, by using the middle fingers, gently press the area between the jawbone and the ear for two minutes while breathing deeply.

A number of homeopathic remedies can be used for the treatment of mumps. For example, belladonna may be useful for flushing, redness, and swelling. Bryonia (wild hops) may be useful for irritability, lack of energy, or thirst. Phytolacca (poke root) may be prescribed for extremely swollen glands. A homeopathic physician should always be consulted for appropriate doses for children, and remedies that do not work within one day should be stopped. A homeopathic preparation of the mumps virus can also be used prophylactically or as a treatment for the disease.

Several herbal remedies may be useful in helping the body recover from the infection or may help alleviate the discomfort associated with the disease. **Echinacea** (*Echinacea* spp.) can be used to boost the immune system and help the body fight the infection. Other herbs taken internally, such as cleavers (*Galium aparine*), calendula (*Calendula officinalis*), and phytolacca (poke root), target the lymphatic system and may help to enhance the activity of the body's internal filtration system. Since phytolacca can be toxic, it should only be used by patients under the care of a skilled practitioner. Topical applications are also useful in relieving the discomfort of mumps. A cloth dipped in a heated mixture of vinegar and cayenne

(*Capsicum frutescens*) can be wrapped around the neck several times a day. Cleavers or calendula can also be combined with vinegar, heated, and applied in a similar manner.

Prognosis

When mumps is uncomplicated, prognosis is excellent. However, in rare cases, a relapse occurs after about two weeks. Complications can also delay complete recovery.

Prevention

A vaccine exists to protect against mumps. The vaccine preparation (MMR) is usually given as part of a combination injection that helps protect against measles, mumps, and **rubella**. MMR is a live vaccine administered in one dose between the ages of 12-15 months, 4-6 years, or 11-12 years. Persons who are unsure of their mumps history and/or mumps vaccination history should be vaccinated. Susceptible health care workers, especially those who work in hospitals, should be vaccinated. Because mumps is still prevalent throughout the world, susceptible persons over age one who are traveling abroad would benefit from receiving the mumps vaccine.

The mumps vaccine is extremely effective, and virtually everyone should be vaccinated against this disease. There are, however, a few reasons why people should *not* be vaccinated against mumps:

- Pregnant women who contract mumps during pregnancy have an increased rate of miscarriage, but not birth defects. As a result, pregnant women should not receive the mumps vaccine because of the possibility of damage to the fetus. Women who have had the vaccine should postpone pregnancy for three months after vaccination.
- Unvaccinated persons who have been exposed to mumps should not get the vaccine, as it may not provide protection. The person should, however, be vaccinated if no symptoms result from the exposure to mumps.
- Persons with minor fever-producing illnesses, such as an upper respiratory infection, should not get the vaccine until the illness has subsided.
- Because mumps vaccine is produced using eggs, individuals who develop hives, swelling of the mouth or throat, dizziness, or breathing difficulties after eating eggs should not receive the mumps vaccine.
- Persons with immune deficiency diseases and/or those whose immunity has been suppressed with anticancer drugs, corticosteroids, or radiation should not receive the vaccine. Family members of immunocompromised people, however, should get vaccinated to reduce the risk of mumps.
- The CDC recommends that all children infected with human immunodeficiency disease (HIV) who are asymptomatic should receive an the MMR vaccine at 15 months of age.

The mumps vaccine has been controversial in recent years because of concern that its use was linked to a rise in the rate of childhood **autism**. The negative publicity given to the vaccine in the mass media led some parents to refuse to immunize their children with the MMR vaccine. One result has been an increase in the number of mumps outbreaks in several European countries, including Italy and the United Kingdom.

In the fall of 2002, the *New England Journal of Medicine* published a major Danish study disproving the hypothesis of a connection between the MMR vaccine and autism. A second study in Finland showed that the vaccine is not associated with aseptic meningitis or encephalitis as well as autism. Since these studies were published, American primary care physicians have once again reminded parents of the importance of immunizing their children against mumps and other childhood diseases.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Gabutti, G., M. C. Rota, S. Salmaso, et al. "Epidemiology of Measles, Mumps and Rubella in Italy." *Epidemiology and Infection* 129 (December 2002): 543–550.

Kimmel, S. R. "Vaccine Adverse Events: Separating Myth from Reality." *American Family Physician* 66 (December 1, 2002): 2113–2120.

Madsen, K. M., A. Hviid, M. Vestergaard, et al. "A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism." *New England Journal of Medicine* 347 (November 7, 2002): 1477–1482.

Makela, A., J. P. Nuorti, and H. Peltola. "Neurologic Disorders after Measles-Mumps-Rubella Vaccination." *Pediatrics* 110 (November 2002): 957–963.

McKie, A., D. Samuel, B. Cohen, and N. A. Saunders. "A Quantitative Immuno-PCR Assay for the Detection of Mumps-Specific IgG." *Journal of Immunological Methods* 270 (December 1, 2002): 135–141.

Nielsen, S. E., O. H. Nielsen, B. Vainer, and M. H. Claesson. "Inflammatory Bowel Disease—Do Microorganisms Play a Role?" [in Danish] *Ugeskrift for laeger* 164 (December 9, 2002): 5947–5950.

Pugh, R. N., B. Akinosi, S. Pooransingh, et al. "An Outbreak of Mumps in the Metropolitan Area of Walsall, UK." *International Journal of Infectious Diseases* 6 (December 2002): 283–287.

ORGANIZATIONS

American Academy of Pediatrics (AAP), 141 Northwest Point Boulevard, Elk Grove Village, IL, 60007-1098, (847) 434-4000, (847) 424-8000, kidsdocs@aap.org, http://www.aap.org.

Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

Ron Gasbarro, PharmD
Rebecca J. Frey, PhD

Munchausen syndrome

Definition

Munchausen syndrome is a psychiatric disorder that causes an individual to self-inflict injury or illness or to fabricate symptoms of physical or mental illness, in order to receive medical care or hospitalization. In a variation of the disorder, Munchausen by proxy (MSBP), an individual, typically a mother, intentionally causes or fabricates illness in a child or other person under her care.

Description

Munchausen syndrome takes its name from Baron Karl Friederich von Munchausen, an 18th century German military man known for his tall tales. The disorder first appeared in psychiatric literature in the early 1950s when it was used to describe patients who sought hospitalization by inventing symptoms and complicated medical histories, and/or inducing illness and injury in themselves. Categorized as a factitious disorder (a disorder in which the physical or psychological symptoms are under voluntary control), Munchausen's syndrome seems to be motivated by a need to assume the role of a patient. Unlike **malingering**, there does not seem to be any clear secondary gain (e.g., money) in Munchausen syndrome.

Individuals with Munchausen by proxy syndrome use their child (or another dependent person) to fulfill their need to step into the patient role. The disorder most commonly victimizes children from birth to 8 years old. Parents with MSBP may only exaggerate or fabricate their child's symptoms, or they may deliberately induce symptoms through various methods, including **poisoning**, suffocation, **starvation**, or infecting the child's bloodstream.

Causes and symptoms

The exact cause of Munchausen syndrome is unknown. It has been theorized that Munchausen patients are motivated by a desire to be cared for, a need for attention, dependency, an ambivalence toward doctors, or a need to suffer. Factors that may predispose an individual to Munchausen's include a serious illness in childhood or an existing personality disorder.

The Munchausen patient presents a wide array of physical or psychiatric symptoms, usually limited only by their medical knowledge. Many Munchausen patients are very familiar with medical terminology and symptoms. Some common complaints include fevers, **rashes**, abscesses, bleeding, and **vomiting**. Common Munchausen by proxy symptoms include apnea (cessation of breathing), **fever**, **vomiting**, and **diarrhea**. In both Munchausen and MSBP syndromes, the suspected illness does not respond to a normal course of treatment. Patients or parents may push for invasive diagnostic procedures and display an extraordinary depth of knowledge of medical procedures.

Diagnosis

Because Munchausen sufferers often go from doctor to doctor, gaining admission into many hospitals along the way, diagnosis can be difficult. They are typically detected rather than diagnosed. During a course of treatment, they may be discovered by a hospital employee who encountered them during a previous hospitalization. Their caregivers may also notice that symptoms such as high fever occur only when the patient is left unattended. Occasionally, unprescribed medication used to induce symptoms is found with the patient's belongings. When the patient is confronted, they often react with outrage and check out of the hospital to seek treatment at another facility with a new caregiver.

Treatment

There is no clearly effective treatment for Munchausen syndrome. Extensive **psychotherapy** may be helpful with some Munchausen patients. If Munchausen syndrome co-exists with other mental disorders, such as a personality disorder, the underlying disorder is typically treated first.

Prognosis

The infections and injuries Munchausen patients self-inflict can cause serious illness. Patients often undergo countless unnecessary surgeries throughout their lifetimes. In addition, because of their frequent

KEY TERMS

Apnea—A cessation of breathing.

Factitious disorder—A disorder in which the physical or psychological symptoms are under voluntary control.

hospitalizations, they have difficulty holding down a job. Further, their chronic health complaints may damage interpersonal relationships with family and friends. Children victimized by sufferers of MSBP are at a real risk for serious injury and possible **death**. Those who survive physically unscathed may suffer developmental problems later in life.

Prevention

Because the cause of Munchausen syndrome is unknown, formulating a prevention strategy is difficult. Some medical facilities and healthcare practitioners have attempted to limit hospital admissions for Munchausen patients by sharing medical records. While these attempts may curb the number of hospital admissions, they do not treat the underlying disorder and may endanger Munchausen sufferers that have made themselves critically ill and require treatment. Children who are found to be victims of persons with Munchausen by proxy syndrome should be immediately removed from the care of the abusing parent or guardian.

ORGANIZATIONS

American Psychiatric Association (APA), 1000 Wilson Boulevard, Suite 1825, Arlington, VA, 22209, (888) 357-7924, apa@psych.org, http://www.psych.org.

American Psychological Association (APA), 750 First St. NE, Washington, DC, 20002-4242, (202) 336-5500, (800) 374-2721, http://www.apa.org/.

National Alliance for the Mentally Ill (NAMI), 3803 N. Fairfax Dr., Suite 100, Arlington, VA, 22203, (703) 524-7600, (703) 524-9094, (800) 950-6264, http://www.nami.org.

National Institute of Mental Health (NIMH). http://www.nimh.nih.gov

Paula Anne Ford-Martin

Mupirocin *see* **Antibiotics, topical**

Murine (endemic) typhus *see* **Typhus**

Muscle cramps *see* **Muscle spasms and cramps**

Muscle relaxants

Definition

Skeletal muscle relaxants are drugs that help loosen up or relax the muscles that control skeletal (body) movements. They are a separate class of drugs from the muscle relaxant drugs, given intravenously, to relax the same muscles for surgery or intubation.

Purpose

Skeletal muscle relaxants may be used to relieve spastic or tight muscles in diseases like **tetanus**, **multiple sclerosis**, **spinal cord injury**, or **stroke**. They are also used to relieve **muscle spasms** following injuries or minor muscle strains. Dantrolene (Dantrium) has been used to prevent or treat malignant hyperthermia in anesthesia or surgery.

Description

Skeletal muscle relaxants are divided into two groups: one, containing most of the drugs in this class, acts via the central nervous system to relax muscles; Dantrium is the only drug that acts directly on muscles.

Baclofen (Lioresal) may be administered orally or injected directly into the spinal-fluid sac to control muscle spasms.

Carisoprodol (Soma), chlorphenesin (Maolate), chlorzoxazone (Paraflex), cyclobenzaprine (Flexeril), diazepam (Valium), metaxalone (Skelaxin), methocarbamol (Robaxin), and orphenadrine (Norflex) are used, along with rest and perhaps **physical therapy**, to treat muscle spasms from sprains and minor injuries and to assist in **rehabilitation** following serious illness, major surgery, or stroke.

Diazepam (Valium) and methocarbamol (Robaxin) can be given by injection to relieve muscle spasms associated with tetanus.

Recommended dosage

Dose varies with the drug, route of administration, and purpose. There may be individual variations in absorption that require doses higher than those usually recommended. Consult specific references for further information.

Precautions

All drugs in this class may cause **sedation**. Baclofen, when injected into the spinal fluid sac, may produce unconsciousness, **shock**, and **respiratory failure**.

KEY TERMS

Central nervous system—The brain and spinal cord.

Sedative—Medicine used to treat nervousness or restlessness.

Spasm—Sudden, involuntary tightening or tensing of a muscle or a group of muscles.

Tranquilizer (minor)—A drug that has a calming effect and is used to treat anxiety and emotional tension.

Diazepam may be addictive.

Dantrolene may damage the liver.

Tizanidine may cause low blood pressure; this may be controlled by starting with a low dose and increasing the dose gradually. Rarely, it can cause liver damage.

Methocarbamol and chlorzoxazone may cause harmless color changes in urine—orange or reddish-purple with chlorzoxazone and purple, brown, or green with methocarbamol. The urine will return to its normal color when the patient stops taking the medicine.

Not all drugs in this group have been evaluated for safety in **pregnancy** and breast feeding.

Baclofen passes into breast milk; breast feeding while taking it is not recommended.

Diazepam crosses the placenta and into breast milk; breast fed babies may become drowsy and lethargic.

Side effects

Drugs in this class may produce **dizziness**, drowsiness, or headaches. Alcohol may increase these effects.

Paradoxically, these drugs may cause stimulation and irritability.

Skeletal muscle relaxant drugs may cause **rashes**, with or without **itching**.

These drugs may produce upset stomach and **nausea**.

Interactions

Skeletal muscle relaxants have many potential **drug interactions**. Individual references should be consulted.

Because these drugs cause sedation, they should be used with caution with other drugs that may also cause drowsiness.

The activity of diazepam may be increased by drugs that inhibit its metabolism in the liver. These include: Cimetidine, **oral contraceptives**, Disulfiram, Fluoxetine, Isoniazid, Ketoconazole, Metoprolol, Propoxyphene, Propranolol, and Valproic acid.

Dantrolene may have an interaction with estrogens. Although no interaction has been demonstrated, the rate of liver damage in women over the age of 35 who were taking estrogens is higher than in other groups.

Samuel D. Uretsky, PharmD

Muscle spasms and cramps

Definition

Muscle spasms and cramps are spontaneous, often painful muscle contractions.

Description

Most people are familiar with the sudden **pain** of a muscle cramp. The rapid, uncontrolled contraction, or spasm, happens unexpectedly, with either no stimulation or some trivially small one. The muscle contraction and pain last for several minutes, and then slowly ease. Cramps may affect any muscle, but are most common in the calves, feet, and hands. While painful, they are harmless, and in most cases, not related to any underlying disorder. Nonetheless, cramps and spasms can be manifestations of many neurological or muscular diseases.

The terms cramp and spasm can be somewhat vague, and they are sometimes used to include types of abnormal muscle activity other than sudden painful contraction. These include stiffness at rest, slow muscle relaxation, and spontaneous contractions of a muscle at rest (fasciculation). Fasciculation is a type of painless muscle spasm, marked by rapid, uncoordinated contraction of many small muscle fibers. A critical part of diagnosis is to distinguish these different meanings and to allow the patient to describe the problem as precisely as possible.

Causes and symptoms

Causes

Normal voluntary muscle contraction begins when electrical signals are sent from the brain through the spinal cord along nerve cells called motor neurons.

These include both the upper motor neurons within the brain and the lower motor neurons within the spinal cord and leading out to the muscle. At the muscle, chemicals released by the motor neuron stimulate the internal release of **calcium** ions from stores within the muscle cell. These calcium ions then interact with muscle proteins within the cell, causing the proteins (actin and myosin) to slide past one another. This motion pulls their fixed ends closer, thereby shortening the cell and, ultimately, the muscle itself. Recapture of calcium and unlinking of actin and myosin allows the muscle fiber to relax.

Abnormal contraction may be caused by abnormal activity at any stage in this process. Certain mechanisms within the brain and the rest of the central nervous system help regulate contraction. Interruption of these mechanisms can cause spasm. Motor neurons that are overly sensitive may fire below their normal thresholds. The muscle membrane itself may be overly sensitive, causing contraction without stimulation. Calcium ions may not be recaptured quickly enough, causing prolonged contraction.

Interruption of brain mechanisms and overly sensitive motor neurons may result from damage to the nerve pathways. Possible causes include **stroke**, **multiple sclerosis**, **cerebral palsy**, neurodegenerative diseases, trauma, **spinal cord injury**, and nervous system poisons such as strychnine, **tetanus**, and certain insecticides. Nerve damage may lead to a prolonged or permanent muscle shortening called contracture.

Changes in muscle responsiveness may be due to or associated with:

- Prolonged exercise. Curiously, relaxation of a muscle actually requires energy to be expended. The energy is used to recapture calcium and to unlink actin and myosin. Normally, sensations of pain and fatigue signal that it is time to rest. Ignoring or overriding those warning signals can lead to such severe energy depletion that the muscle cannot be relaxed, causing a cramp. The familiar advice about not swimming after a heavy meal, when blood flow is directed away from the muscles, is intended to avoid this type of cramp. Rigor mortis, the stiffness of a corpse within the first 24 hours after death, is also due to this phenomenon.
- Dehydration and salt depletion. This may be brought on by protracted vomiting or diarrhea, or by copious sweating during prolonged exercise, especially in high temperatures. Loss of fluids and salts—especially sodium, potassium, magnesium, and calcium—can disrupt ion balances in both muscle and nerves. This can prevent them from responding and recovering normally, and can lead to cramp.
- Metabolic disorders that affect the energy supply in muscle. These are inherited diseases in which particular muscle enzymes are deficient. They include deficiencies of myophosphorylase (McArdle's disease), phosphorylase b kinase, phosphofructokinase, phosphoglycerate kinase, and lactate dehydrogenase.
- Myotonia. This causes stiffness due to delayed relaxation of the muscle, but does not cause the spontaneous contraction usually associated with cramps. However, many patients with myotonia do experience cramping from exercise. Symptoms of myotonia are often worse in the cold. Myotonias include myotonic dystrophy, myotonia congenita, paramyotonia congenita, and neuromyotonia.

Fasciculations may be due to **fatigue**, cold, medications, metabolic disorders, nerve damage, or neurodegenerative disease, including **amyotrophic lateral sclerosis**. Most people experience brief, mild fasciculations from time to time, usually in the calves.

Symptoms

The pain of a muscle cramp is intense, localized, and often debilitating Coming on quickly, it may last for minutes and fade gradually. **Contractures** develop more slowly, over days or weeks, and may be permanent if untreated. Fasciculations may occur at rest or after muscle contraction, and may last several minutes.

Diagnosis

Abnormal contractions are diagnosed through a careful medical history, physical and neurological examination, and **electromyography** of the affected muscles. Electromyography records electrical activity in the muscle during rest and movement.

Treatment

Most cases of simple cramps require no treatment other than patience and stretching. Gently and gradually stretching and massaging the affected muscle may ease the pain and hasten recovery. In some cases **hydrotherapy**, **yoga**, or **massage therapy** may prove beneficial.

More prolonged or regular cramps may be treated with drugs such as carbamazepine, phenytoin, or quinine. Fluid and salt replacement, either orally or intravenously, is used to treat **dehydration**. Treatment of underlying metabolic or neurologic disease, where possible, may help relieve symptoms.

KEY TERMS

Motor neuron—Nerve cells within the central nervous system that carry nerve impulses controlling muscle movement.

Alternative treatment

Cramps may be treated or prevented with Gingko (*Ginkgo biloba*) or Japanese quince (*Chaenomeles speciosa*). Supplements of vitamin E, niacin, calcium, and magnesium may also help. Taken at bedtime, they may help to reduce the likelihood of night cramps.

Prognosis

Occasional cramps are common, and have no special medical significance.

Prevention

The likelihood of developing cramps may be reduced by eating a healthy diet with appropriate levels of **minerals**, and getting regular **exercise** to build up energy reserves in muscle. Avoiding exercising in extreme heat helps prevent heat cramps. Heat cramps can also be avoided by taking salt tablets and water before prolonged exercise in extreme heat. Taking a warm bath before bedtime may increase circulation to the legs and reduce the incidence of nighttime leg cramps.

Resources

BOOKS

Barron, Patrick. *Hydrotherapy Theory & Technique*,4th ed. St. James City, FL: Pine Island Publishers, 2009.

Faye, Leonard J. *Goodbye Back Pain: A Suffers Guide to Full Back Recovery and Future Prevention*. Charleston, SC: BookSurge Publishing, 2008.

Houglum, Peggy. *Therapeutic Exercise for Musculoskeletal Injuries*, 3rd ed. Champaign, IL: Human Kinetics, 2010.

Rountree, Sage. *The Athlete's Pocket Guide to Yoga: 50 Routines for Flexibility, Balance, and Focus*. Boulder, CO: VeloPress, 2009.

Schenkman, Steven. *Massage Therapy: What It Is and How It Works*. Florence, KY; Cengage Learning, 2009.

Sharon, Michael. *Nutrient A–Z: A User's Guide to Foods, Herbs, Vitamins, Minerals & Supplements*, 4th ed. New York, NY: Carlton Publishing Group, 2009.

Weintraub, Michael I., Ravinder Mamtani, and Marc S. Micozzi, editors. *Complementary and Integrative Medicine in Pain Management*. New York: Springer, 2008.

ORGANIZATIONS

American Academy of Neurology , 1080 Montreal Ave., Saint Paul, MN, 55116, (800) 879–1960, http://www.aan.com.

American Association of Naturopathic Physicians, 8201 Greensboro Dr., Suite 300, McLean, VA, 22102, (206) 298–0126, http://naturopathic.org.

American Holistic Medical Association., PO Box 2016, Edmonds, WA, 98020, (425) 967–0737, http://www.holisticmedicine.org.

American Massage Therapy Association., 500 Davis St., Evanston, IL, 60201, (877) 905–2700, www.amtamassage.org.

National Institute of Neurological Disorders and Stroke (NINDS), P.O. Box 5801, Bethesda, MD, 20824, (301) 496–5751, (800) 352–9424, http://www.ninds.nih.gov.

Richard Robinson
Laura Jean Cataldo, RN, Ed.D.

Muscular dystrophy

Definition

Muscular dystrophy (MD) is the name for a group of inherited disorders in which strength and muscle bulk gradually decline. Nine types of muscular dystrophies are generally recognized.

Demographics

According to National Institute for Neurological Disorders and **Stroke** (NINDS), MD occurs worldwide, and affects all races. Its incidence varies, as some types are more common than others. The most common forms in children are Duchenne and Becker MD and affect approximately 1 in every 3,500 to 5,000 boys, or between 400 and 600 live male births each year in the United States. Between 400 and 600 boys in the United States are born with these conditions each year. Females are rarely affected by these forms of muscular dystrophy. In Europe, the prevalence of Duchenne and Becker MD is 5 per 100,000 individuals.

Description

The muscular dystrophies include:

- ***Duchenne muscular dystrophy (DMD)***: DMD affects young boys, causing progressive muscle weakness, usually beginning in the legs. It is a severe form of muscular dystrophy. DMD occurs in about one in 3,500 male births, and affects approximately 8,000 boys and young men in the United States. A milder form occurs in a very small number of female carriers.

- *Becker muscular dystrophy (BMD)*: BMD affects older boys and young men, following a milder course than DMD. It occurs in about one in 30,000 male births.
- *Emery–Dreifuss muscular dystrophy (EDMD)*: EDMD affects both males and females because it can be inherited as an autosomal dominant or recessive disorder. Symptoms include contractures and weakness in the calves, weakness in the shoulders and upper arms, and problems in the way electrical impulses travel through the heart to make it beat (heart conduction defects). Fewer than 300 cases of EDMD have been reported in the medical literature.
- *Limb–girdle muscular dystrophy (LGMD)*: LGMD begins in late childhood to early adulthood and affects both men and women, causing weakness in the muscles around the hips and shoulders, and weakness in the limbs. It is the most variable of the muscular dystrophies, and there are several different forms of the condition now recognized. Many people with suspected LGMD have probably been misdiagnosed in the past, and therefore, the prevalence of the condition is difficult to estimate. The highest prevalence of LGMD is in a small mountainous Basque province in northern Spain, where the condition affects 69 persons per million.
- *Facioscapulohumeral muscular dystrophy (FSH)*: FSH, also known as Landouzy–Dejerine condition, begins in late childhood to early adulthood and affects both men and women, causing weakness in the muscles of the face, shoulders, and upper arms. The hips and legs may also be affected. FSH occurs in about one out of every 20,000 people, and affects approximately 13,000 people in the United States.
- ***Myotonic dystrophy***: Also known as Steinert's disease, it affects both men and women, causing generalized weakness first seen in the face, feet, and hands. It is accompanied by the inability to relax the affected muscles (myotonia). Symptoms may begin from birth through adulthood. It is the most common form of muscular dystrophy, affecting more than 30,000 people in the United States.
- *Oculopharyngeal muscular dystrophy (OPMD)*: OPMD affects adults of both sexes, causing weakness in the eye muscles and throat. It is most common among French Canadian families in Quebec, and in Spanish American families in the southwestern United States.
- *Distal muscular dystrophy (DD)*: DD is a group of rare muscle diseases that have weakness and wasting of the distal (farthest from the center) muscles of the forearms, hands, lower legs, and feet in common. In general, the DDs are less severe, progress more slowly, and involve fewer muscles than the other dystrophies. DD usually begins in middle age or later, causing weakness in the muscles of the feet and hands. It is most common in Sweden, and rare in other parts of the world.
- *Congenital muscular dystrophy (CMD)*: CMD is a rare group of muscular dystrophies that have in common the presence of muscle weakness at birth (congenital), and abnormal muscle biopsies. CMD results in generalized weakness, and usually progresses slowly. A subtype, called Fukuyama CMD, also involves mental retardation and is more common in Japan.

Risk factors

Since the muscular dystrophies are inherited, people with a family history of MD are at increased risk.

Causes and symptoms

The muscular dystrophies are genetic conditions, meaning they are caused by alterations in genes. Genes, which are linked together on chromosomes, have two functions; they code for the production of proteins, and they are the material of inheritance. Parents pass along genes to their children, providing them with a complete set of instructions for making their own proteins.

Because both parents contribute genetic material to their offspring, each child carries two copies of almost every gene, one from each parent. For some conditions to occur, both copies must be altered. Such conditions are called autosomal recessive conditions. Some forms of LGMD and DD exhibit this pattern of inheritance, as does CMD. A person with only one altered copy, called a carrier, will not have the condition, but may pass the altered gene on to his children. When two carriers have children, the chances of having a child with the condition is one in four for each **pregnancy**.

Other conditions occur when only one altered gene copy is present. Such conditions are called autosomal dominant conditions. DM, FSH, and OPMD exhibit this pattern of inheritance, as do some forms of DD and LGMD. When a person affected by the condition has a child with someone not affected, the chances of having an affected child is one in two.

Because of chromosomal differences between the sexes, some genes are not present in two copies. The chromosomes that determine whether a person is male or female are called the X and Y chromosomes. A person with two X chromosomes is female, while a person with one X and one Y is male. While the X chromosome carries many genes, the Y chromosome carries almost none. Therefore, a male has only one copy of each gene

on the X chromosome, and if it is altered, he will have the condition that alteration causes. Such conditions are said to be X–linked. X–linked conditions include DMD, BMD, and EDMD. Women are not usually affected by X–linked conditions, since they will likely have one unaltered copy between the two chromosomes. Some female carriers of DMD have a mild form of the condition, probably because their one unaltered gene copy is shut down in some of their cells.

Women carriers of X–linked conditions have a one in two chance of passing the altered gene on to each child born. Daughters who inherit the altered gene will be carriers. A son born without the altered gene will be free of the condition and cannot pass it on to his children. A son born with the altered gene will have the condition. He will pass the altered gene on to each of his daughters, who will then be carriers, but to none of his sons (because they inherit his Y chromosome).

Not all genetic alterations are inherited. As many as one third of the cases of DMD are due to new mutations that arise during egg formation in the mother. New mutations are less common in other forms of muscular dystrophy.

Several of the muscular dystrophies, including DMD, BMD, CMD, and most forms of LGMD, are due to alterations in the genes for a complex of muscle proteins. This complex spans the muscle cell membrane (a thin sheath that surrounds each muscle cell) to unite a fibrous network on the interior of the cell with a fibrous network on the outside. Theory holds that by linking these two networks, the complex acts as a "shock absorber," redistributing and evening out the forces generated by contraction of the muscle, thereby preventing rupture of the muscle membrane. Alterations in the proteins of the complex lead to deterioration of the muscle during normal contraction and relaxation cycles. Symptoms of these conditions set in as the muscle gradually exhausts its ability to repair itself.

Both DMD and BMD are caused by alterations in the gene for the protein called dystrophin. The alteration leading to DMD prevents the formation of any dystrophin, while that of BMD allows some protein to be made, accounting for the differences in severity and age of onset between the two conditions. Differences among the other muscular dystrophies in terms of the muscles involved and the ages of onset are less easily explained.

A number of genes have been found to cause LGMD. A majority of the more severe autosomal recessive types of LGMD with childhood–onset are caused by alterations in the genes responsible for making proteins called sarcoglycans. The sarcoglycans are a complex of proteins that are normally located in the muscle cell membrane along with dystrophin. Loss of these proteins causes the muscle cell membrane to lose some of its shock absorber qualities. The genes responsible include LGMD2D on chromosome 17, which codes for the alpha–sarcoglycan protein; LGMD2E on chromosome 4, which codes for the beta–sarcoglycan protein; LGMD2C on chromosome 13, which codes for the gamma–sarcoglycan protein; and LGMD2F on chromosome 5, which codes for the delta–sarcoglycan protein. Some cases of autosomal recessive LGMD are caused by an alteration in a gene, LGMD2A, on chromosome 15, which codes for a muscle enzyme, calpain 3. The relationship between this alteration and the symptoms of the condition is unclear. Alterations in a gene called LGMD2B on chromosome 2 that codes for the dysferlin protein, is also responsible for a minority of autosomal recessive LGMD cases. The exact role of dysferlin is not known. Finally, alterations in the LGMD2G gene on chromosome 17 which codes for a protein, telethonin, is responsible for autosomal recessive LGMD in two reported families. The exact role of telethonin is not known. Some families with autosomal recessive LGMD are not accounted for by alterations in any of the above mentioned genes, indicating that there are as yet undiscovered genes which can cause LGMD. The autosomal dominant LGMD genes have mostly been described in single families. These types of LGMD are considered quite rare.

The genes causing these types of LGMD, their chromosomal location, and the proteins they code for (when known) are listed below:

- LGMD1A (chromosome 5): myotilin
- LGMD1B (chromosome 1): laminin
- LGMD1C (chromosome 3): caveolin
- LGMD1D (chromosome 6)
- LGMD1E (chromosome 7)
- COL6A1 (chromosome 21): collagen VI alpha 1
- COL6A2 (chromosome 21): collagen VI alpha 2
- COL6A3 (chromosome 2): collagen VI alpha 3

The causes of the other muscular dystrophies are not as well understood:

- EDMD is due to a alteration in the gene for a protein called emerin, which is found in the membrane of a cell's nucleus, but whose exact function is unknown.
- Myotonic dystrophy is caused by alterations in a gene on chromosome 19 for an enzyme called myotonin protein kinase that may control the flow of charged particles within muscle cells. This gene alteration is called a triple repeat, meaning it contains extra triplets of DNA code. It is possible that this

alteration affects nearby genes as well, and that the widespread symptoms of myotonic dystrophy are due to a range of genetic disruptions.

- The gene for OPMD appears to also be altered with a triple repeat. The function of the affected protein may involve translation of genetic messages in a cell's nucleus.
- The gene(s) for FSH is located on the long arm of chromosome 4 at gene location 4q35. Nearly all cases of FSH are associated with a deletion (missing piece) of genetic material in this region. Researchers are investigating the molecular connection of this deletion and FSH. It is not yet certain whether the deleted material contains an active gene or changes the regulation or activity of a nearby FSH gene. A small number of FSH cases are not linked to chromosome 4. Their linkage to any other chromosome or genetic feature is under investigation.
- The gene(s) responsible for DD have not yet been found.
- About 50% of individuals with CMD have their condition as a result of deficiency in a protein called merosin, which is made by a gene called laminin. The merosin protein usually lies outside muscle cells and links them to the surrounding tissue. When merosin is not produced, the muscle fibers degenerate soon after birth. A second gene called integrin is responsible for CMD in a few individuals but alterations in this gene are a rare cause of CMD. The gene responsible for Fukuyama CMD is FCMD and it is responsible for making a protein called fukutin whose function is not clear.

All of the muscular dystrophies are marked by muscle weakness as the major symptom. The distribution of symptoms, age of onset, and progression differ significantly. **Pain** is sometimes a symptom of each, usually due to the effects of weakness on joint position.

DUCHENNE MUSCULAR DYSTROPHY (DMD). A boy with Duchenne muscular dystrophy usually begins to show symptoms as a pre–schooler. The legs are affected first, making walking difficult and causing balance problems. Most patients walk three to six months later than expected and have difficulty running. Later on, a boy with DMD will push his hands against his knees to rise to a standing position, to compensate for leg weakness. About the same time, his calves will begin to enlarge, though with fibrous tissue rather than with muscle, and feel firm and rubbery; this condition gives DMD one of its alternate names, pseudohypertrophic muscular dystrophy. He will widen his stance to maintain balance, and walk with a waddling gait to advance his weakened legs. **Contractures** (permanent muscle tightening) usually begin by age five or six, most severely in the calf muscles. This pulls the foot down and back, forcing the boy to walk on tip–toes, and further decreases balance. Climbing stairs and rising unaided may become impossible by age nine or ten, and most boys use a wheelchair for mobility by the age of 12. Weakening of the trunk muscles around this age often leads to **scoliosis** (a side–to–side spine curvature) and **kyphosis** (a front–to–back curvature).

The most serious weakness of DMD is weakness of the diaphragm, the sheet of muscles at the top of the abdomen that perform the main work of breathing and coughing. Diaphragm weakness leads to reduced energy and stamina, and increased lung infection because of the inability to **cough** effectively. Young men with DMD often live into their twenties and beyond, provided they have mechanical ventilation assistance and good respiratory hygiene.

Among males with DMD, the incidence of **cardiomyopathy** (weakness of the heart muscle), increases steadily in teenage years. Almost all patients have cardiomyopathy after 18 years of age. It has also been shown that carrier females are at increased risk for cardiomyopathy and should also be screened.

About one third of males with DMD experience specific learning disabilities, including difficulty learning by ear rather than by sight and difficulty paying attention to long lists of instructions. Individualized educational programs usually compensate well for these disabilities.

BECKER MUSCULAR DYSTROPHY (BMD). The symptoms of BMD usually appear in late childhood to early adulthood. Though the progression of symptoms may parallel that of DMD, the symptoms are usually milder and the course more variable. The same pattern of leg weakness, unsteadiness, and contractures occur later for the young man with BMD, often allowing independent walking into the twenties or early thirties. Scoliosis may occur, but is usually milder and progresses more slowly. Cardiomyopathy occurs more commonly in BMD. Problems may include irregular heartbeats (**arrhythmias**) and congestive **heart failure**. Symptoms may include **fatigue**, **shortness of breath**, chest pain, and **dizziness**. Respiratory weakness also occurs, and may lead to the need for mechanical ventilation.

EMERY–DREIFUSS MUSCULAR DYSTROPHY (EDMD). This type of muscular dystrophy usually begins in early childhood, often with contractures preceding muscle weakness. Weakness affects the shoulder and upper arm initially, along with the calf muscles, leading to foot–drop. Most men with EDMD survive into middle age, although an abnormality in the heart's

rhythm (**heart block**) may be fatal if not treated with a pacemaker.

LIMB–GIRDLE MUSCULAR DYSTROPHY (LGMD). While there are several genes that cause the various types of LGMD, two major clinical forms of LGMD are usually recognized. A severe childhood form is similar in appearance to DMD, but is inherited as an autosomal recessive trait. Symptoms of adult–onset LGMD usually appear in a person's teens or twenties, and are marked by progressive weakness and wasting of the muscles closest to the trunk. Contractures may occur, and the ability to walk is usually lost about 20 years after onset. Some people with LGMD develop respiratory weakness that requires use of a ventilator. Life–span may be somewhat shortened. Autosomal dominant forms usually occur later in life and progress relatively slowly.

FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY (FSH). FSH varies in its severity and age of onset, even among members of the same family. Symptoms most commonly begin in the teens or early twenties, though infant or childhood onset is possible. Symptoms tend to be more severe in those with earlier onset. The condition is named for the regions of the body most severely affected by the condition: muscles of the face (facio–), shoulders (scapulo–), and upper arms (humeral). Hips and legs may be affected as well. Children with FSH may develop partial or complete deafness.

The first symptom noticed is often difficulty lifting objects above the shoulders. The weakness may be greater on one side than the other. Shoulder weakness also causes the shoulder blades to jut backward, called scapular winging. Muscles in the upper arm often lose bulk sooner than those of the forearm, giving a "Popeye" appearance to the arms. Facial weakness may lead to loss of facial expression, difficulty closing the eyes completely, and inability to drink through a straw, blow up a balloon, or whistle. A person with FSH may not be able to wrinkle thier forehead. Contracture of the calf muscles may cause foot–drop, leading to frequent tripping over curbs or rough spots. People with earlier onset often require a wheelchair for mobility, while those with later onset rarely do.

MYOTONIC DYSTROPHY. Symptoms of **myotonic dystrophy** include facial weakness and a slack jaw, drooping eyelids (**ptosis**), and muscle wasting in the forearms and calves. A person with myotonic dystrophy has difficulty relaxing his grasp, especially if the object is cold. Myotonic dystrophy affects heart muscle, causing arrhythmias and heart block, and the muscles of the digestive system, leading to motility disorders and **constipation**. Other body systems are affected as well; myotonic dystrophy may cause **cataracts**, retinal degeneration, mental deficiency, frontal balding, skin disorders, testicular atrophy, **sleep apnea**, and **insulin resistance**. An increased need or desire for sleep is common, as is diminished motivation. The condition is extremely variable; some individuals show profound weakness as a newborn (congenital myotonic dystrophy), others show **mental retardation** in childhood, many show characteristic facial features and muscle wasting in adulthood, while the most mildly affected individuals show only cataracts in middle age with no other symptoms. Individuals with a severe form of mytonic dystropy typically have severe disabilities within 20 years of onset, although most do not require a wheelchair even late in life.

OCULOPHARYNGEAL MUSCULAR DYSTROPHY (OPMD). OPMD usually begins in a person's thirties or forties, with weakness in the muscles controlling the eyes and throat. Symptoms include drooping eyelids and difficulty swallowing (dysphagia). Weakness progresses to other muscles of the face, neck, and occasionally the upper limbs. Swallowing difficulty may cause aspiration, or the introduction of food or saliva into the airways. **Pneumonia** may follow.

DISTAL MUSCULAR DYSTROPHY (DD). DD usually begins in the twenties or thirties, with weakness in the hands, forearms, and lower legs. Difficulty with fine movements such as typing or fastening buttons may be the first symptoms. Symptoms progress slowly, and the condition usually does not affect life span.

CONGENITAL MUSCULAR DYSTROPHY (CMD). CMD is marked by severe muscle weakness from birth, with infants displaying "floppiness," very poor muscle tone, and they often have trouble moving their limbs or head against gravity. Mental function is normal but some are never able to walk. They may live into young adulthood or beyond. In contrast, children with Fukuyama CMD are rarely able to walk, and have severe mental retardation. Most children with this type of CMD die in childhood.

Diagnosis

For most forms of muscular dystrophy, accurate diagnosis is not difficult when done by someone familiar with the range of conditions. There are exceptions, however. Even with a muscle biopsy, it may be difficult to distinguish between FSH and another muscle condition, **polymyositis**. Childhood–onset LGMD is often mistaken for the much more common DMD, especially when it occurs in boys. BMD with an early onset appears very similar to DMD, and a genetic test may be needed to accurately distinguish them. The

KEY TERMS

Amniocentesis—A procedure performed at 16–18 weeks of pregnancy in which a needle is inserted through a woman's abdomen into her uterus to draw out a small sample of the amniotic fluid from around the baby. Either the fluid itself or cells from the fluid can be used for a variety of tests to obtain information about genetic disorders and other medical conditions in the fetus.

Autosomal dominant—A pattern of genetic inheritance where only one abnormal gene is needed to display the trait or disease.

Autosomal recessive—A pattern of genetic inheritance where two abnormal genes are needed to display the trait or disease.

Becker muscular dystrophy (BMD)—A type of muscular dystrophy that affects older boys and men, and usually follows a milder course than Duchenne muscular dystrophy.

Chorionic villus sampling (CVS)—A procedure used for prenatal diagnosis at 10–12 weeks gestation. Under ultrasound guidance a needle is inserted either through the mother's vagina or abdominal wall and a sample of cells is collected from around the fetus. These cells are then tested for chromosome abnormalities or other genetic diseases.

Contracture—A tightening of muscles that prevents normal movement of the associated limb or other body part.

Distal muscular dystrophy (DD)—A form of muscular dystrophy that usually begins in middle age or later, causing weakness in the muscles of the feet and hands.

Duchenne muscular dystrophy (DMD)—The most severe form of muscular dystrophy, DMD usually affects young boys and causes progressive muscle weakness, usually beginning in the legs.

Dystrophin—A protein that helps muscle tissue repair itself. Both Duchenne muscular dystrophy and Becker muscular dystrophy are caused by flaws in the gene that instructs the body how to make this protein.

Facioscapulohumeral muscular dystrophy (FSH)—This form of muscular dystrophy, also known as Landouzy–Dejerine condition, begins in late childhood to early adulthood and affects both men and women, causing weakness in the muscles of the face, shoulders, and upper arms.

Limb–girdle muscular dystrophy (LGMD)—Form of muscular dystrophy that begins in late childhood to early adulthood and affects both men and women, causing weakness in the muscles around the hips and shoulders.

Myotonic dystrophy—A form of muscular dystrophy, also known as Steinert's condition, characterized by delay in the ability to relax muscles after forceful contraction, wasting of muscles, as well as other abnormalities.

Oculopharyngeal muscular dystrophy (OPMD)—Form of muscular dystrophy affecting adults of both sexes, and causing weakness in the eye muscles and throat.

muscular dystrophies may be confused with conditions involving the motor neurons, such as spinal muscular atrophy; conditions of the neuromuscular junction, such as **myasthenia gravis**; and other muscle conditions, as all involve generalized weakness of varying distribution.

Examination

The diagnosis of muscular dystrophy involves a careful medical history and a thorough physical exam to determine the distribution of symptoms and to rule out other causes. Family history may give important clues, since all the muscular dystrophies are genetic conditions (though no family history will be evident in the event of new mutations; in autosomal recessive inheritance, the family history may also be negative).

Tests

Lab tests may include:

- Blood level of the muscle enzyme creatine kinase (CK). CK levels rise in the blood due to muscle damage, and may be seen in some conditions even before symptoms appear.
- Muscle biopsy, in which a small piece of muscle tissue is removed for microscopic examination. Changes in the structure of muscle cells and presence of fibrous tissue or other aberrant structures are characteristic of different forms of muscular dystrophy. The muscle tissue can also be stained to detect the presence or absence of particular proteins, including dystrophin.
- Electromyogram (EMG). This electrical test is used to examine the response of the muscles to stimulation.

Decreased response is seen in muscular dystrophy. Other characteristic changes are seen in DM.

- Genetic tests. Several of the muscular dystrophies can be positively identified by testing for the presence of the altered gene involved. Accurate genetic tests are available for DMD, BMD, DM, several forms of LGMD, and EDMD. Genetic testing for some of these conditions in future pregnancies of an affected individual or parents of an affected individual can be done before birth through amniocentesis or chorionic villus sampling. Prenatal testing can only be undertaken after the diagnosis in the affected individual has been genetically confirmed and the couple has been counseled regarding the risks of recurrence.
- Other specific tests as necessary. For EDMD, DMD and BMD, for example, an electrocardiogram may be needed to test heart function, and hearing tests are performed for children with FSH.

Prenatal diagnosis (testing of the baby while in the womb) can be done for those types of muscular dystrophy where the specific disease–causing gene alteration has been identified in a previously affected family member. Prenatal diagnosis can be done utilizing DNA extracted from tissue obtained by **chorionic villus sampling** or **amniocentesis**.

Treatment

There is no specific treatment that can stop or reverse any form of muscular dytrophy. MD management is focused on improving muscle and joint function, and slowing muscle deterioration. Treatment also seeks to prevent the complications of weakness, including decreased mobility and dexterity, contractures, scoliosis, heart alterations, and respiratory insufficiency.

Traditional

Physical therapy, regular stretching in particular, is used to maintain the range of motion of affected muscles and to prevent or delay contractures. Braces are used as well, especially on the ankles and feet to prevent tip–toeing. Full–leg braces may be used in children with DMD to prolong the period of independent walking. Strengthening other muscle groups to compensate for weakness may be possible if the affected muscles are few and isolated, as in the earlier stages of the milder muscular dystrophies. Regular, nonstrenuous **exercise** helps maintain general good health. Strenuous exercise is usually not recommended, since it may damage muscles further.

Occupational therapy also provides techniques and tools to compensate for the loss of strength and dexterity. Strategies may include modifications in the home, adaptive utensils and dressing aids, compensatory movements and positioning, wheelchair accessories, or communication aids.

Good **nutrition** helps to promote general health in all the muscular dystrophies. No special diet or supplement has been shown to be of use in any of the conditions. The weakness in the throat muscles seen especially in OPMD and later DMD may necessitate the use of a **gastrostomy** tube, inserted in the stomach to provide nutrition directly.

Drugs

For DMD, prednisone, a corticosteroid, has been shown to delay the progression of disease somewhat, for reasons that are still unclear. Some have reported improvement in strength and function in patients treated with a single dose. Improvement begins within ten days and plateaus after three months. Long–term benefit has not been demonstrated. Prednisone is also prescribed for BMD, though no controlled studies have tested its benefit.

Anticonvulsants, also known as antiepileptics, are also prescribed to control seizures and some muscle activity. Commonly used oral anticonvulsants include carbamazepine, phenytoin, clonazepam, gabapentin, topiramate, and felbamate. Respiratory infections are usually treated with **antibiotics**.

Alternative

When contractures become more pronounced, tenotomy surgery may be performed. In this operation, the tendon of the contractured muscle is cut, and the limb is braced in its normal resting position while the tendon regrows. In FSH, surgical fixation of the scapula can help compensate for shoulder weakness. For a person with OPMD, surgical lifting of the eyelids may help compensate for weakened muscular control. For a person with DM, sleep apnea may be treated surgically to maintain an open airway. Scoliosis surgery is often needed in boys with DMD, but much less often in other muscular dystrophies. Surgery is recommended at a much lower degree of curvature for DMD than for scoliosis due to other conditions, since the decline in respiratory function in DMD makes surgery at a later time dangerous. In this surgery, the vertebrae are fused together to maintain the spine in the upright position. Steel rods are inserted at the time of operation to keep the spine rigid while the bones grow together.

When any type of surgery is performed in patients with muscular dystrophy, anesthesia must be carefully selected. People with MD are susceptible to a severe

reaction, known as malignant hyperthermia, when given halothane anesthetic.

The arrhythmias of EDMD and BMD may be treatable with antiarrhythmia drugs. A pacemaker may be implanted if these do not provide adequate control. Heart transplants are increasingly common for men with BMD. A complete cardiac evaluation is recommended at least once in all carrier females of DMD and EDMD.

People who develop weakness of the diaphragm or other ventilatory muscles may require a mechanical ventilator to continue breathing deeply enough. Air may be administered through a nasal mask or mouthpiece, or through a tracheostomy tube, which is inserted through a surgical incision through the neck and into the windpipe. Most people with muscular dystrophy do not need a tracheostomy, although some may prefer it to continual use of a mask or mouthpiece. Supplemental oxygen is not needed. Good hygiene of the lungs is critical for health and long–term survival of a person with weakened ventilatory muscles. Assisted cough techniques provide the strength needed to clear the airways of secretions; an assisted cough machine is also available and provides excellent results.

Clinical trials for the treatment of muscular dystrophies are currently sponsored by the National Institutes of Health (NIH) and other agencies. In 2009, NIH reported 23 on–going or recently completed studies. Some examples include the following:

- The evaluation of the efficacy of using far infrared radiation to manage muscular dystrophies. (NCT00674843)
- The evaluation of whether a high–dose weekly course of prednisone therapy is safer than and at least as effective as daily dose therapy for people with Duchenne muscular dystrophy. (NCT00110669)
- The study of the early signs and symptoms of fukutin–related protein (FKRP) muscular dystrophy to determine the reasons for differences in disease severity. (NCT00313677)
- The evaluation of the safety and efficacy of antisense oligonucleotides in Duchenne muscular dystrophy. (NCT00159250)

Clinical trial information is constantly updated by NIH and the most recent information on muscular dystrophy trials can be found at: http://clinicaltrials.gov/search/open/condition=%22Muscular+Dystrophies%22

Prognosis

The expected life span for a male with DMD has increased significantly in the past two decades. Most young men will live into their early or mid–twenties. Respiratory infections become an increasing problem as their breathing becomes weaker, and these infections are usually the cause of **death**.

The course of the other muscular dystrophies is more variable; expected life spans and degrees of disability are hard to predict, but may be related to age of onset and initial symptoms. Prediction is made more difficult because, as new genes are discovered, it is becoming clear that several of the dystrophies are not uniform disorders, but rather symptom groups caused by different genes.

People with dystrophies with significant heart involvement (BMD, EDMD, myotonic dystrophy) may nonetheless have almost normal life spans, provided that cardiac complications are monitored and treated aggressively. The respiratory involvement of BMD and LGMD similarly require careful and prompt treatment.

Prevention

There is no way to prevent any of the muscular dystrophies in a person who has the genes responsible for these disorders. Individuals with muscular dystrophy and their families may benefit from genetic counselling for information on the condition and recurrence risks for future pregnancies.

Resources

BOOKS

Abramovitz, Melissa. *Muscular Dystrophy (Diseases and Disorders)*. San Diego, CA: Lucent Books, 2008.

Emery, Alan. *Muscular Dystrophy: The Facts*. New York, NY: Oxford University Press, 2008.

Patridge, T., editor. *Molecular and Cell Biology of Muscular Dystrophy*. Cambridge, MA: Chapman & Hall, 2007.

Stone, Kate, et al. *Occupational Therapy and Duchenne Muscular Dystrophy*. Chichester, UK: Wiley, 2007.

PERIODICALS

Davidson, Z. E., and H. Truby "A review of nutrition in Duchenne muscular dystrophy." *Journal of Human Nutrition and Dietetics* 22, no. 5 (October 2009): 383–393.

Farini, A., et al. "Cell based therapy for Duchenne muscular dystrophy." *Journal of Cell Physiology* 221, no. 3 (December 2009): 526–534.

Mansur, A. Y., and F. Muntoni. "Diagnosis and new treatments in muscular dystrophies." *Journal of Neurology, Neurosurgery, and Psychiatry* 80, no. 7 (July 2009): 706–714.

Meregalli, M., et al. "Combining stem cells and exon skipping strategy to treat muscular dystrophy." *Expert Opinion on Biological Therapy* 8, no. 8 (August 2008): 1051–1061.

Muir, L. A., and J. S. Chamberlain. "Emerging strategies for cell and gene therapy of the muscular dystrophies." *Expert Reviews in Molecular Medicine* 11 (June 2009): e18.

Trollet, C., et al. "Gene therapy for muscular dystrophy: current progress and future prospects." *Expert Opinion on Biological Therapy* 9, no. 7 (July 2009): 849–866.

Zebracki, K., and D. Drotar. "Pain and activity limitations in children with Duchenne or Becker muscular dystrophy." *Developmental Medicine and Child Neurology* 50, no. 7 (July 2008): 546–552.

OTHER

"Becker Muscular Dystrophy (BMD)." *MDA*. Information Page. http://www.mda.org/disease/bmd.html (accessed December 12, 2009)

"Congenital Muscular Dystrophy (CMD)." *MDA*. Information Page. http://www.mda.org/disease/cmd.html (accessed December 12, 2009)

"Duchenne Muscular Dystrophy (DMD)." *MDA*. Information Page. http://www.mda.org/disease/dmd.html (accessed December 12, 2009)

"Emery–Dreifuss Muscular Dystrophy (EDMD)." *MDA*. Information Page. http://www.mda.org/disease/edmd.html (accessed December 12, 2009)

"Limb–Girdle Muscular Dystrophy (LGMD)." *MDA*. Information Page. http://www.mda.org/disease/lgmd.html (accessed December 12, 2009)

"Muscular Dystrophy." *NINDS*. Information Page. http://www.ninds.nih.gov/disorders/md/md.htm (accessed December 12, 2009)

"Myotonic Muscular Dystrophy (MMD)." *MDA*. Information Page. http://www.mda.org/disease/dm.html (accessed December 12, 2009)

ORGANIZATIONS

Centers for Disease Control and Prevention (CDCP), 1600 Clifton Road, N.E., Atlanta, GA, 30333, (404) 639-3311, (800) 311-3435, inquiry@cdc.gov, http://www.cdc.gov.

Facioscapulohumeral Muscular Dystrophy (FSH) Society, 64 Grove Street, Watertown, MA, 02472, (781) 275-7781, (781) 860-0599, info@fshsociety.org, http://www.fshsociety.org.

Muscular Dystrophy Association (MDA), 3300 East Sunrise Drive, Tucson, AZ, 85718-3208, (520) 529-2000, (800) 572-1717, (520) 529-5300, mda@mdausa.org, http://www.mda.org.

Muscular Dystrophy Canada, 2345 Yonge St., Suite 900, TorontoON, Canada, M4P 2E5, (866) MUSCLE-8, (416) 488-7523, http://www.muscle.ca.

Muscular Dystrophy Family Foundation, 7220 U.S. 31 South, Indianapolis, IN, 46227, (317) 923-6333, (800) 544-1213, (317) 923-6334, mdff@mdff.org, http://www.mdff.org.

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), 31 Center Dr., Rm. 4C02, MSC 2350, Bethesda, MD, 20892-2350, (301) 496-8190, (877) 22-NIAMS, NIAMSinfo@mail.nih.gov, http://www.niams.nih.gov.

National Institute of Child Health and Human Development (NICHD), 31 Center Drive, Rm. 2A32, MSC 2425, Bethesda, MD, 20892-2425, (301) 496-5133, (301) 496-7101, http://www.nichd.nih.gov.

National Institute of Neurological Disorders and Stroke (NINDS), PO Box 5801, Bethesda, MD, 20824, (301) 496-5751, (800) 352-9424, http://www.ninds.nih.gov.

Parent Project Muscular Dystrophy (PPMD), 158 Linwood Plaza, Suite 220, Fort Lee, NJ, 07024, (201) 944-9985, (800) 714-5437, (201) 944-9987, info@parentprojectmd.org, http://www.parentprojectmd.org.

Nada Quercia, Msc, CCGC
Monique Laberge, PhD

Mushroom poisoning

Definition

Mushroom **poisoning** refers to the severe and often deadly effects of various toxins that are found in certain types of mushrooms. One type known as *Amanita phalloides*, appropriately called "death cap," accounts for the majority of cases. The toxins initially cause severe abdominal cramping, **vomiting**, and watery **diarrhea**, and then lead to liver and kidney failure.

Description

The highest reported incidences of mushroom poisoning occur in western Europe, where a popular pastime is amateur mushroom hunting. Since the 1970s, the United States has seen a marked increase in mushroom poisoning due to an increase in the popularity of "natural" foods, the use of mushrooms as recreational hallucinogens, and the gourmet qualities of wild mushrooms. About 90% of the deaths due to mushroom poisoning in the United States and western Europe result from eating *Amanita phalloides*. This mushroom is recognized by its metallic green cap (the color may vary from light yellow to greenish brown), white gills (located under the cap), white stem, and bulb-shaped structure at the base of the stem. A pure white variety of this species also occurs. Poisoning results from ingestion of as few as one to three mushrooms. Higher **death** (mortality) rates of more than 50% occur in children less than 10 years of age.

A poisonous mushroom, Amanita muscaria. *(Photo Researchers, Inc.)*

Causes and symptoms

Poisonous mushrooms contain at least two different types of toxins, each of which can cause death if taken in large enough quantities. Some of the toxins found in poisonous mushrooms are among the most potent ever discovered. One group of poisons, known as amatoxins, blocks the production of DNA, the basis of cell reproduction. This leads to the death of many cells, especially those that reproduce frequently such as in the liver, intestines, and kidney. Other mushroom poisons affect the proteins needed for muscle contraction, and therefore reduce the ability of certain muscle groups to perform.

Symptoms of *Amanita* poisoning occur in different stages or phases. These include:

- First phase. Abdominal cramping, nausea, vomiting, and severe watery diarrhea occur anywhere from 6-24 hours after eating the mushroom and last for about 24 hours. These intestinal symptoms can lead to dehydration and low blood pressure (hypotension).
- Second phase. A period of remission of symptoms that lasts 1-2 days. During this time, the patient feels better, but blood tests begin to show evidence of liver and kidney damage.
- Third phase. Liver and kidney failure develop at this point and either lead to death within about a week or recovery within 2-3 weeks.

Other symptoms are due to either a decrease in blood clotting factors that leads to internal bleeding or reduced muscle function, with the development of weakness and **paralysis**.

Diagnosis

In most cases, the fact that the patient has recently eaten wild mushrooms is the clue to the cause of symptoms. Moreover, the identification of any remaining mushrooms by a qualified mushroom specialist (mycologist) can be a key to diagnosis. When in doubt, the toxin known as alpha-amantin can be found in the blood, urine, or stomach contents of an individual who has ingested poisonous *Amanita* mushrooms.

Treatment

It is important to remember that there is no specific antidote for mushroom poisoning. However, several advances in therapy have decreased the death rate over the last several years. Early replacement of lost body fluids has been a major factor in improving survival rates.

Therapy is aimed at decreasing the amount of toxin in the body. Initially, attempts are made to remove toxins from the upper gastrointestinal tract by inducing **vomiting** or by gastric lavage (stomach pumping). After that continuous aspiration of the upper portion of the small intestine through a nasogastric tube is done and oral charcoal (every four hours for 48 hours) is given to prevent absorption of toxin. These measures work best if started within six hours of ingestion.

In the United States, early removal of mushroom poison by way of an artificial kidney machine (dialysis) has become part of the treatment program. This is combined with the correction of any imbalances of salts (electrolytes) dissolved in the blood, such as **sodium** or potassium. An enzyme called thioctic acid and **corticosteroids** also appear to be beneficial, as well as high doses of penicillin. In Europe, a chemical taken from the milk thistle plant, *Silybum marianum*, is also part of treatment. When liver failure develops, **liver transplantation** may be the only treatment option.

Prognosis

The mortality rate has decreased with improved and rapid treatment. However, according to some medical reports death still occurs in 20-30% of cases,

with a higher mortality rate of 50% in children less than 10 years old.

Prevention

The most important factor in preventing mushroom poisoning is to avoid eating wild or noncultivated mushrooms. For anyone not expert in mushroom identification, there are generally no easily recognizable differences between nonpoisonous and poisonous mushrooms. It is also important to remember that most mushroom poisons are not destroyed or deactivated by cooking, canning, freezing, drying, or other means of food preparation.

Resources

OTHER

BBB–Mushroom Toxins. http://www.fda.gov/Food/FoodSafety/FoodborneIllness/FoodborneIllnessFoodbornePathogensNaturalToxins/BadBugBook/ucm070853.htm.

"Cyclopeptide-Containing Mushroom Toxicity." *The Toxikon Multimedia Project Page*. http://www.uic.edu/com/er/toxikon/mushroo.htm.

"Mushroom Poisoning in Children." *American Association of Family Physicians*. http://www.aafp.org/patientinfo/mushroom.html.

David Kaminstein, MD

Music therapy

Definition

Music therapy is a technique of complementary medicine that uses music prescribed in a skilled manner by trained therapists. Programs are designed to help patients overcome physical, emotional, intellectual, and social challenges. Applications range from improving the well being of geriatric patients in nursing homes to lowering the **stress** level and **pain** of women in labor. Music therapy is used in many settings, including schools, **rehabilitation** centers, hospitals, hospices, nursing homes, community centers, and sometimes even in the home.

Purpose

Music can be beneficial for anyone. Although it can be used therapeutically for people who have physical, emotional, social, or cognitive deficits, even those who are healthy can use music to relax, reduce stress, improve mood, or to accompany **exercise**. There are no potentially harmful or toxic effects. Music therapists help their patients achieve a number of goals through music, including improvement of communication, academic strengths, attention span, and motor skills. They may also assist with behavioral therapy and **pain management**.

Demographics

There are about 5000 board certified music therapists in the United States. The field is growing rapidly as an increasing number of both inpatient and outpatient healthcare settings incorporate music therapy into their treatment modalities.

Description

Origins

Music has been used throughout human history to express and affect human emotion. In biblical accounts, King Saul was reportedly soothed by David's harp music, and the ancient Greeks expressed thoughts about music having healing effects as well. Many cultures are steeped in musical traditions. It can change mood, have stimulant or sedative effects, and alter physiologic processes such as heart rate and breathing. The apparent health benefits of music to patients in Veterans Administration hospitals following World War II lead to it being studied and formalized as a complementary healing practice. Musicians were hired to continue working in the hospitals. Degrees in music therapy became available in the late 1940s, and in 1950, the first professional association of music therapists was formed in the United States. The National Association of Music Therapy merged with the American Association of Music Therapy in 1998 to become the American Music Therapy Association.

Physical effects

Brain function physically changes in response to music. The rhythm can guide the body into breathing in slower, deeper patterns that have a calming effect. Heart rate and blood pressure are also responsive to the types of music that are listened to. The speed of the heartbeat tends to speed or slow depending on the volume and speed of the auditory stimulus. Louder and faster noises tend to raise both heart rate and blood pressure; slower, softer, and more regular tones produce the opposite result. Music can also relieve muscle tension and improve motor skills. It is often used to help rebuild physical patterning skills in rehabilitation clinics. Levels of endorphins, natural pain relievers, are increased while listening to music, and levels of stress hormones are decreased. This latter

KEY TERMS

Adjunctive—Refers to a form of treatment that is not strictly necessary to a therapy regimen but is helpful. Music therapy is an example of an adjunctive form of treatment.

Entrainment—The patterning of body processes and movements to the rhythm of music.

Physiologic—Refers to physiology, particularly normal, healthy, physical functioning.

effect may partially explain the ability of music to improve immune function. A study at Michigan State University showed that even 15 minutes of exposure to music could increase interleukin-1 levels, a consequence which also heightens immunity.

Mental effects

Depending on the type and style of sound, music can either sharpen mental acuity or assist in relaxation. Memory and learning can be enhanced, and this used with good results in children with learning disabilities. This effect may also be partially due to increased concentration that many people have while listening to music. Better productivity is another outcome of an improved ability to concentrate. The term "Mozart effect" was coined after a study showed that college students performed better on math problems when listening to classical music.

Emotional effects

The ability of music to influence human emotion is well known, and is used extensively by moviemakers. A variety of musical moods may be used to create feelings of calmness, tension, excitement, or romance. Lullabies have long been popular for soothing babies to sleep. Music can also be used to express emotion nonverbally, which can be a very valuable therapeutic tool in some settings.

Goals

Music is used to form a relationship between the therapist and the patient. The music therapist sets goals on an individual basis, depending on the reasons for treatment, and selects specific activities and exercises to help the patient progress. Objectives may include development of communication, cognitive, motor, emotional, and social skills. Some of the techniques used to achieve this are singing, listening, instrumental music, composition, creative movement, **guided imagery**, and other methods as appropriate. Other disciplines may be integrated as well, such as dance, art, and psychology. Patients may develop musical abilities as a result of therapy, but this is not a major concern. The primary aim is to improve the patient's ability to function.

Techniques

Learning to play an instrument is an excellent musical activity to develop motor skills in individuals with developmental delays, brain injuries, or other motor impairment. It is also an exercise in impulse control and group cooperation. Creative movement is another activity that can help to improve coordination, as well as strength, balance, and gait. Improvisation facilitates the nonverbal expression of emotion. It encourages socialization and communication about feelings as well. Singing develops articulation, rhythm, and breath control. Remembering lyrics and melody is an exercise in sequencing for **stroke** victims and others who may be intellectually impaired. Composition of words and music is one avenue available to assist the patient in working through fears and negative feelings. Listening is an excellent way to practice attending and remembering. It may also make the patient aware of memories and emotions that need to be acknowledged and perhaps talked about. Singing and discussion is a similar method, which is used with some patient populations to encourage dialogue. Guided Imagery and Music (GIM) is a very popular technique developed by music therapist Helen Bonny. Listening to music is used as a path to invoke emotions, picture, and symbols from the patient. This is a bridge to the exploration and expression of feelings.

Music and children

The sensory stimulation and playful nature of music can help to develop a child's ability to express emotion, communicate, and develop rhythmic movement. There is also some evidence to show that speech and language skills can be improved through the stimulation of both hemispheres of the brain. Just as with adults, appropriately selected music can decrease stress, **anxiety**, and pain. Music therapy in a hospital environment with those who are sick, **preparing for surgery**, or recovering postoperatively is appropriate and beneficial. Children can also experience improved self-esteem through musical activities that allow them to succeed.

Newborns may enjoy even greater benefits from music. Premature infants experience more rapid weight gain and an earlier discharge from the hospital than their peers who are not exposed to music. There is

also anecdotal evidence of improved cognitive function in premature infants from listening to music.

Music and rehabilitation

Patients with brain damage from stroke, traumatic brain injury, or other neurologic conditions have been shown to exhibit significant improvement as a result of music therapy. This is theorized to be partially the result of entrainment, which is the synchronization of movement with the rhythm of the music. Consistent practice leads to gains in motor skill ability and efficiency. Cognitive processes and language skills often benefit from appropriate musical intervention.

Music therapy has also shown effectiveness in rehabilitating the hearing of children and adults who have had cochlear implant surgery to treat impaired hearing. Young children who have never heard sounds face a lengthy rehabilitation in order to learn how to interpret sound and form speech. Music therapy can serve as a bridge between non-verbal communication and the new sounds that toddlers are hearing and processing into language. In older adults with **cochlear implants**, music therapy can offer relaxation to minimize distortion among new sounds, and cues to remembering old sounds. Individualized music therapy is also used to reduce noise levels in people with **tinnitus**, or ringing in the ears.

Music and the elderly

The geriatric population can be particularly prone to anxiety and depression, particularly in nursing home residents. Chronic diseases causing pain are also not uncommon in this setting. Music is an excellent outlet to provide enjoyment, relaxation, relief from pain, and an opportunity to socialize and reminisce about music that has had special importance to the individual. It can have a striking effect on patients with **Alzheimer's disease**, even sometimes allowing them to focus and become more responsive for a time. Music has also been observed to decrease the agitation that is so common with this disease. One study shows that elderly people who play a musical instrument are more physically and emotionally fit as they age than their nonmusical peers are.

Music and psychiatric disorders

Music can be an effective tool for treating the mentally or emotionally ill. **Autism** is one disorder that has been particularly researched. Music therapy has enabled some autistic children to relate to others and have improved learning skills. **Substance abuse**, **schizophrenia**, **paranoia**, and disorders of personality, anxiety, and affect are all conditions that may be benefited by music therapy. In these groups, participation and social interaction are promoted through music. Reality orientation is improved. Patients are helped to develop coping skills, reduce stress, and express their feelings.

In the treatment of psychotic disorders, however, the benefits of music therapy appear to be limited. One study of patients diagnosed with schizophrenia or schizoaffective **psychosis** found that while music therapy improved the patients' social relationships, these benefits were relatively short-lived.

Music and hospice care

Pain, anxiety, and depression are major concerns with patients who are terminally ill, whether they are in hospice or not. Music can provide some relief from pain, through release of endorphins and promotion of relaxation. It can also provide an opportunity for the patient to reminisce and talk about the fears that are associated with **death** and dying. Music may help regulate the rapid breathing of a patient who is anxious, and soothe the mind. The Chalice of Repose project, headquartered at St. Patrick Hospital in Missoula, Montana, is one organization that attends and nurtures dying patients through the use of music, in a practice they called music-thanatology by developer Therese Schroeder-Sheker. Practitioners in this program work to relieve suffering through music prescribed for the individual patient.

Music and gynecologic procedures

Research has proven that women require less pharmaceutical pain relief during labor if they make use of music. Listening to music that is familiar and associated with positive imagery is the most helpful. During early labor, music will promote relaxation. Maternal movement is helpful to get the baby into a proper birthing position and dilate the cervix. Enjoying some "music to move by" can encourage the mother to stay active for as long as possible during labor. The rhythmic auditory stimulation may also prompt the body to release endorphins, which are a natural form of pain relief. Many women select different styles of music for each stage of labor, with a more intense, or faster-moving piece feeling like a natural accompaniment to the more difficult parts of labor. Instrumental music is often preferred.

The benefits of music therapy during **childbirth** have also been shown to apply to other surgical procedures. Women who have listened to music tapes

during gynecologic surgery have more restful sleep following the procedure and less postoperative soreness.

Precautions

Patients making use of music therapy should not discontinue medications or therapies prescribed by other health providers without prior consultation.

Research and general acceptance

There is little disagreement among physicians that music can be of some benefit for patients, although the extent of its effects on physical well-being is not as well acknowledged in the medical community. Acceptance of music therapy as an adjunctive treatment modality is increasing, however, due to the growing diversity of patient populations receiving music therapy. Research has shown that listening to music can decrease anxiety, pain, and recovery time. There are also good data for the specific subpopulations discussed. A therapist referral can be made through the AMTA.

Training and certification

Music therapists are themselves often talented musicians; they also study the ways in which music can be applied to specific groups and circumstances. Coursework includes classes regarding music history and performance, behavioral science, and education. The American Music Therapy Association dictates what classes must be included in order for a music therapy program to be certified. There are approximately 70 colleges with approved curricula. A six-month internship follows the completion of the formal music therapy program, and the graduate is then able to take a national board exam to gain certification.

Resources

BOOKS

Boxill, Edith Hillman, and Kristen M. Chase. *Music Therapy for Developmental Disabilities*. Austin, Tex: Pro-Ed, 2007.

Nordoff, Paul, Clive Robbins, and David Marcus. *Creative Music Therapy: A Guide to Fostering Clinical Musicianship*. Gilsum, N.H.: Barcelona Pub, 2007.

Oldfield, Amelia, and Claire Flower. *Music Therapy with Children and Their Families*. London: Jessica Kingsley Pub, 2008.

Sacks, Oliver W. *Musicophilia: Tales of Music and the Brain*. New York: Alfred A. Knopf, 2007.

Sekeles, Chava. *Music Therapy: Death and Grief*. Gilsum, N.H.: Barcelona Publishers, 2007.

Serlin, Ilene A. *Whole Person Healthcare*. Praeger perspectives. Westport, Conn: Praeger, 2007.

PERIODICALS

Avers, Laura, Ambika Mathur, and Deepak Kamat. "Music Therapy in Pediatrics." *Clinical Pediatrics*. 46 (2007): 575–579.

Parker, A.B., "Music Therapy Clarifications." *Journal of Psychosocial Nursing and Mental Health Services* 47 (2009): 7.

Romo, R., and L. Gifford. "A Cost-Benefit Analysis of Music Therapy in a Home Hospice." *Nursing Economic$*. (2007): 34.

"Sonic Health Boost: Music Therapy Can Fight Pain and Disease." *Prevention*. (2008): 53.

Talwar, N., Crawford, M.J., Maratos, A., Nur, U., McDermott, O., and S. Procter. "Music Therapy for In-Patients with Schizophrenia: Exploratory Randomized Controlled Trial." *The British Journal of Psychiatry: the Journal of Mental Science*. 189 (2006): 405–9.

ORGANIZATIONS

American Music Therapy Association, 8455 Colesville Road, Suite 1000, Silver Spring, MD, 20910, (301) 589–3300, (301) 589–5175 , info@musictherapy.org, http://www.musictherapy.org/.

Judith Turner
Rebecca J. Frey, PhD
Brenda W. Lerner

Mutism

Definition

Mutism is a rare childhood condition characterized by a consistent failure to speak in situations where talking is expected. As of 2010, the childhood disorder is more often called selective mutism or SM to distinguish it from akinetic mutism, a brain disorder in which the patient does not move about as well, as not being able to speak. Akinetic mutism is caused by severe damage to the frontal lobe of the brain. SM, in contrast, is an **anxiety** disorder that affects behavior rather than the structure and functioning of the brain itself. A child with selective mutism has the ability to converse normally, and does so, for example, in the home, but consistently fails to speak in such situations as at school or with strangers. The *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM–IV), classifies selective mutism under the general category of "disorders usually first diagnosed in infancy, childhood, or adolescence."

Demographics

It was estimated in the past that one in every 1,000 school–age children in North America is affected by selective mutism. However, a study carried out by the American Academy of Child and Adolescent Psychiatry (AACAP) reported in 2002 that a more accurate figure is seven children in every 1,000. DSM–IV states that the disorder "is apparently rare and is found in fewer than one percent of individuals seen in mental health settings." The condition is more common in girls, with a sex ratio of 2–2.5 females to one male. So far as is known, the condition is equally common in all racial and ethnic groups.

Description

Experts believe that selective mutism is associated with anxiety and fear in social situations such as in school or in the company of adults. It is, therefore, often considered a type of social phobia. Selective mutism is not a communication disorder because affected children can converse normally in some situations. It is not a developmental disorder because their ability to talk when they choose to do so is appropriate for their age level. This problem has been linked to anxiety, and one of the major ways in which both children and adults attempt to cope with anxiety is by avoiding whatever provokes the anxiety. The onset of selective mutism is often abrupt, occurring after the child has first entered school or suffered some other public humiliation.

Affected children are typically shy, and are especially so in the presence of strangers and unfamiliar surroundings or situations. However, the behaviors of children with this condition go beyond **shyness**. The condition becomes progressive in some cases, meaning that the child gradually stops talking to everyone, including his or her own parents.

Selective mutism was originally termed "elective mutism" when it was first listed in the third (1980) edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM–III). Doctors at the time thought that children with the disorder chose to remain silent when they could speak. It is now recognized that the inability to speak is involuntary and does not reflect stubbornness or opposition. The change from "elective" to "selective" mutism was made in the fourth edition (1994) of DSM (DSM–IV) to correct the misconception that children with SM are simply defiant and willful. They actually have a lower rate of oppositional disorder than their school–age peers.

Risk factors

Known risk factors for SM include a family history of **anxiety disorders**, particularly social phobia or **generalized anxiety disorder** (GAD). Some researchers report that rejection by peers or separation from caregivers due to severe illness or hospitalization in early childhood is also risk factors. According to the Selective Mutism Foundation (SMF), however, physical or emotional **abuse** within the family or family dysfunction is *not* usually causes of selective mutism.

Causes and symptoms

Mutism is believed to arise from anxiety experienced in social situations in which a child may be called upon to speak. Refusing to speak, or speaking in a whisper, spares the child from the possible humiliation or embarrassment of "saying the wrong thing." When asked a direct question by teachers, for example, the affected child may act as if he or she is unable to answer. Some children may communicate via gestures, nodding, or very brief utterances. Additional features may include excessive shyness, oppositional behavior, and impaired learning at school.

Some possible genetic or inborn causes of SM are currently under investigation. Some children appear to have an inborn susceptibility to high anxiety levels. Another theory maintains that children with SM have an overly excitable amygdala, an almond–shaped structure in the brain that governs the so–called fight–or–flight response. Still another theory holds that children with selective mutism suffer from sensory integration dysfunction, a neurological disorder that affects one' ability to process certain information coming from the senses. The resulting difficulties lead to anxiety, which in turn causes the child to "shut down" and stop talking to others.

Diagnosis

Selective mutism is usually diagnosed before a child is five years old, most often about the time the child starts school. The diagnosis is not always easy to make because the signs and symptoms can be confused with those of autism—particularly when the child is shy around the diagnostician. It is also important for the examiner to rule out cultural factors, such as recent immigration and little exposure to spoken English; or recent exposure to a traumatic event of some kind. It is not unusual for children to stop speaking temporarily after witnessing a murder, serious accident, or other frightening event. This type of mutism is transient, however, and usually clears up after a few weeks. For this reason DSM–IV specifies that the child's mutism

KEY TERMS

Amygdala—An almond–shaped structure found deep within each medial temporal lobe of the brain that plays a primary role in the processing and memory of emotional experiences.

Behavior modification—A form of therapy that uses rewards to reinforce desired behavior. An example would be to give a child a piece of chocolate for grooming himself or herself appropriately.

Oppositional defiant disorder—A childhood behavioral disorder characterized by an ongoing pattern of disobedient, hostile, and defiant behavior toward authority figures that goes beyond the bounds of normal childhood conduct.

Sensory integration dysfunction—A neurological disorder in which a person has trouble processing and integrating all the information relayed to the brain by the various senses. Some researchers think that it is a possible cause of selective mutism.

must have lasted for a month or longer to meet the diagnostic criteria for SM. Other disorders that must be ruled out include **schizophrenia**, a pervasive developmental disorder (PDD), or **stuttering** or another communication disorder. Older children or teenagers may be asked about their **caffeine** intake, as heavy consumption of energy drinks can lead to jitteriness and other symptoms that resemble those of anxiety disorders.

Examination

The American Speech–Language–Hearing Association (ASHA) recomments that children who may suffer from SM should be evaluated by a speech–language pathologist in addition to a pediatrician and a child psychiatrist or psychologist. A complete diagnostic workup will include a number of different reviews, interviews, and tests:

- Educational review. The child's school reports, standardized test results, and teacher comments will be reviewed.
- Child Autism Rating Scale (CARS). This is a test administered by a licensed clinical psychologist to rule out autism or PDD.
- Parent/family interview. This interview is intended to gather information on such factors as language problems, family history of anxiety disorders (if any), general level of family functioning, and information from the parents about the history of the child's symptoms at home.
- Hearing test. This test is done to rule out hearing disorders or chronic middle ear infections as factors.
- Oral–motor examination. This is an examination of the strength and coordination of the muscles in the child's lips, jaws, and tongue.
- Speech and language evaluation. This part of the diagnostic workup looks at the child's ability to understand language, his or her patterns of verbal and nonverbal communication, and his or her ability to tell a simple story. If the child has difficulty communicating with the speech–language pathologist, the parents may be asked to make a videotape of the child talking at home.

Treatment

There is no single pattern of treatment for SM. Therapy is highly individualized, with the child's age, family situation, and overall health being taken into account. It is, however, important to start treatment as soon as possible after diagnosis, because children do not grow out of SM. In fact, their anxiety levels typically increase the longer the disorder goes untreated.

Most therapists will use a combination of behavioral strategies in treating a child with selective mutism. The most commonly employed behavioral techniques include:

- Stimulus fading. Stimulus fading refers to a technique in which the patient is brought into a controlled environment with someone with whom they are at ease and can communicate. Stimulus fading is usually used only with younger children, because older children and adolescents can quickly recognize it as a technique to get them to speak.
- Shaping. In shaping, the therapist gives the child positive reinforcement, first for interacting without speech, then for making sounds, then for making fully formed words.
- Self–modeling. In self–modeling, the therapist, parents, or teachers make videotapes of the child successfully communicating at home (or communicating successfully elsewhere, as with playmates). The child is then encouraged to watch him– or herself succeeding in speaking normally, as a way of boosting self–confidence and carrying over speaking normally into the classroom or other setting in which mutism occurs.
- Role–playing. This technique can be helpful in encouraging the child to feel comfortable in a variety of different settings with different participants.

Drugs

The use of drugs in treating SM is controversial. Some doctors recommend low doses of antidepressants like fluoxetine (Prozac) or sertraline (Zoloft) to lower the child's anxiety level and speed up the process of **speech therapy**. If an antidepressant is used, it is not given for longer than nine to 12 months, and it is more likely to be given to older children or teenagers than to younger children. Other doctors, however, refuse to give medications to children with SM because of the risk of possible side effects. In any case, drugs should never be used as the sole treatment of selective mutism.

Prognosis

The prognosis for selective mutism varies considerably, although the overall prognosis is fair–to–good as of 2010. In general, children diagnosed before age 10 do better than those diagnosed and treated after age 12. Children with concurrent social phobia do not do as well as those with selective mutism alone. Individuals with SM who are not diagnosed or treated until they are adolescents have the poorest prognosis, most likely because they have fewer overall communication skills in social settings than children who were treated at younger ages. Although selective mutism was not the only disorder that was diagnosed in Seung–hui Cho, the student responsible for the Virginia Tech massacre of 2007, Cho was not diagnosed with SM or treated for it until he was in eighth grade. He was treated for three years for the disorder but refused further therapy during his junior year of high school.

Prevention

Selective mutism is difficult to prevent because relatively little is known about its causes or risk factors as of 2010. The best preventive approach is regular checkups for possible hearing problems in young children and more extensive evaluation as soon as a speech problem is present.

Resources

BOOKS

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed., text revision. Washington, D.C.: American Psychiatric Association, 2000.

Harrison, Alan E., editor. *Speech Disorders: Causes, Treatment and Social Effects*. Hauppauge, NY: Nova Science Publishers, 2009.

Kearney, Christopher A. *Helping Children with Selective Mutism and Their Parents: A Guide for School–based Professionals*. New York: Oxford University Press, 2010.

PERIODICALS

Golden, Daniel. "From Disturbed High Schooler to College Killer." *Wall Street Journal*, August 20, 2007.

Kaakeh, Y., and J.L. Stumpf. "Treatment of Selective Mutism: Focus on Selective Serotonin Reuptake Inhibitors." *Pharmacotherapy* 28 (February 2008): 214–24.

Keen, D.V., et al. "Selective Mutism: A Consensus–based Care Pathway of Good Practice." *Archives of Disease in Childhood* 93 (October 2008): 838–44.

Manassis, K. "Silent Suffering: Understanding and Treating Children with Selective Mutism." *Expert Review of Neurotherapeutics* 9 (February 2009): 235–43.

Viana, A.G., et al. "Selective Mutism: A Review and Integration of the Last 15 Years." *Clinical Psychology Review* 29 (February 2009): 57–67.

Wong, P. "Selective Mutism: A Review of Etiology, Comorbidities, and Treatment." *Psychiatry (Edgemont)* 7 (March 2010): 23–31.

OTHER

American Speech–Language–Hearing Association (ASHA). "Selective Mutism." http://asha.org/public/speech/disorders/SelectiveMutism.htm (accessed September 8, 2010).

Bernstein, Bettina E. "Anxiety Disorder, Social Phobia and Selective Mutism." eMedicine (September 25, 2009). http://emedicine.medscape.com/article/917147-overview (September 8, 2010).

Selective Mutism Foundation (SMF). "Understanding Selective Mutism." http://www.selectivemutismfoundation.org/about.shtml (September 8, 2010).

ORGANIZATIONS

American Academy of Child and Adolescent Psychiatry (AACAP), 3615 Wisconsin Ave., NW, Washington, DC, 20016-3007, (202) 966-7300, (202) 966-2891, http://www.aacap.org/.

American Psychiatric Association (APA), 1000 Wilson Blvd., Suite 1825, Arlington, VA, 22209-3901, (703) 907-7300, apa@psych.org, http://www.psych.org/.

American Speech–Language–Hearing Association (ASHA), 2200 Research Blvd., Rockville, MD, 20850-3289, (301) 296-5700, http://www.asha.org/default.htm.

Anxiety Disorders Association of America (ADAA), 8730 Georgia Ave., Suite 600, Silver Spring, MD, 20910, (240) 485-1001, (240) 485-1035, information@adaa.org, http://www.adaa.org/.

Selective Mutism Foundation (SMF), P.O. Box 13133, Sissonville, WV, 25360, http://www.selectivemutismfoundation.org/.

Selective Mutism Group/Childhood Anxiety Network, http://www.selectivemutism.org/contactus, http://www.selectivemutism.org/.

Donald G. Barstow, RN
Rebecca J. Frey, Ph.D.

MVP *see* **Mitral valve prolapse**

Myasthenia gravis

Definition

Myasthenia gravis is an autoimmune disease that causes muscle weakness.

Description

Myasthenia gravis (MG) affects the neuromuscular junction, interrupting the communication between nerve and muscle, and thereby causing weakness. A person with MG may have difficulty moving their eyes, walking, speaking clearly, swallowing, and even breathing, depending on the severity and distribution of weakness. Increased weakness with exertion, and improvement with rest, is a characteristic feature of MG.

About 30,000 people in the United States are affected by MG. It can occur at any age, but is most common in women who are in their late teens and early twenties, and in men in their sixties and seventies.

Causes and symptoms

Myasthenia gravis is an autoimmune disease, meaning it is caused by the body's own immune system. In MG, the immune system attacks a receptor on the surface of muscle cells. This prevents the muscle from receiving the nerve impulses that normally make it respond. MG affects "voluntary" muscles, which are those muscles under conscious control responsible for movement. It does not affect heart muscle or the "smooth" muscle found in the digestive system and other internal organs.

A muscle is stimulated to contract when the nerve cell controlling it releases acetylcholine molecules onto its surface. The acetylcholine lands on a muscle protein called the acetylcholine receptor. This leads to rapid chemical changes in the muscle which cause it to contract. Acetylcholine is then broken down by acetylcholinesterase enzyme, to prevent further stimulation.

In MG, immune cells create antibodies against the acetylcholine receptor. Antibodies are proteins normally involved in fighting infection. When these antibodies attach to the receptor, they prevent it from receiving acetylcholine, decreasing the ability of the muscle to respond to stimulation.

Why the immune system creates these self-reactive "autoantibodies" is unknown, although there are several hypotheses:

- During fetal development, the immune system generates many B cells that can make autoantibodies, but B cells that could harm the body's own tissues are screened out and destroyed before birth. It is possible that the stage is set for MG when some of these cells escape detection.
- Genes controlling other parts of the immune system, called MHC genes, appear to influence how susceptible a person is to developing autoimmune disease.
- Infection may trigger some cases of MG. When activated, the immune system may mistake portions of the acetylcholine receptor for portions of an invading virus, though no candidate virus has yet been identified conclusively.
- About 10% of those with MG also have thymomas, or benign tumors of the thymus gland. The thymus is a principal organ of the immune system, and researchers speculate that thymic irregularities are involved in the progression of MG.

Some or all of these factors (developmental, genetic, infectious, and thymic) may interact to create the autoimmune reaction.

The earliest symptoms of MG often result from weakness of the extraocular muscles, which control eye movements. Symptoms involving the eye (ocular symptoms) include double vision (diplopia), especially when not gazing straight ahead, and difficulty raising the eyelids (**ptosis**). A person with ptosis may need to tilt their head back to see. Eye-related symptoms remain the only symptoms for about 15% of MG patients. Another common early symptom is difficulty chewing and swallowing, due to weakness in the bulbar muscles, which are in the mouth and throat. **Choking** becomes more likely, especially with food that requires extensive chewing.

Weakness usually becomes more widespread within several months of the first symptoms, reaching their maximum within a year in two-thirds of patients. Weakness may involve muscles of the arms, legs, neck, trunk, and face, and affect the ability to lift objects, walk, hold the head up, and speak.

Symptoms of MG become worse upon exertion, and better with rest. Heat, including heat from the sun, hot showers, and hot drinks, may increase weakness. Infection and **stress** may worsen symptoms. Symptoms may vary from day to day and month to month, with intervals of no weakness interspersed with a progressive decline in strength.

"Myasthenic crisis" may occur, in which the breathing muscles become too weak to provide adequate respiration. Symptoms include weak and shallow breathing, **shortness of breath**, pale or bluish

skin color, and a racing heart. Myasthenic crisis is an emergency condition requiring immediate treatment. In patients treated with anticholinesterase agents, myasthenic crisis must be differentiated from cholinergic crisis related to overmedication.

Pregnancy worsens MG in about one third of women, has no effect in one third, and improves symptoms in another third. About 12% of infants born to women with MG have "neonatal myasthenia," a temporary but potentially life-threatening condition. It is caused by the transfer of maternal antibodies into the fetal circulation just before birth. Symptoms include weakness, floppiness, feeble cry, and difficulty feeding. The infant may have difficulty breathing, requiring the use of a ventilator. Neonatal myasthenia usually clears up within a month.

Diagnosis

Myasthenia gravis is often diagnosed accurately by a careful medical history and a neuromuscular exam, but several tests are used to confirm the diagnosis. Other conditions causing worsening of bulbar and skeletal muscles must be considered, including drug-induced myasthenia, thyroid disease, Lambert-Eaton myasthenic syndrome, **botulism**, and inherited muscular dystrophies.

MG causes characteristic changes in the electrical responses of muscles that may be observed with an electromyogram, which measures muscular response to electrical stimulation. Repetitive nerve stimulation leads to reduction in the height of the measured muscle response, reflecting the muscle's tendency to become fatigued.

Blood tests may confirm the presence of the antibody to the acetylcholine receptor, though up to a quarter of MG patients will not have detectable levels. A **chest x ray** or chest computed tomography scan (CT scan) may be performed to look for **thymoma**.

Treatment

While there is no cure for myasthenia gravis, there are a number of treatments that effectively control symptoms in most people.

Edrophonium (Tensilon) blocks the action of acetylcholinesterase, prolonging the effect of acetylcholine and increasing strength. An injection of edrophonium rapidly leads to a marked improvement in most people with MG. An alternate drug, neostigmine, may also be used.

Pyridostigmine (Mestinon) is usually the first drug tried. Like edrophonium, pyridostigmine blocks acetylcholinesterase. It is longer-acting, taken by mouth, and well-tolerated. Loss of responsiveness and disease progression combine to eventually make pyridostigmine ineffective in tolerable doses in many patients.

Thymectomy, or removal of the thymus gland, has increasingly become standard treatment for MG. Up to 85% of people with MG improve after thymectomy, with complete remission eventually seen in about 30%. The improvement may take months or even several years to fully develop. Thymectomy is not usually recommended for children with MG, since the thymus continues to play an important immune role throughout childhood.

Immune-suppressing drugs are used to treat MG if response to pyridostigmine and thymectomy are not adequate. Drugs include **corticosteroids** such as prednisone, and the non-steroids azathioprine (Imuran) and cyclosporine (Sandimmune).

Plasma exchange may be performed to treat myasthenic crisis or to improve very weak patients before thymectomy. In this procedure, blood plasma is removed and replaced with purified plasma free of autoantibodies. It can produce a temporary improvement in symptoms, but is too expensive for long-term treatment. Another blood treatment, intravenous immunoglobulin therapy, is also used for myasthenic crisis. In this procedure, large quantities of purified immune proteins (immunoglobulins) are injected. For unknown reasons, this leads to symptomatic improvement in up to 85% of patients. It is also too expensive for long-term treatment.

People with weakness of the bulbar muscles may need to eat softer foods that are easier to chew and swallow. In more severe cases, it may be necessary to obtain **nutrition** through a feeding tube placed into the stomach (**gastrostomy** tube).

Prognosis

Most people with MG can be treated successfully enough to prevent their condition from becoming debilitating. In some cases, however, symptoms may worsen even with vigorous treatment, leading to generalized weakness and disability. MG rarely causes early **death** except from myasthenic crisis.

Prevention

There is no known way to prevent myasthenia gravis. Thymectomy improves symptoms significantly in many patients, and relieves them entirely in some. Avoiding heat can help minimize symptoms.

Some drugs should be avoided by people with MG because they interfere with normal neuromuscular function.

KEY TERMS

Antibody—An immune protein normally used by the body for combating infection and which is made by B cells.

Autoantibody—An antibody that reacts against part of the self.

Autoimmune disease—A disease caused by a reaction of the body's immune system.

Bulbar muscles—Muscles that control chewing, swallowing, and speaking.

Neuromuscular junction—The site at which nerve impulses are transmitted to muscles.

Pyridostigmine bromide (Mestinon)—An anticholinesterase drug used in treating myasthenia gravis.

Tensilon test—A test for diagnosing myasthenia gravis. Tensilon is injected into a vein and, if the person has MG, their muscle strength will improve for about five minutes.

Thymus gland—A small gland located just above the heart, involved in immune system development.

Drugs to be avoided or used with caution include:

- Many types of antibiotics, including erythromycin, streptomycin, and ampicillin
- Some cardiovascular drugs, including Verapamil, betaxolol, and propranolol
- Some drugs used in psychiatric conditions, including chlorpromazine, clozapine, and lithium.

Many other drugs may worsen symptoms as well, so patients should check with the doctor who treats their MG before taking any new drugs.

A Medic-Alert card or bracelet provides an important source of information to emergency providers about the special situation of a person with MG. They are available from health care providers.

ORGANIZATIONS

Muscular Dystrophy Association, 3300 East Sunrise Drive, Tucson, AZ, 85718, (800) 572-1717, http://www.mdausa.org.

Myasthenia Gravis Foundation of America, 355 Lexington Avenue, 15th Floor, New York, NY, 10017, (212) 297-2156, (212) 370-9047, (800) 541-5454, http://www.myasthenia.org/.

Richard Robinson

Mycetoma

Definition

Mycetoma, or maduromycosis, is a slow-growing bacterial or fungal infection focused in one area of the body, usually the foot. For this reason—and because the first medical reports were from doctors in Madura, India—an alternate name for the disease is Madura foot. The infection is characterized by an abnormal tissue mass beneath the skin, formation of cavities within the mass, and a fluid discharge. As the infection progresses, it affects the muscles and bones; at this advanced stage, disability may result.

Description

Although the bacteria and fungi that cause mycetoma are found in soil worldwide, the disease occurs mainly in tropical areas in India, Africa, South America, Central America, and southeast Asia. Mycetoma is an uncommon disease, affecting an unknown number of people annually.

There are more than 30 species of bacteria and fungi that can cause mycetoma. Bacteria or fungi can be introduced into the body through a relatively minor skin wound. The disease advances slowly over months or years, typically with minimal **pain**. When pain is experienced, it is usually due to secondary infections or bone involvement. Although it is rarely fatal, mycetoma causes deformities and potential disability at its advanced stage.

Causes and symptoms

Owing to a wound, bacteria or fungi gain entry into the skin. Approximately one month or more after the injury, a nodule forms under the skin surface. The nodule is painless, even as it increases in size over the following months. Eventually, the nodule forms a tumor, or mass of abnormal tissue. The tumor contains cavities—called sinuses—that discharge blood- or pus-tainted fluid. The fluid also contains tiny grains, less than two thousandths of an inch in size. The color of these grains depends on the type of bacteria or fungi causing the infection.

As the infection continues, surrounding tissue becomes involved, with an accumulation of scarring and loss of function. The infection can extend to the bone, causing inflammation, pain, and severe damage. Mycetoma may be complicated by secondary infections, in which new bacteria become established in the area and cause an additional set of problems.

KEY TERMS

Biopsy—A medical procedure in which a small piece of tissue is surgically removed for microscopic examination.

Grains—Flecks of hardened material such as bacteria or fungi spores.

Nodule—A hardened area or knot sometimes associated with infection.

Secondary infection—Illness caused by new bacteria, viruses, or fungi becoming established in the wake of an initial infection.

Sinuses—Cavities or hollow areas.

Tumor—A mass or clump of abnormal tissue, not necessarily caused by a cancer.

Diagnosis

The primary symptoms of a tumor, sinuses, and grain-flecked discharge often provide enough information to diagnose mycetoma. In the early stages, prior to sinus formation, diagnosis may be more difficult and a biopsy, or microscopic examination of the tissue, may be necessary. If bone involvement is suspected, the area is x rayed to determine the extent of the damage. The species of bacteria or fungi at the root of the infection is identified by staining the discharge grains and inspecting them with a microscope.

Treatment

Combating mycetoma requires both surgery and drug therapy. Surgery usually consists of removing the tumor and a portion of the surrounding tissue. If the infection is extensive, **amputation** is sometimes necessary. Drug therapy is recommended in conjunction with surgery. The specific prescription depends on the type of bacteria or fungi causing the disease. Common medicines include antifungal drugs, such as ketoconazole and **antibiotics** (streptomycin sulfate, amikacin, sulfamethoxazole, penicillin, and rifampin).

Prognosis

Recovery from mycetoma may take months or years, and the infection recurs after surgery in at least 20% of cases. Drug therapy can reduce the chances of a re-established infection. The extent of deformity or disability depends on the severity of infection; the more deeply entrenched the infection, the greater the damage. By itself, mycetoma is rarely fatal, but secondary infections can be fatal.

Prevention

Mycetoma is a rare condition that is not contagious.

Resources

OTHER

The Merck Manuals Online Medical Library, http://www.merckmanuals.com/professional/sec14/ch180/ch180j.html (accessed December 6, 2010).

Julia Barrett

Mycobacterial infections, atypical

Definition

Atypical mycobacterial infections are infections caused by several types of mycobacteria similar to the germ that causes **tuberculosis**. These atypical mycobacterial infections are a frequent complication in patients with human **immunodeficiency** virus (HIV) infection or **AIDS**.

Description

Mycobacteria are a group of rod-shaped bacteria that cause several diseases, among them **leprosy** and tuberculosis. For some time, scientists have known of bacteria that are similar to *Mycobacterium tuberculosis,* the cause of tuberculosis, but that grow and act differently. When tuberculosis was a much more widespread problem and microbiology was much less able to tell the difference between similar microbes, these atypical mycobacteria were ignored. Today, they have been classified more precisely as members of the same species and called atypical (or nontuberculosis) mycobacteria.

Although the medical profession has known about these atypical infections for a long time, they were not considered a serious problem until the early 1980s. It was then that many of these atypical infections were noticed among homosexuals and intravenous drug users in New York City. These bacteria rarely cause infection in humans other than those with HIV or AIDS.

Causes and symptoms

Although there are more than a dozen species of atypical mycobacteria, the two most common are *Mycobacterium kansasii* and *M. avium-intracellulare*. These microbes are found in many places in the environment: tap water, fresh and ocean water, milk, bird droppings, soil, and house dust. The manner in which these bacteria are transmitted is not completely understood. There is no evidence that they are transmitted from person to person.

M. avium-intracellulare (MAC or MAI) is a rare cause of lung disease in otherwise healthy humans but a frequent cause of infection among those whose resistance has been lowered by another disorder (opportunistic infection). According to some experts, MAC infection is an almost inevitable complication of HIV. The infection is caused by one of two similar organisms, *M. avium* and *M. intracellulare*.

AIDS patients are almost always attacked by these mycobacteria. Once inside the body, the atypical mycobacterial organisms colonize and grow in the lungs like tuberculosis. Because AIDS patients have a poorly functioning immune system, the microbes multiply because they aren't stopped by the body's normal response to infection. Once they have colonized the lungs, the organisms enter the bloodstream and spread throughout the body, affecting almost every organ. These devastating infections can invade the lymph nodes, liver, spleen, bone marrow, gastrointestinal tract, skin, and brain.

Symptoms include **shortness of breath**, **fever**, night sweats, weight loss, appetite loss, **fatigue**, and progressively severe **diarrhea**, stomach **pain**, **nausea and vomiting**. If the infection spreads to the brain, the patient may experience weakness, headaches, vision problems, and loss of balance.

MAC and *M. kansasii* sometimes cause lung infections in middle-aged and elderly people with chronic lung conditions. MAC, *M. kansasii*, and *M. scrofulaceum* may cause inflammation of the lymph nodes in otherwise healthy young children. *M. fortuitum* and *M. chelonae* cause skin and wound infections and abscesses after trauma or surgical procedures. *M. marinum* causes a nodular inflammation, usually on the arms and legs. This infection is called "swimming pool granuloma" because it is associated with swimming pools, fish tanks, and other bodies of water. *M. ulcerans* infection causes chronic skin ulcerations, usually on an arm or leg. Atypical mycobacteria infections can also occur without causing any symptoms. In such cases, a **tuberculin skin test** may be positive.

KEY TERMS

Culture—A test in which a sample of body fluid, such as prostatic fluid, is placed on materials specially formulated to grow microorganisms. A culture is used to learn what type of bacterium is causing infection.

Human immunodeficiency virus (HIV)—The virus that causes AIDS.

Diagnosis

The diagnosis is made from the patient's symptoms and organisms grown in culture from the site of infection. In cases of lung infection, a diagnostic workup will include a **chest x ray** and tests on discharges from the respiratory passages (sputum).

Treatment

These nontypical mycobacteria are not easy to treat in any patient and the problem is complicated when the person has AIDS. **Antibiotics** are not particularly effective, although rifabutin (a cousin of the anti-tuberculosis drug rifampin) and clofazimine (an anti-leprosy drug) have helped some patients. It is also possible to contain the infection to some degree by combining different drugs, including ethionamide, cycloserine, ethambutol, and streptomycin.

Prognosis

Because drug therapy is not easily effective, the overwhelming infections caused by these mycobacteria in AIDS patients can be fatal.

Prevention

People with HIV infection can prevent or delay the onset of MAC by taking disease-preventing drugs such as rifabutin.

AIDS patients and persons with tissue damage, such as skin **wounds** or pulmonary disease, can make a number of lifestyle changes to help prevent MAC infection. Since these mycobacteria are found in most city water systems, in hospital water supplies, and in bottled water, at-risk persons should boil drinking water. Persons at risk should also avoid raw foods, especially salads, root vegetables, and unpasteurized milk or cheese. Fruits and vegetables should be peeled and rinsed thoroughly. Conventional cooking (baking, boiling or steaming) destroys mycobacteria, which are killed at 176°F (80°C).

Finally, at-risk patients should avoid contact with animals, especially birds and bird droppings. Pigeons in particular can transmit MAC.

ORGANIZATIONS

National AIDS Treatment Advocacy Project, 580 Broadway, Ste. 1010, New York, NY, 10012, (212) 219-0106, (212) 219-8473, (866) 26-NATAP, info@natap.org, http://www.natap.org.

Carol A. Turkington

Mycobacterium leprae infection *see* **Leprosy**

Mycobacterium tuberculosis see **Tuberculosis**

Mycoplasma infections

Definition

Mycoplasma are the smallest of the free-living organisms. (Unlike viruses, mycoplasma can reproduce outside of living cells.) Many species within the genus *Mycoplasma* thrive as parasites in human, bird, and animal hosts. Some species can cause disease in humans.

Description

Mycoplasma are found most often on the surfaces of mucous membranes. They can cause chronic inflammatory diseases of the respiratory system, urogenital tract, and joints. The most common human illnesses caused by mycoplasma are due to infection with *M. pneumoniae,* which is responsible for 10-20% of all pneumonias. This type of **pneumonia** is also called atypical pneumonia, walking pneumonia, or community-acquired pneumonia. Infection moves easily among people in close contact because it is spread primarily when infected droplets circulate in the air (that is, become aerosolized), usually due to coughing, spitting, or sneezing.

Causes and symptoms

Atypical pneumonias can affect otherwise healthy people who have close contact with one another. Pneumonia caused by *M. pneumoniae* may start out with symptoms of an upper respiratory infection, probably a **sore throat** progressing to a dry **cough** within a few days. Gradually, **fever**, **fatigue**, muscle aches, and a cough that produces thin sputum (spit or phlegm) will emerge. Nonrespiratory symptoms may occur too: abdominal **pain**, **headache**, and **diarrhea**; about 20% of patients may have ear pain.

KEY TERMS

Community-acquired—Refers to an infectious disease that is passed among individuals who have close contact with one another.

Another mycoplasma species, *M. hominis*, is common in the mucous membranes of the genital area (including the cervix), and can cause infection in both males and females. Its presence does not always result in symptoms.

Diagnosis

Usually, mycoplasma pneumonia will be identified after other common diagnoses are set aside. For example, a type of antibiotic known as a beta-lactam might be prescribed for a respiratory infection producing fever and cough. If symptoms do not improve in 3-5 days, the organism causing the disease is not a typical one and not susceptible to these **antibiotics**. If a Gram's stain (a common test done on sputum) does not indicate a gram-positive pathogen, the doctor will suspect a gram-negative organism, such as mycoplasma. The actual underlying organism may not be identified (it is not in almost 50% of cases of atypical pneumonia). Although it is rare, a rash may appear along with pneumonia symptoms.This should trigger suspicion of mycoplasma pneumonia, even if laboratory tests are inconclusive.

Standard x rays may reveal a patchy material that has entered the tissue; this can be evident for months. Laboratory tests include cold agglutinins, complement fixation, culture, and enzyme immunoassay. The presence of infection with *M. pneumoniae* would be indicated by a fourfold rise in *M. pneumoniae*-specific antibody in serum, during the illness or convalescence. Highly sophisticated and specific polymerase chain reaction methods (PCR) have been developed for many respiratory pathogens, including *M. pneumoniae*. They are not readily available and are very expensive.

Treatment

A 2-3 week course of certain antibiotics (erythromycin, azithromycin, clarithromycin, dirithromycin, or doxycycline) is generally prescribed for atypical pneumonia. This disease is infectious for weeks, even after the patient starts antibiotics. A persistent cough may linger for 6 weeks.

Prognosis

Mycoplasma pneumonia may be involved in the onset of **asthma** in adults; other rare complications include meningoencephalitis, **Guillain-Barré syndrome**, mononeuritis multiplex, **myocarditis**, or **pericarditis**. This may increase the risk of acute **arrhythmias** leading to **sudden cardiac death**. However, with proper treatment and rest, recovery should be complete.

Prevention

At this time, there are no vaccines for mycoplasma infection. It is difficult to control its spread, especially in a group setting. The best measures are still the simplest ones. Avoid exposure to people with respiratory infections whenever possible. A person who has a respiratory infection should cover the face while coughing or sneezing.

Resources

BOOKS

Fauci, Anthony S., et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill Professional, 2008.

Jill S. Lasker

Mycoplasmal pneumonia *see* **Mycoplasma infections**

Myelocytic leukemia, acute *see* **Leukemias, acute**

Myelodysplastic syndrome

Definition

Myelodysplastic syndrome (MDS) is a disease that is associated with decreased production of blood cells. Blood cells are produced in the bone marrow, and the blood cells of people with MDS do not mature normally. There are three major types of blood cells — red blood cells, white blood cells and platelets. Patients with MDS can have decreased production of one, two, or all three types of blood cells.

Description

Blood cells are used in the body for many different and important functions, such as carrying oxygen (red blood cells), fighting infection (white blood cells), and controlling bleeding (platelets). Blood cells are formed and stored in the bone marrow, which is the spongy tissue inside large bones. Stem cells, or immature blood cells, are stored in the bone marrow and have the ability to develop into all three types of mature blood cells. When the body needs a specific type of blood cell, the bone marrow uses its stockpile of stem cells to produce the kind of mature cells needed for that particular situation.

In patients who have MDS, blood cells fail to mature normally. In other words, the bone marrow is unable to develop a normal amount of mature blood cells, and is also not able to increase blood cell production when mature cells are needed. Sometimes, even the cells that are produced do not function normally. The marrow eventually becomes filled with the immature cells and there is not room for the normal cells to grow and develop. MDS therefore causes a shortage of functional blood cells.

Subtypes of MDS

MDS is divided into five different subtypes that are classified according to the number and appearance of blast cells in the bone marrow. It is important for doctors to know the type of MDS a patient has, because each subtype affects patients differently and requires specific treatment. The International Prognostic Scoring System (IPSS) can help the doctor to determine the best treatment for an individual patient. The subtypes are as follows:

- Refractory anemia (RA). Bone marrow with less than 5% blast cells and abnormal red blood cell blasts
- Refractory anemia with ring sideroblasts (RARS). Bone marrow with less than 5% blasts and characteristic abnormalities in red blood cells
- Refractory anemia with excess blasts (RAEB). Bone marrow with 5-20% blast cells, and higher risk of changing into acute leukemia over time
- Refractory anemia with excess blasts in transformation (RAEBT). Bone marrow with 21-30% blast cells. This form is most likely to change into acute leukemia.
- Chronic myelomonocytic leukemia (CMMoL). Marrow with 5-20% blasts and excess monocytes (a specific type of white blood cell).

Approximately 15,000 new cases are diagnosed annually in the United States. The average age at diagnosis is 70. The most common types are RA and RARS. It is rare to have MDS before age 50. MDS is slightly more common in males than in females.

Causes and symptoms

Causes

There is no clear cause for the majority of MDS cases, which is referred to as primary or *de novo* myelodysplastic syndrome. In some cases, however, MDS results from earlier **cancer** treatments such as radiation and/or **chemotherapy**. This type of MDS is called secondary or treatment related MDS, is often seen 3 to 7 years after the exposure, and usually occurs in younger people.

Other possible causative agents for MDS include exposure to radiation, cigarette smoke, or toxic chemicals such as benzene. Children with pre-existing chromosomal abnormalities such as **Down syndrome** have a higher risk of developing MDS. MDS does not appear to run in families, nor can it be spread to other individuals.

Symptoms

MDS symptoms are related to the type of blood cells that the body is lacking. The earliest symptoms are usually due to anemia, which results from a shortage of mature red blood cells. Anemia causes patients to feel tired and out of breath because there is a lack of cells transporting oxygen throughout the body. MDS may also lead to a shortage of white blood cells resulting in an increased likelihood of infections. Another symptom of MDS is increased bleeding (e.g., blood in stool, nose bleeds, increased **bruises** or bleeding gums) which is due to low level of platelets. These symptoms can occur in any combination, depending on a given patient's specific subtype of MDS.

Diagnosis

Blood tests

People who have MDS usually visit their primary care doctor first, with symptoms of **fatigue**, and are then referred to a hematologist (a physician who specializes in diseases of the blood). The diagnosis of MDS requires a complete analysis of the patient's blood and bone marrow, which is done by the hematologist. A **complete blood count** (CBC) is done to determine the number of each blood cell type within the sample. Low numbers of red blood cells, white blood cells, and or platelets are signs that a patient has MDS. Numerous other medical problems such as bleeding, nutritional deficiencies, or adverse reaction to a medication can also cause low blood counts. The hematologist will investigate other causes for low blood counts before assigning a diagnosis of MDS. Blood cells in patients with MDS can also be abnormal when viewed under the microscope.

Bone marrow aspiration and biopsy

A **bone marrow biopsy** is required to confirm the diagnosis of MDS and determine the correct MDS subtype. This procedure involves a needle used to take a sample of marrow from inside the bone. The area of the skin where the needle is inserted is numbed and sometimes the patient is also sedated. Patients may experience some discomfort but the procedure is safe and is over fairly quickly. Marrow samples are usually taken from the back of the hip bone (iliac crest). A sample of the marrow, known as an aspirate, and a small piece of bone are both removed with the needle.

A hematologist or a pathologist (a specialist in diagnosing diseases through cell examination) will carefully examine the bone marrow sample through a microscope. Microscopic examination allows the doctor to determine the number and type of blast cells (immature cells) within the marrow in order to identify the MDS subtype. Cells from the bone marrow are also sent for cytogenetic testing, which analyzes the cells' chromosomes. Forty to seventy percent of MDS patients have abnormal bone marrow chromosomes as a result of the disease. The pattern of these abnormalities can be used to predict how a patient will respond to a particular treatment. Thus, the full set of information provided by a bone marrow biopsy and CBC will ultimately allow the doctor to recommend the most effective treatment plan.

International Prognostic Scoring System (IPSS) for MDS

Once a diagnosis of MDS is established, the doctor will calculate the IPSS score for each individual patient. The bone marrow blast percentage, chromosomal abnormalities and number of different blood types that are reduced determine the score. A score of 0 to 3.5 is assigned to each patient. Patients with lower score have a better prognosis and usually should not undertake treatment upon initial diagnosis. Patients with a higher score have more aggressive disease and should consider more aggressive treatment.

Treatments

Supportive care

Treatment for MDS is tailored to the patient's age, general health, specific MDS subtype, and IPSS score. Treatment varies for each patient, but most treatment strategies are designed to control the

symptoms of MDS. This approach is called supportive care and aims to improve the patient's quality of life.

Supportive care for the MDS patients commonly includes red blood cell transfusions to relieve symptoms related to anemia. Red cell transfusions are relatively safe and the physician will review risks and benefits with this approach. Transfusions of any type only last a certain amount of time and therefore need to be repeated at certain intervals. Platelet transfusions can also be a way to control excessive bleeding. The doctor will decide with each individual patient when it is appropriate to give a **transfusion**. **Antibiotics** are used when needed to combat infections that can occur more frequently in patients with low white blood cell counts.

Bone marrow transplantation

Bone marrow transplantation (BMT) is a type of treatment that attempts to provide MDS patients with a cure. This strategy requires the patients to be in fairly good health and are therefore more likely to be used in younger patients. Bone marrow transplantation (BMT) has been found to be a successful treatment for MDS patients under the age of 50 (and some over 50 in good health). Following BMT, many patients are able to achieve long-term, disease-free survival. Unfortunately, most MDS patients cannot receive a traditional bone marrow transplant because of older age or because they do not have a suitable donor. Bone marrow donors are usually siblings or are obtained from the national bone marrow registry. "Mini"-bone marrow transplants use less intense chemotherapy, and are currently being tested in older patients who would otherwise not be candidates for traditional bone marrow transplants.

Chemotherapy

Chemotherapy has been used to treat some MDS patients; however, the disease often recurs after a period of time. This type of therapy uses cell-killing drugs that may also damage healthy cells in the body. Most chemotherapy drugs are associated with some side effects. For these reasons, chemotherapy is generally not used until the MDS becomes more aggressive or the patient has a high IPSS score.

Growth factors

Growth factors are natural proteins that the body normally uses to control blood production. These substances stimulate the patient's bone marrow to produce healthy blood cells. Growth factors that stimulate white cell production are G-CSF (also called neupogen or filgrastim) and GMCSF (Leukine, sargramostim). In order to increase red cell production another growth factor, erythropoietin (Procrit) is used. These growth factors are safe with few side effects and are available only in the injectable form. The physician will decide if this treatment is appropriate for an individual patient.

Alternative treatment

There are no alternative therapies that have been proven to successfully treat MDS. Some of the available alternative drugs can have adverse side effects and therefore a physician should be informed if they are being used.

Prognosis

The prognosis for MDS patients depends on the subtype of their disease and the IPSS score. Patients with RA, RARS or low IPSS score rarely develop leukemia and may live with disease for some years. The higher-risk patients including those with RAEB, RAEBt, CMMoL or high IPSS scores progress more rapidly, and require intensive therapy to control the disease.

Managing MDS requires frequent doctor appointments to monitor disease progression and to evaluate the response to treatment. Fortunately for many patients, recent advances in therapy have significantly enhanced their ability to cope with MDS. Experimental drugs and a better understanding of the disease are likely to improve the overall prognosis in the future.

Prevention

MDS is usually impossible to prevent. Being careful about daily activities and avoiding the use of aspirin-like products that thin the blood may prevent secondary complications of MDS such as bruising and bleeding. Practicing good hygiene and avoiding crowds or people with infections can sometimes prevent infections. A well balanced diet is recommended to increase overall energy.

Resources

BOOKS

Aguayo, Alvaro, Jorge Cortes, and Hagop Kantarjian. "Myelodysplastic Syndromes." In *Cancer Management: A Multidisciplinary Approach*, edited by Richard Pazdur, et al., 4th ed. PRR, Inc, 2000.

ORGANIZATIONS

Aplastic Anemia Foundation of America, P.O. Box 613, Annapolis, MD, 21404, (800) 747-2820, www.aplastic.org.

Leukemia Society of America, 600 Third Avenue, New York, NY, 10016, (800) 955-4572, www.leukemia.org.

Myelodysplastic Syndromes Foundation, 464 Main Street, P.O. Box 477, Crosswicks, NJ, 08515, (800) MDS-0839, www.mds-foundation.org.

Andrea Ruskin, M.D.

Myelofibrosis

Definition

Myelofibrosis is a rare disease of the bone marrow in which collagen builds up fibrous scar tissue inside the marrow cavity. This is caused by the uncontrolled growth of a blood cell precursor, which results in the accumulation of scar tissue in bone marrow. Myelofibrosis goes by many names including idiopathic myelofibrosis, agnogenic myeloid metaplasia, chronic myelosclerosis, aleukemic megakaryocytic myelosis, and leukoerythroblastosis.

Description

Myelofibrosis can be associated with many other conditions including **breast cancer**, **prostate cancer**, Hodgkin's disease, non-Hodgkin's lymphoma, acute myeloid leukemia, acute lymphocytic leukemia, **hairy cell leukemia**, **multiple myeloma**, myeloproliferative diseases, **tuberculosis**, Gaucher's disease, and **Paget's disease of bone**. Myelofibrosis typically becomes progressively worse and can cause **death**.

In myelofibrosis, abnormal cells (hematopoietic stem cells) grow out of control and begin to produce both immature blood cells and excess scar (fibrous) tissue. The fibrous tissue builds up (fibrosis) primarily in the bone marrow, the place where blood cells are produced. The fibrous tissue interferes with the production of normal blood cells. The outcome of this is that the blood made by the bone marrow is of poor quality. To compensate for this, blood cell production occurs in other parts of the body (extramedullary hematopoiesis), but most notably in the spleen and liver. This causes enlargement of the spleen (splenomegaly) and the liver (hepatomegaly). Extramedullary hematopoiesis is not effective and, combined with the reduced production of blood cells by the bone marrow, a condition called anemia results.

The abnormal stem cells can spread throughout the body, settle in other organs, and form tumors that produce more abnormal blood cells and fibrous tissue. These tumors are most commonly found in the adrenals, kidneys, lymph nodes, breast, lungs, skin, bowel, thymus, thyroid, prostate, and urinary tract.

Most patients with myelofibrosis are over 50 years old; the average age at diagnosis is 65 years. However, myelofibrosis can occur at any age. Myelofibrosis occurs with equal frequency in women and men, but in children it affects girls twice as often as it does boys.

Causes and symptoms

Myelofibrosis is caused by an abnormality in a single stem cell, which causes it to grow out of control. Myelofibrosis tumors that have originated from a single cell are called monoclonal. The cause of the stem cell abnormality is unknown. Persons who were exposed to benzene or high doses of radiation have developed myelofibrosis. There may be an association between myelofibrosis and autoimmune diseases, such as **systemic lupus erythematosus** and **scleroderma**, in which the immune system treats certain molecules of the body as foreign invaders.

Symptoms usually appear slowly over a long period of time. About one quarter of all patients with myelofibrosis have no symptoms (asymptomatic). An enlarged spleen discovered at an annual medical examination may be the first clue. Symptoms of myelofibrosis include:

- fatigue
- weight loss
- paleness
- fever
- sweating
- weakness
- heart palpitations
- shortness of breath
- itchiness
- feeling full after eating a small amount of food
- stomach pain or discomfort
- pain in the left shoulder or upper left portion of the body
- unexpected bleeding
- bone pain, especially in the legs

Diagnosis

Because symptoms are similar to other diseases (mostly leukemias), myelofibrosis is not easy to

diagnose. The doctor would use his or her hands to feel (palpate) for enlargement of the spleen and liver. Blood tests and urine tests would be performed. **Bone marrow aspiration and biopsy** can help make a diagnosis, but they often fail because of the fibrosis. X-ray imaging and **magnetic resonance imaging** (MRI) may be performed.

Treatment

Many asymptomatic patients, if stable, do not require treatment. There is no cure for myelofibrosis, although **bone marrow transplantation** is curative in some cases. Treatment is aimed at reducing symptoms and improving quality of life.

Medications

Male hormones (androgens) can be used to treat anemia but, in women, these drugs can cause the development of male characteristics (e.g., hair growth on the face and body). Glucocorticoid therapy is also an effective treatment of anemia and can improve myelofibrosis in children. Nutrients that stimulate blood formation (hematinics), such as iron, **folic acid**, and vitamin B_{12}, may reduce anemia. Cancer-chemotherapy (usually hydroxyurea) can decrease splenomegaly and hepatomegaly, reduce symptoms of myelofibrosis, lessen anemia, and sometimes reduce bone marrow fibrosis. The bone marrow of myelofibrosis patients is often not strong enough to withstand the harsh **chemotherapy** drugs, so this treatment is not always an option. Interferon-alpha has been shown to reduce spleen size, reduce bone **pain**, and, in some cases, increase the number of blood platelets (structures involved in blood clotting).

Other treatments

In certain cases, the enlarged spleen may be removed (**splenectomy**). Conditions that warrant splenectomy include spleen pain, the need for frequent blood **transfusion**, very low levels of platelets (**thrombocytopenia**), and extreme pressure in the blood vessels of the liver (portal **hypertension**).

Radiation therapy is used to treat splenomegaly, spleen pain, bone pain, tumors in certain places such as next to the spinal cord, and fluid accumulation inside the abdomen (**ascites**). Patients who are not strong enough to undergo splenectomy are often treated with radiation therapy.

Bone marrow transplantation may be used to treat some patients with myelofibrosis. This procedure may be performed on patients who are less than 50 years old, have a poor life expectancy, and have a brother or sister with blood-type similarities.

Patients with severe anemia may require blood transfusions.

KEY TERMS

Anemia—Low numbers of red blood cells in the blood.

Benzene—A colorless volatile flammable toxic liquid hydrocarbon used as a solvent and as a motor fuel.

Biopsy—Surgical removal of tissue for microscopic examination.

Fibrosis—Buildup of scar tissue.

Glucocorticoid therapy—Treatment using corticoids that are anti-inflammatory and immunosuppressive.

Leukemia—Cancer of white blood cells.

Portal hypertension—Extreme pressure on the blood vessels of the liver.

Stem cell—A cell that has the ability to become many different specialized cells.

Prognosis

Similar to leukemias, myelofibrosis is progressive and often requires therapy to control the disease. Myelofibrosis can progress to acute lymphocytic leukemia or lymphoma. Although a number of factors to predict the survival time have been proposed, advanced age or severe anemia are consistently associated with a poor prognosis. The average survival rate of patients diagnosed with myelofibrosis is five years. Death is usually caused by infection, bleeding, complications of splenectomy, **heart failure**, or progression to leukemia. Spontaneous remission is rare.

Prevention

Persons who have been exposed to radiation, benzene, or radioactive thorium dioxide (a chemical used during certain diagnostic radiological procedures) are at risk for myelofibrosis.

Resources

BOOKS

Hillman, Robert S., et al. *Hematology in Clinical Practice*. 5th ed. New York: McGraw-Hill Medical, 2011.

Rodak, Bernadette F., George A. Fritsma, and Elaine Keohane. *Hematology Clinical Principles and Applications*. Philadelphia: Saunders, 2011.

Belinda Rowland, Ph.D.
J. Ricker Polsdorfer, MD

Myelogram *see* **Myelography**

Myelography

Definition

Myelography is an x-ray examination of the spinal canal. A contrast agent is injected through a needle into the space around the spinal cord to display the spinal cord, spinal canal, and nerve roots on an x ray.

Purpose

The purpose of a myelogram is to evaluate the spinal cord and/or nerve roots for suspected compression. Pressure on these delicate structures causes **pain** or other symptoms. A myelogram is performed when precise detail about the spinal cord is needed to make a definitive diagnosis. In most cases, myelography is used after other studies, such as **magnetic resonance imaging** (MRI) or a computed tomography scan (CT scan), have not yielded enough information to be sure of the disease process. Sometimes myelography followed by CT scan is an alternative for patients who cannot have an MRI scan, because they have a pacemaker or other implanted metallic device.

A herniated or ruptured intervertebral disc, popularly known as a slipped disc, is one of the most common causes for pressure on the spinal cord or nerve roots. Discs are pads of fiber and cartilage that contain rubbery tissue. They lie between the vertebrae, or individual bones, which make up the spine. Discs act as cushions, accommodating strains, shocks, and position changes. A disc may rupture suddenly, due to injury, or a sudden straining with the spine in an unnatural position. In other cases, the problem may come on gradually as a result of progressive deterioration of the discs with **aging**. The lower back is the most common area for this problem, but it sometimes occurs in the neck, and rarely in the upper back. A myelogram can help accurately locate the disc or discs involved.

Myelography may be used when a tumor is suspected. Tumors can originate in the spinal cord, or in tissues surrounding the cord. Cancers that have started in other parts of the body may spread or metastasize in the spine. It is important to precisely locate the mass causing pressure, so effective treatment can be undertaken. Patients with known **cancer** who develop back pain may require a myelogram for evaluation.

Other conditions that may be diagnosed using myelography include arthritic bony growths, known as spurs, narrowing of the spinal canal, called **spinal stenosis**, or malformations of the spine.

Precautions

Patients who are unable to lie still or cooperate with positioning should not have this examination. Severe congenital spinal abnormalities may make the examination technically difficult to carry out. Patients with a history of severe allergic reaction to contrast material (x-ray dye) should report this to their physician. Pretreatment with medications to minimize the risk of severe reaction may be recommended.

Description

Myelograms can be performed in a hospital x-ray department or in an outpatient radiology facility. The patient lies on the x-ray table on his or her stomach. The radiologist first looks at the spine under fluoroscopy, where the images appear on a monitor screen. This is done to find the best location to position the needle. The skin is cleaned, then numbed with local anesthetic. The needle is inserted. Occasionally, a small amount of cerebrospinal fluid, the clear fluid which surrounds the spinal cord and brain, may be withdrawn through the needle and sent for laboratory studies. Then contrast material is injected. The contrast material (dye) is a liquid that shows up on x rays.

The x-ray table is tilted slowly. This allows the contrast material to reach different levels in the spinal canal. The flow is observed under fluoroscopy, then x rays are taken with the table tilted at various angles. A footrest and shoulder straps or supports will keep the patient from sliding.

In many instances, a CT scan of the spine will be performed immediately after a myelogram, while the contrast material is still in the spinal canal. This helps outline internal structures most clearly.

A myelogram takes approximately 30-60 minutes. A CT scan adds about another hour to the examination. If the procedure is done as an outpatient exam, some facilities prefer the patient to stay in a recovery area for up to four hours.

Preparation

Patients should be well hydrated at the time of a myelogram. Increasing fluids the day before the study is usually recommended. All food and fluid intake should be stopped approximately four hours before the myelogram.

Certain medications may need to be stopped for one to two days before myelography is performed. These include some antipsychotics, antidepressants, blood thinners, and diabetic medications. Patients should consult with their physician and/or the facility where the study is to be done.

Patients who smoke may be asked to stop the day before the test. This helps decrease the chance of **nausea** or headaches after the myelogram. Immediately before the examination, patients should empty their bowels and bladder.

Aftercare

After the examination is completed, the patient usually rests for several hours, with the head elevated. Extra fluids are encouraged, to help eliminate the contrast material and prevent headaches. A regular diet and routine medications may be resumed. Strenuous physical activity, especially any which involve bending over, may be discouraged for one or two days. The doctor should be notified if a **fever**, excessive **nausea and vomiting**, severe **headache**, or stiff neck develops.

Risks

Headache is a common complication of myelography. It may begin several hours to several days after the examination. The cause is thought to be changes in cerebrospinal fluid pressure, not a reaction to the dye. The headache may be mild and easily alleviated with rest and increased fluids. Sometimes, nonprescription medicine are recommended. In some instances, the headache may be more severe and require stronger medication or other measures for relief. Many factors influence whether the patient develops this problem. These include the type of needle used and the age and sex of the patient. Patients with a history of chronic or recurrent headache are more likely to develop a headache after a myelogram.

The chance of reaction to the contrast material is a very small, but potentially significant risk with myelography. It is estimated that only 5-10% of patients experience any effect from contrast exposure. The vast majority of reactions are mild, such as sneezing, nausea, or **anxiety**. These usually resolve by themselves.

KEY TERMS

Contrast agent—Also called a contrast medium, this is usually a barium or iodine dye that is injected into the area under investigation. The dye makes the interior body parts more visible on an x-ray film.

A moderate reaction, like **wheezing** or **hives**, may be treated with medication, but is not considered life threatening. Severe reactions, such as heart or **respiratory failure**, happen very infrequently. These require emergency medical treatment.

Rare complications of myelography include injury to the nerve roots from the needle, or from bleeding into the spaces around the roots. Inflammation of the delicate covering of the spinal cord, called arachnoiditis, or infections, can also occur. Seizures are another very uncommon complication reported after myelography.

Normal results

A normal myelogram would show a spinal canal of normal width, with no areas of constriction or obstruction.

Abnormal results

A myelogram may reveal a **herniated disk**, tumor, bone spurs, or narrowing of the spinal canal (spinal stenosis).

ORGANIZATIONS

Radiological Society of North America, 820 Jorie Boulevard, Oak Brook, IL, 60523-2251, (630) 571-2670, (630) 571-7837, (800) 381-6660, radiologyinfo.org.

Ellen S. Weber, MSN

Myeloma *see* **Multiple myeloma**

Myers-Briggs type indicator

Definition

The Myers-Briggs Type Indicator (MBTI) is a widely used personality inventory, or test, employed in vocational, educational, and **psychotherapy** settings to evaluate personality type in adolescents and adults age 14 and older.

Purpose

In an educational setting, the MBTI may be performed to assess student learning style. Career counselors use the test to help others determine what occupational field they might be best suited for, and it is also used in organizational settings to assess management skills and facilitate teamwork and problem-solving, including communication difficulties. Because the MBTI is also a tool for self-discovery, mental health professionals may administer the test in counseling sessions to provide their patients with insight into their behavior.

As of the early 2000s, the MBTI is also being used in the mental health field to assess vulnerability to **anxiety disorders** and depression. Preliminary results indicate that some of the 16 types are more susceptible to **mood disorders** than others. ISFPs, for example, are overrepresented among patients in treatment for unipolar depression, while the four ST types appear to be more vulnerable to **anxiety** states.

Precautions

The MBTI should be administered, scored, and interpreted only by a professional trained in its use. Cultural and language differences in the test subject may affect performance and may result in inaccurate test results. The test administrator should be informed before testing begins if the test taker is not fluent in English and/or he has a unique cultural background.

Description

In 2000, an estimated two million people took the MBTI, making it the most frequently used personality inventory available. The test was first introduced in 1942, the work of a mother and daughter, Katharine Cook Briggs and Isabel Briggs Myers. There are now several different versions of the test available. Form M, which contains 93 items, is the most commonly used.

The Myers-Briggs inventory is based on Carl Jung's theory of types, outlined in his 1921 work *Psychological Types*. Jung's theory holds that human beings are either *introverts* or *extraverts*, and their behavior follows from these inborn psychological types. He also believed that people take in and process information different ways, based on their personality traits.

The Myers-Briggs evaluates personality type and preference based on the four Jungian psychological types:

- extraversion (E) or introversion (I)
- sensing (S) or intuition (N)
- thinking (T) or feeling (F)
- judging (J) or perceiving (P)

KEY TERMS

Multitasking—Performing multiple duties or taking on multiple responsibilities and roles simultaneously.

Vocational—Relating to an occupation, career, or job.

Preparation

Prior to the administration of the MBTI, the test subject should be fully informed about the nature of the test and its intended use. He or she should also receive standardized instructions for taking the test and any information on the confidentiality of the results.

Normal results

Myers-Briggs results are reported as a four-letter personality type (e.g., ESTP, ISFJ). Each letter corresponds to an individual's preference in each of the four pairs of personality indicators (i.e., E or I, S or N, T or F, and J or P). There are a total of sixteen possible combinations of personality types on the MBTI.

Letter One: E or I

Extraverts focus more on people and things in the outside world, introverts on internal thoughts and ideas.

Letter Two: S or N

Sensing dominant personalities prefer to perceive things through sight, sound, taste, touch, and smell, while intuition dominant types look to past experience and are more abstract in their thinking.

Letter Three: T or F

The third subtype is a measure of how people use judgment. Thinking types use logic to judge the world, while feeling types tend to view things on the basis of what emotions they elicit.

Letter Four: J or P

Everyone judges and perceives, but those who are judging dominant are said to be more methodical and results-oriented, while perceiving dominant personalities are good at multitasking and are flexible.

Resources

BOOKS

Brandt, Tina. *Personality and Leadership: Myers–Briggs Type Indicator and Transformational Leadership—Perspectives of Subordinates and Leaders*. Saarbrücken, Germany: Lambert Academic, 2010.

PERIODICALS

Clack, G. B., J. Allen, D. Cooper, and J. O. Head. "Personality Differences between Doctors and Their Patients: Implications for the Teaching of Communication Skills." *Medical Education* 38 (February 2004): 177–186.

Janowsky, D. S., E. Hong, S. Morter, and L. Howe. "Myers Briggs Type Indicator Personality Profiles in Unipolar Depressed Patients." *World Journal of Biological Psychiatry* 3 (October 2002): 207–215.

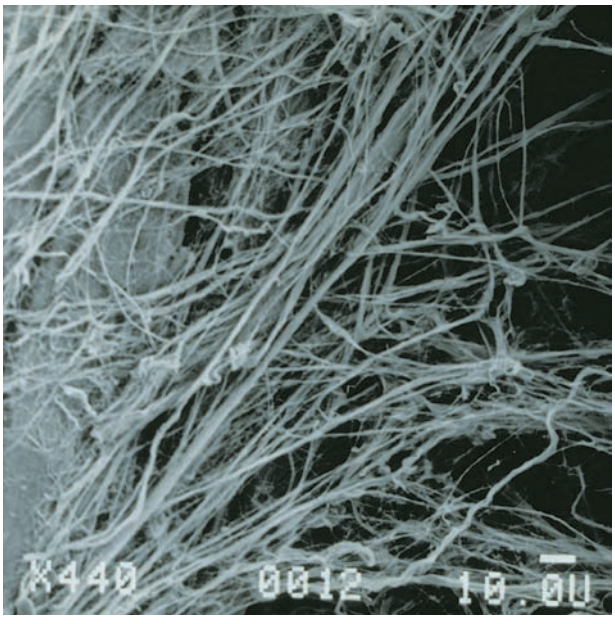
Kameda, D. M., and J. L. Nyland. "Relationship between Psychological Type and Sensitivity to Anxiety." *Perceptual and Motor Skills* 97 (December 2003): 789–793.

Paula Anne Ford-Martin
Rebecca J. Frey, PhD

Myocardial biopsy

Definition

Myocardial biopsy is a procedure wherein a small portion of tissue is removed from the heart muscle for testing. This test is also known as endomyocardial biopsy.



Once the catheter is threaded up into the heart, the surgeon will take several small samples of muscle for laboratory analysis. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

KEY TERMS

Anticoagulant—Medication that thins the blood and slows clot formation.

Aplastic anemia—A greatly decreased production of all of the formed elements of the blood caused by a failure of the cell-generating capacity of the bone marrow.

Electrocardiography—A test that uses electrodes attached to the chest with an adhesive gel to transmit the electrical impulses of the heart muscle to a recording device.

Leukemia—A disease characterized by an increasing number of abnormal cells in the blood.

Purpose

The main reason for a biopsy is to secure tissue samples that will be useful in the diagnosis, treatment, and care of heart muscle disorders. The test is also used to detect rejection after a **heart transplantation** procedure.

Precautions

This procedure is not used when the patient is taking blood-thinning medication (anticoagulant therapy). It should not be done when the patient has leukemia and **aplastic anemia** or if there is a blood clot on the interior wall of the heart.

Description

A long, flexible tube, called a catheter, is inserted into a vein and threaded up into the heart. The doctor can guide the catheter by watching its movement on a TV monitor showing an x-ray image of the area. The tip of the catheter is fitted with tiny jaws that the doctor can open and close. Once the catheter is in place, the doctor will take several small snips of muscle for microscopic examination.

Preparation

Preparation for myocardial biopsy is quite extensive. The patient will be asked not to eat for several hours before the procedure. A technician will shave the hair from the area of the incision and will also insert an intravenous line in the arm. The patient will be given a sedative to relax but will not be fully anesthetized. The patient will be connected to an

electrocardiograph (ECG) to monitor the heart, and a blood-pressure cuff will be placed. Finally, the patient will be covered with sterile drapes, so that the area of the biopsy is kept free of germs. The cardiologist will numb the area where the catheter will be inserted.

Aftercare

At the end of the biopsy, the catheter will be removed and pressure will be applied at the site where it entered the blood vessel in order to encourage healing. The patient will then be taken to the recovery room. It is advisable to remain flat and not to move about for 6-8 hours. After that time, most people begin walking around. Swelling and bruising at the puncture site are common and usually go away without need for further attention.

Risks

The risks involved with myocardial biopsy are small because the patient is monitored closely and attended by well-trained staff. Racing of the heart (**palpitations**) and quivering of the heart muscles (**atrial fibrillation**) are both possible during the procedure.

ORGANIZATIONS

American Heart Association National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, Review.personal.info@heart.org.

Dorothy Elinor Stonely

Myocardial infarction *see* **Heart attack**

Myocardial resection

Definition

Myocardial resection is a surgical procedure in which a portion of the heart muscle is removed.

Purpose

Myocardial resection is done to improve the stability of the heart function or rhythm. Also known as endocardial resection, this open-heart surgery is done to destroy or remove damaged areas of the heart that cause life-threatening heart rhythms. This procedure is often performed in people who have had a **heart attack**, in order to prevent future rapid heart rates. It is also used in people who have **Wolff-Parkinson-White syndrome** (a condition resulting in abnormal heart rhythm).

KEY TERMS

Implantable cardioverter-defibrillator—A device placed in the body to deliver an electrical shock to the heart in response to a serious abnormal rhythm.

Wolff-Parkinson-White syndrome—An abnormal, rapid heart rhythm, due to an extra pathway for the electrical impulses to travel from the atria to the ventricles.

Precautions

This is major surgery and should be the treatment of choice only after medications have failed and the use of an **implantable cardioverter-defibrillator** (a device that delivers electrical shock to control heart rhythm) has been ruled out.

Description

After receiving a general anesthetic, an incision will be made in the chest to expose the heart. When the exact source of the abnormal rhythm is identified, it is removed. If there are areas around the source that may contribute to the problem, they can be frozen with a special probe to further insure against dangerous heart rates. The amount of tissue removed is so small, usually only 2 or 3 millimeters, that there is no damage to the structure of the heart. On some occasions, aneurysms of the heart wall are removed as well.

Preparation

Prior to surgery, the physician will explain the procedure, routine blood tests will be completed, and consent forms will be signed.

Aftercare

Immediately after surgery, the patient will be moved to a recovery room until the affects of anesthesia have worn off. The patient will then be transferred to the intensive care unit for further recovery. In the intensive care unit, the heart will be monitored for any disturbances in rhythm and the patient will be watched for any signs of post-operative problems.

Risks

The risks of myocardial resection are based in large part on the person's underlying heart condition and, therefore, vary greatly. The procedure involves opening the heart, so the person is at risk for the complications associated with major heart surgery such as **stroke**, shock, infection, and hemorrhage.

Normal results

Anywhere from 5-25% of post-heart attack patients do not survive open-heart surgery. The survivors have a 90% arrhythmia-free one-year survival rate, (arrthymia is an irregular heart beat).

ORGANIZATIONS

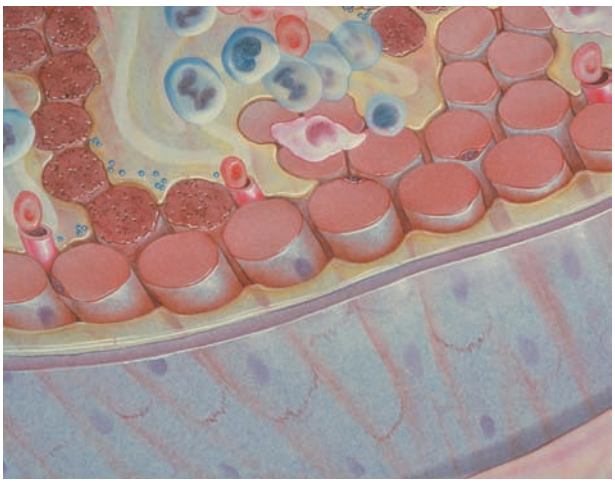
American Heart Association National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, Review.personal.info@heart.org.

Dorothy Elinor Stonely

Myocarditis

Definition

Myocarditis is an inflammatory disease of the heart muscle (myocardium) that can result from a variety of causes. While most cases are produced by a viral infection, an inflammation of the heart muscle may also be instigated by toxins, drugs, and hypersensitive immune reactions. Myocarditis is a rare but serious condition that affects both males and females of any age.



This illustration depicts the inflammation of the myocarditis, the middle muscular layer of the heart wall. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Description

Most cases of myocarditis in the United States originate from a virus, and the disease may remain undiagnosed by doctors due to its general lack of initial symptoms. The disease may also present itself as an acute, catastrophic illness that requires immediate treatment. Although the inflammation or degeneration of the heart muscle that myocarditis causes may be fatal, this disease often goes undetected. It may also disguise itself as ischemic, valvular, or hypertensive heart disease.

An inflammation of the heart muscle may occur as an isolated disorder or be the dominating feature of a systemic disease (one that affects the whole body, like **systemic lupus erythematosus**).

Causes and symptoms

While there are several contributing factors that may lead to myocarditis, the primary cause is viral. Myocarditis usually results from the Coxsackie B virus, and may also result from **measles**, **influenza**, chicken pox, hepatitis virus, or the adenovirus in children. If an acute onset of severe myocarditis occurs, a patient may display the following symptoms:

- Rhythm disturbances of the heart
- Rapid heartbeat (Ventricular tachycardia)
- Left or right ventricular enlargement
- Shortness of breath (Dyspnea)
- Pulmonary edema (the accumulation of fluid in the lungs due to left-sided heart failure)
- Swollen legs.

Additional causes of myocarditis include:

- Bacterial infections, such as tetanus, gonorrhea, or tuberculosis
- Parasite infections, such as Chagas' disease (which is caused by an insect-borne protozoan most commonly seen in Central and South America)
- Rheumatic fever
- Surgery on the heart
- Radiation therapy for cancer that is localized in the chest, such as breast or lung cancer
- Certain medications.

Research has shown that illegal drugs and toxic substances may also produce acute or chronic injury to the myocardium. These studies also indicate an increase in the incidence of toxic results from the use of **cocaine**. This illegal drug causes coronary artery

KEY TERMS

Adenovirus—One type of virus that can cause upper respiratory tract infections.

Angiography—A procedure that uses x ray after injecting a radiopaque substance to examine the blood vessels and lymphatics.

Arrhythmia—An irregular heartbeat or action.

Cardiac catheterization—A diagnostic procedure that gives a comprehensive examination of how the heart and its blood vessels function; performed by inserting one or more catheters through a peripheral blood vessel in the arm or leg.

Coxsackie B virus—A mild virus belonging to a group of viruses (coxsackievirus) that may produce a variety of illnesses, including myocarditis.

Echocardiography—A noninvasive diagnostic procedure that uses ultrasound to examine internal cardiac structures.

Electrocardiogram—A record of the electrical activity of the heart, with each wave being labeled as P, Q, R, S, and T waves. Often used in the diagnosis of cases of abnormal cardiac rhythm and myocardial damage.

Hypertensive heart disease—High blood pressure resulting in a disease of the heart.

Ischemic heart disease—Insufficient blood supply to the heart muscle (myocardium).

Valvular heart disease—A disease of any one of the four valves that controls blood flow into, through, and out of the heart.

Ventricular tachycardia—An abnormally rapid heartbeat. It includes a series of at least three beats arising from a ventricular area at a rate of more than 100 beats per minute, usually ranging from 150-200 beats per minute.

spasm, myocardial infarction (**heart attack**), and **arrhythmias**, as well as myocarditis.

Further studies conducted in 1996 indicate that **malnutrition** encourages the Coxsackie B virus to flourish, leading to the potential development of myocarditis. Human **immunodeficiency** virus (HIV) is also now recognized as a cause of myocarditis, though its prevalence is not known.

Symptoms of myocarditis may start as **fatigue**, **shortness of breath**, **fever**, and aching of the joints, all characteristic of a flu-like illness. In contrast to this type of mild appearance, myocarditis may also appear suddenly in the form of **heart failure**, or **sudden cardiac death** without any prior symptoms. If an inflammation of the heart muscle leads to congestive heart failure, symptoms such as swollen feet and ankles, distended neck veins, a rapid heartbeat, and difficulty breathing while reclining may all appear.

Diagnosis

The best way to diagnose myocarditis may be through a person's observation of his or her own symptoms, followed by a thorough medical history and physical exam conducted by a doctor. Further tests usually include laboratory blood studies and **echocardiography**. An electrocardiogram (ECG) is also routinely used due to its ability to detect a mild case of the disease. **Cardiac catheterization** and **angiography** are additional diagnostic tests used to determine the presence of myocarditis, or to rule out other possible heart diseases that may lead to heart failure.

Another measure used to diagnosis myocarditis is the endomyocardial biopsy procedure. This invasive catheterization procedure examines a biopsied, or "snipped," piece of the endocardium (the lining membrane of the inner surface of the heart). The tissue sample is examined to verify the presence of the disease, as well as to try to determine the infective cause. An approach used only with a patient's consent, this procedure may also confirm acute myocarditis, allowing close monitoring of potential congestive heart failure.

Treatment

While myocarditis is a serious condition, there is no medical treatment necessary if it results from a general viral infection. The only steps to recovery include rest and avoidance of physical exertion. Adequate rest becomes more important to recovery if the case is severe myocarditis with signs of dilated **cardiomyopathy** (disease of the heart muscles). In this case, medical treatment for congestive heart failure may include the following medications: angiotensin converting enzyme (ACE) inhibitors, **diuretics** to reduce fluid retention, digitalis to stimulate a stronger heartbeat, and low-dose beta-blockers.

If myocarditis is caused by a bacterial infection, the disease is treated with **antibiotics** to fight the infection. If severe rhythm disturbances are involved, cardiac

assist devices, an "artificial heart," or **heart transplantation** may be the only option for complete recovery.

Prognosis

The outlook for a diagnosed case of myocarditis caused by a viral infection is excellent, with many cases healing themselves spontaneously. Severe or acute myocarditis may be controlled with medication to prevent heart failure. Because this disease may be mild or may be extreme and cause serious arrhythmias, the prognosis varies. Cases of myocarditis may vary from complete healing (with or without significant scarring), to severe congestive heart failure leading to **death** or requiring a heart transplant.

Inflammation of the myocardium may also cause acute **pericarditis** (inflammation of the outer lining of the heart). Due to the potential effects of the disease, including sudden death, it is imperative that proper medical attention is obtained.

Prevention

Although myocarditis is an unpredictable disease, the following measures may help prevent its onset. Individuals should:

- Take extra measures to avoid infections, and obtain appropriate treatment for infections.
- Limit alcohol consumption to no more than one or two drinks a day, if any.
- Maintain current immunizations against diphtheria, tetanus, measles, rubella, and polio.
- Avoid anything that may cause the abnormal heart to work too hard, including salt and vigorous exercise.

ORGANIZATIONS

American Heart Association National Center, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, Review.personal.info@heart.org.

National Heart Lung and Blood Institute Health Information Center, P.O. Box 30105, Bethesda, MD, 20824-0105, (301) 592-8573, (240) 629-3246, http://www.nhlbi.nih.gov.

Beth A. Kapes

Myoglobin test

Definition

Myoglobin is a protein found in muscle. Myoglobin tests are done to evaluate a person who has symptoms of a **heart attack** (myocardial infarction) or other muscle damage.

Purpose

Myoglobin holds oxygen inside heart and skeletal muscle (muscles that attach to and move bones). It is continually released into the blood in small amounts due to normal turnover of muscle cells. Kidneys discard the myoglobin into urine.

When muscle is damaged, as in a heart attack, larger amounts of myoglobin are released and blood levels rise rapidly. Myoglobin is one of the first tests done to determine if a person with chest **pain** is having a heart attack, as it may be one of the first blood tests to become abnormal.

Damage or injury to skeletal muscle also causes myoglobin to be released into the blood.

Description

Heart attack must be diagnosed quickly. Medications to prevent heart damage are effective only within a limited number of hours. Yet, because of their risk for excessive bleeding, these medications are given only after a diagnosis of heart attack is made.

Myoglobin is one of several cardiac markers used to make the diagnosis. Cardiac markers are substances in blood whose levels rise in the hours following a heart attack. Increased levels help diagnose a heart attack; persistent normal levels rule it out.

Each cardiac marker rises, peaks, and returns to a normal level according to its own timeline, or diagnostic window. Myoglobin is useful because it has the earliest diagnostic window. It is the first marker to rise after chest pain begins. Myoglobin levels rise within two to three hours, and sometimes as early as 30 minutes. They peak after six to nine hours. The levels return to normal within 24-36 hours.

Although a rise in myoglobin supports a diagnosis of heart attack, it is not conclusive. Simultaneous skeletal muscle damage could also cause the increase. Myoglobin rules out, rather than proves, a diagnosis in the following way. If myoglobin levels have not risen after more than five hours, a heart attack in unlikely. Normal levels in the first two to three hours do not rule out an infarction.

The myoglobin test is sometimes repeated every one to two hours to watch for the rise and peak. Results are available within 30 minutes.

Myoglobin in large amounts is toxic to the kidney. When a person has high amounts of myoglobin in the blood, kidney function must be monitored.

KEY TERMS

Cardiac marker—A substance in the blood that rises following a heart attack.

Diagnostic window—A cardiac marker's timeline for rising, peaking, and returning to normal after a heart attack.

Myoglobin—A protein that holds oxygen in heart and skeletal muscle. It rises after damage to either of these muscle types.

Preparation

This test requires 5 mL of blood. Collection of the sample takes only a few minutes. A urine myoglobin test requires 1 mL of urine collected into a urine collection cup.

Aftercare

Discomfort or bruising may occur at the puncture site or the person may feel dizzy or faint. Pressure to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort.

Normal results

Normal results vary based on the laboratory and method used.

Abnormal results

Myoglobin levels and levels of other cardiac markers are usually considered before finally confirming a diagnosis of heart attack. A level that has doubled after one to two hours, even if the level is still in the normal range, indicates a significant rise that may be due to heart attack.

Increased levels are also found with skeletal muscle damage or disease, such as an injury, **muscular dystrophy**, or **polymyositis**. Myoglobin levels also rise during renal failure because kidneys lose their ability to clear myoglobin from blood.

Resources

BOOKS

Morrow, David A. *Cardiovascular Biomarkers: Pathophysiology and Disease Management*. Totowa, NJ: Humana Press, 2006.

Nancy J. Nordenson

Myomas *see* **Uterine fibroids**

Myomectomy

Definition

Myomectomy is the removal of fibroids (noncancerous tumors) from the wall of the uterus. Myomectomy is the preferred treatment for symptomatic fibroids in women who want to keep their uterus. Larger fibroids must be removed with an abdominal incision, but small fibroids can be taken out using **laparoscopy** or **hysteroscopy**.

Purpose

A myomectomy can remove **uterine fibroids** that are causing symptoms. It is an alternative to surgical removal of the whole uterus (**hysterectomy**). The procedure can relieve fibroid-induced menstrual symptoms that have not responded to medication. Myomectomy also may be an effective treatment for **infertility** caused by the presence of fibroids.

Precautions

There is a risk that removal of the fibroids may lead to such severe bleeding that the uterus itself will have to be removed. Because of the risk of blood loss during a myomectomy, patients may want to consider banking their own blood before surgery.

Description

Usually, fibroids are buried in the outer wall of the uterus and abdominal surgery is required. If they are on the inner wall of the uterus, uterine fibroids can be removed using hysteroscopy. If they are on a stalk (pedunculated) on the outer surface of the uterus, laparoscopy can be performed.

Removing fibroids through abdominal surgery is a more difficult and slightly more risky operation than a hysterectomy. This is because the uterus bleeds from the sites where the fibroids were, and it may be difficult or impossible to stop the bleeding. This surgery is usually performed under **general anesthesia**, although some patients may be given a spinal or epidural anesthesia.

The incision may be horizontal (the "bikini" incision) or a vertical incision from the navel downward. After separating the muscle layers underneath the skin, the surgeon makes an opening in the abdominal wall. Next, the surgeon makes an incision over each fibroid, grasping and pulling out each growth.

Every opening in the uterine wall is then stitched with sutures. The uterus must be meticulously repaired

in order to eliminate potential sites of bleeding or infection. Then, the surgeon sutures the abdominal wall and muscle layers above it with absorbable stitches, and closes the skin with clips or nonabsorbable stitches.

When appropriate, a laparoscopic myomectomy may be performed. In this procedure, the surgeon removes fibroids with the help of a viewing tube (laparoscope) inserted into the pelvic cavity through an incision in the navel. The fibroids are removed through a tiny incision under the navel that is much smaller than the 4 or 5 inch opening required for a standard myomectomy.

If the fibroids are small and located on the inner surface of the uterus, they can be removed with a thin telescope-like device called a hysteroscope. The hysteroscope is inserted into the vagina through the cervix and into the uterus. This procedure does not require any abdominal incision, so hospitalization is shorter.

Preparation

Surgeons often recommend hormone treatment with a drug called leuprolide (Lupron) two to six months before surgery in order to shrink the fibroids. This makes the fibroids easier to remove. In addition, Lupron stops menstruation, so women who are anemic have an opportunity to build up their blood count. While the drug treatment may reduce the risk of excess blood loss during surgery, there is a small risk that temporarily smaller fibroids might be missed during myomectomy, only to enlarge later after the surgery is completed.

Aftercare

Patients may need four to six weeks of recovery following a standard myomectomy before they can return to normal activities. Women who have had laparoscopic or hysteroscopic myomectomies, however, can leave the hospital the day after surgery and usually recovery completely within two to three days to one to three weeks.

Risks

The risks of a myomectomy performed by a skilled surgeon are about the same as hysterectomy (one of the most common and safest surgeries). Removing multiple fibroids is more difficult and slightly more risky.

Possible complications include:

- Infection.
- Blood loss.

KEY TERMS

Epidural anesthesia—A method of pain relief for surgery in which local anesthetic is injected into the epidural space in the middle and lower back.

- The wall of the uterus may be weakened if the removal of a large fibroid leaves a wound that extends the complete thickness of the wall. Special precautions may be needed in future pregnancies. For example, the delivery may need to be performed surgically (Caesarean section).
- Adverse reactions to anesthesia.
- Internal scarring (and possible infertility).

Since fibroids tend to appear and grow as a woman ages (until **menopause**), it is possible that new fibroids will appear after myomectomy.

Resources

OTHER

Toaff, Michael E. "Myomectomy." *Alternatives to Hysterectomy Page*. http://www.netreach.net/~hysterectomyedu/myomecto.htm.

Carol A. Turkington

Myopathies

Definition

Myopathies are diseases of skeletal muscle which are not caused by nerve disorders. These diseases cause the skeletal or voluntary muscles to become weak or wasted.

Description

There are many different types of myopathies, some of which are inherited, some inflammatory, and some caused by endocrine problems. Myopathies are rare and not usually fatal. Typically, effects are mild, largely causing muscle weakness and movement problems, and many are transitory. Only rarely will patients become dependent on a wheelchair. However, **muscular dystrophy** (which is technically a form of myopathy) is far more severe. Some types of this disease are fatal in early adulthood.

Causes and symptoms

Myopathies are usually degenerative, but they are sometimes caused by drug side effects, chemical **poisoning**, or a chronic disorder of the immune system.

Genetic myopathies

Among their many functions, genes are responsible for overseeing the production of proteins important in maintaining healthy cells. Muscle cells produce thousands of proteins. With each of the inherited myopathies, a genetic defect is linked to a lack of, or problem with, one of the proteins needed for normal muscle cell function.

There are several different kinds of myopathy caused by defective genes:

- Central core disease
- Centronuclear (myotubular) myopathy
- Myotonia congenita
- Nemaline myopathy
- Paramyotonia congenita
- Periodic paralysis (hypokalemic and hyperkalemic forms)
- Mitochondrial myopathies.

Most of these genetic myopathies are dominant, which means that a child needs to inherit only one copy of the defective gene from one parent in order to have the disease. The parent with the defective gene also has the disorder, and each of this parent's children has a 50% chance of also inheriting the disease. Male and female children are equally at risk.

However, one form of myotonia congenita and some forms of nemaline myopathy must be inherited from both parents, each of whom carry a recessive defective gene but who do not have symptoms of the disease. Each child of such parents has a 25% chance of inheriting both genes and showing signs of the disease, and a 50% chance of inheriting one defective gene from only one parent. If the child inherited just one defective gene, he or she would be a carrier but would not show signs of the disease.

A few forms of centronuclear myopathy develop primarily in males. Females who inherit the defective gene are usually carriers without symptoms, like their mothers, but they can pass on the disease to their sons. Mitochondrial myopathies are inherited through the mother, since sperm do not contain mitochondria. (Mitochondria play a key role in energy production in the body's cells.)

The major symptoms associated with the genetic myopathies include:

- Central core disease: mild weakness of voluntary muscles, especially in the hips and legs; hip displacement; delays in reaching developmental motor milestones; problems with running, jumping, and climbing stairs develop in childhood
- Centronuclear myopathy: weakness of voluntary muscles including those on the face, arms, legs, and trunk; drooping upper eyelids; facial weakness; foot drop; affected muscles almost always lack reflexes
- Myotonia congenita: voluntary muscles of the arms, legs, and face are stiff or slow to relax after contracting (myotonia); stiffness triggered by fatigue, stress, cold, or long rest periods, such as a night's sleep; stiffness can be relieved by repeated movement of the affected muscles
- Nemaline myopathy: moderate weakness of voluntary muscles in the arms, legs, and trunk; mild weakness of facial muscles; delays in reaching developmental motor milestones; decreased or absent reflexes in affected muscles; long, narrow face; high-arched palate; jaw projects beyond upper part of the face
- Paramyotonia congenita: stiffness (myotonia) of voluntary muscles in the face, hands, and forearms; attacks spontaneous or triggered by cold temperatures; stiffness made worse by repeated movement; episodes of stiffness last longer than those seen in myotonia congenita
- Periodic paralysis: attacks of temporary muscle weakness (muscles work normally between attacks); in the hypokalemic (low calcium) form, attacks triggered by vigorous exercise, heavy meals (high in carbohydrates), insulin, stress, alcohol, infection, pregnancy; in the hyperkalemic (normal/high calcium) form, attacks triggered by vigorous exercise, stress, pregnancy, missing a meal, steroid drugs, high potassium intake
- Mitochondrial myopathies: symptoms vary quite widely with the form of the disease and may include progressive weakness of the eye muscles (ocular myopathy), weakness of the arms and legs, or multisystem problems primarily involving the brain and muscles.

Endocrine-related myopathies

In some cases, myopathies can be caused by a malfunctioning gland (or glands), which produces either too much or too little of the chemical messengers called hormones. Hormones are carried by the blood and one of their many functions is to regulate muscle activity. Problems in producing hormones can lead to muscle weakness.

Hyperthyroid myopathy and hypothyroid myopathy affect different muscles in different ways. Hyperthyroid myopathy occurs when the thyroid gland produces too much thyroxine, leading to muscle weakness, some muscle wasting in hips and shoulders, and, sometimes, problems with eye muscles. The hypothyroid type occurs when too little hormone is produced, leading to stiffness, cramps, and weakness of arm and leg muscles.

Inflammatory myopathies

Some myopathies are inflammatory, leading to inflamed, weakened muscles. Inflammation is a protective response of injured tissues characterized by redness, increased heat, swelling, and/or **pain** in the affected area. Examples of this type include **polymyositis**, **dermatomyositis**, and **myositis** ossificans.

Dermatomyositis is a disease of the connective tissue that also involves weak, tender, inflamed muscles. In fact, muscle tissue loss may be so severe that the person may be unable to walk. Skin inflammation is also present. The cause is unknown, but viral infection and **antibiotics** are associated with the condition. In some cases, dermatomyositis is associated with rheumatologic disease or **cancer**. Polymyositis involves inflammation of many muscles usually accompanied by deformity, swelling, sleeplessness, pain, sweating, and tension. It, too, may be associated with cancer. Myositis ossificans is a rare inherited disease in which muscle tissue is replaced by bone, beginning in childhood.

Muscular dystrophy

While considered to be a separate group of diseases, the muscular dystrophies also technically involve muscle wasting and can be described as myopathies. These relatively rare diseases appear during childhood and adolescence, and are caused by muscle destruction or degeneration. They are a group of genetic disorders caused by problems in the production of key proteins.

The forms of muscular dystrophy (MD) differ according to the way they are inherited, the age of onset, the muscles they affect, and how fast they progress. The most common type is Duchenne MD, affecting one or two in every 10,000 boys. Other types of MD include Becker's, **myotonic dystrophy**, limb-girdle MD, and facioscapulohumeral MD.

Diagnosis

Early diagnosis of myopathy is important so that the best possible care can be provided as soon as possible. An experienced physician can diagnose a myopathy by evaluating a person's medical history and by performing a thorough physical exam. Diagnostic tests can help differentiate between the different types of myopathy, as well as between myopathy and other neuromuscular disorders. If the doctor suspects a genetic myopathy, a thorough family history will also be taken.

Diagnostic tests the doctor may order include:

- Measurements of potassium in the blood
- Muscle biopsy
- Electromyogram (EMG).

KEY TERMS

Electromyogram (EMG)—A diagnostic test that records the electrical activity of muscles. In the test, small electrodes are placed on or in the skin; the patterns of electrical activity are projected on a screen or over a loudspeaker. This procedure is used to test for muscle disorders, including muscular dystrophy.

Inflammation—A protective response of injured tissues characterized by redness, increased heat, swelling, and/or pain in the affected area.

Voluntary muscles—Muscles producing voluntary movement.

Treatment

Treatment depends on the specific type of myopathy the person has:

- Periodic paralysis: medication and dietary changes
- Hyperthyroid or hypothyroid myopathy: treatment of the underlying thyroid abnormality
- Myositis ossificans: medication may prevent abnormal bone formation, but there is no cure following onset
- Central core disease: no treatment
- Nemaline myopathy: no treatment
- Centronuclear (myotubular) myopathy: no treatment
- Paramyotonia congenita: treatment often unnecessary
- Myotonia congenita: drug treatment (if necessary), but drugs do not affect the underlying disease, and attacks may still occur.

Prognosis

The prognosis for patients with myopathy depends on the type and severity of the individual disease. In most cases, the myopathy can be successfully treated and the patient returned to normal life.

Muscular dystrophy, however, is generally a much more serious condition. Duchenne's MD is usually fatal by the late teens; Becker's MD is less serious and may not be fatal until the 50s.

ORGANIZATIONS

Muscular Dystrophy Association, 3300 East Sunrise Drive, Tucson, AZ, 85718, (800) 572-1717, http://www.mdausa.org.

Carol A. Turkington

Myopia

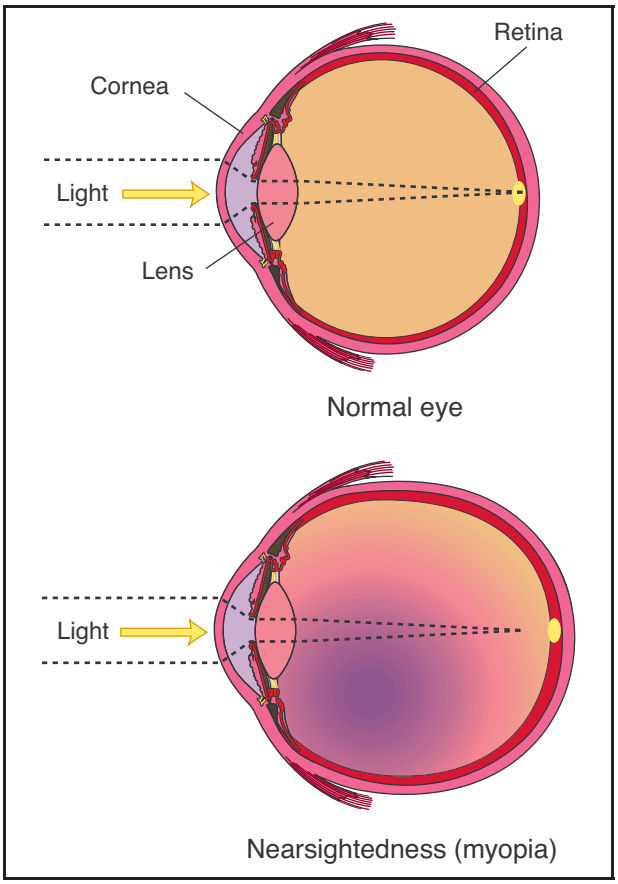
Definition

Myopia is the medical term for nearsightedness. People with myopia see objects more clearly when they are close to the eye, while distant objects appear blurred or fuzzy. Reading and close–up work may be clear, but distance vision is blurry.

Description

To understand myopia it is necessary to have a basic knowledge of the main parts of the eye's focusing system: the cornea, the lens, and the retina. The cornea is a tough, transparent, dome–shaped tissue that covers the front of the eye (not to be confused with the white, opaque sclera). The cornea lies in front of the iris (the colored part of the eye). The lens is a transparent, double–convex structure located behind the iris. The retina is a thin membrane that lines the rear of the eyeball. Light–sensitive retinal cells convert incoming light rays into electrical signals that are sent along the optic nerve to the brain, which then interprets the images.

In people with normal vision, parallel light rays enter the eye and are bent by the cornea and lens (a process called refraction) to focus precisely on the retina, providing a crisp, clear image. In the myopic eye, the focusing power of the cornea (the major refracting structure of the eye) and the lens is too great with respect to the length of the eyeball. Light rays are bent too much, and they converge in front of the retina. This inaccuracy is called a refractive error. In other words, an overfocused fuzzy image is sent to the brain.



Myopia, or nearsightedness, is a condition of the eye in which objects are seen more clearly when close to the eye while distant objects appear blurred or fuzzy. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

There are many types of myopia. Some common types include:

- Physiologic
- Pathologic
- Acquired.

By far the most common form, physiologic myopia develops in children sometime between the ages of five and 10 years and gradually progresses until the eye is fully grown. Physiologic myopia may include refractive myopia (the cornea and lens–bending properties are too strong) and axial myopia (the eyeball is too long). Pathologic myopia is a far less common abnormality. This condition begins as physiologic myopia, but rather than stabilizing, the eye continues to enlarge at an abnormal rate (progressive myopia). This more advanced type of myopia may lead to degenerative changes in the eye (degenerative myopia). Acquired myopia occurs after

infancy. This condition may be seen in association with uncontrolled diabetes and certain types of **cataracts**. **Antihypertensive drugs** and other medications can also affect the refractive power of the lens.

Genetic profile

Eye care professionals have debated the role of genetics in the development of myopia for many years. Some believe that a tendency toward myopia may be inherited, but that the actual disorder results from a combination of environmental and genetic factors. Environmental factors include close work; work with computer monitors or other instruments that emit some light (electron microscopes, photographic equipment, lasers, etc.); emotional **stress**; and eye strain.

A variety of genetic patterns for inheriting myopia have been suggested, ranging from a recessive pattern with complete penetrance in people who are homozygotic for myopia to an autosomal dominant pattern; an autosomal recessive pattern; and various mixtures of these patterns. One explanation for this lack of agreement is that the genetic profile of high myopia (defined as a refractive error greater than –6 diopters) may differ from that of low myopia. Some researchers believe that high myopia is determined by genetic factors to a greater extent than low myopia.

The lack of clear consensus concerning the role of heredity in myopia may be due to the sensitivity of the human eye to very small changes in its anatomical structure. Since even small deviations from normal structure cause significant refractive errors, it may be difficult to single out any specific genetic or environmental factor as their cause.

Genetic markers and gene mapping

Since 1992, genetic markers that may be associated with genes for myopia have been located on human chromosomes 1, 2, 12, and 18. There is some genetic information on the short arm of chromosome 2 in highly myopic people. Genetic information for low myopia appears to be located on the short arm of chromosome 1, but it is not known whether this information governs the structure of the eye itself or vulnerability to environmental factors.

In 1998, a team of American researchers presented evidence that a gene for familial high myopia with an autosomal dominant transmission pattern could be mapped to human chromosome 18 in eight North American families. The same group also found a second locus for this form of myopia on human chromosome 12 in a large German/Italian family. In 1999, a group of French researchers found no linkage between chromosome 18 and 32 French families with familial high myopia. These findings have been taken to indicate that more than one gene is involved in the transmission of the disorder.

As of 2009, the heritability of high–grade myopia has been confirmed. Multiple high–grade myopia genetic loci have been identified, and confirmatory studies identifying high–grade and moderate myopia loci have also occurred. However, myopia susceptibility genes still remain unknown.

Family studies

It has been known for some years that a family history of myopia is one of the most important risk factors for developing the condition. Only 6–15% of children with myopia come from families in which neither parent is myopic. In families with one myopic parent, 23–40% of the children develop myopia. If both parents are myopic, the rate rises to 33–60% for their children. One American study found that children with two myopic parents are six times as likely to develop myopia themselves as children with only one or no myopic parents. The precise interplay of genetic and environmental factors in these family patterns, however, is not yet known.

One multigenerational study of Chinese patients indicated that third generation family members had a higher risk of developing myopia even if their parents were not myopic. The researchers concluded that, at least in China, the genetic factors in myopia have remained constant over the past three generations while the environmental factors have intensified. The increase in the percentage of people with myopia over the last 50 years in the United States has led American researchers to the same conclusion.

Demographics

The prevalence of refractive error in the United States has not been evaluated since the early 1970s. According to a 2006 study sponsored by the National Eye Institute (NEI), refractive errors are estimated to affect 42.2 million (35%) of Americans 40 years or older.

Myopia is the most common eye disorder in humans around the world. It affects some 20% of the adult population in the United States. In various reports, incidence frequently varies with age, sex, race, ethnicity, occupation, environment, and other factors. Myopia is more common in central and eastern Europe than in northern Europe, Britain, and the United States. It is also very common in certain populations, such as Chinese, Japanese, Arab, and Jewish

KEY TERMS

Accommodation—The ability of the lens to change its focus from distant to near objects. It is achieved through the action of the ciliary muscles that change the shape of the lens.

Cornea—The transparent structure of the eye over the lens that is continous with the sclera in forming the outermost, protective, layer of the eye.

Diopter (D)—A unit of measure for describing refractive power.

Epi-LASIK—A surgical procedure that uses a blunt, plastic oscillating blade called an epithelial separator to cut a flap in the cornea.

Laser–assisted sub–epithelial keratomileusis (LASEK)—A surgical procedure in which the epithelium is loosened on the corneal surface. The loosened epithelium is then reflected away from the cornea, and laser ablation performed.

Laser–assisted in–situ keratomileusis (LASIK)—A surgical procedure that uses a cutting tool and a laser to modify the cornea and correct moderate to high levels of myopia.

Lens—The transparent, elastic, curved structure behind the iris (colored part of the eye) that helps focus light on the retina.

Ophthalmologist—A physician specializing in the medical and surgical treatment of eye disorders.

Optic nerve—A bundle of nerve fibers that carries visual messages from the retina in the form of electrical signals to the brain.

Optometrist—A medical professional who examines and tests the eyes for disease and treats visual disorders by prescribing corrective lenses and/or vision therapy. In many states, optometrists are licensed to use diagnostic and therapeutic drugs to treat certain ocular diseases.

Orthokeratology—A method of reshaping the cornea using a contact lens. It is not considered a permanent method to reduce myopia.

Peripheral vision—The ability to see objects that are not located directly in front of the eye. Peripheral vision allows people to see objects located on the side or edge of their field of vision.

Photorefractive keratectomy (PRK)—A procedure that uses an excimer laser to make modifications to the cornea and permanently correct myopia. As of early 1998, only two lasers have been approved by the FDA for this purpose.

Radial keratotomy (RK)—A surgical procedure involving the use of a diamond–tipped blade to make several spoke–like slits in the peripheral (non–viewing) portion of the cornea to improve the focus of the eye and correct myopia by flattening the cornea.

Refraction—The bending of light rays as they pass from one medium through another. Used to describe the action of the cornea and lens on light rays as they enter they eye. Also used to describe the determination and measurement of the eye's focusing system by an optometrist or ophthalmologist.

Refractive eye surgery—A general term for surgical procedures that can improve or correct refractive errors by permanently changing the shape of the cornea.

Retina—The light–sensitive layer of tissue in the back of the eye that receives and transmits visual signals to the brain through the optic nerve.

Visual acuity—The ability to distinguish details and shapes of objects.

persons. Myopia is uncommon in black, Nubian, and Sudanese persons.

Other factors that affect the demographic distribution of myopia are income level and education. The prevalence of myopia is higher among people with above–average incomes and educational attainments. Myopia is also more prevalent among people whose work requires a great deal of close focusing, including work with computers.

Signs and symptoms

Myopia is said to be caused by an elongation of the eyeball. This means that the oblong (as opposed to normal spherical) shape of the myopic eye causes the cornea and lens to focus at a point in front of the retina. A more precise explanation is that there is an inadequate correlation between the focusing power of the cornea and lens and the length of the eye.

People are generally born with a small amount of **hyperopia** (farsightedness), but as the eye grows this decreases and myopia does not become evident until later. This change is one reason why some researchers think that myopia is an acquired rather than an inherited trait.

The symptoms of myopia are blurred distance vision, eye discomfort, squinting, and eye strain.

Diagnosis

The diagnosis of myopia is typically made during the first several years of elementary school when a teacher notices a child having difficulty seeing the chalkboard, reading, or concentrating. The teacher or school nurse often recommends an **eye examination** by an ophthalmologist or optometrist. An ophthalmologist—M.D. or D.O. (Doctor of Osteopathy)—is a medical doctor trained in the diagnosis and treatment of eye problems. Ophthalmologists also perform eye surgery. An optometrist (O.D.) diagnoses, manages and/or treats eye and visual disorders. In many states, optometrists are licensed to use diagnostic and therapeutic drugs.

A patient's distance vision is tested by reading letters or numbers on a chart posted a set distance away (usually 20 ft). The doctor asks the patient to view images through a variety of lenses to obtain the best correction. The doctor also examines the inside of the eye and the retina. An instrument called a slit lamp is used to examine the cornea and lens. The eyeglass prescription is written in terms of diopters (D), which measure the degree of refractive error. Mild to moderate myopia usually falls between -1.00D and -6.00D. Normal vision is commonly referred to as 20/20 to describe the eye's focusing ability at a distance of 20 ft from an object. For example, 20/50 means that a myopic person must stand 20 ft away from an eye chart to see what a normal person can see at 50 ft. The larger the bottom number, the greater the myopia.

Treatment and management

People with myopia have three main options for treatment: optical devices, such as eyeglasses and **contact lenses**, refractive eye surgery, and intraocular surgical procedures.

Optical devices

EYEGLASSES. Eyeglasses are the most common method used to correct myopia. Concave glass or plastic lenses are placed in frames in front of the eyes. The lenses are ground to the thickness and curvature specified in the eyeglass prescription. The lenses cause the light rays to diverge so that they focus further back, directly on the retina, producing clear distance vision.

CONTACT LENSES. Contact lenses are a second option for treatment. Contact lenses are extremely thin round discs of plastic that are worn on the eye in front of the cornea. Although there may be some initial discomfort, most people quickly grow accustomed to contact lenses. Hard contact lenses, made from a material called PMMA, are virtually obsolete. Rigid gas permeable lenses (RGP) are made of plastic that holds its shape but allows the passage of some oxygen into the eye. Some believe that RGP lenses may halt or slow the progression of myopia because they maintain a constant, gentle pressure that flattens the cornea. In 2004, results of a NEI–sponsored study called the Contact Lens and Myopia Progression (CLAMP) Study, were published. Researchers found that RGP contact lenses slowed the progression of myopia in young children. Researchers also found that RGP contact lenses did not slow the growth of the eye, responsible for the majority of myopia in children. Instead of slowing the growth of the eye, RGP lenses kept the cornea from changing shape more than soft contact lenses.

Soft contact lenses are made of flexible plastic and can be up to 80% water. Soft lenses offer increased comfort and the advantage of extended wear; some can be worn continuously for up to one week. While oxygen passes freely through soft lenses, bacterial contamination and other problems can occur, requiring replacement of lenses on a regular basis. It is very important to follow the cleaning and disinfecting regimens prescribed because protein and lipid buildup can occur on the lenses, causing discomfort or increasing the risk of infection. Contact lenses offer several benefits over glasses, including: better vision, less distortion, clear peripheral vision, and cosmetic appeal. In addition, contacts will not fog up from perspiration or changes in temperature.

Refractive eye surgery

For people who find glasses and contact lenses inconvenient or uncomfortable, and who meet selection criteria regarding age, degree of myopia, general health, etc., refractive eye surgery is a third treatment alternative. **Radial keratotomy** was the first such procedure developed, but has been replaced since the mid–1990s by photorefractive keratectomy (PRK), laser–assisted in–situ keratomileusis (LASIK), Epi-LASIK, and laser–assisted sub–epithelial keratomileusis (LASEK). Refractive eye surgery improves myopic vision by permanently changing the shape of the cornea so that light rays focus properly on the retina. These procedures are performed on an outpatient basis and generally take 10–30 minutes.

PHOTOREFRACTIVE KERATECTOMY (PRK). PRK involves the use of a computer to measure the shape of the cornea. Using these measurements, the surgeon uses a computer–controlled excimer laser to make modifications to the cornea. The PRK procedure flattens the cornea by vaporizing small amounts of tissue

from the cornea's surface, thereby improving the cornea's refractive properties in focusing light on the retina. The ultra thin, outer layer of the eye (epithelium) is removed completely by laser energy during the PRK procedure, and eventually grows back. PRK has been approved by the Food and Drug Administration (FDA) for myopia since 1995 and the first excimer lasers used to perform PRK have been improved significantly in terms of size, efficiency, and accuracy. PRK can treat mild to moderate forms of myopia.

LASER–ASSISTED IN–SITU KERATOMILEUSIS (LASIK). As of December 2005, LASIK has been approved by the FDA for several different laser platforms. About 5 million procedures have been performed in the United States since the approval of the excimer laser for refractive surgery in late 1995. It is recommended for moderate to severe cases of myopia. As currently practiced, LASIK is perhaps best thought of as PRK performed under a flap instead of on the corneal surface. The flap is flipped back to expose the inner layers of the cornea. The cornea is treated with a laser to change the shape and focusing properties,then the flap is replaced. For myopic LASIK ablations, most of the laser energy is directed at the center of the treatment zone with the result that the central cornea is thus flattened.

LASER–ASSISTED SUB–EPITHELIAL KERATOMILEUSIS (LASEK). In a LASEK procedure, the epithelium is chemically loosened using dilute alcohol on the corneal surface. The loosened epithelium is then reflected away from the cornea, and laser ablation performed. The procedure preserves the extremely thin epithelial layer by lifting it from the eye's surface before using a laser for reshaping. After the LASEK procedure, the epithelium is replaced on the eye's surface.

EPI–LASIK. In Epi–LASIK, the surgeon uses a blunt, plastic oscillating blade called an epithelial separator to cut a flap in the cornea. Instead of the alcohol used in LASEK to loosen the epithelial sheet, the epithelial separator is used to separate the sheet from the eye. This avoids the possibility of an adverse reaction from the alcohol. Because it is more difficult to create the epithelial flap in people with steeper corneas (who have higher amounts of myopia), the procedure is considered more appropriate for people with less steep corneas (who have low myopia).

Intraocular surgical procedures

These procedures involve extraction of the clear lens with or without lens implantation and the use of intraocular lens (IOL) implants. IOLs have been used since 1999 for correcting large refractive errors in myopia. An IOL is a microscopic lens that can be placed inside the eye to correct certain vision problems. For patients who are extremely nearsighted and may have contraindications to LASIK, an IOL may be implanted in front of the iris to correct their distance vision and provide normal focusing ability and near vision. Although IOLs are intended to be permanent, the procedure is reversible.

Risks

All of these surgical procedures carry risks, the most serious being corneal scarring, corneal rupture, infection, flap problems, dry eye, cataracts, and loss of vision. The National Eye Institute (NEI) warns that before agreeing to refractive surgery, patients should get a clear picture of what they can expect. Surgeons should explain the risks and possible complications, as well as potential side effects.

Since refractive eye surgery does not guarantee 20/20 vision, it is important to have realistic expectations before choosing this treatment. For example, the American Academy of Ophthalmology (AAO) reports that nine out of 10 patients achieve 20/20 vision, but 20/20 does not always mean perfect vision. Detailed, precise vision may be slightly diminished. Even if the patient gains near-perfect vision, irritating side effects are also possible, such as postoperative **pain**, poor night vision, variation in visual acuity, light sensitivity and glare, and optical distortion. Finally, refractive eye surgeries are considered elective procedures and are rarely covered by insurance plans.

Alternative treatments

Some eye care professionals recommend treatments to help improve circulation, reduce eye strain, and relax the eye muscles. It is possible that by combining exercises with changes in behavior, the progression of myopia may be slowed or prevented. Alternative treatments include: visual therapy (also referred to as **vision training** or eye exercises); discontinuing close work; reducing eye strain (taking a rest break during periods of prolonged near vision tasks); and wearing bifocals to decrease the need to accommodate when doing close–up work.

Clinical trials

Clinical trials on myopia are currently sponsored by the National Institutes of Health (NIH) and other agencies. As of 2009, NIH was reporting 121 on–going and completed studies.

Examples include:

- The evaluation of neurovision correction (NVC) technology for the treatment of low myopia. (NCT00469612)
- A study of the inheritance of myopia in families of various nationalities and ethnic backgrounds to identify gene changes that cause myopia or similar diseases. (NCT00272376)
- A study to determine whether the MEL 80 Excimer Laser is effective in the treatment of moderate to high myopia, when used as part of the LASIK procedure. (NCT00762541)

Clinical trial information is constantly updated by NIH and the most recent information on myopia trials can be found at: http://clinicaltrials.gov/ct2/results?term=myopia

Prognosis

Glasses and contact lenses can (but not always) correct the patient's vision to 20/20. Refractive surgery can make permanent improvements for the right candidates.

While the genetic factors that influence the transmission and severity of myopia cannot be changed, some environmental factors can be modified. They include reducing close work; reading and working in good light; taking frequent breaks when working at a computer or microscope for long periods of time; maintaining good **nutrition**; and practicing visual therapy (when recommended).

Eye strain can be prevented by using sufficient light for reading and close work, and by wearing corrective lenses as prescribed. Everyone should have regular eye examinations to see if their prescription has changed or if any other problems have developed. This is particularly important for people with high (degenerative) myopia who are at a greater risk of developing **retinal detachment**, retinal degeneration, glaucoma, or other problems.

Resources

BOOKS

Caster, Andrew. *Lasik: The Eye Laser Miracle: The Complete Guide to Better Vision*. New York, NY: Ballantine Books, 2008.

De Angelis, David. *The Secret of Perfect Vision: How You Can Prevent and Reverse Nearsightedness*. Berkeley, CA: North Atlantic Books, 2008.

PERIODICALS

de Benito–Llopis, L., et al. "Ten–year Follow–up of Excimer Laser Surface Ablation for Myopia in Thin Corneas." *American Journal of Ophthalmology* 147, no. 5 (2009): 768–773.

Kim, M. J., et al. "Congenital axial high myopia detected by prenatal ultrasound." *American Journal of Pediatric Ophthalmology and Strabismus* 46, no. 1 (January–February 2009): 50–53.

McKone, E., et al. "Blurry means good focus: myopia and visual attention." *Perception* 37, no. 11 (2008): 1765–17.

Schäche, M., et al. "Fine mapping linkage analysis identifies a novel susceptibility locus for myopia on chromosome 2q37 adjacent to but not overlapping MYP12." *Molecular Vision* 15 (2009): 722–730.

Young, T. L. "Molecular genetics of human myopia: an update." *Optometry and Vision Science* 86, no. 1 (January 2009): E8–E22.

OTHER

Basic Lasik: Tips on Eye Surgery. Information Page. NEI, October 2008 (April 05, 2009). http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea04.shtm

Myopia. Medical Encyclopedia. Medline, August 22, 2008 (April 05, 2009). http://www.nlm.nih.gov/MEDLINEPLUS/ency/article/001023.htm

Myopia (Nearsightedness). Information Page. AOA. (April 05, 2009). http://www.aoa.org/myopia.xml

Nearsightedness. Information Page. Mayo Clinic, January 17, 2008 (April 05, 2009). http://www.mayoclinic.com/print/nearsightedness/DS00528/DSECTION=all&METHOD=print

Nearsightedness. Fact Sheet. NEI. (April 05, 2009). http://www.nei.nih.gov/healthyeyestoolkit/factsheets/Nearsightedness.pdf

LASIK, Epi–LASIK & LASEK. Information Page. The Eye Digest, June 17, 2007 (April 05, 2009). http://www.agingeye.net/lasik/lasik.php#

Questions and Answers about Refractive Errors. Information Page. NEI, October 2008 (April 05, 2009). http://www.nei.nih.gov/CanWeSee/qa_refractive.asp

Refractive Errors. Information Page. EyeCare America, May 2007 (April 05, 2009). http://www.nlm.nih.gov/MEDLINEPLUS/ency/article/001023.htm

ORGANIZATIONS

American Academy of Ophthalmology (AAO), P.O. Box 7424, San Francisco, CA, 94120-7424, (415)561-8500, (415)561-8533, patientinfo@aao.org, http://www.aao.org.

American Optometric Association, 243 N. Lindbergh Blvd., St. Louis, MO, 63141, (800)365-2219, http://www.aoa.org.

EyeCare America, P.O. Box 429098, San Francisco, CA, 94142-9098, (877)887-6327, (415)561-8567, http://www.eyecareamerica.org/eyecare/.

National Eye Institute (NEI), 31 Center Drive MSC 2510, Bethesda, MD, 20892-3655, (301)496-5248, http://www.nei. nih.gov.

Rebecca J. Frey, PhD

Myositis

Definition

Myositis is a rare disease in which the muscle fibers and skin are inflamed and damaged, resulting in muscle weakness. There are several types of myositis that affect different parts of the body.

Description

The persistent inflammation that is associated with myositis develops slowly over weeks to months and often years, with progressive weakening of the muscles. Later in the course of the disease development muscle wasting or shortening (contracture) may develop. Myositis can range in severity from mild to debilitating.

The forms of myositis include:

- Polymyositis (PM) inflames and weakens muscles in many parts of the body, and especially those parts closest to the trunk. With polymyositis, dysphagia (difficulty, discomfort, or pain in speaking or swallowing), fatigue, and pain in the muscles are common. PM rarely affects people under the age of 20, with the peak onset between the ages of 30 and 60.
- Dermatomyositis (DM) affects both the muscle fibers and skin by damaging the tiny blood vessels (capillaries) that supply blood to the muscle and skin, resulting in muscle weakness, pain, and fatigue. In addition the affected person develops a distinctive patchy, reddish rash on the eyelids, cheeks, bridge of the nose, back or upper chest, elbows, knees, and knuckles. There may also be hardened, tender bumps (possibly caused by inflammation of fat) under the skin. DM can occur at any age and is more common in females than males.
- Inclusion Body Myositis (IBM) typically begins after age 50, and is characterized by gradual weakening of muscles throughout the body, including the wrists or fingers, development of dysphagia, and atrophy of forearms and/or thigh muscles. Unlike the other types of myositis, IBM occurs more often in men than women, and also does not respond very well to drug therapy.
- Juvenile myositis (JM) involves muscle weakness, skin rash, and dysphagia in children. A common characteristic of JM is the formation of calcium deposits in the muscle (calcinosis). These deposits are hard and sometimes painful lumps of calcium under the skin that appear on the child's fingers, hands, elbows, and knees. Painful sores may appear if the lumps break through the skin. The child may also suffer from contractures, which is muscle shortening that results in joints staying bent. About half of the children with JM will have pain in their muscles.

Myositis is rare, affecting about 10 in one million people each year. DM and PM affect mostly women in the forties and fifties but men and children can also affect be affected, some at a young age (between the ages of 5 and 15). About 40,000 people in the United States may have this disease, with about 3,000 to 5,000 children affected.

Causes and symptoms

Myositis is thought to be an autoimmune disease. The body normally fights infections and disease by producing antibodies and white blood cells called lymphocytes in a process called the immune response. In an autoimmune disease, the immune response is overactive, and the immune system attacks and destroys the body's own normal healthy tissues. There is no known cause to the autoimmune response that results in myositis. However, investigators are studying whether the disease is triggered by such environmental agents as the organism that causes **toxoplasmosis**, *Toxoplasma gondii*, the **Lyme disease** organism, *Borrelia burgdorferi*, the coxsackievirus, or by **food allergies**. Some cases of IBM are thought to be inherited.

The first symptoms of most types of myositis are weakness and **pain** in the muscles of the hips and shoulders. The affected person may have trouble getting up from a chair, lifting the arms above the head, or climbing stairs, and may be too tired to walk or stand. DM and PM mostly affects muscles that are close to and within the trunk of the body, while IBM involves a wider range of muscles. Myositis may make it difficult for the person to speak or swallow. When the disease affects the lungs or chest muscles, the person may have difficulty breathing. If the person has DM, they may develop characteristic **rashes**. Other symptoms may include **fever** and joint pain and swelling.

The first signs of JM is usually a red and patchy skin rash and/or a red or purplish rash on the eyelids or cheeks that look like **allergies**. Weak muscles may develop at the same time as the rash, or may develop days, weeks, or months after the appearance of the rash. Other symptoms of JM include falling, a weaker voice (dysophonia), or dysphagia. Calcinosis usually develops later during the course of the disease.

Diagnosis

Myositis can a difficult disease to diagnose, because it is rare, because the symptoms develop

slowly, and because it can be mistaken for other diseases causing muscle weakness such as limb-girdle **muscular dystrophy**. Many cases of myositis go undiagnosed for years. The health care provider must rule out other conditions such as **hypothyroidism**, toxin exposure, drug reactions, and genetic disorders that can also affect muscles. The **physical examination** will include a complete medical history focusing on symptoms and when they occurred, and blood tests for autoantibodies and muscle enzymes (for example, creatine kinase (CK), which when present in the blood indicates muscle damage). Specialized tests may also be performed, including:

- an electromyogram, which measures the electrical pattern of the muscles
- a muscle biopsy, in which a small piece of muscle is removed, stained, and examined by microscopic techniques to determine if muscle fibers are damaged and whether the muscle fibers are being infiltrated by cells of the immune system
- magnetic resonance imaging (MRI) to identify areas of muscle inflammation.

Treatment

There is no cure for myositis. However, prompt and aggressive treatment may reduce muscle inflammation and prevent muscle weakness from progressing. Because of the many different kinds of symptoms and a wide range of reactions to different drugs, each person's treatment for myositis should be individualized.

Drugs that are used for treatment include **corticosteroids**, such as prednisone, to reduce inflammation and improve the body's reaction to infections. Corticosteroids are usually taken in the form of pills, but may also be injected. The amount of creatine kinase (CK) levels in the blood are monitored to determine how well the medicine is working. Corticosteroids may produce a number of side effects, such as weight gain, difficulties in fighting infections, psychiatric changes, sleeping troubles, water retention, bone thinning, facial swelling, diabetes, and **cataracts**. Corticosteroid therapy usually leads to improvement in myositis symptoms within two to three months, after which the dose can be lowered to avoid the side effects. If the dose of corticosteriods is going to be reduced, it is essential to lower the dose over a period of time.

Immunosuppressant drugs are used to slow down the immune system's attack on healthy tissue and improve skin rashes. Persons may be prescribed these drugs to control myositis if they are unable to tolerate corticosteroids or if the corticosteroids are not accomplishing the desired degree of treatment. Immunosuppressant drugs may also be used in conjunction with corticosteroids so that lower doses of corticosteroids can be used. Immunosuppressant drugs include azathioprine, methotrexate, cyclosporine, tacrolimus, etanercept, and mycophenolate mofetil.

Intravenous immunoglobulin (IVIg) appears to aid in improving muscle strength in many persons with myositis, particularly those with DM. It may be less effective in PM, and its role in treating IBM requires more study, although it has been shown to help some patients with IBM if they are diagnosed early. Immunoglobulins are normal proteins in the blood that attack anything foreign in the body, such as viruses and bacteria. IVIg is made from donated blood plasma from people with normal immune systems. Side effects from the the use of IVIg include **headache** and flu-like symptoms.

Topical cream or ointment forms of some of the medicines, such as prednisone and tacrolimus, can be used to heal and soothe the rash associated with DM. Non-steriodal anti-inflammatory drugs (NSAIDS) such as **aspirin** or ibuprofen can be used for pain relief. Calcinosis can be treated with prednisone, plaquenil (also called hydroxychloroquine), intravenous immunoglobin (IVIG), cyclosporine, and methotrexate.

After drug treatment results in improvement, the affected person begins a program of regular stretching exercises to maintain range of motion in the weakened arms and legs. **Physical therapy** may be used to prevent permanent muscle shortening. Whirlpool baths, heat, and gentle massages may also provide relief. Adequate rest is necessary, and affected persons should take frequent breaks throughout the day and limit their activity.

Patients with throat problems should be evaluated by a speech therapist who can evaluate the swallowing-related problems and make recommendations regarding diet changes and safe swallowing techniques.

Before a woman with myositis becomes pregnant, she should discuss the medicines that she is taking with her health care provider and evaluate the possible risks that she and the baby face if she does become pregnant. Many of the drugs used in the treatment of myositis may be harmful to the fetus or to a breast-fed baby.

It is recommended that a doctor experienced in the treatment of myositis, assisted by a rheumatologist, dermatologist, or neurologist, be consulted. Oftentimes a patient may have to be treated at a

major medical center, where the disease has been seen and treated before.

Alternative treatment

Various supplements may be used in conjunction with traditional treatment to offset side effects of conventional drug treatment. The use of these suppplements should be approved by the primary health care provider.

Immunosuppressant drugs such as methotroxate and cyclophosphamide increase the risk of infection, so a healthy well-balanced diet is required. Methotroxate impairs the body's ability to absorb **folic acid**, so foods high in folic acid, such as leafy green vegetables, fruits, and folate-fortified breads and cereals are recommended. The use of folate supplements may also be recommended by the health care provider. **Vitamins** C and E can be used to help with the pain and infections associated with calcinosis.

Corticosteroids may have multiple side effects when taken for long periods of time at high doses. **Calcium** and Vitamin D are recommended to lower the risk of **osteoporosis**, a common side effect of prednisone use. **Hypertension** and fluid retention may be controlled by a diet low in salt. Steroid-induced diabetes (hyperglycemia) can be aided by a diet low in sugar and other simple carbohydrates. Proteinuria, in which the body breaks down protein faster than normal, may mean that more protein should be included in the diet.

Weight gain associated with the use of corticosteroids can be managed by the use of the DASH (Dietary Approach to Stop Hypertension) diet, which is high in fruits, vegetables, dietary fiber, and low-fat dairy products. Information concerning this diet, developed by the National Institutes of Health, can be found at [htpp://www.nhlbi.nih.gov/health/public/heart/hbp/dash/]. Weight gain can overtax weakened muscles and should be avoided if possible.

Prognosis

The progression of PM and DM varies from person to person, but the lifespan of an affected person is not usually significantly affected. DM responds more favorably to therapy than PM. Overall, many patients do improve and have a functional recovery. About half of the patients recover and can discontinue treatment within 5 years of beginning treatment. In children the chances of a cure are better than in adults, although some children do suffer a relapse. Of the remaining 50%, about 20% will still have the active disease and will require ongoing treatment, while up to 30% may have some remaining muscle weakness. However, IBM is disabling, and most patients will require the use of an assistive device such as a cane, walker, or wheel chair. The older the patient is when contracting IBM, the more rapidly the disease progresses.

KEY TERMS

Coxsackievirus—Enterovirus causing a disease resembling poliomyelitis but without paralysis.

Dysphagia—Medical term for any difficulty, discomfort or pain when swallowing.

Limb-girdle muscular dystrophy—An autosomal recessive form of muscular dystrophy that appears anywhere from late childhood to middle age and is characterized by progressive muscular weakness beginning either in the shoulder or pelvic girdle; the disease usually progresses slowly with cardiopulmonary complications in the later stages.

Prevention

There is no known way to prevent myositis.

Resources

BOOKS

Kagen, Lawrence J., ed. *The Inflammatory Myopathies*. Dordrecht; New York: Humana Press, 2009.

Myositis: A Medical Dictionary, Bibliography, and Annotated Research Guide to Internet Resources. San Diego: ICON Health Publications, 2004.

Rider, Lisa G., et al. *Myositis and You: A Guide to Juvenile Dermatomyositis for Patients, Families, and Healthcare Providers*. Washington, DC: Myositis Association, 2007.

ORGANIZATIONS

Muscular Dystrophy Association, 3300 East Sunrise Drive, Tucson, AZ, 85718, (800) 572-1717, http://www. mdausa.org.

The Myositis Association, 1737 King Street, Suite 600, Alexandria, VA, 22314, (800) 821-7356, TMA@myositis. org, http://www.myositis.org.

Myositis Support Group, PO Box 1793, Athens, TX, 75751, http://www.myositissupportgroup.org.

Judith Sims

Myositis *see* **Myopathies**

Myotonia atrophica *see* **Myotonic dystrophy**

Myotonic dystrophy

Definition

Myotonic dystrophy is a progressive disease in which the muscles are weak and are slow to relax after contraction.

Demographics

DM occurs in about 1 per 7,000–8,000 people and has been described in people from all over the world. DM is an inherited disease, affecting males and females approximately equally. About 30,000 people in the United States are affected.

Description

Myotonic dystrophy (DM), also called dystrophia myotonica, myotonia atrophica, or Steinert's disease, is a common form of **muscular dystrophy**. Symptoms may appear at any time from infancy to adulthood. DM causes general weakness, usually beginning in the muscles of the hands, feet, neck, or face. It slowly progresses to involve other muscle groups, including the heart. DM affects a wide variety of other organ systems as well.

A severe form of DM, congenital myotonic dystrophy or Thomsen's disease, may appear in newborns of mothers who have DM. Congenital means that the condition is present from birth. The incidence of congenital myotonic dystrophy is thought to be about 1:20,000.

Risk factors

The most common type of DM is called DM1 and is caused by a mutation in a gene called myotonic dystrophy protein kinase (DMPK). The DMPK gene is located on chromosome 19q. When there is a mutation in this gene, a person develops DM1. The specific mutation that causes DM1 is called a trinucleotide repeat expansion. Risk for DM increases when a parent has a mutation in this gene.

Causes and symptoms

Some families with symptoms of DM do not have a mutation in the DMPK gene. Scientists have found that the DM in many of these families is caused by a mutation in a gene on chromosome 3. These families are said to have DM2.

Congenital myotonic dystrophy has been linked to a region on chromosome 7 that contains a muscle chloride channel gene.

Trinucleotide repeats

In the DMPK gene, there is a section of the genetic code called a CTG repeat. The letters stand for three nucleotides (complex organic molecules) known as cytosine, thymine, and guanine, and are repeated a certain number of times. In people who have DM1, this sequence of nucleotides is repeated too many times—more than the normal number of 37 times—making this section of the gene too big. This enlarged section of the gene is called a trinucleotide repeat expansion.

People who have repeat numbers in the normal range will not develop DM1 and cannot pass it to their children. Having more than 50 repeats causes DM1. People who have 38–49 repeats have a premutation and will not develop DM1, but can pass DM1 onto their children. Having repeats numbers greater than 1,000 causes congenital myotonic dystrophy.

In general, the more repeats in the affected range that someone has, the earlier the age of onset of symptoms and the more severe the symptoms. However, this is a general rule. It is not possible to look at a person's repeat number and predict at what age they will begin to have symptoms or how their condition will progress.

Exactly how the trinucleotide repeat expansion causes myotonia, the inability to relax muscles, is not yet understood. The disease somehow blocks the flow of electrical impulses across the muscle cell membrane. Without proper flow of charged particles, the muscle cannot return to its relaxed state after it has contracted.

Since 2001 it has been discovered that DM2 is caused by a CCTG (cytosine-cytosine-thymine-guanine) expansion on chromosome 3 at locus 3q21, but it is not known how this repeat affects muscle cell function.

Anticipation

Sometimes when a person who has repeat numbers in the affected or premutation range has children, the expansion grows larger. This is called anticipation. A larger expansion can result in an earlier age of onset in children than in their affected parent. Anticipation happens more often when a mother passes DM1 onto her children then when it is passed from the father. Occasionally, repeat sizes stay the same or even get smaller when they are passed to a person's children.

Inheritance

DM is inherited through autosomal dominant inheritance. This means that equal numbers of males and females are affected. It also means that only one

gene in the pair needs to have the mutation in order for a person to be affected. Since a person only passes one copy of each gene onto their children, there is a 50% or one in two chance that a person who has DM will pass it onto each of their children. This percentage is not changed by results of other pregnancies. A person with a premutation also has a 50%, or one in two, chance of passing the altered gene on to each of their children. Whether or not their children will develop DM1 depends on whether the trinucleotide repeat becomes further expanded. A person who has repeat numbers in the normal range cannot pass DM1 onto their children.

There is a range in the severity of symptoms in DM and not everyone will have all of the symptoms.

Myotonic dystrophy causes weakness and delayed muscle relaxation called myotonia. Symptoms of DM include facial weakness and a slack jaw, drooping eyelids called **ptosis**, and muscle wasting in the forearms and calves. A person with DM has difficulty relaxing his or her grasp, especially in the cold. DM affects the heart muscle, causing irregularities in the heartbeat. It also affects the muscles of the digestive system, causing **constipation** and other digestive problems. DM may cause **cataracts**, retinal degeneration, low IQ, frontal balding, skin disorders, atrophy of the testicles, and diabetes. It can also cause sleep apnea—a condition in which normal breathing is interrupted during sleep. DM increases the need for sleep and decreases motivation. Severe disabilities do not set in until about 20 years after symptoms begin. Most people with myotonic dystrophy maintain the ability to walk, even late in life.

A severe form of DM, congenital myotonic dystrophy, may appear in newborns of mothers who have DM1. Congenital myotonic dystrophy is marked by severe weakness, poor sucking and swallowing responses, respiratory difficulty, delayed motor development, and **mental retardation**. **Death** in infancy is common in this type.

Some people who have a trinucleotide repeat expansion in their DMPK gene do not have symptoms or have very mild symptoms that go unnoticed. It is not unusual for a woman to be diagnosed with DM after she has an infant with congenital myotonic dystrophy.

Predictive testing

It is possible to test someone who is at risk for developing DM1 before they are showing symptoms to see whether they inherited an expanded trinucleotide repeat. This is called predictive testing. Predictive testing cannot determine the age of onset that someone will begin to have symptoms, or the course of the disease.

KEY TERMS

Electrocardiogram (ECG, EKG)—A test that uses electrodes attached to the chest with an adhesive gel to transmit the electrical impulses of the heart muscle to a recording device.

Electromyography (EMG)—A test that uses electrodes to record the electrical activity of muscle. The information gathered is used to diagnose neuromuscular disorders.

Muscular dystrophy—A group of inherited diseases characterized by progressive wasting of the muscles.

Nucleotide—Any of a group of organic molecules that link together to form the building blocks of DNA or RNA.

Sleep apnea—Temporary cessation of breathing while sleeping.

Trinucleotide repeat expansion—A sequence of three nucleotides that is repeated too many times in a section of a gene.

Diagnosis

Diagnosis of DM is not difficult once the disease is considered. However, the true problem may be masked because symptoms can begin at any age, can be mild or severe, and can occur with a wide variety of associated complaints.

Examination

Diagnosis of DM begins with a careful medical history and a thorough physical exam to determine the distribution of symptoms and to rule out other causes. A family history of DM or unexplained weakness helps to establish the diagnosis.

Tests

A definitive diagnosis of DM1 is done by **genetic testing**, usually by taking a small amount of blood. The DNA in the blood cells is examined and the number of repeats in the DMPK gene is determined. Various other tests may be done to help establish the diagnosis, but only rarely would other testing be needed. An electromyogram (EMG) is a test is used to examine the response of the muscles to stimulation. Characteristic changes are seen in DM that helps distinguish it from other muscle diseases.

PRENATAL TESTING. Testing a **pregnancy** to determine whether an unborn child is affected is possible if genetic testing in a family has identified a DMPK mutation. This can be done at 10–12 weeks gestation by a procedure called **chorionic villus sampling** (CVS), which involves removing a tiny piece of the placenta and analyzing DNA from its cells. It can also be done by **amniocentesis** after 14 weeks gestation by removing a small amount of the amniotic fluid surrounding the baby and analyzing the cells in the fluid. Each of these procedures has a small risk of **miscarriage** associated with it and those who are interested in learning more should check with their doctor or genetic counselor.

Procedures

Removing a small piece of muscle tissue for microscopic examination is called a muscle biopsy. DM is marked by characteristic changes in the structure of muscle cells that can be seen on a muscle biopsy. An electrocardiogram could be performed to detect characteristic abnormalities in heart rhythm associated with DM. These symptoms often appear later in the course of the disease.

A procedure called preimplantation diagnosis allows a couple to have a child that is unaffected with the genetic condition in their family. This procedure is experimental and not widely available. Those interested in learning more about this procedure should check with their doctor or genetic counselor.

A group of researchers in Houston, Texas, reported in 2004 that they have successfully developed a technique for detecting the CCTG expansion that causes DM2 and estimating the size of the repeat expansion.

Treatment

Myotonic dystrophy cannot be cured, and no treatment can delay its progression. There is no standardized treatment for these disorders because the precise reasons for muscle weakness are not yet fully understood. However, many of the symptoms can be treated. **Physical therapy** can help preserve or increase strength and flexibility in muscles. Ankle and wrist braces can be used to support weakened limbs. **Occupational therapy** is used to develop tools and techniques to compensate for loss of strength and dexterity. A speech-language pathologist can provide retraining for weakness in the muscles controlling speech and swallowing.

Irregularities in the heartbeat may be treated with medication or a pacemaker. A yearly electrocardiogram is usually recommended to monitor the heartbeat. **Diabetes mellitus** in DM is treated in the same way that it is in the general population. A high-fiber diet can help prevent constipation. **Sleep apnea** may be treated with surgical procedures to open the airways or with nighttime ventilation. Treatment of sleep apnea may reduce drowsiness. Lens replacement surgery is available when cataracts develop. Pregnant woman should be followed by an obstetrician familiar with the particular problems of DM because complications can occur during pregnancy, labor and delivery.

Wearing a medical bracelet is advisable. Some emergency medications may have dangerous effects on the heart rhythm in a person with DM. Adverse reactions to **general anesthesia** may also occur.

Prognosis

The course of myotonic dystrophy varies. When symptoms appear earlier in life, disability tends to become more severe. Occasionally, people with DM require a wheelchair later in life. Children with congenital DM usually require special educational programs and physical and occupational therapy. For both types of DM, respiratory infections pose a danger when weakness becomes severe.

Resources

BOOKS

Abramovitz, Melissa. *Muscular Dystrophy (Diseases and Disorders)*. San Diego, CA: Lucent, 2008.

Bennett, Robin L. *The Practical Guide to the Genetic Family History*. 2nd ed. New York: Wiley—Blackwell, 2010.

Emery, Alan E.H. *Muscular Dystrophy (The Facts)*. 3rd ed. New York: Oxford University Press, 2008.

PERIODICALS

International Myotonic Dystrophy Consortium (IMDC). "New Nomenclature and DNA Testing Guidelines for Myotonic Dystrophy Type 1 (DM1)." *Neurology* 54 (2000): 1218–1221.

Meola, G., and V. Sansone. "Treatment in Myotonia and Periodic Paralysis." *Revue neurologique (Paris)* 160, no. 5, Part 2 (May 2004: S55–S69.

Meola, Giovanni. "Myotonic Dystrophies." *Current Opinion in Neurology* 13 (2000): 519–525.

Ranum, L. P., and J. W. Day. "Myotonic Dystrophy: RNA Pathogenesis Comes into Focus." *American Journal of Human Genetics* 74 (May 2004): 793–804.

Sallinen, R., et al. "New Methods for Molecular Diagnosis and Demonstration of the (CCTG)n Mutation in Myotonic Dystrophy Type 2 (DM2)." *Neuromuscular Disorders* 14 (April 2004): 274–283.

OTHER

Bird, Thomas. "Myotonic Dystrophy Type 1." *GeneReviews*. November 15, 2007. http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=myotonic-d (accessed October 9, 2010).

"Myotonic Dystrophy." *Genes and Disease*. http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gnd&part=myotonicdystrophy (accessed October 9, 2010).

ORGANIZATIONS

Muscular Dystrophy Association, 3300 East Sunrise Dr., Tucson, AZ, 85718, (520) 529-2000, (800) 572-1717, http://www.mdausa.org.

National Institutes of Health (NIH), 9000 Rockville Pike, Bethesda, MD, 20892, (301) 496-4000, http://www.nih.gov.

National Organization for Rare Diseases, 55 Kenosia Ave., PO Box 1968, Danbury, CT, 06813, (213) 744-0100, (800) 999-6673, http://www.rarediseases.org.

U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD, 20894, http://www.nlm.nih.gov/medlineplus/medlineplus.html.

Karen M. Krajewski, MS, CGC
Rebecca J. Frey, PhD
Laura Jean Cataldo, RN, EdD

Myringotomy and ear tubes

Definition

Myringotomy is a surgical procedure in which a small incision is made in the eardrum (the tympanic membrane), usually in both ears. The English word is derived from *myringa,* modern Latin for drum membrane, and *tomē,* Greek for cutting. It is also called myringocentesis, tympanotomy, tympanostomy, or **paracentesis** of the tympanic membrane. Fluid in the middle ear can be drawn out through the incision.

Ear tubes, or tympanostomy tubes, are small tubes open at both ends that are inserted into the incisions in the eardrums during myringotomy. They come in various shapes and sizes and are made of plastic, metal, or both. They are left in place until they fall out by themselves or until they are removed by a doctor.

Demographics

In the United States, myringotomy and tube placement have become a mainstay of treatment for recurrent **otitis media** in children. More than 500,000 procedures are performed annually, making myringotomy the most common pediatric, ambulatory operation performed in the United States. Myringotomy in adults is a less common procedure than in children, primarily because adults benefit from certain changes in the anatomy of the middle ear that occur after childhood. In particular, the adult ear is less likely to accumulate fluid because the Eustachian tube, which connects the middle ear to the throat area, lies at about a 45–degree angle from the horizontal. This relatively steep angle means that the force of gravity helps to keep fluids from the throat containing disease organisms out of the middle ear. In children, however, the Eustachian tube is only about 10 degrees above the horizontal, which makes it relatively easy for disease organisms to migrate from the nose and throat into the inner ear. Myringotomies in adults are usually performed as a result of barotrauma, which is also known as pressure–related ear **pain** or barotitis media. Barotrauma refers to earache caused by unequal air pressure on the inside and outside of the eardrum. Adults with very narrow Eustachian tubes may experience barotrauma in relation to scuba diving, using elevators, or frequent flying. A myringotomy with tube insertion may be performed if the condition is not helped by **decongestants** or **antibiotics**.

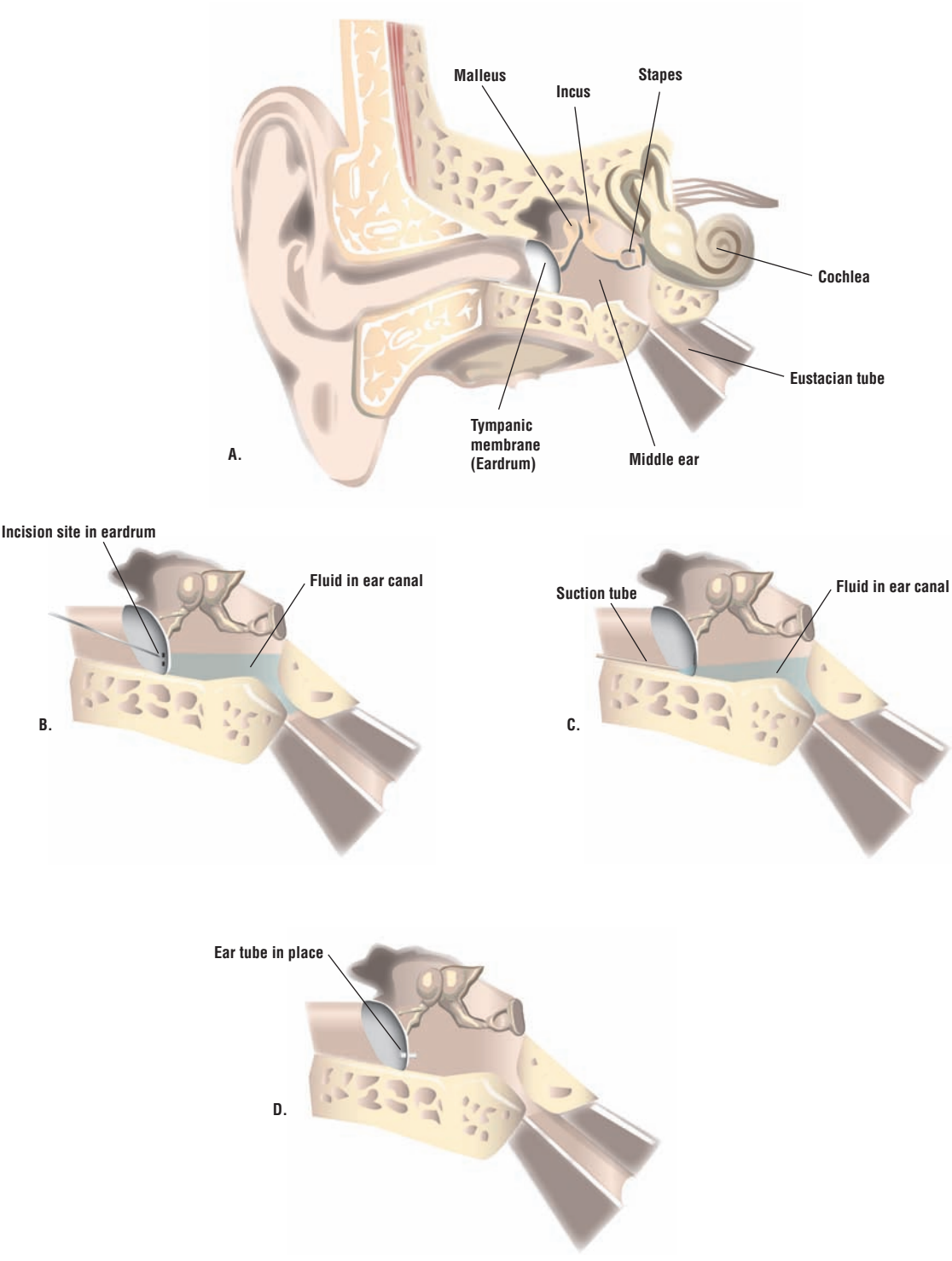
Purpose

Myringotomy with the insertion of ear tubes is an optional treatment for inflammation of the middle ear with fluid collection (effusion) that lasts longer than three months (chronic otitis media with effusion) and does not respond to drug treatment. This condition is also called glue ear. Myringotomy is the recommended treatment if the condition lasts four to six months. Effusion refers to the collection of fluid that escapes from blood vessels or the lymphatic system. In this case, the effusion collects in the middle ear.

Initially, acute inflammation of the middle ear with effusion is treated with one or two courses of antibiotics. **Antihistamines** and decongestants have been used, but they have not been proven effective unless there is also hay **fever** or some other allergic inflammation that contributes to the problem. Myringotomy with or without the insertion of ear tubes is *not* recommended for initial treatment of otherwise healthy children with middle ear inflammation with effusion.

In about 10% of children, the effusion lasts for three months or longer, when the disease is considered chronic. In children with chronic disease, systemic **steroids** may help, but the evidence is not clear, and there are risks.

Myringotomy and ear tubes



During a myringotomy, an incision is made into the ear drum, or tympanic membrane (B). The fluid in the ear canal is suctioned out (C), and a small tube is put in place to allow future drainage in the event of an ear infection (D). *(Illustration by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)*

KEY TERMS

Acute otitis media—Inflammation of the middle ear with signs of infection lasting less than three months.

Adenoids—Clusters of lymphoid tissue located in the upper throat above the roof of the mouth. Some doctors think that removal of the adenoids may lower the rate of recurrent otitis media in high–risk children.

Barotrauma—Ear pain caused by unequal air pressure on the inside and outside of the ear drum. Barotrauma, which is also called pressure–related ear pain or barotitis media, is the most common reason for myringotomies in adults.

Chronic otitis media—Inflammation of the middle ear with signs of infection lasting three months or longer.

Effusion—The escape of fluid from blood vessels or the lymphatic system and its collection in a cavity, in this case, the middle ear.

Eustachian tube—A canal that extends from the middle ear to the pharynx.

Insufflation—Blowing air into the ear as a test for the presence of fluid in the middle ear.

Middle ear—The cavity or space between the eardrum and the inner ear. It includes the eardrum, the three little bones (hammer, anvil, and stirrup) that transmit sound to the inner ear, and the Eustachian tube, which connects the inner ear to the nasopharynx (the back of the nose).

Otolaryngologist—A surgeon who specializes in treating disorders of the ears, nose, and throat.

Tympanic membrane—The eardrum. A thin disc of tissue that separates the outer ear from the middle ear.

Tympanostomy tube—Ear tube. A small tube made of metal or plastic that is inserted during myringotomy to ventilate the middle ear.

When medical treatment does not stop the effusion after three months in a child who is one to three years old, is otherwise healthy, and has **hearing loss** in both ears, myringotomy with insertion of ear tubes becomes an option. If the effusion lasts for four to six months, myringotomy with insertion of ear tubes is recommended.The purpose of myringotomy is to relieve symptoms, to restore hearing, to take a sample of the fluid to examine in the laboratory in order to identify any microorganisms present, or to insert ear tubes.

Ear tubes can be inserted into the incision during myringotomy and left there. The eardrum heals around them, securing them in place. They usually fall out on their own in six to 12 months or are removed by a doctor.While the tubes are in place, they keep the incision from closing, keeping a channel open between the middle ear and the outer ear. This allows fresh air to reach the middle ear, allowing fluid to drain out, and preventing pressure from building up in the middle ear. The patient's hearing returns to normal immediately and the risk of recurrence diminishes.

Most myringotomies in children are performed in children between one to two years of age. One Canadian study found that the number of myringotomies performed was 12.8 per thousand for children 11 months old or younger; 54.2 per thousand for children between 12 and 23 months old; and 11.1 per thousand for children between three and 15 years old. Sex and race do not appear to affect the number of myringotomies in any age group, although boys are reported to have a slightly higher rate of ear infections than girls.

Description

When a conventional myringotomy is performed, the ear is washed, a small incision made in the eardrum, the fluid sucked out, a tube inserted, and the ear packed with cotton to control bleeding.

Recent developments include the use of medical **acupuncture** to control pain during the procedure, and the use of carbon dioxide lasers to perform the myringotomy itself. Laser–assisted myringotomy can be performed in a doctor's office with only a local anesthetic. It has several advantages over the older technique: it is less painful; less frightening to children; and minimizes the need for tube insertion because the hole in the eardrum produced by the laser remains open longer than an incision done with a scalpel.

Another technique to keep the incision in the eardrum open without the need for tube insertion is application of a medication called mitomycin C, which was originally developed to treat **bladder cancer**. The mitomycin prevents the incision from sealing over. As of 2010, however, this approach is still being studied.

There has also been an effort to design ear tubes that are easier to insert or to remove, and to design tubes that stay in place longer. Ear tubes come in various shapes and sizes designed to meet the needs of each specific patient.

Diagnosis/Preparation

The diagnosis of otitis media is based on the doctor's visual examination of the patient's ear and the patient's symptoms. Patients with otitis media complain of earache and usually have a fever, sometimes as high as 105°F (40.5°C). There may or may not be loss of hearing. Small children may have **nausea and vomiting**. When the doctor looks in the ear with an otoscope, the patient's eardrum will look swollen and may bulge outward. The doctor can evaluate the presence of fluid in the middle ear either by blowing air into the ear, known as insufflation, or by tympanometry, which is an indirect measurement of the mobility of the eardrum. If the eardrum has already ruptured, there may be a watery, bloody, or pus–streaked discharge.

Fluid removed from the ear can be taken to a laboratory for culture. The most common bacteria that cause otitis media are *Pneumococcus*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Some cases are caused by viruses, particularly respiratory syncytial virus (RSV).

A child scheduled for a myringotomy should not have food or water for four to six hours before anesthesia. Antibiotics are usually not needed.

If **local anesthesia** is used, a cream containing lidocaine and prilocaine is applied to the ear canal about 30 minutes before the myringotomy. If medical acupuncture is used for pain control, the acupuncture begins about 40 minutes before surgery and is continued during the procedure.

Aftercare

The use of antimicrobial drops is controversial. Water should be kept out of the ear canal until the eardrum is intact. A doctor should be notified if the tubes fall out.

Risks

The risks include:

- cutting the outer ear
- formation at the myringotomy site of granular nodes due to inflammation
- formation of a mass of skin cells and cholesterol in the middle ear that can grow and damage surrounding bone (cholesteatoma)
- permanent perforation of the eardrum

It is also possible that the incision will not heal properly, leaving a permanent hole in the eardrum. This result can cause some hearing loss and increases the risk of infection.

The ear tube may move inward and get trapped in the middle ear, rather than move out into the external ear, where it either falls out on its own or can be retrieved by a doctor. The exact incidence of tubes moving inward is not known, but it could increase the risk of further episodes of middle–ear inflammation, inflammation of the eardrum or the part of the skull directly behind the ear, formation of a mass in the middle ear, or infection due to the presence of a foreign body.

The surgery may not be a permanent cure. As many as 30% of children undergoing myringotomy with insertion of ear tubes need to undergo another procedure within five years.

Other risks include those associated with sedatives or **general anesthesia**. Some patients may prefer acupuncture for pain control in order to minimize these risks.

An additional element of postoperative care is the recommendation of many doctors that the child use ear plugs to keep water out of the ear during bathing or swimming to reduce the risk of infection and discharge.

Normal results

Parents often report that children talk better, hear better, are less irritable, sleep better, and behave better after myringotomy with the insertion of ear tubes. Normal results in adults include relief of ear pain and ability to resume flying or deep–sea diving without barotrauma.

Morbidity and mortality rates

Morbidity following myringotomy usually takes the form of either otorrhea, which is a persistent discharge from the ear, or changes in the size or texture of the eardrum. The risk of otorrhea is about 13%. If the procedure is repeated, the eardrum may shrink, retract, or become flaccid. The eardrum may also develop an area of hardened tissue. This condition is known as tympanosclerosis. The risk of hardening is 51% its effects on hearing are not known, but they appear to be insignificant.

In 2008, it was reported that morbidity following myringotomy in the United States is highest among children from families of low socioeconomic status. The study found that children from poor urban families had more episodes of otorrhea following tube insertion then children from suburban families. In addition, the episodes of otorrhea in the urban children lasted longer.

Mortality rates are extremely low; case studies of fatalities following myringotomy are rare in the medical literature, and most involve adults.

Alternatives

Preventive measures

There are several lifestyle issues related to high rates of middle ear infection. One of the most serious is parental **smoking**. One study of the effects of passive smoking on **children's health** estimated that as many as 165,000 of the myringotomies performed each year on American children are related to the use of tobacco in the household.

Studies have shown that children in daycare have a higher risk of chronic ear infection, and therefore a higher risk of needing myringotomy.

A third factor that affects a child's risk of recurrent middle ear infection is **breastfeeding**. Toddlers who were breastfed as infants for at least four months have a lower risk of ear infection than those who were bottlefed.

Other surgical approaches

Because the adenoids may harbor infection, when myringotomy and tube placement fails, **adenoidectomy** may be performed in order to resolve chronic otitis media.

Alternative medicine

According to Dr. Kenneth Pelletier, former director of the program in complementary and alternative medicine at Stanford University, there is some evidence that homeopathic treatment is effective in reducing the pain of otitis media in children and lowering the risk of recurrence.

Resources

BOOKS

Behrman R.E., et al. *Nelson Textbook of Pediatrics,* 18th ed. Philadelphia: Saunders, 2007.

Cummings, C.W., et al. *Otolayrngology: Head and Neck Surgery,* 5th ed. St. Louis: Mosby, 2010.

Pelletier, Kenneth R., and J.E. Kerschner. "Otitis media." In: R.M. Kliegman, R.E. Behrman, H.B. Jenson, and B.F. Stanton, editors. *Nelson Textbook of Pediatrics,* 8th ed. Philadelphia, Pa: Saunders Elsevier; 2007: chap 639.

PERIODICALS

Desai, S. N., J. D. Kellner, and D. Drummond. "Population–Based, Age–Specific Myringotomy with Tympanostomy Tube Insertion Rates in Calgary, Canada." *Pediatric Infectious Disease Journal* 21 (April 2002): 348–50.

Paradise J.L., et al. "Tympanostomy Tubes and Developmental Outcomes at 9 to 11 years of age." *New England Journal of Medicine*. 356(3) (2007): 248–61.

Perkins, J. A. "Medical and Surgical Management of Otitis Media in Children." *Otolaryngology Clinics of North America* 35 (August 2002): 811–25.

Siegel, G. J., and R. K. Chandra. "Laser Office Ventilation of Ears with Insertion of Tubes." *Otolaryngology—Head and Neck Surgery* 127 (July 2002): 60–66.

OTHER

Lin, Yuan–Chi. "Acupuncture Anesthesia for a Patient with Complex Congenital Anomalies." Medical Acupuncture. 13 (Fall/Winter 2002). http://www.medicalacupuncture.org/aama_marf/journal/vol14_3/article2.html (accessed September 22, 2010).

ORGANIZATIONS

American Academy of Medical Acupuncture (AAMA), 4929 Wilshire Blvd., Suite 428, Los Angeles, CA, 90010, (323) 937–5514, http://www.medicalacupuncture.org.

American Academy of Otolaryngology, Head and Neck Surgery, Inc. (AAOHNSI), One Prince St., Alexandria, VA, 22314–3357, (703) 836–4444, http://www.entnet.org.

American Academy of Pediatrics (AAP), 141 Northwest Point Blvd., Elk Grove Village, IL, 60007, (847) 434–4000, http://www.aap.org.

Mary Zoll, PhD
Rebecca Frey, PhD
Karl Finley

Myxedema *see* **Hypothyroidism**

Myxoma

Definition

A myxoma is a rare, usually noncancerous, primary tumor (a new growth of tissue) of the heart. It is the most common of all benign heart tumors.

Description

Myxoma is an intracardiac tumor; it is found inside the heart. Seventy five percent of all myxomas are found in the left atrium, and almost all other myxomas are found in the right atrium. It is very rare for a myxoma to be found in either of the ventricles. The tumor takes one of two general shapes: a round, firm mass, or an irregular shaped, soft, gelatinous mass. They are attached to the endocardium, the

KEY TERMS

Embolus—A piece of tissue, blood clot, etc., that travels through the blood system and can lodge in smaller blood vessels anywhere in the body.

Metastasis—The spread of a cancer or infectious agent from the site of origin to other areas of the body.

Raynaud's phenomenon—Intermittant ischemia (deficient blood flow) of the fingers or toes, sometimes also affecting the ears and nose.

inside lining of the heart. The cells that make up the tumor are spindle-shaped cells and are embedded in a matrix rich in mucopolysaccharides (a group of carbohydrates). Myxomas may contain **calcium**, which shows up on x rays. The tumor gets its blood supply from capillaries that bring blood from the heart to the tumor. Thrombi (**blood clots**) may be attached to the outside of the myxoma.

There are three major syndromes linked to myxomas: embolic events, obstruction of blood flow, and constitutional syndromes. Embolic events happen when fragments of the tumor, or the thrombi attached to the outside of the tumor, are released and enter the blood stream. Gelatinous myxomas are more likely to embolize than the more firm form of this tumor.

Myxomas may also obstruct blood flow in the heart, usually at a heart valve. The mitral valve is the heart valve most commonly affected. Blood flow restrictions can lead to pulmonary congestion and heart valve disease. Embolization can lead to severe consequences. In cases of left atrial myxoma, 40-50% of patients experience embolization. Emboli usually end up in the brain, kidneys, and extremities.

The third syndrome linked to myxomas are called constitutional syndromes, nonspecific symptoms caused by the myxoma.

Causes and symptoms

There is no known causative agent for myxoma. The main symptoms, if any, produced by myxoma are generic and not specific. These include **fever**, weight loss, anemia, elevated white blood cell (WBC) count, decreased **platelet count**, and Raynaud's phenomenon. Most patients with myxoma are between 30-60 years of age.

Diagnosis

Diagnosis is made following a suspicion that a myxoma might be present, and can usually be confirmed by echocardiogram

Treatment

Surgery is used to remove the tumor. Myxomas can regrow if they are not completely removed. The survival rate for this operation is excellent.

Prognosis

Successful removal of the tumor rids the patient of this disease. Emboli from a myxoma may survive in other areas of the body. However, there is no evidence that myxoma is truly metastatic (able to transfer disease from one area to another), causing tumors in other areas of the body.

Resources

OTHER

"Myxoma, Intracardiac." *OMIM Home Page, Online Mendelian Inheritance in Man*. http://www.ncbi.nlm.nih.gov/Omim.

John T. Lohr, PhD

N

Nail-patella syndrome

Definition

Nail-patella syndrome, is a genetic disease of the connective tissue that produces defects in the fingernails, knee caps, and kidneys.

Description

Nail-patella syndrome is also known as Fong disease, hereditary onycho osteodysplasia (HOOD), iliac horn disease, and Turner-Kieser syndrome. Patients who have nail-patella syndrome may show a variety of physical defects. The hallmark features of this syndrome are poorly developed fingernails, toenails, and patellae (kneecaps). Other common abnormalities include elbow deformities, abnormally shaped pelvis bone (hip bone), and kidney (renal) disease.

Less common medical findings include defects of the upper lip, the roof of the mouth, and unusual skeletal abnormalities. Skeletal abnormalities may include poorly developed scapulae (shoulder blades), sideways-bent fingers (clinodactyly), **clubfoot**, **scoliosis**, and unusual neck bones. There are also other effects, such as thickening of the basement membrane in the skin and of the tiny clusters of capillaries (glomeruli) in the kidney. Scientists have recognized an association between nail-patella syndrome and **colon cancer**. Nail-patella syndrome is associated with open-angle glaucoma, which, if untreated, may lead to blindness. Patients may also have **cataracts**, drooping eyelids (**ptosis**), or corneal problems such as glaucoma.

People with nail-patella syndrome may display only a few or many of the recognized signs of this disease. Symptoms vary widely from person to person. Signs even vary within a single family with multiple affected members.

The incidence of nail-patella syndrome is approximately one in 50,000 births. This disorder affects males and females equally. It is found throughout the world and occurs in all ethnic groups. The strongest risk factor for nail-patella syndrome is a family history of the disease.

Causes and symptoms

Nail-patella syndrome has been recognized as an inherited disorder for more than 100 years. It is caused by mutations in a gene known as LIM homeobox transcription factor 1-beta (LMX1B), located on the long arm of chromosome 9.

The LMX1B gene codes for a protein that is important in organizing embryonic limb development. Mutations in this gene have been detected in many unrelated people with nail-patella syndrome. Scientists have also been able to interrupt this gene in mice to produce defects similar to those seen in human nail-patella syndrome.

Nail-patella syndrome is inherited in an autosomal dominant manner. This means that possession of only one copy of the defective gene is enough to cause disease. When a parent has nail-patella syndrome each of their children has a 50% chance of inheriting the disease-causing mutation.

A new mutation causing nail-patella syndrome can also occur, resulting in disease in a person with no family history. This is called a sporadic occurrence and accounts for approximately 20% of cases of nail-patella syndrome. The children of a person with sporadic nail-patella syndrome are also at a 50% risk of developing signs of the disorder.

Medical signs of nail-patella syndrome vary widely between patients. Some patients with this disorder do not display symptoms. These patients are discovered to have the nail-patella syndrome only when genetic studies trace their family history. Scientists are now working to learn what causes different people to display such different symptoms of nail-patella syndrome.

The most obvious sign associated with nail-patella syndrome is absent, poorly developed, or unusual fingernails. Fingernail abnormalities are found in more than 80% of patients with this disorder. Abnormalities may be found in one or more fingernails. Only rarely are all fingernails affected. This disease most commonly affects the fingernails of the thumbs and index fingers. The pinky fingernail is least likely to be affected. Fingernails may be small and concave with pitting, ridges, splits, and/or discoloration. Toenails are less often affected. The lunulae, or light-colored crescent moons, at the base of the fingernail bed next to the cuticle are sometimes triangularly-shaped in people with nail-patella syndrome.

Kneecap abnormalities are the second most common sign associated with this disorder. Either or both kneecaps may be missing or poorly formed. If present, kneecaps are likely to be dislocated. The knees of people with nail-patella syndrome may have a square appearance. Besides the kneecap, other support structures including bones, ligaments, and tendons may also be malformed. These support structures stabilize the knee, therefore patients with some leg malformations may have difficulty in walking.

The hip bones of approximately 80% of patients with nail-patella syndrome have unusual bony projections called posterior iliac horns. These bony projections, or spurs, are internal and not obvious unless they are detected on X-ray. This unusual pelvic anatomy is not associated with any other disease.

Kidney disease is present in at least 30% of people with nail-patella syndrome. Biopsy shows lesions that resemble those of inflammation of the clusters of capillaries in the kidneys (**glomerulonephritis**), but without any infection present. Kidney failure is the most dangerous consequence of nail-patella syndrome. It occurs in about 30% of patients who have kidney involvement. An early sign of kidney involvement is the presence of protein or blood in the urine (chronic, benign proteinuria and hematuria.) Kidney involvement is progressive, so early diagnosis and treatment of renal disease is important. Kidney disease has been reported in children with nail-patella syndrome, but renal involvement more commonly develops during adulthood.

Various skeletal symptoms may occur. Patients with nail-patella syndrome may not be able to fully straighten their arms at the elbow. This may create a webbed appearance at the elbow joint. Patients may have sideways-bent fingers, poorly developed shoulder blades, clubfoot, hip dislocation, unusual neck bones, or scoliosis.

Eye problems may be present and vary from person to person. Nail-patella syndrome is associated with open angle glaucoma. Open angle glaucoma is caused by fluid blocked into the front chamber of the eye. This blocked fluid builds increasing pressure into the eye. If untreated, this increased pressure may lead to permanent damage of the optic nerve and irreversible blindness. Some patients with nail-patella syndrome have ptosis, or drooping eyelids. Nail-patella syndrome has also been associated with abnormalities of the cornea, cataracts, and **astigmatism**. Additionally, the irises of the eye may be multicolored, possibly displaying a clover-shaped pattern of color.

Diagnosis

Genetic testing for nail-patella syndrome is available only through research institutions that are working to further characterize this disorder. Genetic testing cannot predict which signs of the disease will develop, nor can genetic testing predict the severity of disease symptoms. Improved genetic testing for nail-patella syndrome is anticipated in the future.

Diagnosis of this disease is most often made on visual medical clues such as the characteristic abnormalities of the fingernails and kneecaps. Diagnosis is confirmed by X-ray images of the affected bones and, when indicated, **kidney biopsy**. The bony pelvic spurs found in 80% of patients with nail-patella syndrome are not associated with any other disease.

Prenatal diagnosis for nail-patella syndrome by third-trimester ultrasound was documented in 1998. Prenatal diagnosis via genetic testing of cells obtained by **chorionic villus sampling** was reported the same year. Prenatal genetic testing for nail-patella syndrome is not yet widely available. Controversy surrounds the use of prenatal testing for such a variable disorder. Prenatal testing cannot predict the extent of an individual's disease.

Treatment

Treatment is usually not necessary. Treatment, when required, depends on each patient's specific symptoms. Severe kidney disease is treated with dialysis or a kidney transplant. Patients receiving kidney transplants do not develop nail-patella type renal complications in their new kidney.

A wheelchair may be required if walking becomes painful due to bone, tendon, ligament, or muscle defects. **Orthopedic surgery** may be necessary for congenital clubfoot deformity. Manipulation or surgery may be required to correct hip dislocation. Cataracts are also surgically treated. Medical treatment at early

KEY TERMS

Chorionic villus sampling (CVS)—A procedure used for prenatal diagnosis at 10–12 weeks gestation. Under ultrasound guidance a needle is inserted either through the mother's vagina or abdominal wall and a sample of cells is collected from around the early embryo. These cells are then tested for chromosome abnormalities or other genetic diseases.

Glomeruli—Tiny clusters of capillaries in the kidney.

Hematuria—The presence of blood in the urine.

Patella—The kneecap.

Proteinuria—Excess protein in the urine.

signs of glaucoma prevents progression of the disease to blindness.

Genetic counseling is offered to persons who have the disease. Parents with this disease have a 50% chance of passing it to each of their children. Current genetic testing technology cannot predict the severity or scope of an individual's symptoms.

Because many possible manifestations of nail-patella syndrome exist, patients are advised to pursue extra medical care including regular **urinalysis** and special eye exams. Children with nail-patella syndrome should be screened for scoliosis.

Prognosis

Survival among patients with nail-patella syndrome is not decreased unless a they exhibit renal complications. It is estimated that 8% of individuals with nail-patella syndrome who come to medical attention eventually die of kidney disease.

Resources

BOOKS

Kaplan, Justin L., et al. *The Merck Manual of Medical Information*. New York: Pocket Books, 2007.

OTHER

Gene Clinics. http://www.geneclinics.org.
OMIM—Online Mendelian Inheritance in Man. http://www.ncbi.nlm.nih.gov/omim/.

John T. Lohr, PhD
Judy C. Hawkins, MS

Nail infections *see* **Onychomycosis**

Nail removal

Definition

Nail removal is a form of treatment that is sometimes necessary following traumatic injuries or recurrent infections in the area of the nail. There are nonsurgical as well as surgical methods of nail removal.

Purpose

Nails are removed only when necessary to allow the skin beneath the nail (the nail bed) to heal or in some cases, to remove a nail that has been partially pulled out in an accident. In the case of toenails, it is occasionally necessary to remove the nail of the large toe due to a chronic condition caused by badly fitted shoes. In general, however, doctors prefer to try other forms of treatment before removing the nail. Depending on the cause, nail disorders are usually treated through: the use of oral medications; medicated gels or creams applied directly to the skin around the nail; the avoidance of substances that irritate the nail folds; surgical lancing of abscesses around the nail; or the injection of **corticosteroids** under the nail fold.

The most common causes of nail disorders include:

- Trauma. The nails can be damaged by nail biting, using the fingernails as tools, and incorrect use of nail files and manicure scissors as well as by accidents and sports injuries.
- Infections. These include fungal infections under the nails, bacterial infections of cuts or breaks in the nail folds, or infections of the nails themselves caused by the fungus *Candida albicans*. Inflammation of the nail folds is called paronychia.
- Exposure to harsh detergents, industrial chemicals, hot water, and other irritants. People who work as dishwashers are especially vulnerable to separation of the nail itself from the nail bed (onycholysis).
- Systemic diseases and disorders. These include psoriasis, anemia, and certain congenital disorders.
- Allergic reactions to nail polish, polish remover, or the glue used to attach false nails.

Precautions

In the case of infections, it is necessary to distinguish between fungal, bacterial, and candidal infections before removing the nail. Cultures can usually be obtained from pus or tissue fluid from the affected nail.

KEY TERMS

Avulse—To pull or tear away forcibly. In some cases, a surgeon must remove a nail by avulsing it from its matrix.

Matrix—The tissue at the base of the nail, from which the nail grows.

Nail bed—The layer of tissue underneath the nail.

Onycholysis—The separation of a nail from its underlying bed. Onycholysis is a common symptom of candidal infections of the nail or of exposure to harsh chemicals and detergents.

Paronychia—Inflammation of the folds of skin that surround a nail.

Description

Surgical nail removal

If necessary, the surgeon can remove the nail at its base with an instrument called a needlepoint scalpel. In a few cases, the nail may need to be pulled out (avulsed) from its matrix.

Nonsurgical nail removal

Nails can be removed by applying a mixture of 40% urea, 20% anhydrous lanolin, 5% white wax, 25% white petroleum jelly, and silica gel type H.

Preparation

For nonsurgical nail removal, the nail fold is treated with tincture of benzoin and covered with adhesive tape. The nail itself is thickly coated with the urea mixture, followed by a layer of plastic film and adhesive tape. The mixture is left on the nail for five to 10 days, after which the nail itself can be removed.

Aftercare

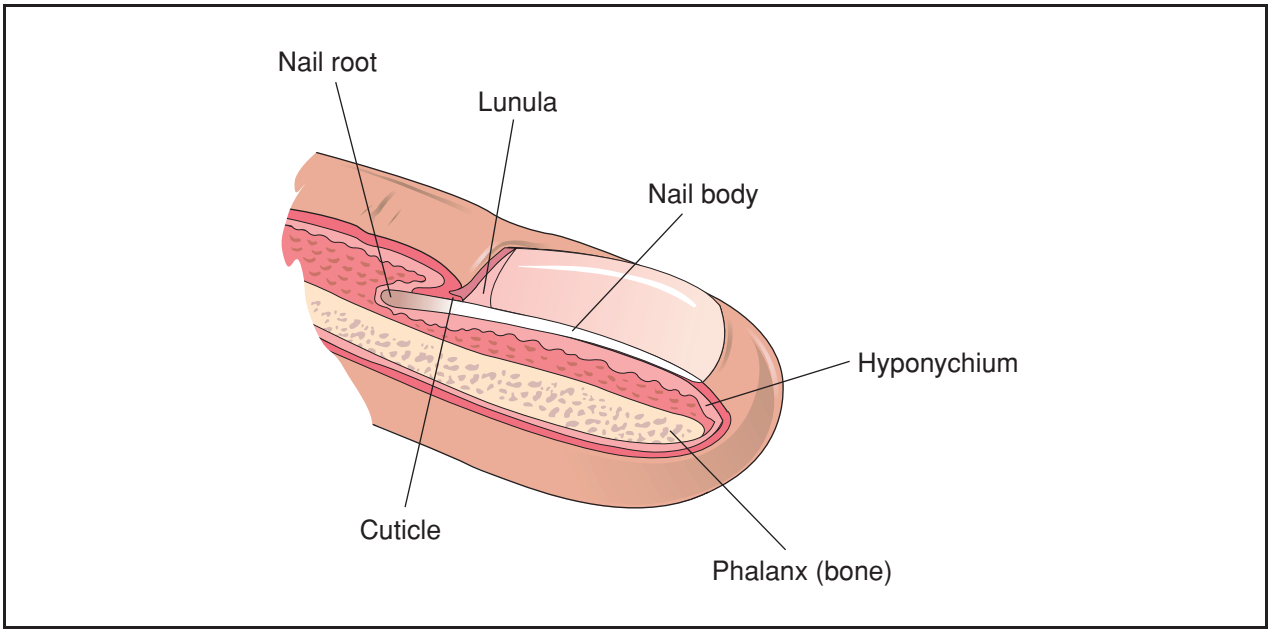
Aftercare of surgical removal is similar to the care of any minor surgical procedure. Aftercare of the urea paste method includes applying medication for the specific infection that is being treated.

Risks

Risks from either procedure are minimal.

Normal results

Normal results include the successful removal of the infected or damaged nail.



The physiology of the human fingernail. The most common causes of nail disorders include trauma, infections, exposure to harsh detergents, hot water and other irritants, systemic diseases and disorders, and allergic reactions to nail polish, nail polish remover, and nail glue.
(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)

Resources

BOOKS

Gupta, Aditya K., and R. Baran. *Nail Disorders and Their Management*. Philadelphia: W.B. Saunders, 2006.

Rebecca J. Frey, PhD

Nalidixic acid *see* **Urinary anti-infectives**

Narcissistic personality disorder *see* **Personality disorders**

Narcolepsy

Definition

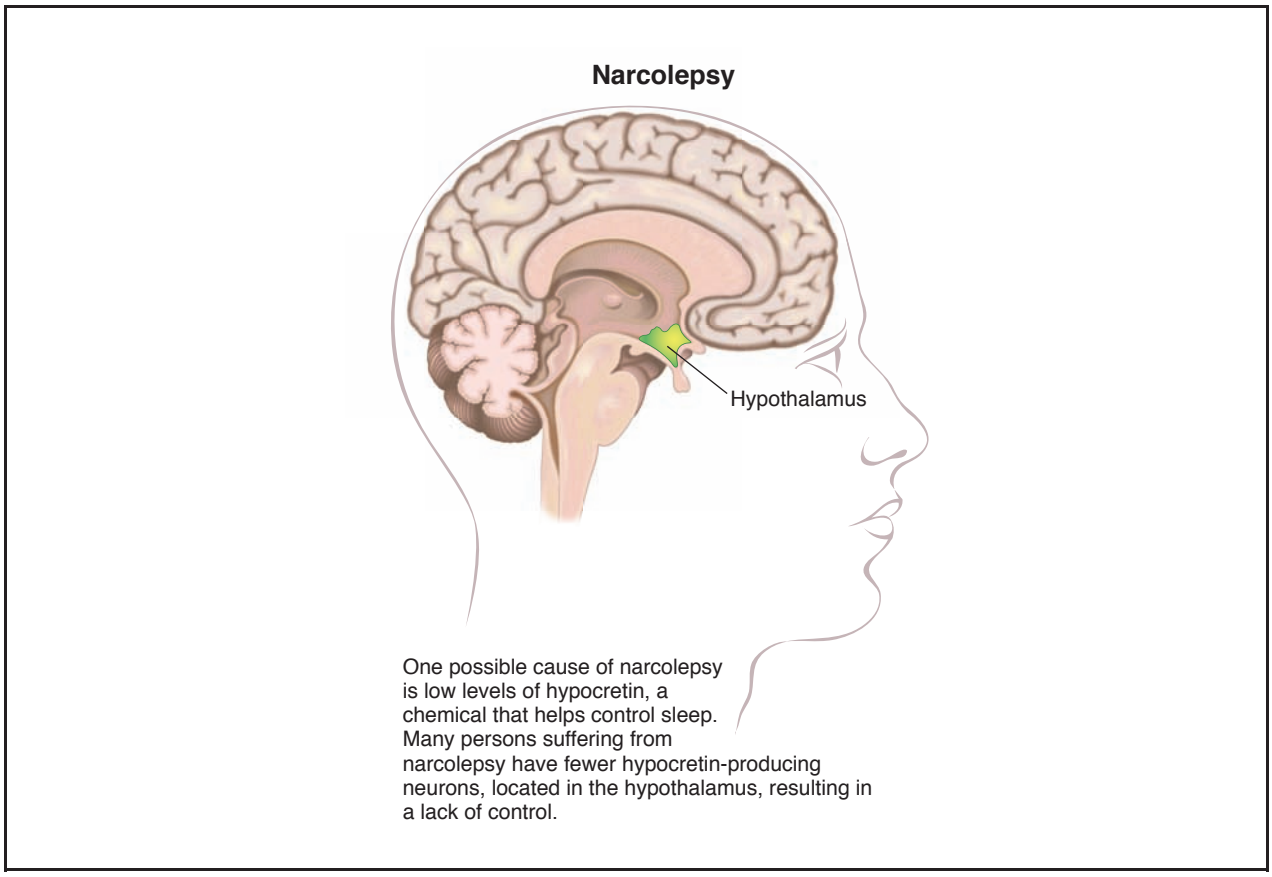
Narcolepsy is a neurological disorder marked by excessive daytime sleepiness, uncontrollable sleep attacks, and cataplexy (a sudden loss of muscle tone, usually lasting up to half an hour).

Demographics

According to the National Institute for Neurological Disorders and Stroke (NINDS), narcolepsy is an underrecognized and underdiagnosed condition in the United States. The exact prevalence is not known, but it is estimated to affect about one in every 2,000 Americans. The disorder occurs worldwide in every racial and ethnic group, affecting males and females equally. However, prevalence varies among populations. For example, narcolepsy is less prevalent in Israel (about one per 500,000) but considerably more prevalent in Japan (about one per 600).

Description

Narcolepsy is the second–leading cause of excessive daytime sleepiness (after obstructive **sleep apnea**). Persistent sleepiness and sleep attacks are the hallmarks of this condition. The sleepiness has been compared to the feeling of trying to stay awake after not sleeping for two or three days.



(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)

KEY TERMS

Cataplexy—A symptom of narcolepsy in which there is a sudden episode of muscle weakness triggered by emotions. The muscle weakness may cause the person's knees to buckle, or the head to drop. In severe cases, the patient may become paralyzed for a few seconds to minutes.

Excessive daytime sleepiness (EDS)—A persistent sense of mental cloudiness, a lack of energy, a depressed mood, or extreme state of exhaustion.

Hypnagogic hallucinations—Dream–like auditory or visual hallucinations that occur while falling asleep.

Hypothalamus—A part of the forebrain that controls heartbeat, body temperature, thirst, hunger, body temperature and pressure, blood sugar levels, and other functions.

Sleep paralysis—An abnormal episode of sleep in which the patient cannot move for a few minutes, usually occurring on falling asleep or waking up. Often found in patients with narcolepsy.

People with narcolepsy fall asleep suddenly—anywhere, at any time, maybe even in the middle of a conversation. These sleep attacks can last from a few seconds to more than an hour. Depending on where they occur, they may be mildly inconvenient or even dangerous to the individual. Some people continue to function outwardly during the sleep episodes, such as talking or putting things away. But when they wake up, they have no memory of the event.

Narcolepsy is related to the deep, dreaming part of sleep known as rapid eye movement (REM) sleep. Normally when people fall asleep, they experience 90 minutes of non–REM sleep, which is then followed by REM sleep. People with narcolepsy, however, enter REM sleep immediately. In addition, REM sleep occurs inappropriately throughout the day.

Risk factors

According to the NINDS, close relatives of people with narcolepsy have a statistically higher risk of developing the condition than do members of the general population.

Causes and symptoms

Narcolepsy sometimes runs in families, but most cases are sporadic, meaning that the disorder occurs independently in individuals without strong evidence of being inherited. Some researchers therefore believe that the inheritance of narcolepsy is similar to that of heart disease. In heart disease, several genes play a role in being susceptible to the disorder, but it usually does not develop without an environmental trigger of some sort. Other factors, such as infection, immune system deficiencies, trauma, hormonal changes, and **stress** may also play a role in the development of the disease.

The immediate cause of narcolepsy remains unknown but as of 2009, medical researchers have made considerable progress in understanding the disorder and in identifying genes strongly associated with it. Abnormalities in various parts of the brain involved in regulating REM sleep were also discovered. Narcolepsy is now known to have one of the tightest associations with a specific form, or allele, of the HLA gene family. The HLA gene family provides instructions for making a group of related proteins known as the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria. From 88% to 98% of patients affected by narcolepsy have been shown to be positive for the allele known as HLA DQB1*0602. This allele strongly increases the susceptibility for cataplexy, although 41% of patients without cataplexy are carriers. DRB1 and DQB1 genes have been sequenced in narcolepsy patients but no mutation has been identified. This suggests that these genes strongly confer susceptibility to narcolepsy without their function being defective. It is accordingly believed that non–HLA genes may also be involved in susceptibility to narcolepsy.

While the symptoms of narcolepsy usually appear during the teens or 20s, the disease may not be diagnosed for many years. The most common major symptom is excessive daytime sleepiness (EDS), an overwhelming feeling of **fatigue**. After several months or years, cataplexy and other symptoms appear.

Cataplexy is the most dramatic symptom of narcolepsy. It affects 75% of people with the disorder. During attacks, the knees buckle and the neck muscles go slack. In extreme cases, the person may become paralyzed and fall to the floor. This loss of muscle tone is temporary, lasting from a few seconds to half an hour, but frightening. The attacks can occur at any time but are often triggered by strong emotions, such as anger, joy, or surprise.

Other symptoms of narcolepsy include:

- sleep attacks: short, uncontrollable sleep episodes throughout the day
- sleep paralysis: a frightening inability to move shortly after awakening or dozing off
- auditory or visual hallucinations: intense, sometimes terrifying experiences at the beginning or end of a sleep period
- disturbed nighttime sleep: tossing and turning, nightmares, and frequent awakenings during the night

Diagnosis

Examination

In most patients, narcolepsy is not diagnosed until 10 to 15 years after the first symptoms appear. This is because the disorder is not familiar to most of the general public. The disorder is suspected when a person reports both excessive daytime sleepiness and cataplexy. Diagnosis is established on the basis of a clinical examination and comprehensive medical history.

Tests

Laboratory tests are required to confirm a diagnosis. These may include an overnight polysomnogram—a test in which sleep is monitored with **electrocardiography**, video, and respiratory parameters. A multiple sleep latency test, which measures sleep latency (onset) and how quickly REM sleep occurs, may be used. People who have narcolepsy usually fall asleep in less than five minutes.

If a diagnosis is in question, a genetic blood test can reveal the existence of certain substances in people who have a tendency to develop narcolepsy. Positive test results suggest, but do not prove, the existence of narcolepsy.

Treatment

Traditional

There is no cure for narcolepsy. It is not progressive, and it is not fatal, but it is chronic. The symptoms can be managed with medication or lifestyle adjustment.

Drugs

Amphetamine–like stimulant drugs are often prescribed to control drowsiness and EDS attacks. Patients who do not like taking high doses of stimulants may choose to take smaller doses and "manage" their lifestyles, such as by napping every couple of hours, to relieve daytime sleepiness. Antidepressants are often effective in treating symptoms of abnormal REM sleep. In 2002, the FDA approved Xyrem® (**sodium** oxybate or gamma hydroxybutyrate, also known as GHB) for treating people with narcolepsy who experience episodes of cataplexy.

Prognosis

Narcolepsy is not a degenerative disease, and patients do not develop other neurologic symptoms. However, narcolepsy can interfere with a person's ability to work, play, drive, and perform other daily activities. In severe cases, the disorder prevents people from living a normal life, leading to depression and a loss of independence.

Prevention

Narcolepsy cannot be prevented.

Resources

BOOKS

Goswami, Meeta, et al., editors. *Narcolepsy: A Clinical Guide*. New York, NY: Springer, 2009.

ICON Health Publications. *Narcolepsy —A Medical Dictionary, Bibliography, and Annotated Research Guide to Internet References*. San Diego, CA: ICON Health Publications, 2004.

Lee–Chiong, Teofilo L. *Sleep Medicine Essentials*. New York, NY: Wiley-Blackwell, 2009.

McBrewster, John, et al., editors. *Rapid eye movement (sleep): Sleep (non–human), Polysomnogram, Sleep disorder, PGO waves, Dream, Narcolepsy, Parasomnia, Lucid dream*. Beau Bassin, Mauritius: Alphascript Publishing, 2009.

Parker, James and Philip Parker, editors. *The Official Patient's Sourcebook on Narcolepsy*. San Diego, CA: ICON Health Publications, 2002.

PERIODICALS

Arias–Carrión, O., and E. Murillo–Rodríguez. "Cell transplantation: a future therapy for narcolepsy?" *CNS & Neurological Disorders Drug Targets* 8, no. 4 (August 2009): 309–314.

Black, J., et al. "The nightly administration of sodium oxybate results in significant reduction in the nocturnal sleep disruption of patients with narcolepsy." *Sleep Medicine* 10, no. 8 (September 2009): 829–835.

Caylak, E. "The genetics of sleep disorders in humans: narcolepsy, restless legs syndrome, and obstructive sleep apnea syndrome." *American Journal of Medical Genetics. Part A* 149A, no. 11 (November 2009): 2612–2626.

Didato, G., and L. Nobili. "Treatment of narcolepsy." *Expert Review of Neurotherapeutics* 9, no. 6 (June 2009): 897–910.

Kroeger, K., and L. de Lecea. "The hypocretins and their role in narcolepsy." *CNS & Neurological Disorders Drug Targets* 8, no. 4 (August 2009): 271–2804.

Todman, D. "Narcolepsy." *European Neurology* 61, no. 4 (2009): 255.

Undurraga, J., et al. "Treatment of narcolepsy complicated by psychotic symptoms." *Psychosomatics* 50, no. 4 (July–August 2009): 427–428.

Vernet, C., and I. Arnulf. "Narcolepsy with long sleep time: a specific entity?" *Sleep* 32, no. 9 (September 2009): 1229–1235.
Wang, W., et al. "Two patients with narcolepsy treated by hypnotic psychotherapy." *Sleep Medicine* 10, no. 10 (December 2009): 1167.

OTHER

"Do I Have Narcolepsy?" *Narcolepsy Network*. Information Page. http://www.narcolepsynetwork.org/?page_id=7 (accessed November 14, 2009)
"Narcolepsy." *Medline Plus*. Encyclopedia. http://www.nlm.nih.gov/medlineplus/ency/article/000802.htm (accessed November 14, 2009)
"Narcolepsy and Sleep." *National Sleep Foundation*. Information Page. http://www.sleepfoundation.org/article/sleep-related-problems/narcolepsy-and-sleep (accessed November 14, 2009)
"Narcolepsy Fact Sheet." *NINDS*. Information Page. http://www.ninds.nih.gov/disorders/narcolepsy/detail_narcolepsy.htm (accessed November 14, 2009)

ORGANIZATIONS

Narcolepsy Network, Inc., 110 Ripple Lane, North Kingstown, RI, 02852, (401) 667-2523, (888) 292-6522, (401) 633-6567, narnet@narcolepsynetwork.org, http://www.narcolepsynetwork.org.
National Heart, Lung, and Blood Institute (NHLBI), Building 31, Room 5A52, 31 Center Drive MSC 2486, Bethesda, MD, 20892, (301) 592-8573, (240) 629-3246, nhlbiinfo@nhlbi.nih.gov, http://www.nhlbi.nih.gov.
National Institute of Neurological Disorders and Stroke (NINDS), P.O. Box 5801, Bethesda, MD, 20824, (301) 496-5751, (800) 352-9424, http://www.ninds.nih.gov.
National Sleep Foundation, 1522 K Street NW, Suite 500, Washington, DC, 20005, (202) 347-3471, (202) 347-3472, nsf@sleepfoundation.org, http://www. sleepfoundation.org.

Michelle Lee Brandt
Monique Laberge, PhD

Narcotics

Definition

Narcotics are natural opioid drugs derived from the Asian poppy *Palaver somniferous*, or semi-synthetic or synthetic substitutes for these drugs.

Purpose

Narcotics are drugs that dull the sense of **pain**, and cause drowsiness or sleep. They are the most effective tool a physician has to relieve severe pain. Narcotics are also given pre-operatively to relieve **anxiety** and induce anesthesia. Other common uses are to suppress **cough** and to control very severe **diarrhea**. In large doses, they can suppress the ability to breathe and cause **coma** and **death**. Narcotics are also taken illegally for recreational use.

Classes of narcotics

Narcotics of natural origin

Codeine
Morphine
Opium
Thebaine

Semi-synthetic narcotics

Heroin
Hydrocodone
Hydromorphone
Oxycodone

Synthetic narcotics

Butorphanol
Dextropropoxyphene
Fentanyl
Meperidine
Pentazocine

Narcotics treatment drugs

Buprenorphine
LAAM
Methadone

SOURCE: U.S. Department of Justice, Drug Enforcement Administration, *Drugs of Abuse*, "Chapter 4: Narcotics." Available online at: http://www.justice.gov/dea/pubs/abuse/4-narc.htm (accessed August 19, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

Precautions

Narcotics should only be taken under the direction of a physician. These drugs depress the central nervous system and should not be taken with other drugs, such as alcohol, **barbiturates**, **antihistamines**, and **benzodiazepines** that also depress the central nervous system.

Opioids are broken down by the liver. Individuals with liver damage may not detoxify these substances as rapidly as healthy individuals, leading to potential accidental overdose. Street narcotics are of uncertain strength and may be contaminated with toxic chemicals or contain a mixture of drugs that can cause life-threatening reactions.

Description

Natural narcotics are derived directly from the sap of the unripe seed pods of the opium poppy. Morphine and codeine are the most familiar natural narcotics and are the narcotics most frequently used in medical settings. Often they are prescribed in combination with other non-narcotic drugs. Heroin is a

semi-synthetic narcotic. It has no medical or legal uses. Other completely synthetic narcotics are made in the laboratory. These include drugs with medical uses such as fentanyl and oxycodone, and illegal "designer drugs" synthesized for recreational use. Some man-made narcotics are hundreds of times more potent than natural narcotics.

Narcotics depress the central nervous system. They work by binding chemically with receptors in a way that blocks the transmission of nerve impulses. These drugs do not cure the source of the pain; they simply block the individual's perception of pain. When used to treat cough or diarrhea, they slow or block muscle contractions.

Morphine (Roxanol, morphine sulfate, morphine hydrochloride) is the most commonly used medical narcotic for managing moderate to severe pain. It can be also be used to control extreme diarrhea caused by **cholera** or similar diseases. Morphine sulfate is a white powder that dissolves in water. It is usually given by injection into a muscle or intravenously by injection into a vein. When given intravenously, its effect occurs almost immediately. Individuals given morphine regularly have a high potential for developing dependence on the drug. Morphine can cause withdrawal symptoms if stopped abruptly. It is not a common street drug.

More codeine is prescribed medically than any other narcotic. Concentrations of codeine in the sap of the opium poppy are low, so most codeine is manufactured by chemical alteration of morphine. For pain control, codeine is combined with other non-narcotic painkillers such as **aspirin** (Empirin with Codeine,) **acetaminophen** (Tylenol with Codeine) or non-steroidal anti-inflammatory drugs. These combination painkillers are manufactured as tablets (most common) or liquids, and come in a variety of strengths based on the amount of codeine they contain. Codeine is also found in some cough syrups (Robitussin A-C, for example) and is used to control dry cough. Occasionally codeine is used to control severe diarrhea, although diphenoxylate (Lomotil) is used more often.

In Canada, certain low-dose codeine pain relievers are sold without prescription. In the United States pain medication with codeine requires a prescription. The likelihood of physical or psychological dependence on codeine is much lower than with morphine.

Hydromorphone (Dilaudid) is a narcotic synthetically produced from morphine. It is available in tablets or as an injectable solution and used for pain relief. It is one of the most common pain relievers prescribed for patients who are terminally ill, because it combines high effectiveness with low side effects.

Mederidine (Demerol) was originally developed to treat **muscle spasms** but is used mainly for pain relief. It is manufactured as tablets of varying strengths. Another synthetic pain relief narcotic whose use parallels mederidine is propoxyphene. When combined with aspirin this narcotic is known under the brand name Darvon. In November 2010, the U.S. Food and Drug Administration banned Darvon, Darvocet, and other pills containing propoxyphene.

Oxycodone (Oxycontin), a synthetic narcotic used for pain relief, is manufactured both alone and with aspirin (Percodan) or acetaminophen (Percoset) in tablets of various strengths. Oxycontin is a controlled release formula of oxycodone that controls pain continuously for 12 hours at a time. Oxycodone has a high potential for prescription-drug and street **abuse**. Hydrocodone with acetaminophen (Vicodin) is another synthetic narcotic whose use and potential abuse parallels oxycodone.

Fentanyl (Sublimaze, Actiq, Duragesic) is used as a surgical anesthetic. It is available as an injectable solution and as a skin patch.

Methadone is a synthetic narcotic used mainly as a substitute for heroin in heroin-withdrawal treatment, although it does have pain-killing properties. Methadone, when taken by mouth (liquid, wafers, tablets) provides little of the euphoria of heroin, but it blocks heroin cravings and withdrawal symptoms.

The first international attempts to control narcotic drugs were made in 1909 with the formation of the Opium Commission Forum, which developed the first international drug control treaty in 1912. Established in 1961, the International Narcotics Control Board (INCB), today regulates narcotics internationally. The INCB regulates the cultivation of raw materials to make narcotics and natural and man-made drugs. **Cocaine** and **marijuana** also fall under the board's control, although they are not technically narcotics. Narcotic drugs are also regulated by federal and state governments. In law enforcement, the term narcotics is extended to include other, mainly illicit drugs such as cocaine that have little medical use.

Preparation

No special preparation is required before being treated with narcotics, although, as with all medications, individuals should tell their physicians about all prescription and non-prescription drugs, supplements,

KEY TERMS

Tapering—Gradually reducing the amount of a drug when stopping it abruptly would cause unpleasant withdrawal symptoms.

and herbal remedies that they are taking, as certain medications may enhance the effects of narcotics.

Aftercare

When an individual is prescribed narcotics regularly for an extended period, tolerance may develop. With tolerance, the individual must take higher and higher doses to achieve the same level of pain control. In some cases, when narcotics are stopped abruptly, withdrawal symptoms may develop. These include:

- anxiety
- irritability
- rapid breathing
- runny nose
- sweating
- vomiting and diarrhea
- confusion
- shaking
- lack of appetite

In order to prevent withdrawal symptoms, the dose of narcotics can be gradually diminished, a process known as tapering, until they can be discontinued completely without unpleasant effects. Individuals may also be treated with the drug cloindine (Catapres) to relieve some withdrawal symptoms.

Risks

All narcotics have the potential to become physically and psychologically addictive. When used regularly, tolerance can develop. Abuse and dependence on narcotic prescription drugs in an increasing problem among the elderly particularly and among members of the middle class generally.

Overdose and withdrawal symptoms and reactions caused by contamination with other drugs or toxic chemicals are common reasons for drug-related visits to the emergency room by individuals using street narcotics recreationally. Overdose is treated with the drug naloxone (ReVia). Naloxone blocks and reverses the effects of narcotics. When given intravenously it is effective within one to two minutes.

Normal results

When used as prescribed, narcotics are a generally safe and effective way to relieve pain and control cough and severe diarrhea. Individuals should not be afraid they will develop an **addiction** after a short-term course of narcotics following a dental or medical procedure, provided that they follow the physician's instructions for taking the drugs.

Resources

OTHER

"Narcotics." U.S. Drug Enforcement Administration (undated) [cited March 25, 2005] http://www.usdoj.gov/dea/concern/narcotics.html.

National Institute on Drug Abuse. February 4, 2005 [cited March 25, 2005]. http://drugabuse.gov/drugpages/prescription.html

Stephens, Everett. *Toxicity, Narcotics* January 7, 2005 [cited March 25, 2005]. http://www.emedicine.com/emerg/topic330.htm.

ORGANIZATIONS

National Institute on Drug Abuse, 6001 Executive Blvd., Room 5213, Bethesda, MD, (301) 443-1124, information@nida.nih.gov, http://drugabuse.gov.

United States Drug Enforcement Administration, Dr Mailstop: AXS, 2401 Jefferson Davis Highway, Alexandria, VA, 22301, (202) 307-1000, http://www.dea.gov.

Tish Davidson, A. M.

Nasal culture *see* **Nasopharyngeal culture**

Nasal irrigation

Definition

Nasal irrigation is the practice of flushing the nasal cavity with a sterile solution. The solution may contain **antibiotics** or steroid medications.

Purpose

Nasal irrigation is used to clear infected sinuses or may be performed after surgery to the nose region. It may be performed by adding antibiotics to the solution to treat **nasal polyps**, nasal septal deviation, allergic nasal inflammation, chronic sinus infection, and swollen mucous membranes. One benefit of nasal irrigation in treating these conditions is that it usually lowers the amount of medication that the patient must take by mouth.

Irrigation is also used to treat long-term users of inhalants, such as illicit drugs (**cocaine**), or such occupational toxins as paint fumes, sawdust, pesticides, and coal dust.

Nasal irrigation may also be used in occupational medicine to monitor workers for exposure to airborne glass fibers, asbestos, and similar materials.

KEY TERMS

Irrigation—In medicine, the practice of washing out or flushing a wound or body opening with a stream of water or another liquid.

Saline—A solution made from salt and water.

Precautions

Nasal irrigation should not be performed on people who have frequent nosebleeds; have recently had nasal surgery; or whose gag reflex is impaired, as fluid may enter the windpipe.

Description

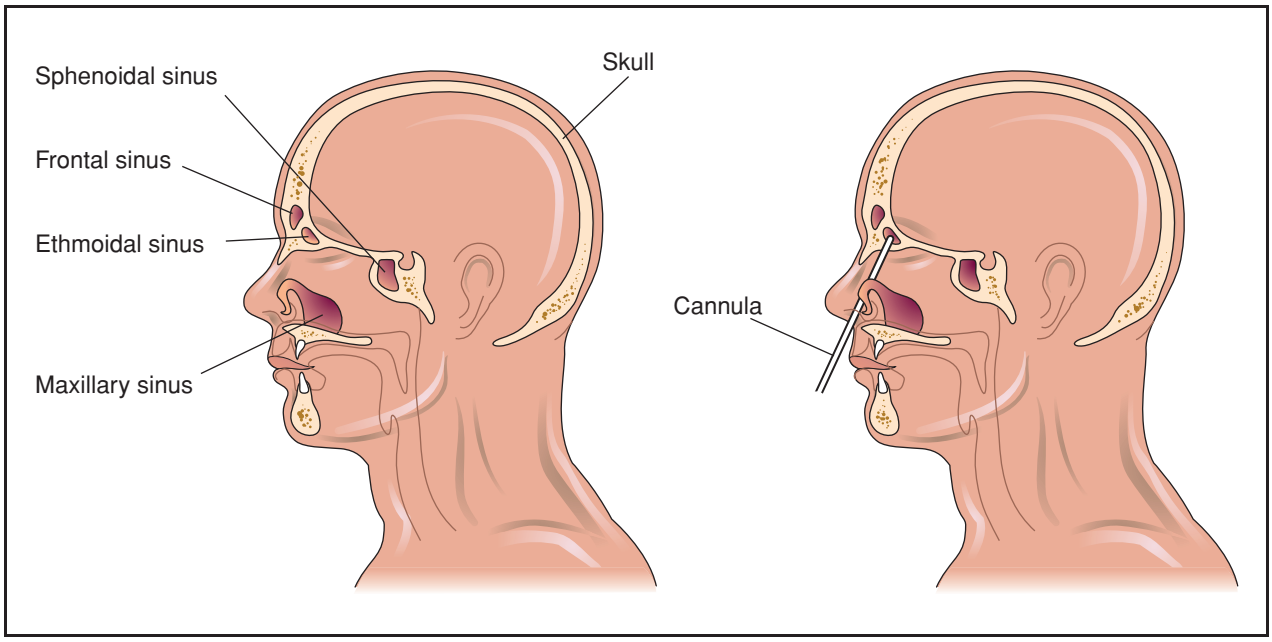
Nasal irrigation can be performed by the patient at home or by a medical professional. A forced-flow instrument, such as a syringe, is filled with a warm saline solution. The solution can be commercially prepared (Ayr, NaSal) or can be prepared by the patient, using one-half teaspoon salt with each eight ounces of warm water. Occasionally, antibiotics or **steroids** are added to the solution to kill bacteria and aid healing of irritated membrane. The syringe is then directed into the nostril. The irrigation solution loosens encrusted material in the nasal passage, and drainage takes place through the nose. The patient leans over a catch basin during irrigation, into which the debris flows. Irrigation continues until all debris is cleared from the passage. Nasal irrigation can be performed up to twice daily, unless the irrigation irritates the mucous membrane.

Preparation

Before nasal irrigation, the patient is instructed not to open his or her mouth or swallow during the procedure. Opening the mouth or swallowing may cause infectious material to move from the nasal passage into the sinuses or the ear.

Risks

Complications of nasal irrigation include irritation of the nasal passages due to extreme temperature of the irrigation solution. Rarely, irrigation



Because surgery in the nasal area has a high incidence rate for contamination with pathogenic bacteria, nasal irrigation is performed to remove loose tissue and prevent infection. The illustration (right) shows a cannula in place while the sinus passages are being flushed. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

fluid may enter the windpipe in people with a poor gag reflex.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Aukema, A. A., and W. J. Fokkens. "Chronic Rhinosinusitis: Management for Optimal Outcomes." *Treatments in Respiratory Medicine* 3 (February 2004): 97–105.

Brown, C. L., and S. M. Graham. "Nasal Irrigations: Good or Bad?" *Current Opinion in Otolaryngology and Head and Neck Surgery* 12 (February 2004): 9–13.

Lavigne, F., M. K. Tulic, J. Gagnon, and Q. Hamid. "Selective Irrigation of the Sinuses in the Management of Chronic Rhinosinusitis Refractory to Medical Therapy: A Promising Start." *Journal of Otolaryngology* 33 (February 2004): 10–16.

Paananen, H., M. Holopainen, P. Kalliokoski, et al. "Evaluation of Exposure to Man-Made Vitreous Fibers by Nasal Lavage." *Journal of Occupational and Environmental Hygiene* 1 (February 2004): 82–87.

ORGANIZATIONS

American Academy of Family Physicians (AAFP), 11400 Tomahawk Creek Parkway, Leawood, KS, 66211-2680, (913) 906-6000, (913) 906-6075, (800) 271-2237, http://www.aafp.org/.

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 836-4444, http://www.entnet.org.

Mary K. Fyke
Rebecca J. Frey, PhD

Nasal packing

Definition

Nasal packing is the application of gauze or cotton packs to the nasal chambers.

Purpose

The most common purpose of nasal packing is to control bleeding following surgery to the septum or nasal reconstruction and to treat chronic nosebleeds. Packing is also used to provide support to the septum after surgery.

Description

Packing is the placement of gauze or cotton into the nasal area. Packing comes in three forms: gauze, cotton balls, and preformed cotton wedges. Packing is usually coated with **antibiotics** and, sometimes, petrolatum. The end of the nose may be taped to keep the packings in place or to prevent the patient from pulling them out. In cases of surgery, packings are frequently removed within 24–48 hours following surgery. In the case of nosebleeds, packing is left in for extended periods of time to promote healing and to prevent the patient from removing scar tissue which might reopen the wound. If both sides of the nose are packed, the patient must breathe through his or her mouth while the packs are in place.

In patients who are chronic nose pickers, frequent bleeding is common and ulceration of nasal tissue is possible. To promote healing and to prevent nose picking, both sides of the nose are packed with cotton that contains antibiotics. The nose is taped shut with surgical tape to prevent the packing from being removed. The packing is left in the nose for seven to 10 days. If the wound is high up in the nasal cavity, gauze strips treated with petrolatum and antibiotics are used. The strips are placed into the nose one layer at a time, folding one layer on top of the other until the area is completely packed.

Local packing is a procedure used when only a small part of the nose must be packed. Typically, this occurs when one blood vessel is prone to bleeding, and there is no need to block breathing through the nose. Local packing is used when the pack can remain in place by itself. This situation can be found at the turbinates. Turbinates are folds of tissue on the insides of the nose. The folds are sufficiently firm to support packing. A small piece of gauze or cotton is wedged in between the turbinates where the blood vessel being treated is located. Local packing is left in place for up to 48 hours and then removed. The main advantage to this type of packing is that it enables the patient to breathe through his or her nose. Local packing is also more comfortable than complete packing, although the patient will still experience a sensation that something is in the nasal cavity. The patient must be instructed not to interfere with or probe the packing while it is in place.

A postnasal pack is used to treat bleeding in the postnasal area. This is a difficult area to pack. Packs used in this area are made from cotton balls or gauze that have been tied into a tubular shape with heavy gauge suture or umbilical tape. Long lengths of suture or tape are left free. The lengths of suture or tape are used to help position the pack during installation and to remove it. An alternative is to cut a vaginal tampon

KEY TERMS

Turbinate—Ridge-shaped cartilage or soft bony tissue inside the nose.

Ulcer—A sore on the skin or mucous tissue that produces pus and in which tissue is destroyed.

and reposition the strings. Balloons have been tried as a method to replace postnasal packing, but have not proved effective. After being tied, the pack is soaked with an antibiotic ointment. Generally, packs are formed larger than needed, so that they completely block the nasal passage. A catheter is passed through the nose and pulled out through the mouth. Strings from one end of the pack are tied to the catheter and the pack pulled into place by passing through the mouth and up the back of the nasal cavity. The pack is removed in a similar manner. Complications may occur if a pack compresses the eustachian tube, causing ear problems. The ear should be examined to ensure that infection is not developing.

Packing of the anterior (front) part of the nose is also performed following surgery such as **septoplasty** and **rhinoplasty**. In these operations, the surgeon cuts through the skin flap covering cartilage and bone in the center, top, and bottom of the nose to correct the shape of the nose. At the conclusion of the surgery, the skin flap is sutured back into place. The purposes of packing are to absorb any drainage from the incision and mucus produced by nasal tissue, and to support the skin flap and cartilage. The packing used is either gauze or preformed adsorbent wedges of cotton. Both are usually treated with antibiotic to reduce the chance of infections at the incision site. Generally, there is little bleeding following septoplasty and rhinoplasty, and the incisions heal normally. These packs are left in place for 24 to 48 hours and then removed.

Aftercare

Ice chips or mouthwash can be used to moisten the mouth while packing is in place, as the mouth may be dry from breathing through it. Humidifiers may also help with breathing. After nasal packing, the nose should not be blown for two to three days.

Since one of the major reasons that packing is performed is to heal damage to nasal blood vessels from nose-picking, follow-up examination should be done to ensure that the patient is no longer practicing this habit. If the patient has restarted nose-picking, therapy to alter this behavior should be pursued. When the packing completely blocks the nasal cavity and prevents breathing through the nose, the patient should adjust to breathing through the mouth. In elderly patients, adjustment may be more difficult. This leads to a drop in the blood oxygen content and an increase in blood carbon dioxide levels (CO_2). This, in turn, can cause respiratory and cardiac complications, including a racing pulse.

Risks

Nasal packing could cause a lack of oxygen in those who have difficulty breathing through their mouths. Rarely, sinus infection or middle-ear infection may occur.

Resources

BOOKS

Shapiro, Nina L. *Handbook of Pediatric Otolaryngology: A Practical Guide for Evaluation and Management of Pediatric Ear, Nose, and Throat Disorders*. Singapore: World Scientific, 2011.

John T. Lohr, PhD

Nasal papillomas

Definition

Nasal papillomas are **warts** located inside the nose.

Description

Two types of tumors can grow inside the nose: polyps and papillomas. By far the most common are polyps, which have smooth surfaces. On the contrary, papillomas have irregular surfaces and are, in fact, warts. Papillomas may be caused by the same viruses that cause warts elsewhere on the body. They are inside the nose, more often on the side near the cheek, and, because of their internal structure, they are much more likely to bleed than polyps.

There is a special type of nasal papilloma called an inverting papilloma because of its unique appearance. About 10 or 15% of these are or can become cancers.

Causes and symptoms

Like polyps, papillomas can plug up the nose and disable the sense of smell. Unlike polyps, papillomas often bleed.

KEY TERMS

Polyp—A tumor commonly found in the nasal cavity or intestine.

Diagnosis

A **physical examination** with special instruments will detect these tumors.

Treatment

Because of the possibility of **cancer**, all nasal papillomas must be removed surgically and sent to the laboratory for analysis. If a cancer is present, further surgery may be necessary to guarantee that all of the cancer has been removed. The initial surgery can be done in an office setting by a specialist in head and neck surgery, also known as otorhinolaryngology and popularly abbreviated ENT (ear, nose, and throat). Cancer surgery is more extensive and often requires hospitalization.

Prognosis

For benign (non-cancerous) lesions, removal is curative, although they tend to recur, just like warts elsewhere. The cancerous papillomas may occasionally escape complete surgical removal and spread to adjacent or distant sites. The prognosis is then much more complex.

Resources

BOOKS

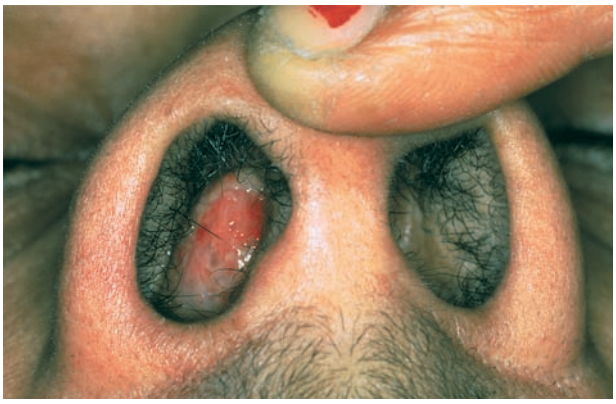
Blair, Robin, and Arnold G. D. Maran. *Logan Turner's Diseases of the Ear, Nose and Throat*. 11th ed. Oxford, UK; New York: Oxford University Press, 2010.

J. Ricker Polsdorfer, MD

Nasal polyps

Definition

A polyp is the medical term for any overgrowth of tissue from the surface of a body organ. Polyps come in all shapes—round, droplet, and irregular being the most common. Nasal polyps are teardrop-shaped while growing and resemble peeled grapes when they have reached their full size. The condition of nasal polyps is sometimes called nasal polyposis.



A nasal polyp inside patient's right nostril. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Description

Nasal polyps tend to occur in people with respiratory **allergies**. Hay fever (**allergic rhinitis**) is an irritation of the membranes of the nose by airborne particles or chemicals. These membranes secrete mucus. When irritated, they can also grow polyps. The nose is not only a passageway for air to reach the lungs; it also provides the connection between the sinuses and the outside world. Sinuses are lined with mucous membranes, just like the nose. Polyps can easily obstruct the drainage of mucus from the sinuses. When any fluid in the body is trapped so it cannot flow freely, it becomes infected. The result, **sinusitis**, is a common complication of allergic **rhinitis**.

Nasal polyps may also develop in children with **cystic fibrosis**.

Causes and symptoms

Some people who are allergic to **aspirin** develop both **asthma** and nasal polyps.

Nasal polyps often plug the nose, usually one side at a time. People with allergic rhinitis are so used to having a stopped-up nose they may not notice the difference when a polyp develops. Other polyps may be closer to a sinus opening, so airflow is not obstructed, but mucus becomes trapped in the sinus. In this case, there is a feeling of fullness in the head, no sense of smell, and perhaps a **headache**. The trapped mucus will eventually get infected, adding **pain**, fever, and perhaps bloody discharge from the nose.

KEY TERMS

Allergen—Any substance that irritates only those who are sensitive (allergic) to it.

Asthma—Wheezing (labored breathing) due to allergies or irritation of the lungs.

Decongestant—Medicines that shrink blood vessels and consequently mucus membranes. Pseudoephedrine, phenylephrine, and phenylpropanolamine are the most common.

Polyposis—The medical term for the development of multiple polyps on a body part.

Sinus—Air-filled cavities surrounding the eyes and nose are lined with mucus-producing membranes. They cleanse the nose, add resonance to the voice, and partially determine the structure of the face.

Diagnosis

A **physical examination** will identify most polyps. Small polyps located higher up or further back may be hidden from view, but they will be detected with more sophisticated medical instruments. The otorhinolaryngologist is equipped to diagnose nasal polyps. In order to perform the examination, the doctor must apply medicine to reduce congestion in the swollen membranes. Cotton balls soaked with one of these agents and left in the nostrils for a few minutes provide adequate shrinkage.

Treatment

Most polyps can be removed by the head and neck surgeon as an office procedure called a nasal polypectomy. Bleeding, the only complication, is usually easy to control. Nose and sinus infections can be treated with **antibiotics** and **decongestants**, but if airflow is restricted, the infection will recur.

Prognosis

Polyps may reappear as long as the allergic irritation continues. In addition, one study of patients who had undergone nasal polypectomy reported that 60% had a recurrence of nasal polyposis, and 47% were advised to have revision surgery. The risk of recurrence is higher among patients with asthma.

Prevention

If aspirin is the cause of the polyps, all aspirin containing medications must be avoided.

Since most nasal polyps are the result of allergic rhinitis, they can be prevented by treating this condition. New treatments have greatly improved control of hay fever. There are now several spray medicines that are quite effective. Spray cortisone-like drugs, usually beclomethasone (Beconase, Vancenase) or flunisolide (Nasalide), are the most popular. Over-the-counter nasal decongestants have an irritating effect similar to the allergy they are supposed to be treating. Continued use can bring more trouble than relief and result in an **addiction** to nose sprays. The resulting disease, rhinitis medicamentosa, is more difficult to treat than allergic rhinitis.

Allergists and ENT surgeons both treat allergic rhinitis with a procedure called desensitization. After identifying suspect allergens using one of several methods, they will give the patient increasing doses of those allergens in order to produce blocking antibodies that will impede the allergic reaction. This approach is effective in a number of patients, but the treatment may take a period of months to years.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Bikhazi, N. B. "Contemporary Management of Nasal Polyps." *Otolaryngologic Clinics of North America* 37 (April 2004): 327–337.

Drake-Lee, A. B. "Nasal Polyps." *Hospital Medicine* 65 (May 2004): 264–267.

Wynn, R., and G. Har-El. "Recurrence Rates after Endoscopic Sinus Surgery for Massive Sinus Polyposis." *Laryngoscope* 114 (May 2004): 811–813.

ORGANIZATIONS

American Academy of Allergy, Asthma & Immunology, 555 East Wells Street, Suite 1100, Milwaukee, WI, 53202-3823, (414) 272-6071, http://www.aaaai.org.

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 836-4444, http://www.entnet.org.

J. Ricker Polsdorfer, MD
Rebecca J. Frey, PhD

Nasal trauma

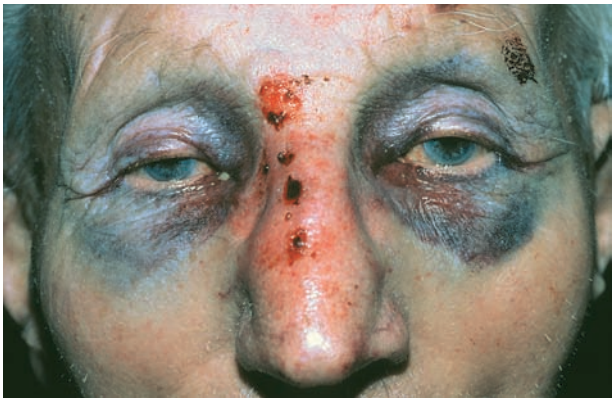
Definition

Nasal trauma is defined as any injury to the nose or related structure that may result in bleeding, a physical deformity, a decreased ability to breathe normally because of obstruction, or an impaired sense of smell. The injury may be either internal or external.

Description

The human nose is composed of bone, soft tissue, and cartilage. It serves as a passageway for air to flow from the outside environment into the lower respiratory tract and lungs. At the same time, the nasal passages warm and humidify the air that enters the body.

Internal injuries to the nose typically occur when a foreign object (including the fingers) is placed in the nose or when a person takes in drugs of **abuse** (inhalants or **cocaine**) through the nose. External injuries to the nose are usually blunt force injuries related to sports participation, criminal violence, parental abuse, or automobile or bicycle accidents. This type of injury may result in a nasal fracture. The nasal bones are the most frequently fractured facial bones due to their position on the face, and are the third most common type of bone fracture in general after **fractures** of the wrist and collarbone. A force of only 30g is required to break the nasal bones, compared to 70g for the bones in the jaw and 200g for the bony ridge above the eyes. The pattern of the fracture depends on the direction of the blow to the nose, whether coming from the front, the side, or above the nose. Although not life-threatening by itself, a fractured nose may lead to difficulties in breathing as well as facial disfigurement.



Fractured nose of an elderly patient. *(Dr. P. Marazzi/Photo Researchers, Inc.)*

Fractures resulting from trauma to the nose may involve the bones of the septum (the partition of bone and cartilage dividing the two nostrils) as well as the bones surrounding the eyes. These bones include the nasal, maxilla, lacrimal, and frontal bones. Direct trauma to the bridge of the nose may also result in damage to a part of the base of the skull known as the cribriform plate. This injury in turn may allow cerebrospinal fluid to leak out of the skull and leave the body through the nose. Fractures may also damage the membranes that line the nasal passages, leading to possible formation of scar tissue, obstruction of the airway, and damage to the child's sense of smell.

In addition to fractures, external injuries of the nose include soft-tissue injuries resulting from **bites** (human and animal), insect **stings**, cuts, or scrapes. Penetrating injuries to the nasal area caused by air gun or BB pellets are also reported with increasing frequency in older children and adolescents. When fired at close range, these pellets can penetrate the skin and cheekbone and lodge in the nasal septum or the sinuses near the nose.

Lastly, nose **piercing** as a fashion trend is a type of intentional injury to the nose that has several possible complications, including infections of the cartilage and soft tissues in the nose; blockage of the airway due to a loosened stud or other nose ornament; and gastrointestinal emergencies caused by accidental swallowing of nose jewelry.

Causes and symptoms

Causes

External trauma to the nose may be accidental (transportation accidents, animal bites, air gun injuries, and **sports injuries**) or intentional (fights, criminal assault, domestic violence, nose piercing). Nasal injuries from athletic activities may result from contact with equipment (being hit in the face by a baseball, or other small ball hit at high speed, or by the bat or stick itself) or the bodies of other players (in sports such as football, boxing, martial arts, rugby). Nasal injuries from piercing include bacterial infections of

the skin and nasal cartilage, allergic reactions to the jewelry, tissue damage, and periodic bleeding.

In a few cases, external trauma to the nose may also be iatrogenic, or caused by medical care. Most of these injuries result from medical examination of the nose—particularly in emergency circumstances—or as complications of **plastic surgery**. In a few cases damage to the nose is caused by **radiation therapy** for **cancer**.

Internal injuries to the nose may be either mechanical (caused by **foreign objects** in the nose or by picking or scratching the tissues lining the nose) or chemical (caused by environmental irritants or **substance abuse**).

Chemical injuries to the nose are caused by accidental or purposeful breathing or sniffing of irritating substances. These may include tobacco smoke; household cleaners (ammonia and chlorine bleach) and furniture polish; ozone and other air pollutants; cocaine; and glue, paint thinners, solvents, and similar household products that produce toxic vapors. An increasingly common form of chemical injury to the nasal membranes in toddlers is alkali **burns** caused by leakage from small batteries placed in the nose. While chemical damage to the nose is usually accidental in younger children, it is more often the result of substance abuse in adolescents. Taking cocaine through the nose ("snorting") or inhalant abuse ("sniffing" or "huffing") are the most common causes of chemical damage to the nose in older children or teenagers.

Symptoms

The symptoms of physical trauma to the nose may include:

- Flattening or other deformation of the shape of the nose
- Infections of the cartilage or soft tissue
- Epistaxis or bleeding from the nose
- Crepitus. Crepitus is the crackling or crunching sound heard when the ends of a fractured bone are rubbed together
- Pain and tissue swelling
- Airway blockage from bleeding, fluid discharge, or tissue swelling
- Rhinitis. Rhinitis is an inflammation of the mucous membranes lining the nose. In the case of a fracture, rhinitis may lead to increased tear production in the eyes and a runny nose
- Septal hematoma. A septal hematoma is a mass of blood from torn tissue that may collect within the cartilage that divides the two nostrils. It may become infected and form an abscess that eventually destroys the cartilage
- Bruising or discoloration (ecchymosis) of the tissues around the eye
- Leakage of cerebrospinal fluid through the nostrils

Chemical trauma to the nose may result in:

- Runny nose and watering of the eyes
- Pain
- Loss of the sense of smell
- Nasal congestion and sneezing
- Reddening and swelling of the mucous membranes lining the nose
- Eventual destruction of the cartilage in the nasal septum and the tissues lining the nose

Some common irritants that may be encountered in the home and workplace include:

- cleaning solutions and powders
- ammonia
- environmental tobacco smoke
- bleach
- metalworking fluids
- ozone
- sulfur dioxide
- paint thinners
- arsenic
- chromic acid
- copper dust and mists

Aftereffects following exposure to these chemicals are based not only on the concentration of the irritant but also on factors specific to the individual. Reactions vary among persons, even with similar exposures.

Diagnosis

Diagnosis of a fracture is normally based on a history of nasal trauma and clinical presentation. Epistaxis may or may not be present. An intranasal examination is performed in order to look for a septal hematoma that may result in serious consequences such as **death** of the septal cartilaginous tissue. The nose is also checked for tenderness, mobility, stability, and crepitance.

X-rays are normally not indicated, however, in more severe fractures involving multiple bones, a computed tomography (CT) scan may be required. The physician should look for associated injuries such as periorbital (surrounding the eye) ecchymosis, watery eyes, or diplopia (double vision) that may indicate orbital injuries. In addition, dental fractures and a cerebrospinal fluid (CSF) leak should be looked for.

CSF leaks indicate a more severe injury possibly involving an ethmoid bone fracture.

The physician may also ask for photographs taken prior to the injury in order to determine the extent of deformity. Photographs may also be taken to document the injury in regards to possible legal actions.

In order to diagnose trauma sustained by a chemical injury, a history of exposure to potentially toxic chemicals should be ascertained. In addition, the patient should also bring information related to the types of chemicals that he or she has been exposed to. If injury occurs in the workplace, Material Safety Data Sheets should be available in the employer's poison control center that list the chemical components of commercial materials. Measurements of air from the patient's work area may also be obtained. Symptomatic improvement on off-days followed by a subsequent return of symptoms when returning to work confirms that the illness is work related. The physician should perform an intranasal examination to determine the extent of the chemical injury. A **chest x-ray** as well as a pulmonary function test may be ordered to determine if there is any subsequent lower respiratory tract involvement.

Treatment

Timing

Nasal injuries should be treated as promptly as possible to prevent complications. Batteries placed in the nose should be removed within four hours to prevent burns and other damage to the tissues from leaking chemicals. If a septal hematoma has developed, the doctor must remove it as quickly as possible to prevent infection or eventual death of the tissues in the nasal septum. Lastly, if the child has been bitten by an animal, the injury must be cleansed as soon as possible to lower the risk of **rabies**.

Treatment of nasal fractures is best performed during the first three hours after the injury. If this is impossible, management of a nasal fracture should be done within three to seven days. Timing is of utmost importance when treating nasal fractures because delays longer than seven to 10 days may allow the broken bones to set without proper alignment, or lead to such complications as scar tissue formation and airway obstruction. Poorly set nasal fractures usually require surgical correction.

Specific procedures

Foreign objects in the nose can be removed by nasal suction in most cases. Most nosebleeds are treated by 5–30 minutes of direct pressure on the nostrils, with the patient's head placed in an upright position. The doctor may also pack the nose with gauze coated with petroleum jelly. If the bleeding does not stop, or if it appears to originate in the upper nose, the doctor will consult a head and neck surgeon or an otolaryngologist for specialized evaluation of the bleeding.

Air gun or BB pellets that have penetrated the nose or nearby sinuses are generally removed with the help of an endoscope, which is a slender tubular instrument that allows the doctor to examine the inside of a body cavity.

Treatment of nasal fractures depends on the extent of the injury; the most difficult fractures to treat are those that involve the nasal septum. The doctor will usually reduce the fracture, which means that he or she will restore the damaged bones to their proper position and alignment. Although **local anesthesia** is usually sufficient for treating nasal fractures in adults and older teenagers, **general anesthesia** is usually given when treating these injuries in younger children.

Reductions of nasal fractures may be either open or closed. A closed reduction involves manipulation of the bones without cutting into the overlying skin. This type of reduction will be performed for fractures of the nasal bones that are limited in size and complexity. Open reductions are performed for more complex nasal fractures. In an open reduction, the nasal bones are moved back to their original location after the surgeon has made an incision in the overlying skin. This procedure is done for fractures involving dislocation of the septum as well as the nasal bones. In addition, an open reduction is necessary if the child has a septal hematoma or an open fracture in which the skin has been perforated. If a septal hematoma is present, the doctor will drain it and pack the nose to prevent subsequent accumulation of blood. The nasal bones are held in the proper position with external splints as well as the internal packing, and the splints are kept in place for seven to 10 days. The patient will be given **antibiotics** to lower the risk of infection and may be referred to an otolaryngologist or plastic surgeon for further evaluation. Ice packs or cold compresses can be applied at home to lower swelling and ease discomfort.

In the case of animal bites, the patient may be given passive or active immunization against rabies if there is a chance that the dog or other animal is rabid. This precaution is particularly important for animal bites on the nose or other parts of the face, as the

KEY TERMS

Crepitus—A crackling or crunching sound heard when the ends of a fractured piece of bone rub against each other.

Diplopia—The medical term for seeing double.

Ecchymosis (plural, ecchymoses)—The medical term for a bruise. Ecchymoses may develop around the eyes following a nasal fracture.

Epistaxis—The medical term for a nosebleed.

Hematoma—A localized collection of blood that accumulates in an organ, tissue, or body space as the result of leakage from a broken blood vessel. Hematomas sometimes develop within the nasal cartilage when the nose is fractured.

Iatrogenic—Referring to injuries caused by a doctor. Nasal trauma may occasionally result from a doctor's examination of the nose or complications from plastic surgery.

Otolaryngologist—A doctor who specializes in diagnosing and treating disorders of the ears, nose, and throat.

Reduce—To restore a part of the body to its normal position or place, as in treating a fracture or dislocation. The repositioning of the bone or body part is called a reduction.

Rhinitis—An inflammation of the mucous membranes that line the nasal passages.

Rhinoplasty—Plastic surgery of the nose to repair or change the shape of the nose.

Septal hematoma—A mass of extravasated blood that is confined within the nasal septum.

Septum—The partition of bone and cartilage in the nose that separates the two nostrils.

incubation period of the rabies virus is much shorter for bites on the head and neck than for bites elsewhere on the body.

Complications can arise following treatment and therefore follow-up is necessary. Problems that may occur resemble symptoms of nasal fractures. Others include infection, CSF leakage, scar tissue build-up, and a saddle nose deformity where the bridge of the nose is markedly depressed.

Treatment for trauma caused by irritant inhalation involves removing the patient from the contaminated area or decreasing exposure time. Other measures include using a saline nasal spray or topical **steroids**. For acute injuries oxygen or supportive treatment for any subsequent lower respiratory tract involvement may be administered.

If the injury is occupation-related, changes should be made in order to eliminate future incidents. These changes may include having the patient wear a respiratory protection device while working. In addition, the employer should be made aware of the situation and employ measures to prevent future incidents.

Prognosis

Most types of nasal trauma have a good prognosis. Nosebleeds or tissue damage caused by scratching or picking at the nose usually clear completely once these habits are stopped. Infections or allergic reactions caused by foreign objects in the nose or piercing usually clear up promptly after the object or piece of jewelry is removed. Nasal fractures that do not involve the nasal septum or other facial bones and receive prompt treatment generally heal without deformities of the nose, cartilage destruction, or other complications. More extensive facial fractures, however, may require a second operation to correct the positioning of the bones and restore the appearance of the nose.

The prognosis for soft-tissue injuries to the nose depends on the cause and extent of the injuries. Such tearing or crushing injuries as those caused by bites take longer to heal than simple cuts, and may require plastic surgery at a later date to restore the appearance of the nose.

Damage to the tissues lining the nose caused by exposure to tobacco smoke or other irritants in the environment is usually reversible once the patient is removed from contact with the irritating substance. Erosion or destruction of the nasal cartilage as a result of inhalant or cocaine abuse, however, usually requires surgical treatment.

Prevention

Although most cases of nasal trauma happen inadvertently, some measures can be employed in order to prevent injury. Patients should be aware of the symptoms of nasal fracture and should seek medical attention as

soon as possible to prevent more invasive reductions. Protective equipment should also be worn when playing sports. Employees should also be aware of irritating chemicals in their workplace and appropriate measures should be taken to avoid exposure.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

McPhee, Stephen, and Maxine Papadakis. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw–Hill Medical, 2009.

PERIODICALS

Alvi, A., T. Doherty, and G. Lewen. "Facial Fractures and Concomitant Injuries in Trauma Patients." *Laryngoscope* 113 (January 2003): 102–106.

Anderson, Carrie E., MD, and Glenn A. Loomis, MD. "Recognition and Prevention of Inhalant Abuse." *American Family Physician* 68 (September 1, 2003): 869–876.

Brinson, G. M., B. A. Senior, and W. G. Yarbrough. "Endoscopic Management of Retained Airgun Projectiles in the Paranasal Sinuses." *Otolaryngology and Head and Neck Surgery* 130 (January 2004): 25–30.

Kalavrezos, N. "Current Trends in the Management of Frontal Sinus Fractures." *Injury* 35 (April 2004): 340–346.

Mahajan, M., and N. Shah. "Accidental Lodgment of an Air Gun Pellet in the Maxillary Sinus of a 6-Year-Old Girl: A Case Report." *Dental Traumatology* 20 (June 2004): 178–180.

Ross, Adam T., MD, and Daniel G. Becker, MD. "Fractures, Nasal and Septal." *eMedicine* July 13, 2004. http://www.emedicine.com/ent/topic159.htm.

Rupp, Timothy J., MD, Marian Bednar, MD, and Stephen Karageanes, DO. "Facial Fractures." *eMedicine* August 29, 2004. http://www.emedicine.com/sports/topic33.htm.

Tu, A. H., J. A. Girotto, N. Singh, et al. "Facial Fractures from Dog Bite Injuries." *Plastic and Reconstructive Surgery* 109 (April 1, 2002): 1259–1265.

ORGANIZATIONS

American Academy of Family Physicians (AAFP), 11400 Tomahawk Creek Parkway, Leawood, KS, 66211-2680, (913) 906-6000, (913) 906-6075, (800) 271-2237, http://www.aafp.org/.

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 836-4444, http://www.entnet.org.

American College of Sports Medicine (ACSM), 401 West Michigan Street, P.O. Box 1440, Indianapolis, IN, 46202-3233, (317) 637-9200, (317) 634-7817, http://www.acsm.org.

Laith Farid Gulli, MD
Robert Ramirez, BS
Rebecca J. Frey, PhD

Nasogastric suction

Definition

Nasogastric suction involves removing solids, liquids, or gasses from the stomach or small intestine by inserting a tube through the nose and suctioning the gastrointestinal material through the tube.

Purpose

Nasogastric suction may be done in the following situations:

- to decompress the stomach or small intestine when intestinal obstruction (ileus) is suspected
- prior to gastrointestinal operations
- to obtain a sample of the gastric contents for analysis
- to remove toxic substances
- to flush the stomach during gastrointestinal bleeding or poisonings

Nasogastric intubation, the insertion of a tube through the nose into the stomach or small intestine, is also done to temporarily feed certain patients. In this case, material is not suctioned out.

Precautions

Nasogastric tubes cannot be placed in patients who have blockages in their esophagus, enlarged esophageal veins or arteries that might bleed, or severe damage to the jaws and face. The tube cannot be inserted in a patient who is having convulsions, or who is losing or has lost consciousness unless a tube has been inserted into his or her airway (intubation).

Description

The patient sits upright while a lubricated tube is slipped through the nose and down the throat. The patient may be asked to sip water at a certain point in the procedure to facilitate the passage of the tube. If the tube is to be placed into the small intestine, the doctor may use an endoscope to help see where the tube is going. Once the tube is in place, material can be removed from the stomach or intestines with gentle suction.

There are several different types of nasogastric tubes, each with a different purpose. Tubes used for **stomach flushing** are called orogastric tubes and are the largest in diameter. Tubes that are threaded through the lower opening of the stomach (pylorus) and into the small intestine are stiffer and have a

KEY TERMS

Endoscope—A piece of equipment with a camera and a light source in a thin tube that can be threaded through the nose into the gastrointestinal system so that the doctor can make a real-time visual examination.

Pylorus—The ring of muscle that controls the passage of material from the stomach into the small intestine.

balloon tip. Other specialized tubes are used for long-term and short-term feeding.

Preparation

Little preparation is necessary for this procedure other than educating the patient as to what will happen. The patient should remove dental appliances before the nasogastric tube is inserted.

Aftercare

After the tube is removed, no special care is needed. The patient's throat may feel irritated from the presence of the tube.

Risks

The most serious risk is that the patient will inhale some of the stomach contents into the lungs (aspiration). This may lead to bronchial infections and aspiration **pneumonia**. There is also the chance that the tube will be misplaced in the windpipe (trachea), causing violent coughing. Irritation to the throat and esophagus can cause bleeding.

Normal results

Nasogastric suctioning is normally well tolerated by patients and is a temporary treatment, performed in conjunction with other therapies.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Tish Davidson, A.M.

Nasopharyngeal culture

Definition

A nasopharyngeal culture is used to identify pathogenic (disease-causing) organisms present in the nasal cavity that may cause upper respiratory tract symptoms.

Purpose

Some organisms that cause upper respiratory infections are carried primarily in the nasopharynx, or back of the nose. The person carrying these pathogenic bacteria may have no symptoms, but can still infect others with the pathogen and resulting illness. The most serious of these organisms is *Neisseriea meningitidis*, which causes **meningitis** or blood stream infection in infants. By culturing a sample from the nasopharynx, the physician can identify this organism, and others, in the asymptomatic carrier. The procedure can also be used as a substitute for a **throat culture** in infants, the elderly patient, the debilitated patient, or in cases where a throat culture is difficult to obtain.

Precautions

The technician taking the specimen should wear gloves to prevent spreading infectious organisms. The patient should not be taking **antibiotics**, as these drugs may influence the test results.

Description

The patient should **cough** before collection of the specimen. Then, as the patient tilts his or her head backwards, the caregiver will inspect the back of the throat using a penlight and tongue depressor. A swab on a flexible wire is inserted into the nostril, back to the nasal cavity and upper part of the throat. The swab is rotated quickly and then removed. Next, the swab is placed into a sterile tube with culture fluid in it for transport to the microbiology laboratory. To prevent contamination, the swab should not touch the patient's tongue or side of the nostrils.

When the sample reaches the laboratory, the swab will be spread onto an agar plate and the agar plate incubated for 24–48 hours, to allow organisms present to grow. These organisms will be identified and any pathogenic organisms may also be tested for susceptibility to specific antibiotics. This allows the treating physician to determine which antibiotics will be effective.

Alternative procedures

In most cases of upper respiratory tract infections, a throat culture is more appropriate than a nasopharyngeal culture. However, the nasopharyngeal culture should be used in cases where throat cultures are difficult to obtain or to detect the carrier states of *Harmophilus influenzae* and meningococcal disease.

Some researchers regard the immunoblot method as preferable to a standard culture to detect certain species of pneumococci and other organisms that cause **pneumonia**. The immunoblot method uses a membrane that changes color in response to a specific antigen-antibody reaction.

As of the early 2000s, polymerase chain reaction (PCR) analysis is considered more sensitive than standard culture in detecting *Bordetella pertussis*, the bacterium that causes **whooping cough**. PCR has the additional advantage of providing test results more rapidly than culture.

Preparation

The procedure of inserting the swab should be described to the patient, as there is a slight discomfort associated with taking the sample. Other than that, no special preparation is necessary.

Aftercare

None

Risks

There is little to no risk involved in a nasopharyngeal culture.

Normal results

Bacteria that normally grow in the nose cavity will be identified by a nasopharyngeal culture. These include nonhemolytic streptococci, alpha-hemolytic streptococci, some *Neisseria* species, and some types of staphylococci.

Abnormal results

Pathogenic organisms that might be identified by this culture include

- Group A beta-hemolytic streptococci
- *Bordetella pertussis*, the causative agent of whooping cough

KEY TERMS

Antibiotic—A drug given to stop the growth of bacteria. Antibiotics are ineffective against viruses.

Nasopharynx—The back wall of the nasal cavity where it meets the throat.

- *Corynebacterium diptheriae*, the causative agent of diptheria
- *Staphylococcus aureus*, the causative agent of many staphylococcal infections

Additional bacteria are abnormal if they are found in large amounts. These include

- *Haemophilus influenzae*, a causative agent for certain types of meningitis and chronic pulmonary disease
- *Streptococcus pneumoniae*, a causative agent of pneumonia
- *Candida albicans*, the causative agent of thrush

Resources

BOOKS

Longe, Jacqueline L., ed. *The Gale Encyclopedia of Nursing & Allied Health*. Detroit: Thomson Gale, 2006.

PERIODICALS

Bronsdon, M. A., K. L. O'Brien, R. R. Facklam, et al. "Immunoblot Method to Detect *Streptococcus pneumoniae* and Identify Multiple Serotypes from Nasopharyngeal Secretions." *Journal of Clinical Microbiology* 42 (April 2004): 1596–1600.

Fry, N. K., O. Tzivra, Y. T. Li, et al. "Laboratory Diagnosis of Pertussis Infections: The Role of PCR and Serology." *Journal of Medical Microbiology* 53 (June 2004): 519–525.

ORGANIZATIONS

American Medical Association, 515 N. State St., Chicago, IL, 60654, (800) 621-8335, http://www.ama-assn.org/.

Centers for Disease Control and Prevention (CDC), 1600 Clifton Road, Atlanta, GA, 30333, (800) 232-4636, cdcinfo@cdc.gov, http://www.cdc.gov.

Cindy L. A. Jones, PhD
Rebecca J. Frey, PhD

Native American health *see* **Minority health**

Naturopathic medicine

Definition

Naturopathic medicine is a branch of medicine in which a variety of natural medicines and treatments are used to heal illness. It uses a system of medical diagnosis and therapeutics based on the patterns of chaos and organization in nature. It is founded on the premise that people are naturally healthy, and that healing can occur through removing obstacles to a cure and by stimulating the body's natural healing abilities. The foundations of health in natural medicine are diet, **nutrition**, homeopathy, physical manipulation, **stress** management, and **exercise**.

Naturopaths are general practitioners who treat a wide variety of illnesses. They believe in treating the "whole person"—the spirit as well as the physical body—and emphasize preventive care. They often recommend changes in diet and lifestyle to enhance the health of their patients.

Purpose

Naturopathic medicine is useful for treating chronic as well as acute diseases. It is sometimes used in conjunction with allopathic care to enhance wellness and relieve chronic symptoms, such as **fatigue** and **pain**. A naturopath treats a wide range of health problems, ranging from back pain to depression.

A naturopathic physician will spend extra time interviewing and examining the patient to find the underlying cause for a medical problem. Emotional and spiritual symptoms and patterns are included in the assessment. The naturopath often spends more time educating patients in preventive health, lifestyle, and nutrition than most MDs.

Description

Origins

People have always seen a connection to diet and disease, and many therapies are built around special **diets**. Naturopathy began in the 18th and 19th centuries, as the industrial revolution brought about unhealthy lifestyles, and the European custom of "taking the cure" at natural spas became popular. Benedict Lust, who believed deeply in natural medicine, organized naturopathy as a formal system of healthcare in the 1890s. By the early 1900s, it was flourishing.

The first naturopaths in the United States emphasized the healing properties of a nutritious diet, as did a number of their contemporaries. In the early 20th century, for instance, John Kellogg, a physician and vegetarian, opened a sanitarium that used healing methods such as **hydrotherapy**, often prescribed by today's naturopaths. His brother Will produced health foods, such as corn flakes and shredded wheat. The Kellogg brothers helped make naturopathic ideas popular and emphasized the value of whole grains over highly refined ones. They and one of their employees, C.W. Post, eventually went on to start the cereal companies that bear their names.

In the early 1900s, most states licensed naturopaths as physicians. There were 20 medical schools of naturopathic medicine. From early on, naturopathic physicians were considered "eclectic," since they drew on a variety of natural therapies and traditions for treating their patients.

In the 1930s, naturopathy dramatically declined for several reasons. Allopathic medicine finally stopped using therapies such as bloodletting and **heavy metal poisoning** as curatives. New therapies were more effective and less toxic. Allopathic medical schools became increasingly well-funded by foundations with links to the emerging drug industry. Also, allopathic physicians became much more organized and wielded political clout. Naturopathy has experienced a resurgence over the last 20 years, however. The lay public is aware of the connection between a healthy diet and lifestyle and avoiding chronic disease. In addition, conventional medicine is often unable to treat these chronic diseases. Patients are now health care consumers, and will seek their own resolution to health problems that cannot be resolved by conventional physicians. As a result, even medical groups which once considered naturopathy ineffective are now beginning to accept it.

Naturopathic medicine modalities include a variety of healing treatments, such as diet and clinical nutrition, homeopathy, botanical medicine, soft tissue and spinal manipulation, ultrasound, and therapeutic exercise. A naturopath provides complete diagnostic and treatment services in sciences such as obstetrics, pediatrics and obstetrics. Some are also licensed midwives.

Naturopaths consider health to be not just the absence of disease, but complete physical, mental and social well being. Naturopathic physicians often say that diseases must be healed not just by suppressing symptoms, but by rooting out the true cause. Symptoms are actually viewed as the body's natural efforts to heal itself and restore balance.

A typical office visit to a naturopath takes an hour. During the first visit, the doctor will ask detailed questions about the patient's symptoms, lifestyle, history of illness, and state of his or her emotions. The

naturopath will take a complete medical history, and may order lab tests such as urine and blood tests. A naturopath may talk with the patient about the possible causes for an illness: poor diet, life stresses, occupational dangers, and mental, emotional, and spiritual problems. Naturopaths believe that even widely varying symptoms can sometimes be traced to one underlying cause. Often environmental or metabolic toxins or serious stress bring on an illness.

In some states, naturopaths prescribe pharmaceuticals. In these cases, naturopaths might prescribe natural medicines, such as natural hormones, glandular **thyroid hormones**, herbal extracts, **vitamins**, etc.

As with most doctors, treatment by a naturopath can range from one office visit to many. Some acute illnesses can be alleviated with one or two visits. Other chronic diseases need regular weekly or monthly attention. Clinical care provided by naturopathic physicians are covered by insurance in a number of states in the United States.

Preparations

There are about 1,500 naturopathic physicians in the United States practicing; nearly 80% of these practitioners entered the profession following the revival of interest in naturopathy in the late 1970s. Consumers can find naturopaths by contacting the American Association of Naturopathic Physicians (AANP) or logging on to their web site. Naturopaths recommended by the AANP have met requirements for state licensure and have taken a national exam that qualifies them to practice. Qualified naturopaths can also be found through the local branch of the national or state association of naturopathic physicians. It is sometimes useful to request names from another health care provider who knows naturopathic practitioners in the community.

Some states license naturopathic physicians. As of late 2010, those states included Hawaii, Alaska, Washington, Oregon, Utah, Montana, Arizona, Connecticut, New Hampshire, Vermont, Maine, California, Idaho, Minnesota, and Kansas, in addition to the territories of Puerto Rico and the Virgin Islands. Training via a correspondence school does not qualify a naturopath for licensure or to take the national qualifying examination.

Precautions

A good naturopath is always willing to work with the patient's other physicians or health care providers. To avoid **drug interactions** and to coordinate care, it is important for a patient to inform his or her allopathic doctor about supplements prescribed by a naturopath.

Many naturopaths give childhood vaccinations, but some do not. If a parent is concerned about this, it is best to go to an allopathic doctor for vaccinations.

Naturopaths are not licensed to perform major surgery, or prescribe **narcotics** and **antidepressant drugs**. They must involve an oncologist when treating a **cancer** patient.

Side effects

Although naturopathic remedies are from natural sources and typically pose much less risk than traditional drugs do, some do have side effects. One problem they can pose is the interaction with prescription medicines. It is important for a patient to inform his or her allopathic physician about any natural remedies or herbs prescribed by a naturopath.

It is also important to note that the U.S. Food and Drug Administration considers medicinal herbs as dietary supplements, not drugs, and so are not subject to the same regulations as drugs are. Because they come from natural sources, the active ingredients may not always be in the same concentration from bottle to bottle, since plants naturally vary. To guard against using too little or too much of a natural remedy, use herbs and supplements recommended by a naturopath or those produced by well-respected companies.

Research and general acceptance

Medical research in naturopathy has increased dramatically in the United States within the last 10 years. Naturopathic research often employs case histories, summaries of practitioners' clinical observations, and medical records. Some U.S. studies have also met today's scientific gold standard; they were double-blind and placebo-controlled. Much naturopathic research has also been done in Germany, France, England, India, and China.

Some mainstream medical practitioners remain distrustful of naturopathy, however. Such problems as health-food store employees without naturopathic credentials giving health-related advice to customers, or occasional rare cases of infections caused by naturopathic injections, continue to damage the reputation of this form of alternative medicine.

Research in naturopathy tends to focus on single treatments used by naturopaths, rather than naturopathy as a whole. In 1998, an extensive review of such single treatment studies found that naturopathic healing methods were effective for 15 different medical conditions, including **osteoarthritis**, **asthma**, and

KEY TERMS

Clinical nutrition—The use of diet and nutritional supplements as a way to enhance health prevent disease.

Cryotherapy—The exposure of body tissue to extremely cold temperatures, often by applying a probe containing liquid nitrogen.

Herb—In naturopathy, a plant or plant derivative or extract prescribed for health or healing.

Homeopathy—The use of diluted remedies that have energetic rather than chemical properties. They are prescribed according to the axiom that "like cures like."

Hydrotherapy—The use of water as baths, poultices, and steams to heal.

Physical manipulation—The use of deep massage, spinal alignment, and joint manipulation to stimulate tissues.

Ultrasound—A therapy employing high frequency sound waves.

middle ear infections. A study of 8,341 men with damaged heart muscles in 1996 revealed that supplementation with niacin, a B vitamin, was associated with an 11% reduced risk of mortality over 15 years. In 1996, a study showed **St. John's wort** was as effective as prescription antidepressants in relieving depression, and had fewer side effects.

Studies have also demonstrated benefits in the arena of **women's health** issues. In one classic 1993 study, women with cervical dysplasia or abnormal Pap smears were treated by naturopaths with topical applications of herbs and dietary supplements. These medications included Bromelian, an enzyme from the pineapple; bloodroot; marigold; and zinc chloride; and suppositories made from herbal and nutritional ingredients, such as **echinacea**, vitamin A, and vitamin E. Thirty eight of the 43 women in the study had normal Pap smears and normal tissue biopsies after treatment. The study concluded that these protocols might benefit the health of patients undergoing more traditional treatments for cervical dysplasia, such as **cryotherapy**.

Other more recent research has documented the benefits of such nutritional foods as soy in relieving hot flashes and vaginal dryness. **Nutritional supplements** prescribed by naturopaths to enhance women's health during **menopause** have also proven effective; in general, naturopathy appears to be as useful as conventional medicine for treating menopausal symptoms. Research shows vitamin E supplements are helpful for 50% of postmenopausal women with thinning vaginal tissue. Studies also reveal that bioflavonoids with vitamin C and gamma-oryzanol, a substance taken from rice bran oil, can relieve hot flashes.

Another area of women's health concerns that naturopathy has taken seriously is a growing preference for skin care and beauty products derived from natural sources rather than from chemical laboratories. Such products are often more beneficial to the skin and less likely to cause **rashes** or other allergic reactions.

Resources

BOOKS

Hechtman, Leah. *Clinical Naturopathic Medicine*. London: Churchill Livingstone, 2010.

Pizzorno, Joseph E., Michael T Murray, and Herb Joiner–Bey. *The Clinician's Handbook of Natural Medicine*. St. Louis: Churchill Livingstone, 2008.

PERIODICALS

Cramer, E. H., P. Jones, N. L. Keenan, and B. L. Thompson. "Is Naturopathy as Effective as Conventional Therapy for Treatment of Menopausal Symptoms?" *Journal of Alternatie and Complementary Medicine* 9 (August 2003): 529–538.

Engelhart, S., F. Saborowski, M. Krakau, et al. "Severe *Serratia liquefaciens* Sepsis Following Vitamin C Infusion Treatment by a Naturopathic Practitioner." *Journal of Clinical Microbiology* 41 (August 2003): 3986–3988.

Hudson, Tori. "Naturopathic Medicine, Integrative Medicine and Women's Health." *Townsend Letter for Doctors and Patients* November 2001: 136.

Mills, E., R. Singh, M. Kawasaki, et al. "Emerging Issues Associated with HIV Patients Seeking Advice from Health Food Stores." *Canadian Journal of Public Health* 94 (September–October 2003): 363–366.

ORGANIZATIONS

American Association of Naturopathic Physicians, 4435 Wisconsin Ave., NW, Suite 403, Washington, DC, 20016, (202) 237-8150, (202) 237-8152, (866) 538-2267, member.services@naturopathic.org, http://naturopathic.org/.

Canadian Association of Naturopathic Doctors, 20 Holly St., Ste. 200, Toronto, Ontario, Canada M4S 3B1, (416) 496-8633, (416) 496-8634, (800) 551-4381, http://www.cand.ca.

Barbara Boughton
Rebecca J. Frey, PhD

Naturopathy *see* **Naturopathic medicine**

Nausea and vomiting

Definition

Nausea is the sensation of being about to vomit. **Vomiting**, or emesis, is the expelling of undigested food through the mouth.

Description

Nausea is a reaction to a number of causes that include overeating, infection, or irritation of the throat or stomach lining. Persistent or recurrent nausea and vomiting should be checked by a doctor.

A doctor should be called if nausea and vomiting occur:

- after eating rich or spoiled food or taking a new medication
- repeatedly or for 48 hours or longer
- following intense dizziness

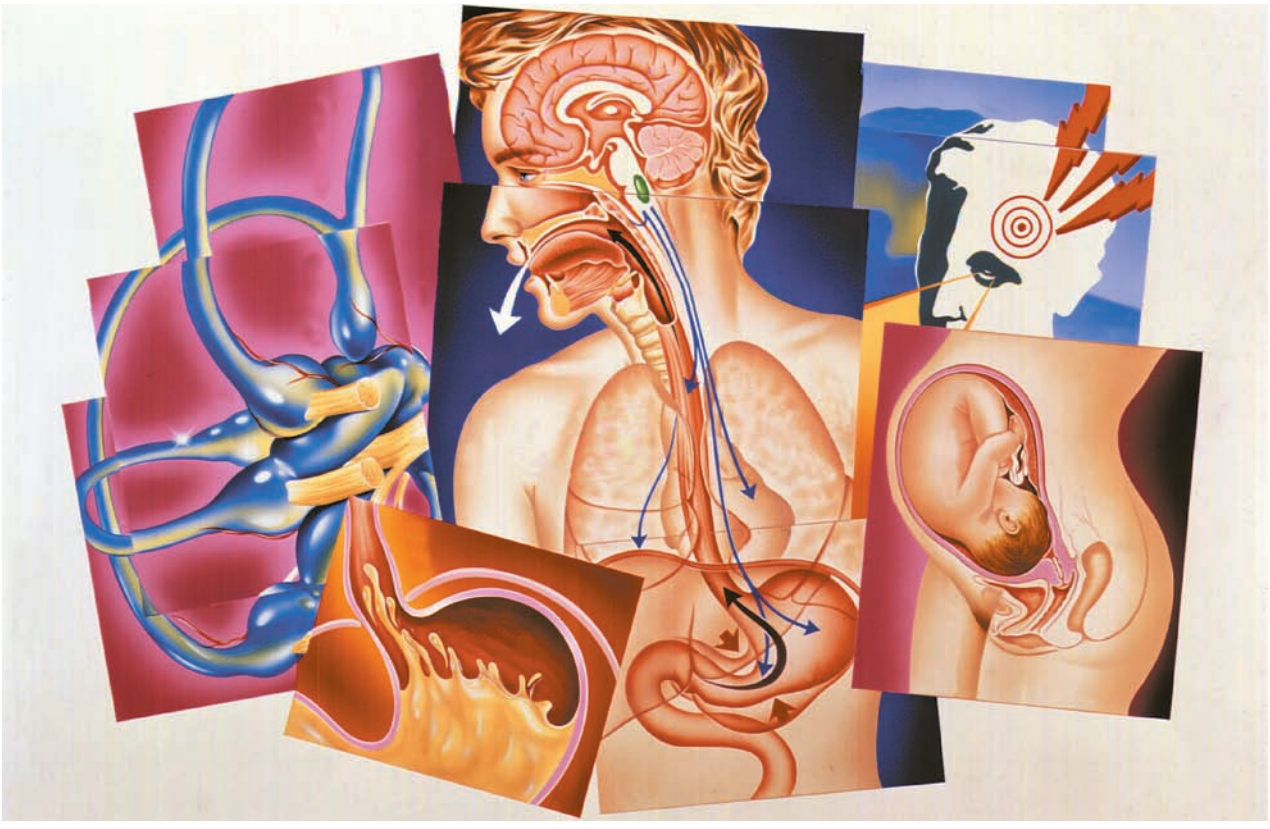
It is important to see a doctor if nausea and vomiting are accompanied by:

- yellowing of the skin and whites of the eyes
- pain in the chest or lower abdomen
- trouble with swallowing or urination
- dehydration or extreme thirst
- drowsiness or confusion
- constant, severe abdominal pain
- a fruity breath odor

A doctor should be notified if vomiting is heavy and/or bloody, if the vomitus looks like feces, or if the patient has been unable to keep food down for 24 hours.

An ambulance or emergency response number should be called immediately if:

- Diabetic shock is suspected.
- Nausea and vomiting continue after other symptoms of viral infection have subsided.



These illustrations depict the mechanism and causes of vomiting in the human body. An impulse from the brain stimulates the vomiting center (top center) in the brain stem. Nerve impulses sent to the stomach, diaphragm, and abdominal wall (bottom center) result in stomach's contents being expelled. Other causes of vomiting include raised pressure in the skull due to injury or tumor (upper right), and hormonal changes during pregnancy. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

- The patient has a severe headache.
- The patient is sweating and having chest pain and trouble breathing.
- The patient is known or suspected to have swallowed a drug overdose or poisonous substance.
- The patient has a high body temperature, muscle cramps, and other signs of heat exhaustion or heat stroke.
- Nausea, vomiting, and breathing problems occur after exposure to a known allergen.

Causes and symptoms

Persistent, unexplained, or recurring nausea and vomiting can be symptoms of a variety of serious illnesses. It can be caused by simply overeating or drinking too much alcohol. It can be due to **stress**, certain medications, or illness. For example, people who are given morphine or other opioid medications for **pain** relief after surgery sometimes feel nauseated by the drug. Such poisonous substances as arsenic and other heavy metals cause nausea and vomiting. Morning sickness is a consequence of pregnancy-related hormone changes. **Motion sickness** can be induced by traveling in a vehicle, plane, or on a boat. Many patients experience nausea after eating spoiled food or foods to which they are allergic. Patients who suffer **migraine headache** often experience nausea. **Cancer** patients on **chemotherapy** are nauseated. **Gallstones**, **gastroenteritis** and stomach ulcer may cause nausea and vomiting. These symptoms should be evaluated by a physician.

Nausea and vomiting may also be psychological in origin. Some people vomit under such conditions of emotional stress as family arguments, academic tests, airplane travel, losing a job, and similar high-stress situations. In addition, some **eating disorders** are characterized by self-induced vomiting.

Diagnosis

Diagnosis is based on the severity, frequency, and duration of symptoms, and other factors that could indicate the presence of a serious illness.

Diagnosis is based on the taking of a careful patient history. In some cases, the doctor may order laboratory tests or imaging studies to determine the presence of drugs or poisonous substances in the patient's blood or urine, or evidence of head injuries or abnormalities in the digestive tract. If the nausea and vomiting appear to be related to **anxiety**, stress, or an eating disorder, the doctor may refer the patient to a psychiatrist for further evaluation.

Treatment

Getting a breath of fresh air or getting away from whatever is causing the nausea can solve the problem. Eating olives or crackers or sucking on a lemon can calm the stomach by absorbing acid and excess fluid. Coke syrup is another proven remedy.

Vomiting relieves nausea right away but can cause **dehydration**. Sipping clear juices, weak tea, and some sports drinks help replace lost fluid and **minerals** without irritating the stomach. Food should be reintroduced gradually, beginning with small amounts of dry, bland food like crackers and toast.

Medications that are given to relieve nausea and vomiting are called antiemetics. Meclizine (Bonine), a medication for motion sickness, also diminishes the feeling of queasiness in the stomach. Dimenhydrinate (Dramamine), another motion-sickness drug, is not effective on other types of nausea and may cause drowsiness.

Newer drugs that have been developed to treat postoperative or postchemotherapy nausea and vomiting include ondansetron (Zofran) and granisetron (Kytril). Another treatment that has been found to lower the risk of nausea after surgery is intravenous administration of supplemental fluid before the operation.

Alternative treatment

Advocates of alternative treatments suggest **biofeedback**, **acupressure** and the use of herbs to calm the stomach. Biofeedback uses **exercise** and deep relaxation to control nausea. Acupressure (applying pressure to specific areas of the body) can be applied by wearing a special wristband or by applying firm pressure to:

- the back of the jawbone
- the webbing between the thumb and index finger
- the top of the foot
- the inside of the wrist
- the base of the rib cage

Acupuncture is another alternative treatment found to be effective in relieving nausea. A few people, however, experience nausea as a side effect of acupuncture.

Chamomile (*Matricaria recutita*) or lemon balm (*Melissa officinalis*) tea may relieve symptoms. Ginger (*Zingiber officinale*), another natural remedy, can be drunk as tea or taken as candy or powered capsules.

Prevention

Massage, **meditation**, **yoga**, and other relaxation techniques can help prevent stress-induced nausea.

KEY TERMS

Acupuncture—A treatment technique associated with traditional Chinese medicine, in which thin needles are inserted into specific points located along energy channels in the human body known as meridians.

Antiemetic—A preparation or medication that relieves nausea and vomiting. Coke syrup, ginger, and motion sickness medications are examples of antiemetics.

Dehydration—Loss of fluid and minerals following vomiting, prolonged diarrhea, or excessive sweating.

Diabetic coma—Reduced level of consciousness that requires immediate medical attention.

Emesis—The medical term for vomiting.

Anti-nausea medication taken before traveling can prevent motion sickness. Sitting in the front seat, focusing on the horizon, and traveling after dark can also minimize symptoms.

Food should be fresh, properly prepared, and eaten slowly. Overeating, tight-fitting clothes, and strenuous activity immediately after a meal should be avoided.

Vomiting related to emotional upsets may be avoided by forms of **psychotherapy** that teach patients to manage stress in healthier ways.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

National Cancer Institute. *Nausea and Vomiting*. [Bethesda, MD]: U.S. Department of Health and Human Services, National Institutes of Health, [2008].

PERIODICALS

Ali, S. Z., A. Taguchi, B. Holtmann, and A. Kurz. "Effect of Supplemental Pre-Operative Fluid on Postoperative Nausea and Vomiting." *Anaesthesia* 58 (August 2003): 780–784.

Cepeda, M. S., J. T. Farrar, M. Baumgarten, et al. "Side Effects of Opioids During Short-Term Administration: Effect of Age, Gender, and Race." *Clinical Pharmacology and Therapeutics* 74 (August 2003): 102–112.

Chung, A., L. Bui, and E. Mills. "Adverse Effects of Acupuncture. Which Are Clinically Significant?" *Canadian Family Physician* 49 (August 2003): 985–989.

O'Brien, C. M., G. Titley, and P. Whitehurst. "A Comparison of Cyclizine, Ondansetron and Placebo as Prophylaxis Against Postoperative Nausea and Vomiting in Children." *Anaesthesia* 58 (July 2003): 707–711.

Quinla, J. D., and D. A. Hill. "Nausea and Vomiting of Pregnancy." *American Family Physician* 68 (July 1, 2003): 121–128.

Ratnaike, R. N. "Acute and Chronic Arsenic Toxicity." *Postgraduate Medical Journal* 79 (July 2003): 391–396.

Tan, M. "Granisetron: New Insights Into Its Use for the Treatment of Chemotherapy-Induced Nausea and Vomiting." *Expert Opinion in Pharmacotherapy* 4 (September 2003): 1563–1571.

Tiwari, A., S. Chan, A. Wong, et al. "Severe Acute Respiratory Syndrome (SARS) in Hong Kong: Patients' Experiences." *Nursing Outlook* 51 (September-October 2003): 212–219.

Walling, Anne D. "Ginger Relieves Nausea and Vomiting During Pregnancy." *American Family Physician* 64 (November 15, 2001): 1745.

ORGANIZATIONS

American Gastroenterological Association (AGA), 4930 Del Ray Avenue, Bethesda, MD, 20814, (301) 654-2055, (301) 654-5920, member@gastro.org, http://www.gastro.org.

Maureen Haggerty
Rebecca J. Frey, PhD

Nberg disease *see* **Osteopetroses**

NCV *see* **Electromyography**

Near-drowning

Definition

Near-drowning is the term for survival after suffocation caused by submersion in water or another fluid. Some experts exclude from this definition cases of temporary survival that end in **death** within 24 hours, which they prefer to classify as drownings.

Demographics

An estimated 15,000–70,000 near-drownings occur in the United States each year (insufficient reporting prevents a better estimate). The typical victim is young and male. Nearly half of all

drownings and near-drownings involve children less than four years old. Home swimming pools pose the greatest risk for children, being the site of 60–90% of drownings in the 0–4 age group. Teenage boys also face a heightened risk of drowning and near-drowning, largely because of their tendency to behave recklessly, and to use drugs and alcohol (drugs and alcohol are implicated in 40–50% of teenage drownings). Males, however, predominate even in the earliest age-groups, possibly because young boys are often granted more freedom from supervision than young girls enjoy, making it more likely that they will stumble into danger and less likely that they will attract an adult's attention in time for a quick rescue. Roughly four out of five drowning victims are males.

Description

Drowning remains a significant public health concern, as it is a major cause of disability and death. Drowning has been previously defined as death secondary to asphyxia while immersed in a liquid, usually water, or within 24 hours of submersion. Near-drowning occurs when the victim survives.

Causes and symptoms

The circumstances leading to near-drownings (and drownings also) cannot be reduced to a single scenario involving nonswimmers accidentally entering deep water. On many occasions, near-drownings are secondary to an event such as a **heart attack** that causes unconsciousness or a head or spinal injury that prevents a diver from resurfacing. Near-drownings, moreover, can occur in shallow as well as deep water. Small children have drowned or almost drowned in bathtubs, toilets, industrial-size cleaning buckets, and washing machines. Bathtubs are especially dangerous for infants six months to one year old, who can sit up straight in a bathtub but may lack the ability to pull themselves out of the water if they slip under the surface.

A reduced concentration of oxygen in the blood (hypoxemia) is common to all near-drownings. Human life, of course, depends on a constant supply of oxygen-laden air reaching the blood by way of the lungs. When drowning begins, the larynx (an air passage) closes involuntarily, preventing both air and water from entering the lungs. In 10–15% of cases, hypoxemia results because the larynx stays closed. This is called "dry drowning." Hypoxemia also occurs in "wet drowning," the 85–90% of cases where the larynx relaxes and water enters the lungs. The physiological mechanisms that produce hypoxemia in wet drowning are different for freshwater and saltwater, but only a small amount of either kind of water is needed to damage the lungs and interfere with the body's oxygen intake. All of this happens very quickly: within three minutes of submersion most people are unconscious, and within five minutes the brain begins to suffer from lack of oxygen. Abnormal heart rhythms (cardiac dysrhythmias) often occur in near-drowning cases, and the heart may stop pumping (cardiac arrest). An increase in blood acidity (acidosis) is another consequence of near-drowning, and under some circumstances near-drowning can cause a substantial increase or decrease in the volume of circulating blood. Many victims experience a severe drop in body temperature (**hypothermia**).

The signs and symptoms of near-drowning can differ widely from person to person. Some victims are alert but agitated, while others are comatose. Breathing may have stopped, or the victim may be gasping for breath. Bluish skin (**cyanosis**), coughing, and frothy pink sputum (material expelled from the respiratory tract by coughing) are often observed. Rapid breathing (tachypnea), a rapid heart rate (tachycardia), and a low-grade **fever** are common during the first few hours after rescue. Conscious victims may appear confused, lethargic, or irritable.

Diagnosis

Diagnosis relies on a **physical examination** of the victim and on a wide range of tests and other procedures. Blood is taken to measure oxygen levels and for many other purposes. Pulse oximetry, another way of assessing oxygen levels, involves attaching a device called a pulse oximeter to the patient's finger. An electrocardiograph is used to monitor heart activity. X-rays can detect head and neck injuries and excess tissue fluid (**edema**) in the lungs.

Treatment

Treatment begins with removing the victim from the water and performing **cardiopulmonary resuscitation** (CPR). One purpose of CPR—which, of course, should be attempted only by people trained in its use—is to bring oxygen to the lungs, heart, brain, and other organs by breathing into the victim's mouth. When the victim's heart has stopped, CPR also attempts to get the heart pumping again by pressing down on the victim's chest. After CPR has been performed and emergency medical help has arrived on the scene, oxygen is administered to the victim. If the victim's breathing has stopped or is otherwise impaired, a tube is inserted into the windpipe (trachea) to maintain the

airway (this is called endotracheal intubation). The victim is also checked for head, neck, and other injuries, and fluids are given intravenously. Hypothermia cases require careful handling to protect the heart.

In the emergency department, victims continue receiving oxygen until blood tests show a return to normal. About one-third are intubated and initially need mechanical support to breathe. Rewarming is undertaken when hypothermia is present. Victims may arrive needing treatment for cardiac arrest or cardiac dysrhythmias. Comatose patients present a special problem: although various treatment approaches have been tried, none have proved beneficial. Patients can be discharged from the emergency department after four to six hours if their blood oxygen level is normal and no signs or symptoms of near-drowning are present. But because lung problems can arise 12 or more hours after submersion, the medical staff must first be satisfied that the patients are willing and able to seek further medical help if necessary. Admission to a hospital for at least 24 hours for further observation and treatment is a must for patients who do not appear to recover fully in the emergency department.

Prognosis

Neurological damage is the major long-term concern in the treatment of near-drowning victims. Patients who arrive at an emergency department awake and alert usually survive with brain function intact, as do about 90% of those who arrive mentally impaired (lethargic, confused, and so forth) but not comatose. Death or permanent neurological damage is very likely when patients arrive comatose. Early rescue of near-drowning victims (within five minutes of submersion) and prompt CPR (within less than 10 minutes of submersion) seem to be the best guarantees of a complete recovery. An analysis of 715 patients admitted to emergency departments in 1971–81 revealed that 69% recovered completely, 25% died, and 6% survived but suffered permanent neurological damage.

Prevention

Prevention depends on educating parents, other adults, and teenagers about water safety. Parents must realize that young children who are left in or near water without adult supervision even for a short time can easily get into trouble, not just at the beach or next to a swimming pool, but in bathtubs and around toilets, buckets, washing machines, and other household articles where water can collect. Research on swimming pool drownings involving young children shows that the victims have usually been left unattended less than five minutes before the accident. Experts consider putting up a fence around a home swimming pool an essential precaution, and estimate that 50–90% of child drownings and near-drownings could be prevented if fences were widely adopted. The fence should be at least five feet high and unclimbable, have a self-closing and self-locking gate, and completely surround the pool.

Pool owners—and, indeed, all other adults—should consider learning CPR. Everyone, of course, should follow the rules for safe swimming and boating. Those who have a medical condition that can cause a seizure or otherwise threaten safety in the water are advised always to swim with a partner. And of course, people need to be aware that alcohol and drug use substantially increase the chances of an accident.

The danger of alcohol and drug use around water is a point that requires special emphasis where teenagers are concerned. Teenagers can also benefit from CPR training and safe swimming and boating classes.

Resources

BOOKS

Modell, Jerome H. "Drowning and Near-Drowning." In *Harrison's Principles of Internal Medicine*, edited by Anthony S. Fauci, et al. New York:McGraw-Hill, 1997.

PERIODICALS

Cortez KJ, Roilides E, Quiroz-Telles F, et al. Infections caused by Scedosporium spp. *Clin Microbiol Rev*. Jan 2008;21(1):157-97.

Mesfin FB, Tobin E, Adamo MA, Dirisio D. Fungal vertebral osteomyelitis due to Scedosporium apiospermum after near-drowning. *J Neurosurg Spine*. Jul 2008;9(1):58-61.

Vayrynen T, Kuisma M, Maatta T, Boyd J. Medical futility in asystolic out-of-hospital cardiac arrest. *Acta Anaesthesiol Scand*. Jan 2008;52(1):81-7.

Howard Baker
Karl Finley

Nearsightedness *see* **Myopia**

Necrotizing enterocolitis

Definition

Necrotizing enterocolitis is a serious bacterial infection in the intestine, primarily of sick or premature newborn infants. It can cause the **death** (necrosis) of intestinal tissue and progress to blood poisoning (septicemia).

KEY TERMS

Enteral nutrition—Liquid nutrition provided through tubes that enter the gastrointestinal tract, usually through the mouth or nose.

Necrosis—The death of cells, a portion of tissue, or a portion of an organ due to permanent damage of some sort, such as a lack of oxygen supply to the tissues.

Parenteral nutrition—Liquid nutrition provided through tubes that are placed in the veins.

Sepsis—The presence of pus–forming or other disease–causing organisms in the blood or tissues. Septicemia, commonly known as blood poisoning, is a common type of sepsis.

Description

Necrotizing enterocolitis develops in approximately 10% of newborns weighing less than two pounds (800 grams). It is a serious infection that can produce complications in the intestine itself—such as ulcers, perforations (holes) in the intestinal wall, and tissue necrosis—as well as progress to life–threatening septicemia. Necrotizing enterocolitis most commonly affects the lower portion of the small intestine (ileum). It is less common in the colon and upper small bowel.

Causes and symptoms

The cause of necrotizing enterocolitis is not clear. It is believed that the infection usually develops after the bowel wall has already been weakened or damaged by a lack of oxygen, predisposing it to bacterial invasion. Bacteria proliferate in the bowel and cause a deep infection that can kill bowel tissue and spread to the bloodstream.

Necrotizing enterocolitis almost always occurs in the first month of life. Infants who require **tube feedings** may have an increased risk for the disorder. A number of other conditions also make newborns susceptible, including **respiratory distress syndrome**, congenital heart problems, and episodes of apnea (cessation of breathing). The primary risk factor, however, is **prematurity**. Not only is the immature digestive tract less able to protect itself, but premature infants are subjected to many stresses on the body in their attempt to survive.

Early symptoms of necrotizing enterocolitis include an intolerance to formula, distended and tender abdomen, **vomiting**, and blood (visible or not) in the stool. One of the earliest signs may also be the need for mechanical support of the infant's breathing. If the infection spreads to the bloodstream, infants may develop lethargy and fluctuations in body temperature, and may periodically stop breathing.

Diagnosis

The key to reducing the complications of this disease is early suspicion by the physician. A series of x-rays of the bowel often reveals the progressive condition, and blood tests confirm infection.

Treatment

Over two–thirds of infants can be treated without surgery. Aggressive medical therapy is begun as soon as the condition is diagnosed or even suspected. Tube feedings into the gastrointestinal tract (enteral **nutrition**) are discontinued, and tube feedings into the veins (parenteral nutrition) are used instead until the condition has resolved. Intravenous fluids are given for several weeks while the bowel heals.

Some infants are placed on a ventilator to help them breathe, and some receive transfusions of platelets, which help the blood clot when there is internal bleeding. **Antibiotics** are usually given intravenously for at least 10 days. These infants require frequent evaluations by the physician, who may order multiple abdominal x-rays and blood tests to monitor their condition during the illness.

Sometimes, necrotizing enterocolitis must be treated with surgery. This is often the case when an infant's condition does not improve with medical therapy or there are signs of worsening infection.

Surgical treatment depends on the individual patient's condition. Patients with infection that has caused serious damage to the bowel may have portions of the bowel removed. It is sometimes necessary to create a substitute bowel by making an opening (**ostomy**) into the abdomen through the skin, from which waste products are discharged temporarily. But many physicians avoiding this procedure and operate to remove diseased bowel and repair the defect at the same time.

Postoperative complications are common, including wound infections and lack of healing, persistent **sepsis** and bowel necrosis, and a serious internal

bleeding disorder known as disseminated intravascular coagulation.

Prognosis

Necrotizing enterocolitis is the most common cause of death in newborns undergoing surgery. The average mortality is 30–40%, even higher in severe cases.

Early identification and treatment are critical to improving the outcome for these infants. Aggressive nonsurgical support and careful timing of surgical intervention have improved overall survival; however, this condition can be fatal in about one–third of cases. With the resolution of the infection, the bowel may begin functioning within weeks or months. But infants need to be carefully monitored by a physician for years because of possible future complications.

About 10–35% of all survivors eventually develop a stricture, or narrowing, of the intestine that occurs with healing. This stricture can create an intestinal obstruction that will require surgery. Infants may also be more susceptible to future bacterial infections in the gastrointestinal tract and to a delay in growth. Infants with severe cases may also suffer neurological impairment.

The most serious long-term gastrointestinal complication associated with necrotizing enterocolitis is short-bowel, or short-gut, syndrome. This term refers to a condition that can develop when a large amount of bowel must be removed, making the intestines less able to absorb certain nutrients and enzymes. These infants gradually evolve from tube feedings to oral feedings, and medications are used to control the malabsorption, **diarrhea**, and other consequences of this condition.

Prevention

In very small or sick premature infants, the risk for necrotizing enterocolitis may be diminished by beginning parenteral nutrition and delaying enteral feedings for several days to weeks.

Some authorities have suggested that breast milk provides substances that may be protective, but there is no evidence that this practice reduces the risk of infection. A large multicenter trial showed that steroid drugs given to women in preterm labor may protect their offspring from necrotizing enterocolitis.

Sometimes necrotizing enterocolitis occurs in clusters, or outbreaks, in hospital newborn (neonatal) units. Because there is an infectious element to the disorder, infants with necrotizing enterocolitis may be isolated to avoid infecting other infants. Persons caring for these infants must also employ strict measures to prevent spreading the infection.

Resources

BOOKS

Adamkin, David H. *Nutritional Strategies for the Very Low Birthweight Infant*. New York, NY: Cambridge University Press, 2009.

Cameron, Kristy M. *Mitchell's Gift–A Parent's Perspective on Surviving Life... With a Premature Baby in the NICU*. Santa Maria, CA: LP Publishing, 2009.

Gunter, Jennifer. *The Preemie Primer: A Complete Guide for Parents of Premature Babies—from Birth through the Toddler Years and Beyond*. Cambridge, MA: Da Capo Lifelong Books, 2010.

OTHER

"Neonatology on the Web." http://www.neonatology.org. (accessed September 13, 2010).

Caroline A. Helwick
Laura Jean Cataldo, RN, Ed.D.

Necrotizing fasciitis *see* **Flesh-eating disease**

Neisseria gonorrheae infection *see* **Gonorrhea**

Neisseria meningitidis bacteremia *see* **Meningococcemia**

Nelfinavir *see* **Protease inhibitors**

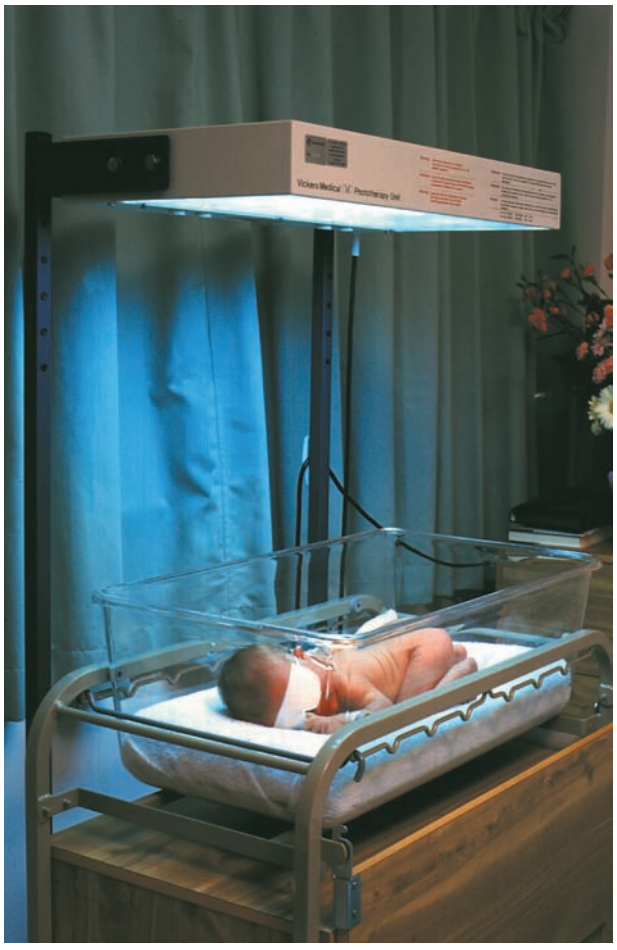
Neonatal jaundice

Definition

Neonatal **jaundice** refers to the yellow discoloration of the skin and sclera (whites) of the eyes in newborns, which results as the breakdown of bilirubin goes faster than the rate at which it can leave the body, causing its level to rise in the blood.

Demographics

Neonatal jaundice is extremely common. In the United States, it is the most common condition needing medical care in newborns. The incidence of neonatal jaundice varies with location and ethnicity. It is highest in those of East Asian, American Indian, and Greek descent. The condition is more common in white than in black babies, and the rate is increased in infants of mothers at high altitudes. Preterm babies have a higher rate of neonatal jaundice than full-term babies.



A newborn baby undergoes phototherapy with visible blue light to treat his jaundice. *(Ron Sutherland/SPL/ Photo Researchers, Inc.)*

Description

Neonatal jaundice and hyperbilirubinemia are terms used when a newborn has a higher-than-normal level of bilirubin in the blood. Bilirubin is an end product of the breakdown of the hemoglobin present in the red blood cells at the end of their life cycle. Hemoglobin carries oxygen to tissues and cells. Before birth the placenta is not as efficient in providing oxygen as the baby's lungs will be after birth. Because of this, infants *in utero* have more red blood cells than they will need after birth to provide enough oxygen. Therefore, newborns have an excess of red blood cells that they need to process and an immature liver with which to complete the job.

When the fetus is *in utero*, bilirubin is processed through the placenta and the maternal-fetal circulation. After birth, the infant's often-immature liver must take over this task. Clinical jaundice (serum bilirubin levels of 5–7 mg/dL and above) occurs in about 60-70% of term newborns and about 80% of premature infants. Ever since hospital stays after delivery decreased to 24–48 hours postpartum, hyperbilirubinemia has become the leading cause of hospital re-admissions in the first two weeks of life. The greatest concern with hyperbilirubinemia is that the unexcreted bilirubin will begin to deposit in the brain of the newborn, resulting in a serious, potentially life-threatening condition called kernicterus. Kernicterus occurs in about 1.5 of every 100,000 live births in the United States. Another term used for kernicterus is brain encephalopathy.

Causes and symptoms

An elevated bilirubin level may be due to its increased production, a decreased rate of conjugation, or abnormalities of the liver. In order for the bilirubin to be excreted in the urine and stool, it must be converted, or conjugated, from a fat- or lipid-soluble form to a water-soluble form. Bilirubin that has not been excreted can be reabsorbed and contributes to increased blood levels.

Initial symptoms of a rising bilirubin level can be subtle, and usually include increased drowsiness, which leads to poor feeding, and the subsequent decreased urine and stool output. The diaper may contain orange spots, an indication of the presence of uric acid crystals, a sign of **dehydration**. A change in the infant's cry to a high-pitched tone may indicate early neurological damage.

There are several types of jaundice. Jaundice that sets in within the first 24 hours after birth is usually due to an Rh factor or ABO blood incompatibility between the mother and infant.

The most common form of neonatal jaundice appears between the first 24 and 72 hours after birth and is usually considered a benign form. It is often referred to as early-onset breast milk jaundice, and is related to insufficient **breastfeeding**, which results in decreased nutritional intake and decreased stool production. With decreased stool volume, the bilirubin in the stool is not adequately excreted, and remains available for reabsorption. Increasing feedings from six to 12 times a day, and checking for latching-on and a good sucking and swallowing patterns, can lead to a decreasing bilirubin level to within normal limits. To encourage adequate maternal milk production, infant supplementation with water or glucose is discouraged.

Late-onset breast milk jaundice may occur in 10–30% of breast-fed infants and appears in the second to sixth weeks of life. This form of jaundice is believed to

KEY TERMS

Bilirubin—A yellowish-brown substance in the blood that forms as old red blood cells are broken down.

Jaundice—a condition in which bilirubin, a waste product caused by the normal breakdown or red blood cells, builds up in the body faster than the liver can break it down. People with jaundice develop yellowish skin and the whites of their eyes become yellow. The condition can occur in newborns and people with liver damage.

Kernicterus—A serious condition in which bilirubin deposits in the brain leading to permanent neurological damage and potentially death.

be related to a substance present in the mother's milk that affects the infant's absorption of bilirubin.

Risk factors

Risk factors for the development of hyperbilirubinemia include:

- premature birth
- East Asian and Native American descent
- maternal diabetes
- hemolytic disease in the neonate
- sepsis
- family history of jaundice
- presence of excessive bruising due to traumatic birth, and cephalhematoma
- oxytocin-induced delivery
- mother's use of sulfa medications during pregnancy
- history of familial liver disease
- delayed cord clamping
- thyroid gland abnormalities
- G6PD (glucose-6-phosphate dehydrogenase) deficiency

Diagnosis

Examination

Diagnosis of hyperbilirubinemia usually begins with the observation of jaundice at the time of **physical examination**. However, a delay in recognition of jaundice may occur since many infants have already gone home before its onset. Pediatric practices vary as to times of follow-up after hospital discharge. Parents may call their pediatric care provider's office because of jaundice, or because of a decreased ability of the infant to feed. Examination of the infant is best done next to a window so that the jaundice can be assessed in natural light.

Tests

Blood tests to check the bilirubin level, blood type, and for signs of dehydration will usually be ordered. Blood is drawn by a heel stick. Heel sticks on an infant can be difficult when the infant is dehydrated. Ways to facilitate a more successful blood draw include:

- Use of a heel warmer to increase circulation to the foot.
- Having a parent hold the infant in a seated position so that the foot is below the level of the heart.
- Having the parent feed the infant prior to the lab visit.

Treatment

Treatment is primarily focused on decreasing the bilirubin level to prevent the progression of the condition to kernicterus. In kernicterus, the bilirubin deposits in the brain. This extreme condition leads to central nervous system damage and can progress to **hearing loss**, seizures, and **death**.

Phototherapy

For many infants, increasing breastfeeding will be sufficient to bring about adequate hydration and an increase in gastric motility and the amount of stool, so that the bilirubin is effectively excreted from the body. Some infants may need the additional assistance of **phototherapy**. The light source most effective in treating hyperbilirubinemia occurs in the blue-green spectrum. Phototherapy may be provided in the hospital. In the hospital the infant is usually placed in a special bassinet, with an overhead light source. The skin is uncovered, exposing as much surface area to the light. The infant's eyes and genitals are usually shielded from direct light and heat, depending on the intensity of the light.

If the bilirubin level is under about 15–20 mg/dL, phototherapy may be administered via a fiberoptic source referred to as a blanket or belt in the home. The home unit is designed to encourage parent-infant bonding. The blanket/belt wraps around the infant's bare middle so that the cool light source is next to the

skin. There is no need to shield the eyes from the light, and parents can hold, feed, and interact with the infant as usual. Most insurance companies cover the cost of the home rental for the phototherapy equipment and the accompanying daily home nursing visits.

In 1994 the American Academy of Pediatrics (AAP) developed guidelines for care and management of neonatal jaundice. These guidelines were reviewed and updated in 2004. In studies where experienced pediatric practitioners evaluated the same infants for jaundice, considerable discrepancies existed. Despite all the research done in this area, there are no consistent predictors of which infants will continue from benign jaundice to kernicterus. Research studies express concern over finding a balance between treating those that need treatment without treating well infants unnecessarily.

Prognosis

Jaundice addressed in its early stages rarely progresses to kernicterus, and therefore the prognosis for complete resolution of the problem is excellent. Phototherapy is extremely effective in bringing down the bilirubin levels. Some extreme cases may require a blood **transfusion**, but those situations are relatively rare. Infants who do develop kernicterus may continue to have long-term neurological effects present if the kernicterus was well established at the time of initiation of treatment.

Prevention

Primary prevention begins with addressing the risk factors mentioned previously. Prevention of kernicterus requires early detection, monitoring and potential treatment of jaundice with rising bilirubin levels. Frequent feedings of ten or more per day help to ensure adequate hydration, **nutrition**, gastric motility, and stool and urine output.

Resources

BOOKS

Robert M. Kliegman, Behrman, Richard E Behrman, Hal B. Jenson and Bonita Stanton. *Nelson Textbook of Pediatrics, 19th ed.* Philadelphia: W. B. Saunders Company, 2007.

OTHER

Hansen, Thor. Jaundice, Neonatal. eMedicine.com. March 24, 2010. http://emedicine.medscape.com/article/974786-overview

Mayo, Colby D. and Brent R. King. Newborn Jaundice. eMedicineHealth.com. October 20, 2005. http://www.emedicinehealth.com/newborn_jaundice/article_em.htm

ORGANIZATIONS

American Academy of Pediatrics, 141 Northwest Point Blvd., Elk Grove Village, IL, 60007-1098, (847) 434-4000, (847) 434-8000, http://www.aap.org.

Association of Women's Health, Obstetric, and Neonatal Nurses, 2000 L St., NW, Suite. 740, Washington, DC, 20036, (202) 261-2400, (800) 673-8499. Toll-free in Canada (800) 245-0231, (202) 728-0575, customerservice@awhonn.org, http://www.awhonn.org.

Esther Csapo Rastegari, R.N., B.S.N., Ed.M.
Tish Davidson, A.M.

Nephrectomy

Definition

Nephrectomy is the surgical procedure of removing a kidney or section of a kidney.

Purpose

Nephrectomy, or kidney removal, is performed on patients with **cancer** of the kidney (renal cell carcinoma); a disease in which cysts (sac-like structures) displace healthy kidney tissue (**polycystic kidney disease**); and serious kidney infections. It is also used to remove a healthy kidney from a donor for the purposes of **kidney transplantation**.

Precautions

Because the kidney is responsible for filtering wastes and fluid from the bloodstream, kidney function is critical to life. Nephrectomy candidates suffering from serious **kidney disease**, cancer, or infection usually have few treatment choices but to undergo the procedure. However, if kidney function is lost in the remaining kidney, the patient will require chronic dialysis treatments or transplantation of a healthy kidney to sustain life.

Description

Nephrectomy may involve removing a small portion of the kidney or the entire organ and surrounding tissues. In partial nephrectomy, only the diseased or infected portion of the kidney is removed. Radical nephrectomy involves removing the entire kidney, a section of the tube leading to the bladder (ureter), the gland that sits atop the kidney (adrenal gland), and the fatty tissue surrounding the kidney. A simple nephrectomy performed for transplant purposes requires removal of the kidney and a section of the attached

ureter. A similar procedure is used to harvest cadaver kidneys, although both kidneys are typically removed at once (bilateral nephrectomy) and blood and cell samples for **tissue typing** are also taken.

The nephrectomy patient is administered **general anesthesia** and the surgeon makes an incision on the side or front of the abdomen. Muscle, fat, and tissue are cut away to reveal the kidney. The blood vessels connecting the kidney to the circulation are cut and clamped. Depending on the type of nephrectomy procedure being performed, the ureter, adrenal gland, and/or surrounding tissue may also be cut. The vessels and the ureter in the patient are then tied off and the incision is sewn up (sutured). The surgical procedure can take up to three hours, depending on the type of nephrectomy being performed.

Laparoscopic nephrectomy is a form of minimally invasive surgery that utilizes instruments on long, narrow rods to view, cut, and remove the kidney. The surgeon views the kidney and surrounding tissue with a flexible videoscope. The videoscope and surgical instruments are maneuvered through four small incisions in the abdomen. Once the kidney is freed, it is secured in a bag and pulled through a fifth incision, approximately 3 in (7.6 cm) wide, in the front of the abdominal wall below the navel. Although this surgical technique takes slightly longer than a traditional nephrectomy, preliminary studies have shown that it promotes a faster recovery time, shorter hospital stays, and less post-operative **pain** for kidney donors.

Preparation

Prior to surgery, blood samples will be taken from the patient to type and crossmatch in case **transfusion** is required during surgery. A catheter will also be inserted into the patient's bladder. The surgical procedure will be described to the patient, along with the possible risks.

Aftercare

Nephrectomy patients may experience considerable discomfort in the area of the incision. Patients may also experience **numbness**, caused by severed nerves, near or on the incision. Pain relievers are administered following the surgical procedure and during the recovery period on an as-needed basis. Although deep breathing and coughing may be painful due to the proximity of the incision to the diaphragm, breathing exercises are encouraged to prevent **pneumonia**. Patients should not drive an automobile for a minimum of two weeks.

KEY TERMS

Cadaver kidney—A kidney from a brain-dead organ donor used for purposes of kidney transplantation.

Polycystic kidney disease—A hereditary kidney disease that causes fluid- or blood-filled pouches of tissue called cysts to form on the tubules of the kidneys. These cysts impair normal kidney function.

Renal cell carcinoma—Cancer of the kidney.

Risks

Possible complications of a nephrectomy procedure include infection, bleeding (hemorrhage), and post-operative pneumonia. There is also the risk of kidney failure in a patient with impaired function or disease in the remaining kidney.

Normal results

Normal results of a nephrectomy are dependent on the purpose of the procedure and the type of nephrectomy performed. Immediately following the procedure, it is normal for patients to experience pain near the incision site, particularly when coughing or breathing deeply. Renal function of the patient is monitored carefully after nephrectomy surgery. If the remaining kidney is healthy, it will increase its functioning over time to compensate for the loss of the removed kidney.

Length of hospitalization depends on the type of nephrectomy procedure. Patients undergoing a laparoscopic radical nephrectomy may be released within two to four days after surgery. Traditional open nephrectomy patients are typically hospitalized for about a week. Recovery time will also vary, on average from three to six weeks.

ORGANIZATIONS

National Kidney Foundation, Inc., 30 East 33rd Street, New York, NY, 10016, (212) 889-2210, (212) 689-9261, (800) 622-9010, http://www.kidney.org/.

Paula Anne Ford-Martin

Nephritic syndrome *see* **Glomerulonephritis**

Nephritis

Definition

Nephritis is inflammation of the kidney.

Description

The most prevalent form of acute nephritis is **glomerulonephritis**. This condition affects children and teenagers far more often than it affects adults. It is inflammation of the glomeruli, or small round filters located in the kidney. **Pyelonephritis** is recognized as inflammation of the kidney and upper urinary tract. It affects adults more than children. A third type of nephritis is hereditary nephritis, a rare inherited condition.

Causes and symptoms

Acute glomerulonephritis usually develops a few weeks after a strep infection of the throat or skin. Symptoms of glomerulonephritis include **fatigue**, high blood pressure, and swelling. Swelling is most notable in the hands, feet, ankles and face.

Pyelonephritis usually occurs suddenly, and the acute form of this disease is more common in adult women. The most common cause of this form of bacterial nephritis is the backward flow of infected urine from the bladder into the upper urinary tract. Its symptoms include **fever** and chills, fatigue, burning or frequent urination, cloudy or bloody urine, and aching **pain** on one or both sides of the lower back or abdomen.

Hereditary nephritis can be present at birth. The rare disease presents in many different forms and can be responsible for up to 5% of end-stage renal disease in men.

Diagnosis

Diagnosis of nephritis is based on:

- the patient's symptoms and medical history
- physical examination
- laboratory tests
- kidney function tests
- imaging studies such as ultrasound or x-rays to determine blockage and inflammation

Urinalysis can reveal the presence of:

- albumin and other proteins
- red and white blood cells
- pus, blood, or bacteria in the urine

Treatment

Treatment of glomerulonephritis normally includes drugs such as cortisone or cytotoxic drugs (those that are destructive to certain cells or antigens). **Diuretics** may be prescribed to increase urination. If high blood pressure is present, drugs may be prescribed to decrease the **hypertension**. Iron and vitamin supplements may be recommended if the patient becomes anemic.

Acute pyelonephritis may require hospitalization for severe illness. **Antibiotics** will be prescribed, with the length of treatment based on the severity of the infection. In the case of chronic pyelonephritis, a six-month course of antibiotics may be necessary to rid the infection. Surgery is sometimes necessary.

Treatment of hereditary nephritis depends of the variety of the disease and severity at the time of treatment.

Alternative treatment

Alternative treatment of nephritis should be used as a complement to medical care and under the supervision of a licensed practitioner. Some herbs thought to relieve symptoms of nephritis include cleavers (*Galium* spp.) and wild hydrangea.

Prognosis

Prognosis for most cases of glomerulonephritis is generally good. Ninety percent of children recover without complications. With proper medical treatment, symptoms usually subside within a few weeks, or at the most, a few months.

Pyelonephritis in the acute form offers a good prognosis if diagnosed and treated early. Follow-up urinalysis studies will determine if the patient remains bacteria-free. If the infection is not cured or continues to recur, it can lead to serious complications such as **bacteremia** (bacterial invasion of the bloodstream), hypertension, chronic pyelonephritis, and even permanent kidney damage.

If hereditary nephritis is not detected or treated, it can lead to complications such as eye problems, deafness or kidney failure.

Prevention

Streptococcal infections that may lead to glomerulonephritis can be prevented by avoiding exposure to strep infection and obtaining prompt medical treatment for **scarlet fever** or other infection.

Pyelonephritis can best be avoided if those with a history of urinary tract infections take care to drink

plenty of fluids, urinate frequently, and practice good hygiene following urination.

Hereditary nephritis can not be prevented, but research to combat the disease continues.

Resources

OTHER

"Glomerulonephritis." *National Institute of Diabetes and Digestive and Kidney Disease*. http://www.niddk.nih.gov.

ORGANIZATIONS

American Kidney Fund (AKF), 6110 Executive Boulevard, Suite 1010, Rockville, MD, 20852, (800) 638-8299, http://www.kidneyfund.org.

National Kidney Foundation, Inc., 30 East 33rd Street, New York, NY, 10016, (212) 889-2210, (212) 689-9261, (800) 622-9010, http://www.kidney.org/.

Maureen Haggerty

Nephroblastoma *see* **Wilms' tumor**

Nephrocarcinoma *see* **Kidney cancer**

Nephrotic syndrome

Definition

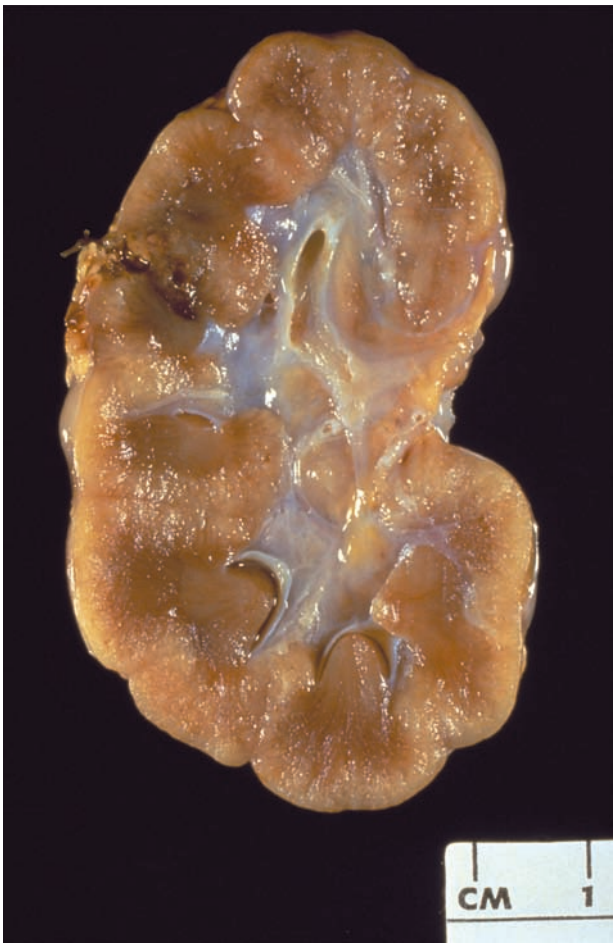
Nephrotic syndrome is a collection of symptoms that occur because the tiny blood vessels (the glomeruli) in the kidney become leaky. This allows protein (normally never passed out in the urine) to leave the body in large amounts.

Demographics

Patients with nephrotic syndrome are from all age groups, although in children children between the ages of 18 months and four years have an increased risk of the disorder. In children, boys are more frequently affected; in adults, the ratio of men to women is closer to equal.

Description

The glomeruli (a single one is called a glomerulus) are tiny tufts of capillaries (the smallest type of blood vessels). Glomeruli are located in the kidneys, where they allow a certain amount of water and waste products to leave the blood, ultimately to be passed out of the body in the form of urine. Normally, proteins are unable to pass through the glomerular filter. Nephrotic syndrome, however, occurs when this filter becomes defective, allowing large quantities of protein to leave the blood circulation and pass out of the body in the urine.



A specimen of a nephrotic human kidney. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Causes and symptoms

Nephrotic syndrome can be caused by a number of different diseases. The common mechanism that seems to cause damage involves the immune system. For some reason, the immune system becomes directed against the person's own kidney. The glomeruli become increasingly leaky as various substances from the immune system are deposited within the kidney.

A number of different kidney disorders are associated with nephrotic syndrome, including:

- minimal change disease or MCD (responsible for about 80% of nephrotic syndrome in children, and about 20% in adults), which is a disorder of the glomeruli
- focal segmental glomerulosclerosis (FSGS)

- membranous glomerulonephritis (MGN)
- membranoproliferative glomerulonephritis (MPGN)

Other types of diseases can also result in nephrotic syndrome. These include diabetes, sickle-cell anemia, **amyloidosis**, **systemic lupus erythematosus**, **sarcoidosis**, leukemia, lymphoma, **cancer** of the breast, colon, and stomach, reactions to drugs (including **nonsteroidal anti-inflammatory drugs**, lithium, and street heroine), allergic reactions (to insect **stings**, snake venom, and **poison ivy**), infections (**malaria**, various bacteria, **hepatitis B**, herpes zoster, and the virus which causes **AIDS**), and severe high blood pressure.

The first symptom of nephrotic syndrome is often foamy urine. As the syndrome progresses, swelling (**edema**) is noticed in the eyelids, hands, feet, knees, scrotum, and abdomen. The patient feels increasingly weak and fatigued. Appetite is greatly decreased. Over time, the loss of protein causes the muscles to become weak and small (called muscle wasting). The patient may note abdominal **pain** and difficulty breathing. Because the kidneys are involved in blood pressure regulation, abnormally low or abnormally high blood pressure may develop.

As the syndrome progresses the protein loss occurring in nephrotic syndrome will result in a generally malnourished state. Hair and nails become brittle, and growth is stunted. Bone becomes weak, and the body begins to lose other important nutrients (sugar, potassium, **calcium**). Infection is a serious and frequent complication, as are disorders of blood clotting. **Acute kidney failure** may develop.

Diagnosis

Tests

Diagnosis is based first on the laboratory examination of the urine and the blood. While the urine will reveal significant quantities of protein, the blood will reveal abnormally low amounts of circulating proteins. Blood tests also reveal a high level of cholesterol.

Procedures

In order to diagnose one of the kidney disorders that cause nephrotic syndrome, a small sample of the kidney will be removed for examination. This biopsy can be done with a long, very thin needle that is inserted through the skin under the ribs.

Treatment

Treatment depends on the underlying disorder that caused nephrotic syndrome.

KEY TERMS

Glomeruli—Tiny tufts of capillaries that carry blood within the kidneys. The blood is filtered by the glomeruli. The blood then continues through the circulatory system, but a certain amount of fluid and specific waste products are filtered out of the blood, to be removed from the body in the form of urine.

Immune system—The complex system within the body that serves to fight off harmful invaders, such as bacteria, viruses, fungi.

Kidney failure—The inability of the kidney to excrete toxic substances from the body.

Drugs

Medications that dampen the immune system are a mainstay of treatment. The first choice is usually a steroid drug (such as prednisone). Some conditions may require more potent medications, such as cyclophosphamide or cyclosporine. Treating the underlying conditions (lymphoma, cancers, heroine use, infections) that have led to nephrotic syndrome often improve the symptoms of nephrotic syndrome as well. Some patients require the use of specific medications to control high blood pressure. Occasionally, the quantity of fluid a patient is allowed to drink is restricted. Some patients benefit from the use of **diuretics** (which allow the kidney to produce more urine) to decrease swelling.

Prognosis

Prognosis depends on the underlying disorder. Minimal change disease has the best prognosis of all the kidney disorders, with 90% of all patients responding to treatment. Other types of kidney diseases have less favorable outcomes, with high rates of progression to kidney failure. When nephrotic syndrome is caused by another, treatable disorder (infection, allergic or drug reaction), the prognosis is very good.

Resources

BOOKS

Clatworthy, Menna. *Nephrology: Clinical Cases Uncovered.* New York, NY: Wiley-Blackwell, 2010.

Deshmukh, Sunita R., and Newton W. K. Wong. *The Renal System Explained: An Illustrated Core Text.* Nottingham, UK: Nottingham University Press, 2009.

Feld, Leonard G., and Frederick J. Kaskel. *Fluid and Electrolytes in Pediatrics: A Comprehensive Handbook.* Totowa, NJ: Humana Press, 2009.

O'Callaghan, Chris. *The Renal System at a Glance*. 3rd ed. New York, NY: Wiley-Blackwell, 2009.
Stam, Lawrence, E. *100 Questions & Answers About Kidney Dialysis*. Sudbury, MA: Jones and Bartlett Publishers, 2009.

ORGANIZATIONS

American Association of Kidney Patients, 3505 E. Frontage Rd., Suite 315, Tampa, FL, 33607, (800) 749-2257, info@aakp.org, http://www.aakp.org.
American Kidney Fund (AKF), 6110 Executive Blvd., Suite 1010, Rockville, MD, 20852, (800) 638-8299, http://www.kidneyfund.org.
American Society of Pediatric Nephrology, 3400 Research Forest Dr., Suite B-7, The Woodlands, TX, 77381, (281) 419-0052, http://www.aspneph.com.
National Kidney Foundation, 30 East 33rd St., New York, NY, 10016, (800) 622-9010, http://www.kidney.org.
National Kidney and Urologic Disease Information Clearinghouse, 3 Information Way, Bethesda, MD, 20892, (800) 891-5390, nkudic@info.niddk.nih.gov, http://kidney.niddk.nih.gov.

Rosalyn DeWitt, MD
Laura Jean Cataldo, RN, EdD

Nephrotoxic injury

Definition

Nephrotoxic injury is damage to one or both of the kidneys that results from exposure to a toxic material, usually through ingestion.

Description

The kidneys are the primary organs of the urinary system, which purifies the blood by removing wastes from it and excreting them from the body in urine. Every day, the kidneys filter about 45 gal (180 l) of blood, about four times as much as the amount that passes through any other organ. Because of this high volume, the kidneys are more often exposed to toxic substances in the blood and are very vulnerable to injury from those sources.

Each kidney contains more than one million structures called nephrons. Each nephron consists of two parts: the renal corpuscle and the renal tubule. The renal corpuscle is where the blood is filtered. It is made up of a network of capillaries (the glomerulus) and the structure that surrounds these capillaries (Bowman's capsule). Blood flows into the glomerulus, where the liquid part of the blood (plasma) passes through the walls of the capillaries and into Bowman's capsule (blood cells and some proteins are too big to pass through and therefore remain in the blood vessels). The plasma, now called filtrate, contains substances that the body needs, such as water, glucose, and other nutrients, as well as wastes, excess salts, and excess water. When the filtrate moves from Bowman's capsule into the renal tubules, about 99% of it is taken back up as the action of the tubules allows beneficial substances to be reabsorbed into the blood stream. The remaining filtrate is then passed to the bladder as urine.

When the kidneys are exposed to a toxic agent, either accidentally or intentionally (as in a **suicide** attempt), damage can occur in a number of different ways, depending upon the agent. One toxin may directly affect the glomerulus or the renal tubules, causing the cells of these structures to die. Another toxin may create other substances or conditions that result in the same cell death. Nephrotoxic injury can lead to acute renal failure, in which the kidneys suddenly lose their ability to function, or chronic renal failure, in which kidney function slowly deteriorates. If unchecked, renal failure can result in death.

Causes and symptoms

Several different substances can be toxic to the kidneys. These include:

- antibiotics, primarily aminoglycosides, sulphonamides, amphotericin B, polymyxin, neomycin, bacitracin, rifampin, trimethoprim, cephaloridine, methicillin, aminosalicylic acid, and oxy- and chlorotetracyclines
- analgesics, including acetaminophen (Tylenol), all nonsteroidal anti-inflammatory drugs, or NSAIDs (e.g. aspirin, ibuprofen), and all prostaglandin synthetase inhibitors
- contrast agents used in some diagnostic tests, such as sodium iodide
- heavy metals, such as lead, mercury, arsenic, and uranium
- anti-cancer drugs, such as cyclosporin, cisplatin, and cyclophosphamide
- methemoglobin-producing agents
- solvents and fuels, such as carbon tetrachloride, methanol, amyl alcohol, and ethylene glycol
- herbicides and pesticides
- overproduction of uric acid

Nephrotoxic injury is most commonly caused by drugs, primarily **antibiotics**, **analgesics**, and contrast agents. In some cases, such as with **aminoglycosides** and amphotericin B, the drug itself will damage the kidneys. In others, such as with methicillin,

KEY TERMS

Bowman's capsule—The structure surrounding the glomerulus.

Chelate—A chemical that binds to heavy metals in the blood, thereby helping the body to excrete them in urine.

Contrast agent—Substance ingested so as to highlight anatomical structures in x-ray imaging tests.

Diuretic—A drug that promotes the excretion of urine.

Glomerulus—A network of capillaries located in the nephron where wastes are filtered from the blood.

Methemoglobin—A compound formed from hemoglobin by oxidation.

Nephron—Basic functional unit of the kidney.

Nephrotoxin—Substance that is poisonous to the kidneys.

Renal failure—Disorder characterized by the kidney's inability to filter wastes from the blood. It may be acute (occuring suddenly and usually reversable) or chronic (developing slowly over time as a result of permanent damage).

sulphonamides, and some contrast agents, the drug provokes an allergic reaction that destroys the kidneys. Some chemicals found in certain drugs and industrial agents damage the kidneys by converting the hemoglobin of red blood cells into methemoglobin, thereby interfering with the blood's transport of oxygen. In hospitals, the most common form of nephrotoxic injury is antibiotic nephropathy, which usually occurs when antibiotics are given to patients with already weakened kidneys. Analgesic nephropathy is another common form of nephrotoxic injury and occurs as a result of long-term **abuse** of analgesics, usually NSAIDs (e.g., ibuprofen). Analgesic nephropathy is most prevalent in women over 30. Lead nephropathy, arising from **lead poisoning**, and nephropathy, from ingestion of the solvent carbon tetrachloride, are also more common forms of nephrotoxic injury. Uric acid nephropathy is one form of nephropathy that is not caused by exposure to an external toxin; instead, it arises from the body's overproduction of uric acid, usually in persons with diseases of the lymph nodes or bone marrow.

Risk factors for nephrotoxic injury include:

- Age. The elderly are more likely to overdose on antibiotics or analgesics.
- Underlying kidney disease. Kidneys already weakened by conditions such as diabetes can be particularly susceptible to nephrotoxic injury.
- Severe dehydration.
- Prolonged exposure to heavy metals or solvents on the job or in the home.
- Presence of diseases that cause the overproduction of uric acid.

Symptoms of nephrotoxic injury are wide ranging and, in some cases, depend upon the type of toxin involved. In general, symptoms are similar to those of renal failure and include excess urea in the blood (azotemia), anemia, increased hydrogen ion concentration in the blood (acidosis), excess fluids in the body (**overhydration**), and high blood pressure (**hypertension**). Blood or pus may be present in the urine, as may uric acid crystals. A decrease in urinary output may also occur. If the toxin's effect on the kidneys remains unchecked, more serious symptoms of kidney failure may occur, including seizures and **coma**.

Diagnosis

Damage to the kidneys is assessed through a combination of **physical examination**, blood tests, urine tests, and imaging procedures. Diagnosis of nephrotoxic injury as the underlying cause results from a thorough investigation of the patient's history. Information regarding preexisting conditions, current prescriptions, and environmental exposures to toxins aid the physician in determining what toxin, if any, has caused the kidneys to malfunction.

Treatment

Treatment of nephrotoxic injury takes place in the hospital and focuses on removing the toxin from the patient's system, while maintaining kidney function. Removal methods are targeted to specific toxins and may include the use of **diuretics** or chelates to enhance excretion of the toxin in urine, or, in extreme cases, the direct removal of toxins from the blood via hemodialysis or passing the blood over an absorbent substance such as charcoal. Support of kidney function depends on the extent of damage to the organs and ranges from monitoring fluid levels to dialysis.

Prognosis

The outcome of nephrotoxic injury is determined by the cause and severity of the damage. In cases where damage has not progressed beyond acute renal failure, kidney function can be fully restored once the toxin is removed from the system and equilibrium restored. However, if permanent damage has resulted in chronic renal failure, lifelong dialysis or a kidney transplant may be required.

Prevention

Exposure to nephrotoxins can be minimized several different ways. When taking antibiotics or analgesics, recommended dosages should be strictly followed. Also, elderly patients on these medications (for example, those taking **aspirin** for heart problems or NSAIDs for arthritis) should be closely monitored to prevent accidental overdose. Health care workers should be aware of any underlying conditions, such as diabetes or **allergies** to antibiotics, that may heighten the effect of a potential nephrotoxin. When using solvents or handling heavy metals, procedures regarding their safe use should be employed.

ORGANIZATIONS

American Kidney Fund (AKF), 6110 Executive Boulevard, Suite 1010, Rockville, MD, 20852, (800) 638-8299, http://www.kidneyfund.org.

National Kidney Foundation, Inc. , 30 East 33rd Street, New York, NY, 10016, (212) 889-2210, (212) 689-9261, (800) 622-9010, http://www.kidney.org/.

Bridget Travers

Nerve conduction velocity testing *see* **Electromyography**

Neural hearing loss *see* **Hearing loss**

Neuralgia

Definition

Neuralgia is defined as an intense burning or stabbing **pain** caused by irritation of or damage to a nerve. The pain is usually brief but may be severe. It often feels as if it is shooting along the course of the affected nerve.

Description

Different types of neuralgia occur depending on the reason the nerve has been irritated. Neuralgia can be triggered by a variety of causes, including **tooth decay**, eye strain, or **shingles** (an infection caused by the herpes zoster virus). Pain is usually felt in the part of the body that is supplied by the irritated nerve.

Causes and symptoms

Neuralgia is caused by irritation or nerve damage from systemic disease, inflammation, infection, and compression or physical irritation of a nerve. The location of the pain depends on the underlying condition that is irritating the nerve or the location of the particular nerve that is being irritated.

Neuralgia can result from tooth decay, poor diet, eye strain, nose infections, or exposure to damp and cold. Postherpetic neuralgia is an intense debilitating pain felt at the site of a previous attack of shingles. **Trigeminal neuralgia** (also called tic douloureux, the most common type of neuralgia), causes a brief, searing pain along the trigeminal nerve, which supplies sensation to the face. The facial pain of migraine neuralgia lasts between 30 minutes and an hour and occurs at the same time on successive days. The cause is not known.

Glossopharyngeal neuralgia is an intense pain felt at the back of the tongue, in the throat, and in the ear—all areas served by the glossopharyngeal nerve. The pain may occur spontaneously, or it can be triggered by talking, eating, or swallowing (especially cold foods such as ice cream). Its cause is not known.

Occipital neuralgia is caused by a pinched occipital nerve. There are two occipital nerves, each located at the back of the neck, each supplying feeling to the skin over half of the back of the head. These nerves can be pinched due to factors ranging from arthritis to injury, but the result is the same: **numbness**, pain, or **tingling** over half the base of the skull.

Diagnosis

Neuralgia is a symptom of an underlying disorder; its diagnosis depends on finding the cause of the condition creating the pain.

To diagnose occipital neuralgia, a doctor can inject a small amount of anesthetic into the region of the occipital nerve. If the pain temporarily disappears, and there are no other physical reasons for the pain, the doctor may recommend surgery to deal with the pinched nerve.

Treatment

Glossopharyngeal, trigeminal, and postherpetic neuralgias sometimes respond to **anticonvulsant**

KEY TERMS

Desensitization—A technique of pain reduction in which the painful area is stimulated with whatever is causing the pain.

Dorsal root entry zone (DREZ)—A type of nerve surgery for postherpetic neuralgia that is occasionally used when the patient can get no other pain relief. The surgery destroys the area where damaged nerves join the central nervous system, thereby interfering with inappropriate pain messages from nerves to the brain.

Glossopharyngeal neuralgia—Sharp recurrent pain deep in the throat that extends to the area around the tonsils and possibly the ear. It is triggered by swallowing or chewing.

Migraine neuralgia—A variant of migraine pain, also called cluster headache, in which severe attacks of pain affect the eye and forehead on one side of the face.

Occipital neuralgia—Pain on one side of the back of the head caused by entrapment or pinching of an occipital nerve.

Postherpetic neuralgia—Persistent pain that occurs as a complication of a herpes zoster infection. Although the pain can be treated, the response is variable.

Shingles—A painful rash with blisters that appears along the course of a nerve. It is caused by infection with herpes zoster virus.

TENS—The abbreviation for transcutaneous electrical nerve stimulation, a technique used to control chronic pain. Electrodes placed over the painful area deliver a mild electrical impulse to nearby nerve pathways, thereby easing pain.

Trigeminal neuralgia—Brief episodes of severe shooting pain on one side of the face caused by inflammation of the root of the trigeminal nerve. Also referred to as tic douloureux.

drugs, such as carbamazepine or phenytoin, or to painkillers, such as **acetaminophen**. Trigeminal neuralgia may also be relieved by surgery in which the nerve is cut or decompressed. In some cases, compression neuralgia (including occipital neuralgia) can be relieved by surgery.

People with shingles should see a doctor within three days of developing the rash, since aggressive treatment of the blisters that appear with the rash can ease the severity of the infection and minimize the risk of developing postherpetic neuralgia. However, it is not clear whether the treatment can prevent postherpetic neuralgia.

If postherpetic neuralgia develops, a variety of treatments can be tried, since their effectiveness varies from person-to-person.

- antidepressants such as amitriptyline (Elavil)
- anticonvulsants (phenytoin, valproate, or carbamazepine)
- capsaicin (Xostrix), the only medication approved by the FDA for treatment of postherpetic neuralgia
- topical painkillers
- desensitization
- TENS (transcutaneous electrical nerve stimulation)
- dorsal root zone (DREZ) surgery (a treatment of last resort)

Alternative treatment

B-complex **vitamins**, primarily given by intramuscular injection, can be an effective treatment. A whole-foods diet with adequate protein, carbohydrates, and fats that also includes yeast, liver, wheat germ, and foods that are high in B vitamins may be helpful. **Acupuncture** is a very effective treatment, especially for postherpetic neuralgia. Homeopathic treatment can also be very effective when the correct remedy is used. Some botanical medicines may also be useful. For example, black cohosh (*Cimicifuga racemosa*) appears to have anti-inflammatory properties based on recent research.

Prognosis

The effectiveness of the treatment depends on the cause of the neuralgia, but many cases respond to pain relief.

Trigeminal neuralgia tends to come and go, but successive attacks may be disabling. Although neuralgia is not fatal, the patient's fear of being in pain can seriously interfere with daily life.

Some people with postherpetic neuralgia respond completely to treatment. Most people, however, experience some pain after treatment, and a few receive no relief at all. Some people live with this type of neuralgia for the rest of their lives, but for most, the condition gradually fades away within five years.

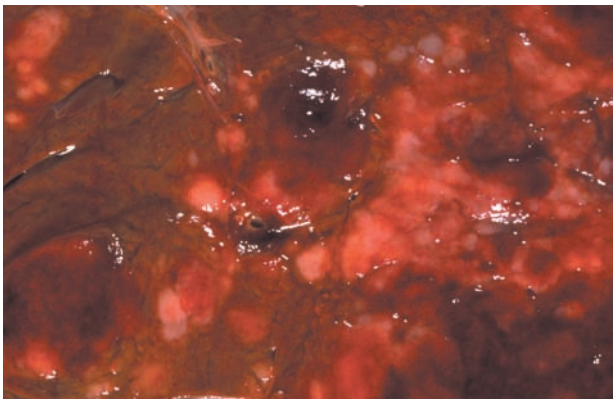
ORGANIZATIONS

American Chronic Pain Association, P.O. Box 850, Rocklin, CA, 95677, (916) 632-3208, (800) 533-3231, APA@pacbell.net, http://www.theacpa.org.

Americna Pain Society, 4700 W. Lake Ave., Glenview, IL, 60025, (847) 375-4715, (866) 574-2654, info@ampainsoc.org, http://www.ampainsoc.org.

National Institute of Neurological Disorders and Stroke (NINDS), NIH Neurological Institute, P. O. Box 5801, Bethesda, MD, 20824, (301) 496-5751, (800) 352-9424, http://www.ninds.nih.gov/.

Carol A. Turkington



A neuroblastoma appearing at the surface of the liver. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Neuroblastoma

Definition

Neuroblastoma is a type of **cancer** that usually originates either in the tissues of the adrenal gland or in the ganglia of the abdomen or in the ganglia of the nervous system. (Ganglia are masses of nerve tissue or groups of nerve cells.) Tumors develop in the nerve tissue in the neck, chest, abdomen, or pelvis.

Description

Neuroblastoma is one of the few cancer types known to secrete hormones. It occurs most often in children, and it is the third most common cancer that occurs in children. Approximately 7.5% of the childhood cancers diagnosed in 2001 were neuroblastomas, affecting one in 80,000 to 100,000 children in the United States. Close to 50% of cases of neuroblastoma occur in children younger than two years old. The disease is sometimes present at birth, but is usually not noticed until later. By the time the disease is diagnosed, it has often spread to the lymph nodes, liver, lungs, bones, or bone marrow. Approximately one-third of neuroblastomas start in the adrenal glands.

Demographics

According to some reports, African-American children develop the disease at a slightly higher rate than Caucasian children (8.7 per million compared to 8.0 per million cases diagnosed).

Causes and symptoms

The causes of neuroblastoma are not precisely known. Current research holds that neuroblastomas develop when cells produced by the fetus (neuroblast cells) fail to mature into normal nerve or adrenal cells and keep growing and proliferating. The first symptom of a neuroblastoma is usually an unusual growth or lump, found in most cases in the abdomen of the child, causing discomfort or a sensation of fullness and **pain**. Other symptoms such as **numbness** and **fatigue**, arise because of pressure caused by the tumor. Bone pain also occurs if the cancer has spread to the bone. If it has spread to the area behind the eye, the cancer may cause protruding eyes and dark circles around the eyes; in a few cases, blindness may be the presenting symptom. **Paralysis** may result from compression of the spinal cord. **Fever** is also reported in one case out of four. High blood pressure, persistent **diarrhea**, rapid heartbeat, reddening of the skin, and sweating occur occasionally. Some children may also have uncoordinated or jerky muscle movements, or uncontrollable eye movements, but these symptoms are rare. If the disease spreads to the skin, blue or purple patches may appear.

Diagnosis

A diagnosis of neuroblastoma usually requires blood and urine tests to investigate the nature and quantity of chemicals (neurotransmitters) released by the nerve cells. These are broken down by the body and released in urine. Additionally, scanning techniques are used to confirm the diagnosis of neuroblastoma. These techniques produce images or pictures of the inside of the body and they include computed tomography scan (CT scan) and **magnetic resonance imaging** (MRI). To confirm the diagnosis, the physician will surgically remove some of the tissue from the tumor or bone marrow, and examine the cells under the microscope (biopsy).

Treatment

The treatment team usually consists of an oncologist specialized in the treatment of neuroblastoma, a surgeon to perform biopsies and possibly attempt surgical removal of the tumor, a **radiation therapy** team and, if indicated, a **bone marrow transplantation** team.

Staging

Once neuroblastoma has been diagnosed, the physician will perform more tests to determine if the cancer has spread to other tissues in the body. This process, called staging, is important for the physician to determine how to treat the cancer and check liver and kidney function. The staging system for neuroblastoma is based on how far the disease has spread from its original site to other tissues in the body.

Localized resectable (able to be cut out) neuroblastoma is confined to the site of origin, with no evidence that it has spread to other tissues, and the cancer can be surgically removed. Localized unresectable neuroblastoma is confined to the site of origin, but the cancer cannot be completely removed surgically. Regional neuroblastoma has extended beyond its original site to regional lymph nodes, and/or surrounding organs or tissues, but has not spread to distant sites in the body. Disseminated neuroblastoma has spread to distant lymph nodes, bone, liver, skin, bone marrow, and/or other organs. Stage 4S (or IVS, or "special") neuroblastoma has spread only to liver, skin, and/or, to a very limited extent, bone marrow. Recurrent neuroblastoma means that the cancer has come back, or continued to spread after it has been treated. It may come back in the original site or in another part of the body.

Treatments are available for children with all stages of neuroblastoma. More than one of these treatments may be used, depending on the stage of the disease. The four types of treatment used are:

- surgery (removing the tumor in an operation)
- radiation therapy (using high-energy x-rays to kill cancer cells)
- chemotherapy (using drugs to kill cancer cells)
- bone marrow transplantation (replacing the patient's bone marrow cells with those from a healthy person)

Surgery is used whenever possible, to remove as much of the cancer as possible, and can generally cure the disease if the cancer has not spread to other areas of the body. Before surgery, **chemotherapy** may be used to shrink the tumor so that it can be more easily removed during surgery; this is called neoadjuvant chemotherapy. Radiation therapy is often used after surgery; high-energy rays (radiation) are used to kill as many of the remaining cancer cells as possible. Chemotherapy (called adjuvant chemotherapy) may also be used after surgery to kill remaining cells. Bone marrow transplantation is used to replace bone marrow cells killed by radiation or chemotherapy. In some cases the patient's own bone marrow is removed prior to treatment and saved for transplantation later. Other times the bone marrow comes from a "matched" donor, such as a sibling.

One novel approach to treatment of neuroblastomas is therapy with desferoxamine (DFO), which is ordinarily used to treat iron **poisoning**. DFO has been shown to have antitumor activity in neuroblastomas and other cancers of the central nervous system. It is thought that the drug works by lowering the increased iron levels in the body associated with cancer.

There are significant differences in treatment protocols for neuroblastoma between the major North American study group (Children's Oncology Group) and its European counterpart, the Société Internationale d'Oncologie Pédiatrique (SIOP). These differences include biopsy techniques, the timing and extent of surgery, chemotherapy dosages, and the types of salvage therapy employed.

Alternative treatment

No alternative therapy has yet been reported as a substitute for conventional neuroblastoma treatment. Complementary therapies—such as retinoic acid therapy—have been shown to be beneficial to patients when administered after a conventional course of chemotherapy or transplantation.

Prognosis

The chances of recovery from neuroblastoma depend on the stage of the cancer, the age of the child at diagnosis, the location of the tumor, and the state and nature of the tumor cells evaluated under the microscope. Infants have a higher rate of cure than do children over one year of age, even when the disease has spread. In general, the prognosis for a young child with neuroblastoma is good: the predicted five-year survival rate is approximately 85% for children who had the onset of the disease in infancy, and 35% for those whose disease developed later.

Prevention

Neuroblastoma may be a genetic disease passed down from the parents. In 2004, a group of German researchers reported that a series of neuroblastomas demonstrated a consistent pattern of deletions and

KEY TERMS

Adjuvant chemotherapy—Treatment of the tumor with drugs after surgery to kill as many of the remaining cancer cells as possible.

Adrenal gland—Gland located above each kidney consisting of an outer wall (cortex) that produces steroid hormones and an inner section (medulla) that produces other important hormones, such as adrenaline and noradrenaline.

Alternative therapy—A therapy is generally called alternative when it is used instead of conventional cancer treatments.

Biopsy—A small sample of tissue removed from the site of the tumor to be examined under a microscope.

Conventional therapy—Treatments that are widely accepted and practiced by the mainstream medical community.

Complementary therapy—A therapy is called complementary when it is used in addition to conventional cancer treatments.

Disseminated—Spread to other tissues.

Hormone—A substance produced by specialized cells that affects the way the body carries out the biochemical and energy-producing processes required to maintain health (metabolism.

Localized—Confined to a small area.

Neoadjuvant chemotherapy—Treatment of the tumor with drugs before surgery to reduce the size of the tumor.

Neuroblast cells—Cells produced by the fetus which mature into nerve cells and adrenal medulla cells.

Monoclonal antibody—A protein substance which is produced in the laboratory by a single population of cells. They are being tested as a possible form of cancer treatment.

Resectable cancer—A tumor that can be surgically removed.

Salvage therapy—Treatment measures taken late in the course of a disease after other therapies have failed. It is also known as rescue therapy.

Staging system—A system based on how far the cancer has spread from its original site, developed to help the physician determine how best to treat the disease.

Unresectable cancer—A tumor that cannot be completely removed by surgery.

overrepresentations on chromosomes 3, 10, 17q, and 20. There is currently no known method for its prevention.

Special concerns

After completion of a course of treatment for neuroblastoma, physicians sometimes recommend that the child undergo an investigative operation. This procedure allows the treatment team to evaluate how effective treatment has been, and may offer an opportunity to remove more of the tumor if it is still present.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Cheung, Nai–Kong V., and Susan L. Cohn. *Neuroblastoma*. Berlin; New York: Springer–Verlag, 2005.

PERIODICALS

Bockmuhl, U., X. You, M. Pacyna-Gengelbach, et al. "CGH Pattern of Esthesioneuroblastoma and Their Metastases." *Brain Pathology* 14 (April 2004): 158–163.

Dayani, P. N., M. C. Bishop, K. Plack, and P. M. Zeltzer. "Desferoxamine (DFO)—Mediated Iron Chelation: Rationale for a Novel Approach to Therapy for Brain Cancer." *Journal of Neurooncology* 67 (May 2004): 367–377.

Lau, J. J., J. D. Trobe, R. E. Ruiz, et al. "Metastatic Neuroblastoma Presenting with Binocular Blindness from Intracranial Compression of the Optic Nerves." *Journal of Neuroophthalmology* 24 (June 2004): 119–124.

Morgenstern, B. Z., A. P. Krivoshik, V. Rodriguez, and P. M. Anderson. "Wilms' Tumor and Neuroblastoma." *Acta Paediatrica Supplementum* 93 (May 2004): 78–84.

ORGANIZATIONS

National Cancer Institute (National Institutes of Health), NCI Office of Communications and Education, 6116 Executive Blvd. Suite 300, Bethesda, MD, 20892-8322, (800) 4-CANCER (422-6237), cancergovstaff@mail.nih.gov, http://www.cancer.gov/.

National Institutes of Health and National Cancer Institute, 6116 Executive Boulevard Suite 300, Bethesda, MD, 20892-8322, (800) 422-6237, cancergovstaff@mail.nih.gov, http://www.cancer.gov.

Lisa Christenson, PhD
Monique Laberge, PhD
Rebecca J. Frey, PhD

Neuroendocrine tumors

Definition

Neuroendocrine tumor refers to the type of cell that a tumor grows from rather than where that tumor is located. Neuroendocrine cells produce hormones or regulatory proteins, and so tumors of these cells usually have symptoms that are related to the specific hormones that they produce.

Description

Neuroendocrine cells have roles both in the endocrine system and the nervous system. They produce and secrete a variety of regulatory hormones, or neuropeptides, which include neurotransmitters and growth factors. When these cells become cancerous, they grow and overproduce their specific neuropeptide. Neuroendocrine tumors are generally rare. One type of neuroendocrine tumor is a carcinoid tumor. This type of tumor can occur in the intestinal tract, appendix, rectum, bronchial tubes, or ovary. Most carcinoid tumors secrete serotonin. When the blood concentration of this hormone is high enough, it causes carcinoid syndrome. This syndrome refers to a variety of symptoms that are caused by the excessive amount of hormone secreted rather than the tumor itself.

The total incidence of neuroendocrine tumors is thought to be between five and nine million people in the United States. It is possible that these tumors are underreported because they grow slowly and do not always produce dramatic symptoms.

Causes and symptoms

Many of the symptoms of carcinoid tumor are due to the hormones that the tumor secretes. These hormones can affect the whole body and cause what is referred to as carcinoid syndrome. The most common symptom of carcinoid syndrome is flushing, a sudden appearance of redness and warmth in the face and neck that can last from minutes to hours. Other symptoms of carcinoid syndrome are **diarrhea**, asthma-like symptoms and heart problems. Since most carcinoid tumors are found in the appendix, the symptoms are often similar to **appendicitis**, primarily **pain** in the abdomen. When these tumors are found in the small intestine, they can cause abdominal pain that is often initially diagnosed as bowel obstruction. Many patients have no symptoms and the carcinoids are found during routine **endoscopy** of the intestines.

Diagnosis

The diagnosis of carcinoid syndrome is made by the measurement of 5–hydroxy indole acetic acid (5–HIAA) in the urine. 5–HIAA is a breakdown (waste) product of serotonin. If the syndrome is diagnosed, the presence of carcinoid tumor is a given. When the syndrome is not present, diagnosis may be delayed, due to the vague symptoms present. Diagnosis can sometimes take up to two years. It is made by performing a number of tests, and the specific test used depends on the tumor's suspected location. The tests that may be performed include gastrointestinal endoscopy, **chest x-ray**, computed tomography scan (CT scan), **magnetic resonance imaging**, or ultrasound. A biopsy of the tumor is performed for diagnosis. A variety of hormones can be measured in the blood as well to indicate the presence of a carcinoid.

Treatment

The only effective treatment for carcinoid tumor is surgical removal of the tumor. Although **chemotherapy** is sometimes used when metastasis has occurred, it is rarely effective. The treatment for carcinoid syndrome is typically meant to decrease the severity of symptoms. Patients should avoid **stress** as well as foods that bring on the syndrome. Some medications can be given for symptomatic relief; for example, tumors of the gastrointestinal tract may be treated with octreotide (Sandostatin) or lanreotide (Somatuline) to relieve such symptoms as diarrhea and flushing. These drugs are known as somatostatin analogs.

Liver transplantation is a treatment option for patients with neuroendocrine tumors that have metastasized only to the liver. This approach is reported to offer patients long, disease-free periods and relief of symptoms.

Prognosis

The prognosis of carcinoid tumors is related to the specific growth patterns of that tumor, as well as its location. For example, a group of researchers at the University of Wisconsin reported in 2004 that patients with gastrointestinal tumors in the hindgut had longer

KEY TERMS

Appendicitis—Inflammation of the appendix.

Growth factor—A local hormone produced by some cells that initiates growth.

Metastasis—The spread of disease from one part of the body to another, as when cancer cells appear in parts of the body remote from the site of the primary tumor.

Neurotransmitter—A chemical messenger used to transmit information in the nervous system.

periods of disease-free survival than those with foregut or midgut cancers. For localized disease the five-year survival rate can be 94%, whereas for patients where metastasis has occurred, the average five-year survival rate is 18%. It is not unusual for patients with carcinoid tumors to live 10–15 years after the initial diagnosis.

Prevention

Neuroendocrine tumors such as carcinoid tumors are rare, and no information consequently is yet available on cause or prevention.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Ahlman, H., S. Friman, C. Cahli, et al. "Liver Transplantation for Treatment of Metastatic Neuroendocrine Tumors." *Annals of the New York Academy of Sciences* 1014 (April 2004): 265–269.

Oberg, K., L. Kvols, M. Caplin, et al. "Consensus Report on the Use of Somatostatin Analogs for the Management of Neuroendocrine Tumors of the Gastroenteropancreatic System." *Annals of Oncology* 15 (June 2004): 966–973.

Van Gompel, J. J., R. S. Sippel, T. F. Warner, and H. Chen. "Gastrointestinal Carcinoid Tumors: Factors That Predict Outcome." *World Journal of Surgery* 28 (April 2004): 387–392.

ORGANIZATIONS

Carcinoid Cancer Foundation, 333 Mamaroneck Ave. #492, New York, NY, 10605, (888) 722-3132, http://www.carcinoid.org/.

Cindy L. A. Jones, PhD
Rebecca J. Frey, PhD

Neurofibromatosis

Definition

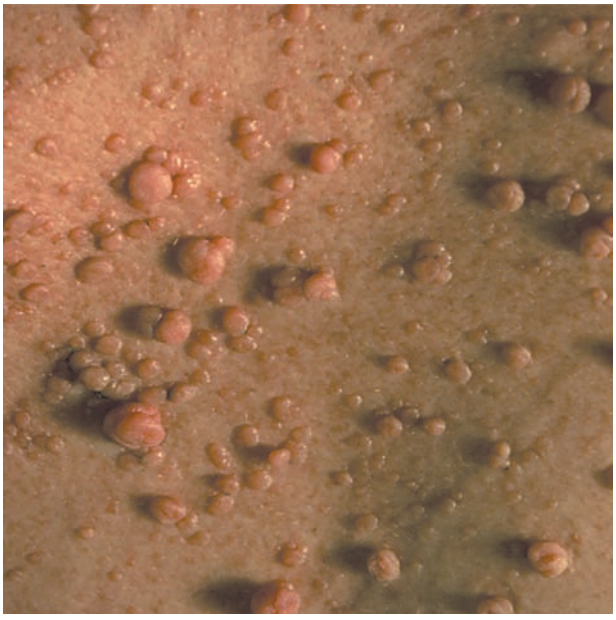
Neurofibromatosis (NF), or von Recklinghausen disease, is a genetic disease in which patients develop multiple soft tumors (neurofibromas). These tumors occur under the skin and throughout the nervous system.

Description

Neural crest cells are primitive cells which exist during fetal development. These cells eventually turn into:

- cells which form nerves throughout the brain, spinal cord, and body
- cells which serve as coverings around the nerves that course through the body
- pigment cells, which provide color to structures
- the meninges, the thin, membranous coverings of the brain and spinal cord
- cells which ultimately develop into the bony structures of the head and neck

In neurofibromatosis, a genetic defect causes these neural crest cells to develop abnormally. This results in numerous tumors and malformations of the nerves, bones, and skin.



This person's skin has multiple soft tumors, or neurofibromas. Such tumors develop underneath the skin. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Neurofibromatosis occurs in about one of every 4,000 births. Two types of NF exist: NF-1 (90% of all cases), and NF-2 (10% of all cases).

Causes and symptoms

Both forms of neurofibromatosis are caused by a defective gene. NF-1 is due to a defect on chromosome 17; NF-2 results from a defect on chromosome 22. Both of these disorders are inherited in a dominant fashion. This means that anybody who receives just one defective gene will have the disease. However, a family pattern of NF is only evident in about half of all cases of NF. The other cases of NF occur due to a spontaneous mutation (a permanent change in the structure of a specific gene). Once such a spontaneous mutation has been established in an individual, however, it is then possible to be passed on to any offspring. The chance of a person with NF passing on the NF gene to a child is 50%.

NF-1 has a number of possible signs and can be diagnosed if any two of the following are present:

- The presence of café-au-lait (French for coffee-with-milk) spots. These are patches of tan or light brown skin, usually about 5-15 mm in diameter. Nearly all patients with NF-1 will display these spots.
- Multiple freckles in the armpit or groin area.
- Ninty percent of patients with NF-1 have tiny tumors called Lisch nodules in the iris (colored area) of the eye.
- Neurofibromas. These soft tumors are the hallmark of NF-1. They occur under the skin, often located along nerves or within the gastrointestinal tract. Neurofibromas are small and rubbery, and the skin overlying them may be somewhat purple in color.
- Skeletal deformities, such as a twisted spine (scoliosis), curved spine (humpback), or bowed legs.
- Tumors along the optic nerve, which cause vision disturbance in about 20% of patients.
- The presence of NF-1 in a patient's parent, child, or sibling.

There are very high rates of speech impairment, learning disabilities, and attention deficit disorder in children with NF-1. Other complications include the development of a **seizure disorder**, or the abnormal accumulation of fluid within the brain (**hydrocephalus**). A number of cancers are more common in patients with NF-1. These include a variety of types of malignant brain tumors, as well as leukemia, and cancerous tumors of certain muscles (rhabdomyosarcoma), the adrenal glands (**pheochromocytoma**), or the kidneys (**Wilms' tumor**).

Patients with NF-2 do not necessarily have the same characteristic skin symptoms (café-au-lait spots, freckling, and neurofibromas of the skin) that appear in NF-1. The characteristic symptoms of NF-2 are due to tumors along the acoustic nerve. Interfering with the function of this nerve results in the loss of hearing; and the tumor may spread to neighboring nervous system structures, causing weakness of the muscles of the face, **headache**, **dizziness**, poor balance, and uncoordinated walking. Cloudy areas on the lens of the eye (called **cataracts**) frequently develop at an unusually early age. As in NF-1, the chance of brain tumors developing is unusually high.

Diagnosis

Diagnosis is based on the symptoms outlined above. Diagnosis of NF-1 requires that at least two of the listed signs are present. Diagnosis of NF-2 requires the presence of either a mass on the acoustic nerve or another distinctive nervous system tumor. An important diagnostic clue for either NF-1 or NF-2 is the presence of the disorder in a patient's parent, child, or sibling.

Monitoring the progression of neurofibromatosis involves careful testing of vision and hearing. X-ray studies of the bones are frequently done to watch for the development of deformities. CT scans and MRI scans are performed to track the development/progression of tumors in the brain and along the nerves. Auditory evoked potentials (the electric response evoked in the cerebral cortex by stimulation of the acoustic nerve) may be helpful to determine involvement of the acoustic nerve, and EEG (electroencephalogram, a record of electrical currents in the brain) may be needed for patients with suspected seizures.

Treatment

There are no available treatments for the disorders that underlie either type of neurofibromatosis. To some extent, the symptoms of NF-1 and NF-2 can be treated individually. Skin tumors can be surgically removed. Some brain tumors, and tumors along the nerves, can be surgically removed, or treated with drugs (**chemotherapy**) or x-ray treatments (**radiation therapy**). Twisting or curving of the spine and bowed legs may require surgical treatment, or the wearing of a special brace.

Prognosis

Prognosis varies depending on the types of tumors which an individual develops. As tumors grow, they begin to destroy surrounding nerves and structures. Ultimately, this destruction can result in blindness, deafness, increasingly poor balance, and increasing difficulty with

KEY TERMS

Chromosome—A structure within the nucleus of every cell, which contains genetic information governing the organism's development.

Mutation—A permanent change to the genetic code of an organism. Once established, a mutation can be passed on to offspring.

Neurofibroma—A soft tumor usually located on a nerve.

Tumor—An abnormal multiplying mass of cells.

the coordination necessary for walking. Deformities of the bones and spine can also interfere with walking and movement. When cancers develop, prognosis worsens according to the specific type of **cancer**.

Prevention

There is no known way to prevent the approximately 50% of all NF cases that occur due to a spontaneous change in the genes (mutation). New cases of inherited NF can be prevented with careful **genetic counseling** so that a person with NF understands that each of his or her offspring has a 50% chance of also having NF. When a parent has NF, and the specific genetic defect causing the parent's disease has been identified, tests can be performed on the fetus so that a during **pregnancy**. **Amniocentesis** or **chorionic villus sampling** are two techniques which allow small amounts of the developing baby's cells to be removed for examination. The tissue can then be examined for the presence of the parent's genetic defect. Some families choose to use this information in order to prepare for the arrival of a child with a serious medical problem. Other families may choose not to continue the pregnancy.

ORGANIZATIONS

Children's Foundation, 95 Pine St., 16th Floor, New York, NY, 10005-4002, (212) 344-6633, (800) 323-7938, info@ctf.org, http://www.ctf.org.

March of Dimes Birth Defects Foundation, 1275 Mamaroneck Ave., White Plains, NY, 10605, (914) 997-4488, http://www.modimes.org.

Neurofibromatosis, Inc. 8855 Annapolis Rd., #110, Lanham, P.O. Box 66884, Chicago, IL, 60666, (800) 942-6825, http://www.nfinc.org.

Rosalyn Carson-DeWitt, MD

Neurogenic arthropathy *see* **Charcot's joints**

Neurogenic bladder

Definition

Neurogenic bladder is a dysfunction that results from interference with the normal nerve pathways associated with urination.

Description

Normal bladder function is dependent on the nerves that sense the fullness of the bladder (sensory nerves) and on those that trigger the muscle movements that either empty it or retain urine (motor nerves). The reflex to urinate is triggered when the bladder fills to 300-500 mL. The bladder is then emptied when the contraction of the bladder wall muscles forces urine out through the urethra. The bladder, internal sphincters, and external sphincters may all be affected by nerve disorders that create abnormalities in bladder function.

There are two categories of neurogenic bladder dysfunction: overactive (spastic or hyper-reflexive) and underactive (flaccid or hypotonic). An overactive neurogenic bladder is characterized by uncontrolled, frequent expulsion of urine from the bladder. There is reduced bladder capacity and incomplete emptying of urine. An underactive neurogenic bladder has a capacity that is extremely large (up to 2000 mL). Due to a loss of the sensation of bladder filling, the bladder does not contract forcefully, and small amounts of urine dribble from the urethra as the bladder pressure reaches a breakthrough point.

Causes and symptoms

There are numerous causes for neurogenic bladder dysfunction and symptoms vary depending on the cause. An **overactive bladder** is caused by interruptions in the nerve pathways to the bladder occurring above the sacrum (five fused spinal vertebrae located just above the tailbone, or coccyx). This nerve damage results in a loss of sensation and motor control and is often seen in **stroke**, Parkinson's disease, and most forms of spinal-cord injuries. An underactive bladder is the result of interrupted bladder stimulation at the level of the sacral nerves. This may result from certain types of surgery on the spinal cord, sacral spinal tumors, or congenital defects. It also may be a complication of various diseases, such as **syphilis**, **diabetes mellitus**, or **polio**.

Diagnosis

Neurogenic bladder is diagnosed by carefully recording fluid intake and urinary output and by measuring the quantity of urine remaining in the bladder after voiding (residual urine volume). This measurement is done by draining the bladder with a small rubber tube (catheter) after the person has urinated. Kidney function also is evaluated by regular laboratory testing of the blood and urine. **Cystometry** may be used to estimate the capacity of the bladder and the pressure changes within it. These measurements can help determine changes in bladder compliance in order to assess the effectiveness of treatment. Doctors may use a cystoscope to look inside the bladder and tubes that lead to it from the kidneys (ureters). **Cystoscopy** may be used to assess the loss of muscle fibers and elastic tissues and, in some cases, for removing small pieces of tissue for examination (biopsy).

Treatment

Doctors begin treating neurogenic bladder by attempting to reduce bladder stretching (distension) through intermittent or continuous catheterization. In intermittent catheterization, a small rubber catheter is inserted at regular intervals (four to six times per day) to approximate normal bladder function. This avoids the complications that may occur when a catheter remains in the bladder's outside opening (urethra) continuously (an indwelling catheter). Intermittent catheterization should be performed using strict sterile technique (asepsis) by skilled personnel, and hourly fluid intake and output must be recorded. Patients who can use their arms may be taught to catheterize themselves.

Indwelling catheters avoid distension by emptying the bladder continuously into a bedside drainage collector. Individuals with indwelling catheters are encouraged to maintain a high fluid intake in order to prevent bacteria from accumulating and growing in the urine. Increased fluid intake also decreases the concentration of **calcium** in the urine, minimizing urine crystallization and the subsequent formation of stones. Moving around as much as possible and a low calcium diet also help to reduce stone formation.

Drugs may be used to control the symptoms produced by a neurogenic bladder. The unwanted contractions of an overactive bladder with only small volumes of urine may be suppressed by drugs that relax the bladder (anticholinergics) such as propantheline (ProBanthine) and oxybutynin (Ditropan). Contraction of an underactive bladder with normal bladder volumes may be stimulated with parasympathomimetics (drugs that mimic the action resulting from stimulation of the parasympathetic nerves) such as bethanechol (Urecholine).

Long-term management for the individual with an overactive bladder is aimed at establishing an effective spontaneous reflex voiding. The amount of fluid taken in is controlled in measured amounts during the waking hours, with sips only toward bedtime to avoid bladder distension. At regular intervals during the day (every four to six hours when fluid intake is two to three liters per 24 hours), the patient attempts to void using pressure over the bladder (Crede maneuver). The patient may also stimulate reflex voiding by abdominal tapping or stretching of the anal sphincter. The **Valsalva maneuver**, involving efforts similar to those used when straining to pass stool, produces an increase in intra-abdominal pressure that is sometimes adequate to completely empty the bladder. The amount of urine remaining in the bladder (residual volume) is estimated by a comparison of fluid intake and output. The patient also may be catheterized immediately following the voiding attempt to determine residual urine. Catheterization intervals are lengthened as the residual urine volume decreases and catheterization may be discontinued when urine residuals are at an acceptable level to prevent **urinary tract infection**.

For an underactive bladder, the patient may be placed on a similar bladder routine with fluid intake and output adjusted to prevent bladder distension. If an adequate voiding reflex cannot be induced, the patient may be maintained on clean intermittent catheterization.

Some individuals who are unable to control urine output (**urinary incontinence**) due to deficient sphincter tone may benefit from perineal exercises. Although this is a somewhat dated technique, male patients with extensive sphincter damage may be helped by the use of a Cunningham clamp. The clamp is applied in a horizontal fashion behind the glans of the penis and must be removed approximately every four hours for bladder emptying to prevent bacteria from growing in the urine and causing an infection. Alternation of the Cunningham clamp with use of a condom collection device will reduce the skin irritation sometimes caused by the clamp.

Surgery is another treatment option for incontinence. Urinary diversion away from the bladder may involve creation of a urostomy or a continent diversion. The surgical implantation of an inflatable sphincter is another option for certain patients. An indwelling urinary catheter is sometimes used when all other methods of incontinence management have failed. The long-term use of an indwelling catheter almost inevitably leads to some urinary tract infections, and contributes to the formation of urinary stones (calculi). Doctors may prescribe **antibiotics** preventively to reduce recurrent urinary tract infection.

KEY TERMS

Anticholinergic—An agent that blocks certain nerve impulses.

Catheterization—Insertion of a slender, flexible tube into the bladder to drain urine.

Compliance—A term used to describe how well a patient's behavior follows medical advice.

Cystometry—A test of bladder function in which pressure and volume of fluid in the bladder are measured during filling, storage, and voiding.

Cystoscopy—A direct method of bladder study and visualization using a cystoscope (self-contained optical lens system). The cystoscope can be manipulated to view the entire bladder, with a guide system to pass it up into the ureters (tubes leading from the kidneys to the bladder).

Glans penis—The bulbous tip of the penis.

Motor nerves—Nerves that cause movement when stimulated.

Parasympathomimetic—An agent whose effects mimic those resulting from stimulation of the parasympathetic nerves.

Perineal—The diamond-shaped region of the body between the pubic arch and the anus.

Reflex—An involuntary response to a particular stimulus.

Sensory nerves—Nerves that convey impulses from sense organs to the higher parts of the nervous system, including the brain.

Sphincter—A band of muscles that surrounds a natural opening in the body; these muscles can open or close the opening by relaxing or contracting.

Ureter—A tube leading from one of the kidneys to the bladder.

Urethra—The tube that leads from the bladder to the outside of the body.

Urostomy—A diversion of the urinary flow away from the bladder, resulting in output through the abdominal wall. The most common method involves use of a portion of intestine to conduct the urine out through the abdomen and into an external pouch worn for urine collection.

Alternative treatment

The cause of the bladder problem must be determined and treated appropriately. If nerve damage is not permanent, homeopathy and **acupuncture** may help restore function.

Prognosis

Individuals with an overactive bladder caused by spinal cord lesions at or above the seventh thoracic vertebra, are at risk for sympathetic dysreflexia, a life-threatening condition which can occur when the bladder (and/or rectum) becomes overly full. Initial symptoms include sweating (particularly on the forehead) and **headache**, with progression to slow heart rate (bradycardia) and high blood pressure (**hypertension**). Patients should notify their physician promptly if symptoms do not subside after the bladder (or rectum) is emptied, or if the bladder (or rectum) is full and cannot be emptied.

ORGANIZATIONS

American Urological Association (AUA), 1000 Corporate Boulevard, Linthicum, MD, 21090, (410) 689-3700, (410) 689-3800, (866) 746-4282, aua@AUAnet.org, http://www.auanet.org.

National Association for Continence, P.O. Box 1019, Charleston, SC, 29402-1019, (843) 377-0900, (843) 377-0905, (800) 252-3337, memberservices@nafc.org, http://www.nafc.org.

Simon Foundation for Continence, P.O. Box 815, Wilmette, IL, 60091, (800) 2237-4666, http://www.simonfoundation.org.

Kathleen D. Wright, RN

Neuroleptics *see* **Antipsychotic drugs**

Neurolinguistic programming

Definition

Neurolinguistic programming (NLP) is aimed at enhancing the healing process by changing the conscious and subconscious beliefs of patients about themselves, their illnesses, and the world. These limiting beliefs are "reprogrammed" using a variety of techniques drawn from other disciplines including **hypnotherapy** and **psychotherapy**.

Purpose

Neurolinguistic programming has been used to change the limiting beliefs of patients about their prospects of recovery from a wide variety of medical conditions including Parkinson's disease, **AIDS**, migraines, arthritis, and **cancer**. Practitioners claim to be able to cure most **phobias** in less than one hour, and to help in making lifestyle changes regarding **exercise**, diet, **smoking**, etc. NLP has also been used to treat **allergies**. In other fields, claimed benefits include improved relationships, communication, motivation, and business performance.

Description

Origins

NLP was originally developed during the early 1970s by linguistics professor John Grinder, and psychology and mathematics student Richard Bandler, both of the University of California at Santa Cruz.

Studying the well-known psychotherapist Virginia Satir, the hypnotherapist Milton Erickson, the anthropologist Gregory Bateson, and others whom they considered "charismatic superstars" in their fields, Grinder and Bandler identified psychological, linguistic, and behavioral characteristics that they said contributed to the greatness of these individuals. On the other hand, they found that persons experiencing emotional difficulties could be similarly identified by posture, breathing pattern, choice of words, voice tone, eye movements, body language, and other characteristics.

Grinder and Bandler then focused on using these indicators to analyze and alter patterns of thought and behavior. After publishing their findings in two books in 1975, Grinder and Bandler parted company with one another, with a number of other collaborators, and with the University of California, continuing their work on NLP outside the formal world of academia. As a result, NLP split into a number of competing schools.

Popularized by television "infomercial" personality Anthony Robbins and others, NLP was quickly adopted in management and self-improvement circles. During the 1990s, there was growing interest in NLP's healing potential.

In a health-care context, practitioners of neurolinguistic programming first seek to identify the negative attitudes and beliefs with which a client has been "programmed" since birth. This is accomplished by asking questions and observing physical responses such as changes in skin color, muscle tension, etc. Then, a wide variety of techniques is employed to "reprogram" limiting beliefs. For example, clients with chronic illness such as AIDS or cancer might be asked to displace the despair and loss of identity caused by the disease by visualizing themselves in vigorous health. Treatment by NLP practitioners is often of shorter duration than that of other alternative practitioners, but NLP self-help seminars and courses can be quite expensive.

For those who wish to try self-treatment with NLP, a wide variety of books, audio tapes, and videos are available.

Precautions

NLP is particularly popular in the self-improvement and career-development fields, and some trainers and practitioners have little experience in its use for healing. Practitioners should be specifically asked about this.

Because NLP is intended to enhance the healing process, it should not be used independently of other healing methods. In all cases of serious illness, a physician should be consulted.

Side effects

NLP is believed to be generally free of harmful side effects.

Research and general acceptance

Although some physicians and mental health practitioners employ principles of neurolinguistic programming, the field is generally considered outside of mainstream medical practice and academic thinking.

ORGANIZATIONS

Association for NLP, Room, 11, Apsley Mills Cottage, London Road, Hemel Hempstead, Herts, HP3 9RL, (020) 3384 3217, (0845) 053 1176, http://www.anlp.org/.

International NLP Trainers Association, 1201 Delta Glen Court, Vienna, VA, 22182, wyatt.woodsmall@inlpta.org, http://www.inlpta.org.

Society of Neuro-Lingustic Programming, 7065 Bella Vista Road, Vernon, Canada, BC, V1H 1X3, (250) 545-6448, access@nlpmind.com, http://www.nlpmind.com/contact.

David Helwig

Neurologic bladder dysfunction *see* **Neurogenic bladder**

Neurological exam

Definition

A neurological exam—also called a neurologic or neuro exam—is an evaluation of the nervous system, including the brain, spinal cord, the 12 cranial nerves that come from the brain, and the nerves that come from the spinal cord. A neurological exam uses observation and simple tests to assess motor and sensory skills and mental status. Motor skills include reflexes, muscle strength, eye and mouth movement, and coordination, balance, and gait. Sensory skills include hearing and speech, vision, taste, and smell. Mental status includes alertness, awareness of and interaction with one's environment, and mood and behavioral changes.

Purpose

Neurological exams are performed for a variety of purposes:

- as part of a complete physical exam
- as part of a newborn physical exam
- to assess or follow the effects of a head or spine birth defect
- for the diagnosis of a wide variety of diseases and conditions
- to follow the progression or management of a disease or condition
- to monitor an injury to the head, neck, or back
- to monitor recovery following brain surgery

Neurological exams are becoming routine in some sports, most notably preseason exams for all National Football League players to provide a baseline in case of **concussion**. A neurological exam can reveal signs of increased intracranial pressure or decreased brain function. In addition to concussions, neurological exams are performed on patients with any of the following symptoms:

- fatigue
- headaches
- blurred vision
- fever of unknown origin
- numbness or tingling in the arms or legs
- decreased arm or leg movement
- tremor
- uncontrollable jerky body movements
- problems with balance or coordination
- behavioral changes

A neurological exam is often one of the first procedures in the diagnosis of many diseases and conditions including:

- central nervous system (CNS) infections, such as encephalitis and meningitis
- stroke
- transient ischemic attacks—in which the exam results may be abnormal during the episode but normal immediately afterwards
- bleeding in the brain
- spinal cord injuries
- carotid artery disease
- peripheral neuropathy
- alcoholic neuropathy
- erectile dysfunction
- brain and spinal cord tumors, including pituitary tumors and primary CNS lymphomas
- nasopharyngeal cancer
- brain abscesses
- brain herniation
- epilepsy
- cerebral palsy
- dementia
- Alzheimer's disease
- Parkinson's disease
- Huntington's disease
- multiple sclerosis
- myasthenia gravis—a muscle weakness disorder
- neurological complications of HIV/AIDS
- systemic lupus erythematosus, a chronic inflammatory autoimmune disease
- amyotrophic lateral sclerosis (ALS)
- congenital toxoplasmosis
- craniosynostosis, a congenital defect in which one or more sutures on a infant's head close too early
- mitochondrial diseases
- motor neuron diseases
- metabolic diseases of muscle

Description

A neurological exam is neither invasive nor painful. It can be performed in a physician's office and involves only simple instruments such as a reflex hammer, tuning fork, needles, a light, and an ophthalmoscope. The simplest aspects of a neurological exam involve observing a patient's gait and coordination and whether the eyelids are drooping. However some specialized exams may require a neurologist to

perform the tests and analyze the results. The extent of a neurological exam depends on the symptoms being evaluating and the patient's age and medical condition. For some injuries it may be necessary to repeat portions of the exam after swelling from the injury has decreased. In some cases, such as after a **stroke**, neurological exams may be repeated at regular intervals to monitor the condition.

A neurological exam focuses on:

- motor skills, including reflexes, muscle strength, head and facial movements, coordination, balance, and gait
- sensory skills
- mental status and basic cognitive skills
- cranial nerves

Motor nerve function—especially deep tendon reflexes—are central to a neurological exam. Deep tendon reflexes, also known as muscle stretch reflexes, are tendon responses to stimuli. Normally, tapping specific areas of tendons with a soft rubber hammer causes the muscle fibers to contract. The physician taps various points with a reflex hammer and observes any decrease in responsiveness.

The Babinski reflex is an important component of motor system evaluation. In patients over the age of two, stroking or scratching the outer side of the sole of the foot in a heel-to-toe direction normally causes the toes to curl downward. A brain or **spinal cord injury** is indicated by the toes fanning upward.

The physician will examine the patient's muscles for atrophy (shrinkage), twitching, or abnormal movements. Tests may be performed to evaluate the strength of all major muscle groups. Specific tests may include:

- squeezing fingers
- using the arms and legs to push and pull against the physician's hands
- passive movement of the joints by the physician and active movement by the patient

Head and facial movement tests may include:

- touching various areas of the face
- biting down
- swallowing
- smiling, grimacing, moving the cheeks, and baring the teeth
- tongue movement
- testing the gag reflex using a tongue blade
- head movements such as turning side to side against mild resistance
- shrugging the shoulders

Tests of coordination, balance, and gait may include:

- observation of a patient's walk and general coordination
- moving one's finger back and forth between one's nose and the examiner's finger, touching the tip of each
- tapping one's fingers together rapidly in a coordinated manner
- moving one's hands back and forth on top of one another as smoothly as possible
- rubbing one heel smoothly over the other shin
- drawing a spiral
- touching a finger to one's nose with the eyes closed
- balancing with the feet together and eyes closed
- standing with the eyes closed while being gently pushed to one side
- heel-to-toe walking in a straight line
- walking on one's toes
- turning abruptly
- running, hopping, skipping, or jumping
- evaluation of any functional limitations, such as difficulty writing or holding a cup or utensil

Sensory tests may include:

- hearing tests using a ticking watch or a tuning fork
- clarity, fluency, and coherence of speech
- vision tests
- examining the eye with a special light to evaluate the optic nerve
- using a light to evaluate pupil size reflex
- evaluating eye movement by having the patient follow a light or the examiner's finger in various directions with the eyes
- identifying various tastes—such as sweet, sour, and bitter—on the back of the tongue
- identifying different smells with the eyes closed
- identifying objects and sensations—such as sharp or dull—as the physician touches parts of the patient's body with a finger, sharp object, cotton ball, paint brush, dull needle, tuning fork, or alcohol swab
- identifying numbers or letters traced on the body
- using pinpricks to test a patient's pain response on different parts or opposite sides of the body
- using cold or warm objects to test temperature sensations
- sense of position by identifying the direction in which the examiner is moving a part of the patient's body, such as a big toe

KEY TERMS

Automatism—An automatic action or reflex.

Babinski reflex—A reflex movement by the big toe when the sole is tickled: an upward response is normal in infancy, but indicates central nervous system damage in older children and adults.

Moro reflex—A reflex startle reaction in infants: the arms and legs move away from the body and to the side and are then drawn together.

Ophthalmoscope—An instrument for viewing the interior of the eye.

Stroke—A sudden diminishment of consciousness, sensation, or voluntary movement caused by a rupture or clot in a blood vessel in the brain.

Tendon reflex—A reflex action, such as a knee jerk, in which a light blow to the tendon causes the muscle to contract.

Evaluating mental status is particularly important when other parts of a neurological exam yield normal results. Sometimes small changes in memory or other intellectual abilities are the only indication of a problem. Evaluating mental skills can also be useful for determining a course of treatment and making a prognosis. Mental status tests may involve:

- observing a patient's state of consciousness or awareness of and responsiveness to the environment and the senses
- ability to follow simple and complex directions
- orientation with reference to time, place, and person, such as knowing the current time and date and the current president
- attentiveness
- ability to appropriately answer simple but detailed questions
- ability to read and write
- intellectual capacity including comprehension, insight, and judgment
- solving simple mathematical problems
- copying a three-dimensional drawing
- drawing a clock with the numbers and hands placed appropriately
- abstract reasoning tests such as explaining the meaning of common sayings
- memory tests, such as repeating sentences or a list of objects used early in the exam or describing yesterday's breakfast or what happened on the last holiday
- the patient's appearance, mood, and general behavior
- with an infant, observing the child's interaction with parents

Specific components of a neurological exam evaluate the function of each of the 12 cranial nerves:

- cranial nerve I—the olfactory nerve
- cranial nerve II—the optic nerve
- cranial nerve III—the oculomotor nerve responsible for pupil size and eye movement
- cranial nerve IV—the trochlear nerve involved in eye movement
- cranial nerve V—the trigeminal nerve—which has various functions including the ability to feel the face and inside the mouth, and moving muscles involved in chewing
- cranial nerve VI—the abducens nerve involved in eye movement
- cranial nerve VII—the facial nerve—which has various functions including taste and movement
- cranial nerve VIII—the acoustic nerve
- cranial nerve IX—the glossopharyngeal nerve involved in taste
- cranial nerve X—the vagus nerve involved in swallowing, gag reflex, and aspects of taste and speech
- cranial nerve XI—the accessory nerve involved in moving the head and shoulders
- cranial nerve XII—the hypoglossal nerve responsible for tongue movement

A newborn or infant neurological exam evaluates reflexes or automatisms, each of which disappears at a certain stage of normal development. These reflexes include, but are not limited to, the following:

- blinking—closing the eyes in response to a bright light
- Babinski reflex—the toes extending upward as an infant's foot is stroked
- crawling—infants making crawling motions when placed on their stomach
- Moro reflex—infants throw out their arms, open their hands, and throw back their heads when startled or moved rapidly
- palmar and plantar grasps—infants fingers and toes curl around a nearby finger

- startle reflex—infants extend and flex the arms with the hands fisted in response to loud noise A measurement of head circumference is also part of a neurological exam in infants and younger children.

Benefits

A neurological exam is a relatively simple, quick, and inexpensive means of identifying a wide range of neurological abnormalities. In many cases a simple neurological exam has been found to be superior to expensive computed tomography (CT) scans for diagnoses. Neurological problems and nervous system damage can cause delays in infant and child development and functioning: early diagnosis of problems using a neurological exam can help identify the cause and decrease the likelihood of long-term complications.

Precautions

Precautions concerning a neurological exam include:

- The exam requires skill and patience on the part of the physician.
- Importantly, the exam requires the patient's cooperation.
- Responses can be affected by the wakefulness, awareness, and alertness of the patient, so the mental status portion of a neurological exam is usually performed early on.
- The sensory exam should be repeated for accuracy.

Aftercare

There are no special preparations or risks involved in a neurological exam. However abnormal results may require further procedures such as a CT scan, **magnetic resonance imaging** (MRI), x-rays, or laboratory tests. The patient may be referred to a neurologist or other specialist.

Resources

BOOKS

Levy, Michael. *Patient Encounters: The Neurology and Psychiatric Work-Up*. Philadelphia: Wolters Kluwer/ Lippincott Williams & Wilkins, 2010.

PERIODICALS

Gruber, Nancy. "Beyond Discharge: Impairment After Critical Illness." *RN* 71, no. 5 (May 2008): 29.

OTHER

"Chapter 5: Diagnosis & Follow-Up Testing." *A Primer of Brain Tumors*. http://www.abta.org/siteFiles/SitePages/CB001386B9BE886833764351A83EFA8B.pdf

"Neurological Diagnostic Tests and Procedures." *National Institute of Neurological Disorders and Stroke*. http://www.ninds.nih.gov/disorders/misc/diagnostic_tests.htm#examination

"Neurological Exam." *Children's Hospital Boston*. http://www.childrenshospital.org/az/Site1350/mainpageS1350P0.html

"What Is a Neurological Exam?" *Diagnostic Tests*. http://www.neurologychannel.com/neuroexam.shtml

ORGANIZATIONS

American Brain Tumor Association, 2720 River Road, Des Plaines, IL, 60018, (847) 827-9910, (800) 886-2282 , (847) 827-9918, infor@abta.org, http://www.abta.org.

National Institute of Neurological Disorders and Stroke (NINDS), NIH Neurological Institute, P.O. Box 5801, Bethesda, MD, 20824, (301) 496-5751, (800) 352-9424, http://www.ninds.nih.gov/index.htm.

Margaret Alic, PhD
Brenda Lerner

Neurosurgery

Definition

Neurosurgery is a specialized field of surgery for the treatment of diseases or conditions of the central nervous system (CNS) and spine.

Description

Neurosurgery is the specialized field of surgery that treats diseases that affect the CNS—the brain and the spine. A neurosurgeon is a medical doctor who has received extensive training in the surgical and medical management of neurological diseases. The field of neurosurgery is one of the most sophisticated surgical specialties and encompasses advanced surgical and imaging technology and new research in molecular neurosurgery and **gene therapy**. There are five general categories of neurosurgical diseases that are commonly managed by neurosurgeons: cerebrovascular (hemorrhage [bleeding] and aneurysms); traumatic **head injury**, or THI traumatic injury caused by accident); degenerative diseases of the spine; tumors in the CNS; functional neurosurgery; surgery for congenital abnormalities; and neurosurgical management of the CNS.

Cerebrovascular diseases that usually require surgery include spontaneous intracranial hemorrhage (bleeding within the skull), spontaneous **subarachnoid hemorrhage** (bleeding beneath the outer membranous covering of the brain), spontaneous intracerebral

hemorrhage (bleeding within the brain), cerebral aneurysms (outpouchings of the blood vessel), hypertensive intracerebral hemorrhage (due to high blood pressure), and angiomatous malformations.

Brain hemorrhage

Spontaneous intracranial hemorrhage is a condition characterized by hemorrhage in the brain (hemorrhagic **stroke**) that results in a sudden onset of neurologically worsening symptoms (that include focal neurologic deficits and loss of consciousness). CT scans are helpful in identifying the intracranial hemorrhage, of which there are two types—subarachnoid hemorrhage and intracerebral hematoma.

The subarachnoid space is an area that exists between two layers of coverings (membranes) that wrap around the brain. A spontaneous subarachnoid hemorrhage is defined as blood (not caused by trauma), in the subarachnoid space. The amount of blood in the subarachnoid space can be a focal (small area) amount or a larger, more diffuse hemorrhage, which can be further complicated by having an intraventricular hemorrhage or intracerebral hematoma at the same time.

The incidence of subarachnoid hemorrhage is 10 per 100,000 persons per year; approximately 30% of Americans will sustain a subarachnoid hemorrhage annually. **Smoking** is a major factor in increasing the odds of sustaining a subarachnoid hemorrhage. Subarachnoid hemorrhage can affect adults of all ages, but usually peaks in the fourth and fifth decades of life. Approximately 60% of patients are female. Approximately 30% of subarachnoid hemorrhages occur during sleep.

The most frequent cause of spontaneous subarachnoid hemorrhage is rupture of an intracranial aneurysm. The symptoms of subarachnoid hemorrhage are a sudden onset of severe **headache** that worsens over time, **nausea**, loss of consciousness (with or without seizure), and **vomiting**. Depending on the severity of bleeding, additional symptoms can also include visual sensitivity to light (photophobia), a stiff neck, and minor (low-grade) **fever**. Symptoms occur before rupture of the aneurysm in 40% of patients, usually in those with a minor hemorrhage. These symptoms can also include headache or **dizziness**, and tend to go unnoticed.

After a subarachnoid hemorrhage, most patients are hypertensive (have high blood pressure) and experience changes in heart rate and rhythm. CT scans are the best diagnostic tool for subarachnoid hemorrhage. The hemorrhage can be visualized in the first 24 hours after onset in 90% of patients and in more than 50% in the first week. Spinal taps to sample the cerebrospinal fluid (CSF) may be required to evaluate some patients who have the potential to suffer a subarachnoid hemorrhage. This procedure involves the insertion of a thin needle between the lumbar vertebral bodies (L–4 and L–5) to allow the removal of a small amount of fluid to look for either red (RBCs) or white blood cells (WBCs). Once the aneurysm has been identified, the patient is taken for surgery. A **craniotomy** is performed using microsurgical techniques. The operative microscope helps to identify the aneurysm, which is then clipped. A berry aneurysm, or congenital aneurysm, is the reason for more than half of all cases of spontaneous subarachnoid hemorrhage.

A spontaneous intracerebral hemorrhage (or hematoma) (SICH) is a blood clot in brain tissue that can arise abruptly and is strongly correlated with **hypertension**. There are approximately 40,000 new

KEY TERMS

Angiomatous malformations—Tumors in blood vessels.

Cerebral aneurysms—A sac in a blood vessel in the brain that can rupture and cause bleeding in the brain.

Craniosynostosis—Premature closure of the skull, which results in skull deformities.

Craniotomy—Procedure to remove a lesion in the brain through an opening in the skull.

Desiccation—Extreme drying.

Encephaloceles—Protrusion of the brain through a defect in the skull.

Germinoma—A tumor of germ cells (ovum and sperm cells that participate in production of the developing embryo).

Hydrocephalus—A defect characterized by an increase in cerebrospinal fluid (CSF), which bathes and nourishes the brain and spinal cord.

Intraventricular hemorrhage—Hemorrhage in the ventricles of the brain.

Lymphoma—A tumor of lymph glands or lymph tissues.

Meninges—Membranes that cover the brain.

Myelomeningoceles (MMC)—A protrusion in the vertebral column containing spinal cord and meninges.

Subarachnoid space—A space between membranes that covers and protects the brain.

cases of SICH in the United States annually. Stroke is the third leading cause of **death** in the United States, and SICH accounts for 10% of all stroke cases. Advancing age is a major predisposing factor for SICH: The incidence of SICH is two per 1,000 persons per year by age 45, and rises to 350 per 100,000 persons per year in those aged 80 years or more. Hypertensive intracerebral hemorrhage can occur in different areas within the brain. Damage to some areas may be associated with a very high death rate. Treatment includes comprehensive ICU (intensive care unit) management of hypertension and maintenance of adequate cerebral perfusion (oxygenated blood going to the brain).

Accidental head injury is a major public health problem. Trauma causes approximately 150,000 deaths annually in the United States; approximately half of these deaths were caused by fatal head trauma. Additionally, there are 10,000 new spinal cord injuries annually. The cost of disability (e.g., chronic long-term care, lost wages, and work) is very high. Approximately 200,000 persons in the United States are living with disabilities associated with head and spinal cord trauma.

Severe head injury is defined as an injury that produces **coma** (patient will not open eyes even to painful stimulus; is incapable of following simple commands; and cannot utter words). These clinical criteria are defined on the well-established Glasgow Coma Scale (GCS). A **physical examination** and neurologic assessment by a neurosurgeon and brain scan imaging (CT scan) are necessary for the initial evaluation. Additionally, a special catheter to monitor intracranial pressure (due to brain swelling) is necessary. A blood clot larger than 25 to 30 cubic centimeters is considered clinically large enough to cause progressive brain injury.

Tumors inside the brain (intracranial tumors) are typically of two types: primary and secondary intracranial tumors. Primary intracranial tumors (PICT) rarely metastasize and usually originate in the brain, coverings (membranes) of the brain, or the pituitary gland. The incidence of primary intracranial tumors is 11.5 per 100,000, or approximately 35,000 persons per year.

Secondary intracranial tumors arise from outside the brain coverings (meninges). Quite commonly, secondary intracranial tumors are bloodborne metastatic disease from primary malignant **cancer** outside the brain (i.e., cancer from some other location that has spread to the brain). Approximately 250,000 persons per year are affected by secondary intracranial tumors. A tumor in the brain can cause increased intracranial pressure, or cause symptoms associated with localized compression of the brain (i.e., a tumor grows and compresses part of the brain against the skull). One common cause of increased intracranial pressure is growth of a tumor that obstructs the duct system of cerebrospinal fluid (CSF), which bathes and nourishes the brain and spinal cord. Common symptoms can include nausea, **vomiting**, headache that is worse in the morning, and a reduced level of consciousness that causes drowsiness. Tumors causing focal compression on or irritation of the brain usually result in loss of neurologic function. This progressive loss of neurologic function can manifest as **tinnitus** (ringing in the ears) or **aphasia** (language problems).

Technical advancement has made surgical removal of brain tumors more effective and safer. Surgical management of intracranial tumors focuses on diagnosis and reduction of tumor mass. Depending on tumor location and patient health status, the neurosurgeon may perform a needle biopsy (called image-directed stereotactic needle biopsy) or a craniotomy to extract a piece of tumor for pathologic analysis. If the tumor is located in an area where surgery can be performed, the neurosurgeon generally will remove the mass if the patient can tolerate **general anesthesia**. Exceptions to a surgical option may be exercised to treat malignant tumors that are very sensitive to **chemotherapy** or **radiation therapy** (i.e., to manage lymphoma or germinoma). One of the most common types of tumors is the glioma, which accounts for 50% of all primary brain tumors.

Degenerative disorders of the spine

Degenerative disorders of the spine are a common problem. Between 50% and 90% of the population will experience back **pain** at some point in their lifetime. Most of these symptoms subside on their own within a few weeks; the cost, however, is realized in decreased productivity and lost wages—a public health problem. Pain in the lumbar spine is the most common reason adults seek medical attention. The lumbar spine comprises five lumbar vertebra and supports the weight of the entire vertebral column and head. Lower back disorders are among the most frequent reasons for referral to a neurosurgeon. Lumbar discs are prone to herniation and desiccation (drying out) as a result of the heavy load they bear and the motion to which they are subject. Nerves that run from the vertebrae extend out to distant body parts, and degeneration of the discs may change bony structures in such a manner that can cause nerve compression. Typically, patients with degenerative disorders of the spine may experience pain, **numbness**, paresthesia (**tingling**), and restriction of

neck movement (if the affected vertebra is in the cervical spine, which is located in the back of the neck).

Surgery for congenital abnormalities

Congenital abnormalities arise during embryonic development. Important changes in growth and chemistry occur during the second week of human gestation; these changes contribute to the development of the nervous system. Several different types of cells proliferate as they move together or separate into other structures according to an orchestrated, natural timeline. Defects can occur at different stages of development. Among the defects with which infants can be born include myelomeningoceles, encephaloceles, **hydrocephalus**, and craniosynostosis.

Central nervous system infections

Solitary or multiple brain abscesses can occur as a result of infection in the brain. Patients present with clinical symptoms such as focal (a specific area is affected) neurologic signs, seizures, altered mental status, and increased intracranial pressure. CT scans and **magnetic resonance imaging** (MRI) are helpful for identification of brain abscesses. Surgery is usually indicated if the **abscess** fails to resolve or worsens following antibiotic treatment, or if there are signs of mass effect and brain herniation. Although rare, a spinal epidural abscess can occur. Typically, bacteria can spread in patients who have acute bacterial **meningitis** (infection of the subarachnoid spaces and meninges). The specific type of problem bacteria varies according to the patient's age.

Functional neurosurgery

Functional neurosurgery is a special type of surgical procedure used to manage movement disorder, **epilepsy**, and pain. Stereotactic neurosurgery makes use of a coordinate system that provides accurate navigation to a specific point or region in the brain. This is usually done by placing and fixing into position a frame on the scalp (using four threaded pins that penetrate the outer skull to stabilize the frame in position) under **local anesthesia**. A special box and sterotactic arc are placed to precisely determine X, Y, and Z coordinates of any point within the frame.

Epilepsy surgery

Approximately 70 people per 100,000 in the United States takes antiepileptic medications for seizure disorders. The risk of developing epilepsy over a lifetime is 3%, and there are 100,000 new cases per year. The majority of cases (approximately 60,000) are epilepsy of the temporal lobe (the brain lobes located on the sides of the head). Approximately 25% of temporal lobe seizure patients who are prescribed antiepileptic drugs continue to have seizures that are not controlled or that can be controlled, but the side effects of the medication outweigh the therapeutic benefits. Approximately 5,000 new cases per year require epilepsy surgery (partial anterior temporal **lobectomy**). The patient and neurosurgeon should consider surgery if continued seizures cause injuries due to repeated falls; driving restrictions; limitation of social interactions; problems related to education and learning; and employment limitations.

The future of neurosurgery

Neurosurgery as a field is faced with many new opportunities and challenges, based on advanced technological approaches and molecular approaches to neurosurgical problems. Advances in technology have allowed the neurosurgeon to precisely locate abnormal tissue in the brain and spinal cord, thereby preserving normal tissues from surgical trauma. In addition to cardiovascular neurosurgery, functional neurosurgery, neuro-oncologic neurosurgery (surgical removal of brain tumors), and spinal surgery, the future holds many new research innovations. In the new millennium, the field of molecular neurosurgery can make it possible to introduce genetic material into nerve cells and to redirect protein synthesis—to work toward reversing the disease process, in general.

Resources

BOOKS

Goetz, CG. *Goetz's Textbook of Clinical Neurology*. 3rd ed. Philadelphia: Saunders, 2007.

Khatri, VP and JA Asensio. *Operative Surgery Manual*. 1st ed. Philadelphia: Saunders, 2003.

Townsend, CM et al. *Sabiston Textbook of Surgery*. 17th ed. Philadelphia: Saunders, 2004.

PERIODICALS

Freese, A., Simeone, F. "Ocular Surgery for the New Millennium." and "Treatment of Neurosurgical Disease in the New Millennium." *Ophthalmology Clinics of North America* 12, no. 4 (December 1999).

ORGANIZATIONS

The American Board of Neurological Surgery, 6550 Fannin Street, Suite 2139, Houston, TX, 77030, (713) 441-6015, http://www.abns.org.

Laith Farid Gulli, MD, MS
Miguel A. Melgar, MD, PhD
Nicole Mallory, MS, PA-C

Neuromuscular junction disease *see* **Myasthenia gravis**

Neuropathic bladder *see* **Neurogenic bladder**

Neutropenia

Definition

Neutropenia is an abnormally low level of neutrophils in the blood. Neutrophils are white blood cells (WBCs) produced in the bone marrow that ingest bacteria. Neutropenia is sometimes called agranulocytosis or granulocytopenia because neutrophils make up about 60% of WBCs and have granules inside their cell walls. Neutropenia is a serious disorder because it makes the body vulnerable to bacterial and fungal infections.

Description

The normal level of neutrophils in human blood varies slightly by age and race. Infants have lower counts than older children and adults, and African Americans have lower counts than Caucasians or Asians. The average adult level is 1,500 cells/mm^3 of blood. Neutrophil counts (in cells/mm^3) are interpreted as follows:

- greater than 1,000–normal protection against infection
- 500–1,000–some increased risk of infection
- 200–500–great risk of severe infection
- lower than 200–risk of overwhelming infection; requires hospital treatment with antibiotics

Causes and symptoms

Causes

Neutropenia may result from three processes:

DECREASED WBC PRODUCTION. Lowered production of white blood cells is the most common cause of neutropenia. It can result from:

- medications that affect the bone marrow, including cancer drugs, chloramphenicol (Chloromycetin), anticonvulsant medications, and antipsychotic drugs (Thorazine, Prolixin, and other phenothiazines)
- hereditary and congenital disorders that affect the bone marrow, including familial neutropenia, cyclic neutropenia, and infantile agranulocytosis
- cancer, including certain types of leukemia
- radiation therapy
- exposure to pesticides
- vitamin B_{12} and folate (folic acid) deficiency

DESTRUCTION OF WBCS. WBCs are used up at a faster rate by:

- acute bacterial infections in adults
- infections in newborns
- certain autoimmune disorders, including systemic lupus erythematosus (SLE)
- penicillin, phenytoin (Dilantin), and sulfonamide medications (Benemid, Bactrim, Gantanol)

SEQUESTRATION AND MARGINATION OF WBCS. Sequestration and margination are processes in which neutrophils are removed from the general blood circulation and redistributed within the body. These processes can occur because of:

- hemodialysis
- Felty's syndrome or malaria, in which the neutrophils accumulate in the spleen
- bacterial infections, in which the neutrophils remain in the infected tissues without returning to the bloodstream

Symptoms

Neutropenia has no specific symptoms except the severity of the patient's current infection. In severe neutropenia, the patient is likely to develop **periodontal disease**, oral and rectal ulcers, **fever**, and bacterial **pneumonia**. Fever recurring every 19–30 days suggests cyclical neutropenia.

Diagnosis

Diagnosis is made on the basis of a **white blood cell count** and **differential** (determines the percentage of different types of WBCs). The cause of neutropenia is often difficult to establish and depends on a combination of the patient's history, genetic evaluation, **bone marrow biopsy**, and repeated measurements of the WBCs.

Treatment

Treatment of neutropenia depends on the underlying cause.

Medications

Patients with fever and other signs of infection are treated for seven to 10 days with **antibiotics**. Nutritional deficiencies are corrected by green vegetables to supply **folic acid**, and by vitamin B supplements.

KEY TERMS

Cyclical neutropenia—A rare genetic blood disorder in which the patient's neutrophil level drops below 500/mm^3 for six to eight days every three weeks.

Differential—A blood cell count in which the percentages of cell types are calculated as well as the total number of cells.

Felty's syndrome—An autoimmune disorder in which neutropenia is associated with rheumatoid arthritis and an enlarged spleen.

Granulocyte—Any of several types of white blood cells that have granules in their cell substance. Neutrophils are the most common type of granulocyte.

Neutrophil—A granular white blood cell that ingests bacteria, dead tissue cells, and foreign matter.

Sargramostim—A medication made from yeast that stimulates WBC production. It is sold under the trade names Leukine and Prokine.

Sequestration and margination—The removal of neutrophils from circulating blood by cell changes that trap them in the lungs and spleen.

Medications known to cause neutropenia are stopped. Neutropenia related to pesticide exposure is treated by removing the patient from the contaminated environment.

Patients receiving **chemotherapy** for **cancer** may be given a blood growth factor called sargramostim (Leukine, Prokine) to stimulate WBC production.

Surgery

Patients with Felty's syndrome who have repeated infections may have their spleens removed.

Prognosis

The prognosis for mild or chronic neutropenia is excellent. Recovery from acute neutropenia depends on the severity of the patient's infection and the promptness of treatment.

Resources

BOOKS

McPhee, Stephen, and Maxine Papadakis. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw–Hill Medical, 2009.

Rebecca J. Frey, PhD

Nevirapine *see* **Non-nucleoside reverse transcriptase inhibitors**

Nevus *see* **Moles**

Newborn life support *see* **Extracorporeal membrane oxygenation**

Niacin deficiency *see* **Pellagra**

Nicotine *see* **Smoking; Smoking-cessation drugs**

Nicotine and related disorders

Definition

Nicotine disorders are caused by the main psychoactive ingredient in tobacco. Nicotine is a physically and psychologically addictive drug. It is the most influential dependence-producing drug in the United States and worldwide, and its use is associated with many serious health risks.

Demographics

Although the prevalence of **smoking** has gradually decreased in the United States and many other industrialized countries since the 1970s, the use of tobacco products is rapidly increasing in developing nations, where approximately 80% of current smokers live. Younger populations may be particularly vulnerable. For example, a CDC survey from 2003 found that almost 42% of teenaged boys in one city in Mali were cigarette smokers. The World Health Organization currently attributes 4.9 million deaths per year globally to tobacco use among the estimated 1.2 billion smokers worldwide, a **death** total expected to double in two to three decades. Use of tobacco products in developing countries is of particular concern because these countries often lack adequate health care resources to treat smoking-related diseases, let alone support smoking cessation programs.

In the United States, the percentage of men who smoke outnumbers that of women 23% to 18.7%. In developing countries, male smokers outnumber women smokers, but among adolescent populations, girls and boys are becoming more equal in their rates of smoking. In the United States, people who smoke tend to have lower levels of formal education than those who do not. About half of patients diagnosed with psychiatric problems are smokers, while more

Nicotine effects and trends

Effects:

- Nicotine is highly addictive.
- The tar in cigarettes increases a person's chance of developing lung cancer, emphysema, or chronic bronchitis.
- The carbon monoxide in smoke increases the risk of developing a cardiovascular disease.
- Pregnant smokers are more likely to have miscarriages or babies born with low birth weights.
- Secondhand smoke can cause lung cancer in adults and greatly increases the risk of respiratory illnesses in children.

Statistics and trends:

In 2008, nearly 71 million Americans aged 12 and older used a tobacco product at least once in the past month.

- Almost 60 million smoked cigarettes
- 8.7 million used smokeless tobacco
- More than 13 million smoked cigars
- Just under 2 million smoked pipe tobacco

SOURCE: National Institutes of Health, National Institute on Drug Abuse, "Tobacco/Nicotine." Available online at: http://www.drugabuse.gov/drugpages/nicotine.html (accessed August 16, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

than three-quarters of those who abuse other substances also smoke.

From 1997 to 2005, smoking among high-school students had declined after increasing dramatically in the 1990s; however, in 2005, there appears to have been a slight uptick in percentage of smokers in this group. Smoking among women with less than a high school education has shown a steady decline since a bump upward in 1995, but there was a slight increase from 2002 to 2004 among women with a high-school education. Smoking rates among white and African American males overall were almost identical in 2004, but African American males between the ages of 45 and 65 had the highest rates of any group, at 29% in 2004. Among pregnant women, the highest rates of smoking in 2003 occurred among American Indian or Alaska Native women, at 18%. In an age breakdown, women in the 18- to 19-year age group had the highest rates of smoking during **pregnancy**, at 17%, while education plays a strong role in whether a pregnant woman smokes: rates among women without a high-school diploma were 25.5%, while rates among women with at least a four-year degree were 1.6%.

Recent research suggests that there may be a genetic component to nicotine dependence, just as there is for alcohol dependence. Studies show that girls (but not boys) whose mothers smoked during pregnancy are four times more likely to smoke than those whose mothers were tobacco-free during pregnancy. Other research suggests that the absence of a certain enzyme in the body protects the body against nicotine dependence. In addition, there appears to be a sex-based difference among smokers: women may have a harder time quitting smoking.

Description

Nicotine is the most addictive and psychoactive chemical in tobacco, a plant native to the North America. Early European explorers learned to smoke its leaves from indigenous peoples who had been using tobacco for hundreds of years. They took tobacco back to Europe, where it became immensely popular. Tobacco became a major source of income for the American colonies and later for the United States. Advances in cigarette-making technology caused a boom in cigarette smoking in the early 1900s. Before the early twentieth century, most people who used tobacco used pipes, cigars, or chewing tobacco.

In the 1950s, researchers began to link cigarette smoking to certain respiratory diseases and cancers. In 1964 the Surgeon General of the United States issued the first health report on smoking. Cigarette smoking peaked in the United States in the 1960s, then began to decline as health concerns about tobacco increased. In 1971 cigarette advertising was banned from television, although tobacco products are still advertised in other media today. There are about 91.5 million current and former smokers in the United States, and in a 2004 survey, almost 4 million adolescents had tried smoking in the previous month. Most active smokers are addicted to nicotine.

Pure nicotine is a colorless liquid that turns brown and smells like tobacco when exposed to air. Nicotine can be absorbed through the skin, the lining of the mouth and nose, and the moist tissues lining the lungs. Cigarettes are the most efficient nicotine delivery system. Once tobacco smoke is inhaled, nicotine reaches the brain in less than 15 seconds. Because people who smoke pipes and cigars do not inhale, they absorb nicotine more slowly. Nicotine in chewing tobacco and snuff is absorbed through the mucous membranes lining the mouth and nasal passages. There are also several "hard snuff" and other new tobacco products being produced and marketed as alternative to traditional tobacco products. At least one study of the nicotine content of these products has found that some have lower levels of nicotine than regular tobacco products, but others contain comparable levels.

KEY TERMS

Tapering—Gradually reducing the intake of an addictive substance (such as nicotine) as part of a cessation effort.

Withdrawal—Physical symptoms and psychological discomforts experienced after eliminating the intake of an addictive substance (such as nicotine) from the body.

Causes and symptoms

How nicotine works

Nicotine is the main addictive drug among the 4,000 compounds found in tobacco smoke. Such other substances in smoke as tar and carbon monoxide present documented health hazards, but they are not addictive and do not cause cravings or withdrawal symptoms to the extent that nicotine does. Neuroimaging technology has shown that levels of monoamine oxidase, the enzyme responsible for boosting mood-enhancing molecule levels in the brain, increase in response to smoking, even though nicotine does not affect levels of this enzyme. Thus, some other compound in cigarette smoke must be acting to exert this effect. In addition, a compound in cigarette smoke called acetylaldehyde may contribute to tobacco addiction and may have a stronger effect in adolescents.

Nicotine is both a stimulant and a sedative. It is a psychoactive drug, meaning that it works in the brain, alters brain chemistry, and changes mood. Once tobacco smoke is inhaled, nicotine passes rapidly through the linings of the lungs and into the blood. It quickly circulates to the brain where it stimulates release of dopamine, a neurotransmitter (nerve signaling molecule) in the brain that affects mood. Drugs that elicit an increase in dopamine influence the brain's "reward" pathway, causing the user to turn again to the drug for another pleasurable, rewarding dopamine response. This release accounts for the pleasurable sensation that most smokers feel almost as soon as they light a cigarette. Nicotine also decreases anger and increases the efficiency of a person's performance on long, dull tasks.

At the same time nicotine affects the brain, it also stimulates the adrenal glands. The adrenal glands are small, pea-sized organs located above each kidney that really act as two different endocrine organs. The adrenal gland produces several hormones in the medulla, or inner layer, including epinephrine, also called adrenaline. Under normal circumstances, adrenaline is released in response to stress or a perceived threat. It is sometimes called the "fight or flight" hormone, because it prepares the body for action. When adrenaline is released, blood pressure, heart rate, blood flow, and oxygen use increase. Glucose, a simple form of sugar used by the body, floods the body to provide extra energy to muscles. The overall effect of the release of the stress hormones is strain on the cardiovascular (heart and blood vessels) system. This response to stress produces inflammation in the blood vessels that ultimately results in buildup of plaque, which can block the vessels and cause stroke or heart attack.

Most people begin smoking between the ages of 12 and 20. Few people start smoking as adults over 21. Adolescents who smoke tend to begin as casual smokers, out of rebelliousness or a perceived need for social acceptance. Dependence on nicotine develops rapidly, however; one study suggests that 85–90% of adolescents who smoke four or more cigarettes become regular smokers. Nicotine is addictive, so being tobacco-free soon feels uncomfortable for users. In addition, smokers quickly develop tolerance to nicotine. Tolerance is a condition that occurs when the body needs a larger and larger dose of a substance to produce the same effect. For smokers, tolerance to nicotine means more frequent and more rapid smoking. Soon most smokers develop physical withdrawal symptoms when they try to stop smoking. Users of other forms of tobacco experience the same effects; however, the delivery of nicotine is slower and the effects may not be as pronounced.

Nicotine dependence

In addition to the physical dependence caused by the actions of nicotine on the brain, there is a strong psychological component to the dependency of most users of tobacco products, especially cigarette smokers. Most people who start smoking or using smokeless tobacco products do so because of social factors. These include:

- the desire to fit in with peers
- acceptance by family members who use tobacco
- rebelliousness
- the association of tobacco products with maturity and sophistication
- positive response to tobacco advertising

Such personal factors as mental illness (depression, anxiety, schizophrenia, or alcoholism); the need to reduce stress and anxiety; or a desire to avoid weight gain also influence people to start smoking. Once

smoking has become a habit, whether physical addiction occurs or not, psychological factors play a significant role in continuing to smoke. People who want to stop smoking may be discouraged from doing so because:

- they live or work with people who smoke and who are not supportive of their quitting
- they believe they are incapable of quitting
- they perceive no health benefits to quitting
- they have tried to quit before and failed
- they associate cigarettes with specific pleasurable activities or social situations that they are not willing to give up
- they fear gaining weight

Successful smoking cessation programs must treat both the physical and psychological aspects of nicotine addiction.

Nicotine withdrawal

The American Psychiatric Association first recognized nicotine dependence and nicotine withdrawal as serious psychological problems in 1980. Today nicotine is considered an addictive drug, although a common and legalized one.

As is widely recognized, quitting can be difficult. Among people who try, between 75% and 80% will relapse within six months. Because of this rate, research has found that smoking cessation programs that last longer than six months can greatly enhance quit rates, achieving rates as high as 50% at one year. Combining a nicotine-withdrawal product (described in this article) with a behavioral-modification or support program has produced the greatest success rates.

The combination of physiological and psychological factors make withdrawal from nicotine very difficult. Symptoms of nicotine withdrawal include:

- irritability
- restlessness
- increased anger or frustration
- sleep disturbances
- inability to concentrate
- increased appetite or desire for sweets
- depression
- anxiety
- constant thoughts about smoking
- cravings for cigarettes
- decreased heart rate
- coughing

Withdrawal symptoms are usually more pronounced in smokers than in those who use smokeless tobacco products, and heavy smokers tend to have more symptoms than light smokers when they try to stop smoking. People with depression, schizophrenia, alcoholism, or mood disorders find it especially difficult to quit, as nicotine offers temporary relief for some of the symptoms of these disorders.

Symptoms of nicotine withdrawal begin rapidly and peak within one to three days. Withdrawal symptoms generally last three to four weeks, but a significant number of smokers have withdrawal symptoms lasting longer than one month. Some people have strong cravings for tobacco that last for months, even though the physical addiction to nicotine is gone. These cravings often occur in settings in which the person formerly smoked, such as at a party or while driving, or after a meal. Researchers believe that much of this extended craving is psychological.

Diagnosis

Smokers usually self-diagnose their nicotine dependence and nicotine withdrawal. Such questionnaires as the Fagerstrom Test for Nicotine Dependence (FTND), a short six-item assessment of cigarette use, help to determine the level of tobacco dependence. Physicians and mental health professionals are less concerned with diagnosis, which is usually straightforward, than with determining the physical and psychological factors in each patient that must be addressed for successful smoking cessation.

Treatments

Most people do not decide to stop smoking all of the sudden. Instead, they go through several preparatory stages before taking action. First is the precontemplation stage, in which the smoker does not even consider quitting. Precontemplation is followed by the contemplation stage, in which the smoker thinks about quitting, but takes no action. Contemplation eventually turns to preparation, often when counselors or family members encourage or urge the smoker to quit. Now the smoker starts making plans to quit soon. Finally the smoker arrives at the point of taking action.

Having decided to stop smoking, a person has many choices of programs and approaches. When mental health professionals are involved in smoking cessation efforts, one of their first jobs is to identify the physical and psychological factors that keep the person smoking. This identification helps to direct the smoker to the most appropriate type of program. Assessment examines the frequency of the person's

smoking, his or her social and emotional attachment to cigarettes, commitment to change, available support system, and barriers to change. These conditions vary from person to person, which is why some smoking cessation programs work for one person and not another.

Medications

Before 1984, there were no medications to help smokers quit. In that year, a nicotine chewing gum (Nicorette) was approved by the United States Food and Drug Administration (FDA) as a prescription drug for smoking cessation. In 1996 it became available without prescription. Nicorette was the first of several medications used for nicotine replacement therapy, intended to gradually reduce nicotine dependence to prevent or reduce withdrawal symptoms. This approach, called tapering, is used in withdrawal of other addictive drugs. Studies indicate that people using these replacement therapies do not become addicted to them.

Nicotine gum comes in two strengths, 2 mg and 4 mg. As the gum is chewed, nicotine is released and absorbed through the lining of the mouth. Over a six- to 12-week period, the amount and strength of gum chewed can be decreased, until the smoker is weaned from his or her dependence on nicotine. People trying to quit smoking are instructed to use the gum when they feel a craving. Products with caffeine may limit nicotine absorption and should be avoided in a window of time around the gum "dose." Some people may not like the taste of the gum, and other common side effects include burning mouth and sore jaw. Anyone with heart problems, diabetes, ulcers, or who is pregnant or breastfeeding should consult with a doctor before beginning any nicotine-replacement product.

The nicotine transdermal patches have been available without prescription since 1996. They are marketed under several brand names, including Habitrol, Nicoderm, NicoDerm CQ, Prostep and Nicotrol. All but Nicotrol are 24-hour patches. Nicotrol is a 16-hour patch designed to be removed at night. The patches are worn on the skin between the neck and the waist, and provide a steady delivery of nicotine through the skin. Patches like Nicoderm come in varying strengths, and after several weeks, users can move down to a patch that delivers a lower dose. With the Nicotrol patch, a user simply ceases use after six weeks. Some people using the 24-hour patches experience sleep disturbances, and a few develop mild skin irritations, but generally side effects are few. Although fears that using a patch and smoking simultaneously have not been borne out, doctors still recommend not using the patch while smoking.

Two other nicotine delivery devices are available by prescription only. One is a nicotine nasal spray. It has the advantage of delivering nicotine rapidly, just as a cigarette does, although it delivers a much lower dose than a cigarette. Treatment with nasal spray usually lasts four to six weeks. Side effects include cold-like symptoms (runny nose, sneezing, etc.). A nicotine inhaler is also available that delivers nicotine through the tissues of the mouth. A major advantage of the inhaler is that it provides an alternative to having a cigarette in one's hands while still delivering nicotine. It delivers less nicotine in cold weather (under 50°F). Recommendations for both the spray and the inhaler are that they be used at least hourly at first.

There are two prescription drugs that are not nicotine replacement therapy that have been approved for treatment of nicotine dependence. The first-approved drug was buproprion (Zyban), an antidepressant that acts to cut down withdrawal symptoms. This drug may be used in combination with a nicotine-replacement therapy and behavioral therapy.

The newer drug is varenicline (Chantix), which was developed to help people stop smoking. This drug acts directly on the proteins in the brain that recognize and bind nicotine. Interfering with their action not only stops the brain from sending the pleasurable message of nicotine but also reduces the feelings of nicotine withdrawal. Some studies indicate that this drug can double a person's chances of quitting smoking. Side effects of this drug can include headache, nausea, vomiting, sleep problems, gas, and changes in taste sensation.

There is also a combination therapy of atropine and scopolamine that some nicotine cessation programs use. These are two anticholinergic (they block the effects of a class of protein receptors, the acetocholine receptors) drugs that affect dopamine levels in the brain and are administered in the form of shots, followed by self-administration with pills or patches. Side effects of these drugs include dry mouth, constipation, dizziness, or blurry vision, and people with conditions such as heart problems, high blood pressure, or glaucoma, cannot use these programs. In addition, use of this combination for smoking cessation is "off-label" (not approved by the FDA for this purpose), and there are no published studies on success rates with this approach.

Behavioral treatments

Behavioral treatments are used to help smokers learn to recognize and avoid specific situations that

trigger desire for a cigarette. They also help the smoker learn to substitute other activities for smoking. Behavioral treatments are almost always combined with smoker education, and usually involve forming a support network of other smokers who are trying to quit.

Behavioral treatments often take place in support groups either in person or online. They are most effective when combined with nicotine reduction therapy. Other supportive techniques include the use of rewards for achieving certain goals and contracts to clarify and reinforce the goals. Aversive techniques include asking the smoker to inhale the tobacco smoke deeply and repeatedly to the point of nausea, so that smoking is no longer associated with pleasurable sensations. Overall, quit rates are highest when behavior modification is combined with nicotine replacement therapy and tapering. Behavior modification once was conducted in person, but with the advent of a telephonic and virtual world on the Internet, behavioral approaches have been adapted to mail, telephone, and the Web for greater access and flexibility. In 2004, the U.S. Department of Health and Human Services created a toll-free number for people who want to quit: 800-QUIT-NOW (800-784-8669). This number serves as the point of contact for smokers who want information and help.

Alternative treatments

Many alternative therapies have been tried to help smokers withdraw from nicotine. Hypnosis has proved helpful in some cases, but has not been tested in controlled clinical trials. **Acupuncture**, relaxation techniques, restricted environmental stimulation therapy (REST, a combination of relaxation and hypnosis techniques), special **diets**, and herbal supplements have all been used to help people stop smoking. Of these alternative techniques, clinical studies of REST showed substantial promise in helping people stop smoking permanently.

Prognosis

Smoking is a major health risk associated with nicotine dependence. About half of all smokers die of a smoking-related illness, often **cancer**. Most lung cancers are linked to smoking, and smoking is linked to about one-third of all cancer deaths. It kills an estimated 440,000 U.S. citizens each year—more than alcohol, **cocaine**, heroin, homicide, **suicide**, car accidents, fire, and **AIDS** combined. Smoking also causes such other lung problems as chronic **bronchitis** and **emphysema**, as well as worsening the symptoms of **asthma**. Other cancers associated with smoking include cancers of the mouth, esophagus, stomach, kidney, colon, and bladder. Smoking accounts for 20% of cardiovascular deaths. It significantly increases the risk of heart disease, **heart attack**, **stroke**, and aneurysm. Women who smoke during pregnancy have more miscarriages, premature babies, and low-birth-weight babies than nonsmokers. In addition, there is a two-fold increased risk that a child born to a mother who smokes will die of **Sudden Infant Death Syndrome**, thus making smoking an avoidable factor in this tragic occurrence. Secondhand smoke also endangers the health of nonsmokers in the smoker's family or workplace. Although most of these effects are not caused directly by nicotine, it is dependence on nicotine that keeps people smoking.

Even though it is difficult for smokers to break their chemical and psychological dependence on nicotine, they should remember that most of the negative health effects of smoking are reduced or reversed after quitting. Therefore, it is worth trying to quit smoking at any age, regardless of the length of time a person has had the habit.

Prevention

The best way to avoid nicotine dependence and withdrawal is to avoid the use of tobacco products.

Resources

BOOKS

Cooper, Grant. *Never Smoke Again: The Top10 Ways to Stop Smoking Now & Forever*. Garden City Park, NY: Square One Publishers, 2007.

Henningfield, Jack E., Edythe D. London, and Sakire Pöğün. *Nicotine Psychopharmacology*. Berlin: Springer, 2009.

Miller, Michael W. ed. *Brain Development: Normal Processes and the Effects of Alcohol and Nicotine*. Oxford: Oxford University Press, 2006.

Naff, Clay Farris. *Nicotine and Tobacco*. San Diego, CA: ReferencePoint Press, Inc, 2007.

Symposium on Understanding Nicotine and Tobacco Addiction, Gregory Bock, and Jamie Goode. *Understanding Nicotine and Tobacco Addiction*. Novartis Foundation symposium, 275. Chichester, UK: John Wiley & Sons, 2006.

PERIODICALS

Berrettini W. "Nicotine addiction." *The American Journal of Psychiatry* 165 (2008): 1089–92.

Caggiula AR, EC Donny, MI Palmatier, X Liu, N Chaudhri, and AF Sved. "The role of nicotine in smoking: a dual-reinforcement model." *Nebraska Symposium on Motivation. Nebraska Symposium on Motivation*. 55 (2009): 91–109.

DiFranza JR. "Hooked from the first cigarette." *Scientific American*. 298 (2008): 82–7.
Glasser, I. "Nicotine Anonymous May Benefit Nicotine-Dependent Individuals." *American Journal of Public Health*. 100 (2010): 196.
Oncken C, E Dornelas, J Greene, H Sankey, A Glasmann, R Feinn, and HR Kranzler. "Nicotine gum for pregnant smokers: a randomized controlled trial." *Obstetrics and Gynecology*. 112 (2008): 859–67.

OTHER

Nicotine Anonymous. http://www.nicotine-anonymous.org (accessed February 4, 2010).
"Quit Smoking Today." *smokefree.gov*http://www.smokefree.gov/ (accessed February 4, 2010).

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329-4251, (800) 227–2345, http://www.cancer.org.
American Lung Association, 1740 Broadway, New York, NY, 10019, (212) 315–8700, http://www.lungusa.org.

Tish Davidson, A.M.
Emily Jane Willingham, PhD
Brenda W. Lerner

Nicotinic acid deficiency *see* **Pellagra**
Niemann-Pick disease *see* **Lipidoses**
Nifedipine *see* **Calcium channel blockers**
Night blindness *see* **Vitamin A deficiency**

Night terrors

Definition

Night terrors are a sleep disorder characterized by **anxiety** episodes with extreme panic, often accompanied by screaming, flailing, fast breathing, and sweating that usually occur within a few hours after going to sleep.

Demographics

Night terrors occur most commonly in children between the ages of three and seven, especially boys ages five to seven; however, they can also occur in girls. After the age of seven they are not common at all. Night terrors may run in families. They can also occur in adults, especially with adults who use alcohol or have emotional problems. Affected individuals usually suffer these episodes within a few hours after going to sleep. They appear to bolt up suddenly, and wake up screaming, sweating and panicked. The episode may last anywhere from five to 20 minutes. During this time, the individual is actually asleep, although the eyes may open. Quite often, nothing can be done to comfort the affected person. Very often, the person has no memory of the episode upon waking the next day.

Description

Night terrors are differentiated from nightmares in that they have been shown to occur during Stage 4 of sleep, or in REM sleep, while nightmares can occur anytime throughout the sleep cycle.

Causes and symptoms

Suffering from night terrors seems to run in families. Extreme tension or **stress** can increase the incidence of the episodes. In adults, the use of alcohol also contributes to an increased incidence of night terrors. Episodes sometimes occur after an accident involving **head injury**. Other factors thought to contribute to episodic night terrors, but not actually cause them, include:

- medications
- excessive tiredness at bedtime
- eating a heavy meal prior to bedtime drug **abuse**

Diagnosis

Night terrors are primarily diagnosed by observing the person suffering from an episode. The following symptoms are characteristic of a person suffering from a night terror:

- panic
- sweating
- gasping, moaning, crying, or screaming during sleep
- little or no recollection of the episode upon awakening

Treatment

In most cases, the individual will still be asleep as the night terror episode happens and will prove difficult to awaken. The goal should be to help the affected person go back into a calm state of sleep. The lights should be turned on, and soothing comments should be directed at the person, avoiding brusque gestures such as shaking the person or shouting to startle them out of the episode. Any form of stress should be avoided.

Individuals affected by night terrors should be evaluated by a physician if they are really severe and occur frequently. A physician can recommend the best treatment for the particular circumstances of

KEY TERMS

Benzodiazepines—A class of drugs that suppresses Stage 4 of sleep.

REM sleep—Rapid Eye Movement phase of sleep, a mentally active period during which dreaming occurs.

Sleep disorder—Any disorder that keep a person from falling asleep or staying asleep.

the night terrors. In some severe cases, the physician may prescribe a benzodiazepine tranquilizer, such as Diazepam, known to suppress Stage 4 of sleep. The physician may also refer the affected person for further evaluation by a sleep disorder specialist. It should be noted that episodic night terrors in children are normal and do not suggest the presence of psychological problems. In adults, night terrors are more likely to be related to a significant stress–related or emotional problem.

Prognosis

In children, night terror episodes in children usually end by the age of 12.

Prevention

If a child seems to have a regular pattern of night terror episodes, he should be gently awakened about 15 minutes before the episode usually happens. The child should be kept awake and out of the bed for a short period of time and then allowed to return to bed.

Since **sleep deprivation** is a strong trigger for night terror episodes, children should not be allowed to become overtired. Having children take a nap during the day may be useful.

Adults affected by night terror episodes should avoid stress, the consumption of alcohol and stimulants before going to sleep.

Resources

PERIODICALS

Stores, G. "Aspects of Parasomnias in Childhood and Adolescence." *Archives of Disease in Childhood.* 94(1) (January 2009): 63–9.

ORGANIZATIONS

American Sleep Disorders Association (ASDA), 6301 Bandel Rd., Suite 101, Rochester, MN, 55901, (507) 287–6008, http://www.asda.org.

National Foundation for Sleep and Related Disorders in Children (NFSRDC), 4200 W. Peterson, Suite 109, Chicago, IL, 60646, (708) 971–1086

Kim A. Sharp, M.L n.
Karl Finley

Nitrates *see* **Antiangina drugs**

Nitrofurantoin *see* **Urinary anti-infectives**

Nitrogen narcosis

Definition

Nitrogen narcosis is a condition that occurs in divers breathing compressed air. When divers go below depths of approximately 100 ft, increase in the partial pressure of nitrogen produces an altered mental state similar to alcohol intoxication.

Description

Nitrogen narcosis, commonly referred to as "rapture of the deep," typically becomes noticeable at 100 ft underwater and is incapacitating at 300 ft, causing stupor, blindness, unconsciousness, and even **death**. Nitrogen narcosis is also called "the martini effect" because divers experience an effect comparable to that from one martini on an empty stomach for every 50 ft of depth beyond the initial 100 ft.

Causes and symptoms

Nitrogen narcosis is caused by gases in the body acting in a manner described by Dalton's law of partial pressures: The total pressure of a gas mixture is equal to the sum of the partial pressures of gases in the mixture. As the total gas pressure increases with increasing dive depth, the partial pressure of nitrogen increases and more nitrogen becomes dissolved in the blood. This high nitrogen concentration impairs the conduction of nerve impulses and mimics the effects of alcohol or **narcotics**.

Symptoms of nitrogen narcosis include: wooziness; giddiness; euphoria; disorientation; loss of balance; loss of manual dexterity; slowing of reaction time; fixation of ideas; and impairment of complex reasoning. These effects are exacerbated by cold, **stress**, and a rapid rate of compression.

KEY TERMS

Compressed air—Air that is held under pressure in a tank to be breathed by underwater divers. A tank of compressed air is part of a diver's scuba (self-contained underwater breathing apparatus) gear.

Compression—An increase in pressure from the surrounding water that occurs with increasing diving depth.

Partial pressure—The pressure exerted by one of the gases in a mixture of gases. The partial pressure of the gas is proportional to its concentration in the mixture. The total pressure of the gas mixture is the sum of the partial pressures of the gases in it (Dalton's law of partial pressure) and as the total pressure increases, each partial pressure increases proportionally.

Diagnosis

A diagnosis must be made on circumstantial evidence of atypical behavior, taking into consideration the depth of the dive and the rate of compression. Nitrogen narcosis may be differentiated from toxicity of oxygen, carbon monoxide, or carbon dioxide by the absence of such symptoms as **headache**, seizure, and bluish color of the lips and nail beds.

Treatment

The effects of nitrogen narcosis are totally reversed as the gas pressure decreases. They are typically gone by the time the diver returns to a water depth of 60 ft. Nitrogen narcosis has no hangover or lasting effects requiring further treatment. However, a doctor should be consulted whenever a diver has lost consciousness.

Prognosis

When a diver returns to a safe depth, the effects of nitrogen narcosis disappear completely. Some evidence exists that certain divers may become partially acclimated to the effects of nitrogen narcosis with frequency—the more often they dive, the less the increased nitrogen seems to affect them.

Prevention

Helium may be used as a substitute for nitrogen to dilute oxygen for deep water diving. It is colorless, odorless, tasteless, and chemically inert. However, it is more expensive than nitrogen and drains body heat from a diver. In diving with rapid compression, the helium-oxygen mixture may produce **nausea**, **dizziness**, and trembling, but these adverse reactions are less severe than nitrogen narcosis.

Nitrogen narcosis can be avoided by limiting the depth of dives. The risk of nitrogen narcosis may also be minimized by following safe diving practices, including proper equipment maintenance, low work effort, proper buoyancy, maintenance of visual cues, and focused thinking. In addition, no alcohol should be consumed within 24 hours of diving.

ORGANIZATIONS

Divers Alert Network, 6 West Colony Place, Durham, NC, 27705, (919) 684-2948, (919) 490-6630, (800) 446-2671, http://www.diversalertnetwork.org.

Undersea and Hyperbaric Medical Society, 21 West Colony Place, Suite 280, Durham, NC, 27705, (919) 490-5140, (919) 490-5149, (877) 533-UHMS (8467), uhms@ uhms@ org, http://www.uhms.org.

Bethany Thivierge

Nitroglycerin *see* **Antiangina drugs**

Nlein purpura *see* **Allergic purpura**

NMR *see* **Magnetic resonance imaging**

Nocardia asteroides infection *see* **Nocardiosis**

Nocardiosis

Definition

Nocardiosis is a serious infection caused by a fungus-like bacterium. The infection begins in the lungs and can spread to the brain.

Description

Nocardiosis is found throughout the world among people of all ages, although it is most common in older people and males. While people with poor immunity are vulnerable to this infection, it sometimes strikes individuals who have no history of other diseases. Nocardiosis is rare in **AIDS** patients. It is not transmitted by person-to-person contact.

Causes and symptoms

Nocardiosis is caused by a bacterium of the *Nocardia* species—usually *N. asteroides*, an organism

KEY TERMS

Abscess—A localized area of infection in a body tissue. Abscesses in the brain or skin are possible complications of nocardiosis.

Meningitis—An infection of the outer covering of the brain (meninges) that can be caused by either bacteria or a virus.

that is normally found in the soil. The incubation period is not known, but is probably several weeks.

The bacteria can enter the human body when a person inhales contaminated dust. Less often, people can pick up the bacteria in contaminated puncture **wounds** or cuts.

Symptoms

The infection causes a **cough** similar to **pneumonia** or **tuberculosis**, producing thick, sometimes bloody, sputum. Other symptoms include chills, night sweats, chest **pain**, weakness, loss of appetite and weight loss. Nocardiosis does not, however, respond to short-term **antibiotics**.

Complications

In about one-third of patients, the infection spreads from the blood into the brain, causing brain abscesses. This complication can trigger a range of symptoms including severe **headache**, confusion, disorientation, **dizziness**, **nausea** and seizures, and problems in walking. If a **brain abscess** ruptures, it can lead to **meningitis**.

About a third of patients with nocardiosis also have abscesses in the skin or directly underneath the skin. They may also have lesions in other organs, such as the kidneys, liver, or bones.

Diagnosis

Nocardia is not easily identified from cultures of sputum or discharge. A doctor can diagnose the condition using special staining techniques and taking a thorough medical history. Lung biopsies or x-rays also may be required. Up to 40% of the time, however, a diagnosis can't be made until an **autopsy** is done.

Treatment

Treatment of nocardiosis includes bed rest and high doses of medication for a period of 12 to 18 months, including sulfonamide drugs or a combination of trimethoprim-sulfamethoxazole (Bactrim, Septra). If the patient doesn't respond to these drugs, antibiotics such as ampicillin (Amcill, Principen) or erythromycin (E-Mycin, Eryc) may be tried.

The abscesses may need to be drained and dead tissue cut away. Other symptoms are treated as necessary.

Prognosis

Nocardiosis is a serious disease with a high mortality rate. If it has been diagnosed early and caught before spreading to the brain, the prognosis is better. Even with appropriate treatment, however, the **death** rate is still 50%. Once the infection reaches the brain, the death rate is above 80%. This outcome is most commonly seen in patients with a weakened immune system.

Resources

BOOKS

Bordow, Richard A., Andrew L. Ries, and Timothy A. Morris. *Manual of Clinical Problems in Pulmonary Medicine*. Philadelphia: Lippincott Williams & Williams, 2005.

Carol A. Turkington

Nodule *see* **Skin lesions**

Non-A, non-B hepatitis *see* **Hepatitis C**

Non-Hodgkin's lymphomas *see* **Malignant lymphomas**

Non-melanoma skin cancer *see* **Skin cancer, non-melanoma**

Nongonococcal urethritis

Definition

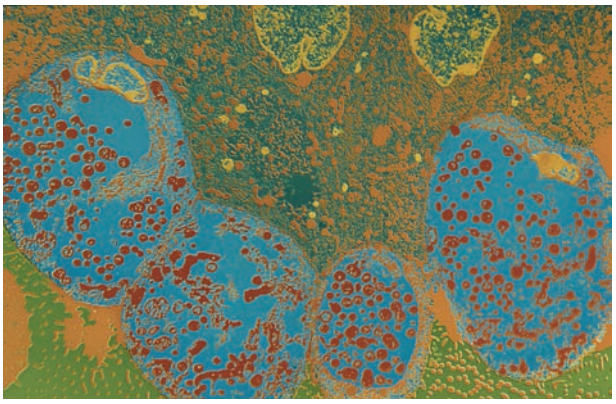
Nongonococcal urethritis (NGU) is any inflammation of the urethra not due to **gonorrhea**. NGU is almost always contracted through sexual intercourse and is found far more often in men.

Description

Men between the ages of 15 and 30 who have multiple sex partners are most at risk for nongonococcal **urethritis** (NGU), which is believed to be the most common sexually transmitted disease in the United States.

Causes and symptoms

NGU is spread almost exclusively via sexual contact, and appears most often in men because a woman's urethra is less easily infected during sex. The



A microscopic image of non-specific urethritis. This sexually transmitted disease is usually caused by a bacterium of the genus *Chlamydia*. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

infection is most often due to *Chlamydia trachomatis*, the organism that causes chlamydia. Those that aren't caused by *Chlamydia trachomatis* are usually due to another bacterium, *Ureaplasma urealyticum*. In 10% to 20% of NGU cases, the cause is unknown.

Symptoms appear within one to five weeks after infection, and include a slight clear discharge (the color of the discharge can vary from one patient to the next), and **itching** or burning during or after urination.

However, some men never develop symptoms, and women almost never show signs of infection. However, it's possible that symptoms of burning or itching in or around the vagina may be due to NGU.

The disease is communicable from the time of first infection until the patient is cured. Past infection doesn't make a person immune.

Diagnosis

Nongonococcal urethritis is diagnosed by excluding other causes, since inflammation that is not caused by gonorrhea is classified as NGU. A microscopic and/or culture test of the discharge or urine can reveal the infection.

Since many people are infected with both NGU and **syphilis** at the same time, infected patients also should have a test for syphilis before treatment for NGU begins, and three months after treatment ends.

Treatment

Antibiotics such as tetracycline or azithromycin will cure NGU; both sexual partners should be treated at the same time.

KEY TERMS

Chlamydia—One of the most common sexually transmitted diseases in the United States. It causes discharge, inflammation and burning during urination. About half of the cases of nongonococcal urethritis are due to chlamydia.

Gonorrhea—A sexually transmitted disease that affects the genital mucous membranes of men and women.

Urethra—The tube that carries urine from the bladder through the outside of the body.

Patients taking tetracycline should avoid milk or milk products and take the medication at least one hour before or two hours after meals. On the last day of treatment, a male should have a urine test to make sure the infection has cleared. If it hasn't, he should take a second course of therapy. Men should use a condom during treatment and for several months after treatment is completed.

If urine tests indicate the infection is gone but symptoms persist, the doctor will check for signs of prostate inflammation.

Prognosis

NGU is completely curable with proper antibiotic treatment. Untreated, NGU can lead to sterility in both men and women, inflammation of the mouth of the uterus, and infections of the woman's internal sexual organs. An infection during **pregnancy** may lead to **pneumonia** or eye infections in the newborn child. Untreated men may develop swelling of the testicles and an infected prostate gland.

Prevention

People can prevent the spread of NGU by:

- using a condom
- limiting the number of sex partners
- washing the genital area after sex
- if infected, avoid sexual contact; take antibiotics, notify all partners

Resources

OTHER

Sexually Transmitted Diseases Hotline. (800) 227-8922.

ORGANIZATIONS

American Social Health Association, P.O. Box 13827, Research Triangle Park, NC, 27709, (919) 361-8400, (919) 361-8425, http://www.ashastd.org/.

Carol A. Turkington

Non-nucleoside reverse transcriptase inhibitors

Definition

Non-nucleoside reverse transcriptase inhibitors (NRTI) are a type of drug that interferes with an enzyme that is key to the replication (reproduction) of the human **immunodeficiency** virus (HIV). The drug is designed to help suppress the growth of HIV, but does not eliminate it.

Purpose

This medication is used to treat patients with the HIV virus and **AIDS** in combination with one or more other AIDS drugs. Combining NRTIs with older drugs improves their ability to lower the levels of HIV in the bloodstream, and strengthens the immune system.

HIV becomes rapidly resistant to this class of drugs when they are used alone. However, in combination with older drugs, they can interfere with the virus's ability to become resistant because they attack the virus on several fronts. As the virus tries to evade one drug, another attacks. This combination can lower the level of HIV in the blood to undetectable levels.

Precautions

Patients should not discontinue this drug without first consulting a physician–even if symptoms improve.

Description

Nucleoside analogues, the first class of HIV drugs to be developed, worked by incorporating themselves into the virus's DNA, making the DNA incomplete and therefore unable to create a new virus. Non-nucleoside inhibitors work at the same stage as nucleoside analogues, but act in a completely different way, preventing the conversion of RNA to DNA.

This class of drugs includes nevirapine (Viramune) and delavirdine (Rescriptor). It may take several weeks or months before the full benefits are apparent.

KEY TERMS

Human immunodeficiency virus (HIV)—The virus that causes AIDS.

Depending on the drug prescribed, doses may start with a lower amount and be increased after a short period of time.

Risks

A mild skin rash is common; a severe skin rash can be a life-threatening reaction. Other possible side effects include **fever**, blistering skin, mouth sores, aching joints, eye inflammation, **headache**, **nausea**, and tiredness.

Because the drug passes into breast milk, **breast-feeding** mothers should avoid the drug, or not nurse until the treatment is completed.

ORGANIZATIONS

National AIDS Treatment Advocacy Project, 580 Broadway, Ste. 1010, New York, NY, 10012, (212) 219-0106, (212) 219-8473, (866) 26-NATAP, info@natap.org, http://www.natap.org.

Carol A. Turkington

Non-small cell lung cancer *see* **Lung cancer, non-small cell**

Non-tuberculous mycobacteria *see* **Mycobacterial infections, atypical**

Nonbacterial regional lymphadenitis *see* **Cat-scratch disease**

Noncholera vibrio infections *see* **Vibriosis**

Nonerosive gastritis *see* **Gastritis**

Nonsteroidal anti-inflammatory drugs

Definition

Nonsteroidal anti-inflammatory drugs are medicines that relieve **pain**, swelling, stiffness, and inflammation.

Types of nonsteroidal anti-inflammatory drugs (NSAIDS)

Over-the-counter (OTC)

Aspirin (Bayer, Bufferin)

Ibuprofen (Advil, Motrin)

Naproxen sodium (Aleve)

Prescription

Celecoxib (Celebrex®)

Diclofenac (Cataflam®, Voltaren®, Arthrotec™ [combined with misoprostol])

Diflunisal (Dolobid®)

Etodolac (Lodine®, Lodine® XL)

Fenoprofen (Nalfon®, Nalfon® 200)

Flurbiprofen (Ansaid®)

Ibuprofen (Motrin®, Tab-Profen®, Vicoprofen® [combined with hydrocodone], Combunox™ [combined with oxycodone])

Indomethacin (Indocin®, Indocin® SR, Indo-Lemmon™, Indomethagan™)

Ketoprofen (Oruvail®)

Ketorolac (Toradol®)

Mefenamic Acid (Ponstel®)

Meloxicam (Mobic®)

Nabumetone (Relafen®)

Naproxen (Naprosyn®, Anaprox®, Anaprox® DS, EC-Naprosyn®, Naprelan®, Naprapac® [copackaged with lansoprazole])

Oxaprozin (Daypro®)

Piroxicam (Feldene®)

Sulindac (Clinoril®)

Tolmetin (Tolectin®, Tolectin DS®, Tolectin® 600)

SOURCE: U.S. Food and Drug Administration, "Medication Guide for Non-steroidal Anti-Inflammatory Drugs (NSAIDS)." Available online at: http://www.fda.gov/downloads/Drugs/DrugSafety/ucm089822.pdf (accessed August 17, 2010).

(Table by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)

Purpose

Nonsteroidal anti-inflammatory drugs (NSAIDs) are prescribed for a variety of painful conditions, including arthritis, **bursitis**, **tendinitis**, **gout**, menstrual cramps, sprains, strains, and other injuries. They are also given to control the pain of **cancer** and the side effects of **radiation therapy**.

A group of researchers associated with the Women's Health Initiative reported in 2003 that regular use of **aspirin**, ibuprofen, and other NSAIDs may help to lower a woman's risk of developing **breast cancer**. Further clinical trials are needed, however, to confirm the group's findings.

Description

Nonsteroidal anti-inflammatory drugs relieve pain, stiffness, swelling, and inflammation, but they do not cure the diseases or injuries responsible for these problems. Two drugs in this category, ibuprofen and naproxen, also reduce **fever**. Some nonsteroidal anti-inflammatory drugs can be bought over the counter; others are available only with a prescription from a physician or dentist.

Among the drugs in this group are diclofenac (Voltaren), etodolac (Lodine), flurbiprofen (Ansaid), ibuprofen (Motrin, Advil, Rufen), ketorolac (Toradol), nabumetone (Relafen), naproxen (Naprosyn); naproxen **sodium** (Aleve, Anaprox, Naprelan); and oxaprozin (Daypro). They are sold as tablets, capsules, caplets, liquids, and rectal suppositories, and some are available in chewable, extended-release, or delayed-release forms.

A newer group of NSAIDs known as **COX-2 inhibitors** are being used successfully to treat patients with allergic reactions to the older NSAIDs. Their name comes from the fact that they block an enzyme known as cyclooxygenase-2, or COX-2, which is involved in the inflammation pathway. The COX-2 inhibitors are also less likely to affect the patient's digestive tract. They include such drugs as celecoxib (Celebrex), rofecoxib (Vioxx), etoricoxib (Arcoxia), and valdecoxib (Bextra). With regard to cancer treatment, some studies indicate that the use of COX-2 inhibitors may postpone the need to prescribe narcotic medications for severe pain.

Recommended dosage

Recommended doses vary, depending on the patient, the type of nonsteroidal anti-inflammatory drug prescribed, the condition for which the drug is prescribed, and the form in which it is used. Always take nonsteroidal anti-inflammatory drugs exactly as directed. If using non-prescription (over-the-counter) types, follow the directions on the package label. For prescription types, check with the physician who prescribed the medicine or the pharmacist who filled the prescription. Never take larger or more frequent doses, and do not take the drug for longer than directed. Patients who take nonsteroidal anti-inflammatory drugs for severe arthritis must take them regularly over a long time. Several weeks may be needed to feel the results, so it is important to keep taking the medicine, even if it does not seem to be working at first.

When taking nonsteroidal anti-inflammatory drugs in tablet, capsule, or caplet form, always take them with a full, 8-ounce glass of water or milk. Taking these drugs with food or an antacid will help prevent stomach irritation.

Precautions

Nonsteroidal anti-inflammatory drugs can cause a number of side effects, some of which may be very serious. These side effects are more likely when the drugs are taken in large doses or for a long time, or when two or more nonsteroidal anti-inflammatory drugs are taken together. Health care professionals can help patients weigh the risks or benefits of taking these medicines for long periods.

Do not take **acetaminophen**, aspirin, or other salicylates along with other nonsteroidal anti-inflammatory drugs for more than a few days unless directed to do so by a physician. Do not take ketorolac (Toradol) while taking other nonsteroidal anti-inflammatory drugs unless directed to do so by a physician.

Because older people are more sensitive than younger adults to nonsteroidal anti-inflammatory drugs, they may be more likely to have side effects. Some side effects, such as stomach problems, may also be more serious in older people.

Serious side effects are especially likely with one nonsteroidal anti-inflammatory drug, phenylbutazone. Patients age 40 and over are especially at risk of side effects from this drug, and the likelihood of serious side effects increases with age. Because of these potential problems, it is especially important to check with a physician before taking this medicine. Never take it for anything other than the condition for which it was prescribed, and never share it—or any other prescription drug—with another person.

Some nonsteroidal anti-inflammatory drugs can increase the chance of bleeding after surgery (including dental surgery), so anyone who is taking the drugs should alert the physician or dentist before surgery. Avoiding the medicine or switching to another type in the days prior to surgery may be necessary.

Some people feel drowsy, dizzy, confused, lightheaded, or less alert when using these drugs. Blurred vision or other vision problems also are possible side effects. For these reasons, anyone who takes these drugs should not drive, use machines or do anything else that might be dangerous until they have found out how the drugs affect them.

Nonsteroidal anti-inflammatory drugs make some people more sensitive to sunlight. Even brief exposure to sunlight can cause severe **sunburn**, **rashes**, redness, **itching**, blisters, or discoloration. Vision changes also may occur. To reduce the chance of these problems, avoid direct sunlight, especially from mid-morning to mid-afternoon; wear protective clothing, a hat, and sunglasses; and use a sunscreen with a skin protection factor (SPF) rating of at least 15. Do not use sunlamps, **tanning** booths or tanning beds while taking these drugs.

Special conditions

People with certain medical conditions and people who are taking some other medicines can have problems if they take nonsteroidal anti-inflammatory drugs. Before taking these drugs, be sure to let the physician know about any of these conditions:

ALLERGIES. Let the physician know about any **allergies** to foods, dyes, preservatives, or other substances. Anyone who has had reactions to nonsteroidal anti-inflammatory drugs in the past should also check with a physician before taking them again.

PREGNANCY. Women who are pregnant or who plan to become pregnant should check with their physicians before taking these medicines. Whether nonsteroidal anti-inflammatory drugs cause **birth defects** in people is unknown, but some do cause birth defects in laboratory animals. If taken late in **pregnancy**, these drugs may prolong pregnancy, lengthen labor time, cause problems during delivery, or affect the heart or blood flow of the fetus.

BREASTFEEDING. Some nonsteroidal anti-inflammatory drugs pass into breast milk. Women who are **breastfeeding** should check with their physicians before taking these drugs.

OTHER MEDICAL CONDITIONS. A number of medical conditions may influence the effects of nonsteroidal anti-inflammatory drugs. Anyone who has any of the conditions listed here should tell his or her physician about the condition before taking nonsteroidal anti-inflammatory drugs.

- stomach or intestinal problems, such as colitis or Crohn's disease
- liver disease
- current or past kidney disease; current or past kidney stones
- heart disease
- high blood pressure
- blood disorders, such as anemia, low platelet count, low white blood cell count
- bleeding problems
- diabetes mellitus
- hemorrhoids, rectal bleeding, or rectal irritation
- asthma
- Parkinson's disease
- epilepsy
- systemic lupus erythematosus

KEY TERMS

Anemia—A lack of hemoglobin—the compound in blood that carries oxygen from the lungs throughout the body and brings waste carbon dioxide from the cells to the lungs, where it is released.

Bursitis—Inflammation of the tissue around a joint.

Colitis—Inflammation of the colon (large bowel)

COX-2 inhibitors—A class of newer nonsteroidal anti-inflammatory drugs (NSAIDs) that are less likely to cause side effects in the digestive tract. COX-2 inhibitors work by inhibiting the production of cyclo-oxygenase-2, an enzyme involved in inflammation.

Inflammation—Pain, redness, swelling, and heat that usually develop in response to injury or illness.

Salicylates—A group of drugs that includes aspirin and related compounds. Salicylates are used to relieve pain, reduce inflammation, and lower fever.

Tendinitis—Inflammation of a tendon, which is a tough band of tissue that connects muscle to bone.

- diseases of the blood vessels, such as polymyalgia rheumatica and temporal arteritis
- fluid retention
- alcohol abuse
- mental illness

People who have sores or white spots in the mouth should tell the physician about them before starting to take nonsteroidal anti-inflammatory drugs. Sores or white spots that appear while taking the drug can be a sign of serious side effects.

SPECIAL DIETS. Some nonsteroidal anti-inflammatory drugs contain sugar or sodium, so anyone on a low-sugar or low-sodium diet should be sure to tell his or her physician.

SMOKING. People who smoke cigarettes may be more likely to have unwanted side effects from this medicine.

USE OF CERTAIN MEDICINES. Taking nonsteroidal anti-inflammatory drugs with certain other drugs may affect the way the drugs work or increase the risk of unwanted side effects.

Side effects

The most common side effects are stomach pain or cramps, **nausea**, **vomiting**, **indigestion**, **diarrhea**, **heartburn**, **headache**, **dizziness** or lightheadedness, and drowsiness. As the patient's body adjusts to the medicine, these symptoms usually disappear. If they do not, check with the physician who prescribed the medicine.

Serious side effects are rare, but do sometimes occur. If any of the following side effects occur, stop taking the medicine and get emergency medical care immediately:

- swelling or puffiness of the face
- swelling of the hands, feet, or lower legs
- rapid weight gain
- fainting
- breathing problems
- fast or irregular heartbeat
- tightness in the chest

Other side effects do not require emergency medical care, but should receive medical attention. If any of the following side effects occur, stop taking the medicine and call the physician who prescribed the medicine as soon as possible:

- severe pain, cramps, or burning in the stomach or abdomen
- convulsions
- fever
- severe nausea, heartburn, or indigestion
- white spots or sores in the mouth or on the lips
- rashes or red spots on the skin
- any unusual bleeding, including nosebleeds, spitting up or vomiting blood or dark material
- black, tarry stool
- chest pain
- unusual bruising
- severe headaches

A number of less common, temporary side effects are also possible. They usually do not need medical attention and will disappear once the body adjusts to the medicine. If they continue or interfere with normal activity, check with the physician. Among these side effects are:

- gas, bloating, or constipation
- bitter taste or other taste changes
- sweating
- restlessness, irritability, anxiety
- trembling or twitching

Some patients who have had problems with side effects from NSAIDs may benefit from **acupuncture** as an adjunctive treatment in **pain management**. A recent study done in New York found that older patients with lower back pain related to cancer reported that their pain was relieved by acupuncture with fewer side effects than those caused by NSAIDs.

Interactions

Nonsteroidal anti-inflammatory drugs may interact with a variety of other medicines. When this happens, the effects of the drugs may change, and the risk of side effects may be greater. Anyone who takes these drugs should let the physician know all other medicines he or she is taking. Among the drugs that may interact with nonsteroidal anti-inflammatory drugs are:

- blood thinning drugs, such as warfarin (Coumadin)
- other nonsteroidal anti-inflammatory drugs
- heparin
- tetracyclines
- cyclosprorine
- digitalis drugs
- lithium
- phenytoin (Dilantin)
- zidovudine (AZT, Retrovir).

NSAIDs may also interact with certain herbal preparations sold as dietary supplements. Among the herbs known to interact with NSAIDs are bearberry (*Arctostaphylos uva-ursi*), feverfew (*Tanacetum parthenium*), evening primrose (*Oenothera biennis*), and gossypol, a pigment obtained from cottonseed oil and used as a male contraceptive. In most cases, the herb increases the tendency of NSAIDs to irritate the digestive tract. It is just as important for patients to inform their doctor of herbal remedies that they take on a regular basis as it is to give the doctor a list of their other prescription medications.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Lehne, Richard A. *Pharmacology for Nursing Care*. 6th ed. St. Louis: Saunders Elsevier, 2007.

Wilson, Billie A., et al. *Nurses Drug Guide 2008*. Upper Saddle River, NJ: Prentice Hall, 2008.

PERIODICALS

Birbara, C. A., A. D. Puopolo, D. R. Munoz, et al. "Treatment of Chronic Low Back Pain with Etoricoxib, A New Cyclo-Oxygenase-2 Selective Inhibitor: Improvement in Pain and Disability—A Randomized, Placebo-Controlled, 3-Month Trial." *Journal of Pain* 4 (August 2003): 307–315.

Gordon, D. B. "Nonopioid and Adjuvant Analgesics in Chronic Pain Management: Strategies for Effective Use." *Nursing Clinics of North America* 38 (September 2003): 447–464.

Graf, C., and K. Puntillo. "Pain in the Older Adult in the Intensive Care Unit." *Critical Care Clinics* 19 (October 2003): 749–770.

Harris, R. E., R. T. Chlebowski, R. D. Jackson, et al. "Breast cancer and Nonsteroidal Anti-Inflammatory Drugs: Prospective Results from the Women's Health Initiative." *Cancer Research* 63 (September 15, 2003): 6096–6101.

Hatsiopoulou, O., R. I. Cohen, and E. V. Lang. "Postprocedure Pain Management of Interventional Radiology Patients." *Journal of Vascular and Interventional Radiology* 14 (November 2003): 1373–1385.

Meng, C. F., D. Wang, J. Ngeow, et al. "Acupuncture for Chronic Low Back Pain in Older Patients: A Randomized, Controlled Trial." *Rheumatology (Oxford)* 42 (December 2003): 1508–1517.

Perrone, M. R., M. C. Artesani, M. Viola, et al. "Tolerability of Rofecoxib in Patients with Adverse Reactions to Nonsteroidal Anti-Inflammatory Drugs: A Study of 216 Patients and Literature Review." *International Archives of Allergy and Immunology* 132 (September 2003): 82–86.

Raffa, R. B., R. Clark-Vetri, R. J. Tallarida, and A. I. Wertheimer. "Combination Strategies for Pain Management." *Expert Opinion in Pharmacotherapy* 4 (October 2003): 1697–1708.

Small, R. C., and A. Schuna. "Optimizing Outcomes in Rheumatoid Arthritis." *Journal of the American Pharmaceutical Association* 43, no. 5, Supplement 1 (September-October 2003): S16–S17.

Stephens, J., B. Laskin, C. Pashos, et al. "The Burden of Acute Postoperative Pain and the Potential Role of the COX-2-Specific Inhibitors." *Rheumatology (Oxford)* 42, Supplement 3 (November 2003): iii40–iii52.

ORGANIZATIONS

United States Food and Drug Administration (FDA), 10903 New Hampshire Ave, Silver Spring, MD, 02993-0002, (888) 463-6332, http://www.fda.gov.

Nancy Ross-Flanigan
Rebecca J. Frey, PhD

Nontropical sprue *see* **Celiac disease**

Nonvenereal syphilis *see* **Bejel**

Norfloxacin *see* **Fluoroquinolones**

Noroviruses

Definition

Noroviruses are a group of related, single-stranded RNA (ribonucleic acid) viruses that cause infection resulting in acute **gastroenteritis** in humans. Gastroenteritis, also commonly called stomach flu, involves an inflammation of the gastrointestinal tract, which results in **diarrhea**, abdominal **pain**, and **vomiting**. The infection caused by noroviruses is very highly contagious, being commonly spread through water or food that has been contaminated with fecal matter; or through contact with an infected person. Norovirus infections occur frequently in closed, and often-times crowded, environments where the viruses can quickly spread. Such places include as hospitals and medical facilities, schools, nursing/retirement homes and day-care facilities, and cruise ships.

Demographics

Anyone can become infected with a norovirus. During norovirus outbreaks there are high rates of infection among people of all ages. There are a large number of genetically distinct strains of noroviruses. Immunity appears to be specific for the norovirus strain and lasts for only a few months. Therefore, norovirus infection can recur throughout a person's lifetime. Because of genetic (inherited) differences among humans, some people appear to be more susceptible to norovirus infection and may suffer more severe illness. People with type O blood are at the highest risk for severe infection.

Description

Norovirus infection is caused by a variety of viruses. All such viruses cause acute gastroenteritis, an inflammation of the stomach and intestines. The illness is highly contagious, and usually requires professional medical care to treat the most serious of the symptoms, which often times included **dehydration**, bloody stool, abdominal pain, and **vomiting**. Noroviruses are difficult to eliminate in the environment because they can withstand very high and low temperatures, along with being able to resist most disinfectants.

Noroviral infection

Noroviruses are a major cause of viral gastroenteritis—an inflammation of the linings of the stomach and small and large intestines that causes vomiting and diarrhea. Viruses are responsible for 30 to 40% of all cases of infectious diarrhea, and viral gastroenteritis is the second most common illness in the United States, exceeded only by the **common cold**.

Infected individuals are contagious from the first onset of symptoms until at least three days after full recovery. Some people may remain contagious for as long as two weeks after recovery.

Gastroenteritis

Gastroenteritis often is referred to as the stomach flu even though the flu is a respiratory illness caused by an **influenza** virus. Other common names for viral gastroenteritis include:

- food poisoning
- winter-vomiting disease
- non-bacterial gastroenteritis
- calicivirus infection.

The U.S. Centers for Disease Control and Prevention (CDC) estimate, in 2010, that noroviruses are responsible for some 21 million cases of acute gastroenteritis in the United States every year. Epidemiologists estimate that about 50,000 Americans are hospitalized annually and about 400 people die each year because of norovirus infection. However, the CDC reported in 2006 that many reports of acute gastroenteritis go unreported. Consequently, the U.S. health organization suggests that up to 300,000 hospitalizations occur annually and about 5,000 deaths occur each year, all due to noroviruses. In developing countries, noroviruses are a major cause of human illness. The CDC estimate that about 900,000 visits to clinics and other medical facilities by children in developed countries of the world result in about 64,000 hospitalizations. Even worse, about 200,000 children under the age of five years die from noroviruses each year in developing countries of the world.

Gastroenteritis caused by infection with a norovirus is rarely a serious illness. Typically an infected person suddenly feels very ill and may vomit many times in a single day. The symptoms, although quite unpleasant, usually last only 24 to 60 hours.

Transmission

Noroviruses are ubiquitous in the environment. They are highly contagious and are considered to be among the most infectious of viruses. The reasons for this include:

- Only a small number of viral particles—as few as 10—are required for infection.
- Although noroviruses cannot reproduce outside of their human hosts, they can remain viable for weeks or even months on objects and surfaces.

- Human immunity to norovirus is short-lived and strain-specific.

Noroviruses are transmitted among people by a fecal-oral route, either by ingestion of food or water contaminated with feces or by contact with the vomit or feces of an infected person. Norovirus infection can occur by:

- consuming contaminated food or liquids
- hand contact with contaminated objects or surfaces, followed by hand contact with the mouth
- contact with an infected person, including caring for the sick person or sharing food or utensils
- aerosolized vomit that is swallowed or that contaminates surfaces.

Environmental contamination or contact with infected clothing or linen also may be a source of transmission. Although evidence is not available that norovirus infection can occur via the respiratory system, the sudden and violent vomiting of noroviral gastroenteritis can lead to contamination of the surroundings and of public areas. Particles laden with virus can be suspended in the air and swallowed.

FOODBORNE TRANSMISSION. Noroviruses account for at least 50% of food-related outbreaks of gastroenteritis. A European study, published in 2010, showed that 21% of all norovirus outbreaks are caused by foodborne transmission. In addition, 25% of the outbreaks were initially reported to be "food handler-associated." This was later found to be caused from contamination of the food source. In addition, restaurant or catered foods are common sources of norovirus transmission, with subsequent infection of household members. The majority of norovirus outbreaks occur via contamination by a food handler immediately before the food is consumed.

Foods that frequently are associated with norovirus outbreaks include:

- foods that are eaten without further cooking, including sandwiches, salads, and bakery products
- liquids such as salad dressing or cake icing in which the virus becomes evenly distributed
- food that is contaminated at its source, including oysters and clams from contaminated waters and raspberries irrigated with sewage-contaminated water
- food that becomes contaminated before distribution, including salads and frozen fruit.
- Shellfish, including oysters and clams, concentrate norovirus from contaminated water in their tissues. Steaming shellfish may not completely inactivate the virus.

WATERBORNE TRANSMISSION. There is widespread norovirus contamination of rivers and seas, often with more than one strain of the virus. Waterborne outbreaks of norovirus have been associated with:

- sewage-contaminated wells
- contaminated municipal water systems
- stream and lake water
- swimming pools and spas
- commercial ice.

Outbreaks

Norovirus infection can spread rapidly through daycare centers, schools, prisons, hospitals, nursing homes, camps, and other confined spaces. Norovirus is responsible for about 40% of group- or institution-related outbreaks of diarrhea. Outbreaks usually peak during the winter months.

In 2008, it was reported that outbreaks of the norovirus occurred on several university campuses in California, Michigan, and Wisconsin. The CDC, along with state and local health departments, found that approximately 1,000 cases of illness resulted from these outbreaks, including 10 hospitalizations. In addition, one college campus was closed temporarily due to an outbreak.

Cruise ships have become notorious for norovirus outbreaks among passengers and staff. Cruise ships and naval vessels are at increased risk for contamination when docking in regions that lack adequate sanitation and where contaminated food or water may be brought onboard. Close living quarters and the arrival of new, susceptible passengers every one to two weeks exacerbate outbreaks on cruise ships. Norovirus outbreaks have been reported to continue through more than 12 successive cruises on a single ship.

Noroviruses are relatively rare on cruise ships but they do happen. In 2006, the CDC reported that 34 cases of norovirus were reported, while 27 were reported in 2007, 15 in 2008, and 13 in 2009—all from cruises originating from U.S. ports. In 2010, for instance, the Celebrity Cruises company had about 15% of its passengers come down with norovirus-like symptoms on its cruise ship that departed from Charleston, South Carolina, on February 15, 2010. A year before the incident, a paper published in the medical journal *Clinical Infectious Diseases* found that a large number of norovirus outbreaks on cruise ships were the result of dirty public restroom facilities. However, in 2010, the CDC reported that the trend was down for contracting a norovirus on a cruise ship sailing from a

U.S. port. In fact, the incidence of noroviruses on a cruise ship was at a decade-long low as of January 2010. The International Council of Cruise Lines reported that less than 1% of passengers become infected with norovirus each year. As reported by the CDC the outbreaks on cruise ships during the 2000s were on the decline. However, it is too early in the 2010s to tell if the trend will continue.

Generally, outbreaks of norovirus appear on the increase. Near the end of the 2000s, the CDC reported that norovirus outbreaks were increasing in many closed, crowded facilities across the country.

Risk factors

Humans are at increased risk from contracting noroviruses if they:

- travel frequently on cruise ships or stay at lodging establishments where many people are living in close surroundings
- live with children that attend school or day care
- have a weakened immune system
- live in nursing homes, retirement centers, or other such facilities.

Causes and symptoms

Norovirus strains

Noroviruses lack outer envelopes and their genetic material is carried as single-stranded RNA rather than DNA (deoxyribonucleic acid). Although noroviruses are not new, the extent of norovirus infection was not recognized until the 1990s. This has led to increased research on noroviruses and more monitoring of outbreaks.

Until 2004 noroviruses were commonly referred to as:

- Norwalk virus
- Norwalk-like viruses (NLVs)
- caliciviruses
- small, round-structured viruses (SRSVs).

Noroviruses are named after the original strain—the Norwalk virus—that caused an outbreak of gastroenteritis in a Norwalk, Ohio, school in 1968. The virus was identified in 1972. Since then many related viruses have been identified. In 2004, these viruses were grouped together in the genus *Norovirus* within the Caliciviridae family of viruses. Eight to 10 distinct genogroups of norovirus have been found in various parts of the world. There are five common genogroups and, of those, three (GI, GII, and GIV) affect humans. Each of these groups can be further differentiated into at least 20 genetic clusters. Evidence suggests that noroviruses in different genetic clusters can recombine to form new, genetically distinct noroviruses. As of 2010, GII strains, especially GII4, are the most prevalent, and have caused the most norovirus outbreaks since 2002. However the most common method of identifying noroviruses—the reverse transcription-polymerase chain reaction (RT-PCR)—may not always identify GII genetic clusters correctly.

The increased number of norovirus outbreaks in European countries in the early 2000s—occurring in the spring and summer rather than in winter—were found to be associated with the emergence of a new variant of the GII4 strain. Increased international outbreaks in 2003 and 2004 also were caused by a GII4-related norovirus that was found to mutate rapidly. Mutations in the viral capsid—the virus' outer protective layer—were used to determine the predominant routes of norovirus transmission.

Then, in the first quarter of 2010, 334 cases of norovirus were reported at 65 different locations within the United Kingdom, Norway, France, Sweden, and Denmark. All of the cases were associated with the eating of raw oysters. The International Society of Infectious Diseases reports that the Rapid Alert System for Food and Feed database contained 19 reports of norovirus in oysters between March 2006 and March 2010—all within the European Union.

Symptoms

Symptoms of norovirus infection usually appear within 24–48 hours after exposure, with a median incubation period during outbreaks of 33–36 hours. However symptoms can occur as early as 12 hours or less after exposure.

Typical symptoms of norovirus infection are:

- nausea
- vomiting
- fever
- malaise (general feeling of sickness)
- watery or loose diarrhea without blood
- abdominal cramping and pain
- bloody stool
- dehydration
- weight loss.

Among children, vomiting is the predominant symptom, whereas diarrhea is more common in adults. Vomiting can be frequent and violent and may occur without warning.

Additional symptoms of norovirus infection may include:

- low-grade fever
- chills
- headache
- muscle aches
- fatigue.

Dehydration is the major risk from gastroenteritis caused by norovirus, particularly among infants, young children, the elderly, and those with underlying health conditions. Symptoms of dehydration include:

- dry mouth
- increased or excessive thirst
- low urine output
- nausea
- dizziness or faintness
- sunken eyes
- sunken fontanelle—the soft spot on an infant's head
- confusion.

As many as 30–50% of norovirus infections do not produce symptoms. It is not known whether individuals with asymptomatic infections can transmit the virus.

Diagnosis

Identifying noroviruses

Viral gastroenteritis usually is diagnosed on the basis of the symptoms. Many types of viruses cause gastroenteritis. Rotoviruses are a leading cause of gastroenteritis in children who then transmit the virus to adults. In addition to noroviruses, viral gastroenteritis in humans can be caused by another genus of viruses within the Caliciviridae family. Formerly known as the Sapporo-like virus, or classic or typical calicivirus, these now are grouped in the genus *Sapovirus*. Other genera in the Caliciviridae family are not pathogenic in humans. Some bacteria and parasites also cause illnesses that are similar to norovirus infection.

The cloning and sequencing of noroviruses in the early 1990s made it easier to identify norovirus outbreaks. RT-PCR is the most commonly used method for identifying norovirus. With this technique the virus' RNA is used as the template for transcribing the corresponding DNA using the enzyme reverse transcriptase. The DNA is amplified into many copies using the polymerase chain reaction. Many state public health laboratories use this method to detect norovirus in vomit and stools. The best identification usually comes from stool samples taken within 48–72 hours after the onset of symptoms; however norovirus can be detected in stool samples taken five days after the onset of symptoms and sometimes even in samples taken up to two weeks after recovery.

Norovirus from fecal samples can be visualized using electron microscopy. With immune electron microscopy (IEM), antibodies against norovirus are collected from blood serum and used to trap and visualize the virus from fecal samples. However these methods require high concentrations of norovirus in the stool, as well as a fourfold increase in norovirus-specific antibodies in blood samples taken during the acute or recovery phases of gastroenteritis.

Enzyme-linked immunosorbent assays may be used to detect noroviruses in fecal samples. In these assays noroviral-specific antibodies bound to the virus are detected by the reaction of an enzyme that is attached to the antibody. Nucleic acid probes that hybridize with noroviral RNA also can be used for virus detection in feces.

A Japanese chemical company was producing a reagent kit that can be used to detect norovirus in two hours rather than the 12–24 hours needed for conventional detection. Other simpler methods for rapidly identifying norovirus are under development. As of 2010, further research is continuing on commercial devices for detecting norovirsuses. For example, scientists at the Department of Infectious Diseases, Osaka Prefectural Institute of Public Health (Osaka, Japan) are developing modified reagent kits for norovirus genogroups I and II. They reported their advancement in the *Journal of Medical Virology* (December 2009).

Investigating outbreaks

Epidemiological studies often involve sequencing the norovirus RNA. This can help to determine whether outbreaks in different geographical locations are connected to each other and can help trace the source of the norovirus to contaminated food or water. CaliciNet is a database that stores the RNA sequences of all norovirus strains that cause gastroenteritis in the United States.

Criteria that are sometimes used to determine whether an outbreak of gastroenteritis is caused by a norovirus include:

- a mean incubation period of 24–48 hours
- a mean duration time for illness of 12–60 hours
- vomiting in more than 50% of patients
- failure to find a bacterial cause for the illness.

During investigations of norovirus outbreaks, food handlers may be asked to provide a stool sample and possibly a blood sample. Food rarely is tested for norovirus since each type of food requires a specific assay. However, tests are used to detect the virus in shellfish. When large amounts—1–26 gallons (5–100 liters)—of water are processed through specially designed filters, the norovirus can be concentrated and assayed by RT-PCR.

Treatment

Gastroenteritis caused by noroviruses usually resolves itself without treatment within a very few days. As of 2010, medications or vaccines are not available that are effective against the norovirus. Viruses are not affected by **antibiotics** and antidiarrheal medications may prolong the infection.

Norovirus infections should be treated by:

- drinking plenty of fluids, such as water and juice, to prevent dehydration caused by vomiting and diarrhea
- intravenous fluids if severe nausea prevents drinking, particularly in small children
- drinking oral rehydration fluids (ORFs) to prevent dehydration and to replace electrolytes (salt and minerals) and glucose
- avoiding alcohol and caffeine which can increase urination.

Commercially available ORFs include Naturalyte, Pedialyte, Infalyte, and Rehydralyte.

Juice, soda, and water do not replace lost electrolytes; nor do sports drinks replace nutrients and **minerals** lost through vomiting and diarrhea. In fact, drinks containing sugar may make diarrhea worse. Those taking **diuretics** should ask their healthcare provider whether to stop taking the medication during acute diarrhea.

Since the risk of dehydration is higher for infants and young children, the number of wet diapers per day should be closely monitored. Severely dehydrated children may receive rapid **intravenous rehydration** in a hospital or emergency-room setting.

A health care provider should be consulted if:

- symptoms of dehydration appear
- diarrhea persists for longer than a few days
- there is blood in the stool.

Alternative treatment

An infusion of meadowsweet (*Filipendula ulmaria*) may reduce **nausea**. Once the symptoms are reduced, slippery elm (*Ulmus fulva*) may calm the digestive system. Castor oil packs placed on the abdomen can reduce inflammation and discomfort.

Homeopathic remedies for gastroenteritis include *Arsenicum album*, **ipecac**, and *Nux vomica*. Chinese patent herbal remedies include Po Chai and Pill Curing.

During recovery from viral gastroenteritis, live cultures of *Lactobacillus acidophilus*, found in live-culture yogurt or as powder or capsules, may be useful for restoring the native flora of the digestive tract.

Prognosis

Norovirus infection is usually followed by complete recovery. Any long-term health effects are not known. Infected persons do not become long-term carriers of the virus. However, in some cases dehydration can become a very serious possible consequence of noroviral infection and can be fatal, particularly among young children, older people, and anyone with debilitating medical conditions or impaired immune systems.

Prevention

Noroviruses are difficult to destroy. They can survive freezing as well as temperatures as high as 140°F (60°C). Noroviruses can survive chlorine levels as high as 10 parts per million (ppm), far higher than the levels present in most public water systems. A 2004 study from the Netherlands found that inactivation of norovirus with 70% ethanol was inefficient and that **sodium** hypochlorite solutions were effective only at concentrations above 300 ppm.

The best prevention against noroviral infection is frequent, thorough hand washing with soap and water. All soaped hand surfaces should be rubbed vigorously for at least 10 seconds. The hands should be thoroughly rinsed under a stream of water. In particular hands always should be washed before handling food and after using the toilet or changing diapers.

Other important measures for preventing norovirus infection include:

- proper handling of cold foods
- careful washing of fruits and vegetables
- steaming oysters before eating, although even this may be insufficient for destroying norovirus
- taking particular care when handing the diapers of children with diarrhea
- properly disposing of sewage and diapers
- excluding sick infants and children from food preparation areas.

KEY TERMS

Antibody—A blood protein produced in response to foreign material such as a virus; the antibody attaches to the virus and destroys it.

Calicivirus—A member of the Caliciviridae family of viruses that includes noroviruses.

Capsid—The outer protein coat of a virus.

Gastroenteritis—An inflammation of the lining of the stomach and intestines, usually caused by a viral or bacterial infection.

Genetic cluster—A group of viral strains with very similar, yet distinct, nucleic acid sequences.

Genogroup—Related viruses within a genus; may be further subdivided into genetic clusters.

Reverse transcription-polymerase chain reaction (RT-PCR)—A method of polymerase-chain-reaction amplification of nucleic acid sequences that uses RNA as the template for transcribing the corresponding DNA using reverse transcriptase.

To prevent further transmission of norovirus:

- All surfaces exposed to vomit or otherwise contaminated should be immediately cleaned and disinfected with a solution of between 5 to 10% bleach, followed by rinsing.
- Contaminated clothing and linens should be removed immediately and washed with hot water and detergent on the maximum machine cycle and with a minimum of handling, followed by machine drying.
- Vomit and feces should be discarded or flushed immediately and the toilet area should be kept clean.
- Exposed or contaminated food should be discarded.
- Masks may be worn while cleaning areas that have been badly contaminated with vomit or feces, such as in hospitals or nursing homes.
- Stay home and do not go to work or school in order to prevent further passing on of the virus.

Scientific studies have found that detergent-based cleaning with a cloth consistently fails to eliminate norovirus contamination. With fecal contamination, detergent-based cleaning, followed by cleaning with a combination hypochlorite/detergent formula containing 5,000 ppm of available chlorine significantly reduced contamination. However, norovirus still could be detected on as much as 28% of the surfaces. When this procedure failed to eliminate contamination, the virus was transmitted to the cleaner's hands. Contaminated fingers consistently transferred norovirus to up to seven different surfaces including doorknobs and telephones. However the contamination was diluted during secondary transmission and treatment with the combined bleach/detergent eliminated the virus without prior cleaning.

In situations where there is a periodic renewal of susceptible people, such as on cruise ships and at camps, the facility may have to be closed until cleaning is complete. Although many state and local health departments require that food handlers with gastroenteritis not return to work until two to three days following recovery, this may not be an adequate length of time to prevent noroviral transmission.

The prevention of norovirus outbreaks include reducing contamination of water supplies with human waste and using high-level chlorination—at least 10 ppm for more than 30 minutes. Surveillance of shorelines for potential sources of fecal contamination and for boats that are dumping human waste may help prevent shellfish-associated norovirus outbreaks.

In 2004, researchers at Washington University (St. Louis, Missouri) became the first to grow a norovirus in a laboratory setting. They grew a mouse norovirus, with the goal of studying the virus and developing a vaccine against it. Research is ongoing in the early 2010s. New surveillance systems also are being developed to detect norovirus outbreaks at an early stage.

Resources

BOOKS

Richman, Douglas D., et al., editors. *Clinical Virology*. 3rd ed. Washington, D.C.: ASM Press, 2009.

PERIODICALS

"Use of Norovirus Genotype Profiles to Differentiate Origins of Foodborne Outbreaks." *Emerging Infectious Diseases* April 16, 2010: 16(4).

OTHER

Application of a Modified Loop-mediated Isothermal Amplification Kit for Detecting Norovirus Genogroups I and II. National Library of Medicine and National Institutes of Health. (December 2009), *http://www.ncbi.nlm.nih.gov/pubmed/19856470* (accessed September 17, 2010).

Celebrity Cruises ship in Caribbean Hit by Major Outbreak of Stomach Illness.USA Today. (February 22, 2010), *http://travel.usatoday.com/cruises/legacy/item.aspx?*

type=blog&ak;=80136.blog(accessed September 17, 2010).

Norovirus. Division of Viral Diseases, Centers for Disease Control and Prevention. (February 23, 2010), *http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus.htm* (accessed September 15, 2010).

Norovirus. Environmental Health Services, Centers for Disease Control and Prevention. (February 3, 2010), *http://www.cdc.gov/nceh/ehs/Topics/norovirus.htm* (accessed September 15, 2010).

Norovirus Cultured for the First Time. Public Library of Science Biology. (November 30, 2004), *http://www.plosbiology.org/article/info:doi%2F10.1371%2Fjournal.pbio.0020445* (accessed September 15, 2010).

Norovirus Infection. Mayo Clinic. (April 8, 2009), *http://www.mayoclinic.com/health/norovirus/DS00942* (accessed September 15, 2010).

Norovirus Outbreaks on Cruise Ships Drop to Lowest Level in Nearly a Decade.USA Today. (January 5, 2010), *http://travel.usatoday.com/cruises/legacy/item.aspx?type=blog&ak;=13584.blog* (accessed September 17, 2010).

Norovirus Outbreaks on Three College Campuses — California, Michigan, and Wisconsin, 2008. MMWR Weekly, Centers for Disease Control and Prevention. (October 9, 2009), *http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5839a2.htm* (accessed September 17, 2010).

Norovirus, Oysters — Europe: (UK, Norway, France, Sweden, Denmark). International Society of Infectious Diseases. (March 25, 2010), *http://www.promedmail.org/pls/otn/f?p=2400:1001:8352811240744308::NO::F2400_P1001_BACK_PAGE,F2400_P1001_PUB_MAIL_ID:1011,81927* (accessed September 17, 2010).

Scientists Grow Norovirus in Lab. Washington University. (December 9, 2004), *http://news.wustl.edu/news/Pages/4418.aspx* (accessed September 17, 2010).

Study: Dirty Restrooms on Cruise Ships Linked to Norovirus Outbreaks.USA Today. (November 4, 2009), *http://travel.usatoday.com/cruises/legacy/item.aspx?type=blog&ak;=620000957.blog* (accessed September 17, 2010).

ORGANIZATIONS

National Health Information Center. Office of Disease Prevention and Health Promotion. U.S. Department of Health and Human Services, Post Office Box 1133, Washington, DC, 20013-1133, (847) 434-4000, http://www.health.gov/nhic/.

Office of Health Communication. National Center for Infectious Diseases. Centers for Disease Control and Prevention, Mailstop C-14, 1600 Clifton Rd., Atlanta, GA, 30333, (800) 311-3435, http://www. cdc.gov/ncidod/index.htm.

Norplant *see* **Depo-Provera/Norplant**

Norwalk virus infection *see* **Gastroenteritis**

Nose injuries *see* **Nasal trauma**

Nose irrigation *see* **Nasal irrigation**

Nose job *see* **Rhinoplasty**

Nose packing *see* **Nasal packing**

Nose papillomas *see* **Nasal papillomas**

Nose polyps *see* **Nasal polyps**

Nosebleed

Definition

A nosebleed is bleeding from the nose; the medical term for it is epistaxis.

Description

Unexpected bleeding from anywhere is cause for alarm. Persistent bleeding should always be investigated because it may be the earliest sign of **cancer**. Fortunately, nosebleeds are rarely a sign of cancer. A much more common cause of nosebleeds is injury from picking, blowing, or fisticuffs. People with hay fever have swollen membranes that are fragile and more likely to bleed.

Most nosebleeds (about 90%) come from the front of the septum, that plane of cartilage that separates the nostrils. These are called anterior nosebleeds. The lower front part of the septum has a mass of blood vessels on either side called Kiesselbach's plexus that is easy to injure. Nosebleeds from the more remote reaches of the nose are called posterior nosebleeds. They are less common, are less likely to have a benign cause, and are much harder to manage.

Nosebleeds are most likely to occur in children between the ages of two and 10 years, in part because younger children frequently insert small objects in the nose or pick at the tissues lining the nose. Nosebleeds in adolescents may indicate cocaine abuse. Nosebleeds in older adults may result from arteriosclerosis or high blood pressure.

Causes and symptoms

Nosebleeds may result from a number of different causes:

- local infections (colds, sinus infections)
- systemic infections (scarlet fever, typhoid fever, malaria)
- drying of the membranes lining the nose, often during heating season in colder climates

KEY TERMS

Cautery—The use of heat, electricity, or chemicals to destroy tissue.

Embolization—A technique for stopping bleeding by introducing a substance into larger blood vessels that blocks or closes them.

Epistaxis—The medical term for nosebleed.

Kiesselbach's plexus—An area on the anterior part of the nasal septum that has a rich supply of blood vessels and is a common site of nosebleeds. It is named for Wilhelm Kiesselbach, a 19th-century German otolaryngologist.

Septum—The partition that separates the two nostrils. It consists of membranes, cartilage, and bone.

Styptic—Any remedy with an astringent and hemostatic (stopping bleeding) quality.

- medications, most commonly, overuse of nasal decongestant sprays
- trauma (from foreign objects in the nose; scratching or picking with the fingers; or blunt trauma to the face)
- tumors in the nasopharynx or paranasal sinuses
- cocaine abuse
- bleeding disorders (leukemia, liver disease, hemophilia and other hereditary clotting disorders)

Treatment

The first treatment is to pinch the patient's nostrils together, have them sit forward, and ask them to stay that way for 5–10 minutes. This method usually stops nosebleeds originating in Kiesselbach's plexus. The patient should not tilt his or her head backward, as this position may cause blood to drip backward into the throat or windpipe. It is best to hold the head upright.

In the case of small children, the doctor may examine the inside of the nose to check for foreign bodies, evidence of scratching or picking, etc. Small foreign bodies (watch batteries, dried peas or beans, buttons, etc.) can be removed by suction if necessary. The doctor may also have to remove clotted blood by suction.

Bleeding that continues originates from the back of the nose in most cases and will flow down the throat. If that happens, emergency intervention is needed.

As an emergency procedure, the nose will be packed front and/or back with cotton gauze and a rubber balloon from a Foley catheter. This treatment is not comfortable. Having no place to flow, the blood should clot, giving the ear, nose and throat specialists (otorhinolaryngologists) a chance to find the source and permanently repair it. If the packing has to remain for any length of time, **antibiotics** and **pain** medication will be necessary—antibiotics because the sinuses will be plugged up and prone to infection. Nose packing may so interfere with breathing that the patient will need supplemental oxygen.

Newer options for controlling posterior nosebleeds include the use of Surgicel, Merocel, or other oxidized cellulose products that expand with moisture. These may control the bleeding without the need for bulky **nasal packing**.

Many bleeds are from small exposed blood vessels with no other disease. They can be destroyed by cautery, usually done by applying silver nitrate to the affected area. Larger vessels may not respond to cautery. The surgeon may have to tie them off, which is known as ligation. Another technique that is sometimes used with larger vessels is embolization, in which the doctor injects a chemical to block or close the blood vessel.

Alternative treatment

Estrogen cream, the same preparation used to revitalize vaginal tissue, can toughen fragile blood vessels in the anterior septum and forestall the need for cauterization. Botanical medicines known as styptics, which slow down and can stop bleeding, may be taken internally or applied topically. Some of the plants used are *Achillea* (yarrow), trillium, geranium, and shepherd's purse (*Capsella bursa-pastoris*). Homeopathic remedies can be one of the quickest and most effective treatments for epistaxis.

Prevention

Both before and after a nosebleed, the patient should blow the nose gently and avoid picking or scratching the tissues that line it. Children with recurrent nosebleeds during heating season may benefit from the use of a cool-mist vaporizer to humidify the bedroom at night, or from the application of a small quantity of petroleum jelly to the inside of each nostril.

Treatment of hay fever helps reduce the fragility of the tissues.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

Bhatnagar, R. K., and S. Berry. "Selective Surgicel Packing for the Treatment of Posterior Epistaxis." *Ear, Nose, and Throat Journal* 83 (September 2004): 633–634.

Gurney, T. A., C. F. Dowd, and A. H. Murr. "Embolization for the Treatment of Idiopathic Posterior Epistaxis." *American Journal of Rhinology* 18 (September-October 2004): 335–339.

ORGANIZATIONS

American Academy of Family Physicians (AAFP), 11400 Tomahawk Creek Parkway, Leawood, KS, 66211-2680, (913) 906-6000, (913) 906-6075, (800) 271-2237, http://www.aafp.org/.

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703) 836-4444, http://www.entnet.org.

J. Ricker Polsdorfer, MD
Rebecca J. Frey, PhD

Nosocomial infections *see* **Hospital-acquired infections**

NS *see* **Nephrotic syndrome**

NSAIDs *see* **Nonsteroidal anti-inflammatory drugs**

Nther's disease *see* **Porphyrias**

Nuclear magnetic resonance *see* **Magnetic resonance imaging**

Nucleoside analogs *see* **Antiretroviral drugs**

Numbness and tingling

Definition

Numbness and tingling are decreased or abnormal sensations caused by altered sensory nerve function.

Demographics

People of all ages experience episodes of numbness and tingling; however, these generally become more common as people age. Episodes of numbness and tingling are more common among people with diabetes, **hypothyroidism**, **alcoholism**, **malnutrition**, or who experience mechanical trauma, especially to their limbs, neck, or spine.

Description

The feeling of having a foot "fall asleep" is a familiar one. This same combination of numbness and tingling can occur in any region of the body and may be caused by a wide variety of disorders. Sensations such as these, which occur without any associated stimulus, are called paresthesias. Other types of paresthesias include feelings of cold, warmth, burning, **itching**, and skin crawling.

Causes and symptoms

Causes

Sensation is carried to the brain by neurons (nerve cells) running from the outer parts of the body to the spinal cord in bundles called nerves. In the spinal cord, these neurons make connections with other neurons that run up to the brain. Paresthesias are caused by disturbances in the function of neurons in the sensory pathway. This disturbance can occur in the central nervous system (the brain and spinal cord), the nerve roots that are attached to the spinal cord, or the peripheral nervous system (nerves outside the brain and spinal cord).

Peripheral disturbances are the most common cause of paresthesias. "Falling asleep" occurs when the blood supply to a nerve is cut off—a condition called **ischemia**. Ischemia usually occurs when an artery is compressed as it passes through a tightly flexed joint. Sleeping with the arms above the head or sitting with the legs tightly crossed frequently cause numbness and tingling.

Direct compression of the nerve also causes paresthesias. Compression can be short-lived, as when a heavy backpack compresses the nerves passing across the shoulders. Compression may also be chronic. Chronic nerve compression occurs in entrapment syndromes. The most common example is **carpal tunnel syndrome**. Carpal tunnel syndrome occurs when the median nerve is compressed as it passes through a narrow channel in the wrist. Repetitive motion or prolonged vibration can cause the lining of the channel to swell and press on the nerve. Chronic nerve root

compression, or radiculopathy, can occur in disk disease or spinal arthritis.

Other causes of paresthesias related to disorders of the peripheral nerves include:

- Metabolic or nutritional disturbances. These disturbances include diabetes, hypothyroidism (a condition caused by too little activity of the thyroid gland), alcoholism, malnutrition, and vitamin B_{12} deficiency.
- Trauma. Trauma includes injuries that crush, sever, or pull on nerves.
- Inflammation.
- Connective tissue disease. These diseases include arthritis, systemic lupus erythematosus (a chronic inflammatory disease that affects many systems of the body, including the nervous system), polyarteritis nodosa (a vascular disease that causes widespread inflammation and ischemia of small and medium-size arteries), and Sjögren's syndrome (a disorder marked by insufficient moisture in the tear ducts, salivary glands, and other glands).
- Toxins. Toxins include heavy metals (metallic elements such as arsenic, lead, and mercury which can, in large amounts, cause poisoning), certain antibiotics and chemotherapy agents, solvents, and overdose of pyridoxine (vitamin B_6).
- Malignancy.
- Infections. Infections include Lyme disease, human immunodeficiency virus (HIV), and leprosy.
- Hereditary disease. These diseases include Charcot-Marie-Tooth disease (a hereditary disorder that causes wasting of the leg muscles, resulting in malformation of the foot), porphyria (a group of inherited disorders in which there is abnormally increased production of substances called porphyrins), and Denny-Brown's syndrome (a hereditary disorder of the nerve root).

Paresthesias can also be caused by central nervous system disturbances, including **stroke**, TIA (**transient ischemic attack**), tumor, trauma, **multiple sclerosis**, or infection.

Symptoms

Sensory nerves supply or innervate particular regions of the body. Determining the distribution of symptoms is an important way to identify the nerves involved. For instance, the median nerve innervates the thumb, the first two fingers, half of the ring finger, and the part of the hand to which they connect. The ulnar nerve innervates the other half of the ring finger, the little finger, and the remainder of the hand. Distribution of symptoms may also aid diagnosis of the underlying disease. Diabetes usually causes a symmetrical "glove and stocking" distribution in the hands and feet. Multiple sclerosis may cause symptoms in several, widely separated areas.

Other symptoms may accompany paresthesias, depending on the type and severity of the nerve disturbance. For instance, weakness may accompany damage to nerves that carry both sensory and motor neurons. (Motor neurons are those that carry messages outward from the brain.)

Diagnosis

A careful history of the patient is needed for a diagnosis of paresthesias. The medical history should focus on the onset, duration, and location of symptoms. The history may also reveal current related medical problems and recent or past exposure to drugs, toxins, infection, or trauma. The family medical history may suggest a familial disorder. A work history may reveal repetitive motion, chronic vibration, or industrial chemical exposure.

The physical and neurological examination tests for distribution of symptoms and alterations in reflexes, sensation, or strength. The distribution of symptoms may be mapped by successive stimulation over the affected area of the body.

Lab tests for paresthesia may include blood tests and **urinalysis** to detect metabolic or nutritional abnormalities. Other tests are used to look for specific suspected causes. Nerve conduction velocity tests, **electromyography**, and imaging studies of the affected area may be employed. Nerve biopsy may be indicated in selected cases.

Treatment

Treatment of paresthesias depends on the underlying cause. For limbs that have "fallen asleep," restoring circulation by stretching, exercising, or massaging the affected limb can quickly dissipate the numbness and tingling. If the paresthesia is caused by a chronic disease such as diabetes or occurs as a complication of treatments such as **chemotherapy**, most treatments are aimed at relieving symptoms. Anti-inflammatory drugs such as **aspirin** or ibuprofen are recommended if symptoms are mild. In more difficult cases, **antidepressant drugs** such as amitriptyline (Elavil) are sometimes prescribed. These drugs are given at a much lower dosage for this purpose than for relief of depression. They are thought to help because they alter the body's perception of **pain**. In

KEY TERMS

Electromyography—A test that uses electrodes to record the electrical activity of muscle. The information gathered is used to diagnose neuromuscular disorders.

Motor nerve—Motor or efferent nerve cells carry impulses from the brain to muscle or organ tissue.

Nerve conduction velocity test—A test that measures the time it takes a nerve impulse to travel a specific distance over the nerve after electronic stimulation.

Nerve growth factor—A protein resembling insulin that affects growth and maintenance of nerve cells

Peripheral nervous system—The part of the nervous system that is outside the brain and spinal cord. Sensory, motor, and autonomic nerves are included.

Sensory nerves—Sensory or afferent nerves carry impulses of sensation from the periphery or outward parts of the body to the brain. Sensations include feelings, impressions, and awareness of the state of the body.

severe cases, opium derivatives such as codeine can be prescribed. Currently trials are being done to determine whether treatment with human nerve growth factor will be effective in regenerating the damaged nerves.

Alternative treatment

Several alternative treatments are available to help relieve symptoms of paresthesia. Nutritional therapy includes supplementation with B complex **vitamins**, especially vitamin B_{12} (intramuscular injection of vitamin B_{12} is most effective). Vitamin supplements should be used cautiously however. Overdose of vitamin B_6 is one of the causes of paresthesias. People experiencing paresthesia should also avoid alcohol. **Acupuncture** and massage are said to relieve symptoms. Self-massage with aromatic oils is sometimes helpful. The application of topical ointments containing capsaicin, the substance that makes hot peppers hot, provides relief for some. It may also be helpful to wear loosely fitting shoes and clothing. None of these alternatives should be used in place of traditional therapy for the underlying condition.

Prognosis

Treating the underlying disorder may reduce the occurrence of paresthesias. Paresthesias resulting from damaged nerves may persist throughout or even beyond the recovery period. The overall prognosis depends on the cause.

Prevention

Preventing the underlying disorder may reduce the incidence of paresthesias. For those with frequent paresthesias caused by ischemia, changes in posture may help.

Resources

BOOKS

Creager MA, Libby P. Peripheral Arterial Disease. In: Libby P, Bonow RO, Mann DL, Zipes DP, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Saunders; 2007:chap 57.

Rowland LP. Diagnosis of Pain and Paresthesias. In: Rowland LP, ed. *Merritt's Neurology*. 11th ed. Baltimore, Md: Lippincott Williams & Wilkins; 2005:chap 5.

PERIODICALS

American Diabetes Association (ADA). Standards of Medical Care in Diabetes. VI. *Prevention and Management of Diabetes Complications*. *Diabetes Care*. 2007 Jan;30(Suppl 1):S15-24.

Richard Robinson
Karl Finley

Nummular dermatitis *see* **Dermatitis**

Nutrition

Definition

Nutrition is the sum of all the processes by which food enters and is utilized by the body. Nutrients include protein, carbohydrates, fats, **vitamins**, **minerals**, and water. Fiber in foods helps prevent disease and control weight.

Purpose

Nutrition is essential to life. It is required for growth and development from infancy through young adulthood and throughout life to provide energy and maintain bodily tissues and functions. Good nutrition

promotes health and helps prevent **obesity** and disease. Nutrition is especially important during **pregnancy** and childhood to prevent growth retardation. Childhood and adolescent nutrition can have major ramifications on health in later life.

Demographics

Throughout much of the world families struggle to obtain adequate nutrition. In the United States and other developed countries nutrition is more often a matter of choice. According to the Centers for Disease Control (CDC), American society has become "obesogenic," with increased consumption of non-nutritional foods. Only 25% of Americans consume at least five daily servings of fruits and vegetables—the cornerstones of good nutrition. Americans are also eating more restaurant and fast food than in the past, along with larger portions and other changes in meal patterns and frequency.

Pediatric

The nutritional status and health of American children and adolescents has declined in recent years:

- The Healthy Eating Index from the U.S. Department of Agriculture (USDA) has found that among children aged two through nine, 60–80% have diets in need of improvement and 4–8% have poor diets, with 63% eating too little fruit and 78% eating too few vegetables.
- Only 21% of high school students report eating five or more daily servings of fruits and vegetables (other than fried potatoes and chips).
- Whole grains account for only 14% of the total daily grain consumption of children and adolescents.
- Only 39% of children aged two through 17 meet dietary recommendations for fiber (fruits, vegetables, dried beans and peas, and whole grains).
- More than 60% of children and teens eat too much saturated fat.
- Almost two-thirds of teens eat more than the recommended amount of total fat.
- Most teens eat too much processed, prepared, and junk foods.
- Among adolescent girls, 85% do not consume adequate calcium. Milk consumption by teenage girls has decreased 36% in recent decades, while soft-drink consumption has almost doubled among girls and almost tripled among adolescent boys.
- Eating disorders are the third most common chronic illness in adolescent girls, affecting as many as 5%.

Geriatric

According to a report by the Merck Institute of Aging and Health and the CDC, two-thirds of older Americans fail to practice good nutrition. Almost 90% of Americans over the age of 65 have one or more degenerative disorders that may have been prevented by better nutrition.

Pregnant or breastfeeding

Breast milk is ideal nutrition for most infants. **Breastfeeding** has increased significantly in the United States in recent decades, from 60% in 1993–1994 to 77% in 2005–2006. Breastfeeding rates by black Americans increased from 36% in 1993–1994 to 65% in 2005–2006. Breastfeeding rates are significantly higher among mothers with higher incomes and those aged 30 and over.

Description

The human body absorbs many different nutrients from food. A good nutrition plan includes a variety of foods from the different food groups, with adequate amounts of the nutrients in each group. Keys to good nutrition include:

- fruits, vegetables, and whole grains
- protein, fiber, calcium, iron, magnesium, potassium, and vitamins A, C, and E
- low-fat dairy products, lean meats, poultry, fish, and beans
- no more than 20–35% of total calories from fat, mostly from polyunsaturated and monounsaturated fats
- plenty of water
- more fluids and carbohydrates from fruits and whole grains for athletes and other physically active individuals
- additional vitamin D from fortified foods and/or supplements for older adults, those with darker skin, and people with insufficient exposure to sunlight
- limited salt (less than about one teaspoon daily for most people), added sugar, saturated fat, trans fat, cholesterol, and alcohol (no more than one drink per day for women and two for men)

Vitamins are required for regulating metabolism and maintaining normal growth and functioning. Minerals are vital for building tissue, muscles, and bones, and for many life-supporting systems, including hormones, oxygen transport, and enzyme function. Although foods are the preferred source of these nutrients, they can also be obtained from **nutritional supplements**.

In 2005 the USDA and the U.S. Department of Health and Human Services revised their *Dietary*

Guidelines for Americans, with caloric requirements and servings adjusted for gender, age, and physical activity. The guidelines also make recommendations for special populations and incorporate the 2006 DASH (Dietary Approaches to Stop **Hypertension**) Eating Plan developed by the U.S. National Heart, Lung and Blood Institute. The USDA revised the traditional food pyramid to be customizable for individuals. The new guidelines and pyramid focus on balancing calories consumed and utilized by the body, with managed portions from the different food groups and the avoidance of high-sugar and high-fat foods.

USDA/DASH recommendations for a 2,000-calorie daily diet include:

- fruit group: 2–2.5 cups (4–5 servings) of fresh, frozen, canned, or dried fruit, with only limited juice
- vegetable group: 2–2.5 cups (4–5 servings)
- grain group: 6–8 ounce-equivalents of cereal, bread, crackers, rice, or pasta; with at least 50% whole grain
- meat and beans group: 5.5–6 ounce-equivalents of baked, broiled, or grilled lean meat, poultry, or fish, eggs, nuts, seeds, beans, peas, or tofu
- milk group: 2–3 cups low-fat/fat-free milk, yogurt, or cheese, or lactose-free, calcium-fortified products
- oils: 2–6 teaspoons
- discretionary: 267 calories; for example, solid fats (saturated fat such as butter, margarine, shortening, or lard) or added sugar

The vegetable group includes:

- dark greens, such as broccoli and leafy greens: three cups per week
- orange vegetables, such as carrots and sweet potatoes: two cups per week
- legumes, such as pinto or kidney beans, split peas, or lentils: three cups per week
- starchy vegetables: three cups per week
- other vegetables: 6.5 cups per week

Benefits

In addition to its essential role in growth and development, maintenance of bodily functions, and energy supply, good nutrition helps prevent weight gain with calories that are high in nutrients other than sugars and fats. Good nutrition also helps prevent various disorders including:

- dental caries
- iron-deficiency anemia
- osteoporosis
- hypertension
- heart disease
- type 2 diabetes
- some types of cancer

Precautions

In general:

- Fresh foods are usually more nutritious than packaged and processed foods.
- Fast and processed foods contain excess fat and sodium and high amounts of sugar, as well as artificial preservatives, and other additives.
- Fast and processed foods are deficient in fiber and essential vitamins and minerals, such as vitamin A, riboflavin, folic acid, vitamin E, calcium, magnesium, and potassium.
- It is difficult to gauge nutrition and calories when eating out and buying packaged foods.
- Vegetarians need to choose carefully from the basic foods groups to achieve recommended nutrient intakes, especially of protein, vitamins, and iron.
- Iron-deficiency anemia is very common in women. The recommended iron intake is 15–18 mg daily for females. Good sources of iron include dark-green leafy vegetables, legumes, iron-fortified breads and cereals, and red meat.
- Many adults do not obtain enough calcium from their diets, which can lead to osteoporosis in later life. Women aged 19–50 should consume 1,000 mg of calcium daily. Women over 50 require 1,200 mg. Good sources of calcium include dark-green leafy vegetables, calcium-fortified orange juice, bread, cereal, fish, and low-fat dairy products.
- Although nutritional supplementation is sometimes necessary, if possible, nutrients should come from food. Excessive use of vitamin and mineral supplements can lead to serious health problems.
- Diets should not be radically altered except under medical supervision.

Pediatric

Childhood nutrition requires adequate essential nutrients, fiber, and calories to maintain proper growth, maximize cognitive development, and promote health, while preventing excess weight gain. Poor nutrition in adolescence can cause growth and developmental problems and long-term complications including obesity, heart disease, and **osteoporosis**. Children's **diets** should include a variety of foods with high nutrient-to-calorie ratios. In addition:

- At age two, 25–33% of grains should be whole-grain, gradually increasing to 50% by age five.

KEY TERMS

Calorie—A unit of food energy.

Carbohydrate—Sugars, starches, celluloses, and gums that are a major source of calories from foods.

Cholesterol—A fat-soluble steroid alcohol (sterol) found in animal fats and oils, and produced in the body from saturated fats. Cholesterol is required to produce vitamin D and various hormones and for the formation of cell membranes. High cholesterol levels contribute to the development of atherosclerosis.

Fat—Molecules composed of fatty acids and glycerol; the slowest utilized source of energy, but the most energy-efficient form of food. Each gram of fat supplies about nine calories, more than twice that supplied by the same amount of protein or carbohydrate.

Monounsaturated fat—Fats that contain one double or triple bond per molecule; examples include canola oil and olive oil.

Polyunsaturated fat—Fats that contain two or more double or triple bonds per molecule; examples include fish, safflower, sunflower, corn, and soybean oils.

Protein—Chains of amino acids that are essential constituents of all living cells and include structural components, enzymes, hormones, and antibodies.

Saturated fat—Fat molecules that contain only single bonds; examples include whole milk, cream, palm and coconut oils, and solid fats such as cheese, butter, and meat.

Trans fat—Fat that is produced by hydrogenation during food processing; trans fats increase bad cholesterol and decrease good cholesterol.

- The average adolescent protein requirement is about 300 mg per 0.4 in (1 cm) of height.
- Physically active adolescents require more fluids and more carbohydrates from fruit and whole grains.
- Requirements for vitamins and minerals increase during adolescence. Teenagers require 1,300 mg of calcium daily. Boys require 10-12 mg of iron and 15 mg of zinc daily. Girls require 15 mg of iron and 12 mg of zinc.
- Vegan and macrobiotic diets for adolescents may require nutritional supplements.

Geriatric

Various factors can interfere with nutrition in the elderly:

- medical conditions and/or medications
- reduced capacity to absorb and utilize nutrients
- oral/dental problems or difficulty chewing or swallowing
- gastrointestinal disturbances
- loss of appetite
- diminishing taste and smell
- changes in taste preferences
- loss of dexterity
- social isolation, loneliness, or depression
- economic limitations
- lack of cooking skills or desire to cook
- inadequate knowledge of nutrition
- dementia

The rate of metabolism can decline by as much as 30% over a lifetime and lean muscle mass can decrease by as much as 25% in the elderly, accompanied by an increase in body fat. Therefore, seniors need foods with high nutrient-to-calorie ratios. Although caloric requirements vary greatly, it has been recommended that, after age 50, men reduce their daily intake by 600 calories and women by 300 calories. Because seniors eat less and take in fewer calories, they also consume fewer vitamins and minerals, even though the body's need for some micronutrients may actually increase with age. This is especially true for vitamin D and **calcium**. A single daily multivitamin/mineral supplement can address nutritional gaps.

Other nutritional recommendations for seniors include:

- adequate protein for immune system health and maintenance and repair of body tissues
- dietary fiber from fruits, vegetables, beans, nuts, seeds, brown rice, and whole grains
- only small amounts of fats, oils, and sweets
- no more than 1,500 mg of sodium daily from all food sources (two-thirds of a teaspoon of table salt)
- adequate fluids—the elderly can easily become dehydrated
- vitamin B_{12} from fortified foods or supplements
- potassium from leafy green vegetables, tomatoes, bananas, and root vegetables such as potatoes to counter the effects of salt on blood pressure

Pregnant or breastfeeding

Women have special nutritional needs during menstruation, pregnancy, **lactation**, and **menopause**. Pregnant and breastfeeding women have increased requirements for calories and for most nutrients. Pregnant and breastfeeding teenagers have even higher nutritional requirements than other pregnant women. Pregnant women should consume iron-rich plant foods and vitamin-C-rich foods that aid in the absorption of iron. **Folic acid**, a B vitamin, is particularly important during pregnancy, since it helps protect against brain and spinal cord **birth defects**. All women of childbearing age should consume 400 micrograms (μg) of folic acid daily and 600 μg during pregnancy. Pregnancy and breastfeeding deplete maternal calcium. Pregnant and lactating adult women should consume 1,000 mg of calcium daily. Pregnant and lactating teenagers require 1,300 mg.

Hormonal changes during pregnancy can trigger **gestational diabetes**, characterized by high levels of sugar in the blood. Changes in diet and **exercise** are often sufficient to keep blood sugar levels within the normal range. Women who experience gestational diabetes are more likely to develop type 2 diabetes later in life.

Other conditions and allergies

Many people with **allergies** or medical conditions require special diets, such as a low-fat, low-cholesterol diet for heart disease, a low-sodium diet for high blood pressure, or a low-calorie diet for weight reduction. Chronic illnesses, such as diabetes, as well as **substance abuse**, also create special nutritional requirements.

Resources

BOOKS

Bales, Connie Watkins, and Christine Seel Ritchie, eds. *Handbook of Clinical Nutrition and Aging*. 2nd ed. Totowa, NJ: Humana Press, 2009.

Bender, David A. *A Dictionary of Food and Nutrition*. 3rd ed. New York: Oxford University Press, 2009.

Duyff, Roberta Larson. *American Dietetic Association Complete Food and Nutrition Guide*. 3rd ed. Hoboken, NJ: John Wiley & Sons, 2007.

Insel, Paul M., R. Elaine Turner, and Don Ross. *Discovering Nutrition*. 3rd ed. Sudbury, MA: Jones & Bartlett, 2010.

U.S. Department of Health and Human Services, U.S. Department of Agriculture. *Dietary Guidelines for Americans, 2005*. 6th ed. Washington, DC: GPO, 2005.

PERIODICALS

Drewnowski, Adam. "The Nutrient Rich Foods Index Helps to Identify Healthy, Affordable Foods." *American Journal of Clinical Nutrition* 91, no. 4 (April 1, 2010): 1095S.

Galson, Steven K. "Improving Nutrition for Older Americans." *Journal of the American Dietetic Association* 109, no. 10 (October 2009): 1672.

Rolls, Barbara J., Liane S. Roe, and Jennifer S. Meengs. "Portion Size Can Be Used Strategically to Increase Vegetable Consumption in Adults." *American Journal of Clinical Nutrition* 91, no. 4 (April 1, 2010): 931.

OTHER

AHA Scientific Statement. "Dietary Recommendations for Children and Adolescents." *Circulation* 112 (2005): 2061-2075. http://circ.ahajournals.org/cgi/content/full/112/13/2061 (accessed September 25, 2010).

"Dietary Guidelines for Americans, 2005." U.S. Department of Health and Human Services. January 2005. http://www.health.gov/dietaryguidelines/dga2005/document/default.htm (accessed September 25, 2010).

"Dietary Recommendations for Healthy Children." *American Heart Association*. June 1, 2010. http://www.americanheart.org/presenter.jhtml?identifier=4575 (accessed September 25, 2010).

"Eat Right Nutrition Tips." *American Dietetic Association*. http://www.eatright.org/Public/content. aspx?id=206 (accessed September 25, 2010).

United States Department of Agriculture. *MyPyramid. gov*. http://www.mypyramid.gov (accessed September 25, 2010).

ORGANIZATIONS

American Dietetic Association, 120 South Riverside Plaza, Suite 2000, Chicago, IL, 60606-6995, (800) 877-1600, http://www.eatright.org.

American Heart Association, 7272 Greenville Avenue, Dallas, TX, 75231, (800) 242-8721, http://www.americanheart.org.

Center for Nutrition Policy and Promotion, 3101 Park Center Drive, 10th Floor, Alexandria, VA, 22302-1594, (703) 305-7600, (888) 7-PYRAMID (779-7264), (703) 305-3300, Support@cnpp.usda.gov, http://www.cnpp.usda.gov.

Food and Nutrition Information Center, National Agricultural Library, 10301 Baltimore Avenue, Room 105, Beltsville, MD, 20705, (301) 504-5414, (301) 504-6409, http://fnic.nal.usda.gov.

National Heart, Lung and Blood Institute, NHLBI Health Information Center, P.O. Box 30105, Bethesda, MD, 20824-0105, (301) 592-8573, (240) 629-3246, nhlbiinfo@nhlbi.nih.gov, http://www.nhlbi.nih.gov.

U.S. Centers for Disease Control and Prevention, 1600 Clifton Rd., Atlanta, GA, 30333, (800) CDC-INFO (232-4636), cdcinfo@cdc.gov, http://www.cdc.gov.

Margaret Alic, PhD

Nutrition through an intravenous line

Definition

Sterile solutions containing some or all of the nutrients necessary to support life, are injected into the body through a tube attached to a needle, which is inserted into a vein, either temporarily or for long-term treatment.

Purpose

Patients who cannot consume enough nutrients or who cannot eat at all due to an illness, surgery, or accident, can be fed through an intravenous (IV) line or tube. An IV can be used for as little as a few hours, to provide fluids to a patient during a short surgical procedure, or to rehydrate a patient after a viral illness.

Patients with more serious and long-term illnesses and conditions may require months or even years of intravenous therapy to meet their nutritional needs. These patients may require a central **venous access** port. A specialized catheter (silastic Broviac or Hickman) is inserted beneath the skin and positioned below the collarbone. Fluids can then be injected directly into the bloodstream for long periods of time. X-rays are taken to ensure that the permanent catheter is properly positioned.

Precautions

Patients receiving IV therapy need to be monitored to ensure that the IV solutions are providing the correct amounts of fluids, **minerals**, and other nutrients needed.

Description

There are two types of IV, or parenteral, **nutrition**. Parenteral nutrition is that which is delivered through a system other than the digestive system. In this case, the nutrition is delivered through a vein. Partial parenteral nutrition (PPN) is given for short periods of time, to replace some of the nutrients required daily and only supplements a normal diet. **Total parenteral nutrition** (TPN) is given to someone who cannot eat anything and must receive all nutrients required daily through an intravenous line. Both of these types of nutrition can be performed in a medical facility or at the patient's home. Home parenteral nutrition (HPN) usually requires a central venous catheter, which must first be inserted in a fully equipped medical facility. After it is inserted, therapy can continue at home.

Basic IV solutions are sterile water with small amounts of **sodium** (salt) or dextrose (sugar) supplied in bottles or thick plastic bags that can hang on a stand mounted next to the patient's bed. Additional minerals, like potassium and **calcium**, **vitamins**, or drugs can be added to the IV solution by injecting them into the bottle or bag with a needle. These simple sugar and salt solutions can provide fluids, calories, and electrolytes necessary for short periods of time. If a patient requires intravenous feeding for more than a few days, additional nutrients like proteins and fats will be included. The amounts of each of the nutrients to be added will depend on the patient's age, medical condition, and particular nutritional requirements.

Preparation

A doctor orders the IV solution and any additional nutrients or drugs to be added to it. The doctor also specifies the rate at which the IV will be infused. The IV solutions are prepared under the supervision of a doctor, pharmacist, or nurse, using sanitary techniques that prevent bacterial contamination. Just like a prescription, the IV is clearly labeled to show its contents and the amounts of any additives. The skin around the area where the needle is inserted is cleaned and sanitized. Once the needle is in place, it will be taped to the skin to prevent it from dislodging.

In the case of HPN, the IV solution is delivered to the patient's home on a regular basis and should be kept refrigerated. Each bag will have an expiration date, by which time the bag should be used. The solution should be allowed to be warmed to room temperature before intravenous nutrition begins.

Aftercare

Patients who have been on IV therapy for more than a few days may need to have foods reintroduced gradually to give the digestive tract time to start working again. After the IV needle is removed, the site should be inspected for any signs of bleeding or infection.

When using HPN, the catheter should be kept clean at all times. The **dressings** around the site should be changed at least once a week and the catheter site should be monitored closely for signs of redness, swelling, and drainage. The patient's extremities

KEY TERMS

Home parenteral nutrition (HPN)—Long-term parenteral nutrition, given through a central venous catheter and administered in the patient's home.

Intravenous—Into a vein; a needle is inserted into a vein in the back of the hand, inside the elbow, or some other location on the body. Fluids, nutrients, and drugs can be injected.

Parenteral—Not in or through the digestive system. Parenteral nutrition is given through the veins of the circulatory system, rather than through the digestive system.

Partial parenteral nutrition (PPN)—A solution, containing some essential nutrients, is injected into a vein to supplement other means of nutrition, usually a partially normal diet of food.

Total parenteral nutrition (TPN)—A solution containing all the required nutrients including protein, fat, calories, vitamins, and minerals, is injected over the course of several hours, into a vein. TPN provides a complete and balanced source of nutrients for patients who cannot consume a normal diet.

should be watched for swelling, which is a sign of nutritional imbalance.

Risks

There is a risk of infection at the injection site, and for patients on long term IV therapy, the risk of an infection spreading to the entire body is fairly high. It is possible that the IV solution may not provide all of the nutrients needed, leading to a deficiency or an imbalance. If the needle becomes dislodged, it is possible that the solution may flow into tissues around the injection site rather than into the vein. The patient should be monitored regularly, particulary if receiving HPN, as intravenous nutrition can potentially cause infection at the site of the catheter, high blood sugar, and low blood potassium, which can all be life-threatening.

Resources

OTHER

"Clinical Management: Parenteral Nutrition" In *Revised Intravenous Nursing Standards of Practice*. http://www.ins1.org.

Altha Roberts Edgren

Nutritional supplements

Definition

Nutritional supplements include **vitamins**, **minerals**, herbs, meal supplements, sports **nutrition** products, natural food supplements, and other related products used to boost the nutritional content of the diet.

Purpose

Nutritional supplements are used for many purposes. They can be added to the diet to boost overall health and energy, to provide immune system support and reduce the risks of illness and age-related conditions, to improve performance in athletic and mental activities, and to support the healing process during illness and disease. Although some supplements may be prescribed by a doctor or used for medical purposes, most of these products are regulated by the U.S. Food and Drug Administration (FDA) as food products, not as drugs. This means that they do not have to meet the strict standards that drugs do.

Description

According to the U.S. National Institute of Health's Office of Dietary Supplements, sales of dietary supplements in the United States reached $21.3 billion in 2005. By category, vitamins provided $3.0 billion in sales, herbs $4.4 billion, minerals $1.8 billion, sports nutrition products $2.2 billion, multivitamins/minerals $4.2 billion, and other supplements totaling $5.7 billion.

Vitamins

Vitamins are micronutrients, or substances that the body uses in small amounts, as compared to macronutrients, which are the proteins, fats, and carbohydrates that make up most of food. Vitamins are present in food, but adequate quantities of vitamins may be reduced when food is overcooked, processed, or improperly stored. For instance, processing whole wheat grain into white flour reduces the contents of vitamins B and E, fiber, and minerals, including zinc and iron. The body requires vitamins to support its basic biochemical functions, and deficiencies over time can lead to serious disorders and have other negative health consequences.

Vitamins are either water-soluble or fat-soluble. Water-soluble vitamins dissolve in water and are not stored in the body, meaning that the body needs them on a regular basis. Water-soluble vitamins include the B-complex vitamins and vitamin C. Fat-soluble vitamins are stored in the body's fatty tissue, meaning that

extra quantities can be stored for use by the body later. Fat-soluble vitamins include vitamins A, D, E, and K.

The amount of vitamins needed by the body has been the subject of much research. The U.S. government has published recommended dietary allowances (RDAs) for each vitamin for the general population. These figures can be used as guidelines, but individuals may have different needs depending on gender, age, activity level, and health conditions.

Vitamins can be natural or synthetic. Natural vitamins are extracted from food sources, while synthetic vitamins are formulated in laboratory processes. The only vitamin for which there is a noted difference between the natural and synthetic forms is vitamin E. The natural form is labeled d-alpha-tocopherol while the synthetic form is named dl-alpha-tocopherol, with the extra "l" signifying laboratory production. Natural vitamin E has been shown to be absorbed slightly more efficiently by the body than the synthetic version. For other vitamins no significant differences in absorption have been noted.

Minerals

Minerals are micronutrients and are essential for the proper functioning of the body. Cells in the body require minerals as part of their basic make-up and chemical balance, and minerals are present in all foods. Minerals can either be bulk minerals, used by the body in larger quantities, or trace minerals, used by the body in minute or trace amounts. Bulk minerals include **sodium**, potassium, **calcium**, magnesium, and phosphorus. Trace minerals include iron, zinc, selenium, iodine, chromium, copper, manganese, and others. Some studies have shown that the amount of minerals, particularly trace minerals, may be decreasing in foods due to mineral depletion of the soil caused by unsustainable farming practices and soil erosion. Supplemental minerals are available in chelated form, in which they are bonded to proteins in order to improve their absorption by the body.

Herbs

Herbal supplements may be added to the diet for both nutritional and medicinal purposes. Herbs have been used for centuries in many traditional medicine systems, and as sources of phytochemicals, or substances found in plants that have notable effects on the body. Chinese medicine and **Ayurvedic medicine** from India, two of the world's oldest healing systems, use hundreds of herbal medications. Naturopathy and homeopathy, two other systems of natural healing, also rely on herbal preparations as their main sources of medication. Some of the medicinal effects of herbs are getting scientific validation; about one-fourth of all pharmaceuticals have been derived directly from plant sources, including **aspirin** (found in willow bark); codeine (from poppy seeds); paclitaxel (Taxol), a patented drug for ovarian and **breast cancer** (from the Pacific yew tree); and many others.

Herbs can supplement the diet to aid in overall health or may be intended to stimulate healing for specific conditions. For instance, **ginseng** is often used to increase overall health and vitality, while **echinacea** is popularly believed to stimulate the body's resistance to colds and infections. Herbs come in many forms. They can be purchased as capsules and tablets, as well as in tinctures, teas, syrups, and ointments.

Meal supplements

Meal supplements are used to replace or fortify meals. They may be designed for people with special needs, or for people with illnesses that may affect digestion capabilities and nutritional requirements. Meal supplements may contain specific blends of macronutrients, or proteins, carbohydrates, fats, and fiber. Some meal supplements consist of raw, unprocessed foods, or may be vegetarian or vegan, or have high protein and low fat composition. Meal supplements are available to support some popular diet programs. They are often fortified with vitamins, minerals, herbs, and nutrient-dense foods.

Sports nutrition

Nutritional supplements may be designed to provide specialized support for athletes. Some of these consist of high-protein products, such as amino acid supplements, while other products contain nutrients that support metabolism, energy, and athletic performance and recovery. People engaging in intense athletic activity may have increased needs for water-soluble vitamins, **antioxidants**, and certain minerals, including chromium. Sports drinks may contain blends of electrolytes (salts) that the body loses during exertion and sweating, as well as vitamins, minerals, and performance-supporting herbs.

Other nutritional supplements

Other nutritional supplements include nutrient-dense food products. Examples of these are brewer's yeast, spirulina (sea algea), bee pollen and royal jelly, fish oil and essential fatty acid supplements, colostrum (a specialty dairy product), psyllium seed husks (a source of fiber), wheat germ, wheatgrass, and medicinal mushrooms such as the shiitake and reishi varieties.

Specialty products may offer particular health benefits or are targeted for specific conditions. These products may consist of whole foods or may be isolated compounds from natural or synthetic sources. Examples include antioxidants, probiotics (supplements containing bacteria helpful to the digestion process), digestive enzymes, shark cartilage, other animal products, and chemical extracts such as the hormone DHEA (dehydroepiandrosterone) and coenzyme Q10, an antioxidant.

General guidelines

Considering average dietary needs and the prevalence of certain health conditions, some basic guidelines may provide the foundation for the effective use of nutritional supplements. First, a high quality, broad-spectrum multivitamin and mineral supplement, taken once per day, may be recommended for some people. This should contain the B-complex vitamins B_6, B_{12}, and **folic acid**, which may help prevent heart disease, and the minerals zinc and copper, which aid immunity. In addition to a multivitamin, antioxidants can be added to a supplementation routine. These include vitamin A (or beta-carotene), vitamin C, and vitamin E, and the mineral selenium. Antioxidants are popularly believed have several positive effects on the body, such as slowing the **aging** process, reducing the risks of **cancer** and heart disease, and reducing the risks of illness and infection by supporting the immune system. Coenzyme Q10 is another antioxidant in wide usage, as studies have shown it may improve the health of the heart and reduce the effects of heart disease. Essential fatty acids, particularly omega-3, are also recommended as they are involved in many important processes in the body, including brain function. Calcium supplementation is recommended for the elderly and for women, to support bone strength. Calcium supplements that are balanced with magnesium have a less constipating effect and are better absorbed.

After basic nutritional requirements are supported, supplements may be used to target specific needs and health conditions. For instance, athletes, men, women, children, the elderly, and vegetarians have differing needs for nutrients, and an informed use of supplements would take these differences into account. People suffering from health conditions and diseases may use specific supplements to target their condition and to support the body's healing capacity by providing optimal amounts of nutrients.

Recommended dosage

Dosages of nutritional supplements vary widely, depending on the product and individual needs. For vitamins and minerals, U.S. RDA's are general guidelines. For other products, manufacturers' guidelines, consumer information sources such as nutritional books and magazines, and practitioners including nutritionists and naturopathic physicians may be consulted.

Precautions

Nutritional supplements are not regulated by the FDA in the same way that prescription and over-the-counter drugs are. Instead, nutritional supplements are regulated in the same way as food. This means that makers of nutritional supplements do not have to prove the effectiveness of their products before putting them on the market. Nutritional supplements that make claims about the benefits of their product are required to carry a label stating that "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."

Because nutritional supplements are regulated in the same way as food products, the FDA may only take action against a product once it is already on the market. This means that sometimes products that are harmful, contaminated, or that make misleading claims can make onto retail shelves. In the past products have been identified by the FDA as containing more, or less, of the vitamin, mineral, or herb, than stated on the package, as contaminated with pesticides, heavy metals, or prescription drugs, as containing herbs not identified on the label, and as possibly causing dangerous interactions with prescription drugs. Because of these concerns it is extremely important that individuals exercise caution when making decisions about taking nutritional supplements.

Overall diet is an important first consideration for those considering nutritional supplementation. Healthy dietary habits can help optimize nutrition and the absorption of supplements, and nutritional supplements cannot substitute for a diet that is not nutritionally balanced. A good diet contain a variety of wholesome foods. The U.S. Department of Agriculture's MyPyramid food guide provides guidelines for a healthy diet, and can be found at www.MyPyramid.gov. Variety in the diet is important to provide a full range of vitamins and minerals. Overeating inhibits digestion and absorption of nutrients, while regular exercise contributes to sound nutrition, by improving metabolism and digestion. Drinking plenty of water prevents **dehydration**, improves digestion, and helps the body flush out impurities.

Generally, nutrients from food sources are more efficiently utilized by the body than isolated substances. For instance, fresh fruit and vegetable juice could be used to provide concentrated amounts of particular nutrients, such as vitamins A and C, to the diet. Eating plenty of leafy green vegetables is a healthy option for those wishing to add calcium to the diet.

Vitamins and minerals are most easily digested with food. Fat-soluble vitamins should be taken with food that contains fat. Vitamins tend to work synergistically, meaning that they work together in order to be effective. For instance, vitamin E requires some of the B-complex vitamins and the minerals selenium and zinc for most effective absorption. Some minerals may not be absorbed or may inhibit each other when taken in improper ratios. Generally, a high quality, broad-spectrum vitamin and mineral supplement is formulated to prevent unfavorable interactions.

Many vitamins, minerals, and herbs are toxic when taken in large quantities. Vitamin A can become toxic when taken in large amounts (more than 100,000 International Units), as can vitamin D. Substituting beta-carotene for vitamin A can alleviate this risk. Large doses of fat-soluble vitamins, because extra amounts of the vitamin are stored in the body, can have serious negative health consequences. Water-soluble vitamins are not stored in the body, and therefore extra quantities are excreted in the urine. Large doses of minerals, especially taken over time, may also have toxic effects in the body. Dosages far exceeding RDA's of vitamins are not recommended, nor are large doses of other supplements.

Vitamins, minerals, and herbs may interact dangerously with prescription or over-the-counter medications, may make some medications less effective, or may cause some medical conditions to become worse. For example, **St. John's wort** can interfere with birth control medications, with medications used to treat cancer and HIV infection, and medications taken by organ transplant patients. Ginseng can cause lowered blood sugar levels, which can be dangerous when used in combination with some medications used to treat diabetes. It is extremely important that individuals talk with their doctor or pharmacist about how a nutritional supplement may interact with their medications and affect their health conditions before beginning to take it.

Consumers can make wise choices for nutritional supplementation by consulting a physician, pharmacist, nutritionist, or other health professionals. Nutritional supplements are best added into the diet slowly, starting with small dosages and working up to the manufacturers' recommended amounts over time.

KEY TERMS

Antioxidants—A class of biochemicals that have been found to protect cells from free-radical damage.

Enzymes—Chemical catalysts that help initiate biochemical processes.

Essential fatty acids—Sources of fat in the diet, including omega-3 and omega-6 fatty acids.

Naturopathic physicians—Physicians specializing in the treatment of disease using a variety of natural methods and plant-based medicines.

Also, some supplements, such as herbal medications that may stimulate processes in the body, are best taken intermittently, allowing the body occasional rest periods without the supplement. To avoid unfavorable interactions, nutritional supplements are best used moderately and individually, rather than taking handfuls of capsules and tablets for various needs and conditions at the same time. Finally, consumers should be wary of excessive or grandiose health claims made by manufacturers of nutritional supplements and rely on scientific information to validate these claims.

Side effects

Some nutritional supplements can cause upset stomach and allergic reactions, including **rashes**, flushing, **nausea**, sweating, and headaches.

Interactions

Herbal preparations and nutritional supplements may interact unfavorably with pharmaceutical drugs. For instance, some nutritional supplements such as taking 5-HTP, a nutritional supplement for the brain, or the herb St. John's Wort, may not be recommended for those taking pharmaceutical antidepressants. Vitamin C should not be taken with aspirin, as it can irritate the stomach and limit absorption. Minerals should be taken in proper proportions to prevent unfavorable interactions; large amounts of zinc may deplete the body of the mineral copper, while too much calcium adversely affects the magnesium levels in the body. Balanced mineral supplements are recommended to alleviate these interactions.

Resources

BOOKS

Adele, Stephen, and Rehan Jalali. *Sports Supplement Buyer's Guide: Complete Nutrition for Your Active Lifestyle*. Laguna Beach, CA: Basic Health Publications, 2007.

Balch, Phyllis A. *Prescription for Nutritional Healing*. East Rutherford, NJ: Penguin Group, 2005.
Shannon, Joyce Brennfleck. *Diet and Nutrition Sourcebook*. Detroit: Omnigraphics, 2006.

ORGANIZATIONS

Center for Science in the Public Interest, 1875 Connecticut Avenue NW, Suite 300, Washington, DC, 20009, (202) 332-9110, (202) 265-4954, cspinews@cspinet.org, http://www.cspinet.org.
USDA Food and Nutrition Information Center, http://www.nal.usda.gov/fnic.

Douglas Dupler

Nystagmus

Definition

Rhythmic, oscillating motions of the eyes are called nystagmus. The to-and-fro motion is generally involuntary. Vertical nystagmus occurs much less frequently than horizontal nystagmus and is often, but not necessarily, a sign of serious brain damage. Nystagmus can be a normal physiological response or a result of a pathologic problem.

Description

The eyes play a critical role in maintaining balance. They are directly connected to other organs of equilibrium, most important of which is the inner ear. Paired structures called the semicircular canals deep in the skull behind the ears sense motion and relay that information to balance control centers in the brain. The eyes send visual information to the same centers. A third set of sensors consists of nerve endings all over the body, particularly in joints, that detect position. All this information is integrated to allow the body to navigate in space and gravity.

It is possible to fool this system or to overload it with information so that it malfunctions. A spinning ride at the amusement park is a good way to overload it with information. The system has adapted to the spinning, expects it to go on forever, and carries that momentum for some time after it is over. Nystagmus is the lingering adjustment of the eyes to tracking the world as it revolves around them.

Nystagmus can be classified depending upon the type of motion of the eyes. In pendular nystagmus the speed of motion of the eyes is the same in both directions. In jerk nystagmus there is a slow and fast phase. The eyes move slowly in one direction and then seem to jerk back in the other direction.

Nystagmus can be present at birth (congenital) or acquired later on in life. A certain type of acquired nystagmus, called spasmus nutans, includes a head tilt and head bobbing and generally occurs between four to 12 months of age. It may last a few months to a few years, but generally goes away by itself.

Railway nystagmus is a physiological type of nystagmus. It happens when someone is on a moving train (thus the term railway) and is watching a stationary object which appears to be going by. The eyes slowly follow the object and then quickly jerk back to start over. Railway nystagmus (also called optokinetic nystagmus) is a type of jerk nystagmus. This phenomenon can be used to check vision in infants. Nystagmus can also be induced by fooling the semicircular canals. Caloric stimulation refers to a medical method of testing their connections to the brain, and therefore to the eyes. Cold or warm water flushed into the ear canal will generate motion signals from the inner ear. The eyes will respond to this signal with nystagmus if the pathways are intact.

Causes and symptoms

There are many causes of nystagmus. Nystagmus may be present at birth. It may be a result of the lack of development of normal binocular fixation early on in life. This can occur if there is a cataract at birth or a problem is some other part of the visual system. Some other conditions that nystagmus may be associated with include:

- Albinism. This condition is caused by a decrease in pigmentation and may affect the eyes.
- Disorders of the eyes. This may include optic atrophy, color blindness, very high nearsightedness (myopia) or severe astigmatism, or opacities in the structures of the eyes.
- Acute labyrinthitis. This is an inflammation in the inner ear. The patient may have dizziness (vertigo), nausea and vomiting, and nystagmus.
- Brain lesions. Disease in many parts of the brain can result in nystagmus.
- Alcohol and drugs. Alcohol and some medications (e.g., anti-epilepsy medications) can induce or exaggerate nystagmus.
- Multiple sclerosis. A disease of the central nervous system.

KEY TERMS

Binocular fixation—Both eyes pointed to and looking at the same object.

Cataract—A clouding of the lens of the eye.

Optic atrophy—Degeneration of the optic nerve.

Semicircular canals—Structures of the inner ear that help in maintaining balance.

Vertigo—A sense of spinning usually accompanied by unsteadiness and nausea.

Diagnosis

Nystagmus is a sign, not a disease. If abnormal, it indicates a problem in one of the systems controlling it. An ophthalmologist and/or neuro-ophthalmologist should be consulted.

Treatment

There is one kind of nystagmus that seems to occur harmlessly by itself. The condition, benign positional vertigo, produces vertigo and nystagmus when the head is moved in certain directions. It can arise spontaneously or after a **concussion**. **Motion sickness** medicines sometimes help. But the reaction will dissipate if continuously evoked. Each morning a patient is asked to produce the symptom by moving his or her head around until it no longer happens. This prevents it from returning for several hours or the entire day.

Prisms, **contact lenses**, eyeglasses, or **eye muscle surgery** are some possible treatments. These therapies may reduce the nystagmus but may not alleviate it. Again, because nystagmus may be a symptom, it is important to determine the cause.

ORGANIZATIONS

American Academy of Ophthalmology (AAO), P.O. Box 7424, San Francisco, CA, 94120-7424, (415) 561-8500, (415) 561-8500, http://www.aao.org.

American Optometric Association, 243 North Lindbergh Blvd., St. Louis, MO, 63141, (314) 991-4100, (314) 991-4101, (800) 365-2219, http://www.aoa.org/.

J. Ricker Polsdorfer, MD

O

Obesity

Definition

Obesity is the excessive accumulation of body fat resulting in a body mass index (BMI) that is significantly above the norm and is associated with increased risk of illness, disability, and **death**. Medical professionals generally consider obesity to be a chronic illness requiring lifelong treatment and management. It is often grouped with other chronic conditions—such as high blood pressure and diabetes—that can be controlled but not cured.

Demographics

Obesity is a serious public-health problem that affects both sexes and all ethnic, racial, age, and socioeconomic groups in the United States and around the world. According to the U.S. Centers for Disease Control (CDC), more than one-third of adults in the United States are obese—more than 71 million people. Approximately 300,000 deaths a year are attributed to obesity, prompting public-health officials such as former Surgeon General C. Everett Koop to label obesity "the second leading cause of preventable deaths in the United States."

Slightly more women than men are obese in all adult age groups—35.3% of women and 33.3% of men. The highest percentage of obesity is in the 40–50-year age group. Approximately 53% of non-Hispanic black U.S. women and 51% of Mexican-American women aged 40-59 years are obese, compared with about 39% of non-Hispanic white women of the same age. Among women 60 years and older, 61% of non-Hispanic blacks are obese compared with 32% of non-Hispanic white women and 37% of Mexican-American women. These racial/ethnic differences in obesity rates are not seen among men.

Obesity is the most common nutritional disorder among U.S. children and teens. African-American and Hispanic children are considerably more likely to be overweight than Caucasian-American children.

According to the CDC, between the mid-1970s and the mid-2000s:

- The percentage of overweight and obese Americans aged 20–74 increased from 15.0% to 32.9%.
- The percentage of overweight children aged 2–5 increased from 5.0% to 13.9%.
- The percentage of overweight children aged 6–11 increased from 6.5% to 18.8%.
- The percentage of overweight and obese teenagers increased from 5.0% to 17.4%.

Similar trends are reported by the World Health Organization (WHO), which refers to the escalating global epidemic of obesity as "globesity." WHO estimated that in 2007, 1.6 billion people over age 15 were overweight and at least 400 million were obese.

Description

Obesity is excessive body weight that develops over time as people consume more calories than they expend in energy. As excess calories accumulate in the body, people first become overweight, then obese. The ability of the human body to store energy can mean the difference between life and death in times of famine. However this protective mechanism becomes a potential problem when food is readily available in unlimited quantities. This is evident in the increasing prevalence of obesity in modern society, particularly in the developed world. As obesity rates have increased, bariatrics—the branch of medicine that studies and treats obesity—has become a separate medical and surgical specialty.

The human body is composed of bone, muscle, specialized organ tissues, and fat. Together these comprise the total body mass, measured in pounds (lb) or kilograms (kg). Fat, or adipose tissue, is a combination of essential and storage fats. Essential fat is an energy source for the normal physiologic function of cells and

organs, is tucked in and around internal organs, and is an important building block for all cells of the body. Storage fat is a reserve supply of energy. It accumulates in the chest and abdomen and, in much greater volume, under the skin. When the amount of energy consumed as food exceeds the amount of energy expended in the maintenance of life processes and physical activity, storage fat accumulates in excessive amounts.

In the past obesity was defined as body weight that was at least 20% above one's ideal weight, defined as the weight at which individuals of the same height, gender, and age had the lowest rate of death. Mild obesity was defined as 20–40% over ideal weight, moderate obesity as 40–100% over ideal, and gross or morbid obesity 100% over ideal weight.

Current guidelines use the body mass index (BMI) to define obesity. The BMI utilizes height and weight to compare the ratio of body fat to total body mass. To calculate BMI using metric units, weight in kilograms is divided by height in meters squared. To calculate BMI in English units, weight in pounds is divided by height in inches squared and then multiplied by 703. This calculated BMI is compared to the statistical distribution of BMIs for adults aged 20–29 to determine whether an individual is underweight, average, overweight, or obese. The 20- to 29-year age group was chosen as the standard because it represents fully developed adults at the point in their lives when they have the least amount of body fat. Ideally body fat is about 15% of total body mass for adult males and about 20–25% for adult females. A simple BMI calculator is available at http://www.nhlbisupport.com/bmi. However BMI does not distinguish between fat and muscle.

Adult BMIs are age- and gender-independent. All adults aged 20 and older are evaluated on the same BMI scale as follows:

- underweight: BMI below 18.5
- normal weight: BMI 18.5–24.9
- overweight: BMI 25.0–29.9
- obese: BMI 30 and above Research has shown that adults with BMIs within the normal weight range live longest and enjoy the best health.

The BMI for children and teens is calculated in the same way as for adults, but the results are interpreted differently. A child's BMI is compared to those of other children of the same age and gender and assigned to a percentile. For example, a girl in the 75th percentile for her age group weighs more than 74 of every 100 girls her age and less than 25 of every 100 girls her age:

- underweight: below the 5th percentile
- healthy weight: 5th percentile to below the 85th percentile
- at risk of overweight: 85th percentile to below the 95th percentile
- overweight: 95th percentile and above. The CDC does not use the term "obese" for children and teens because the proportion of body fat fluctuates during growth and development and is slightly higher than in mature adults.

Obesity places **stress** on the body's organs and puts people at higher risk for many serious and potentially life-threatening health problems:

- fatigue
- joint problems
- poor physical fitness
- digestive disorders
- dizzy spells
- rashes
- hypertension (high blood pressure)
- menstrual disorders
- complications during childbirth and surgery
- type 2 diabetes mellitus (non-insulin dependent)
- heart disease
- unexplained heart attack
- gallstones
- breathing problems
- hyperlipidemia
- infertility
- colon, prostate, endometrial, and breast cancers
- premature aging
- Alzheimer's disease

Obese individuals have a shorter life expectancy than people of normal weight. Many diseases, especially degenerative diseases of the joints, heart, and blood vessels, tend to be more severe in obese individuals, increasing the need for some surgical procedures. Obesity is directly related to the increasing prevalence of type 2 diabetes in the United States and for the appearance of type 2 diabetes in children, previously a rarity.

Although acute complications of obesity are rare in children, **childhood obesity** is a risk factor for **insulin resistance** and type 2 diabetes, **hypertension**, hyperlipidemia, liver and renal disease, and reproductive dysfunction. Childhood obesity increases the risk of deformed bones in the legs and feet. It can also result in emotional disorders such as depression caused by social isolation and negative comments by peers. Moreover childhood obesity increases the risks of adult obesity and cardiovascular disease.

The cost of obesity to the U.S. economy in 2006 was estimated at about $100 billion, of which $52 billion were for direct healthcare costs and $33 billion were for weight-loss products and services. The increasing prevalence of obesity and diabetes in children and young adults heralds spiraling healthcare costs in the future. The social costs of obesity, including decreased productivity, discrimination, depression, and low self-esteem, are less easily measured.

In 1995 the Institute of Medicine of the U.S. National Academies published a report describing obesity as a "complex, multifactorial disease of appetite regulation and energy metabolism." The report cited the following outcomes from even relatively modest weight loss:

- lower blood pressure (and lower risk of heart attack and stroke)
- reduction of abnormally high levels of blood glucose
- lower blood levels of cholesterol and triglycerides (and lower risk of cardiovascular disease)
- lower incidence of sleep apnea
- lower risk for osteoarthritis in weight-bearing joints
- lower incidence of depression
- improved self-esteem

Risk factors

Obesity tends to run in families. Children of obese parents are about 13 times more likely than other children to be obese. Additional obese family members, including siblings and grandparents, greatly increases the likelihood of childhood obesity. The tendency toward a body type with an unusually high number of fat cells—termed *endomorphic*—appears to be inherited. Other genetic factors influence appetite and the metabolic rate at which food is transformed into energy. However family eating habits are major contributors to the development of obesity. Although the majority of adopted children have patterns of weight gain that more closely resemble those of their birth parents than those of their adoptive parents, normal-weight children adopted into obese families are more likely than other children to become obese. Longitudinal studies of juvenile-onset obesity have demonstrated parental and peer encouragement of overeating and even deliberate overfeeding of obese children.

Low socioeconomic status is a risk factor for adult-onset obesity.

Causes and symptoms

Obesity is caused by the consumption of more calories than the body uses for energy. The excess calories are stored as adipose tissue. Although inheritance may play a role, a genetic predisposition toward weight gain does not in itself cause obesity. Hormonal and genetic disorders account for less than 10% of obesity in children. Eating habits, physical activity, and environmental, behavioral, social, and cultural factors all contribute to the development of obesity.

Sometimes obesity does have a purely physiological cause:

- Cushing's syndrome, a disorder involving the excessive release of the hormone cortisol
- hypothyroidism caused by an under-active thyroid gland, resulting in low levels of the hormone thyroxin and the slow metabolism of food, causing excess unburned calories to be stored as fat
- some cases of hypoglycemia, or low blood sugar, due to a metabolic disorder that results in carbohydrates being stored as fat
- neurological disturbances, such as damage to the hypothalamus, a structure located deep within the brain that helps regulate appetite
- certain drugs such as steroids, antipsychotic medications, and antidepressants

Some researchers have suggested that low levels of the neurotransmitter serotonin increase cravings for carbohydrates. In addition, a combination of genetics and early nutritional habits may result in a higher "set point" for body weight that causes obese individuals to feel hunger more often than others. Recent obesity research has focused on two peptide hormones, leptin and ghrelin. Leptin produced by fat cells affects hunger and eating behavior and an insensitivity to leptin may contribute to obesity. Ghrelin is secreted by cells in the lining of the stomach and is important in appetite regulation and maintaining the body's energy balance.

However most obesity is caused by overeating. During the past decades American eating habits have changed significantly, with many people consuming larger meals and more high-calorie processed foods. School and workplace cafeterias often have a poor selection of nutritional food offerings. Furthermore it is estimated that in a given six-month period, 2–5% of Americans binge eat. It has been estimated that approximately 15% of the mildly obese participating in weight-loss programs have binge-eating disorder and that the percentage is much higher among the morbidly obese.

Some recent studies have suggested that the amount of fat in a person's diet may have a greater impact on weight than the total number of calories. Carbohydrates from cereals, breads, fruits, and vegetables, and protein from fish, lean meat, turkey breasts, and skim milk are converted into fuel almost as soon as they are consumed. In contrast most fats are immediately stored in fat cells, which multiply and expand, adding to the body's weight and girth. However current evidence indicates that weight gain depends primarily on total calories consumed, rather than the amount from carbohydrates versus fats, and that low-fat **diets** are no more effective for weight reduction than low-calorie diets.

Sedentary lifestyles, which are particularly prevalent in affluent societies such as the United States, also contribute to obesity. Rather than physical labor on farms and in factories, people are now employed at sedentary jobs in post-industrial service industries. Calorie-saving; machines and devices—cars, computers, remote control devices, household electric appliances, and power tools—have become standard equipment. One study found that the average Western European adult walks about 8,000–9,000 steps daily. In contrast, among the Amish of Pennsylvania who do not use cars or electricity, men accumulate 18,425 steps daily and have no obesity. Amish women walk 14,196 steps daily and have an obesity rate of only 9%.

Psychological factors, such as depression and low self-esteem, can contribute to overeating and obesity. People may eat compulsively to overcome fear or social maladjustment, express defiance, or avoid intimate relationships.

Some babies are born obese. This can be caused by excessive insulin production in the fetuses of diabetic mothers or excess trans-placental nutrients in the case of obese mothers or those who gain excessive weight during **pregnancy**.

Some babies become obese because they are overfed. Grandmothers may value a "nice plump baby" or caregivers may use a bottle to quiet an infant or to demonstrate their own competence as child-rearers. Because obese one-year-olds may be physically delayed in crawling and walking, they become less active toddlers, burning fewer calories. By the age of 10, obese boys and girls are taller than their peers by as much as 10 centimeters. Their skeletal maturation, called "bone-age," is also accelerated, so they stop growing earlier. Sexual maturation is advanced. It is not uncommon for obese girls to experience precocious menarche (early onset of menstruation), sometimes even before age 10. Parental separation and divorce or other psychological stresses may stimulate compensatory overeating in children. Obese teenagers and, increasingly, obese preteens may combine periods of **binge eating** and caloric deprivation, leading to bulimia or **anorexia nervosa**.

In developed countries people generally experience increased BMI with age. The proportion of intra-abdominal fat, which correlates with disease and death, increases progressively with age. There is also a progressive decline in daily total energy expenditure, associated with decreased physical activity and lower metabolic activity, especially in those with chronic disabilities and diseases.

The major symptoms of obesity are excessive weight and large amounts of fatty tissue. Common secondary symptoms include **shortness of breath** and lower back pain from carrying excessive body weight. Obesity can also give rise to secondary conditions including:

- arthritis and other orthopedic problems
- hernias
- heartburn
- adult-onset asthma
- gum disease
- high cholesterol levels
- gallstones
- high blood pressure
- menstrual irregularities or cessation of menstruation (amenorhhea)
- decreased fertility and pregnancy complications
- incapacitating shortness of breath
- sleep apnea and sleeping disorders
- skin disorders from the bacterial breakdown of sweat and cellular material in thick folds of skin or from increased friction between folds
- emotional and social difficulties

Diagnosis

Examination

Obesity is usually diagnosed by observation of excessive storage fat and by calculating BMI from weight and height. Physicians also observe how the excess weight is carried by comparing waist and hip measurements: "apple-shaped" patients—who store most of their weight around the waist and abdomen—are at greater risk for **cancer**, heart disease, **stroke**, and diabetes than "pear-shaped" patients whose extra pounds settle primarily in their hips and thighs.

KEY TERMS

Adipose tissue—Fat tissue.

Anemia—Red blood cell deficiency.

Appetite suppressant—A drug that reduces appetite.

Bariatrics—The branch of medicine that deals with the prevention and treatment of obesity and related disorders.

Binge-eating disorder—A condition characterized by uncontrolled eating.

Body Mass Index (BMI)—A measure of body fat: the ratio of weight in kilograms to the square of height in meters.

Calorie—A unit of food energy.

Carbohydrate—Sugars, starches, celluloses, and gums that are a major source of calories from foods.

Catecholamines—Hormones and neurotransmitters including dopamine, epinephrine, and norepinephrine.

Eating disorder—A condition characterized by an abnormal attitude towards food, altered appetite control, and unhealthy eating habits that affect health and the ability to function normally.

Epidemic—Affecting many individuals in a community or population and spreading rapidly.

Fat—Molecules composed of fatty acids and glycerol; the slowest utilized source of energy, but the most energy-efficient form of food. Each gram of fat supplies about nine calories, more than twice that supplied by the same amount of protein or carbohydrate.

Gastroplasty—A surgical procedure used to reduce digestive capacity by shortening the small intestine or shrinking the side of the stomach.

Ghrelin—A peptide hormone secreted primarily by the stomach that has been implicated in the control of food intake and fat storage.

Hyperlipidemia—Abnormally high levels of lipids in the blood.

Hyperplastic obesity—Excessive weight gain in childhood, characterized by an increase in the number of fat cells.

Hypertension—Abnormally high arterial blood pressure, which if left untreated can lead to heart disease and stroke.

Hypertrophic obesity—Excessive weight gain in adulthood, characterized by expansion of pre-existing fat cells.

Ideal weight—Weight corresponding to the lowest death rate for individuals of a specific height, gender, and age.

Leptin—A peptide hormone produced by fat cells that acts on the hypothalamus to suppress appetite and burn stored fat.

Metabolic activity—The sum of the chemical processes in the body that are necessary to maintain life.

Metabolic bone disease—Weakening of bones due to a deficiency of certain minerals, especially calcium.

Normal weight—A BMI of less than 25.0.

Obesity—An abnormal accumulation of body fat, usually 20% or more above ideal body weight or a BMI of 30.0 or above.

Osteoporosis—A disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility.

Overweight—A BMI between 25.0 and 30.0.

Serotonin—A neurotransmitter located primarily in the brain, blood serum, and stomach membrane.

Procedures

BMIs and other measurements do not necessarily accurately reflect body composition and muscle mass. A heavily muscled football player may weigh far more than a sedentary man of similar height, but have significantly less body fat. Chronic dieters, who have lost significant muscle mass during periods of caloric deprivation, may look slim and weigh little but have elevated body fat. Therefore direct measurements of body fat are obtained using calipers to measure skin-fold thickness at the back of the upper arm and other sites, which distinguishes between muscle and adipose tissue.

The most accurate means of estimating body fat is hydrostatic weighing—calculating the volume of water displaced by the body. The patient exhales as completely as possible and is immersed in water and the relative displacement is measured. Women whose body fat exceeds 30–32% of total body mass by this method and men whose body fat exceeds 25–27% are generally considered obese. Since this method is unpleasant and impractical, it is usually used only in scientific studies.

Treatment

Traditional

Treatment of obesity aims at reducing weight to a BMI within the normal range (below 25.0). The best way to achieve weight loss is to reduce dietary caloric intake and increase physical activity. However obesity will return unless the weight loss includes lifes long behavioral changes. "Yo-yo" dieting, in which weight is repeatedly lost and regained, has been shown to increase the likelihood of fatal health problems even more than no weight loss at all.

Behavioral treatment for obesity is goal-directed and process-oriented and relies heavily on self-monitoring, with emphasis on:

- Food intake: This may involve keeping a food diary and learning the nutritional value, caloric content, and fat content of foods. It may involve changing shopping habits, such as only shopping on a certain day and buying only what is on the grocery list, timing meals and planning frequent small meals to prevent hunger pangs, and eating slowly to allow for satiation.
- Response to food: This may involve understanding psychological issues underlying eating habits. For example, some people binge eat when under stress, whereas others use food as a reward. By recognizing psychological triggers, alternate coping mechanisms, which do not focus on food, can be developed.
- Time usage: Integrating exercise into everyday life is a key to achieving and maintaining weight loss. Starting slowly and building endurance keeps patients from becoming discouraged. Varying routines and trying new activities keeps interest high.
- Stimulus control: This may involve removing environmental cues for inappropriate eating.
- Contingency management: A system of positive and negative reinforcements may help with behavioral modification.

Most mildly obese patients can make these lifestyle changes independently with medical supervision. Others may utilize a commercial weight-loss program such as Weight Watchers. The effectiveness of these programs is difficult to assess, since they vary widely, dropout rates are high, and few employ medical professionals. However programs that emphasize realistic goals, gradual progress, sensible eating, and **exercise** can be very helpful and are recommended by many physicians. Programs that promise instant weight loss or utilize severely restricted diets are not effective and, in some cases, can be dangerous.

Moderately obese patients require medically supervised behavior modification and weight loss. A realistic goal is a 10% weight loss over a six-month period. Most doctors use a balanced, low-calorie diet of 1200–1500 calories a day. However sometimes certain patients may be put on a medically supervised very-low 400–700 calorie liquid protein diet, with supplementation of **vitamins** and **minerals**, for as long as three months. This therapy should not be confused with commercial liquid-protein diets or weight-loss shakes and drinks. Very-low-calorie diets must be designed for specific patients who are monitored carefully and are used for only short periods. Physicians will also refer patients to professional therapists or psychiatrists for help in changing eating behaviors. Without changing eating habits and exercise patterns, the lost weight will be regained quickly.

For morbidly obese patients, dietary changes and behavior modification may be accompanied by **bariatric surgery**. Gastroplasty involves inserting staples to decrease the size of the stomach. Gastric banding is an inflatable band inserted around the upper stomach to create a small pouch and narrow passage into the remainder of the stomach. Although bariatric surgery has become less risky in recent years with innovations in equipment and surgical techniques, it is still performed only on patients for whom supervised diet and exercise strategies have failed, who are at least 100 lb (45 kg) overweight or twice their ideal body weight, and whose obesity seriously threatens their health. Risks and possible complications include infections, hernias, and **blood clots**. Overall, 10–20% of patients who undergo weight-loss surgery require additional operations to correct complications, more than 33% develop **gallstones**, and 30% develop nutritional deficiencies such as anemia, **osteoporosis**, or metabolic bone disease.

Other bariatric surgical procedures—including **liposuction**, a purely cosmetic procedure in which a suction device removes fat from beneath the skin, and **jaw wiring**, which can damage gums and teeth and cause painful muscle spasms—have no place in obesity treatment.

Weight loss is recommended for obese children over age seven and for obese children over age two who have medical complications. Weight maintenance is an appropriate goal for children over the age of two who have no medical complications. Most treatment approaches to childhood obesity involve a combination of caloric restriction, physical exercise, and behavioral therapy. Bariatric surgery is considered as a last resort only for adolescents who are fully grown.

Drugs

The short-term use of prescription medications may assist some individuals in managing their condition, but it is never the sole treatment for obesity, nor are drugs ever considered as a cure for obesity. Diet drugs are designed to help medically at-risk obese patients "jump-start" their weight-loss effort and lose 10% or more of their starting body weight, in combination with a diet and exercise regimen. Prescription weight-loss drugs are approved by the U.S. Food and Drug Administration (FDA) only for patients with a BMI of 30 or above or a BMI of 27 or above and an obesity-related condition such as high blood pressure, type 2 diabetes, or dyslipidemia (abnormal amounts of fats in the blood). The weight is usually regained as soon as the drugs are discontinued, unless eating and exercise habits have changed.

Most appetite-suppressants are based on amphetamine. They increase levels of serotonin or catecholamine, brain chemicals that control feelings of fullness. Serotonin also regulates mood and may be linked to mood-related eating behaviors. Prescription weight-loss medications include:

- diethylpropion (Tenuate, Tenuate Dospan)
- mazindol (Mazanor, Sanorex)
- phendimetrazine (Bontril, Melfiat)
- phentermine (Adipex-P, Ionamin)
- sibutramine (Meridia)

Sibutramine should be taken only under close medical supervision. It can significantly elevate blood pressure and should not be used by patients with a history of congestive **heart failure**, heart disease, stroke, or uncontrolled high blood pressure.

While most of the immediate side effects of appetite suppressants are harmless, their long-term effects may be unknown. Dexfenfluramine hydrochloride (Redux), fenfluramine (Pondimin), and the fenfluramine-phentermine combination (Fen/Phen) were taken off the market after they were shown to cause potentially fatal cardiac effects. Phenylpropanolamine, a component of many nonprescription weight-loss and cold and **cough** medications (Acutrim, Dex-A-Diet, Dexatrim, Phenldrine, Phenoxine, PPA, Propagest, Rhindecon, Unitrol) was removed from shelves because of an increased risk of stroke. Appetite-suppressants can be habit-forming and have the potential for **abuse**. Appetite suppressants should not be used by patients taking **monoamine oxidase inhibitors** (MAOIs) and are not recommended for children.

Side effects of prescription and over-the-counter weight-loss products may include:

- constipation
- dry mouth
- headache
- irritability
- nausea
- nervousness
- sweating

Unlike appetite suppressants, orlistat is a lipase inhibitor that reduces the breakdown and absorption of dietary fat in the intestines. It is available in both prescription (Xenical) and non-prescription (alli) forms. Side effects of orlistat may include abdominal cramping, gas, fecal urgency, oily stools, frequent bowel movements, and **diarrhea**.

Other drugs are sometimes prescribed off-label for treating obesity. For example, fluoxetine (Prozac) is an antidepressant that sometimes aids in temporary weight loss. Side effects of this medication include diarrhea, **fatigue**, **insomnia**, **nausea**, and thirst.

Alternative

Functional food diets are newer, as yet unproven, approaches to weight loss:

- carbohydrates with a low glycemic index, which may help suppress appetite
- green tea extract, which may increase the body's energy expenditure
- chromium, which may encourage the burning of stored fat rather than lean muscle tissue

Various herbs and supplements are promoted for weight loss:

- Diuretic herbs, which increase urine production, can result in short-term weight loss, but do not help with lasting weight control. Increased urine output increases thirst to replace lost fluids and patients who use diuretics for an extended period of time eventually start retaining water anyway.
- In moderate doses, psyllium, a mucilaginous herb available in bulk-forming laxatives like Metamucil, absorbs fluid and provides a feeling of fullness.
- Red peppers and mustard may help encourage weight loss by accelerating the body's metabolic rate. They also cause thirst, so patients crave water instead of food.
- Walnuts can be a natural source of serotonin for providing a feeling of satiation.
- Dandelion (*Taraxacum officinale*) can increase metabolism and counter a desire for sugary foods.
- The amino acid 5-hydroxytryptophan (5-HTP), which is extracted from the seeds of *Griffonia simplicifolia*, is thought to increase serotonin levels in the brain. Patients should consult with their healthcare

provider before taking 5-HTP, as it may interact with other medications and can have potentially serious side effects.

Acupressure and **acupuncture** can suppress food cravings. Visualization and **meditation** can create and reinforce a positive self-image that can enhance a patient's determination to lose weight. By improving physical strength, mental concentration, and emotional serenity, **yoga** can provide the same benefits. Patients who play soft slow music during meals often find that they eat less food but enjoy it more.

Home remedies

Eating the correct ratios of protein, carbohydrates, and high-quality fats are important for weight loss. Support and self-help groups—such as Overeaters Anonymous and TOPS (Taking Off Pounds Sensibly)—that promote nutritious, balanced diets can help patients maintain proper eating regimens.

Fad dieting can have harmful health effects. Weight should be lost gradually and steadily by decreasing calories while maintaining an adequate nutrient intake and level of physical activity. A daily caloric intake of 1,000–1,200 calories for women and 1,200–1,600 for men enables most people to lose weight safely. A loss of about 2 lb (1 kg) per week is recommended. Diets of less than 800 calories a day should never be attempted unless prescribed and monitored by a physician.

At least 60–90 minutes of daily moderate-intensity physical activity is usually recommended to maintain weight loss. Obese people who have led sedentary lives may need monitoring to avoid injury as they begin to increase their physical activity. Exercise should be increased gradually, perhaps starting by climbing stairs instead of taking elevators, followed by walking, biking, or swimming at a slow pace. Eventually 15-minute walks can be built up to brisk, 45–60-minute walks.

The American Academy of Family Physicians offers advice for families with children who need to maintain or lose weight:

- Weight-loss interventions should begin as soon as possible in children over 2 years of age.
- The family must be ready for change; if not, the program is likely to fail.
- The physician should educate the family as to the medical complications of obesity.
- All family members and caregivers should be involved in the treatment program.
- The physician should encourage the child and family, not criticize them.
- The treatment program should institute permanent changes in eating habits and other behaviors.
- The program should help the family to make small gradual changes.
- The program should include learning ways to monitor eating and exercise.
- Goals should be realistic; even a 5% weight loss, if maintained, can reduce risks to health.

Prognosis

The primary factor in achieving and maintaining weight loss is a lifelong commitment to sensible eating habits and regular exercise. As many as 85% of dieters who do not exercise on a regular basis regain their lost weight within two years and 90% regain it within five years. Short-term diet programs and repeatedly losing and regaining weight encourage the storage of fat and may increase the risk of heart disease.

However prudent dieting and exercise are not quick cures for obesity. With decreased caloric intake, the body breaks down muscle for carbohydrates. Much of the early weight loss on a very low-calorie diet represents loss of muscle tissue rather than fat. Similarly, fat is not easily accessed as fuel for exercise.

The chronically or habitually obese tend to come from families with a larger number of risk factors for obesity and have a much more difficult time losing weight than the newly obese. Likewise, previously obese people have a high probability of reverting to obesity.

When obesity develops in childhood, the total number of fat cells increases (hyperplastic obesity), whereas in adulthood the total amount of fat in each cell increases (hypertrophic obesity). Patients who were obese as children may have up to five times as many fat cells as a patient who became obese as an adult. Decreasing the amount of energy (food) consumed or increasing the amount of energy expended reduces the amount of fat in the cells—but does not reduce the number of fat cells already present—and this process is slow, just like the accumulation of excess fat.

Neonatal obesity does not necessarily translate into childhood or adult obesity, but there is an increased probability if the child is born or adopted into a family with multiple obese members. Likewise excess weight in a child under age three does not necessarily predict adult obesity unless one of the parents is obese.

Summer camps specializing in habitually obese children, especially girls, have little long-term success in reducing obesity and a high degree of recidivism for

habitual overeating and under-exercising. About 30% of overweight girls eventually develop **eating disorders**.

According to the Obesity Prevention Center at the University of Minnesota, obesity-control programs that rely on educational messages encouraging greater physical activity and a healthier diet have been only modestly successful. The best outcomes have been with children's programs that have high levels of physical activity.

Prevention

Prevention is far superior to any available treatment for obesity. Obesity can be prevented by eating a healthy diet, being physically active, and making lifestyle changes that help maintain a normal weight. Examples include

- eating smaller portions of food
- taking the time to prepare healthy meals
- avoiding processed foods
- parking farther away from a store
- walking or bicycling instead of driving
- walking the dog instead of just letting it out

Obesity experts suggest that monitoring fat consumption, as well as counting calories, is a key to preventing excess weight gain. The National Cholesterol Education Program of the National Heart, Lung, and Blood Institute maintains that only 30% of calories should be derived from fat and only one-third of those should be saturated fats. High concentrations of saturated fats are found in meat, poultry, and dairy products. Fat replacers or substitutes are now added to many foods. They reduce the amount of fat and usually also reduce the number of calories. It is not clear what effect these will have on the long-term battle against obesity.

However total caloric intake cannot be ignored, since it is usually the slow accumulation of excess calories, regardless of the source, that results in obesity. A single daily cookie providing 25 excess calories will result in a 5-lb weight gain by the end of one year. Because most people eat more than they think they do, keeping a detailed and honest food diary is a useful way to assess eating habits. Eating three balanced, moderate-portion meals a day—with the main meal at mid-day—is a more effective way to prevent obesity than **fasting** or crash diets that trick the body into believing it is starving. After 12 hours without food, the body has depleted its stores of readily available energy and begins to protect itself for the long term. Metabolic rate starts to slow and muscle tissue is broken down for the raw materials needed for energy maintenance.

The U.S. Department of Agriculture (USDA) food pyramid, called *MyPyramid* to distinguish it from earlier versions, contains recommendations on diet and exercise based on the *Dietary Guidelines for Americans 2005*, tailored for an individual's BMI. It includes recommendations on physical activity and in seven food categories: grains, vegetables, fruits, milk, meat and beans, oils, and discretionary calories.

It has been suggested that there may be little benefit in encouraging weight loss in older people, especially when there are no obesity-related complications or when promoting changes in lifelong eating habits creates stress. However studies have shown that weight loss in seniors can lower the incidence of arthritis, diabetes, and other conditions, reduce cardiovascular risk factors, and improve well-being. Increased physical activity in the elderly also improves muscle strength and endurance.

The poor prognosis for reversing adult obesity makes childhood prevention imperative. Unhealthy eating patterns and behaviors associated with obesity can be addressed by programs in **nutrition**, exercise, and stress management involving the entire family.

Health care team roles

- Physicians diagnose obesity and prescribe drugs.
- Nutritionists and dietitians can design safe and effective meal plans based on individual requirements.
- Nurses also make nutritional recommendations and monitor daily dietary intake.
- Personal trainers and fitness instructors teach weight training and cardiovascular exercise to increase the amount of lean muscle mass and decrease body fat.
- Physical therapists design exercise programs for obese people with back or knee problems that prevent conventional exercising.
- Psychologists use therapies including hypnotism and imagery to help improve emotional well-being, self-esteem, and body image.
- Psychiatrists prescribe drugs to treat depression and anxiety disorders that result from and contribute to obesity.
- Holistic health professionals may use sound therapy, relaxation, and yoga to treat obesity.

Resources

BOOKS

Adolfsson, Birgitta, and Marilynn S. Arnold. *Behavioral Approaches to Treating Obesity*. Alexandria, VA: American Diabetes Association, 2006.

Apovian, Caroline M., and Carine M. Lenders, eds. *Clinical Guide for Management of Overweight and Obese Children and Adults*. Boca Raton, FL: Taylor and Francis, 2006.

Apple, Robin F., James Lock, and Rebecka Peebles. *Is Weight Loss Surgery Right for You?* New York: Oxford University Press, 2006.

Duyff, Roberta Larson. *ADA Complete Food and Nutrition Guide*, 3rd ed. Chicago: American Dietetic Association, 2006.

Finkelstein, Eric A., and Laurie Zuckerman. *The Fattening of America: How the Economy Makes Us Fat, If It Matters, and What To Do About It*. New York: John Wiley & Sons, 2008.

Flamenbaum, Richard K., ed. *Childhood Obesity and Health Research*. New York: Nova Science Publishers, 2006.

Hassink, Sandra Gibson. *Guide to Pediatric Weight Management and Obesity*. Philadelphia: Lippincott Williams and Wilkins, 2007.

Marcovitz, Hal. *Diet Drugs*. Farmington Hills, MI: Lucent Books, 2007.

PERIODICALS

Birch, Leann L. "Child Feeding Practices and the Etiology of Obesity." *Obesity* 14, no. 3 (March 2006): 343–344.

Chen, H., and X. Guo. "Obesity and Functional Disability in Elderly America." *Journal of the American Geriatric Society* 56, no. 4 (April 2008): 689–694.

Fabricatore, Anthony N., and Thomas A. Wadden. "Obesity." *Annual Review of Clinical Psychology* 2 (2006): 357–377.

Johannsen, Darcy L., Neil M. Johannsen, and Bonny L. Specker. "Influence of Parents' Eating Behaviors and Child Feeding Practices on Children's Weight Status." *Obesity* 14, no. 3 (March 2006): 431–439.

Masi, C. M., et al. "Respiratory Sinus Arrhythmia and Diseases of Aging: Obesity, Diabetes Mellitus, and Hypertension." *Biological Psychology* 74, no. 2 (February 2007): 212–223.

Ogden, C., et al. "High Body Mass Index for Age Among U.S. Children and Adolescents, 2003–2006." *Journal of the American Medical Association* 299 (2008): 2401–2405.

OTHER

"Body Percentile Calculator for Child and Teen." *Centers for Disease Control and Prevention*. http://apps.nccd.cdc.gov/dnpabmi/Calculator.aspx

"Dietary Guidelines for Americans." *U.S. Department of Health & Human Services*. http://www.health.gov/dietaryguidelines/

"MyPyramid: Steps to a Healthier You." *U.S. Department of Agriculture*. http://www.mypyramid.gov

National Heart, Lung, and Blood Institute. "Information for Patients and the Public." *Aim for a Healthy Weight*. http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/risk.htm

Office on Women's Health. "Overweight, Obesity, and Weight Loss." *Womens Health.gov*. http://womenshealth. gov/faq/weightloss.htm

Ogden, C. L., et al. "Obesity Among Adults in the United States—No Change since 2003–2004." *NCHS Data Brief No. 1*. http://www.cdc.gov/nchs/data/databriefs/db01.pdf

"Overweight and Obesity." *Centers for Disease Control and Prevention*. http://www.cdc.gov/nccdphp/dnpa/obesity/faq.htm

"Overweight and Obesity: How Are Overweight and Obesity Diagnosed?" *National Heart, Lung, and Blood Institute*. http://www.nhlbi.nih.gov/health/dci/Diseases/obe/obe_diagnosis.html

Weight-Control Information Network. "Prescription Medications for the Treatment of Obesity." *NIH Publication No. 07-4191*. http://win.niddk.nih.gov/publications/prescription.htm

ORGANIZATIONS

American Academy of Family Physicians, 11400 Tomahawk Creek Parkway, Leawood, KS, 66211-2680, (913) 906-6000, (800) 274-6000, (913) 906-6075, http://www.aafp. org/online/en/home.html.

American Council for Fitness and Nutrition, 1350 I Street, Suite 300, Washington, DC, 20005, (614) 442-8793, input@acfn.org, http://www.acfn.org.

American Dietetic Association, 120 South Riverside Plaza, Suite 2000, Chicago, IL, 60606-6995, (800) 877-1600, http://www.eatright.org.

American Society for Metabolic and Bariatric Surgery, 100 SW 75th Street, Suite 201, Gainesville, FL, 32607, (352) 331-4900, (352) 331-4975, info@asmbs.org, http://www.asbs.org.

Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA, 30333, (888) 232-6348, (301) 563-6595, cdcinfor@cdc.gov, http://www.cdc.gov.

National Heart, Lung, and Blood Institute, NHLBI Health Information Center, P.O. Box 30105, Bethesda, MD, 20824-0105, (301) 592-8573, (240) 629-3246, nhlbiinfo@nhlbi.nih.gov, http://www.nhlbi.nih.gov.

Obesity Prevention Center, University of Minnesota, 1300 South Second Street, Suite 300, Minneapolis, MN, 55454, (612) 625-6200, umopc@epi.umn.edu, http://www.ahc.umn.edu/opc/home.html.

The Obesity Society, 8630 Fenton Street, Suite 814, Silver Spring, MD, 20910, (301) 563-6526, (301) 563-6595, http://www.obesity.org.

Overeaters Anonymous, P.O. Box 44020, Rio Rancho, NM, 87174-4020, (505) 891-2664, (505) 891-4320, http://www.oa.org.

Weight-Control Information Network (WIN), 1 WIN Way, Bethesda, MD, 20892-3665, (888) 232-6348, (202) 828-1028, win@info.niddk.nih.gov, http://win.niddk.nih.gov.

Rosalyn Carson-DeWitt, MD
Tish Davidson, AM
Rebecca J. Frey, PhD
Stanley Garn, PhD
Elizabeth Reid Holter, MD
Maia Appleby
Monique Laberge, PhD
Margaret Alic, PhD

Obesity surgery

Definition

Obesity surgery is an operation that either reduces the size of the stomach or bypasses a part of the digestive system so that severely overweight people obtain fewer calories and can achieve significant and permanent weight loss. Obesity surgery is also called **bariatric surgery**.

Purpose

Obesity is the second leading cause of preventable **death** in the United States after tobacco use. It is linked to the increased likelihood of developing more than 20 different diseases and disorders including high blood pressure (**hypertension**), type 2 diabetes, heart disease, **stroke**, deep vein **blood clots**, fatty **liver disease**, **sleep apnea**, **heartburn**, **gastroesophageal reflux disease** (GERD), gallstone disease, arthritis, **colon cancer**, breathing problems, and depression.

Obesity surgery is most often performed on severely overweight people who are more than twice their ideal weight or who has a body mass index (BMI) of 40 or above. BMI is a measure of body fatness that compares height to weight. This level of obesity often is referred to as morbid obesity since it substantially increases the risk of developing any of the health problems listed above. According to the National Institutes of Health, in 2006, 34% of Americans were overweight and 27% were obese. The average patient having obesity surgery is a woman in her late 30s who weighs about 300 pounds (135 kg).

Beginning in the early 2000s, some researchers concluded that obesity surgery could cure type 2 diabetes in many people who were not yet morbidly obese. Therefore, this surgery is now performed more often on less obese people whose risk of complications of surgery is outweighed by the need to lose weight to prevent health complications and for whom supervised weight loss and **exercise** programs have repeatedly failed. Obesity surgery, however, does not make people thin. Most people lose about 60% of their excess weight through this treatment. Changes in diet and exercise are required to maintain a normal weight. This surgery also has a high risk of complications, and therefore, is not undertaken for primarily cosmetic reasons.

The theory behind obesity surgery is that if the volume the stomach holds is reduced and the entrance into the intestine is made smaller to slow stomach emptying and/or if part of the small intestine is bypassed or shortened, people will not be able to consume and/or absorb as many calories. With obesity surgery, the volume of food the stomach can hold is reduced from about 4 cups to about 1/2 cup.

Insurers vary in whether they cover the costs of this surgery. Some insurers consider obesity surgery elective surgery and do not cover it. Others will cover these procedures when serious health risks can be documented. Documentation of the necessity for surgery and approval from the insurer should be sought before this operation is performed.

Precautions

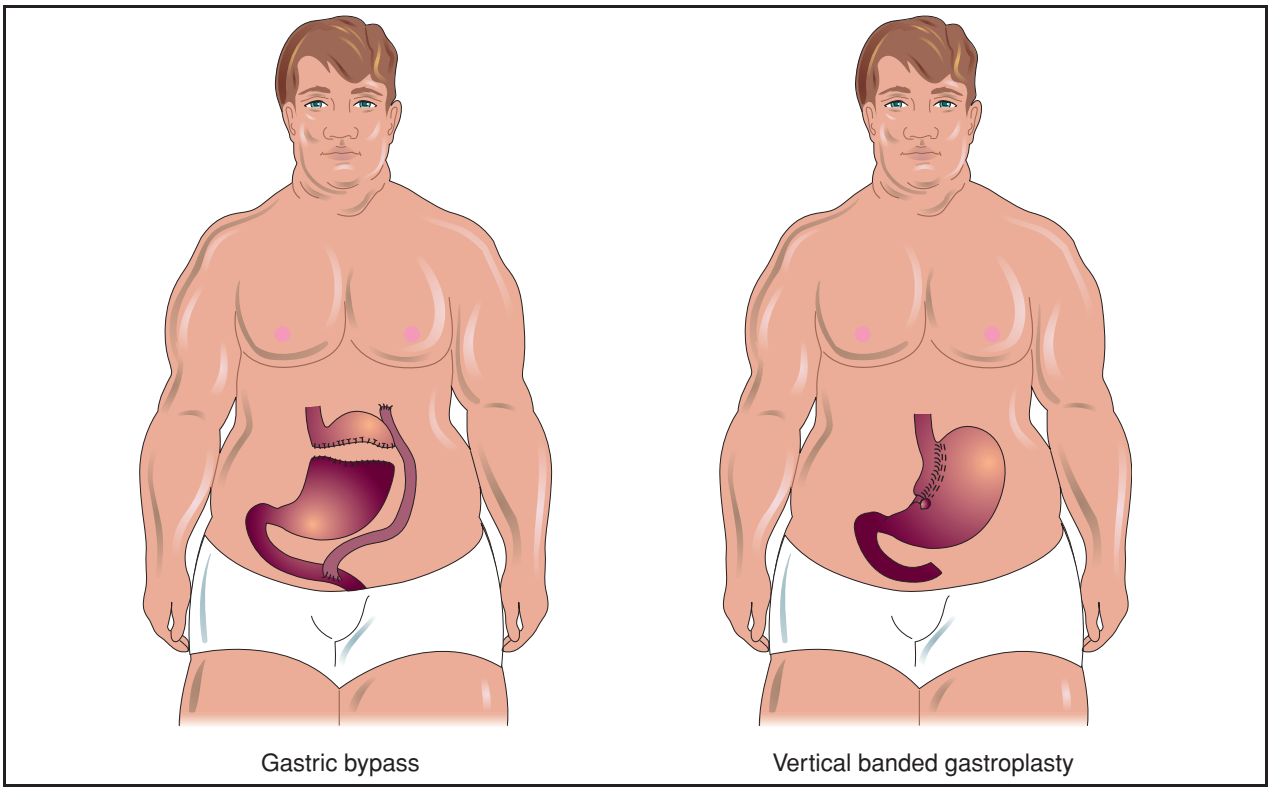
Obesity surgery should not be performed on people who have substance addictions or who have psychological disorders. Other considerations in choosing candidates for obesity surgery include the general health of the person, the health risks posed by continued obesity, and the individual's willingness to comply with follow-up treatment.

Description

Obesity surgery is usually performed in a hospital by a surgeon who has experience with obesity surgery (a bariatric surgeon) or at a center that specializes in the procedure. **General anesthesia** is used, and the operation takes two-three hours. The hospital stay lasts about a week.

Restrictive surgeries

Adjustable gastric band, or Lap-Band surgery restricts the size of the stomach by placing a saline (salt water) filled bag around the stomach, pinching off a portion of it and leaving only a small pouch at the top. The exit to the pouch is narrowed so that the rate at which the pouch empties is slowed. Because the pouch is so small, the individual can only eat about half a cup of food at a time without feeling nauseated.



The purpose of obesity surgery is to reduce the size of the stomach and slow the stomach emptying process by narrowing the entrance into the intestine. With this surgery, the volume of food the stomach can hold is reduced from approximately 4 cups to approximately one-half cup. There are two types of procedures used for obesity surgery: gastric bypass surgery and vertical banded gastroplasty, as shown in the illustration above. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

Adjustable gastric band surgery is the safest surgical weight-loss procedure. Recovery time is rapid compared to other weight-loss surgeries because no part of the digestive system is removed; digestion continues normally just with much smaller amounts of food. A port in the skin allows access to the saline bag so that the size of the stomach pouch opening can be adjusted without additional surgery. The surgery is reversible. The band can be removed because no part of the digestive system was surgically altered.

People who have adjustable band surgery do not feel hungry because stretch sensors in the wall of the stomach tell the brain that the stomach is full. Weight loss averages 50–65% of the excess body weight during the first two years.

Adjustable gastric band surgery also has disadvantages. Individuals must eat five or six very small meals a day. They will vomit if too much food is consumed at once or if it is not chewed well. They also must learn not to fill their stomachs with liquids during their meals. People who have had this surgery must still eat a healthy diet. A steady diet of high-calorie foods such as ice cream will cause weight gain.

Another type of restrictive surgery is vertical banded gastroplasty (VBG), also known as stomach stapling. This surgery is performed less often than Lap-Band surgery. With VBG, part of the stomach is stapled and banded shut making it smaller, so that individuals feel full sooner. The advantage of VBG is that the procedure is quick and has few complications. Disadvantages are that average weight loss is less than with other weight-loss surgeries, and staples can pull out allowing small leaks between the stomach and the abdomen to develop.

Surgery reducing absorption of nutrients

Gastric bypass surgery, also called malabsorptive surgery, has been performed in the United States for about 30 years. This surgery shortens the route that food takes through the digestive system, so that fewer nutrients are absorbed. Gastric bypass surgery is almost always combined with some type of stomach-

restricting surgery so that less food is also moving through the digestive tract.

The most common type of gastric bypass surgery is Roux-en Y gastric bypass. Stapling and banding the stomach creates a small stomach pouch, then a Y-shaped piece of intestine is attached to the pouch on one end, and to the jejunum, or second part of the small intestine, on the other. This allows food to bypass the duodenum (the first part of the intestine) where many calories and nutrients are absorbed. The food then continues normally through the rest of the small intestine and the large intestine.

Roux-en Y gastric bypass allows individuals lose on average 60–70% of their excess weight. Many people are able to maintain the weight loss for 10 years or more and many of their obesity-related health problems are reduced or cured. Nevertheless, Roux-en Y surgery has serious disadvantages. This surgery permanently alters the digestive system. By bypassing the first part of the small intestine, many **vitamins** and **minerals** are no longer adequately absorbed. People who have Roux-en Y surgery must take **nutritional supplements** for the remainder of their lives to prevent vitamin and mineral deficiencies. In addition, dumping syndrome may develop. Dumping occurs when food moves too fast through the intestine and causes symptoms of **nausea**, bloating, weakness, sweating, **fainting** and **diarrhea**.

Billopancreatic diversion (BPD) is a more extreme surgery that bypasses about 9 ft (3 m) of the small intestine. In BPD, about two-thirds of the stomach is surgically removed, and a bypass is created to the ileum, or final portion of the small intestine. This severely restricts the amount of calories and nutrients that are absorbed into the bloodstream. Although large amounts of excess weight—between 75% and 80%—can be lost with BPD, nutrient deficiencies are greater and fat is poorly digested, so that bowel movements are frequent and stools are especially foul smelling.

KEY TERMS

Body Mass Index (BMI)—A measurement of fatness that compares height to weight.

Gastroesophageal reflux disease (GERD)—A condition where gastric juice from the stomach backs up into the bottom of the esophagus and causes irritation, inflammation or erosion of the cells lining the esophagus.

Heartburn—A pain in the center of the chest behind the breastbone caused by the contents of the stomach backflowing (refluxing) into the lower end of the esophagus and causing irritation.

Mineral—An inorganic substance found in the earth that is necessary in small quantities for the body to maintain health. Examples: zinc, copper, iron.

Morbidly obese—Defines a person who is 100 lb (45 kg) or more than 50% overweight and has a body mass index above 40.

Sleep apnea—A temporary interruption in breathing during sleep.

Type 2 diabetes—Sometimes called adult-onset diabetes, this disease prevents the body from properly using glucose (sugar), but can often be controlled with diet and exercise.

Vitamin—A nutrient that the body needs in small amounts to remain healthy but that the body cannot manufacture for itself and must acquire through diet.

Preparation

Many weight loss surgery centers require that patients receive pre-surgery nutritional and psychological counseling. After patients are carefully selected as appropriate for obesity surgery, they receive standard preoperative blood and urine tests and meet with an anesthesiologist to discuss how their health may affect the administration of anesthesia.

Aftercare

Immediately after the operation, most patients are restricted to a liquid diet for two-three weeks; however, some may remain on it for up to 12 weeks depending on the type of surgery they have and how fast they heal. Patients then move on to a diet of pureed food for about a month, and, after about two months, most can tolerate solid food. High-fat food is restricted because it is hard to digest and causes diarrhea. Patients are expected to work on changing their eating and exercise habits to assist in weight loss. Most people eat three-five small meals a day once they return to solid food. Eating too quickly or too much after obesity surgery can cause **nausea and vomiting** as well as intestinal "dumping," a condition in which undigested food is shunted too quickly into the small intestine, causing **pain**, diarrhea, weakness, and **dizziness**.

Risks

As in any abdominal surgery, there is always a risk of excessive bleeding, infection, and allergic reaction to anesthesia. Specific risks associated with obesity

surgery include leaking or stretching of the pouch and loosening of the gastric staples. Although the average death rate associated with this procedure is less than 1%, the rate varies from center to center, ranging from 0–4%. Long-term failure rates can reach 50%. Additional surgery is sometimes required. Other complications of obesity surgery include an intolerance to foods high in fats, **lactose intolerance**, bouts of **vomiting**, diarrhea, and intestinal discomfort

Studies on the risks of these surgeries continue. A 2003 report showed that gastric bypass surgery risks increase with age, weight, and male gender. Patients age 55 and older experienced more complications than did younger patients and male patients had more life-threatening complications than female patients, particularly those who were more severely obese.

Normal results

Many people lose about 60% of the weight they need to reach their ideal weight through obesity surgery. However, surgery is not a magic weight-loss operation, and success depends on the patient's willingness to exercise and eat low-calorie foods. A 2003 report showed that extremely morbidly obese patients had a lower success rate with laparoscopic vertical banding gastroplasty than those considered simply morbidly obese. However, overall about 77% of patients reduce their excess weight by about 50% four years after the procedure.

Resources

BOOKS

Apple, Robin F., James Lock, and Rebecka Peebles. *Is Weight Loss Surgery Right for You?* New York: Oxford University Press, 2006.

Furtado, Margaret M., and Lynette Schultz. *Recipes for Life After Weight–Loss Surgery: Delicious Dishes for Nourishing the New You*. Gloucester, MA: Fair Winds Press, 2007.

Kurian, Marina S., Barbara Thompson, and Brian K. Davidson. *Weight Loss Surgery for Dummies*. Hoboken, NJ: Wiley, 2005.

Leach, Susan M. *Before & After, Revised Edition: Living and Eating Well After Weight–Loss Surgery*. New York: Morrow Cookbooks, 2007.

OTHER

Centers for Disease Control and Prevention. "About BMI for Adults." National Institutes of Health. August 26, 2006 http://www.cdc.gov/nccdphp/dnpa/bmi/adult_BMI/about_adult_BMI.htm

Cleveland Clinic Staff. "Bariatric Surgery for Severe Obesity." The Cleveland Clinic, March 28, 2008. http://my.clevelandclinic.org/services/gastrointestinal_surgery/hic_gastrointestinal_surgery_for_severe_ obesity.aspx

Department of Health and Human Services. "Calculate Your Body Mass Index." National Institutes of Health. Undated, accessed March 26, 2007. http://www.nhlbisupport.com/bmi.

Mayo Clinic Staff. "Gastric Bypass Diet: Nutritional Needs After Weight-loss Surgery." MayoClinic.com, October 14, 2005. http://www.mayoclinic.com/health/gastric-bypass-diet/WT000007

Padda, Sukdeep and Francisco Ramirez. "Dumping Syndrome." eMedicine.com, October 6, 2005. http://www.emedicine.com/med/topic589.htm

Saber, Alan A. and Kathryn L. Hale. "Surgery in the Treatment of Obesity." eMedicineHealth.com, January 13, 2006. http://www.emedicinehealth.com/surgery_in_the_treatment_of_obesity/article_em.htm

Weight-control Information Network (WIN). "Gastrointestinal Surgery for Severe Obesity." National Institute of Diabetes and Digestive and Kidney Diseases, December 2004. http://win.niddk.nih.gov/publications/gastric.htm

ORGANIZATIONS

The Obesity Society, 8630 Fenton St., Suite 814, Silver Spring, MD, 20910, (301)563-6526, (301)563-6595, http://www.obesity.org/.

Weight-control Information Network, 1 WIN Way, Bethesda, MD, 20892-3665, (202)828-1028, (877)946-4627, win@info.niddk.nih.gov, http://win.-niddk. nih.gov.

Tish Davidson, AM
Teresa G. Odle

Obsessive-compulsive disorder

Definition

Obsessive-compulsive disorder (OCD) is a type of **anxiety** disorder. Anxiety disorder is the experience of prolonged, excessive worry about circumstances in one's life. OCD is characterized by distressing repetitive thoughts, impulses or images that are intense, or frightening, and that are unusual or not reasonable. These thoughts are usually followed by ritualized actions that can be either bizarre and irrational themselves, or can be perfectly reasonable actions, such as cleaning or hand washing, that are taken to extremes. These ritual actions, known as compulsions, help reduce anxiety caused by the individual's obsessive thoughts. Often described as the "disease of doubt," the sufferer usually knows the obsessive thoughts and compulsions are irrational but, on another level, fears they may be true.

Description

According to the National Institutes of Health, approximately 2.2 million Americans adults have obsessive-compulsive disorder. The number of children affected with the disorder is not clear, however the Obsessive Compulsive Foundation reports that one in 25 Americans will experience OCD at some point during their lives. It can occur in children and adults. In children, symptoms often begin to appear around age 10 and in adults symptoms most commonly appear around age 21. According to the Obsessive Compulsive Foundation, up to one half of adults with OCD say that it began in childhood. Men and women are believed to be effected by OCD in approximately equal numbers. OCD affects people of all ethnicities.

It can be many years before an individual with obsessive-compulsive disorder is diagnosed. This is because individuals often try to hide their problems for fear of being labeled. Individuals with OCD are not in any way "crazy," but have repeating thoughts and fears that are so distressing, the individual cannot avoid acting on them. Individuals with OCD may recognize on some level that their fears are not rational, but find them so overwhelming that they are unable not to act upon them.

Most people with obsessive-compulsive disorder have both obsessions and compulsions, but some people have just one or the other. The degree to which this condition can interfere with daily living also varies. Some people are barely bothered, while others find the obsessions and compulsions to be profoundly traumatic and spend much time each day in compulsive actions.

Obsessions are intrusive, irrational thoughts that keep popping up in a person's mind, such as "my hands are dirty, I must wash them again." Typical obsessions include fears of dirt, germs, contamination, and violent or aggressive impulses. Other obsessions include feeling responsible for others' safety, or even the repeated thoughts that the person injured someone in a traffic accident when that is not the case. Additional obsessions can involve excessive religious feelings or intrusive sexual thoughts. The individual may need to confess frequently to a religious counselor or may fear acting out the strong sexual thoughts. People with obsessive-compulsive disorder may have an intense preoccupation with order and symmetry, or be unable to throw anything out.

Compulsions usually involve repetitive rituals such as excessive washing (especially hand washing or bathing), cleaning, checking and touching, counting, arranging or hoarding. Often, a person with obsessive-compulsive disorder is driven to perform the rituals because of a fear that if he or she does not something dreadful will happen. As the person performs these acts, he or she may feel better temporarily, but there is no lasting sense of satisfaction, completion, or safety after the act is performed. Although performing the compulsions may temporarily ease **stress**, this short-term comfort has a very high cost. A large quantity of time spent repeating compulsive actions can significantly interfere with activities like school and work, can put a significant strain on relationships, and not leave time for the individual to pursue other activities.

The difference between OCD and other compulsive behavior is that while people who have problems with gambling, overeating or with **substance abuse** may appear to be compulsive, these activities also provide pleasure to some degree. The compulsions of OCD, on the other hand, are never pleasurable.

OCD may be related to some other conditions, such as the continual urge to pull out body hair (trichotillomania), fear of having a serious disease (**hypochondriasis**), or preoccupation with imagined defects in personal appearance (body dysmorphia). Some people with OCD also have **Tourette syndrome**, a condition featuring tics and unwanted vocalizations (such as swearing). OCD can occur alongside depression and with other **anxiety disorders**.

Causes and symptoms

Research suggests that people who have a family member with OCD are more likely to develop obsessive-compulsive disorder themselves. Although no gene for OCD has been identified, it is believed that there may be a genetic predisposition that can be inherited. No one is certain what causes OCD, however there are several theories that have been suggested. Some experts believe that OCD is related to a chemical imbalance within the brain that causes a communication problem between the front part of the brain (frontal lobe) and deeper parts of the brain responsible for the repetitive behavior. Research has shown that the orbital cortex located on the underside of the brain's frontal lobe is overactive in OCD patients. This may be one reason for the feeling of alarm that pushes the patient to perform compulsive, repetitive actions. It is possible that people with OCD experience overactivity deep within the brain that causes the cells to get "stuck," much like a jammed transmission in a car damages the gears. This could lead to the development of rigid thinking and repetitive movements common to the disorder. The fact that drugs which boost the levels of serotonin, a brain

messenger substance linked to emotion and many different anxiety disorders, in the brain can reduce OCD symptoms in many patients may indicate that OCD is related to decreased levels of serotonin in the brain.

Scientists believe there may be a link between childhood episodes of **strep throat** and the development of OCD. It appears that in some vulnerable children, strep throat (infection with group A beta-hemolytic streptococcal pharyngitis) may precede the onset of OCD symptoms. Some scientists hypothesize that this occurs because the antibodies (cells that the body produces to fight specific diseases) that fight strep throat may act on the brain in ways that cause problems with the way neurons communicate. When this happens OCD may result.

Diagnosis

People with obsessive-compulsive disorder may feel ashamed of their problem, may try to hide their symptoms, and may avoid seeking treatment for many reasons. OCD may become more severe as time goes on and it goes untreated, and more severe OCD may be more difficult to treat successfully. OCD may be frequently misdiagnosed or not diagnosed at all. According to the Obsessive Compulsive Foundation, an average of 17 years elapse between the time the OCD symptoms begin and the time appropriate treatment begins. The foundation also reports that individuals with OCD usually see three or four different doctors while seeking treatment.

There is no blood or other test that can determine whether or not an individual has obsessive-compulsive disorder. Instead, doctors must obtain and assess detailed information about an individual's symptoms and history, and may even talk to friends or relatives of the individual to try to obtain as much information as possible. Only after the doctor assesses all the information gathered can a diagnosis be made.

Treatment

Obsessive-compulsive disorder can be treated by **cognitive-behavioral therapy**, medication that regulates the brain's serotonin levels, or a combination of both. Drugs that are approved to treat obsessive-compulsive disorder include fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), and sertraline (Zoloft), all **selective serotonin reuptake inhibitors** (SSRIs) that affect the level of serotonin in the brain. Older drugs include the antidepressant clomipramine (Anafranil), a widely-studied drug in the treatment of OCD, but one that carries a greater risk of side effects than some other available drugs. Drugs may need to be taken for 12 or more weeks before it is possible to determine if they are effective for the particular individual.

KEY TERMS

Anxiety disorder—The experience of prolonged, excessive worry about circumstances in one's life that is severe enough to disrupt daily life.

Cognitive-behavior therapy—A form of psychotherapy that seeks to modify behavior and change the patient's response to stimuli.

Compulsion—A rigid behavior that is repeated over and over unnecessarily.

Obsession—A recurring, distressing idea, thought or impulse that feels "foreign" or alien to the individual.

Selective serotonin reuptake inhibitors (SSRIs)—A class of antidepressants that work by blocking the reabsorption of serotonin in brain cells, raising the level of the chemical in the brain. SSRIs include Prozac, Zoloft, Luvex, and Paxil.

Serotonin—One of three major neurotransmitters found in the brain that is related to emotion, and is linked to the development of depression and obsessive-compulsive disorder.

Cognitive-behavioral therapy (CBT) helps individuals learn new ways of thinking, helping them end the obsessive thought patterns and learn new ways to cope with their fears that do not involve performing the compulsive rituals. Over time, the obsessive thoughts can be reduced, compulsive activities can be stopped, and the individual can spend more time doing enjoyable activities. Times of stress may increase an individual's worry or need to perform rituals, but cognitive-behavioral therapy also provides individuals with techniques to help them make it through such times.

In a few severe cases where patients have not responded to medication or behavioral therapy, brain surgery may be tried as a way of relieving the unwanted symptoms. Surgery can help up to a third of patients with the most severe form of OCD. The most common operation involves removing a section of the brain called the cingulate cortex. The serious side effects of this surgery for some patients include seizures, personality changes and decreased ability to plan.

Alternative treatment

Because OCD sometimes responds to SSRI antidepressants, a botanical medicine called **St. John's**

wort (*Hypericum perforatum*) might have some beneficial effect as well, according to herbalists. St. John's wort is prescribed by herbalists for the treatment of anxiety and depression. They believe that this herb affects brain levels of serotonin in the same way that SSRI antidepressants do. In about one out of 400 people, St. John's wort may initially increase the level of anxiety. Homeopathic constitutional therapy can help rebalance the patient's mental, emotional, and physical well-being, allowing the behaviors of OCD to abate over time.

Prognosis

Obsessive-compulsive disorder is a chronic disease that, if untreated, can last for decades, fluctuating from mild to severe and often worsening with age. When treated by a combination of drugs and behavioral therapy, most patients experience a significant reduction of symptoms, and some patients go into complete remission. Unfortunately, not all patients have such a good response. Some people cannot find relief with either drugs or behavioral therapy. Hospitalization may be required in some extreme cases.

Resources

BOOKS

Abramowitz, Jonathan S., and Arthur C. Houts, eds. *Handbook of OCD: Concepts and Controversies*. New York: Springer, 2005.

Antony, Martin M., Christine Purdon, and Laura Summerfeldt, eds. *Psychological Treatment of Obsessive–Compulsive Disorder: Fundamentals and Beyond*. Washington, DC: American Psychological Association, 2007.

Ling, B.E., ed. *Obsessive Compulsive Disorder Research*. New York: Nova Science, 2005.

ORGANIZATIONS

Anxiety Disorders Association of America, 8730 Georgia Ave., Suite 600, Silver Spring, MD, 20910, (240)485-1001 http://www.adaa.org.

International OCD Foundation, P.O. Box 961029, Boston, MA, 02196, (617)973-5801, (617)973-5803, info@ocfoundation.org, http://www.ocfoundation.org.

National Alliance for the Mentally Ill (NAMI), 3803 N. Fairfax Dr., Suite 100, Arlington, VA, 22203, (703)524-7600, (703)524-9094, (800)950-6264, http://www. nami.org.

Obsessive-Compulsive Anonymous, P.O. Box 215, New Hyde Park, NY, 11040, (516)739-0662, http://obsessivecompulsiveanonymous.org.

Carol A. Turkington
Helen M. Davidson

Obsessive compulsive personality disorder *see* **Personality disorders**

Obstetric sonogram *see* **Pelvic ultrasound**

Obstetrical emergencies

Definition

Obstetrical emergencies are life-threatening medical conditions that occur in **pregnancy** or during or after labor and delivery.

Description

There are a number of illnesses and disorders of pregnancy that can threaten the well-being of both mother and child. Obstetrical emergencies may also occur during active labor, and after delivery (postpartum).

Obstetrical emergencies of pregnancy

ECTOPIC PREGNANCY. An ectopic, or tubal, pregnancy occurs when the fertilized egg implants itself in the fallopian tube rather than the uterine wall. If the pregnancy is not terminated at an early stage, the fallopian tube will rupture, causing internal hemorrhaging and potentially resulting in permanent **infertility**.

PLACENTAL ABRUPTION. Also called *abruptio placenta*, **placental abruption** occurs when the placenta separates from the uterus prematurely, causing bleeding and contractions. If more than 50% of the placenta separates, both the fetus and mother are at risk.

PLACENTA PREVIA. When the placenta attaches to the mouth of the uterus and partially or completely blocks the cervix, the position is termed *placenta previa* (or low-lying placenta). **Placenta previa** can result in premature bleeding and possible postpartum hemorrhage.

PREECLAMPSIA/ECLAMPSIA. Preeclampsia (toxemia), or pregnancy-induced high blood pressure, causes severe **edema** (swelling due to water retention) and can impair kidney and liver function. The condition occurs in approximately 5% of all United States pregnancies. If it progresses to **eclampsia**, toxemia is potentially fatal for mother and child.

PREMATURE RUPTURE OF MEMBRANES (PROM). Premature rupture of membranes is the breaking of the bag of waters (amniotic fluid) before contractions or labor begins. The situation is only considered an emergency if the break occurs before 37 weeks and results in significant leakage of amniotic fluid and/or infection of the amniotic sac.

Obstetrical emergencies during labor and delivery

AMNIOTIC FLUID EMBOLISM. A rare but frequently fatal complication of labor, this condition occurs when amniotic fluid embolizes from the amniotic sac and through the veins of the uterus and into the circulatory system of the mother. The fetal cells present in the fluid then block or clog the pulmonary artery, resulting in **heart attack**. This complication can also happen during pregnancy, but usually occurs in the presence of strong contractions.

INVERSION OR RUPTURE OF UTERUS. During labor, a weak spot in the uterus (such as a scar or a uterine wall that is thinned by a **multiple pregnancy**) may tear, resulting in a uterine rupture. In certain circumstances, a portion of the placenta may stay attached to the wall and will pull the uterus out with it during delivery. This is called uterine inversion.

PLACENTA ACCRETA. *Placenta accreta* occurs when the placenta is implanted too deeply into the uterine wall, and will not detach during the late stages of **childbirth**, resulting in uncontrolled bleeding.

PROLAPSED UMBILICAL CORD. A prolapse of the umbilical cord occurs when the cord is pushed down into the cervix or vagina. If the cord becomes compressed, the oxygen supply to the fetus could be diminished, resulting in brain damage or possible **death**.

SHOULDER DYSTOCIA. Shoulder dystocia occurs when the baby's shoulder(s) becomes wedged in the birth canal after the head has been delivered.

Obstetrical emergencies postpartum

POSTPARTUM HEMORRHAGE OR INFECTION. Severe bleeding or uterine infection occurring after delivery is a serious, potentially fatal situation.

Causes and symptoms

Obstetrical emergencies can be caused by a number of factors, including **stress**, trauma, genetics, and other variables. In some cases, past medical history, including previous pregnancies and deliveries, may help an obstetrician anticipate the possibility of complications.

Signs and symptoms of an obstetrical emergency include, but are not limited to:

- Diminished fetal activity. In the late third trimester, fewer than 10 movements in a two-hour period may indicate that the fetus is in distress.
- Abnormal bleeding. During pregnancy, brown or white to pink vaginal discharge is normal, bright red blood or blood containing large clots is not. After delivery, continual blood loss of more than 500 mL indicates hemorrhage.
- Leaking amniotic fluid. Amniotic fluid is straw-colored and may easily be confused with urine leakage, but can be differentiated by its slightly sweet odor.
- Severe abdominal pain. Stomach or lower back pain can indicate preeclampsia or an undiagnosed ectopic pregnancy. Postpartum stomach pain can be a sign of infection or hemorrhage.
- Contractions. Regular contractions before 37 weeks of gestation can signal the onset of preterm labor due to obstetrical complications.
- Abrupt and rapid increase in blood pressure. Hypertension is one of the first signs of toxemia.
- Edema. Sudden and significant swelling of hands and feet caused by fluid retention from toxemia.
- Unpleasant smelling vaginal discharge. A thick, malodorous discharge from the vagina can indicate a postpartum infection.
- Fever. Fever may indicate an active infection.
- Loss of consciousness. Shock due to blood loss (hemorrhage) or amniotic embolism can precipitate a loss of consciousness in the mother.
- Blurred vision and headaches. Vision problems and headache are possible symptoms of preeclampsia.

Diagnosis

Diagnosis of an obstetrical emergency typically takes place in a hospital or other urgent care facility. A specialist will take the patient's medical history and perform a pelvic and general **physical examination**. The mother's vital signs are taken, and if preeclampsia is suspected, blood pressure may be monitored over a period of time. The fetal heartbeat is assessed with a doppler stethoscope, and diagnostic blood and urine tests of the mother may also be performed, including laboratory analysis for protein and/or bacterial infection. An **abdominal ultrasound** may aid in the diagnosis of any condition that involves a malpositioned placenta, such as placenta previa or placenta abruption.

In cases where an obstetrical complication is suspected, a fetal heart monitor is positioned externally on the mother's abdomen. If the fetal heart rate is erratic or weak, or if it does not respond to movement, the fetus may be in distress. A biophysical profile (BPP) may also be performed to evaluate the health of the fetus. The BPP uses data from an ultrasound examination to analyze the fetus size, movement, heart rate, and surrounding amniotic fluid.

If the mother's membranes have ruptured and her cervix is partially dilated, an internal fetal scalp electrode can be inserted through the vagina to assess heart rate. A fetal oximetry monitor that measures the oxygen saturation levels of the fetus may also be attached to the scalp.

Treatment

Obstetrical emergencies of pregnancy

ECTOPIC PREGNANCY. Treatment of an **ectopic pregnancy** is laparoscopic surgical removal of the fertilized ovum. If the fallopian tube has burst or been damaged, further surgery will be necessary.

PLACENTAL ABRUPTION. In mild cases of placental abruption, bed rest may prevent further separation of the placenta and stem bleeding. If a significant abruption (more than 50%) occurs, the fetus may have to be delivered immediately and a blood **transfusion** may be required.

PLACENTA PREVIA. Hospitalization or highly restricted at-home bed rest is usually recommended if placenta previa is diagnosed after the twentieth week of pregnancy. If the fetus is at least 36 weeks old and the lungs are mature, a **cesarean section** is performed to deliver the baby.

PREECLAMPSIA/ECLAMPSIA. Treatment of preeclampsia depends upon the age of the fetus and the acuteness of the condition. A woman near full term who has only mild toxemia may have labor induced to deliver the child as soon as possible. Severe preeclampsia in a woman near term also calls for immediate delivery of the child, as this is the only known cure for the condition. However, if the fetus is under 28 weeks, the mother may be hospitalized and **steroids** may be administered to try to hasten lung development in the fetus. If the life of the mother or fetus appears to be in danger, the baby is delivered immediately, usually by cesarean section.

PREMATURE RUPTURE OF MEMBRANES (PROM). If PROM occurs before 37 weeks and/or results in significant leakage of amniotic fluid, a course of intravenous **antibiotics** is started. A culture of the cervix may be taken to analyze for the presence of bacterial infection. If the fetus is close to term, labor is typically induced if contractions do not start within 24 hours of rupture.

Obstetrical emergencies during labor and delivery

AMNIOTIC FLUID EMBOLISM. The stress of contractions can cause this complication, which has a high mortality rate. Administering steroids to the mother and delivering the fetus as soon as possible is the standard treatment.

INVERSION OR RUPTURE OF UTERUS. An inverted uterus is either manually or surgical replaced to the proper position. A ruptured uterus is repaired if possible, although if the damage is extreme, a **hysterectomy** (removal of the uterus) may be performed. A blood transfusion may be required in either case if hemorrhaging occurs.

PLACENTA ACCRETA. Women who experience placenta accreta will typically need to have their placenta surgically removed after delivery. Hysterectomy is necessary in some cases.

PROLAPSED UMBILICAL CORD. Saline may be infused into the vagina to relieve the compression. If the cord has prolapsed out the vaginal opening, it may be replaced, but immediate delivery by cesarean section is usually indicated.

Obstetrical emergencies postpartum

POSTPARTUM HEMORRHAGE OR INFECTION. The source of the hemorrhage is determined, and blood transfusion and IV fluids are given as necessary. Oxytocic drugs may be administered to encourage contraction of the uterus. Retained placenta is a frequent cause of persistent bleeding, and surgical removal of the remaining fragments (curettage) may be required. Surgical repair of lacerations to the birth canal or uterus may be required. Drugs that encourage coagulation (clotting) of the blood may be administered to stem the bleeding. Infrequently, hysterectomy is required.

In cases of infection, a course of intravenous antibiotics is prescribed. Most postpartum infections occur in the endometrium, or lining of the uterus, and may be also caused by a piece of retained placenta. If this is the case, it will also require surgical removal.

SHOULDER DYSTOCIA. The mother is usually positioned with her knees to her chest, known as the McRoberts maneuver, in an effort to free the child's shoulder. An **episiotomy** is also performed to widen the vaginal opening. If the shoulder cannot be dislodged from the pelvis, the baby's clavicle (collarbone) may have to be broken to complete the delivery before a lack of oxygen causes brain damage to the infant.

Prognosis

If a fetus is close to full-term (37 weeks) and the complication is detected early enough, the prognosis is usually good for mother and child. With advances in neonatal care, approximately 85% of infants weighing less than 3 lbs 5 oz survive, and these infants are being delivered at 28 weeks and younger. However, preterm infants have a greater chance of serious medical problems, and developmental disabilities occur in 25–50%. They also have a higher incidence of **learning disorders**,

KEY TERMS

Amniotic fluid—The liquid in the placental sac that cushions the fetus and regulates temperature in the placental environment. Amniotic fluid also contains fetal cells.

Cesarean section—The surgical delivery of a fetus through an incision in the uterus.

Embolism—Blood vessel obstruction by a blood clot or other substance (e.g., air, cell matter).

Episiotomy—Incision of the perineum, the area between the vulva and the anus, to assist delivery and avoid severe tearing of the perineum.

Laparoscopic—A minimally-invasive surgical or diagnostic procedure that uses a flexible endoscope (laparoscope) to view and operate on structures in the abdomen.

Postpartum—After childbirth.

and are four to six times more likely to be diagnosed with attention-deficit hyperactivity disorder (**ADHD**).

Prevention

Proper prenatal care is the best prevention for obstetrical emergencies. When complications of pregnancy do arise, pregnant women who see their OB/GYN on a regular basis are more likely to get an early diagnosis, and with it, the best chance for fast and effective treatment. In addition, eating right and taking prenatal **vitamins** and supplements as recommended by a physician will also contribute to the health of both mother and child.

ORGANIZATIONS

National Institute of Child Health and Human Development, Bldg. 31, Room 2A32, MSC 2425, 31 Center Drive, Bethesda, MD, 20892-2425, (866)760-5947, (800)370-2943, http://www.nichd.nih.gov/.

Paula Anne Ford-Martin

Occupational asthma

Definition

Occupational **asthma** is a form of lung disease in which the breathing passages shrink, swell, or become inflamed or congested as a result of exposure to irritants in the workplace.

Description

As many as 15% of all cases of asthma may be related to on-the-job exposure to:

- animal hair
- dander
- dust composed of bacteria, protein, or organic matter like cereal, grains, cotton, and flax
- fumes created by metal soldering
- insulation and packaging materials
- mites and other insects
- paints

Hundreds of different types of jobs involve exposure to substances that could trigger occupational asthma, but only a small fraction of people who do such work develop this disorder. Occupational asthma is most apt to affect workers who have personal or family histories of **allergies** or asthma, or who are often required to handle or breathe dust or fumes created by especially irritating material.

Causes and symptoms

Although occupational asthma is not new, today, more than 240 causes of occupational asthma have been identified. It was probably first recorded in 1713 when one of the fathers of occupational health, Bernadina Ramazzini said bakers and textile workers had problems with coughing, **shortness of breath**, hoarseness and asthma. Even short-term exposure to low levels of one or more irritating substances can cause a very sensitive person to develop symptoms of occupational asthma. A person who has occupational asthma has one or more symptoms, including coughing, shortness of breath, tightness in the chest, and **wheezing**. Symptoms may appear less than 24 hours after the person is first exposed to the irritant or may develop two or three years later.

At first, symptoms appear while the person is at work or several hours after the end of the workday. Symptoms disappear or diminish when the person spends time away from the workplace and return or intensify when exposure is renewed.

As the condition becomes more advanced, symptoms sometimes occur even when the person is not in the workplace. Symptoms may also develop in response to minor sources of lung irritation.

Diagnosis

An allergist, occupational medicine specialist, or a doctor who treats lung disease performs a thorough

ALICE HAMILTON (1869–1970)

(The Library of Congress.)

Alice Hamilton was born on February 27, 1869, in New York City, the second of five children born to Montgomery Hamilton, a wholesale grocer, and Gertrude (Pond) Hamilton. She earned a medical degree from the University of Michigan in 1893, without having completed an undergraduate degree and taking surprisingly few science courses. Realizing that she wanted to pursue research rather than medical practice, Hamilton went on to do further studies both in the United States and abroad: from 1895–1896 at Leipzig and Munich; 1896–1897 at Johns Hopkins; and 1902 in Paris at the Pasteur Institute. In 1897 she accepted a post as professor of pathology at the Women's Medical College at Northwestern University in Chicago.

In Chicago Hamilton became a resident of Hull House, the pioneering settlement designed to give care and advice to the poor of Chicago. Here, under the influence of Jane Addams, the founder of Hull House, Hamilton saw the effects of poverty up close, leading her to a lifelong career focused on industrial medicine.

Alice Hamilton was a pioneer in correcting the medical problems caused by industrialization, awakening the country in the early 20th century to the dangers of industrial poisons and hazardous working conditions. Through her untiring efforts, toxic substances in the lead, mining, painting, pottery, and rayon industries were exposed and legislation passed to protect workers. She was also a champion of worker's compensation laws, and was instrumental in bringing about this type of legislation in the state of Illinois. A medical doctor and researcher, she was the first woman of faculty status at Harvard University, and was a consultant on governmental commissions, both domestic and foreign.

physical examination and takes a medical history that explores:

- the kind of work the patient has done
- the types of exposures the patient may have experienced
- what symptoms the patient has had
- when, how often, and how severely symptoms have occurred

Performed before and after work, **pulmonary function tests** can show how job-related exposures affect the airway. Laboratory analysis of blood and sputum may confirm a diagnosis of workplace asthma. To pinpoint the cause more precisely, the doctor may ask the patient to inhale specific substances and monitor the body's response to them. This is called a challenge test.

Treatment

The most effective treatment for occupational asthma is to reduce or eliminate exposure to symptom-producing substances.

Medication may be prescribed for workers who can not prevent occasional exposure. Leukotriene modifiers (montelukast and zafirlukast) are new drugs that help manage asthma. They work by counteracting leukotrienes, which are substances released by white blood cells in the lung that cause the air passages to constrict and promote mucus secretion. Leukotriene modifiers also fight off some forms of **rhinitis**, an added bonus for people with asthma. Medication, **physical therapy**, and breathing aids may be needed to relieve symptoms of advanced occupational asthma involving airway damage.

A patient who has occupational asthma should learn what causes symptoms and how to control them, and what to do when an asthma attack occurs.

Because asthma symptoms and the substances that provoke them can change, a patient who has occupational asthma should be closely monitored by a family physician, allergist, or doctor who specializes in occupational medicine or lung disease.

Prognosis

Occupational asthma can be reversible. However, continued exposure to the symptom-producing substance can cause permanent lung damage. Follow-up studies of people with occupational asthma show that some cannot be protected from the exposure or are forced to change jobs, lose their jobs, or have worse prospects for future jobs based on their allergies and asthma.

In time, occupational asthma can cause asthma-like symptoms to occur when the patient is exposed to tobacco smoke, household dust, and other ordinary irritants.

Smoking aggravates symptoms of occupational asthma. Patients who eliminate workplace exposure and stop smoking are more apt to recover fully than those who change jobs but continue to smoke.

Prevention

Industries and environments where employees have a heightened exposure to substances known to cause occupational asthma can take measures to diminish or eliminate the amount of pollution in the atmosphere or decrease the number of exposed workers.

Regular medical screening of workers in these environments may enable doctors to diagnose occupational asthma before permanent lung damage takes place.

Resources

PERIODICALS

"Allergic to Work? Occupational Asthma Accounts for Up to 18 Million Lost Working Days a Year and Affects Thousand of Workers." *The Safety & Health Practitioner* September 2004: 38–41.

Solomon, Gina, Elizabeth H. Humphreys, and Mark D. Miller. "Asthma and the Environment: Connecting the Dots: What Role Do Environmental Exposures Play in the Rising Prevalence and Severity of Asthma?" *Contemporary Peditatrics* August 2004: 73–81.

"What's New in: Asthma and Allergic Rhinitis." *Pulse* September 20, 2004: 50.

ORGANIZATIONS

American College of Allergy, Asthma & Immunology, 85 West Algonquin Road, Suite 550, Arlington Heights, IL, 60005, (847)427-1200, (847)427-1294, mail @acaai.org, http://acaai.org.

Maureen Haggerty
Teresa G. Odle

Occupational therapy

Definition

Occupational therapy (OT) is a holistic, patient-centered, occupation-based approach to life-skills development for people with developmental disabilities, physical or mental diseases, injuries, or other health problems. Occupational therapy addresses physical, psychological, social, and environmental factors that interfere with functioning in various ways.

Purpose

The goal of occupational therapy is to help patients develop the skills and obtain the support necessary to live productive lives as independently as possible, to improve quality of life, and to decrease hospitalization and institutionalization.

Occupational therapy is used to treat a variety of physical and developmental disabilities, including:

- cerebral palsy, spina bifida, and other birth injuries and defects
- Down syndrome
- muscular dystrophy, arthritis, multiple sclerosis, or other serious chronic conditions
- developmental delays
- mental retardation
- autism
- learning disabilities
- attention deficit disorder (ADD)
- sensory processing/integrative disorders
- broken bones and other injuries from falls, sports injuries, or accidents
- brain and spinal cord injuries
- hand injuries
- amputations
- post-surgical conditions
- burns
- work-related injuries including lower-back problems and repetitive stress injury (RSI)
- limitations following a heart attack or stroke
- diabetes
- cancer
- Parkinson's disease

In recent years occupational therapy has expanded its scope into new areas, including:

- mental health and behavioral problems such as depression, dementia, Alzheimer's disease, schizophrenia,

posttraumatic stress, substance abuse, and eating disorders
- visual impairment
- home modification
- ergonomics consulting

Demographics

The demand for occupational therapy is expected to continue grow, as the baby-boomer generation (those born between 1945 and 1965) ages and requires various services, such as modifications in order to stay in their homes. As people live longer despite serious illness and disability, occupational therapy will facilitate independence in daily living and working. For example, **stroke** is the major cause of disability in adults and it is estimated that 5.4 million Americans are living with the effects of stroke.

Description

Occupational therapy provides direct care to patients with physical, developmental, and mental disabilities, in settings that include:

- long-term-care (LTC) facilities
- skilled-nursing facilities (SNFs) and nursing homes
- assisted-living facilities
- mental-health facilities
- hospitals
- rehabilitation centers
- outpatient and children's clinics
- adult daycare centers
- home healthcare agencies
- schools
- foster-care residences
- group and private homes
- sheltered workplaces
- senior centers
- wellness education programs
- business-to-business consulting firms that specialize in ergonomics
- private practices

Occupational therapists may work with and receive referrals from:

- physicians and nurses
- psychologists and psychiatrists
- other health professionals
- social workers
- case managers
- courts
- teachers, and vocational and guidance counselors
- foster-care providers
- families
- clients themselves

Regardless of the setting, occupational therapy is centered on the needs of patients and the environments in which they live. The therapist may perform activities-of-daily-living (ADL) evaluations to determine patients' competence and independence in performing daily tasks at home, work or school, and within their social environments. Examples of activities of daily living might include dialing a phone, paying bills, using a computer, or driving a car. Children are evaluated by their abilities to perform activities such as writing the alphabet, drawing shapes, playing games, tying shoes, brushing teeth, combing hair, or squeezing a special grip meter. Following the evaluation the occupational therapist may implement a treatment plan or interventions to facilitate a more independent lifestyle. The OT may evaluate the need for special equipment such as splints, wheelchairs, bathing equipment, dressing devices, or communication aids.

Occupational therapists work within six broad fields:

- rehabilitation, disability, and participation
- productive aging
- children and youth
- mental health
- health and wellness
- work and industry

Within these broad categories occupational therapy can involve a wide range of interventions, including:

- exercises for improving mobility
- prevention of falls
- sensory integration
- home modifications for independent living
- analysis of home lighting and contrast for the visually impaired
- slings or splints to provide support to body parts
- assistive devices for activities such as opening a jar, putting on shoes, or taking a bath or shower
- chronic disease management
- home healthcare
- driving and alternative transportation
- stress management
- communication skills
- assertiveness skills
- problem solving

KEY TERMS

Activities of daily living (ADL)—The skills and practices that determine how well individuals function in their daily lives and relate to and participate in their environment.

Alzheimer's disease—A progressive, neurodegenerative disease characterized by loss of function and death of nerve cells in several areas of the brain, leading to loss of mental functions, such as memory and learning. Alzheimer's disease is the most common cause of dementia.

Arthritis—Inflammation of one or more joints.

Attention deficit disorder (ADD)—A condition characterized by age-inappropriate attention span; often accompanied by age-inappropriate hyperactivity and impulsive behavior.

Autism—A variable developmental disorder that includes an impaired ability to communicate and form normal social relationships.

Ergonomics—The study of the relationship between people and their working environment.

Home modification—The altering of the physical environment of the home to remove hazards and provide a more functional environment; examples include the installation of grab bars and no-slip foot mats in the bathroom to prevent falls.

Parkinson's disease—A disorder of the brain characterized by shaking and difficulty with walking, movement, and coordination. The disease is associated with damage to a part of the brain that controls muscle movement.

Repetitive stress injury; repetitive strain injury (RSI)—Any of various musculoskeletal disorders—such as tendonitis or carpal tunnel syndrome—that are caused by cumulative damage to muscles, tendons, ligaments, nerves, or joints from highly repetitive movements, such as of the hand, wrist, arm, or shoulder.

Stroke—A sudden diminishing or loss of consciousness, sensation, or voluntary movement from a rupture or obstruction of a blood vessel in the brain.

- time management
- management of medications
- safety in the home and community
- pursuing vocational interests
- developing self-awareness
- interpersonal and social skills
- hygiene
- parenting skills

Occupational therapy provides early intervention for children with physical, sensory, or cognitive disabilities in daycare centers, preschools, and elementary and high schools. Occupational therapists also have an important role in disaster relief. OT can help children with disabilities become as independent as possible or successfully return to school after a long illness or serious injury. Childhood interventions may involve:

- working with children to brush their teeth, dress, tie their shoes, and feed themselves
- handwriting and drawing to improve finger dexterity
- coloring within the lines
- working on hand-eye coordination by hitting a target, batting a ball, or copying from the blackboard
- using a computer
- alternative ways for playing popular games
- teaching strategies for improving focus and attentiveness
- homework help
- managing a wheelchair in school
- interacting with others and improving social skills
- learning anger-management skills, such as writing about feelings or pursuing a physical activity

Occupational therapy often breaks tasks down into smaller steps, such as learning a song note by note. To learn to bathe, the client may first learn to turn on the water, then adjust the temperature, find soap and a towel, and then climb in the tub.

Occupational therapy also includes:

- adapting the home, school, or work environment to a client's needs
- developing educational programs, experiential learning, and treatment groups or classes
- housing and job placement, and ongoing monitoring
- assisting with client-run support groups
- consulting with employers about the requirements of the Americans with Disabilities Act
- developing transitional work programs

Occupational therapy in the workplace may involve:

- evaluating a worker on the job
- recommending job modifications
- implementing and supervising a return-to-work program
- monitoring progress
- improving productivity
- ergonomics to maximize function and comfort and minimize repetitive stress injuries from jobs such as typing or assembly-line work

Origins

Occupational therapy developed as a healthcare specialty during World War I, to work with soldiers suffering from shell shock, amputations, and other injuries. In the early 20th century, occupational therapists also treated **tuberculosis** and **polio** patients. The advent of managed healthcare in the United States dramatically expanded the role of occupational therapy.

Benefits

In addition to helping the injured and disabled to perform everyday tasks, live independently, and work or attend school, occupational therapy can improve skills and help prevent injuries in people of any age and ability. Benefits of occupational therapy include:

- assessments of performance and skills
- customized treatment programs for improving clients' abilities to perform daily activities
- home and workplace evaluations and recommendations for adaptations
- guidance for family members and caregivers
- providing fun, positive activities for improving children's cognitive, physical, and motor skills and enhancing self-esteem and sense of accomplishment

Preparation

Client attitude and cooperation are key to successful occupational therapy. Clients should be active participants, aware of the short-term and long-term goals of their therapy and able to communicate with their therapists.

Aftercare

Clients must continue to practice what they have learned in their occupational therapy and make appropriate adjustments in their lives. Many clients have long-term monitoring and assessments.

Training and certification

Occupational therapists have master's or doctoral degrees in OT. Practitioners must complete supervised clinical internships in a variety of healthcare settings and pass a national examination. Occupational therapy assistants (OTAs) usually have associate degrees. OTAs are able to carry out treatment plans developed by occupational therapists, but do not perform evaluations and assessments. The National Board for Certification in Occupational Therapy provides certification for the profession.

Regular continuing education courses and additional training are necessary for occupational therapists to maintain competency. Practitioners can take advantage of continuing education courses offered by the American Occupational Therapy Association, as well as online courses, annual conference and exposition workshops, and educational sessions offered by leaders in occupational therapy.

The practice of occupational therapy is regulated in every state and licensing of occupational therapists is required in most states. Licensure defines the scope of OT practice and provides guidance to facilities and healthcare providers on the appropriate applications of occupational therapy.

Resources

BOOKS

Creek, Jennifer, and Lesley Lougher. *Occupational Therapy and Mental Health,* 4th ed. New York: Churchill Livingstone Elsevier, 2008.

Parham, L. Diane, and Linda S. Fazio. *Play in Occupational Therapy for Children,* 2nd ed. St. Louis, MO: Mosby Elsevier, 2008.

Radomski, Mary Vining, and Catherine A. Trombly Latham. *Occupational Therapy for Physical Dysfunction,* 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2008.

Willard, Helen S., et al. *Willard & Spackman's Occupational Therapy,* 11th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2009.

OTHER

American Occupational Therapy Association. "Occupational Therapy: Fact Sheets and Articles." *Living Life To Its Fullest*.http://www.aota.org/Consumers/WhatisOT.aspx

Nemours Foundation. "Going to an Occupational Therapist." *KidsHealth*.http://kidshealth.org/kid/feel_better/people/occupational_therapist.html#

Nemours Foundation. "Occupational Therapy." *KidsHealth*.http://kidshealth.org/kid/feel_better/people/occupational_therapist.html#

ORGANIZATIONS

American Occupational Therapy Association, Inc., 4720 Montgomery Lane, P.O. Box 31220, Bethesda, MD, 20824-1220, (301) 652-2682, (301) 652-7711, http://www.aota.org.

National Board for Certification in Occupational Therapy, Inc., 12 South Summit Avenue, Suite 100, Gaithersburg, MD, 20877-4150, (301) 990-7979, (301) 869-8492, info@nbcot.org, http://www.nbcot.org.

World Federation of Occupational Therapists, P.O. Box 30, Forrestfield, Western Australia, Australia, 6058, 61-8-9453-9746, admin@wfot.org.au, http://www.wfot.org.

Margaret Alic, PhD
Brenda W. Lerner

Ocular myopathy *see* **Ophthalmoplegia**

Ocular rosacea *see* **Rosacea**

Ofloxacin *see* **Fluoroquinolones**

Ohio Valley disease *see* **Histoplasmosis**

Oil spills: health effects

Definition

Along with fouling marine and coastal ecosystems, offshore oil spills also pose potential health hazards for humans, both as workers respond to the spill and as oil impacts the environment where people live. After the 1989 *Exxon Valdez* oil spill that occurred in Prince William Sound off the coast of Alaska, one study published in the *American Journal of Psychiatry* showed that residents living in areas impacted by the spill were more likely to suffer mental health problems than the general population, even years after the spill. Few studies were conducted, however, on the health impacts of workers who were exposed to the oil during clean-up efforts. In the wake of the 2010 BP *Deepwater Horizon* oil spill in the Gulf of Mexico, the information remains inconclusive on the actual health hazards that could result from the spill. At a gathering of public health experts in late June 2010, U.S. Surgeon General Regina Benjamin described some scientists as predicting little or no toxic effect from short-term exposure to the oil, while indicating that "other scientists express serious concerns about the potential short-term and long-term impacts the exposure to oil and dispersants could have on the health of responders and our communities."

Demographics

Virtually everyone who lives near a coastline could be affected by an oil spill, as more than 38,000 oil tankers traverse the world's oceans and seas, delivering oil in its various stages from ports near the extraction site to ports where it is refined and later consumed. Offshore drilling fields are located primarily in the North Sea, the Gulf of Mexico, the South China Sea, and off the coasts of Nigeria, Angola, Brazil, the Canadian Provinces of Nova Scotia and Newfoundland, and eastern Russia. Large land-based oil fields are located in the Middle East, the United States, Russia, Mexico, and Venezuela. Persons especially at risk to the potentially harmful effects of oil exposure include those with existing respiratory problems, pregnant women, and children.

Description

Although the composition of crude oil varies somewhat according to its source, crude oil is a naturally occurring brown or black liquid that is composed of a mixture of hydrocarbons and other organic compounds. Crude oil is toxic, flammable, and contains volatile organic compounds (VOCs) that have known adverse effects on human health. OVCs include benzene, a carcinogen, and polycyclic aromatic hydrocarbons (PACs), which are toxic to the central nervous system. The VOCs evaporate easily, moving from the oil into the air, and can be carried by prevailing winds miles from the source of the spill and into coastal communities. There is evidence that some dispersants, solvents, and collecting agents used to manage the spill, when combined with the oil, can potentiate some of the toxic effects of crude oil alone. Harmful airborne pollution released by burning the oil on the surface of a spill is also a health concern for both responders and local populations on nearby shores.

Causes and symptoms

People are exposed to oil-spill toxins through direct contact with oil on the skin, by breathing VOCs and other chemicals released into the air, or through oil-contaminated sand, soil, water, or food. Multiple exposure paths can occur simultaneously. All adverse reactions to oil are dependent upon both the duration of the exposure and a person's particular susceptibility to the particular toxins in the oil.

Hundreds of workers cleaning Alaskan shores, marshes, and oiled waterways during the *Exxon Valdez* spill complained of skin **rashes**, **dizziness**, headaches, and **nausea** during their work and for a short time afterwards. Some experienced longer-lasting

KEY TERMS

Carcinogen—An agent that is known to cause cancer.

Dispersant—Chemicals that break up spilled oil into small particles that can be further scattered and broken down by water and wind, thus sparing oil damage to marine and coastal environments.

Mousse oil—Crude oil that has emulsified or weathered, mixed with dispersants, water, and marine material to form a spongy, light brown, mousse-like material.

Post-traumatic stress syndrome—A type of severe anxiety disorder that can develop after experiencing traumatic events or situations.

Teratogen—An agent that is known to disturb the development of an embryo or fetus.

Volatile organic compounds—VOCs, a large class of carbon-based chemicals that release gases into the air as they evaporate at room temperature. Found both in natural sources such as living trees, decomposing vegetation, and crude oil, and in manmade sources such as solvents, adhesives, and gasoline, VOCs help form ozone at ground levels and are major air contaminants.

symptoms including **shortness of breath**, muscle aches, and neurological problems including **numbness and tingling** of the extremities.

Public health officials along the Gulf coast are monitoring for these symptoms in communities affected by the *Deepwater Horizon* spill, as well as establishing data-collection methods to document possible longer-term consequences of oil exposure, such as kidney damage, **birth defects**, and **cancer**. As of late 2010, complaints among coastal residents, along with workers cleaning the oil both on land and at sea, have included skin rashes, headaches, nausea, and irritation in the throat and eyes. Several workers have also experienced heat **stress** due to working outside in hot and humid conditions.

Although high levels of mental and emotional stress are expected during a natural or technological disaster, the *Deepwater Horizon* oil spill impacted an area whose vulnerable population was still recovering from hurricanes Ivan, Katrina, and Rita. Benjamin Springgate, a physician and public health researcher at Tulane University in New Orleans, estimated that more than 30 % of people in the impact zone of Hurricane Katrina experienced symptoms of **anxiety**, depression, or other mental illness after the storm, and also predicted that the impacts of the *Deepwater Horizon* oil spill on the mental health of coastal residents will be a long-term situation. The most frequent symptoms of stress-related mental disorders include feelings of hopelessness, disturbances in sleep patterns, lack of concentration, mood swings, irritability, inability to make productive decisions, nightmares or persistent memories of disturbing or frightening events, and general anxiety.

Diagnosis

The most frequent mental disorders diagnosed among people affected by an oil spill include post-traumatic syndrome, **anxiety disorders**, and depression. These are diagnosed by a psychiatrist or other mental health professional, mostly after a careful discussion of the symptoms. Other oil-spill-related illnesses are diagnosed according to the nature of symptoms, **physical examination**, and additional diagnostic or laboratory tests. Chemical **pneumonia**, for example, is caused by respiratory irritation from exposure to VOCs or other chemicals, followed by inflammation and decreased lung function. It is most often diagnosed by history and physical examination, especially auscultation of (listening to) the lungs, examination of the sputum, and x-ray, as are other types of pneumonia.

Treatment

Mousse oil on the skin or tar balls can be cleaned with soap and water or mineral oil. Treatment of more serious illnesses of various body systems and organs exposed to oil depends on the system affected, the nature and length of the exposure, and the symptoms present. The U.S. Department of Health and Human Services has created a $10 million fund to track *Deepwater Horizon*-related illnesses in order to get a clear picture of their nature and to devise the most effective treatments. Also, more than 14,000 oil spill workers have volunteered to participate in a similar study for the Centers for Disease Control and Prevention (CDC).

Prognosis

The full effects of the *Deepwater Horizon* oil spill on the health and well-being of people living in communities along the northern Gulf of Mexico will not be fully known until the oil is cleaned and the physical, ecological, and economic environments are restored, a process that will take years. Scientists anticipate that the information gained from careful study of the

detrimental effects of the oil spill on the physical and mental health of spill responders and Gulf coast residents will help identify both short-term and long-term health issues related to the spill, and allow for an effective response now and during future technological disasters.

Prevention

Avoiding contact with the oil is the most effective way to prevent negative health effects from an oil spill. Beaches along the northern Gulf Coast have "no swimming" signs and flags posted in locations where oil from the *Deepwater Horizon* spill has impacted the shore. Workers both offshore and at the spill site utilize a variety of personal protective equipment including gloves, white plastic protective (hazmat) suits, respirators, and other barrier methods designed to prevent exposure to oil.

Authorities have closed more than 30% of Gulf Coast federal fishing waters to both commercial and personal fishing in order to prevent oil-contaminated fish and shellfish from entering the food supply. Increased inspection of allowable catches helps ensure that Gulf fish making its way to the market are uncontaminated and of the usual high quality.

When winds bring fumes from the spill onshore, residents with existing respiratory problems are advised to remain indoors with re-circulating air. Pregnant women should avoid oil-contaminated beaches or air, as components of crude oil are known teratogens and exposure to crude oil can result in decreased fetal survival. Children are also particularly vulnerable to DNA damage from long-term exposure to airborne toxins emanating from oil spills. The U.S. Environmental Protection Agency has set up more than 100 monitoring stations along affected areas of the Gulf Coast to detect unhealthy levels of VOCs, overall ozone, and particulate matter in the air, and to issue regular air quality reports.

Innovative approaches are being taken along the Gulf Coast to reach people who may be experiencing symptoms of stress, but are unlikely to seek help for them. Peer listeners have been trained to identify signs of distress during conversation, to offer encouragement that help is available, and to provide referrals to nearby mental health services. Personnel with knowledge of and sensitivities to local cultures, including those who speak Vietnamese and Spanish, are also available to hear the needs and concerns of fishermen and other close-knit communities.

Resources

BOOKS

California Environmental Protection Agency. *San Francisco Bay Oil Spill Health Questions and Answers*. Sacramento, CA: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, 2007.

Ott, Riki. *Not One Drop: Betrayal and Courage in the Wake of the Exxon Valdez Oil Spill*. White River Junction, VT: Chelsea Green Pub, 2008.

Ott, Riki. *Sound Truth and Corporate Myth$: The Legacy of the Exxon Valdez Oil Spill*. Cordova, Alaska: Dragonfly Sisters Press, 2005.

Thayer, Evan C. *Chemical Human Health Hazards Associated with Oil Spill Response*. Washington, D.C.: American Petroleum Institute, 2001.

PERIODICALS

Arata, C.M., Picou, J.S., Johnson, G.D., and T.S. McNally. "Coping with Technological Disaster: an Application of the Conservation of Resources Model to the Exxon Valdez Oil Spill." *Journal of Traumatic Stress* 13, no.1 (2000): 23–39.

Ha, M., Lee, W.J., Lee, S., and H.K. Cheong. "A Literature Review on Health Effects of Exposure to Oil Spill." *Journal of Preventive Medicine and Public Health* 41, no. 5 (2008): 345–354.

Palinkas, L.A., Petterson, J.S., Russell, J., and M.A. Downs. "Community Patterns of Psychiatric Disorders After the Exxon Valdez Oil Spill." *The American Journal of Psychiatry* 150, no. 10 (1993): 1517–1523.

OTHER

Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. "Interim Guidance for Protecting Deepwater Horizon Response Workers and Volunteers." http://www.cdc.gov/niosh/topics/oilspillresponse/protecting/default.html (accessed July 12, 2010).

Brenda Wilmoth Lerner, RN

Oligomenorrhea

Definition

Medical dictionaries define oligomenorrhea as infrequent or very light menstruation. But physicians typically apply a narrower definition, restricting the diagnosis of oligomenorrhea to women whose periods were regularly established before they developed problems with infrequent flow. With oligomenorrhea, menstrual periods occur at intervals of greater than 35 days, with only four to nine periods in a year.

Description

True oligomenorrhea cannot occur until menstrual periods have been established. In the United States, 97.5% of women have begun normal menstrual cycles by age 16. The complete absence of menstruation, whether menstrual periods never start or whether they stop after having been established, is called **amenorrhea**. Oligomenorrhea can become amenorrhea if menstruation stops for six months or more.

It is quite common for women at the beginning and end of their reproductive lives to miss or have irregular periods. This is normal and is usually the result of imperfect coordination between the hypothalamus, the pituitary gland, and the ovaries. For no apparent reason, a few women menstruate (with ovulation occurring) on a regular schedule as infrequently as once every two months. For them that schedule is normal and not a cause for concern.

Women with **polycystic ovary syndrome** (PCOS) are also likely to suffer from oligomenorrhea. PCOS is a condition in which the ovaries become filled with small cysts. Women with PCOS show menstrual irregularities that range from oligomenorrhea and amenorrhea on the one hand to very heavy, irregular periods on the other. The condition affects about 6% of premenopausal women and is related to excess androgen production.

Other physical and emotional factors also cause a woman to miss periods. These include:

- emotional stress
- chronic illness
- poor nutrition
- eating disorders such as anorexia nervosa
- excessive exercise
- estrogen-secreting tumors
- illicit use of anabolic steriod drugs to enhance athletic performance

Professional ballet dancers, gymnasts, and ice skaters are especially at risk for oligomenorrhea because they combine strenuous physical activity with a diet intended to keep their weight down. Menstrual irregularities are now known to be one of the three disorders comprising the so-called "female athlete triad," the other disorders being disordered eating and **osteoporosis**. The triad was first formally named at the annual meeting of the American College of Sports Medicine in 1993, but doctors were aware of the combination of bone mineral loss, **stress**, **fractures**, **eating disorders**, and participation in women's sports for several decades before the triad was named. Women's coaches have become increasingly aware of the problem since the early 1990s, and are encouraging female athletes to seek medical advice.

Causes and symptoms

Symptoms of oligomenorrhea include:

- menstrual periods at intervals of more than 35 days
- irregular menstrual periods with unpredictable flow
- some women with oligomenorrhea may have difficulty conceiving

Oligomenorrhea that occurs in adolescents is often caused by immaturity or lack of synchronization between the hypothalamus, pituitary gland, and ovaries. The hypothalamus is part of the brain that controls body temperature, cellular metabolism, and basic functions such as eating, sleeping, and reproduction. It secretes hormones that regulate the pituitary gland.

The pituitary gland is then stimulated to produce hormones that affect growth and reproduction. At the beginning and end of a woman's reproductive life, some of these hormone messages may not be synchronized, causing menstrual irregularities.

In PCOS, oligomenorrhea is probably caused by inappropriate levels of both female and male hormones. Male hormones are produced in small quantities by all women, but in women with PCOS, levels of male hormone (androgens) are slightly higher than in other women. More recently, however, some researchers are hypothesizing that the ovaries of women with PCOS are abnormal in other respects. In 2003, a group of researchers in London reported that there are fundamental differences between the development of egg follicles in normal ovaries and follicle development in the ovaries of women with PCOS.

In athletes, models, actresses, dancers, and women with **anorexia nervosa**, oligomenorrhea occurs because the ratio of body fat to weight drops too low.

Diagnosis

History and physical examination

Diagnosis of oligomenorrhea begins with the patient informing the doctor about infrequent periods. The doctor will ask for a detailed description of the problem and take a history of how long it has existed and any patterns the patient has observed. A woman can assist the doctor in diagnosing the cause of oligomenorrhea by keeping a record of the time, frequency, length, and quantity of bleeding. She should also tell the doctor about any recent illnesses, including long-standing conditions like **diabetes mellitus**. The doctor

may also inquire about the patient's diet, **exercise** patterns, sexual activity, contraceptive use, current medications, or past surgical procedures.

The doctor will then perform a **physical examination** to evaluate the patient's weight in proportion to her height, to check for signs of normal sexual development, to make sure the heart rhythm and other vital signs are normal, and to palpate (feel) the thyroid gland for evidence of swelling.

In the case of female athletes, the doctor may need to establish a relationship of trust with the patient before asking about such matters as diet, practice and workout schedules, and the use of such drugs as **steroids** or ephedrine. The presence of stress fractures in young women should be investigated. In some cases, the doctor may give the patients the Eating Disorder Inventory (EDI) or a similar screening questionnaire to help determine whether the patient is at risk for developing anorexia or bulimia.

Laboratory tests

After taking the woman's history, the gynecologist or family practitioner does a pelvic examination and **Pap test**. To rule out specific causes of oligomenorrhea, the doctor may also do a **pregnancy** test and blood tests to check the level of thyroid hormone. Based on the initial test results, the doctor may want to do tests to determine the level of other hormones that play a role in reproduction.

More sensitive monoclonal assays have been developed for measuring hormone levels in the blood serum of women with PCOS, thus allowing earlier and more accurate diagnosis.

Imaging studies

In some cases the doctor may order an ultrasound study of the pelvic region to check for anatomical abnormalities, or x-rays or a **bone scan** to check for bone fractures. In a few cases the doctor may order an MRI to rule out tumors affecting the hypothalamus or pituitary gland.

Treatment

Treatment of oligomenorrhea depends on the cause. In adolescents and women near **menopause**, oligomenorrhea usually needs no treatment. For some athletes, changes in training routines and eating habits may be enough to return the woman to a regular menstrual cycle.

Most patients suffering from oligomenorrhea are treated with birth-control pills. Other women, including those with PCOS, are treated with hormones. Prescribed hormones depend on which particular hormones are deficient or out of balance. When oligomenorrhea is associated with an eating disorder or the female athlete triad, the underlying condition must be treated. Consultation with a psychiatrist and nutritionist is usually necessary to manage an eating disorder. Female athletes may require **physical therapy** or **rehabilitation** as well.

Alternative treatment

As with conventional medicial treatments, alternative treatments are based on the cause of the condition. If a hormonal imbalance is revealed by laboratory testing, hormone replacements that are more "natural" for the body (including tri-estrogen and natural progesterone) are recommended. Glandular therapy can assist in bringing about a balance in the glands involved in the reproductive cycle, including the hypothalmus, pituitary, thyroid, ovarian, and adrenal glands. Since homeopathy and **acupuncture** work on deep, energetic levels to rebalance the body, these two modalities may be helpful in treating oligomenorrhea. Western and Chinese herbal medicines also can be very effective. Herbs used to treat oligomenorrhea include dong quai (*Angelica sinensis*), black cohosh (*Cimicifuga racemosa*), and chaste tree (*Vitex agnus-castus*). Herbal preparations used to bring on the menstrual period are known as emmenagogues. For some women, **meditation**, **guided imagery**, and visualization can play a key role in the treatment of oligomenorrhea by relieving emotional stress.

Diet and adequate **nutrition**, including adequate protein, essential fatty acids, whole grains, and fresh fruits and vegetables, are important for every woman, especially if deficiencies are present or if she regularly exercises very strenuously. Female athletes at the high school or college level should consult a nutritionist to make sure that they are eating a well-balanced diet that is adequate to maintain a healthy weight for their height. Girls participating in dance or in sports that emphasize weight control or a slender body type (gymnastics, track and field, swimming, and cheerleading) are at higher risk of developing eating disorders than those that are involved in such sports as softball, weight lifting, or basketball. In some cases the athlete may be given **calcium** or vitamin D supplements to lower the risk of osteoporosis.

Many women, including those with PCOS, are successfully treated with hormones for oligomenorrhea. They have more frequent periods and begin ovulating during their menstrual cycle, restoring their fertility.

For women who do not respond to hormones or who continue to have an underlying condition that

KEY TERMS

Anorexia nervosa—A disorder of the mind and body in which people starve themselves in a desire to be thin, despite being of normal or below normal body weight for their size and age.

Cyst—An abnormal sac containing fluid or semi-solid material.

Emmenagogue—A medication or herbal preparation given to bring on a woman's menstrual period.

Female athlete triad—A combination of disorders frequently found in female athletes that includes disordered eating, osteoporosis, and oligo- or amenorrhea. The triad was first officially named in 1993.

Osteoporosis—The excessive loss of calcium from the bones, causing the bones to become fragile and break easily. Women who are not menstruating are especially vulnerable to this condition because estrogen, a hormone that protects bones against calcium loss, decreases drastically after menopause.

causes oligomenorrhea, the outlook is less positive. Women who have oligomenorrhea may have difficulty conceiving children and may receive fertility drugs. The absence of adequate estrogen increases risk for bone loss (osteoporosis) and cardiovascular disease. Women who do not have regular periods also are more likely to develop uterine **cancer**. Oligomenorrhea can become amenorrhea at any time, increasing the chance of having these complications.

Prevention

Oligomenorrhea is preventable only in women whose low body fat to weight ratio is keeping them from maintaining a regular menstrual cycle. Adequate nutrition and a less vigorous training schedules will normally prevent oligomenorrhea. When oligomenorrhea is caused by hormonal factors, it is not preventable, but it is often treatable.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Ehrenthal, Deborah, Paula Adams Hillard, and Matthew Hoffman *Menstrual Disorders*. Philadelphia: American College of Physicians, 2006.

PERIODICALS

Barrow, Boone, MD. "Female Athlete Triad." *eMedicine* June 17, 2004. http://www.emedicine.com/sports/topic163.htm.

Hopkinson, R. A., and J. Lock. "Athletics, Perfectionism, and Disordered Eating." *Eating and Weight Disorders* 9 (June 2004): 99–106.

Klentrou, P., and M. Plyley. "Onset of Puberty, Menstrual Frequency, and Body Fat in Elite Rhythmic Gymnasts Compared with Normal Controls." *British Journal of Sports Medicine* 37 (December 2003): 490–494.

Milsom, S. R., M. C. Sowter, M. A. Carter, et al. "LH Levels in Women with Polycystic Ovarian Syndrome: Have Modern Assays Made Them Irrelevant?" *BJOG* 110 (August 2003): 760–764.

Suliman, A. M., T. P. Smith, J. Gibney, and T. J. McKenna. "Frequent Misdiagnosis and Mismanagement of Hyperprolactinemic Patients Before the Introduction of Macroprolactin Screening: Application of a New Strict Laboratory Definition of Macroprolactinemia." *Clinical Chemistry* 49 (September 2003): 1504–1509.

Webber, L. J., S. Stubbs, J. Stark, et al. "Formation and Early Development of Follicles in the Polycystic Ovary." *Lancet* 362 (September 27, 2003): 1017–1021.

OTHER

Clinical Research Bulletin. vol. 1, no. 14. http://www.herbsinfo.com.

ORGANIZATIONS

American Academy of Child and Adolescent Psychiatry (AACAP), 3615 Wisconsin Ave. NW, Washington, DC, 20013-3007, (202)966-7300, (202)966-2891, communications@aacap.org, http://www.aacap.org/.

American College of Sports Medicine (ACSM), 401 West Michigan Street, P.O. Box 1440, Indianapolis, IN, 46202-3233, (317)637-9200, (317)634-7817, http://www.acsm.org.

Polycystic Ovarian Syndrome Association, P.O. Box 3403, Englewood, CO, 80155-3403, info@pcosupport.org, http://www.pcosupport.org.

Tish Davidson, AM
Rebecca J. Frey, PhD

Omega-3 fatty acids

Definition

Essential to human health, omega-3 fatty acids are a form of polyunsaturated fats that are not made by the body and must be obtained from a person's food.

Purpose

Eating foods rich in omega-3 fatty acids is part of a healthy diet and helps people maintain their health.

Description

In recent years, a great deal of attention has been placed on the value of eating a low-fat diet. In some cases, people have taken this advice to the extreme by adopting a diet that is far too low in fat or, worse yet, a diet that has no fat at all. But the truth is that not all fat is bad. Although it is true that trans and saturated fats, which are found in high amounts in red meat, butter, whole milk, and some prepackaged foods, have been shown to raise a person's total cholesterol, polyunsaturated fats can actually play a part in keeping cholesterol low. Two especially good fats are the omega-3 fatty acids and the omega-6 fatty acids, which are polyunsaturated.

Two types of omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA), which are found mainly in oily cold-water fish, such as tuna, salmon, trout, herring, sardines, bass, swordfish, and mackerel. With the exception of seaweed, most plants do not contain EPA or DHA. However, alpha-linolenic acid (ALA), which is another kind of omega-3 fatty acid, is found in dark green leafy vegetables, flaxseed oil, fish oil, and canola oil, as well as nuts and beans, such as walnuts and soybeans. Enzymes in a person's body can convert ALA to EPA and DHA, which are the two kinds of omega-3 fatty acids easily utilized by the body.

Many experts agree that it is important to maintain a healthy balance between omega-3 fatty acids and omega-6 fatty acids. As Dr. Penny Kris-Etherton and her colleagues reported in their article published in the *American Journal of Nutrition* an overconsumption of omega-6 fatty acids has resulted in an unhealthy dietary shift in the American diet. The authors point out that what used to be a 1:1 ratio between omega-3 and omega-6 fatty acids is now estimated to be a 10:1 ratio. This poses a problem, researchers say, because consuming some of the beneficial effects gained from omega-3 fatty acids are negated by an overconsumption of omega-6 fatty acids. For example, omega-3 fatty acids have anti-inflammatory properties, whereas omega-6 fatty acids tend to promote inflammation. Cereals, whole grain bread, margarine, and vegetable oils, such as corn, peanut, and sunflower oil, are examples of omega-6 fatty acids. In addition, people consume a lot of omega-6 fatty acid simply by eating the meat of animals that were fed grain rich in omega-6. Some experts suggest that eating one to four times more omega-6 fatty acids than omega-3 fatty acids is a reasonable ratio. In other words, as dietitians often say, the key to a healthy diet is moderation and balance.

The health benefits of omega-3 fatty acids

There is strong evidence that omega-3 fatty acids protect a person against **atherosclerosis** and therefore against heart disease and **stroke**, as well as abnormal heart rhythms that cause **sudden cardiac death**, and possibly **autoimmune disorders**, such as lupus and **rheumatoid arthritis**. In fact, Drs. Dean Ornish and Mehmet Oz, renowned heart physicians, said in a 2002 article published in *O Magazine* that the benefits derived from consuming the proper daily dose of omega-3 fatty acids may help to reduce sudden cardiac **death** by as much as 50%. In fact, in an article published by *American Family Physician*, Dr. Maggie Covington, a clinical assistant professor at the University of Maryland, also emphasized the value of omega-3 fatty acids with regard to cardiovascular health and referred to one of the largest clinical trials to date, the GISSI-Prevenzione Trial, to illustrate her point. In the study, 11,324 patients with coronary heart disease were divided into four groups: one group received 300 mg of vitamin E, one group received 850 mg of omega-3 fatty acids, one group received the vitamin E and fatty acids, and one group served as the control group. After a little more than three years, "the group given omega-3 fatty acids only had a 45% reduction in sudden death and a 20% reduction in all-cause mortality," as stated by Dr. Covington.

According to the American Heart Association (AHA), the ways in which omega-3 fatty acids may reduce cardiovascular disease are still being studied. However, the AHA indicates that research as shown that omega-3 fatty acids:

- decrease the risk of arrthythmias, which can lead to sudden cardiac death
- decrease triglyceride levels
- decrease the growth rate of atherosclerotic plaque
- lower blood pressure slightly

In fact, numerous studies show that a diet rich in omega-3 fatty acids not only lowers bad cholesterol, known as LDL, but also lowers **triglycerides**, the fatty material that circulates in the blood. Interestingly, researchers have found that the cholesterol levels of Inuit Eskimos tend to be quite good, despite the fact that they have a high fat diet. The reason for

this, research has found, is that their diet is high in fatty fish, which is loaded with omega-3 fatty acids. The same has often been said about the typical Mediterranean-style diet.

Said to reduce joint inflammation, omega-3 fatty acid supplements have been the focus of many studies attempting to validate its effectiveness in treating rheumatoid arthritis. According to a large body of research in the area, omega-3 fatty acid supplements are clearly effective in reducing the symptoms associated with rheumatoid arthritis, such as joint tenderness and stiffness. In some cases, a reduction in the amount of medication needed by rheumatoid arthritis patients has been noted.

More research needs to be done to substantiate the effectiveness of omega-3 fatty acids in treating **eating disorders**, attention deficit disorder, and depression. Some studies have indicated, for example, that children with behavioral problems and attention deficit disorder have lower than normal amounts of omega-3 fatty acids in their bodies. However, until there is more data in these very important areas of research, a conservative approach should be taken, especially when making changes to a child's diet. Parents should to talk to their child's pediatrician to ascertain if adding more omega-3 fatty acids to their child's diet is appropriate. In addition, parents should take special care to avoid feeding their children fish high in mercury. A food list containing items rich in omega-3 fatty acids can be obtained from a licensed dietitian.

Mercury levels and concerns about safety

A great deal of media attention has been focused on the high mercury levels found in some types of fish. People concerned about fish consumption and mercury levels can review public releases on the subject issued by the U. S. Food and Drug Administration and the Environmental Protection Agency. Special precautions exist for children and pregnant or **breastfeeding** women. They are advised to avoid shark, mackerel, swordfish, and tilefish. However, both the U.S. Food and Drug Administration and the Environmental Protection Agency emphasize the importance of dietary fish. Fish, they caution, should not be eliminated from the diet. In fact, Robert Oh, MD, stated in his 2005 article, which was published in *The Journal of the American Board of Family Practice,* "with the potential health benefits of fish, women of childbearing age should be encouraged to eat one to two low-mercury fish meals per week."

Contaminants and concerns about safety

Other concerns regarding fish safety have also been reported. In 2004, Hites and colleagues assessed organic contaminants in salmon in an article published in *Science*. Their conclusion that farmed salmon had higher concentrations of polychlorinated biphenyls than wild salmon prompted public concerns and a response from the American Cancer Society. Farmed fish in Europe was found to have higher levels of mercury than farmed salmon in North and South America; however, the American Cancer Society reminded the public that the "levels of toxins Hites and his colleagues found in the farmed salmon were still below what the U.S. Food and Drug Administration, which regulates food, considers hazardous." The American Cancer Society still continues to promote a healthy, varied diet, which includes fish as a food source.

Recommended dosage

The AHA recommends that people eat two servings of fish, such as tuna or salmon, at least twice a week. A person with coronary heart disease, according to the AHA, should consume 1 gram of omega-3 fatty acids daily through food intake, most preferably through the consumption of fatty fish. The AHA also states that "people with elevated triglycerides may need 2 to 4 grams of EPA and DHA per day provided as a supplement," which is available in liquid or capsule form. Ground or cracked flaxseed can easily be incorporated into a person's diet by sprinkling it over salads, soup, and cereal.

Sources differ, but here are some general examples:

- 3 ounces of pickled herring = 1.2 grams of omega-3 fatty acids
- 3 ounces of salmon = 1.3 grams of omega-3 fatty acids
- 3 ounces of halibut = 1.0 grams of omega-3 fatty acids
- 3 ounces of mackerel = 1.6 grams of omega-3 fatty acids
- 1 1/2 teaspoons of flaxseeds = 3 grams of omega-3 fatty acids

Precautions

In early 2004, the U.S. Food and Drug Administration along with the the Environmental Protection Agency issued a statement that women who are or may be pregnant, as well as breastfeeding mothers and children, should avoid eating some types of fish thought to contain high levels of mercury. Fish that

typically contain high levels of mercury are shark, swordfish, and mackerel, whereas shrimp, canned light tuna, salmon, and catfish are generally thought to have low levels of mercury. Because many people engage in fishing as a hobby, women should be sure before they eat any fish caught by friends and family that the local stream or lake is considered low in mercury.

Conflicting information exists whether it is safe for patients with **macular degeneration** to take omega-3 fatty acids in supplement form. Until more data becomes available, it is better for people with macular degeneration to receive their omega-3 fatty acids from the food they eat.

Side effects

Fish oil supplements can cause **diarrhea** and gas. Also, some fish oil capsules may have a fishy aftertaste.

Interactions

Although there are no significant **drug interactions** associated with eating foods containing omega-3 fatty acids, patients who are being treated with blood-thinning medications should not take omega-3 fatty acid supplements without seeking the advice of their physicians. Excessive bleeding could result. For the same reason, some patients who plan to take more than 3 grams of omega-3 fatty acids in supplement form should first seek the approval of their physicians.

Resources

PERIODICALS

Covington, M. B. "Omega-3 fatty acids." *American Family Physician* 70 (2004): 133–140.

Kris-Etherton, P. M., Harris, W. S., Appel, L. J., and American Heart Association Nutrition Committee. "Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease." *Circulation* 106 (2003): 2747–2757.

Oh, R. "Practical applications of fish oil (omega-3 fatty acids) in primary care." *The Journal of the American Board of Family Practice* 18 (2005): 28–36.

Ornish, Dean, and Oz, Mehmet. "Caution: Strong at Heart." *O: The Oprah Magazine* November 2002:163–168.

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd. NE, Atlanta, GA, 30329, (800)227-2345, http://www.cancer.org.

Lee Ann Paradise

Omeprazole *see* **Antiulcer drugs**

Omphalocele *see* **Abdominal wall defects**

Onchocerciasis *see* **Filariasis**

Onychomycosis

Definition

Onychomycosis is a fungal infection of the fingernails or toenails. The actual infection is of the bed of the nail and of the plate under the surface of the nail.

Description

Onychomycosis is the most common of all diseases of the nails in adults. In North America, the incidence falls roughly between 2–13%. The incidence of onychomycosis is also greater in older adults, and up to 90% of the elderly may be affected. Men are more commonly infected than women.

Individuals who are especially susceptible include those with chronic diseases such as diabetes and circulatory problems and those with diseases that suppress the immune system. Other risk factors include a family history, previous trauma to the nails, warm climate, and occlusive or tight footwear.

Causes and symptoms

Onychomycosis is caused by three types of fung: dermatophytes, yeasts, and nondermatophyte molds. Fungi are simple parasitic plant organisms that do not need sunlight to grow. Toenails are especially susceptible because fungi prefer dark damp places. Swimming pools, locker rooms, and showers typically harbor fungi. Chronic diseases such as diabetes, problems with the circulatory system, or immune deficiency disease are risk factors. A history of **athlete's foot** and excess perspiration are also risk factors.

Onychomycosis can be present for years without causing **pain** or disturbing symptoms. Typically, the nail becomes thicker and changes to a yellowish-brown. Foul-smelling debris may collect under the nail. The infection can spread to the surrounding nails and even the skin.

Diagnosis

To make a diagnosis of onychomycosis, the clinician must collect a specimen of the nail in which infection is suspected. A clipping is taken from the nail plate, and a sample of the debris from underneath the nail bed is also taken, usually with a sharp curette.

Debris from the nail surface may also be taken. These will be sent for microscopic analysis to a laboratory, as well as cultured to determine what types of fungus are growing there.

Treatment

Onychomycosis is very difficult and sometimes impossible to treat, and therapy is often long-term. Therapy consists of topical treatments that are applied directly to the nails, as well as two systemic drugs, griseofulvin and ketoconazole. Topical therapy is reserved for only the mildest cases. The use of griseofulvin and ketoconazole is problematic, and there are typically high relapse rates of 50–85%. In addition, treatment must be continued for a long duration (10–18 months for toenails), with monthly laboratory monitoring for several side effects, including liver toxicity. Individuals taking these medications must also abstain from alcohol consumption.

In the past few years, newer oral antifungal agents have been developed, and include itraconazole (Sporanox), terbinafine (Lamisil), and fluconazole (Diflucan). These agents, when taken orally for as little as 12 weeks, bring about better cure rates and fewer side effects than either griseofulvin or ketoconazole. The most common side effect is stomach upset. Patients taking oral antifungal therapy must have a **complete blood count** and liver enzyme workup every four to six weeks. Terbinafine in particular has markedly less toxicity to the liver, one of the more severe side effects of the older agents, griseofulvin and ketoconazole.

Treatment should be continued until microscopic exam or culture shows no more fungal infection. Nails may, however, continue to look damaged even after a clinical cure is achieved. Nails may take up to a full year to return to normal. If the nail growth slows or stops, additional doses of antifungal therapy should be taken.

Nail **debridement** is another treatment option, but it is considered by many to be primitive compared with topical or systemic treatment. Clinicians perform nail debridement in their offices. The nail is cut and then thinned using surgical tools or chemicals, and then the loose debris under the nail is removed. The procedure is painless, and often improves the appearance of the nails immediately. In addition, it helps whatever medication being used to penetrate the newly thinned nail. Patients with very thickened nails will sometimes undergo chemical removal of a nail. A combination of oral, topical, and surgical removal can increase the chances of curing the infection.

KEY TERMS

Curette—Spoon-shaped instrument for removing debris, growths, or infected nail matter.

Dermatophytes, yeasts, and nondermatophyte molds—Three types of fungi responsible for fungal infections of the nails.

Alternative treatment

For controlling onychomycosis, as opposed to curing it, some experts advocate using Lotrimin cream, available over the counter. The cream should be thoroughly rubbed into the nail daily in order to control the infection.

In general, **nutrition** may also play a role in promoting good nail health and thus preventing nail disease. Adequate protein and **minerals**, in the form of nuts, seeds, whole grains, legumes, fresh vegetables, and fish, should be consumed. Sugars, alcohol, and **caffeine** should be avoided. Certain supplements may also be beneficial, including vitamin A (10,000 IU per day), zinc (15–30 mg per day), iron (ferrous glycinate 100 mg per day, vitamin B_{12} (1,000 mcg per day), and essential fatty acids in the form of flax, borage, or evening primrose oil (1,000–1,5000 mg twice daily).

Herbal remedies may also relieve some of the symptoms of onychomycosis. A combination of coneflower, oregano, spilanthes, usnea, Oregon grape root, and myrrh can be used as a tincture (20 drops four times daily).

Undiluted grapefruit seed extract and tea tree oil are also said to be beneficial when applied topically to the infected nails.

Prognosis

Onychomycosis is typically quite difficult to cure completely. Even if a clinical cure is achieved after long therapy with either topical or oral drugs, normal regrowth takes four to six months in the fingernails, and eight to 12 months in the toenails, which grow more slowly. Relapse is common, and often, the nail or nail bed is permanently damaged. For toenails infected with onychomycosis, terbinafine seems to offer the highest cure rate (35–50%). Itraconazole cure rates typically range from 25–40%, and those with fluconazole, which was recently approved in the United States, have not been documented by long-term trials

Prevention

Keeping the feet clean and dry, and washing with soap and water and drying thoroughly are important preventive steps to take to prevent onychomycosis. Other preventive measures include keeping the nails cut short and wearing shower shoes whenever walking or showering in public places. Daily changes of shoes, socks, or hosiery are also helpful. Excessively tight hose or shoes promote moisture, which in turn, provides a wonderful environment for onychomycotic infections. To prevent this, individuals should wear only socks made of synthetic fibers, which can absorb moisture more quickly than those made of cotton or wools. Manicure and pedicure tools should be disinfected after each use. Finally, nail polish should not be applied to nails that are infected, as this causes the water or moisture that collects under the surface of the nail to not evaporate and be trapped.

Resources

PERIODICALS

Harrell T. K., et al. "Onychomycosis: Improved Cure Rates with Itraconazole and Terbinafine." *Journal of the American Board of Family Practitioners* July-August 2001: 268- 73.

OTHER

Zeina, Bassam. "Jessner Lymphocytic Infiltration of the Skin." eMedicine.com. http://www.emedicine.com/derm/topic200.htm.

Nailfungus.org. http://www.nailfungus.org/about.html.

ORGANIZATIONS

American Academy of Dermatology, P.O. Box 4014, Schaumburg, IL, 60168-4014, (847)240-1859, (866)503-SKIN (7546), http://www.aad.org.

Liz Meszaros

Oophorectomy

Definition

Unilateral oophorectomy (also called an ovariectomy) is the surgical removal of an ovary. If one ovary is removed, a woman may continue to menstruate and have children. If both ovaries are removed, a procedure called a bilateral oophorectomy, menstruation stops and a woman loses the ability to have children.

Purpose

Oophorectomy is performed to:

- remove cancerous ovaries
- remove the source of estrogen that stimulates some cancers
- remove a large ovarian cyst
- excise an abscess
- treat endometriosis

In an oophorectomy, one or a portion of one ovary may be removed or both ovaries may be removed. When an oophorectomy is done to treat **ovarian cancer** or other spreading cancers, both ovaries are removed (called a bilateral oophorectomy). Removal of the ovaries and fallopian tubes is performed in about one-third of hysterectomies (surgical removal of the uterus), often to reduce the risk of ovarian **cancer**.

Oophorectomies are sometimes performed on premenopausal women who have estrogen-sensitive **breast cancer** in an effort to remove the main source of estrogen from their bodies. This procedure has become less common than it was in the 1990s. In the early 2000s, **chemotherapy** drugs are available that alter the production of estrogen, and tamoxifen blocks any of the effects any remaining estrogen may have on cancer cells.

Until the 1980s, women over age 40 had hysterectomies routinely, removing healthy ovaries and fallopian tubes at the same time. This operation is called a bilateral **salpingo-oophorectomy**. Many physicians reasoned that a woman over 40 was approaching **menopause** and soon her ovaries would stop secreting estrogen and releasing eggs. Removing the ovaries would eliminate her risk of ovarian cancer and only accelerate menopause by a few years.

In the 1990s, the thinking about routine oophorectomy began to change. The risk of ovarian cancer in women who have no family history of the disease is less than 1%. Furthermore, removing the ovaries increases the risk of cardiovascular disease and accelerates **osteoporosis** unless a woman takes prescribed hormone replacements.

Under certain circumstances, oophorectomy may still be the treatment of choice to prevent breast and ovarian cancer in certain high-risk women. A study done at the University of Pennsylvania and released in 2000 showed that healthy women who carried the BRCA1 or BRCA2 genetic mutations that predisposed them to breast cancer had their risk of breast cancer drop from 80% to 19% when their ovaries were removed before age 40. Women between the ages of 40 and 50 showed less risk reduction, and there

KEY TERMS

Cyst—An abnormal sac containing fluid or semi-solid material.

Endometriosis—A benign condition that occurs when cells from the lining of the uterus begin growing outside the uterus.

Fallopian tubes—Slender tubes that carry ova from the ovaries to the uterus.

Hysterectomy—Surgical removal of the uterus.

Osteoporosis—The excessive loss of calcium from the bones, causing the bones to become fragile and break easily.

was no significant reduction of breast cancer risk in women over age 50. A 2002 study showed that five years after being identified as carrying BRCA1 or BRCA2 genetic mutations, 94% of women who had received a bilateral salpingo-oophorectomy were cancer-free, compared to 79% of women who had not received surgery.

The value of ovary removal in preventing both breast and ovarian cancer has been documented. However, there are disagreements within the medical community about when and at what age this treatment should be offered. Preventative oophorectomy, also called prophylactic oophorectomy, is not always covered by insurance. One study conducted in 2000 at the University of California at San Francisco found that only 20% of insurers paid for preventive bilateral oophorectomy (PBO). Another 25% had a policy against paying for the operation, and the remaining 55% said that they would decide about payment on an individual basis.

Demographics

Overall, ovarian cancer accounts for only 4% of all cancers in women. But the lifetime risk for developing ovarian cancer in women who have mutations in BRCA1 is significantly increased over the general population and may cause an ovarian cancer risk of 30% by age 60. For women at increased risk, oophorectomy may be considered after the age of 35 if childbearing is complete.

Other factors that increase a woman's risk of developing ovarian cancer include age (most ovarian cancers occur after menopause), the number of menstrual periods a woman has had (affected by age of onset, **pregnancy**, **breastfeeding**, and oral contraceptive use), history of breast cancer, diet, and family history. The incidence of ovarian cancer is highest among Native Americans (17.5 cases per 100,000 population), white (15.8 per 100,000), Vietnamese (13.8 per 100,000), white Hispanic (12.1 per 100,000), and Hawaiian (11.8 per 100,000) women; it is lowest among Korean (7.0 per 100,000) and Chinese (9.3 per 100,000) women. African American women have an ovarian cancer incidence of 10.2 per 100,000 population.

Description

Oophorectomy is done under general or regional anesthesia. It is often performed through the same type of incision, either vertical or horizontal, as an abdominal **hysterectomy**. Horizontal incisions leave a less noticeable scar, but vertical incisions give the surgeon a better view of the abdominal cavity. After the incision is made, the abdominal muscles are stretched apart, not cut, so that the surgeon can see the ovaries. Then the ovaries, and often the fallopian tubes, are removed.

Oophorectomy can sometimes be done with a laparoscopic procedure. With this surgery, a tube containing a tiny lens and light source is inserted through a small incision in the navel. A camera can be attached that allows the surgeon to see the abdominal cavity on a video monitor. When the ovaries are detached, they are removed though a small incision at the top of the vagina. The ovaries can also be cut into smaller sections and removed.

The advantages of abdominal incision are that the ovaries can be removed even if a woman has many **adhesions** from previous surgery. The surgeon gets a good view of the abdominal cavity and can check the surrounding tissue for disease. A vertical abdominal incision is mandatory if cancer is suspected. The disadvantages are that bleeding is more likely to be a complication of this type of operation. The operation is more painful than a laparoscopic operation and the recovery period is longer. A woman can expect to be in the hospital two to five days and will need three to six weeks to return to normal activities.

Diagnosis/Preparation

Before surgery, the doctor will order blood and urine tests, and any additional tests such as ultrasound or x-rays to help the surgeon visualize the woman's condition. The woman may also meet with the anesthesiologist to evaluate any special conditions that might affect the administration of anesthesia. A colon preparation may be done, if extensive surgery is anticipated.

On the evening before the operation, the woman should eat a light dinner, then take nothing by mouth, including water or other liquids, after midnight.

Aftercare

After surgery a woman will feel discomfort. The degree of discomfort varies and is generally greatest with abdominal incisions, because the abdominal muscles must be stretched out of the way so that the surgeon can reach the ovaries. In order to minimize the risk of postoperative infection, **antibiotics** will be given.

When both ovaries are removed, women who do not have cancer are started on **hormone replacement therapy** to ease the symptoms of menopause that occur because estrogen produced by the ovaries is no longer present. If even part of one ovary remains, it will produce enough estrogen that a woman will continue to menstruate, unless her uterus was removed in a hysterectomy. To help offset the higher risks of heart and bone disease after loss of the ovaries, women should get plenty of **exercise**, maintain a low-fat diet, and ensure intake of **calcium** is adequate.

Return to normal activities takes anywhere from two to six weeks, depending on the type of surgery. When women have cancer, chemotherapy or radiation are often given in addition to surgery. Some women have emotional trauma following an oophorectomy, and can benefit from counseling and support groups.

Risks

Oophorectomy is a relatively safe operation, although, like all major surgery, it does carry some risks. These include unanticipated reaction to anesthesia, internal bleeding, **blood clots**, accidental damage to other organs, and post-surgery infection.

Complications after an oophorectomy include changes in sex drive, hot flashes, and other symptoms of menopause if both ovaries are removed. Women who have both ovaries removed and who do not take estrogen replacement therapy run an increased risk for cardiovascular disease and osteoporosis. Women with a history of psychological and emotional problems before an oophorectomy are more likely to experience psychological difficulties after the operation.

Complications may arise if the surgeon finds that cancer has spread to other places in the abdomen. If the cancer cannot be removed by surgery, it must be treated with chemotherapy and radiation.

Normal results

If the surgery is successful, the ovaries will be removed without complication, and the underlying problem resolved. In the case of cancer, all the cancer will be removed. A woman will become infertile following a bilateral oophorectomy.

Morbidity and mortality rates

Studies have shown that the complication rate following oophorectomy is essentially the same as that following hysterectomy. The rate of complications associated with hysterectomy differs by the procedure performed. Abdominal hysterectomy is associated with a higher rate of complications (9.3%), while the overall complication rate for vaginal hysterectomy is 5.3%, and 3.6% for laparoscopic vaginal hysterectomy. The risk of **death** is about one in every 1,000 women having a hysterectomy. The rates of some of the more commonly reported complications are:

- excessive bleeding (hemorrhaging): 1.8–3.4%
- fever or infection: 0.8–4.0%
- accidental injury to another organ or structure: 1.5–1.8%

Because of the cessation of hormone production that occurs with a bilateral oophorectomy, women who lose both ovaries also prematurely lose the protection these hormones provide against heart disease and osteoporosis. Women who have undergone bilateral oophorectomy are seven times more likely to develop coronary heart disease and much more likely to develop bone problems at an early age than are premenopausal women whose ovaries are intact.

Alternatives

Depending on the specific condition that warrants an oophorectomy, it may be possible to modify the surgery so at least a portion of one ovary remains, allowing the woman to avoid early menopause. In the case of prophylactic oophorectomy, drugs such as tamoxifen may be administered to block the effects that estrogen may have on cancer cells.

Resources

OTHER

"BRCA1 and BRCA2: Cancer Risk and Genetic Testing." National Cancer Institute (accessed February 8, 2010). http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA

"Oophorectomy (ovary removal surgery)." Mayo Clinic, April 16, 2009. http://www.mayoclinic.com/health/oophorectomy/MY00554/METHOD=print

"Ovarian Cancer." MedlinePlus, November 5, 2009. http://www.nlm.nih.gov/medlineplus/ency/article/000889.htm

ORGANIZATIONS

American Cancer Society, 1599 Clifton Road NE, Atlanta, GA, 30329-4251, (800) 227-2345, http://www.cancer.org.

American College of Obstetricians and Gynecologists, 409 23th Street SW, P.O. Box 96920, Washington, DC, 20090-6920, (202)638-5577, http://www.acog.org.
National Cancer Institute, Building 31, Room 10A31, 31 Center Drive, MSC 2580, Bethesda, MD, 20892-2580, (800) 422-6237, http://www.nci.nih.gov.

Tish Davidson, AM
Stephanie Dionne Sherk
Brenda W. Lerner

Open fracture reduction *see* **Fracture repair**
Ophthalmic antibiotics *see* **Antibiotics, ophthalmic**

Ophthalmoplegia

Definition

Ophthalmoplegia is a **paralysis** or weakness of one or more of the muscles that control eye movement. The condition can be caused by any of several neurologic disorders. It may be myopathic, meaning that the muscles controlling eye movement are directly involved, or neurogenic, meaning that the nerve pathways controlling eye muscles are affected. Diseases associated with ophthalmoplegia are ocular myopathy, which affects muscles, and internuclear ophthalmoplegia, a disorder caused by **multiple sclerosis**, a disease which affects nerves.

Description

Because the eyes do not move together in ophthalmoplegia, patients may complain of double vision. Double vision is especially troublesome if the ophthalmoplegia comes on suddenly or affects each eye differently. Because ophthalmoplegia is caused by another, underlying disease, it is often associated with other neurologic symptoms, including limb weakness, lack of coordination, and **numbness**.

Causes and symptoms

Ocular myopathy is also known as mitochondrial encephalomyelopathy with ophthalmoplegia or progressive external ophthalmoplegia. Because it is so often associated with diseases affecting many levels of the neurologic system, it is often referred to as "ophthalmoplegia plus." The main feature is progressive limitation of eye movements, usually with drooping of the eyelids (**ptosis**). Ptosis may occur years before other symptoms of ophthalmoplegia. Because both eyes are equally involved and because ability to move the eyes lessens gradually over the course of years, double vision is rare. On examination, the eyelids may appear thin. This disease usually begins in childhood or adolescence but may start later.

When ophthalmoplegia is caused by muscle degeneration (myopathic), muscle biopsy, in which a small piece of muscle is surgically removed and examined microscopically, will find characteristic abnormal muscle fibers called ragged red fibers. In this form of ophthalmoplegia, the patient may experience weakness of the face, the muscles involved in swallowing, the neck, or the limbs.

Progressive external ophthalmoplegia is sometimes associated with specific neurologic syndromes. These syndromes include familial forms of spastic paraplegia, spinocerebellar disorders, or sensorimotor **peripheral neuropathy**. Kearns-Sayre syndrome causes ophthalmoplegia along with loss of pigment in the retina, the light-sensitive membrane lining the eye. In addition, the disease may cause **heart block** that must be corrected with a pacemaker, increased protein in the cerebrospinal fluid, and a progressively disabling lack of muscular coordination (cerebellar syndrome). Symptoms of the disease appear before age 15.

Some of the progressive external ophthalmoplegia syndromes are unusual in that inheritance is controlled by DNA in the mitochondria. The mitochondria are rod-shaped structures within a cell that convert food to usable energy. Most inherited diseases are passed on by DNA in the cell nucleus, the core that contains the hereditary material. Mitochondrial inheritance tends to be passed on by the mother. Other forms of progressive external ophthalmoplegia are not inherited but occur sporadically with no clear family history. It is not known why some forms are neurogenic and others are myopathic. In the forms inherited through mitochondrial DNA, it is not known which gene product is affected.

Internuclear ophthalmoplegia in multiple sclerosis is caused by damage to a bundle of fibers in the brainstem called the medial longitudinal fasciculus. In this syndrome, the eye on the same side as the damaged medial longitudinal fasciculus is unable to look outward (that is, the left eye cannot look left). The other eye exhibits jerking movements (**nystagmus**) when the patient tries to look left. Internuclear ophthalmoplegia may be seen rarely without multiple sclerosis in patients with certain types of **cancer** or with Chiari type II malformation.

Eye **movement disorders** and ophthalmoplegia can also be seen with **progressive supranuclear palsy**, thyroid disease, **diabetes mellitus**, brainstem tumors,

migraine, basilar artery **stroke**, pituitary stroke, **myasthenia gravis**, **muscular dystrophy**, and the Fisher variant of **Guillain-Barré syndrome**. A tumor or aneurysm in the cavernous sinus, located behind the eyes, can cause painful ophthalmoplegia. Painful ophthalmoplegia can also be caused by an inflammatory process, called Tolosa-Hunt syndrome,in the same area.

Diagnosis

The patient's medical and family history and the examination findings will usually help differentiate the various syndromes associated with ophthalmoplegia. In addition, each syndrome is associated with characteristic features, such as nystagmus or ptosis. All patients with progressive external ophthalmoplegia should have a muscle biopsy to look for ragged red fibers or changes suggesting muscular dystrophy. A sample should be sent for analysis of mitochondrial DNA. Electromyogram (EMG), measurement of electrical activity in the muscle, helps diagnose myopathy.

Computed tomography scan (CT scan) or **magnetic resonance imaging** (MRI) scans of the brain may be needed to rule out **brain tumor**, stroke, aneurysm, or multiple sclerosis. When multiple sclerosis is suspected, evoked potential testing of nerve response may also be helpful. Analysis of cerebrospinal fluid may show changes characteristic of multiple sclerosis or Kearns-Sayre syndrome. Other tests that may be helpful in Kearns-Sayre include electrocardiogram (measuring electrical activity of the heart muscles), retinal examination, and a hearing test (audiogram). For possible myasthenia gravis, the Tensilon (edrophonium) test should be done. Tests should also be done to measure activity of the cell-surface receptors for acetylcholine, a chemical that helps pass electrical impulses along nerve cells in the muscles. Thyroid disease and diabetes mellitus should be excluded by appropriate blood work.

Treatment

There are no specific cures for ocular myopathy or progressive external ophthalmoplegia. Vitamin E therapy has been used to treat Kearns-Sayre syndrome. Coenzyme Q (ubiquinone), a naturally occurring substance similar to vitamin K, is widely used to treat other forms of progressive external ophthalmoplegia, but the degree of success varies. Specific treatments are available for multiple sclerosis, myasthenia gravis, diabetes mellitus, and thyroid disease. Symptoms of ophthalmoplegia can be relieved by mechanical treatment. Surgical procedures can lift drooping eyelids or a patch over one eye can be used to relieve double vision. Because there is no blink response, a surgically lifted eyelid exposes the cornea of the eye so that it may become dry or be scratched. These complications must be avoided by using artificial tears and wearing eyepatches at night. In Kearns-Sayre syndrome, a pacemaker may be needed.

KEY TERMS

Cerebellar—Involving the cerebellum, which controls walking, balance, and coordination.

Cerebrospinal fluid—Fluid bathing the brain and spinal cord.

Heart block—A problem with electrical conduction in the heart muscle that may lead to irregular heart beat and require a pacemaker for treatment.

Mitochondria—Spherical or rod shaped parts of the cell. Mitochondria contain genetic material (DNA and RNA) and are responsible for converting food to energy.

Prognosis

The prognosis of progressive external ophthalmoplegia depends on the associated neurological problems; in particular, whether there is severe limb weakness or cerebellar symptoms that may be mild or disabling. As with most chronic neurologic diseases, mortality increases with disability. Progressive external ophthalmoplegia itself is not a life-threatening condition. Kearns-Sayre syndrome is disabling, probably shortens the life span, and few if any patients have children. Overall life expectancy for multiple sclerosis patients is seven years less than normal; **death** rates are higher for women than for men.

Prevention

There is no way to prevent ophthalmoplegia.

ORGANIZATIONS

American Academy of Neurology, 1080 Montreal Ave., St. Paul, MN, 55116, (651)695-2717, (651)695-2791, (800)879-1960, memberservices@aan.com, http://www.aan.com/.

Laurie Barclay, MD

Ophthalmoscopic examination *see* **Eye examination**

Opiate withdrawal *see* **Withdrawal syndromes**

Opioid analgesics *see* **Analgesics, opioid**

Oppositional defiant disorder

Definition

Oppositional defiant disorder (ODD) is defined by the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV), as a recurring pattern of negative, hostile, disobedient, and defiant behavior in a child or adolescent, lasting for at least six months without serious violation of the basic rights of others. The incidence of ODD in the U.S. population varies somewhat according to the sample studied; DSM-IV gives the rate as between 2–16% while the American Academy of Child and Adolescent Psychiatry (AACAP) gives a figure of 5%–15%, and a researcher at a children's hospital gives a rate of 6–10%.

Description

In order to meet DSM-IV criteria for ODD, the behavior disturbances must cause clinically significant problems in social, school, or work functioning. The course of oppositional defiant disorder varies among patients. In males, the disorder is more common among those who had problem temperaments or high motor activity in the preschool years. During the school years, patients may have low self-esteem, changing moods, and a low frustration tolerance. Patients may swear and use alcohol, tobacco, or illicit drugs at an early age. There are frequent conflicts with parents, teachers, and peers.

Children with this disorder show their negative and defiant behaviors by being persistently stubborn and resisting directions. They may be unwilling to compromise, give in, or negotiate with adults. Patients may deliberately or persistently test limits, ignore orders, argue, and fail to accept blame for misdeeds. Hostility is directed at adults or peers and is shown by verbal aggression or deliberately annoying others.

Causes and symptoms

Oppositional defiant disorder is more common in boys than girls before **puberty**; the disorder typically begins by age eight. After puberty the male:female ratio is about 1:1. Although the specific causes of the disorder are unknown, parents who are overly concerned with power and control may cause an eruption to occur. Symptoms often appear at home, but over time may appear in other settings as well. Usually the disorder occurs gradually over months or years. Several theories about the causes of oppositional defiant disorder are being investigated. Oppositional defiant disorder may be related to:

- the child's temperament and the family's response to that temperament
- an inherited predisposition to the disorder in some families
- marital discord or violence between husband and wife
- frequent or multiple geographical moves
- a neurological cause, like a head injury
- a chemical imbalance in the brain (especially with the brain chemical serotonin)

Oppositional defiant disorder appears to be more common in families where at least one parent has a history of a mood disorder, **conduct disorder**, **attention deficit hyperactivity disorder**, antisocial personality disorder, or a substance-related disorder. Additionally, some studies suggest that mothers with a depressive disorder are more likely to have children with oppositional behavior. However, it is unclear to what extent the mother's depression results from or causes oppositional behavior in children.

Symptoms include a pattern of negative, hostile, and defiant behavior lasting at least six months. During this time four or more specific behaviors must be present. These behaviors include the child who:

- often loses his/her temper
- often argues with adults
- often actively defies or refuses to comply with adults' requests or rules
- often deliberately annoys people
- often blames others for his/her mistakes or misbehavior
- is often touchy or easily annoyed by others
- is often angry and resentful
- is often spiteful or vindictive
- misbehaves
- swears or uses obscene language
- has a low opinion of him/herself

The diagnosis of oppositional defiant disorder is not made if the symptoms occur exclusively in psychotic or **mood disorders**. Criteria are not met for conduct disorder, and, if the child is 18 years old or older, criteria are not met for antisocial personality disorder. In other words, a child with oppositional defiant disorder does not show serious aggressive behaviors or exhibit the physical cruelty that is common in other disorders.

Additional problems may be present, including:

- learning problems
- a depressed mood
- hyperactivity (although attention deficit hyperactivity disorder must be ruled out)

- substance abuse or dependence
- dramatic and erratic behavior

The patient with oppositional defiant disorder is moody, easily frustrated, and may abuse drugs.

Diagnosis

While psychological testing may be needed, the doctor must examine and talk with the child, talk with the parents, and review the medical history. Diagnosis is complicated because oppositional defiant disorder rarely travels alone. Children with attention deficit hyperactivity disorder will also have oppositional defiant disorder 50% of the time. Children with depression/anxiety will have oppositional defiant disorder 10–29% of the time. Because all of the features of this disorder are usually present in conduct disorder, oppositional defiant disorder is not diagnosed if the criteria are met for conduct disorder.

A diagnosis of oppositional defiant disorder should be considered only if the behaviors occur more frequently and have more serious consequences than is typically observed in other children of a similar developmental stage. Further, the behavior must lead to significant impairment in social, school, or work functioning.

A new evaluation scale known as the Oppositional Defiant Behavior Inventory (ODBI) has been developed as an aid to diagnosis. The ODBI appears to meet accepted standards of reliability and validity.

Treatment

Treatment of oppositional defiant disorder usually consists of group, individual and/or **family therapy**, and education. Of these, individual therapy is the most common. Therapy can provide a consistent daily schedule, support, consistent rules, discipline, and limits. It can also help train patients to get along with others and modify behaviors. Therapy can occur in residential, day treatment, or medical settings. Additionally, having a healthy role model as an example is important for the patient.

Parent management training focuses on teaching the parents specific and more effective techniques for handling the child's opposition and defiance. Research has shown that parent management training is more effective than family therapy. One variation of parent management training known as parent-child interaction therapy (PCIT) appears to be helpful over the long term; a group of Australian researchers reported in 2004 that families who were given a course of PCIT maintained their gains two years after the program ended.

As of the early 2000s, elementary school teachers are being trained to deal more effectively with classroom disruptions caused by children with ODD. The long-term effectiveness of these interventions, however, will require further study.

KEY TERMS

Attention deficit hyperactivity disorder—A persistent pattern of inattention, hyperactivity and/or impulsiveness; the pattern is more frequent and severe than is typically observed in people at a similar level of development.

Conduct disorder—A repetitive and persistent pattern of behavior in which the basic rights of others are violated or major age-appropriate rules of society are broken.

Whether involved in therapy or working on this disorder at home, the patient must work with his or her parents' guidance to make the fullest possible recovery. According to the New York Hospital/Cornell Medical Center, the patients must:

- use self timeouts
- identify what increases anxiety
- talk about feelings instead of acting on them
- find and use ways to calm themselves
- frequently remind themselves of their goals
- get involved in tasks and physical activities that provide a healthy outlet for energy
- learn how to talk with others
- develop a predictable, consistent, daily schedule of activity
- develop ways to obtain pleasure and feel good
- learn how to get along with other people
- find ways to limit stimulation
- learn to admit mistakes in a matter-of-fact way

Stimulant medication is used only when oppositional defiant disorder coexists with attention deficit hyperactivity disorder. Currently, no research is currently available on the use of other psychiatric medications in the treatment of oppositional defiant disorder.

Prognosis

The outcome varies. In some children the disorder evolves into a conduct disorder or a mood disorder. Later in life, oppositional defiant disorder can develop into passive aggressive personality disorder or antisocial personality disorder. Some children respond well to treatment and some do not. Generally, with

treatment, reasonable adjustment in social settings and in the workplace can be made in adulthood.

Resources

BOOKS

Matthys, Walter, and John E. Lochman. *Oppositional Defiant Disorder and Conduct Disorder in Children*. New York: Wiley, 2010.

PERIODICALS

Harada, Y., K. Saitoh, J. Iida, et al. "The Reliability and Validity of the Oppositional Defiant Behavior Inventory." *European Child and Adolescent Psychiatry* 13 (June 2004): 185–190.

Nixon, R. D., L. Sweeney, D. B. Erickson, and S. W. Touyz. "Parent-Child Interaction Therapy: One- and Two-Year Follow-Up of Standard and Abbreviated Treatments for Oppositional Preschoolers." *Journal of Abnormal Child Psychology* 32 (June 2004): 263–271.

van Leer, P. A., B. O. Muthen, R. M. van der Sar, and A. A. Crijnen. "Preventing Disruptive Behavior in Elementary Schoolchildren: Impact of a Universal Classroom-Based Intervention." *Journal of Consulting and Clinical Psychology* 72 (June 2004): 467–478.

OTHER

American Academy of Child and Adolescent Psychiatry (AACAP). *Children with Oppositional Defiant Disorder*. AACAP Facts for Families #72. Washington, DC: AACAP, 2000.

ORGANIZATIONS

American Academy of Child and Adolescent Psychiatry (AACAP), 3615 Wisconsin Ave. NW, Washington, DC, 20013-3007, (202)966-7300, (202)966-2891, communications@aacap.org, http://www.aacap.org/.

American Psychiatric Association (APA), 1000 Wilson Boulevard, Suite 1825, Arlington, VA, 22209, (888)357-7924, apa@psych.org, http://www.psych.org.

Families Anonymous, Inc., P.O. Box 3475, Culver City, CA, 90231-3475, (310)815-9682, (800)736-9805, famanon@FamiliesAnonymous.org, http://www.familiesanonymous.org/.

David James Doermann
Rebecca Frey, PhD

Optic atrophy

Definition

Optic atrophy can be defined as damage to the optic nerve resulting in a degeneration or destruction of the optic nerve. Optic atrophy may also be referred to as optic nerve head pallor because of the pale appearance of the optic nerve head as seen at the back of the eye. Possible causes of optic atrophy include: **optic neuritis**, Leber's hereditary optic atrophy, toxic or nutritional optic neuropathy, glaucoma, vascular disorders, trauma, and other systemic disorders.

Description

The process of vision involves light entering the eye and triggering chemical changes in the retina, a pigmented layer lining the back of the eye. Nerve impulses created by this process travel to the brain via the optic nerve. Using a hand-held instrument called an ophthalmoscope, the doctor can see the optic nerve head (optic disc) which is the part of the optic nerve that enters at the back of the eyeball. In optic atrophy, the disc is pale and has fewer blood vessels than normal.

Causes and symptoms

Symptoms of optic atrophy are a change in the optic disc and a decrease in visual function. This change in visual function can be a decrease in sharpness and clarity of vision (visual acuity) or decreases in side (peripheral) vision. Color vision and contrast sensitivity can also be affected.

There are many possible causes of optic atrophy. The causes can range from trauma to systemic disorders. Some possible causes of optic atrophy include:

- Optic neuritis. Optic neuritis is an inflammation of the optic nerve. It may be associated with eye pain worsened by eye movement. It is more common in young to middle-aged women. Some patients with optic neuritis may develop multiple sclerosis later on in life.
- Leber's hereditary optic neuropathy. This is a disease of young men (late teens, early 20s), characterized by an onset over a few weeks of painless, severe, central visual loss in one eye, followed weeks or months later by the same process in the other eye. At first the optic disc may be slightly swollen, but eventually there is optic atrophy. The visual loss is generally permanent. This condition is hereditary. If a patient knows that Leber's runs in the family, genetic counseling should be considered.
- Toxic optic neuropathy. Nutritional deficiencies and poisons can be associated with gradual vision loss and optic atrophy, or with sudden vision loss and optic disc swelling. Toxic and nutritional optic neuropathies are uncommon in the United States, but took on epidemic proportions in Cuba in 1992–1993. The most common toxic optic neuropathy is known as tobacco-alcohol amblyopia, thought to be caused by exposure to cyanide from tobacco smoking, and by low levels of vitamin B_{12} because of poor nutrition

and poor absorption associated with drinking alcohol. Other possible toxins included ethambutol, methyl alcohol (moonshine), ethylene glycol (antifreeze), cyanide, lead, and carbon monoxide. Certain medications have also been implicated. Nutritional optic neuropathy may be caused by deficiencies of protein, or of the B vitamins and folate, associated with starvation, malabsorption, or alcoholism.

- Glaucoma. Glaucoma may be caused by an increase of pressure inside the eye. This increased pressure may eventually affect the optic nerve if left untreated.
- Compressive optic neuropathy. This is the result of a tumor or other lesion putting pressure on the optic nerve. Another possible cause is enlargement of muscles involved in eye movement seen in hyperthyroidism (Graves' disease).
- Retinitis pigmentosa. This is a hereditary ocular disorder.
- Syphilis. Left untreated, this disease may result in optic atrophy.

Diagnosis

Diagnosis involves recognizing the characteristic changes in the optic disc with an ophthalmoscope, and measuring visual acuity, usually with an eye chart. Visual field testing can test peripheral vision. Color vision and contrast sensitivity can also be tested. Family history is important in the diagnosis of inherited conditions. Exposure to poisons, drugs, and even medications should be determined. Suspected **poisoning** can be confirmed through blood and urine analysis, as can vitamin deficiency.

Brain **magnetic resonance imaging** (MRI) may show a tumor or other structure putting pressure on the optic nerve, or may show plaques characteristic of **multiple sclerosis**, which is frequently associated with optic neuritis. However, similar MRI lesions may appear in Leber's hereditary optic neuropathy. Mitochondrial DNA testing can be done on a blood sample, and can identify the mutation responsible for Leber's.

Visual evoked potentials (VEP), which measure speed of conduction over the nerve pathways involved in sight, may detect abnormalities in the clinically unaffected eye in early cases of Leber's. Fluorescein **angiography** gives more detail about blood vessels in the retina.

Treatment

Treatment of optic neuritis with **steroids** is controversial. There is no known treatment for Leber's hereditary optic neuropathy. Treatment of other causes of optic atrophy varies depending upon the underlying disease.

KEY TERMS

Atrophy—A destruction or dying of cells, tissues, or organs.

Cerebellar—Involving the part of the brain (cerebellum), which controls walking, balance, and coordination.

Mitochondia—A structure in the cell responsible for producing energy. A defect in the DNA in the mitochondria is involved in Leber's optic neuropathy.

Neuritis—An inflammation of the nerves.

Neuropathy—A disturbance of the nerves, not caused by an inflammation. For example, the cause may be toxins, or unknown.

Prognosis

Many patients with optic neuritis eventually develop multiple sclerosis. Most patients have a gradual recovery of vision after a single episode of optic neuritis, even without treatment. Prognosis for visual improvement in Leber's hereditary optic neuropathy is poor, with the specific rate highly dependent on which mitochondrial DNA mutation is present. If the cause of toxic or nutritional deficiency optic neuropathy can be found and treated early, such as stopping **smoking** and taking **vitamins** in tobacco-alcohol **amblyopia**, vision generally returns to near normal over several months' time. However, visual loss is often permanent in cases of long-standing toxic or nutritional deficiency optic neuropathy.

Prevention

People noticing a decrease in vision (central and/or side vision) should ask their eye care practitioner for a check up. Patients should also go for regular vision exams. Patients should ask their doctor how often that should be, as certain conditons may warrant more frequent exams. Early detection of inflammations or other problems lessens the chance of developing optic atrophy.

There are no preventive measures that can definitely abort Leber's hereditary optic neuropathy in those genetically at risk, or in those at risk based on earlier involvement of one eye. However, some

doctors recommend that their patients take vitamin C, vitamin E, coenzyme Q_{10}, or other **antioxidants**, and that they avoid the use of tobacco or alcohol. Patients should ask their doctors about the use of vitamins. Avoiding toxin exposure and nutritional deficiency should prevent toxic or nutritional deficiency optic neuropathy.

ORGANIZATIONS

American Academy of Neurology, 1080 Montreal Ave., St. Paul, MN, 55116, (651)695-2717, (651) 695-2791, (800) 879-1960, memberservices@aan.com, http://www.aan.com/.

Prevent Blindness America, 211 West Wacker Drive, Suite 1700, Chicago, IL, 60606, (800)331-2020, http://www. preventblindness.org.

Laurie Barclay, MD

Optic neuritis

Definition

Optic neuritis is a vision disorder characterized by inflammation of the optic nerve.

Description

Optic neuritis occurs when the optic nerve, the pathway that transmits visual information to the brain, becomes inflamed and the myelin sheath that surrounds the nerve is destroyed (a process known as demyelination). It typically occurs in one eye at a time (70%), and the resulting vision loss is rapid and progressive, but only temporary. Thirty percent of patients experience occurrence in both eyes. Optic neuritis tends to afflict young adults with an average age in their 30s. Seventy-five percent of patients with optic neuritis are women.

Nerve damage that occurs in the section of the optic nerve located behind the eyeball, is called *retrobulbar neuritis*, and is most often associated with **multiple sclerosis**. Optic nerve inflammation and **edema** (swelling) caused by intracranial pressure at the place where the nerve enters the eyeball is termed *papillitis*.

Causes and symptoms

Symptoms of optic neuritis include one or more of the following:

- blurred or dimmed vision
- blind spots, particularly with central vision
- pain with eye movement
- headache
- sudden color blindness
- impaired night vision
- impaired contrast sensitivity

Optic neuritis is most commonly associated with multiple sclerosis (MS). Other causes include viral or fungal infections, encephalomyelitis, autoimmune diseases, or pressure on the nerve from tumors or vascular diseases (i.e., **temporal arteritis**). Some toxins, such as methanol and lead, can also damage the optic nerve, as can long-term **abuse** of alcohol and tobacco. Patients with non-MS related optic neuritis are usually immunocompromised in some way.

Diagnosis

An ophthalmologist, a physician trained in diseases of the eye, will typically make a diagnosis of optic neuritis. A complete visual exam, including a visual acuity test, color vision test, and examination of the retina and optic disc with an ophthalmoscope, will be performed. Clinical signs such as impaired pupil response may be apparent during an eye exam, but in some cases the eye may appear normal. A medical history will also be performed to determine if exposure to toxins such as lead may have caused the optic neuritis.

Further diagnostic testing such as **magnetic resonance imaging** (MRI) may be necessary to confirm a diagnosis of optic neuritis. An MRI can also reveal signs of multiple sclerosis.

Treatment

Treatment of optic neuritis depends on the underlying cause of the condition. Vision loss resulting from a viral condition usually resolves itself once the virus is treated, and optic neuritis resulting from toxin damage may improve once the source of the toxin is removed.

A course of intravenous **corticosteroids** (**steroids**) followed by oral steroids has been found to be helpful in restoring vision quickly to patients with MS-related episodes of optic neuritis, but its efficacy in preventing relapse is debatable. The Optic Neuritis Treatment Trial (ONTT) has shown that IV steroids may be effective in reducing the onset of MS for up to two years, but further studies are necessary. Oral prednisone has been found to increase the likelihood of recurrent episodes of optic neuritis, and is not recommended for treating the disorder.

KEY TERMS

Atrophy—Cell wasting or death.

Multiple sclerosis—An autoimmune disease of the central nervous system characterized by damage to the myelin sheath that covers nerves.

Temporal arteritis—Also known as giant cell arteritis. Inflammation of the large arteries located in the temples which is marked by the presence of giant cells and symptoms of headache and facial pain.

Visual acuity test—An eye examination that determines sharpness of vision, typically performed by identifying objects and/or letters on an eye chart.

Prognosis

The vision loss associated with optic neuritis is usually temporary. Spontaneous remission occurs in two to eight weeks. Sixty-five to eighty percent of patients can expect 20/30 or better vision after recovery. Long-term prognosis depends on the underlying cause of the condition. If a viral infection has triggered the episode, it frequently resolves itself with no after effects. If optic neuritis is associated with multiple sclerosis, future episodes are not uncommon. Thirty-three percent of optic neuritis cases recur within five years. Each recurrence results in less recovery and worsening vision. There is a strong association between optic neuritis and MS. In those without multiple sclerosis, half who experience an episode of vision loss related to optic neuritis will develop the disease within 15 years.

Prevention

Regular annual eye exams are critical to maintaining healthy vision. Early treatment of vision problems can prevent permanent optic nerve damage (atrophy).

Resources

BOOKS

Leitman, Mark. *Manual for Eye Examination and Diagnosis*. 7th ed. New York: Wiley–Blackwell, 2007.

PERIODICALS

Cohen, Joyce Render, et al. "Living with Low Vision." *Inside MS* 1 (2001): 46.

ORGANIZATIONS

Prevent Blindness America, 211 West Wacker Drive, Suite 1700, Chicago, IL, 60606, (800)331-2020, http://www.preventblindness.org.

Paula Anne Ford-Martin

Oral cancer *see* **Head and neck cancer**
Oral cholecystography *see* **Gallbladder x rays**

Oral contraceptives

Definition

Oral contraceptives are medicines taken by mouth to help prevent **pregnancy**. They are also known as "the Pill," OCs, or birth-control pills.

Purpose

Oral contraceptives, birth-control pills, contain artificially made forms of two hormones produced naturally in the body. These hormones, estrogen and progestin, regulate a woman's menstrual cycle. When taken in the proper amounts, following a specific schedule, oral contraceptives are very effective in preventing pregnancy. Studies show that fewer than one of every 100 women who use oral contraceptives correctly becomes pregnant during the first year of use.

These pills have several effects that help prevent pregnancy. For pregnancy to occur, an egg must become mature inside a woman's ovary, be released, and travel to the fallopian tube. A male sperm must also reach the fallopian tube, where it fertilizes the egg. Then the fertilized egg must travel to the woman's uterus (womb), where it lodges in the uterus' lining and develops into a fetus. The main way that oral contraceptives prevent pregnancy is by keeping an egg from ripening fully. Eggs that do not ripen fully cannot be fertilized. In addition, birth-control pills thicken mucus in the woman's cervix, through which the sperm has to swim. This makes it more difficult for the sperm to reach the egg. Oral contraceptives also thin the uterine lining so that a fertilized egg cannot lodge there and develop.

Birth-control pills may cause good or bad side effects. For example, a woman's menstrual periods are regular and usually lighter when she is taking oral contraceptives, and the pills may reduce the risk of **ovarian cysts**, breast lumps, **pelvic inflammatory disease**, and other medical problems. However, taking birth-control pills increases the risk of **heart attack**, **stroke**, and **blood clots** in women with a family history of heart disease. Serious side effects such as these are more likely in women over 35 years of age who smoke cigarettes and in those with specific health problems such as high blood pressure, diabetes, or a history of breast or uterine **cancer**. A woman who wants to use

A package of birth-control pills, an oral contraceptive. *(Lew Robertson/Brand X Pictures/Getty Images.)*

oral contraceptives should ask her physician for the latest information on the risks and benefits of all types of birth control and should consider her age, health, and medical history when deciding what to use.

Precautions

No form of birth control (except not having sex) is 100% effective. However, oral contraceptives can be highly effective when used properly. Discuss the options with a healthcare professional.

Oral contraceptives do not protect against **AIDS** or other **sexually transmitted diseases**. For protection against such diseases, use a latex condom.

Oral contraceptives are not effective immediately after a woman begins taking them. Physicians recommend using other forms of birth control for the first 1–3 weeks. Follow the instructions of the physician who prescribed the medicine.

Smoking cigarettes while taking oral contraceptives greatly increases the risk of serious side effects. *Women who take oral contraceptives should not smoke cigarettes.*

Seeing a physician regularly while taking this medicine is very important. The physician will note unwanted side effects. Follow his or her advice on how often you should be seen.

Anyone taking oral contraceptives should be sure to tell the healthcare professional in charge before having any surgical or dental procedures, laboratory tests, or emergency treatment.

This medicine may increase sensitivity to sunlight. Women using oral contraceptives should avoid too much sun exposure and should not use **tanning** beds, tanning booths, or sunlamps until they know how the medicine affects them. Some women taking oral contraceptives may get brown splotches on exposed areas of their skin. These usually go away over time after the women stop taking birth-control pills.

When possible, birth-control pills ought to be stopped for one month prior to, and not started again until two weeks after, major surgery involving prolonged immobility and/or an increased risk of blood clots.

Oral contraceptives may cause the gums to become tender and swollen, or to bleed. Careful brushing and flossing, gum massage, and regular cleaning may help prevent this problem. Check with a physician or dentist if gum problems develop.

Women who have certain medical conditions or who are taking certain other medicines may have problems if they take oral contraceptives. Before taking these drugs, be sure to let the physician know about any of these conditions:

ALLERGIES. Anyone who has had unusual reactions to estrogens or progestins in the past should let her physician know before taking oral contraceptives. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

PREGNANCY. Women who become pregnant or think they may have become pregnant while taking birth-control pills should stop taking them immediately and check with their physicians. Women who want to start taking oral contraceptives again after pregnancy should not refill their old prescriptions without checking with their physicians. The physician may need to change the prescription.

BREASTFEEDING. Women who are **breastfeeding** should check with their physicians before using oral contraceptives. The hormones in the pills may reduce

the amount of breast milk and may pass to babies via milk. They may also cause **jaundice** and enlarged breasts in nursing babies whose mothers take the medicine.

OTHER MEDICAL CONDITIONS. Oral contraceptives may improve or worsen some medical conditions. The possibility that they may make a condition worse does not necessarily mean they cannot be used. In some cases, women may need only to be tested or followed more closely for medical problems while using oral contraceptives. Before using oral contraceptives, women with any of these medical problems should make sure their physicians are aware of their conditions:

- Female conditions such as menstrual problems, endometriosis, or fibroid tumors of the uterus. Birth-control pills usually make these problems better, but may sometimes make them worse or more difficult to diagnose.
- Heart or circulation problems; recent or past blood clots or stroke. Women who already have these problems may be at greater risk of developing blood clots or circulation problems if they use oral contraceptives. However, healthy women who do not smoke may lower their risk of circulation problems and heart disease by taking the pills.
- Breast cysts, lumps, or other non-cancerous breast problems. Oral contraceptives generally protect against these conditions, but physicians may recommend more frequent breast exams for women taking the pills.
- Breast cancer or other cancer (now or in the past, or family history). Oral contraceptives may make some existing cancers worse. Women with a family history of breast cancer may need more frequent screening for the disease if they decide to take birth-control pills.
- Migraine headaches. This condition may improve, but sometimes worsens with the use of birth-control pills.
- Diabetes. Blood sugar levels may increase slightly when oral contraceptives are used. Usually this increase is not enough to affect the amount of diabetes medicine needed. However, blood sugar will need to be monitored closely while taking oral contraceptives.
- Depression. This condition may worsen in women who already have it or may (rarely) occur again in women who were depressed in the past.
- Gallbladder disease, gallstones, high blood cholesterol, or chorea gravidarum (a nervous disorder). Oral contraceptives may make these conditions worse.
- Epilepsy, high blood pressure, heart or circulation problems. By increasing fluid build-up, oral contraceptives may make these conditions worse.

Description

Oral contraceptives (birth-control pills) come in a wide range of estrogen-progestin combinations. The pills in use today contain much lower doses of estrogen than those available in the past; these changes have reduced the likelihood of serious side effects. Some pills contain only progestin. These are prescribed mainly for women who need to avoid estrogens and may not be as effective in preventing pregnancy as the estrogen-progestin combinations.

These medicines come in tablet form, in containers designed to help women keep track of which tablet to take each day. The tablets are different colors, indicating amounts of hormones they contain. Some may contain no hormones at all. These are included simply to help women stay in the habit of taking a pill every day, as the hormone combination needs to be taken only on certain days of the menstrual cycle. Keeping the tablets in their original container and taking them exactly on schedule is very important. They will not be as effective if taken in the wrong order or if doses are missed.

Oral contraceptives are available only with a physician's prescription. Some commonly used brands are Demulen, Desogen, Loestrin, Lo/Ovral, Nordette, Ortho-Novum, Ortho-Tri-Cyclen, Estrostep, Ortho-cept, Alesse, Levlite and Ovcon.

The dose schedule depends on the type of oral contraceptive. The two basic schedules are a 21-day schedule and a 28-day schedule. On the 21-day schedule, take one tablet a day for 21 days, then skip 7 days and repeat the cycle. On the 28-day schedule, take one tablet a day for 28 days; then repeat the cycle. Be sure to carefully follow the instructions provided with the medicine. For additional information or explanations, check with the physician who prescribed the medicine or the pharmacist who filled the prescription.

Taking doses more than 24 hours apart may increase the chance of side effects or pregnancy. Try to take the medicine at the same time every day. Take care not to run out of pills. If possible, keep an extra month's supply on hand and replace it every month with the most recently filled prescription.

Try not to miss a dose, as this increases the risk of pregnancy. If a dose is missed, follow the package directions or check with the physician who prescribed the medicine for instructions. It may be necessary to use another form of birth control for some time after missing a dose.

Taking this medicine with food or at bedtime will help prevent **nausea**, a side effect that sometimes occurs during the first few weeks. Nausea usually goes away as the body adjusts to the medicine.

Taking oral contraceptives may have several benefits outside of their ability to prevent pregnancy. Research indicates that with 10 to 12 years of oral contraceptive use, a woman's risk of **ovarian cancer** is reduced by up to 80%. There may also be an approximate 50% decrease in the rate of endometrial cancers in women. Another well-known, non-contraceptive benefit of taking oral contraceptives is improvement in **acne**. The combination oral contraceptive ethinyl estradiol/norgestimate has been approved by the U.S. Food and Drug Administration for the treatment of acne. Another positive effect of oral contraceptive use is improvement in abnormal uterine bleeding. Older women may also benefit from using oral contraceptives, because the pills can increase bone mass as women enter their menopausal years, when **osteoporosis** is a growing concern.

Oral contraceptives may be used on an emergency basis as a means of preventing pregnancy in women who have had unprotected intercourse. Plan B is available for this use, over the counter, in most drug stores.

Risks

Taking oral contraceptives with certain other drugs may affect the way the drugs work or may increase the chance of side effects.

Side effects

Serious side effects are rare in healthy women who do not smoke cigarettes. In women with certain health problems, however, oral contraceptives may cause problems such as **liver cancer**, non-cancerous liver tumors, blood clots, or stroke. Health-care professionals can help women weigh the benefits of being protected against unwanted pregnancy against the risks of possible health problems.

The most common minor side effects include emotional lability (swings), nausea; **vomiting**; abdominal cramping or bloating; breast **pain**, tenderness or swelling; swollen ankles or feet; tiredness; and acne. These usually go away as the body adjusts to the drug, and do not need medical attention unless they persist or interfere with normal activities.

Other side effects should be brought to the attention of the physician who prescribed the medicine. Check with the physician as soon as possible if any of the following side effects occur:

- missed periods, longer periods, or bleeding or spotting between periods
- headaches
- vaginal infection, itching, or irritation
- increased blood pressure

Women who have any of the following symptoms should get emergency help right away. These symptoms may be signs of blood clots:

- sudden changes in vision, speech, breathing, or coordination
- severe or sudden headache
- coughing up blood
- sudden, severe, or continuing pain in the abdomen or stomach
- pain in the chest, groin, or leg (especially in the calf)
- weakness, numbness, or pain in an arm or leg

Oral contraceptives may continue to affect the menstrual cycle for some time after a woman stops taking them. Women who miss periods for several months after stopping this medicine should check with their physicians.

Other rare side effects may occur. Anyone who has unusual symptoms while taking oral contraceptives should get in touch with her physician.

Interactions

Oral contraceptives interact with a number of other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Anyone who takes oral contraceptives should let the physician know all other medicines she is taking and should ask whether the possible interactions can interfere with drug therapy.

These drugs may make oral contraceptives less effective in preventing pregnancy. Anyone who takes these drugs should use an additional birth control method for the entire cycle in which the medicine is used:

- ampicillin
- penicillin V
- rifampin (Rifadin)
- tetracyclines
- griseofulvin (Gris-PEG, Fulvicin)
- corticosteroids
- barbiturates
- carbamazepine (Tegretol)
- phenytoin (Dilantin)
- primidone (Mysoline)
- ritonavir (Norvir)
- modafinil (Provigil)
- oxcarbazepine (Trileptal)
- St John's wort

In addition, taking these medicines with oral contraceptives may increase the risk of side effects or interfere with the medicine's effects:

KEY TERMS

Cyst—An abnormal sac or enclosed cavity in the body, filled with liquid or partially solid material.

Endometriosis—A condition in which tissue, like that normally found in the lining of the uterus, is present outside the uterus. The condition often causes pain and bleeding.

Fallopian tube—One of a pair of slender tubes that extend from each ovary to the uterus. Eggs pass through the fallopian tubes to reach the uterus.

Fetus—A developing baby inside the womb.

Fibroid tumor—A noncancerous tumor formed of fibrous tissue.

Hormone—A substance that is produced in one part of the body, then travels through the bloodstream to another part of the body where it has its effect.

Jaundice—Yellowing of the eyes and skin due to the build up of a bile pigment (bilirubin) in the blood.

Migraine—A throbbing headache that usually affects only one side of the head. Nausea, vomiting, increased sensitivity to light, and other symptoms often accompany migraine.

Mucus—Thick fluid produced by the moist membranes that line many body cavities and structures.

Ovary—A reproductive organ in females that produces eggs and hormones.

Pelvic inflammatory disease—Inflammation of the female reproductive tract, caused by any of several microorganisms. Symptoms include severe abdominal pain, high fever, and vaginal discharge. Severe cases can result in sterility. Also called PID.

Uterus—A hollow organ in a female in which a fetus develops until birth.

- theophylline–effects of this medicine may increase, along with the chance of unwanted side effects and possible toxicity
- cyclosporine–effects of this medicine may increase, along with the chance of unwanted side effects

The list above does not include every drug that may interact with oral contraceptives. Be sure to check with a physician or pharmacist before combining oral contraceptives with any other prescription or nonprescription (over-the-counter) medicine.

As with any medication, the benefits and risks should be discussed with a physician.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

PERIODICALS

"Current Perspectives on OC Formulations." *Family Practice News* January 15, 2001: 2.

"Physician Group Supports Safety, Availability of Over-the-Counter Emergency Option." *Medical Letter on the CDC and FDA* March 18, 2001.

OTHER

Medline Plus Health Information, U.S. National Library of Medicine. http://www.nlm.nih.gov/medlineplus.

Deanna M. Swartout-Corbeil, RN

Oral herpes *see* **Cold sore**

Oral hygiene

Definition

Oral hygiene is the practice of keeping the mouth clean and healthy by brushing and flossing to prevent **tooth decay** and gum disease.

Purpose

The purpose of oral hygiene is to prevent the build-up of plaque, the sticky film of bacteria and food that forms on the teeth. Plaque adheres to the crevices and fissures of the teeth and generates acids that, when not removed on a regular basis, slowly eat away, or decay, the protective enamel surface of the teeth, causing holes (cavities) to form. Plaque also irritates gums and can lead to gum disease (**periodontal disease**) and tooth loss. Toothbrushing and flossing remove plaque from teeth, and antiseptic mouthwashes kill some of the bacteria that help form plaque. Fluoride—in toothpaste, drinking water, or dental treatments—also helps to protect teeth by binding with enamel to make it stronger. In addition to such daily oral care, regular visits to the dentist promote oral health. Preventative services that he or she can perform include fluoride treatments, sealant application, and scaling (scraping off the hardened plaque, called tartar). The dentist can also perform such diagnostic services as x-ray imaging and oral **cancer** screening as well as such treatment services as fillings, crowns, and bridges.

Precautions

Maintaining oral hygiene should be a lifelong habit. An infant's gums and, later, teeth should be kept clean by wiping them with a moist cloth or a soft toothbrush. However, only a very small amount (the size of a pea) of toothpaste containing fluoride should be used since too much fluoride may be toxic to infants.

An adult who has partial or full dentures should also maintain good oral hygiene. Bridges and dentures must be kept clean to prevent gum disease. Dentures should be relined and adjusted by a dentist as necessary to maintain proper fit so the gums do not become red, swollen, and tender.

Brushing and flossing should be performed thoroughly but not too vigorously. Rough mechanical action may irritate or damage sensitive oral tissues. Sore or bleeding gums may be experienced for the first few days after flossing is begun. However, bleeding continuing beyond one week should be brought to the attention of a dentist. As a general rule, any sore or abnormal condition that does not disappear after 10 days should be examined by a dentist.

Description

Brushing

Brushing should be performed with a toothbrush and a fluoride toothpaste at least twice a day and preferably after every meal and snack. Effective brushing must clean each outer tooth surface, inner tooth surface, and the flat chewing surfaces of the back teeth. To clean the outer and inner surfaces, the toothbrush should be held at a 45-degree angle against the gums and moved back and forth in short strokes (no more than one toothwidth distance). To clean the inside surfaces of the front teeth, the toothbrush should be held vertically and the bristles at the tip (called the toe of the brush) moved gently up and down against each tooth. To clean the chewing surfaces of the large back teeth, the brush should be held flat and moved back and forth. Finally, the tongue should also be brushed using a back-to-front sweeping motion to remove food particles and bacteria that may sour the breath.

Toothbrushes wear out and should be replaced every three months. Consumers should look for toothbrushes with soft, nylon, rounded bristles in a size and shape that allows them to reach all tooth surfaces easily.

Holding a toothbrush may be difficult for people with limited use of their hands. The toothbrush handle may be modified by inserting it into a rubber ball for easier gripping.

Flossing

Flossing once a day helps prevent gum disease by removing food particles and plaque at and below the gumline as well as between teeth. To begin, most of an 18-in (45-cm) strand of floss is wrapped around the third finger of one hand. A 1-in (2.5-cm) section is then grasped firmly between the thumb and forefinger of each hand. The floss is eased between two teeth and worked gently up and down several times with a rubbing motion. At the gumline, the floss is curved first around one tooth and then the other with gentle sliding into the space between the tooth and gum. After each tooth contact is cleaned, a fresh section of floss is unwrapped from one hand as the used section of floss is wrapped around the third finger of the opposite hand. Flossing proceeds between all teeth and behind the last teeth. Flossing should also be performed around the abutment (support) teeth of a bridge and under any artificial teeth using a device called a floss threader.

Dental floss comes in many varieties (waxed, unwaxed, flavored, tape) and may be chosen on personal preference. For people who have difficulty handling floss, floss holders and other types of interdental (between the teeth) cleaning aids, such as brushes and picks, are available.

Risks

Negative consequences arise from improper or infrequent brushing and flossing. The five major oral health problems are plaque, tartar, gingivitis, periodontitis, and tooth decay.

Plaque is a soft, sticky, colorless bacterial film that grows on the hard, rough surfaces of teeth. These bacteria use the sugar and starch from food particles in the mouth to produce acid. Left to accumulate, this acid destroys the outer enamel of the tooth, irritates the gums to the point of bleeding, and produces foul breath. Plaque starts forming again on teeth four to 12 hours after brushing, so brushing a minimum of twice a day is necessary for adequate oral hygiene.

When plaque is not regularly removed by brushing and flossing, it hardens into a yellow or brown mineral deposit called tartar or calculus. This formation is crusty and provides additional rough surfaces for the growth of plaque. When tartar forms below the gumline, it can lead to periodontal (gum) disease.

Gingivitis is an early form of periodontal disease, characterized by inflammation of the gums with painless bleeding during brushing and flossing. This common condition is reversible with proper dental care but

KEY TERMS

Calculus—A hardened yellow or brown mineral deposit from unremoved plaque; also called tartar.

Cavity—A hole or weak spot in the tooth surface caused by decay.

Gingivitis—Inflammation of the gums, seen as painless bleeding during brushing and flossing.

Interdental—Between the teeth.

Periodontal—Pertaining to the gums.

Periodontitis—A gum disease that destroys the structures supporting the teeth, including bone.

Plaque—A thin, sticky, colorless film of bacteria that forms on teeth.

Tartar—A hardened yellow or brown mineral deposit from unremoved plaque; also called calculus.

if left untreated, it will progress into a more serious periodontal disease, periodontitis.

Periodontitis is a gum disease that destroys the structures supporting the teeth, including bone. Without support, the teeth will loosen and may fall out or have to be removed. To diagnose periodontitis, a dentist looks for gums that are red, swollen, bleeding, and shrinking away from the teeth, leaving widening spaces between teeth and exposed root surfaces vulnerable to decay.

Tooth decay, also called dental caries or cavities, is a common dental problem that results when the acid produced by plaque bacteria destroys the outer surface of a tooth. A dentist will remove the decay and fill the cavity with an appropriate dental material to restore and protect the tooth; left untreated, the decay will expand, destroying the entire tooth and causing significant **pain**.

Normal results

With proper brushing and flossing, oral hygiene may be maintained and oral health problems may be avoided. Older adults may no longer assume that they will lose all of their teeth in their lifetime. Regular oral care preserves speech and eating functions, thus prolonging the quality of life.

ORGANIZATIONS

American Dental Association, 211 E. Chicago Ave., Chicago, IL, 60611-2678, (312)440-2500, http://www.ada.org.

American Dental Hygienists' Association, 444 North Michigan Avenue, Suite 3400, Chicago, IL, 60611, (312)440-8900, mail@adha.net, http://www.adha.org/.

Bethany Thivierge

Oral hypoglycemics *see* **Antidiabetic drugs**

Orbital and periorbital cellulitis

Definition

Periorbital **cellulitis** is an inflammation and infection of the eyelid and the skin surrounding the eye. Orbital cellulitis affects the eye socket (orbit) as well as the skin closest to it.

Description

Inside the eyelid is a septum. The septum divides the eyelid into outer and inner areas. This orbital septum helps prevent the spread of infection to the eye socket. Periorbital and orbital cellulitis are more common in children than in adults. Periorbital cellulitis, which accounts for 85–90% of all ocular cellulitis, usually occurs in children under the age of five. Responsible for the remaining 10–15% of these infections, orbital cellulitis is most common in children over the age of five.

These conditions usually begin with swelling or inflammation of one eye. Infection spreads rapidly and can cause serious problems that affect the eye or the whole body.

Causes and symptoms

Orbital and periorbital cellulitis are usually caused by infection of the sinuses near the nose. Insect **bites** or injuries that break the skin cause about one-third of these cellulitis infections. Orbital and periorbital cellulitis may also occur in people with a history of dental infections.

The blood of about 33 of every 100 patients with orbital or periorbital cellulitis contains bacteria known to cause:

- acute ear infections
- inflammation of the epiglottis (the cartilage flap that covers the opening of the windpipe during swallowing)
- meningitis (inflammation of the membranes that enclose and protect the brain)

- pneumonia
- sinus infection

People with periorbital cellulitis will have swollen, painful lids and redness, but probably no **fever**. About one child in five has a runny nose, and 20% have **conjunctivitis**. Conjunctivitis, also called pinkeye, is an inflammation of the mucous membrane that lines the eyelid and covers the front white part of the eye. It can be caused by allergy, irritation, or bacterial or viral infection.

As well as a swollen lid, other symptoms of orbital cellulitis include:

- bulging or displacement of the eyeball (proptosis)
- chemosis (swelling of the mucous membrane of the eyeball and eyelid as a result of infection, injury, or systemic disorders like anemia or kidney disease)
- diminished ability to see clearly
- eye pain
- fever
- paralysis of nerves that control eye movements (ophthalmoplegia)

Diagnosis

An eye doctor may use special instruments to open a swollen lid in order to:

- examine the position of the eyeball
- evaluate eye movement
- test the patient's vision.

If the source of infection is not apparent, the position of the eyeball may suggest its location. **Computed tomography scans** (CT scans) can indicate which sinuses and bones are involved or whether abscesses have developed.

Treatment

A child who has orbital or periorbital cellulitis should be hospitalized without delay. **Antibiotics** are used to stop the spread of infection and prevent damage to the optic nerve, which transmits visual images to the brain.

Symptoms of optic-nerve damage or infection that has spread to sinus cavities close to the brain include:

- very limited ability to move the eye
- impaired response of the pupil to light and other stimulus
- loss of visual acuity
- papilledema (swelling of the optic disk—where the optic nerve enters the eye)

One or both eyes may be affected, and eye sockets or sinus cavities may have to be drained. These surgical procedures should be performed by an ophthalmologist or otolaryngologist.

Prognosis

If diagnosed promptly and treated with antibiotics, most orbital and periorbital cellulitis can be cured. These conditions are serious and need prompt treatment.

Infections that spread beyond the eye socket can cause:

- abscesses in the brain or in the protective membranes that enclose it
- bacterial meningitis
- blood clots
- vision loss

ORGANIZATIONS

American Academy of Ophthalmology (AAO), P. O. Box 7424, San Francisco, CA, 94120-7424, (415)561-8500, (415)561-8500, http://www.aao.org.

American Optometric Association, 243 North Lindbergh Blvd., St. Louis, MO, 63141, (314)991-4100, (314)991-4101, (800)365-2219, http://www.aoa.org/.

Maureen Haggerty

Orchiectomy *see* **Testicular surgery**

Orchiopexy *see* **Testicular surgery**

Orchitis

Definition

Orchitis is an inflammation of the testis, accompanied by swelling, **pain**, **fever**, and a sensation of heaviness in the affected area.

Description

Viral **mumps** is the most common cause of orchitis. Bacterial infections associated with the disorder are **tuberculosis**, **syphilis**, **gonorrhea**, and chlamydia. A mechanical injury to the groin area may also cause orchitis. Fifteen to twenty-five % of males past the age of **puberty** with mumps develop orchitis. Epididymo-orchitis (inflammation of both testes and part of the spermatic duct) is the most common bacterial type of orchitis. This form of the

condition occurs most often in sexually active males 15 years and older, and in men over 45 with enlarged prostates.

Causes and symptoms

The people most susceptible to orchitis are those with inadequate mumps inoculation and, in the case of sexually transmitted orchitis, those who practice unsafe sex or have a history of sexually transmitted disease. Inadequate protection of the groin area during contact sports or other potentially harmful physical activities may result in injury leading to orchitis. Symptoms of orchitis include swelling of one or both testicles, tenderness in the groin area, fever, **headache**, and **nausea**. Symptoms may also include bloody discharge from the penis, and pain during urination, intercourse, or ejaculation.

Diagnosis

In most cases, Orchitis can be diagnosed by an urologist, general practitioner, or emergency room physician. Diagnosis is usually based on the results of a **physical examination** and patient history. Other testing may include a **urinalysis** and **urine culture**, screening for chlamydia and gonorrhea, ultrasound imaging, or blood tests.

Treatment

Elevation and support of the scrotum, and the application of cold packs to the groin area give some relief from the pain of orchitis. Medication for pain such as codeine and meperidine may be given. Only the symptoms of viral mumps orchitis are treated. **Antibiotics** are used to alleviate orchitis that is bacterial in origin. Sexually transmitted orchitis (especially when resultant from chlamydia or gonorrhea) is often treated with the antibiotic Ceftriaxone in conjunction with azithromycin or doxycycline.

Alternative treatment

For relief from swelling, the drinking of dandelion tea is recommended in **traditional Chinese medicine** (TCM). Another traditional Chinese treatment for swelling is the application of a poultice of ground dandelion and aloe to the affected area. Homeopathic remedies to reduce swelling include apis mel, belladonna, and pulsatilla. Consult a homeopathic physician before taking or administering these remedies to ensure safe and correct dosage.

KEY TERMS

Atrophy—A wasting away or withering.

Epididymo-orchitis—Inflammation of both the testes and a part of the spermatic duct system.

Unilateral—Affecting only one side.

Prognosis

Orchitis is usually unilateral and lasts between one and two weeks. Atrophy of the scrotum occurs in 60% of orchitis cases. However, hormonal function is not affected and resulting sterility is rare from mumps.

Prevention

Keeping mumps inoculations current and diligently practicing safe sex are the best ways to prevent orchitis from occurring. For males involved in contact sports or other potentially harmful physical activities, the wearing of a protective cup over the genitals will help guard against mechanical injuries that could lead to orchitis.

Resources

OTHER

Mycyck, Mark, MD. "Orchitis from Emergency Medicine/Genitourinary." *Emedicine, Instant Access to the Minds of Medicine*. February 2001. http://www.emedicine.com/emerg/topic344.htm.

Mary Jane Tenerelli, MS

Organ donation

Definition

Organ donation is the giving of a healthy body part from either a living or dead individual to another person.

Purpose

The purpose of organ donation is to improve and prolong the life of an ill or impaired individual.

Demographics

In the United States there is a mismatch between the number of people needing donated organs and the number of donors. At the end of June 2010, according

to the United Network for Organ Sharing (UNOS), about 108,000 people were awaiting donor organs. Of those, about 85,000 needed a kidney donation and about 16,000 needed a liver donation. This compares to 1,892 deceased donors and 1,548 living donors who provided organs for donation in the first three months of 2010. Deceased donors often provided more than one organ for donation and accounted for 5,162 transplantations during that three month period.

There is a special need for donors from minority ethnic groups. For example, about 12% of African Americans become organ donors but about 23% of individuals on the waiting list for a donated kidney are African American because of higher rates of **kidney disease** in the African American community. Although it is possible to make a match between people of different ethnic or racial groups, the likelihood of an appropriate genetic match (to prevent organ rejection) is much higher within ethnic groups.

Internationally, the rate of organ donation varies with religious and cultural norms and the level of sophistication of medical care. Many countries, such as the United States, are opt-in donation countries. This means that an individual must positively state his or her desire to donate body parts after **death**. A few countries have an opt-out donor system where individuals must state before death that they *do not* want to donate organs when they die. In all cases, individuals can specify which organs they wish to donate.

Description

Organ donation involves the matching of a person willing to give a healthy body part to an ill person who needs that part. There are two types of organ donation: living donation and donation after death (cadaver donation). In the United States and in many other countries, the costs of the donation to both donor and recipient are paid by health insurance. In the United States, it is illegal to buy an organ or receive money for a donated organ. Both citizens and non-citizens can donate and receive body parts.

All organ donations in the United States are regulated by UNOS. A person approved for an organ donation is registered with UNOS and placed on their waiting list. UNOS has organ transplant specialists who run a national computer network that connects all the transplant centers and organ-donation organizations. Patients are grouped in terms of priority based on how long they can live without a transplant. The list is national and independent of the medical transplant center where the surgery will take place.

When a donor organ becomes available, information about the donor organ is entered into the UNOS computer and compared to information about patients on the waiting list. The computer program produces a list of patients ranked according to blood type and how urgently they need the organ. Because some organs (e.g., the heart) must be transplanted as quickly as possible, a list of local patients may be checked first for a good match. After that, a regional list and then a national list are checked. The patient's transplant team and transplant specialists at UNOS make the final decision as to whether a donor is suitable for a specific recipient.

Living donation

Donation of a body part by a living person is the less common type of organ donation. Usually, but not always, the person who donates is biologically related to the recipient (e.g., parent, sibling, cousin). Related individuals are more likely to have the same blood type and similar immune system markers. This helps prevent organ rejection by the recipient's body. Sometimes a relative is willing to donate an organ, but is not an adequate match for the recipient. In this case, UNOS may be able to arrange a paired organ exchange with another donor-recipient pair. Living donor transplants are slightly more successful (rejected less frequently) than after-death donations.

To be a living donor, the individual cannot have certain diseases such as **cancer**, HIV infection, hepatitis, or major organ disease. Minors must have parental permission to donate, and all donors undergo extensive medical testing before the donation occurs. The type of body parts that can be donated by a living person include.

- kidney (most common)
- liver (second most common)
- lung
- intestine
- pancreas
- bone marrow

Donation after death

Individuals who want to donate body parts after death should indicate this desire on their driver's license and in a living will or medical directive, as well as making their wishes known to relatives. Donation after death does not disfigure the body and a regular funeral can be held. There is no age limit to donation after death; the suitability of body parts is determined at the time of death. Individuals can specify in advance which organs they want or do not want to donate. Agreeing to donate after death does not

KEY TERMS

Cornea—The clear tissue covering the eye.

Pancreas—A gland near the liver and stomach that secretes digestive fluid into the intestine and the hormones insulin and glucagon into the bloodstream.

compromise the quality of medical care the individual receives before death.

Organs and tissues that can be transplanted after death include:

- kidneys
- liver
- lungs
- heart
- pancreas
- intestines
- cornea
- skin
- bone
- cartilage
- tendons
- ligaments
- veins
- heart valves
- middle ear

Benefits

The benefit to the recipient is an extended and improved life. Many living donors and the families of deceased donors find satisfaction in knowing that their donation has given the gift of life to another person.

Precautions

Living donors undergo extensive medical testing in order to assure that they are healthy enough to make a donation and that the donated material is compatible with the recipient, as organ and tissue rejection is the most common cause for transplant failure.

Preparation

Living donors receive counseling and must sign a statement of informed consent. Minors must have parental consent to be living donors. Living donors receive a standard pre-operative work up as well as extensive cross matching with the recipient to assure tissue compatibility.

Individuals who wish to donate after death should make this known in advance in writing as well as informing their families and their doctors.

Aftercare

The length of the hospital stay and specific aftercare for living donors depends on the organ donated.

Risks

For living donors, the risks are the same as with any operation, mainly infection at the surgical site, uncontrolled bleeding, and adverse reaction to anesthesia. People can live healthy, active lives after donating a kidney, lung, or part of a liver or pancreas. There is always the risk, however, that damage by disease or injury to the remaining organ may result in medical problems.

Research and general acceptance

Ethical organ donation is accepted by the medical community as a positive, life-saving procedure. Most religions support organ donation, but when in doubt, individuals should consult their religious leaders.

Resources

BOOKS

Farber, Steve, and Harlan Abrahms. *On the List: Fixing America's Failing Organ Transplant System*. Emmaus, PA: Rodale Press, 2009.

OTHER

"Donation Basics." OrganDonor.gov. http://www.organdonor.gov/donation/index.htm (accessed August 21, 2010).

"Organ Donation." MedlinePlus. December 21, 2009. http://www.nlm.nih.gov/medlineplus/organdonation.html (accessed August 21, 2010).

"Organ Donation and Transplantation: Frequently Asked Questions." U.S. Department of Health and Human Services, WomensHealth.gov. February 17, 2010. http://www.womenshealth.gov/faq/organ-donation.cfm (accessed August 21, 2010).

ORGANIZATIONS

Donate Life America, 700 N. Fourth Street, Richmond, VA, 23219, (804) 782-4920, (804) 782-4643, http://www.donatelife.net.

National Living Donor Assistance Center, 2461 S. Clark Street, Suite 640, Arlington, VA, 22202, (703) 414-1600, (703) 414-7874, NLDCA@livingdonorassistance.org, http://www.livingdonorassistance.org.

United Network for Organ sharing, P.O. Box 2484, Richmond, VA, 23218, (804) 782-4800, (888)894-6361, (804) 782-4800, http://www.unos.org.

Tish Davidson, AM

Organic food

Definition

Organic foods are not specific foods, but are any foods that are grown and handled after harvesting in a particular way. In the United States, organic foods are crops that are raised without using synthetic pesticides, synthetic fertilizers, or sewage sludge fertilizer, and they have not been altered by genetic engineering. Organic animal products come from animals that have been fed 100% organic feed and raised without the use of growth hormones or **antibiotics** in an environment where they have access to the outdoors. Standards for organic foods vary from country to country. The requirements in Canada and Western Europe are similar to those in the United States. Many developing countries have no standards for certifying food as "organic."

Purpose

The organic food movement has the following goals:

- improve human health by decreasing the level of chemical toxins in food
- decrease the level of agricultural chemicals in the environment, especially in groundwater
- promote sustainable agriculture
- promote biodiversity
- promote genetic diversity among plants and animals by rejecting genetically modified organisms (GMOs)
- provide fresh, healthy, safe food at competitive prices

Description

Organic farming is the oldest method of farming. Before the 1940s, what is today called organic farming was the standard method of raising crops and animals. World War II accelerated research into new chemicals that could be used either in fighting the war or as replacements for resources that were in short supply because of their usefulness to the military. After the war ended, many of the new technological discoveries were applied to civilian uses and synthetic fertilizers, new insecticides, and herbicides became available. Fertilizers increased the yield per acre, and pesticides encouraged the development of single-crop mega-farms, resulting in the consolidation of agricultural land and the decline of the family farm.

Organic farming, although only a tiny part of American agriculture, originally offered a niche market for smaller, family-style farms. In the early 1980s this method of food production began to gain popularity, especially in California, Oregon, and Washington. The first commercial organic crops were vegetables that were usually sold locally at farmers' markets and health food stores.

By the late 1980s interest in organic food had reached a level of public awareness high enough that the United States Congress took action and passed the Organic Food Production Act of 1990. This act established the National Organic Standards Board (NOSB) under the United States Department of Agriculture (USDA). NOSB has developed regulations and enforcement procedures for the growing and handling of all agricultural products that are labeled "organic." These regulations went into effect on October 21, 2002.

Since the 1990s, the market for organic food has expanded from primarily fruits and vegetables to eggs, dairy products, meat, poultry, and commercially processed frozen and canned foods. In 2000, for the first time, more organic food was purchased in mainstream supermarkets than in specialty food outlets. By 2005, every state had some farmland that was certified organic, and some supermarket chains had begun selling their own brand-name organic foods. The demand for organic food was expected to continue to grow rapidly through at least 2010.

Organic certification is voluntary and applies to anyone who sells more than $5,000 worth of organic produce annually. (This exempts most small farmers who sell organic produce from their own farm stands). If a product carries the USDA Organic Seal indicating that it is "certified organic" it must meet the following conditions:

- The product must be raised or produced under an Organic Systems Plan that demonstrates and documents that the food meets the standards for growing, harvesting, transporting, processing, and selling an organic product.
- The producer and/or processor are subject to audits and evaluations by agents certified to enforce organic standards.
- The grower must have distinct boundaries between organic crops and non-organic crops to prevent accidental contamination with forbidden substances through wind drift or water runoff.
- No forbidden substances can have been applied to the land organic food is raised on for three years prior to organic certification.
- Seed should be organic, when available, and never genetically altered through bioengineering.
- Good soil, crop, and animal management practices must be followed to prevent contamination of groundwater, contamination of the product by living

pathogens, heavy metals, or forbidden chemicals, and to reduce soil erosion and environmental pollution.

To meet these requirements, organic farmers use natural fertilizers such as composted manure to add nutrients to the soil. They control pests by crop rotation and interplanting. Interplanting is growing several different species of plants in an alternating pattern in the same field to slow the spread of disease. Pest control is also achieved by using natural insect predators, traps, and physical barriers. If these methods do not control pests, organic farmers may apply certain non-synthetic pesticides made from substances that occur naturally in plants. Weed control is achieved by mulching, hand or mechanical weeding, the use of cover crops, and selective burning.

Animals products that are USDA certified organic must come from animals that are fed only organic feed, are not given growth hormones, antibiotics, or other drugs for the purpose of preventing disease, and have access to the outdoors. This last requirement is rather vague, as regulations set neither a minimum amount of time the animal must spend outdoors nor any minimums concerning the amount of outdoor space available per animal.

Selecting organic food

The USDA allows three label statements to help consumers determine if a food is organic.

- Labels stating "100% organic" indicate that all of the ingredients in the product are certified organic. These items have the USDA Organic Seal on the label.
- Labels stating "organic" indicate that at least 95% of the ingredients are certified organic. These items also carry the USDA Organic Seal on the label.
- Labels stating "made with organic ingredients" indicate that at least 70% of the ingredients are certified organic. These items are not permitted to have the USDA Organic Seal on the label.
- Items that contain fewer than 70% organic ingredients are not permitted to use either the word "organic" or the USDA Organic Seal on the label.

Consumers may be bewildered by other words on food labels such as "natural" or "grass-fed" that may be confused with organic. Natural and organic are not interchangeable. "Natural" foods are minimally processed foods but, they are not necessarily grown or raised under the strict conditions of organic foods. "Grass-fed" indicates that the livestock were fed natural forage ("grass"), but not necessarily in open pasture or for their entire lives.

Debate continues about the exact requirements to label animal products "cage-free," "free-range," or "open pasture." Cage-free simply means the animals were not kept caged, but does not necessarily mean that they were raised outdoors or allowed to roam freely. There is no certification process for the designation "cage-free." Animals can spend as little as five minutes per day outdoors and still be considered "free-range." Animal rights organizations are working to clarify these designations and improve the conditions under which all animals, are raised.

Organic food and health

Certified organic food requires more labor to produce, which generally makes it more expensive than non-certified food. Some consumers buy organic food primarily because the way it is raised benefits the environment. Others believe absolutely in the health benefits of organic food. A larger group of consumers are uncertain if organic food offers enough health benefits to justify the additional cost.

Discussions of the health benefits of organic food can become quite heated and emotional. Advocates of buying organic foods firmly believe that they are preserving their health by preventing their bodies from becoming receptacles for poisonous chemicals that can cause **cancer**, **asthma**, and other chronic diseases. Non-organic food buyers take the position that the level pesticide and fertilizer residue in non-organic food is small and harmless. Neither side is likely to change the other's view. However, below are some conclusions from studies done comparing organic and non-organic foods.

- The food supply in the United States, whether organic or non-organic, is extremely safe.
- Fresh organic and non-organic produce are equally likely to become contaminated with pathogens such as *E. coli* that cause health concerns.
- Many, but not all, chemical contaminants can be removed from non-organic food by peeling or thorough washing in cool running water.
- Organic foods are not 100% pesticide- and chemical-free. However, their chemical load appears to be lower than that of non-organic foods.
- The nutrient value of identical organic and non-organic foods is the same.
- The long-term effect on humans of trace amounts of hormones, antibiotics, and drugs found in milk, meat, and other non-organic animal products is unclear.
- The long-term effect of genetically modified foods on both humans and the environment cannot yet be known.

Precautions

Individuals should be informed about food labeling requirements and read food labels carefully so that they can make informed decisions about their purchases.

Interactions

Organic food does not interact with drugs or other foods in a way that is different from non-organic foods.

Complications

No complications are expected from eating organic food.

Parental concerns

Chemicals found in foods may have a greater effect on the growth and development of younger children than older ones. Young children are rapidly growing while still developing their nervous system, immune system, and other organs. Chemicals may have a greater effect on these developing tissues than on adult tissues.

Resources

BOOKS

Fromartz, Samuel. *Organic, Inc.: Natural Foods and How They Grew*. Orlando, FL: Harcourt, 2006.

Goodman, Myra, with Linday Holland, and Pamela McKinstry, Pamela. *Food to Live By: The Earthbound Farm Organic Cookbook*. New York: Workman Pub., 2006.

Lipson, Elaine. *The Organic Foods Sourcebook*. Chicago, IL: Contemporary Books, 2001.

Meyerowitz, Steve. *The Organic Food Guide: How to Shop Smarter and Eat Healthier*. Guilford, CT: Globe Pequot Press, 2004.

OTHER

Barrett, Stephen. "'Organic' Foods: Certification Does Not Protect Consumers." Quackwatch, July 17, 2006. http://www.quackwatch.org/01Quackery Related Topics/organic.html

Mayo Clinic Staff. "Organic Foods: Are They Safer? More Nutritious?" MayoClinic.com, December 26, 2006. http://www.mayoclinic.com/health/organic-food/NU00255

National Organic Program. "Organic Food Standards & Labels: The Facts." United States Department of Agriculture, Agricultural Marketing Service, January 2007. http://www.ams.usda.gov/nop/Consumers/brochure.html

Nemours Foundation. "Organic and Other Environmentally Friendly Foods." March 2007. http://kidshealth.org/teen/food_fitness/nutrition/organics.html

"Organic Foods in Relation to Nutrition and Health Key Facts." Medical News Today. July 11, 2004. http://www.medicalnewstoday.com/medicalnews.php?newsid=10587

Organic Trade Association. "Questions and Answers About Organic." 2003. http://www.ota.com/organic/faq.html

Pames, Robin B. "How Organic Food Works." How Stuff Works, undated, accessed April 26, 2007. http://home.howstuffworks.com/organic-food.htm;

ORGANIZATIONS

National Organic Program, USDA-AMS-TM-NOP, Room 4008-S. Bldg, Ag Stop 0268, 1400 Independence Avenue, S.W., Room 1180, Washington, DC, 20250, (202)720-3252, http://www.ams.usda.gov/nop.

Organic Trade Association, P.O. Box 547, Greenfield, MA, 01302, (413)774-7511, (413) 774-6432, http://www.ota.com.

Helen M. Davidson

Organophosphates *see* **Insecticide poisoning**

Oriental sore *see* **Leishmaniasis**

Ornithosis *see* **Parrot fever**

Oroya fever *see* **Bartonellosis**

Orthodontics

Definition

Orthodontics is a specialized branch of dentistry that diagnoses, prevents, and treats dental and facial irregularities called malocclusions. Orthodontics includes dentofacial orthopedics, which is used to correct problems involving the growth of the jaw.

Purpose

Humans have attempted to straighten teeth for thousands of years before orthodontics became a dental specialty in 1900. Although orthodontic treatment often improves facial appearance and occasionally is performed for solely cosmetic reasons, it is used primarily to correct health problems and to ensure the proper functioning of the mouth. Properly aligned teeth, which close together correctly, simplify **oral hygiene** and enable children to chew their food efficiently. Orthodontic treatment provides the following:

- straightens teeth that are rotated, tilted, or otherwise improperly aligned
- corrects crowded or unevenly spaced teeth
- corrects bite problems
- aligns the upper and lower jaws

An orthodontist attaches braces to the teeth of a teenage patient. *(Antonia Reeve/Photo Researchers, Inc.)*

Malocclusions

Few children have perfectly symmetrical teeth and a perfect bite. In an ideal bite, the following are characteristics:

- All of the teeth fit easily without crowding or spacing.
- The teeth are not rotated, twisted, or leaning forward or backward.
- The teeth of the upper jaw slightly overlap those of the lower jaw.
- The points of the molars fit into the grooves of the opposite molars.

Types of malocclusions include the following:

- crowded, crooked, or misaligned teeth
- extra or missing teeth
- bite problems
- jaws that are out of alignment

Causes of malocclusion

Most malocclusions are caused by hereditary factors that affect the contours of the face and the size of the teeth and jaw. The most common cause of **malocclusion** is a disproportion in size between the jaw and teeth or between the upper and lower jaws. A child who inherits a mother's small jaw and a father's large teeth may have teeth that are too big for the jaw, causing overcrowding. Specific inherited malocclusions include:

- overcrowded teeth
- too much space between teeth
- extra or missing teeth
- various irregularities in the teeth, jaw, or face

Malocclusions can be acquired through the following:

- accidents such as a jaw fracture that causes misalignment
- prolonged sucking on thumbs, fingers, or pacifiers, particularly after the age of four
- fingernail or lip biting
- a lost tooth that causes nearby teeth to move into the empty space, throwing them out of alignment
- airways that are obstructed by tonsils or adenoids
- dental disease
- tumors in the mouth or jaw
- improperly fitted fillings, crowns, or braces
- premature loss of baby teeth or permanent teeth
- late loss of baby teeth

Symptoms of malocclusion

Occasionally children have mild, temporary symptoms of malocclusion resulting from a growth spurt. However, symptoms of malocclusion usually develop gradually beginning at the age of six. Symptoms may include the following:

- crowded or misaligned teeth
- abnormal spacing between teeth, most often occurring because teeth are small or missing or the dental arch (the arch-shaped jawbone that supports the teeth) is very wide
- incisors (front teeth) that do not meet
- an open bite, occurring when the upper and lower incisors do not touch each other during biting, thereby putting all of the chewing pressure on the back teeth and resulting in inefficient chewing and excessive tooth wear
- an overbite or overjet, in which the upper incisors protrude, often caused by a lower jaw that is significantly shorter than the upper jaw

- a deep or closed bite, an excessive overbite in which the lower incisors bite too closely to or into the gum tissue or palate behind the upper teeth
- a crossbite, in which a protruding lower jaw that is longer than the upper jaw causes the upper front or back teeth to bite inside the lower teeth

Early intervention

Although orthodontic treatment can be performed at any age, children are easier, faster, and less expensive to treat than adults. Most often orthodontic treatment is used on older children and adolescents whose teeth are still developing. However some types of problems are corrected more readily before all of the permanent teeth have erupted and facial growth is complete. If a child's permanent lower incisors erupt behind each other, braces may be required at a young age. Crossbites are usually treated early because they can interfere with biting and chewing. Early treatment also is used when thumb- or finger-sucking has affected teeth positioning.

Early orthodontic intervention can provide the following:

- straighten crooked teeth
- preserve or create space for incoming permanent teeth
- guide erupting permanent teeth into the correct positions
- prevent impacted permanent teeth, those that remain partially covered by gum tissue, or partially or completely buried in the jawbone
- correct harmful habits such as thumb- or finger-sucking
- lower the risk of accidents to protruding upper incisors

Other advantages of early orthodontic treatment include the following:

- correction of bite problems by guiding jaw growth and controlling the width of the upper and lower dental arches
- reduction or elimination of abnormal swallowing or speech problems
- shortening and simplification of later orthodontic treatment
- prevention of later tooth extractions
- improvements in appearance and self-esteem

Untreated malocclusions

Minor misalignment or crowding may not require treatment. However untreated malocclusions can cause the following:

- teeth that are partially impacted or fail to erupt
- lips, tongue, or cheeks that contact biting surfaces due to poor tooth alignment
- inefficient or uncomfortable biting, chewing, and digestion
- speech impairments
- teeth that are hard to clean, leading to cavities and gum disease
- abnormal wear of tooth surfaces
- chipped teeth
- loosening or fracturing of a misaligned tooth that is overstrained
- injury to a protruding upper incisor
- thinning and receding of bone and gums covering the roots of very crowded teeth
- accelerated gum disease and bone loss
- temporomandibular joint (TMJ) misalignments at the point where the lower jaw attaches to the skull
- stress and trauma to the teeth, gum tissue, ligaments, muscles, jawbone, and jaw joints
- premature loss of teeth
- adverse effects on facial development and appearance
- the need for surgery

Untreated malocclusions often worsen with time. TMJ problems can cause chronic headaches or **pain** in the face and neck. A deep overbite can cause significant pain and bone damage and may contribute to excessive wear on the incisors.

Orthodontics in young children

Alignment problems usually become apparent as the permanent teeth begin erupting at about age six. Dentists monitor the development of a child's permanent teeth and refer the child to an orthodontist if a problem is suspected. The American Association of Orthodontists recommends that all children be screened by an orthodontist by the age of seven.

Once a child's lower baby incisors have erupted, an orthodontist can measure the child's jaw and tooth size, project their growth rate, and possibly predict whether the child will have orthodontic problems with their permanent teeth. The orthodontist may be able to perform preventative or interceptive orthodontics that can reduce or eliminate the need for braces later.

In a procedure called selective serial extraction, the orthodontist removes one or more baby or permanent teeth. Doing so creates space for the permanent teeth, especially unerupted canine teeth that might become impacted or erupt in the wrong position. After the removal or loss of a tooth, braces or another

orthodontic appliance may be used to prevent the remaining teeth from moving into the empty space. If a baby molar that acts as a space-holder for later permanent teeth is lost, a fixed orthodontic wire is inserted between the teeth to keep the space available.

Preparation

The orthodontist compiles pretreatment records that are used for diagnosis, determining the course of treatment, and measuring the progress of treatment. These records may include:

- a complete medical and dental history
- a clinical examination
- x-rays revealing the positions of erupted and unerupted teeth, development of unerupted teeth, any missing or impacted teeth, shortened or damaged tooth roots, and the amount of bone supporting the teeth
- a facial-profile x-ray or cephalometric film revealing the sizes, positions, and relationships of the teeth and jaw, as well as facial form, growth pattern, and the inclinations of tipped or tilted incisors
- plastic impressions of the bite and plaster models made from the impressions
- photographs and other measurements of the teeth and face

Based on the diagnosis the orthodontist develops a custom treatment plan and designs the appropriate corrective appliances that will gradually straighten or move the teeth. Severe overcrowding may necessitate the extraction of permanent teeth, usually the premolars, to create space prior to using braces to move teeth.

Braces and other orthodontic appliances

By applying constant gentle pressure in a specific direction, braces can slowly move teeth through the supporting bone to a new position. Springs and wires put pressure on teeth in order to straighten them. The pressure causes bone in the jaw to dissolve in front of the moving tooth as new bone grows behind the tooth. Braces and other appliances may be removable or fixed and are made of clear or colored metal, ceramic, or plastic. Removable appliances are often plastic plates that fit into the roof of the mouth and clip onto a tooth.

Fixed braces exert more pressure than removable braces and can achieve more complex movements. They consist of wires and springs that are held in place by small brackets glued to the outside surfaces of the incisors and sometimes the premolars. Lingual braces have brackets bonded to the back of the teeth. Bands encircling the molars also can be used for attachments. The wires, springs, and other devices attached to the brackets or bands put pressure on the teeth, gradually shifting them into new positions. The nickel-titanium wires are very light, and some are heat-activated. These are very flexible at room temperature and actively begin to move the teeth as they warm to body temperature. Elastic bands sometimes connect the upper and lower teeth to create tension.

Appliances used to direct jaw growth and development in growing children and adolescents include:

- Headgear attached to braces and usually worn for 10 to 12 hours at night puts pressure on the upper teeth and jaw and influences the direction and speed of upper jaw growth and upper teeth eruption.
- Herbst appliances attached to the upper and lower molars correct a severe overbite by holding the lower jaw forward, influencing jaw growth and tooth position; they force the jaw muscles to work in ways that promote forward development of the lower jaw; treatment with Herbst appliances must begin several years before the jaw stops growing and they must remain in place throughout the treatment.
- Palatal or upper jaw expansion devices can widen a narrow upper jaw and correct a crossbite within months.
- Removable bionators hold the lower jaw forward and guide tooth eruption while helping the upper and lower jaws to grow proportionately.

Headgear and Herbst appliances can significantly reduce protrusion of the four top incisors and enable the growing lower jaw to catch up with the upper jaw, eliminating swallowing problems.

Duration of treatment

Orthodontic treatment usually continues until the desired outcome is reached. Active orthodontic treatment lasts an average of two years, with a range of one to three years. Some children respond to treatment faster than others and interceptive or early treatments may continue for only a few months. Appliances are adjusted periodically during treatment. Factors affecting the duration of treatment include:

- the growth of the mouth and face
- the severity of the problem
- the health of the teeth, gums, and supporting bones
- the child's level of cooperation

Precautions

Orthodontic appliances trap food, bacteria, and plaque, leading to **tooth decay**. Extra brushing with specially shaped and/or electric toothbrush and

KEY TERMS

Active treatment stage—The period during which orthodontic appliances or braces are used.

Bicuspid—Premolar; the two-cupped tooth between the first molar and the cuspid.

Canines—The two sharp teeth located next to the front incisor teeth in mammals that are used to grip and tear. Also called cuspids.

Crossbite—The condition in which the upper teeth bite inside the lower teeth.

Crown—The natural part of the tooth covered by enamel. A restorative crown is a protective shell that fits over a tooth.

Deep bite—A closed bite; a deep or excessive overbite in which the lower incisors bite too closely to or into the gum tissue or palate behind the upper teeth.

Eruption—The process of a tooth breaking through the gum tissue to grow into place in the mouth.

Impacted tooth—Any tooth that is prevented from reaching its normal position in the mouth by another tooth, bone, or soft tissue.

Incisors—The eight front teeth.

Interceptive orthodontics—Preventative orthodontics; early, simpler orthodontic treatment.

Malocclusion—The misalignment of opposing teeth in the upper and lower jaws.

Molars—The teeth behind the primary canines or the permanent premolars, with large crowns and broad chewing surfaces for grinding food.

Open bite—A malocclusion in which some teeth do not meet the opposing teeth.

Orthognathic surgery—Surgery to alter the relationships of the teeth and/or supporting bones, usually in conjunction with orthodontic treatment.

Overbite—Protrusion of the upper teeth over the lower teeth.

Plaque—A sticky film of saliva, food particles, and bacteria that attaches to the tooth surface and causes decay.

Retainer—An orthodontic appliance that is worn to stabilize teeth in a new position.

Retention treatment stage—The passive treatment period following orthodontic treatment, when retainers may be used to stabilize the teeth.

Temporomandibular joint (TMJ)—One of a pair of joints that attaches the mandible of the jaw to the temporal bone of the skull. It is a combination of a hinge and a gliding joint.

fluoride toothpaste is required around the areas where the braces or appliances attach to the teeth. Both the tops and bottoms of braces must be brushed and irrigated with a water jet directed from the top down and the bottom up. If possible, teeth should be flossed. A fluoride mouthwash may be recommended. Removable appliances should be brushed every time the teeth are brushed. Regular dental check-ups and cleanings must be continued.

Children with braces should eat raw fruits and vegetables and avoid soft, processed, and refined foods that attract bacteria, as well as hard or sticky foods, including gum, caramels, peanuts, ice chips, and popcorn. Chewing on hard items, such as fingernails or pencils, can damage braces. Children with braces should wear a protective mouth guard while playing contact sports.

Aftercare

After braces are removed the teeth must be stabilized in their new positions. This phase of treatment commonly takes two to three years. Occasionally it continues indefinitely. Types of retainers used for stabilization include:

- positioners, rubber-like mouthpieces that are worn at night and bitten into for a few hours during the day
- removable retainers with a plastic plate that snaps onto the roof of the mouth and wires on the outside of the teeth
- removable, clear, plastic retainers that completely cover the sides and biting surfaces of the teeth
- semi-rigid wires that are bonded onto the inside of the incisors.

Risks

Braces may cause discomfort when they are first installed or adjusted during treatment. For the first three to five days teeth may hurt during biting. Lips, cheeks, and tongue may be irritated for one to two weeks before they toughen and adapt to the braces. Some appliances may interfere with speech for the first day or two. Damaged appliances can extend the length of treatment and negatively affect the outcome.

Food particles and plaque deposits around orthodontic appliances can cause demineralization of the tooth enamel, leading to cavities and permanent whitish **scars** on the teeth.

Normal results

Orthodontic treatment is usually very successful at correcting malocclusions. Even a significant size discrepancy between the upper and lower jaws often can be corrected. Sometimes, particularly in adults, corrective orthognathic surgery is required to shorten or lengthen a jawbone. The height of the lower face also can be shortened or lengthened. Sometimes surgery reduces the duration of the orthodontic treatment.

Maturational change can cause teeth to gradually shift with age—at least until one's early 20s—causing crowding. Nighttime retainers can prevent maturational movement.

Parental concerns

In general the earlier an orthodontic problem is detected, the easier and less expensive it is to correct. Parents can compare their child's dental development with standard charts and pictures.

Children with problems involving the width or length of the jaws should be evaluated no later than age 10 for girls and age 12 for boys. For children receiving orthodontic care, the orthodontist should be notified immediately if an appliance breaks. Indications that children may need an early orthodontic examination include:

- early or late loss of baby teeth
- crowded, misplaced, or blocked-out teeth
- upper and lower teeth that do not meet normally
- thumb- or finger-sucking
- biting of the cheek or roof of the mouth
- difficulty biting or chewing
- breathing through the mouth
- jaws that shift or make noise
- jaws and teeth that are out of proportion to the rest of the face

Resources

BOOKS

Ireland, Anthony J., and Fraser McDonald. *The Orthodontic Patient: Treatment and Biomechanics*. New York: Oxford University Press, 2003.

Sutton, Amy L., ed. *Dental Care and Oral Health Sourcebook: Basic Consumer Health Info*, 3rd ed. Detroit, MI: Omnigraphics, 2008.

Van der Linden, Frans P. G. M. *Orthodontic Concepts and Strategies*. Chicago: Quintessence, 2004.

OTHER

Braces and Orthodontics. American Dental Association. http://www.ada.org/public/topics/braces_faq.asp (accessed February 3, 2010).

Oral Hygiene for the Orthodontic Patient. Columbia University Medical Center, School of Dental & Oral Surgery). http://www.simplestepsdental.com/SS/ihtSS/r.WSIHW000/st.32578/t.32586/pr.3.html (accessed February 3, 2010).

ORGANIZATIONS

American Academy of Pediatric Dentistry, 211 East Chicago Avenue, Suite 1700, Chicago, IL, 60611-2637, (312) 337-2169, (312) 337-6329, www.aapd.org.

American Association of Orthodontists, 401 N. Lindbergh Boulevard, St. Louis, MO, 63141-7816, www.braces.org.

American Dental Association, 211 East Chicago Avenue, Chicago, IL, 60611-2678, (312) 440-2500, http://www.ada.org.

Margaret Alic, PhD
Brenda W. Lerner

Orthopedic surgery

Definition

Orthopedic (sometimes spelled orthopaedic) surgery is an operation performed by a medical specialist such as an orthopedist or orthopedic surgeon, who is trained to assess and treat problems that develop in the bones, joints, and ligaments of the human body.

Purpose

Orthopedic surgery addresses and attempts to correct problems that arise in the skeleton and its attachments, the ligaments and tendons. It may also include some problems of the nervous system, such as those that arise from injury of the spine. These problems can occur at birth, through injury, or as the result of **aging**. They may be acute, as in an accident or injury, or chronic, as in many problems related to aging.

Orthopedics comes from two Greek words, *ortho*, meaning straight, and *pais*, meaning child. Originally, orthopedic surgeons treated skeletal deformities in children, using braces to straighten the child's bones. With the development of anesthesia and an understanding of the importance of aseptic technique in surgery, orthopedic surgeons extended their role to

KEY TERMS

Arthroplasty—The surgical reconstruction or replacement of a joint.

Prosthesis—A synthetic replacement for a missing part of the body such as a knee or a hip.

Range of motion—The normal extent of movement (flexion and extension) of a joint.

include surgery involving the bones and related nerves and connective tissue.

The terms orthopedic surgeon and orthopedist are used interchangeably today to indicate a medical doctor with special training and certification in orthopedics.

Many orthopedic surgeons maintain a general practice, while some specialize in one particular aspect of orthopedics such as hand surgery, joint replacements, or disorders of the spine. Orthopedists treat both acute and chronic disorders. Some orthopedic surgeons specialize in trauma medicine and can be found in emergency rooms and trauma centers, treating injuries. Others find their work overlapping with plastic surgeons, geriatric specialists, pediatricians, or podiatrists (**foot care** specialists). A rapidly growing area of orthopedics is sports medicine, and many sports medicine doctors are board certified in orthopedic surgery.

Demographics

The American Academy of Orthopedic Surgeons reported that in January 2008, there were 31,309 members within all categories of orthopedic surgeons in the United States.

Description

The range of treatments provided by orthopedists is extensive. They include procedures such as **traction**, **amputation**, hand reconstruction, spinal fusion, and joint replacements. They also treat strains and sprains, broken bones, and **dislocations**. Some specific procedures performed by orthopedic surgeons are listed as separate entries in this book, including **arthroplasty**, **arthroscopic surgery**, **bone grafting**, **fasciotomy**, **fracture repair**, **kneecap removal**, and traction.

In general, orthopedists are employed by hospitals, medical centers, trauma centers, or free-standing surgical centers where they work closely with a surgical team, including an anesthesiologist and surgical nurse. Orthopedic surgery can be performed under general, regional, or **local anesthesia**.

Much of the work of an orthopedic surgeon involves adding foreign material to the body in the form of screws, wires, pins, tongs, and prosthetics to hold damaged bones in their proper alignment or to replace damaged bone or connective tissue. Great improvements have been made in the development of artificial limbs and joints, and in the materials available to repair damage to bones and connective tissue. As developments occur in the fields of metallurgy and plastics, changes will take place in orthopedic surgery that will allow surgeons to more nearly duplicate the natural functions of bones, joints, and ligaments, and to more accurately restore damaged parts to their original ranges of motion.

Diagnosis/Preparation

Persons are usually referred to an orthopedic surgeon by a primary care physician, emergency room physician, or other doctor. Prior to any surgery, candidates undergo extensive testing to determine appropriate corrective procedures. Tests may include x-rays, computed tomography (CT) scans, **magnetic resonance imaging** (MRI), myelograms, diagnostic arthroplasty, and blood tests. The orthopedist will determine the history of the disorder and any treatments that were previously tried. A period of rest to the injured part may be recommended before surgery is undertaken.

Surgical candidates undergo standard blood and urine tests before surgery and, for major procedures, may be given an electrocardiogram or other diagnostic tests prior to the operation. Individuals may choose to donate some of their own blood to be held in reserve for their use in major surgery such as knee replacement, during which heavy bleeding is common.

Aftercare

Rehabilitation from orthopedic injuries can require long periods of time. Rehabilitation is usually physically and mentally taxing. Orthopedic surgeons will work closely with physical therapists to ensure that patients receive treatment that will enhance the range of motion and return function to all affected body parts.

Risks

As with any surgery, there is always the risk of excessive bleeding, infection, and allergic reaction to anesthesia. Risks specifically associated with orthopedic surgery include inflammation at the site where foreign materials (pins, prostheses, or wires) are

introduced into the body, infection as the result of surgery, and damage to nerves or to the spinal cord.

Normal results

Thousands of people have successful orthopedic surgery each year to recover from injuries or to restore lost function. The degree of success in individual recoveries depends on an individual's age and general health, the medical problem being treated, and a person's willingness to comply with rehabilitative therapy after the surgery.

Abnormal results from orthopedic surgery include persistent **pain**, swelling, redness, drainage or bleeding in the surgical area, surgical wound infection resulting in slow healing, and incomplete restoration of pre-surgical function.

Morbidity and mortality rates

Mortality from orthopedic surgical procedures is not common. The most common causes for mortality are adverse reactions to anesthetic agents or drugs used to control pain, post-surgical clot formation in the veins, and post-surgical heart attacks or strokes.

Alternatives

For the removal of diseased, non-functional, or non-vital tissue, there is no alternative to orthopedic surgery. Alternatives to orthopedic surgery depend on the condition being treated. Medications, **acupuncture**, or hypnosis are used to relieve pain. Radiation is an occasional alternative for shrinking growths. **Chemotherapy** may be used to treat bone **cancer**. Some foreign bodies may remain in the body without harm.

Resources

BOOKS

Browner, Bruce D., et al. *Skeletal Trauma: Basic Science, Management, and Reconstruction*. 4th ed. Philadelphia: Saunders, 2008.

Canale, S. Terry, ed. *Campbell's Operative Orthopaedics*. 11th ed. St. Louis: Mosby, 2007.

DeLee, Jesse C., and David Drez. *DeLee and Drez's Orthopaedic Sports Medicine*. 3rd ed. Philadelphia: Saunders, 2009.

OTHER

"Joint Health and Care: Prevention, Symptoms, Diagnosis and Treatment." Medline Plus, spring 2009. http://www.nlm.nih.gov/medlineplus/magazine/issues/spring09/articles/spring09pg14.html

"Targeting Musculoskeletal Pain." Medline Plus, spring 2009. http://www.nlm.nih.gov/medlineplus/magazine/issues/spring09/articles/spring09pg12-13.html

ORGANIZATIONS

American Academy of Orthopedic Surgeons, 6300 North River Road, Rosemont, IL, 60018-4262, (847) 823-7186, (800) 346-2267, (847) 823-8125, http://www.aaos.org.

American College of Sports Medicine, P.O. Box 1440, Indianapolis, IN, 46206-1440, (317) 637-9200, (317) 634-7817, MSSR@Online, http://acsm.org.

American College of Surgeons, 633 North Saint Claire Street, Chicago, IL, 60611, (312) 202-5000, (800) 621-4111, 312-202-5001, postmaster@facs.org, http://www.facs.org.

American Society for Bone and Mineral Research, 2025 M Street NW, Suite 800, Washington, DC, 20036-3309, (202) 367-1161, (202) 367-2161, asbmr@asbmr.org, http://www.asbmr.org.

Orthopedic Trauma Association, 6300 N. River Road, Suite 727, Rosemont, IL, 60018-4226, (847) 698-1631, (847) 823-0536, OTA@aaos.org, http://www.ota.org.

L. Fleming Fallon, Jr., MD, DrPH
Brenda W. Lerner

Orthopedic x rays *see* **Bone x rays**

Orthostatic hypotension

Definition

Orthostatic **hypotension** is an abnormal decrease in blood pressure when a person stands up. This may lead to **fainting**.

Description

When a person stands upright, a certain amount of blood normally pools in the veins of the ankles and legs. This pooling means that there is slightly less blood for the heart to pump and causes a drop in blood pressure. Usually, the body responds to this drop so quickly, a person is unaware of the change. The brain tells the blood vessels to constrict so they have less capacity to carry blood, and at the same time tells the heart to beat faster and harder. These responses last for a very brief time. If the body's response to a change in vertical position is slow or absent, the result is orthostatic hypotension. It is not a true disease, but the inability to regulate blood pressure quickly.

Causes and symptoms

Orthostatic hypotension has many possible causes. The most common cause is medications used to treat other conditions. **Diuretics** reduce the amount of fluid in the body which reduces the volume of blood. Medicines

used to expand the blood vessels increase the vessel's ability to carry blood and so lower blood pressure.

If there is a severe loss of body fluid from **vomiting**, **diarrhea**, untreated diabetes, or even excessive sweating, blood volume will be reduced enough to lower blood pressure. Severe bleeding can also result in orthostatic hypotension.

Any disease or **spinal cord injury** that damages the nerves which control blood vessel diameter can cause orthostatic hypotension.

Symptoms of orthostatic hypotension include faintness, **dizziness**, confusion, or blurry vision, when standing up quickly. An excessive loss of blood pressure can cause a person to pass out.

Diagnosis

When a person experiences any of the symptoms above, a physician can confirm orthostatic hypotension if the person's blood pressure falls significantly on standing up and returns to normal when lying down. The physician will then look for the cause of the condition.

Treatment

When the cause of orthostatic hypotension is related to medication, it is often possible to treat it by reducing dosage or changing the prescription. If it is caused by low blood volume, an increase in fluid intake and retention will solve the problem.

Medications designed to keep blood pressure from falling can be used when they will not interfere with other medical problems.

When orthostatic hypotension cannot be treated, the symptoms can be significantly reduced by remembering to stand up slowly or by wearing elastic stockings.

Prognosis

The prognosis for people who have orthostatic hypotension depends on the underlying cause of the problem.

Prevention

There is no way to prevent orthostatic hypotension, since it is usually the result of another medical condition.

ORGANIZATIONS

National Heart Lung and Blood Institute Health Information Center, P.O. Box 30105, Bethesda, MD, 20824-0105, (301)592-8573, (240)629-3246, http://www.nhlbi.nih.gov.

National Organization for Rare Disorders, 55 Kenosia Avenue, P.O. Box 1968, Danbury, CT, 06813-1968, (203) 744-0100, http://www.rarediseases.org.

Dorothy Elinor Stonely

Orthotopic transplantation *see* **Liver transplantation**

Osgood-Schlatter disease *see* **Osteochondroses**

Osteitis deformans *see* **Paget's disease of bone**

Osteoarthritis

Definition

Osteoarthritis is a degenerative joint disease characterized by the breakdown of the joint's cartilage.

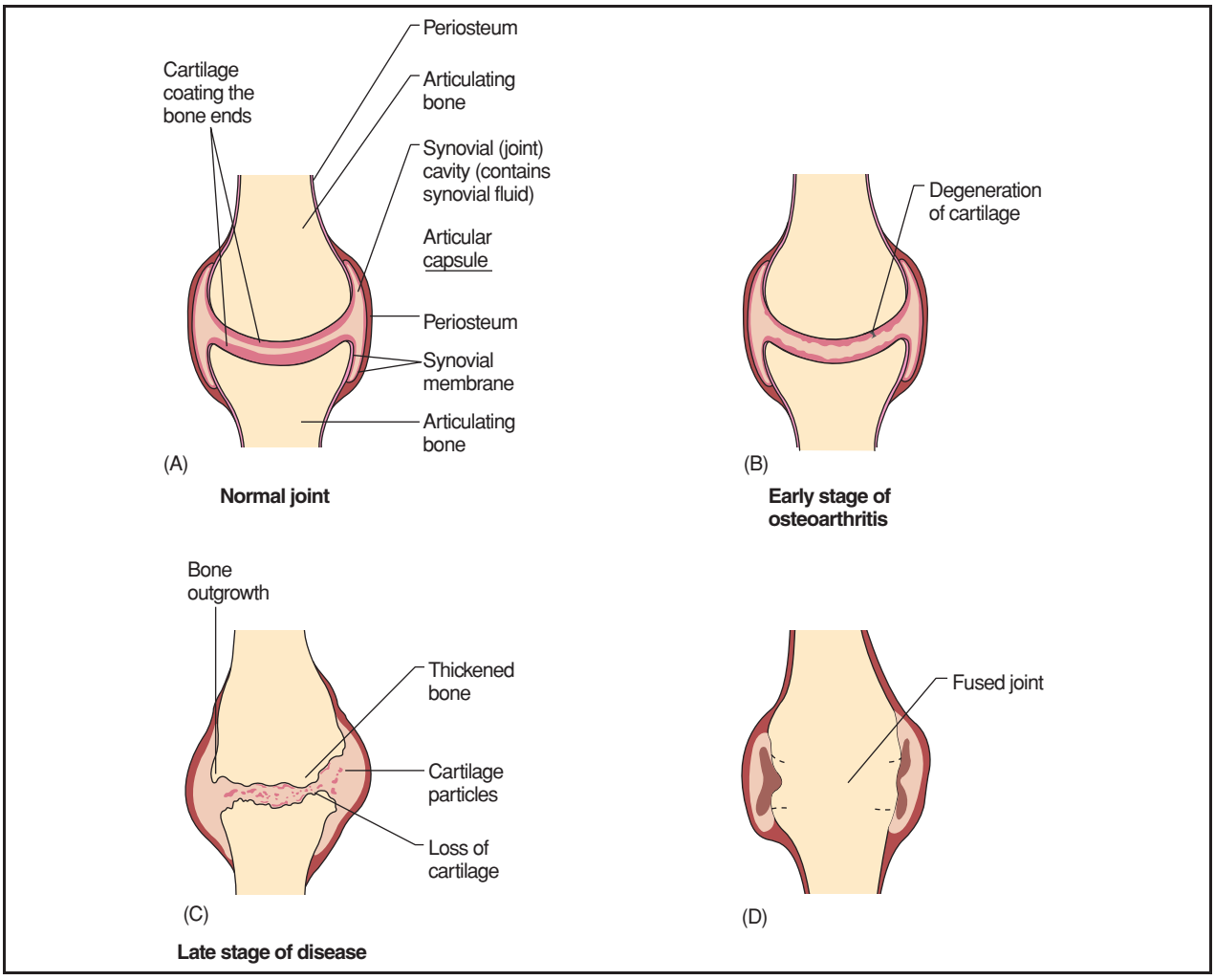
Demographics

According to the American College of Rheumatology, osteoarthritis affects people of all ages, but is more common in older populations, with 70% of people over the age of 70 showing x–ray evidence of the disease. Of this number, only half ever develop symptoms. Before age 45, more men than women have osteoarthritis; after age 45, it is more common in women, affecting especially their fingers and knees. The condition is also more likely to occur in people who are overweight and in people with jobs that stress particular joints. As of 2009, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) estimates that osteoarthritis is by far the most common type of arthritis, with some 12.1% of Americans (nearly 27 million) aged 25 and older affected. By 2030, 20% of Americans, or some 72 million people, will be older than 65 and will be at high risk for the disease.

Studies are indicative of some ethnic and geographical differences in prevalence. African American females are more prone than Caucasian females to osteoarthritis of the knee, but not for the hip. Osteoarthritis of the hip occurs more often in European Caucasians than in Jamaican blacks, African or South African blacks, Chinese, or Asian Indians.

Description

Osteoarthritis is one of the oldest and most common types of arthritis that mostly affects cartilage, the slippery part of the joint that cushions the ends of bones. Unlike some other types of arthritis,



The progression of osteoarthritis. *(Illustration by Hans & Cassady, Inc. Reproduced by permission of Gale, a part of Cengage Learning.)*

osteoarthritis affects only joints and not internal organs. With the breakdown of cartilage, bones rub against each other, causing **pain** and loss of movement. Over time, the affected joint may lose its normal shape. Also, bone spurs may grow on the edges of the joint. Bone or cartilage can break off and migrate inside the joint space, causing more pain and damage.

Osteoarthritis can occur in any joint, but commonly affects hands, knees, hips or spine.

Risk factors

Age increases the risk of osteoarthritis, which typically occurs in older adults. Women are also more likely to develop osteoarthritis. People born with malformed joints or defective cartilage are also at increased risk. **Obesity** is another factor, as more body weight places more stress on weight–bearing joints. Diseases such as **gout**, **rheumatoid arthritis**, **Paget's disease of bone** or septic arthritis can also increase the risk of developing osteoarthritis.

People with joint injuries from sports, work–related activity, or accidents may also be at increased risk. Individuals with mismatched surfaces on the joints that could be damaged over time by abnormal stress may be prone to osteoarthritis. One study reported that wearing shoes with 2.5 in (6.3 cm) heels or higher may also be a contributing factor. High heels force women to alter the way they normally maintain balance, putting strain on the areas between the kneecap and thigh bone and on the inside of the knee joint.

Causes and symptoms

The biological causes of the disorder are currently unknown. Although osteoarthritis is generally more prevalent in the older population, it does not appear to

be caused by **aging** itself, since osteoarthritic cartilage has been shown to be chemically different from normal aged cartilage.

Genetics plays a role in the development of osteoarthritis, particularly in the hands and hips. One study found that heredity may be involved in 30% of people with osteoarthritic hands and 65% of those with osteoarthritic knees. Another study found a higher correlation of osteoarthritis between parents and children and between siblings than between spouses. Other research has shown that a genetic abnormality may promote a breakdown in the protective structure of cartilage.

Abnormal collagen genes have been identified in some families with osteoarthritis. One recent study found that the type IX collagen gene COL9A1 (6q12–q13) may be a susceptibility locus for female hip osteoarthritis. Other research has suggested that mutations in the COL2A1 gene may be associated with osteoarthritis.

Some evidence also suggests that a female–specific susceptibility gene for idiopathic osteoarthritis is located on 11q. There is some evidence of genetic abnormality at the IL1R1 marker on gene 2q12 in individuals with severe osteoarthritis and Heberden nodes (bony lumps on the end joint of fingers).

Although many people over 70 show evidence of osteoarthritis on x–ray, only 50% experience symptoms. Symptoms range from very mild to very severe, affecting hands and weight–bearing joints such as knees, hips, feet, and the back. The pain of osteoarthritis usually begins gradually and progresses slowly over many years.

Osteoarthritis is commonly identified by aching pain in one or more joints, stiffness, and loss of mobility. The disease can cause significant trouble walking and stair climbing. Inflammation may or may not be present. Extensive use of the joint often exacerbates pain in the joints. Osteoarthritis is often more bothersome at night than in the morning and in humid weather than dry weather. Periods of inactivity, such as sleeping or sitting, may result in stiffness, which can be eased by stretching and **exercise**. Osteoarthritis pain tends to fade within a year of appearing.

Bony lumps on the end joint of the finger, called Herberden's nodes, and on the middle joint of the finger, called Bouchard's nodes, may also develop.

KEY TERMS

Cartilage—Supportive connective tissue which cushions bone at the joints or which connects muscle to bone.

Collagen—The main supportive protein of cartilage, connective tissue, tendon, skin, and bone.

Corticosteroids—Anti-inflammatory medications. Related to cortisol, a naturally produced hormone that controls many body functions.

Diagnosis

Examination

A diagnosis of osteoarthritis is made based on a physical exam and history of symptoms.

It is possible to distinguish osteoarthritis from other joint diseases by considering a number of factors together:

- Osteoarthritis usually occurs in older people.
- It is usually located in only one or a few joints.
- The joints are less inflamed than in other arthritic conditions.
- Progression of pain is almost always gradual.

A few of the most common disorders that might be confused with osteoarthritis are rheumatoid arthritis, chondrocalcinosis, and **Charcot's joints**.

Tests

X–rays are used to confirm diagnosis. In people over 60, the disease can often be observed on x–ray. An indication of cartilage loss arises if the normal space between the bones in a joint is narrowed, if there is an abnormal increase in bone density, or if bony projections or erosions are evident. Any cysts that might develop in osteoarthritic joints are also detectable by x–ray.

Additional tests can be performed if other conditions are suspected or if the diagnosis is uncertain. Blood tests can rule out rheumatoid arthritis or other forms of arthritis. Synovial fluid analysis may also be performed to detect crystals that may be present in the joint and to look for signs of joint infection. MRI (**magnetic resonance imaging**) may also be used to examine affected joints.

Treatment

Traditional

There is no known way to prevent osteoarthritis or slow its progression. Some lifestyle changes can

reduce or delay symptoms. Treatment often focuses on decreasing pain and improving joint movement. Prevention and treatment measures may include:

- Exercises to maintain joint flexibility and improve muscle strength. By strengthening the supporting muscles, tendons, and ligaments, regular weight–bearing exercise helps protect joints, even possibly stimulating growth of the cartilage.
- Joint protection, which prevents strain and stress on painful joints.
- Heat/cold therapy for temporary pain relief.
- Weight control, which prevents extra stress on weight–bearing joints. One study reported that weight loss seemed to reduce the risk for symptomatic osteoarthritis of the knee in women, and in another, women who lost 11 pounds or more cut their risk for developing osteoarthritis in half.
- Surgery may be needed to relieve chronic pain in damaged joints. Osteoarthritis is the most common indication for total joint replacement of the hip and knee.

Drugs

Various pain control medications, including **corticosteroids** and NSAIDs (nonsteroidal anti–inflammatory drugs such as **aspirin**, **acetaminophen**, ibuprofen, and naproxen) are available. For inflamed joints that are not responsive to NSAIDS, injectable glucocorticoids may be used. For mild pain without inflammation, acetaminophen is commonly used.

Alternative

Clinical trials for the treatment of osteoarthritis are currently sponsored by the National Institutes of Health (NIH) and other agencies. In 2009, NIH reported 236 on going studies. Some examples include the following:

- A pilot study of group physical therapy for knee osteoarthritis. (NCT00642772)
- The evaluation of whether implanting gold beads extra–articularly in five acupuncture points around a knee improves pain, stiffness and function in patients with knee osteoarthritis. (NCT00487370)
- The evaluation of the effectiveness of a novel biomechanical device consisting of four individually calibrated elements attached onto foot–worn platforms in reducing pain and improving function in patients with knee osteoarthritis. (NCT00457132)
- The evaluation of certain exercises designed to improve knee stability, reduce pain, and improve physical function in people with knee osteoarthritis. (NCT00078624)

Clinical trial information is constantly updated by NIH and the most recent information on osteoarthritis trials can be found at: http://clinicaltrials.gov/search/open/condition=%22Osteoarthritis%22

Home remedies

Glucosamine and chondroitin sulfate are popular **nutritional supplements** that may diminish the symptoms of osteoarthritis. According to some reports, a daily dose of 750–1,500 mg of glucosamine and chondroitin sulfate may result in reduced joint pain, stiffness, and swelling, however these supplements are not approved by the U.S. Food and Drug Administration as effective treatment of osteoarthritis. A person with osteoarthritis should consult with a doctor before using dietary supplements to treat symptoms.

Prognosis

Osteoarthritis is not life-threatening, but quality of life can deteriorate significantly due to the pain and loss of mobility that it causes. Advanced osteoarthritis can force the patient to forgo activities, even walking, unless the condition is alleviated by medication or corrected by surgery.

There is no cure for osteoarthritis, and no treatment alters its progression with any certainty. Only heart disease has a greater impact on work, and 5% of those who leave the work force do so because of osteoarthritis.

Prevention

Preventive measures include maintaining an ideal body weight, exercising, standing straight, avoiding repetitive stress on the joints, using the strongest joints and muscles to lift or move big objects, and avoiding injuries to joints, as articular cartilage wears away in previously injured joints. It has also been reported that deficiencies in vitamin D in older people may worsen their condition, so individuals with osteoarthritis should strive to get the recommended 400 IU a day. To protect bones, adults should also consume at least 1,000 mg of **calcium** daily.

Resources

BOOKS

Adams, Casey. *Arthritis —The Botanical Solution: Nature's Answer to Rheumatoid Arthritis, Osteoarthritis, Gout and Other Forms of Arthritis*. Wilmington, DE: Sacred Earth Publishing, 2009.

Arden, Nigel K., et al. *Osteoarthritis (The Facts)*. Oxford, UK: Oxford University Press, 2008.

Cooper, Grant. *The Arthritis Handbook: Improve Your Health and Manage the Pain of Osteoarthritis*. New York, NY: DiaMedica, 2008.

Foltz–Gray, Dorothy. *The Arthritis Foundation's Guide to Good Living with Osteoarthritis,* 2nd edition. Atlanta, GA: Arthritis Foundation, 2006.

Rosenstein, Ann A. *Water Exercises for Osteoarthritis: The Effective Way to Reduce Pain and Stiffness, While Increasing Endurance and Strength*. Enumclaw, WA: Idyll Arbor, 2007.

Sharma, Leena, and Francis Berenbaum. *Osteoarthritis*. Philadelphia, PA: Mosby (Elsevier), 2007.

PERIODICALS

Argenson, J. N., et al. "The new arthritic patient and arthroplasty treatment options." *Journal of Bone and Joint Surgery* 91, suppl. 7 (August 2009): 43–48.

Blackham, J., et al. "Does regular exercise reduce the pain and stiffness of osteoarthritis?" *Journal of Family Practice* 57, no. 7 (July 2008): 476–477.

De Ceuninck, F. "The application of proteomics to articular cartilage: a new hope for the treatment of osteoarthritis." *Joint Bone Spine* 75, no. 4 (July 2008): 376–378.

Hepper, C. T., et al. "The efficacy and duration of intra–articular corticosteroid injection for knee osteoarthritis: a systematic review of level I studies." *Journal of the American Academy of Orthopaedic Surgeons* 17, no. 10 (October 2009): 638–646.

Jamtvedt, G., et al. "Measuring physiotherapy performance in patients with osteoarthritis of the knee: a prospective study." *JBMC Health Services Research* 8, no. 1 (July 2008): 145.

Minns Lowe, C. J., et al. "Effectiveness of physiotherapy exercise following hip arthroplasty for osteoarthritis: a systematic review of clinical trials." *BMC Musculoskeletal Disorders* 10 (August 2009): 98.

Mollenhauer, J. A. "Perspectives on articular cartilage biology and osteoarthritis." *Injury* 39, suppl. 1 (April 2008): S5–S12.

Richmond, J., et al. "Treatment of osteoarthritis of the knee (nonarthroplasty)." *Journal of the American Academy of Orthopaedic Surgeons* 17, no. 9 (September 2009): 591–600.

Wollheim, F. A. "A pain in the knee—is it osteoarthritis?" *Clinical and Experimental Rheumatology* 26, no. 2 (March–April 2008): 227–229.

OTHER

"Arthritis Advice." *National Institute on Aging*. Information Page. http://www.nia.nih.gov/HealthInformation/Publications/arthritis.htm (accessed December 12, 2009)

"Choosing Pain Medicine For Osteoarthritis." *US Department of Health & Human Services*. Information Page. http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=4 (accessed December 12, 2009)

"Osteoarthritis." *Medline Plus*. Health Topic. http://www.nlm.nih.gov/medlineplus/osteoarthritis.html (accessed December 12, 2009)

"Osteoarthritis." *NIAMS*. Information Page. http://www.niams.nih.gov/Health_Info/Osteoarthritis/default.asp (accessed December 12, 2009)

"Osteoarthritis." *Arthritis Foundation*. Information Page. http://www.arthritis.org/disease-center.php?disease_id=32 (accessed December 12, 2009)

"What Is Osteoarthritis?" *NIAMS*. Information Page. http://www.niams.nih.gov/Health_Info/Osteoarthritis/osteoarthritis_ff.asp (accessed December 12, 2009)

ORGANIZATIONS

American College of Rheumatology, 2200 Lake Blvd. NE, Atlanta, GA, 30319, (404) 633 3777, (404) 633 1870, http://www.rheumatology.org.

Arthritis Foundation, P.O. Box 7669, Atlanta, GA, 30357-0669, (800) 283-7800, http://www.arthritis.org.

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), 31 Center Dr., Rm. 4C02, MSC 2350, Bethesda, MD, 20892-2350, (301) 496-8190, (877) 22-NIAMS, NIAMSinfo@mail.nih.gov, http://www.niams.nih.gov.

Jennifer F. Wilson, MS
Monique Laberge, PhD

Osteoarthrosis *see* **Osteoarthritis**

Osteochondroses

Definition

Osteochondroses comprise group of diseases of children and adolescents in which localized tissue **death** (necrosis) occurs, usually followed by full regeneration of healthy bone tissue. The singular term is osteochondrosis.

Description

During the years of rapid bone growth, blood supply to the growing ends of bones (epiphyses) may become insufficient resulting in necrotic bone, usually near joints. The term avascular necrosis is used to describe osteochondrosis. Since bone is normally undergoing a continuous rebuilding process, the necrotic areas are most often self-repaired over a period of weeks or months.

Osteochondrosis can affect different areas of the body and is often categorized by one of three locations: articular, non-articular, and physeal.

Physeal osteochondrosis is known as Scheuermann's disease. It occurs in the spine at the intervertebral joints (physes), especially in the chest (thoracic) region.

Articular disease occurs at the joints (articulations). One of the more common forms is Legg-Calvé-Perthes disease, occurring at the hip. Other forms include Köhler's disease (foot), Freiberg's disease (second toe), and Panner's disease (elbow). Freiberg's disease is the one type of osteochondrosis that is more common in females than in males. All others affect the sexes equally.

Non-articular osteochondrosis occurs at any other skeletal location. For instance, Osgood-Schlatter disease of the tibia (the large inner bone of the leg between the knee and ankle) is relatively common.

Osteochondritis dissecans is a form of osteochondrosis in which loose bone fragments may form in a joint.

Causes and symptoms

Many theories have been advanced to account for osteochondrosis, but none has proven fully satisfactory. **Stress** and **ischemia** (reduced blood supply) are two of the most commonly mentioned factors. Athletic young children are often affected when they overstress their developing limbs with a particular repetitive motion. Many cases are idiopathic, meaning that no specific cause is known.

The most common symptom for most types of osteochondrosis is simply **pain** at the affected joint, especially when pressure is applied. Locking of a joint or limited range of motion at a joint can also occur.

Scheuermann's disease can lead to serious **kyphosis** (hunchback condition) due to erosion of the vertebral bodies. Usually, however, the kyphosis is mild, causing no further symptoms and requiring no special treatment.

Diagnosis

Diagnosis can be confirmed by x-ray findings.

Treatment

Conservative treatment is usually attempted first. In many cases, simply resting the affected body part for a period of days or weeks will bring relief. A cast may be applied if needed to prevent movement of a joint.

Surgical intervention may be needed in some cases of osteochondritis dissecans to remove abnormal bone fragments in a joint.

Prognosis

Accurate prediction of the outcome for individual patients is difficult with osteochondrosis. Some patients will heal spontaneously. Others will heal with little treatment other than keeping weight or stress off the affected limb. The earlier the age of onset, the better the prospects for full recovery. Surgical intervention is often successful in osteochondritis dissecans.

Prevention

No preventive measures are known.

Resources

BOOKS

Hay, William W., et al. *Current Pediatric Diagnosis & Treatment*. 18th ed. New York: Lange Medical Books/McGraw–Hill, 2007.

Victor Leipzig, PhD

Osteogenesis imperfecta

Definition

Osteogenesis imperfecta (OI) is a group of genetic diseases of collagen in which the bones are formed improperly, making them fragile and prone to breaking.

Description

Collagen is a fibrous protein material. It serves as the structural foundation of skin, bone, cartilage, and ligaments. In osteogenesis imperfecta, the collagen produced is abnormal and disorganized. This results in a number of abnormalities throughout the body, the most notable being fragile, easily broken bones.

There are four forms of OI, Types I through IV. Of these, Type II is the most severe, and is usually fatal within a short time after birth. Types I, III, and IV have some overlapping and some distinctive symptoms, particularly weak bones.

Evidence suggests that OI results from abnormalities in the collagen gene COL1A1 or COL1A2, and possibly abnormalities in other genes. In OI Type I, II, and III, the gene map locus is 17q21.31-q22, 7q22.1, and in OI Type IV, the gene map locus is 17q21.31-q22.

In OI, the genetic abnormality causes one of two things to occur. It may direct cells to make an altered collagen protein and the presence of this altered

collagen causes OI Type II, III, or IV. Alternately, the dominant altered gene may fail to direct cells to make any collagen protein. Although some collagen is produced by instructions from the normal gene, an overall decrease in the total amount of collagen produced results in OI Type I.

A child with only one parent who is a carrier of a single altered copy of the gene has no chance of actually having the disease, but a 50% chance of being a carrier.

If both parents have OI caused by an autosomal dominant gene change, there is a 75% chance that the child will inherit one or both OI genes. In other words, there is a 25% chance the child will inherit only the mother's OI gene (and the father's unaffected gene), a 25% chance the child will inherit only the father's OI gene (and the mother's unaffected gene), and a 25% chance the child will inherit both parents' OI genes. Because this situation has been uncommon, the outcome of a child inheriting two OI genes is hard to predict. It is likely that the child would have a severe, possibly lethal, form of the disorder.

About 25% of children with OI are born into a family with no history of the disorder. This occurs when the gene spontaneously mutates in either the sperm or the egg before the child's conception. No triggers for this type of mutation are known. This is called a new dominant mutation. The child has a 50% chance of passing the disorder on to his or her children. In most cases, when a family with no history of OI has a child with OI, they are not at greater risk than the general population for having a second child with OI, and unaffected siblings of a person with OI are at no greater risk of having children with OI than the general population.

In studies of families into which infants with OI Type II were born, most of the babies had a new dominant mutation in a collagen gene. In some of these families, however, more than one infant was born with OI. Previously, researchers had seen this recurrence as evidence of recessive inheritance of this form of OI. More recently, however, researchers have concluded that the rare recurrence of OI to a couple with a child with autosomal dominant OI is more likely due to gonadal mosaicism. Instead of mutation occurring in an individual sperm or egg, it occurs in a percentage of the cells that give rise to a parent's multiple sperm or eggs. This mutation, present in a percentage of his or her reproductive cells, can result in more than one affected child without affecting the parent with the disorder. An estimated 2%–4% of families into which an infant with OI Type II is born are at risk of having another affected child because of gonadal mosaicism.

Demographics

OI affects equal numbers of males and females. It occurs in about one of every 20,000 births.

Causes and symptoms

OI is usually inherited as an autosomal dominant condition. In autosomal dominant inheritance, a single abnormal gene on one of the autosomal chromosomes (one of the first 22 "non-sex" chromosomes) from either parent can cause the disease. One of the parents will have the disease (since it is dominant) and is the carrier. Only one parent needs to be a carrier in order for the child to inherit the disease. A child who has one parent with the disease has a 50% chance of also having the disease.

Type I

This is the most common and mildest type. Among the common features of Type I are the following:

- Bones are predisposed to fracture, with most fractures occurring before puberty; people with OI type I typically have about 20–40 fractures before puberty.
- Stature is normal or near-normal.
- Joints are loose and muscle tone is low.
- Usually sclera (whites of the eyes) have blue, purple, or gray tint.
- Face shape is triangular.
- Tendency toward scoliosis (a curvature of the spine).
- Bone deformity is absent or minimal.
- Dentinogenesis imperfecta may occur, causing brittle teeth.
- Hearing loss is a possible symptom, often beginning in the early 20s or 30s.
- Structure of collagen is normal, but the amount is less than normal.

Type II

Sometimes called the lethal form, Type II is the most severe form of OI. Among the common features of Type II are the following:

- Frequently, OI Type II is lethal at or shortly after birth, often as a result of respiratory problems.
- Fractures are numerous and bone deformity is severe.
- Stature is small with underdeveloped lungs.
- Collagen is formed improperly.

Type III

Among the common features of Type III are the following:

- Bones fracture easily (fractures are often present at birth, and x-rays may reveal healed fractures that occurred before birth; people with OI Type III may have more than 100 fractures before puberty).
- Stature is significantly shorter than normal.
- Sclera (whites of the eyes) have blue, purple, or gray tint.
- Joints are loose and muscle development is poor in arms and legs.
- Rib cage is barrel-shaped.
- Face shape is triangular.
- Scoliosis (a curvature of the spine) is present.
- Respiratory problems are possible.
- Bones are deformed and deformity is often severe.
- Dentinogenesis imperfecta may occur, causing brittle teeth.
- Hearing loss is possible.
- Collagen is formed improperly.

Type IV

OI Type IV falls between Type I and Type III in severity. Among the common features of Type IV are the following:

- Bones fracture easily, with most fractures occurring before puberty.
- Stature is shorter than average.
- Sclera (whites of the eyes) are normal in color, appearing white or near-white.
- Bone deformity is mild to moderate.
- Scoliosis (curvature of the spine) is likely.
- Rib cage is barrel-shaped.
- Face is triangular in shape.
- Dentinogenesis imperfecta may occur, causing brittle teeth.
- Hearing loss is possible.
- Collagen is formed improperly.

Diagnosis

It is often possible to diagnose OI solely on clinical features and x-ray findings. Collagen or DNA tests may help confirm a diagnosis of OI. These tests generally require several weeks before results are known. Approximately 10–15% of individuals with mild OI who have collagen testing, and approximately 5% of those who have **genetic testing**, test negative for OI despite having the disorder.

Diagnosis is usually suspected when a baby has bone **fractures** after having suffered no apparent injury. Another indication is small, irregular, isolated bones in the sutures between the bones of the skull (wormian bones). Sometimes the bluish sclera serves as a diagnostic clue. Unfortunately, because of the unusual nature of the fractures occurring in a baby who cannot yet move, some parents have been accused of **child abuse** before the actual diagnosis of osteogenesis imperfecta was reached.

Prenatal diagnosis

Testing is available to assist in prenatal diagnosis. Women with OI who become pregnant, or women who conceive a child with a man who has OI, may wish to explore prenatal diagnosis. Because of the relatively small risk (2–4%) of recurrence of OI Type II in a family, families may opt for ultrasound studies to determine if a developing fetus has the disorder.

Ultrasound is the least-invasive procedure for prenatal diagnosis, and carries the least risk. Using ultrasound, a doctor can examine the fetus's skeleton for bowing of the leg or arm bones, fractures, shortening, or other bone abnormalities that may indicate OI. Different forms of OI may be detected by ultrasound in the second trimester. The reality is that when it occurs as a new dominant mutation, it is found inadvertantly on ultrasound, and it may be difficult to know the diagnosis until after delivery since other genetic conditions can cause bowing and/or fractures prenatally.

Chorionic villus sampling is a procedure to obtain chorionic villi tissue for testing. Examination of fetal collagen proteins in the tissue can reveal information about the quantitative or qualitative collagen defects that leads to OI. When a parent has OI, it is necessary for the affected parent to have the results of his or her own collagen test available. Chorionic villus sampling can be performed at 10–12 weeks of **pregnancy**.

Amniocentesis is a procedure that involves inserting a thin needle into the uterus, into the amniotic sac, and withdrawing a small amount of amniotic fluid. DNA can be extracted from the fetal cells contained in the amniotic fluid and tested for the specific mutation known to cause OI in that family. This technique is useful only when the mutation causing OI in a particular family has been identified through previous genetic testing of affected family members, including previous

KEY TERMS

Collagen—The main supportive protein of cartilage, connective tissue, tendon, skin, and bone.

Ligament—A type of connective tissue that connects bones or cartilage and provides support and strength to joints.

Mutation—A permanent change in the genetic material that may alter a trait or characteristic of an individual, or manifest as disease, and can be transmitted to offspring.

Sclera—The tough white membrane that forms the outer layer of the eyeball.

Scoliosis—An abnormal, side-to-side curvature of the spine.

pregnancies involving a baby with OI. Amniocentesis is performed at 16–18 weeks of pregnancy.

Treatment

There are no treatments available to cure OI, nor to prevent most of its complications. Most treatments are aimed at treating the fractures and bone deformities caused by OI. Splints, casts, braces, and rods are all used. Rodding refers to a surgical procedure in which a metal rod is implanted within a bone (usually the long bones of the thigh and leg). This is done when bowing or repeated fractures of these bones has interfered with a child's ability to begin to walk.

Other treatments include **hearing aids** and early capping of teeth. Patients may require the use of a walker or wheelchair. **Pain** may be treated with a variety of medications. **Exercise** is encouraged as a means to promote muscle and bone strength. Swimming is a form of exercise that puts a minimal amount of strain on muscles, joints, and bones. Walking is encouraged for those who are able.

Smoking, excessive alcohol and **caffeine** consumption, and steroid medications may deplete bone and exacerbate bone fragility.

Alternative treatment such as **acupuncture**, naturopathic therapies, hypnosis, relaxation training, visual imagery, and **biofeedback** have all been used to try to decrease the constant pain of fractures.

Prognosis

Lifespan for people with OI Type I, III, and IV is not generally shortened. The prognosis for people with these types of OI is quite variable, depending on the severity of the disorder and the number and severity of the fractures and bony deformities.

Fifty percent of all babies with OI Type II are stillborn. The rest of these babies usually die within a very short time after birth. In recent years, some people with Type II have lived into young adulthood.

Resources

PERIODICALS

Smith, R. "Severe osteogenesis imperfecta: new therapeutic options?" *British Medical Journal* 322 (January 13, 2001): 63+.

OTHER

"Osteogenesis Imperfecta." *National Institutes of Health Osteoporosis and Related Bone Diseases–National Resource Center*. http://www.osteo.org/oi.html.

ORGANIZATIONS

Children's Brittle Bone Foundation, 7701 95th St, Pleasant Prairie, WI, 53158, (773)263-2223, (262)947-0724, bonelink@oif.org, http://www.cbbf.org.

Jennifer F. Wilson, MS

Osteogenic sarcoma *see* **Sarcomas**

Osteomalacia *see* **Vitamin D deficiency**

Osteomyelitis

Definition

Osteomyelitis refers to a bone infection, almost always caused by a bacteria. Over time, the result can be destruction of the bone itself.

Description

Bone infections may occur at any age. Certain conditions increase the risk of developing such an infection, including sickle cell anemia, injury, the presence of a foreign body (such as a bullet or a screw placed to hold together a broken bone), intravenous drug use (such as heroin), diabetes, **kidney dialysis**, surgical procedures to bony areas, untreated infections of tissue near a bone (for example, extreme cases of untreated sinus infections have led to osteomyelitis of the bones of the skull).

Causes and symptoms

Staphylococcus aureus, a bacterium, is the most common organism involved in osteomyelitis. Other

types of organisms include the mycobacterium which causes **tuberculosis**, a type of *Salmonella* bacteria in patients with sickle cell anemia, *Pseudomonas aeurginosa* in drug addicts, and organisms which usually reside in the gastrointestinal tract in the elderly. Extremely rarely, the viruses which cause **chickenpox** and **smallpox** have been found to cause a viral osteomyelitis.

There are two main ways that infecting bacteria find their way to bone, resulting in the development of osteomyelitis. These include:

- Spread via the bloodstream; 95% of these types of infections are due to *Staphylococcus aureus*. In this situation, the bacteria travels through the bloodstream to reach the bone. In children, the most likely site of infection is within one of the long bones, particularly the thigh bone (femur), one of the bones of the lower leg (tibia), or the bone of the upper arm (humerus). This is because in children these bones have particularly extensive blood circulation, making them more susceptible to invasion by bacteria. Different patterns of blood circulation in adults make the long bones less well-served by the circulatory system. These bones are therefore unlikely to develop osteomyelitis in adult patients. Instead, the bones of the spine (vertebrae) receive a lot of blood flow. Therefore, osteomyelitis in adults is most likely to affect a vertebra. Drug addicts may have osteomyelitis in the pubic bone or clavicle.
- Spread from adjacent infected soft tissue; about 50% of all such cases are infected by *Staphylococcus aureus*. This often occurs in cases where recent surgery or injury has resulted in a soft tissue infection. The bacteria can then spread to nearby bone, resulting in osteomyelitis. Patients with diabetes are particularly susceptible to this source of osteomyelitis. The diabetes interferes with both nerve sensation and good blood flow to the feet. Diabetic patients are therefore prone to developing poorly healing wounds to their feet, which can then spread to bone, causing osteomyelitis.

Acute osteomyelitis refers to an infection which develops and peaks over a relatively short period of time. In children, acute osteomyelitis usually presents itself as **pain** in the affected bone, tenderness to pressure over the infected area, **fever** and chills. Patients who develop osteomyelitis, due to spread from a nearby area of soft tissue infection, may only note poor healing of the original wound or infection.

Adult patients with osteomyelitis of the spine usually have a longer period of dull, aching pain in the back, and no fever. Some patients note pain in the chest, abdomen, arm, or leg. This occurs when the inflammation in the spine causes pressure on a nerve root serving one of these other areas. The lower back is the most common location for osteomyelitis. When caused by tuberculosis, osteomyelitis usually affects the thoracic spine (that section of the spine running approximately from the base of the neck down to where the ribs stop).

When osteomyelitis is not properly treated, a chronic (long-term) type of infection may occur. In this case, the infection may wax and wane indefinitely, despite treatment during its active phases. An abnormal opening in the skin overlaying the area of bone infection (called a sinus tract) may occasionally drain pus. This type of smoldering infection may also result in areas of dead bone, called sequestra. These areas occur when the infection interferes with blood flow to a particular part of the bone. Such sequestra lack cells called osteocytes, which in normal bone are continuously involved in the process of producing bony material.

Diagnosis

Diagnosis of osteomyelitis involves several procedures. Blood is usually drawn and tested to demonstrate an increased number of the infection-fighting white blood cells (particularly elevated in children with acute osteomyelitis). Blood is also cultured in a laboratory, a process which allows any bacteria present to multiply. A specimen from the culture is then specially treated, and examined under a microscope to try to identify the causative bacteria.

Injection of certain radioactive elements into the bloodstream, followed by a series of x-ray pictures, called a scan (radionuclide scanning), will reveal areas of bone inflammation. Another type of scan used to diagnose osteomyelitis is called **magnetic resonance imaging**, or MRI

When pockets of pus are available, or overlaying soft tissue infection exists, these can serve as sources for samples which can be cultured to allow identification of bacteria present. A long, sharp needle can be used to obtain a specimen of bone (biopsy), which can then be tested to attempt to identify any bacteria present.

Treatment

Antibiotics are medications used to kill bacteria. These medications are usually given through a needle in a vein (intravenously) for at least part of the time. In children, these antibiotics can be given by mouth after initial treatment by vein. In adults, four to six weeks of intravenous antibiotic treatment is usually recommended, along with bed-rest for part or all of that time. Occasionally, a patient will have such extensive

KEY TERMS

Abscess—A pus-filled pocket of infection.

Femur—The thighbone.

Humerus—The bone of the upper arm.

Thoracic—Pertaining to the area bounded by the rib cage.

Tibia—One of the two bones of the lower leg.

ostemyelitis that surgery will be required to drain any pockets of pus, and to clean the infected area.

Alternative treatment

General recommendations for the treatment of infections include increasing vitamin supplements, such as **vitamins** A and C. Liquid garlic extract is sometimes suggested. **Guided imagery** can help induce relaxation and improve pain, both of which are considered to improve healing. Herbs such as **echinacea** (*Echinacea* spp.), goldenseal (*Hydrastis canadensis*), Siberian **ginseng** (*Eleutherococcus senticosus*), and myrrh (*Commiphora molmol*) are all suggested for infections. Juice therapists recommend drinking combinations of carrot, celery, beet, and cantaloupe juices. A variety of homeopathic remedies may be helpful, especially those used to counter inflammation.

Prognosis

Prognosis varies depending on how quickly an infection is identified, and what other underlying conditions exist to complicate the infection. With quick, appropriate treatment, only about 5% of all cases of acute osteomyelitis will eventually become chronic osteomyelitis. Patients with chronic osteomyelitis may require antibiotics periodically for the rest of their lives.

Prevention

About the only way to have any impact on the development of osteomyelitis involves excellent care of any **wounds** or injuries.

Resources

PERIODICALS

Calhoun, Jason H., et al. "Osteomyelitis: Diagnosis, Staging, Management." *Patient Care* 32 (January 30, 1998): 93+.

Rosalyn Carson-DeWitt, MD

Osteopathic medicine *see* **Osteopathy**

Osteopathy

Definition

Osteopathy is a system and philosophy of health care that separated from traditional (allopathic) medical practice about a century ago. It places emphasis on the musculoskeletal system, hence the name—*osteo* refers to bone and *path* refers to disease. Osteopaths also believe strongly in the healing power of the body and do their best to facilitate that strength. During this century, the disciplines of osteopathy and allopathic medicine have been converging.

Purpose

Osteopathy shares many of the same goals as traditional medicine, but places greater emphasis on the relationship between the organs and the musculoskeletal system as well as on treating the whole individual rather than just the disease.

Precautions

Pain is the chief reason patients seek musculoskeletal treatment. Pain is a symptom, not a disease by itself. Of critical importance is first to determine the cause of the pain. Cancers, brain or spinal cord disease, and many other causes may be lying beneath this symptom. Once it is clear that the pain is originating in the musculoskeletal system, treatment that includes manipulation is appropriate.

Description

History

Osteopathy was founded in the 1890s by Dr. Andrew Taylor, who believed that the musculoskeletal system was central to health. The primacy of the musculoskeletal system is also fundamental to **chiropractic**, a related health discipline. The original theory behind both approaches presumed that energy flowing through the nervous system is influenced by the supporting structure that encase and protect it—the skull and vertebral column. A defect in the musculoskeletal system was believed to alter the flow of this energy and cause disease. Correcting the defect cured the disease. Defects were thought to be misalignments—parts out of place by tiny distances. Treating misalignments became a matter of restoring the parts to their natural arrangement by adjusting them.

As medical science advanced, defining causes of disease and discovering cures, schools of osteopathy adopted modern science, incorporated it into their

Osteopathic physician demonstrating the articulation of a foot. *(Photo Researchers, Inc.)*

curriculum, and redefined their original theory of disease in light of these discoveries. Near the middle of the 20th century the equivalance of medical education between osteopathy and allopathic medicine was recognized, and the DO degree (doctor of osteopathy) was granted official parity with the MD (doctor of medicine) degree. Physicians could adopt either set of initials.

However, osteopaths have continued their emphasis on the musculoskeletal system and their traditional focus on "whole person" medicine. Osteopaths constitute 5.5% of U.S. physicians, approximately 45,000. They provide 100 million patient visits a year. From its origins in the United States, osteopathy has spread to countries all over the world.

Practice

Osteopaths, chiropractors, and physical therapists are the experts in manipulations (adjustments). The place of manipulation in medical care is far from settled, but millions of patients find relief from it. Particularly backs, but also necks, command most of the attention of the musculoskeletal community. This community includes orthopedic surgeons, osteopaths, general and family physicians, orthopedic physicians, chiropractors, physical therapists, massage therapists, specialists in orthotics and prosthetics, and even some dentists and podiatrists. Many types of headaches also originate in the musculoskeletal system. Studies comparing different methods of treating musculoskeletal back, head, and neck pain have not reached a consensus, in spite of the huge numbers of people that suffer from it.

The theory behind manipulation focuses on joints, mostly those of the vertebrae and ribs. Some believe there is a very slight offset of the joint members—a subluxation. Others believe there is a vacuum lock of the joint surfaces, similar to two suction cups stuck together. Such a condition would squeeze joint lubricant out and produce abrasion of the joint surfaces with movement. Another theory focuses on weakness of the ligaments that support the joint, allowing it freedom to get into trouble. Everyone agrees that the result produces pain, that pain produces **muscle spasms and cramps**, which further aggravates the pain.

Some, but not all, practitioners in this field believe that the skull bones can also be manipulated. The skull is, in fact, several bones that are all moveable in infants. Whether they can be moved in adults is controversial. Other practitioners manipulate peripheral joints to relieve arthritis and similar afflictions.

Manipulation returns the joint to its normal configuration. There are several approaches. Techniques vary among practitioners more than between disciplines. Muscle relaxation of some degree is often required for the manipulation to be successful. This can be done with heat or medication. Muscles can also be induced to relax by gentle but persistent stretching. The manipulation is most often done by a short, fast motion called a thrust, precisely in the right direction. A satisfying "pop" is evidence of success. Others prefer steady force until relaxation permits movement.

Return of the joint to its normal status may be only the first step in treating these disorders. There is a reason for the initial event. It may be a fall, a stumble, or a mild impact, in which case the manipulation is a cure. On the other hand, there may be a postural misalignment (such as a short leg), a limp, or a stretched ligament that permits the joint to slip back into dysfunction. Tension, as well as pain, for emotional reasons causes muscles to tighten. If the pain has been present for any length of time, there will also be muscle deterioration. The osteopathic approach to the whole person takes all these factors into account in returning the patient to a state of health.

Other repairs may be needed. A short leg is thought by some to be a subluxation in the pelvis that may be manipulated back into position. Other short legs may require a lift in one shoe. Long-standing pain requires

KEY TERMS

Orthotics—Mechanical devices that assist function.

Prosthetics—Mechanical devices that replace missing body parts.

additional methods of **physical therapy** to rehabilitate muscles, correct posture, and extinguish habits that arose to compensate for the pain. Medications that relieve muscle spasm and pain are usually part of the treatment. Psychological problems may need attention and medication.

Risks

Manipulation has rarely caused problems. Once in a while too forceful a thrust has damaged structures in the neck and caused serious problems. The most common adverse event, though, is misdiagnosis. Cancers have been missed; surgical back disease has been ignored until spinal nerves have been permanently damaged.

Normal results

Many patients find that one or a series of manipulations cures long-standing pain. Other patients need repeated treatments. Some do not respond at all. It is always a good idea to reassess any treatment that is not producing the expected results.

ORGANIZATIONS

American Association of Colleges of Osteopathic Medicine, 5550 Friendship Blvd., Suite 310, Chevy Chase, MD, 20815-7231, (301)968-4100, (301)968-4101, http://www.aacom.org.

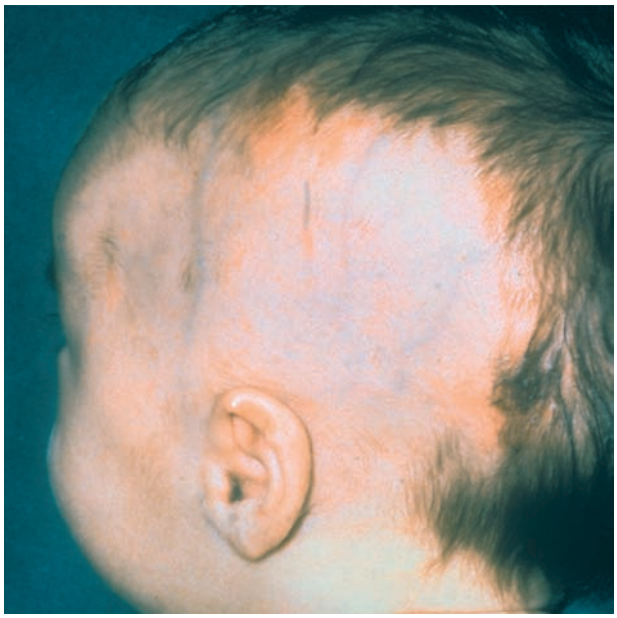
American Osteopathic Association (AOA), 142 East Ontario Street, Chicago, IL, 60611, (312)202-8000, (312)202-8200, (800)621-1773, info@osteotech.org, http://www.osteopathic.org/.

J. Ricker Polsdorfer, MD

Osteopetroses

Definition

Osteopetrosis (plural osteopetroses) is a rare hereditary disorder that makes bones increase in both density and fragility. A potentially fatal condition that can deform bone structure and distort the appearance, osteopetrosis is also called chalk bones, ivory bones, or marble bones.



This infant has osteopetrosis, a condition which thickens and hardens the bone. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Description

Osteopetrosis occurs when bones are spongy or porous, or new bone is repeatedly added to calcified cartilage (hardened connective tissue).

Bone density begins to increase at birth or earlier, but symptoms may not become evident until adulthood. In mild cases, bone density increases at gradual, irregular intervals until full adult height is attained. Some bones are not affected.

More severe osteopetrosis progresses at a rapid pace and destroys bone structure. This condition involves bones throughout the body, but the lower jaw is never affected.

Types of osteopetroses

In early-onset osteopetrosis ends of the long bones of the arms and legs appear clubbed (widened and thickened) at birth, and bone density continues to increase sporadically or without pause. Early-onset osteopetroses can be a fatal condition, resulting in **death** before the age of two.

Malignant infantile osteopetrosis is most often discovered by the time a baby is a few months old. One-third of all malignant infantile osteopetroses cases result in death before the age of 10.

Intermediate osteopetrosis generally appears in children under 10. This condition, usually less severe than early-onset or malignant infantile osteopetrosis, is not life-threatening.

Symptoms of adult or delayed-onset osteopetrosis may not become evident until the child becomes a teenager or adult.

Relatively common in many parts of the world, Albers-Schönberg disease is a mild form of this condition. People who have this disease are born with normal bone structure. Bone density increases as they age but does not affect appearance, health, intelligence, or life span.

Causes and symptoms

Osteopetrosis is the result of a genetic defect that causes the body to add new bone more rapidly than existing bone disintegrates.

When fibrous or bony tissue invades bone marrow and displaces red blood cells, the patient may develop anemia. Infection results when excess bone impairs the immune system, and hemorrhage can occur when platelet production is disrupted. When the skeleton grows so thick that nerves are unable to pass between bones, the patient may have a **stroke** or become blind or deaf.

Other symptoms associated with osteopetrosis include:

- bones that break easily and do not heal properly
- bruising
- convulsions
- enlargement of the liver, lymph glands, or spleen
- failure to thrive (delayed growth, weight gain, and development)
- hydrocephalus (fluid on the brain)
- macrocephaly (abnormal enlargement of the head)
- paralysis or loss of control of muscles in the face or eyes

Diagnosis

Osteopetrosis is usually diagnosed when x-rays reveal abnormalities or increases in bone density. **Bone biopsy** can confirm the presence of osteopetrosis, but additional tests may be needed to distinguish one type of the disorder from another.

Treatment

High doses of vitamin D can stimulate cells responsible for disintegration of old bone and significantly alleviate symptoms of severe disease. Experimental interferon gamma 1-b therapy has been shown to reduce the risk of infection experienced by patients who are severely ill.

When bone overgrowth deforms the shape of the skull, surgery may be required to relieve pressure on the brain. Orthodontic treatment is sometimes necessary to correct **malocclusion** (a condition that shifts the position of the teeth and makes closing the mouth impossible).

Professional counseling can help patients cope with the emotional aspects of deformed features.

Bone marrow transplants (BMT) have cured some cases of early-onset and malignant infantile osteopetrosis. Because 30–60% of children who undergo BMT do not survive, this procedure is rarely performed.

Prognosis

The severity of anemia seems to determine the course of an individual's osteopetrosis. When pronounced symptoms are present at the time of birth, the child's condition deteriorates rapidly. Death usually occurs within two years. When mild or moderate disease develops in older children or adults, and symptoms can be controlled, the patient is likely to survive.

ORGANIZATIONS

Osteoporosis and Related Bone Diseases—National Resource Center, 2 AMS Circle, Bethesda, MD, 20892-3676, (202)223-0344, (202)293-2356, NIAMS BoneInfo@mail.nih.gov, http://www.niams.nih.gov/Health_Info/ bone/default.asp.

Maureen Haggerty

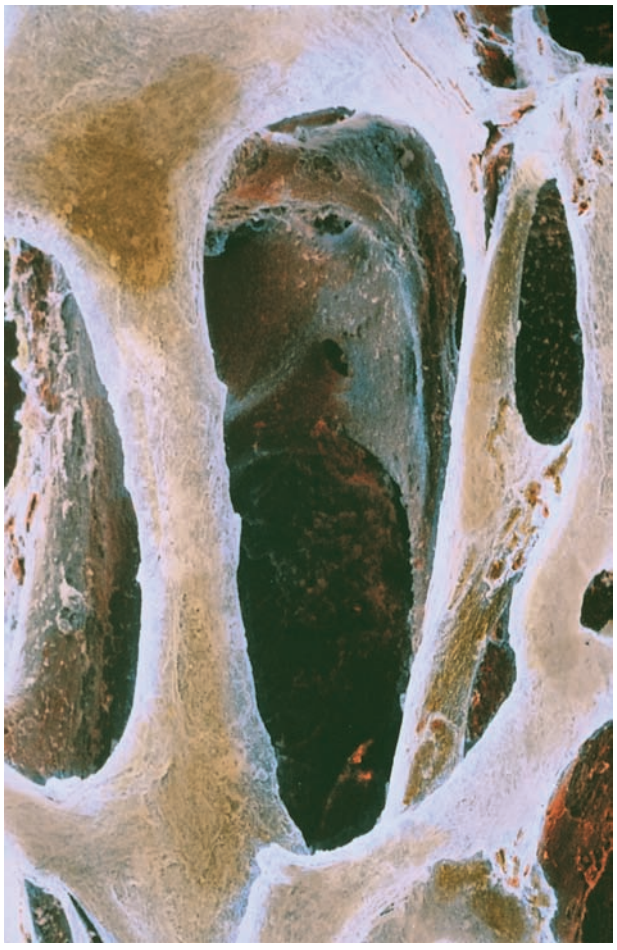
Osteoporosis

Definition

Osteoporosis is a disease characterized by low bone mass and deterioration of bone tissues, leading to bone fragility and, consequently, an increase in fracture risk. The term osteoporosis comes from the Greek word *osteon*, meaning bone, and *porus*, meaning pore or passage. Osteoporosis literally makes bones porous. The amount of **calcium** stored in human bones decreases over time, causing the skeleton to weaken.

Demographics

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) estimates that 10



A scanning electron microscopy (SEM) image of cancellous (spongy) bone from an osteoporosis patient. Osteoporosis is characterized by increased brittleness of the bones and a greater risk of fractures. This is reflected here in the thin appearance of the bony network of the cancellous bone that forms the core of the body's long bones. *(Professor P. Motta/ Photo Researchers, Inc.)*

million people (8 million women and 2 million men) in the United States have osteoporosis as of 2009, with another 34 million adults having low bone density, a condition called **osteopenia**. Osteopenia can develop into osteoporosis if it is not treated. Osteoporosis is responsible for more than 1.5 million **fractures** annually in the United States, including 300,000 hip fractures, 700,000 vertebral fractures, 250,000 wrist fractures, and more than 300,000 fractures in other parts of the body. The costs of treating osteoporosis and the fractures that it causes come to $14 billion each year. An osteoporosis-related fracture will occur in one in two women and one in eight men over the age of 50.

Although osteoporosis is often thought of as a woman's disease, it affects men, too. Men who take certain medications—particularly cortisone and other steroid drugs— have the same risk of developing osteoporosis as women who take these medications. Each year, 80,000 American men with osteoporosis will suffer a hip fracture, and one-third of them will die within a year.

Worldwide, osteoporosis is estimated to affect one in three women and one in 12 men over the age of 50. It is the most common metabolic bone disease in the world.

Osteoporosis in children is very unusual. There is a rare condition called juvenile idiopathic osteoporosis: About 60 cases have been reported worldwide. The word idiopathic means that the cause of the condition is unknown.

Description

Osteoporosis is a disease that has no noticeable symptoms until the weakening of the bones leads to problems with posture, lower back **pain**, and brittle or easily broken bones. Although osteoporosis can appear at any age, it is most commonly a disease of adults. It develops when the wearing-out and removal of old bone—a process known as resorption—outpaces the production of new bone tissue.

Bone is living material. It is constantly broken down by cells called osteoclasts and built up again by cells called osteoblasts. This process is called bone remodeling, and it continues throughout an individual's life. Normally, more bone is built up than is broken down from birth through adolescence. In the late teens or early 20s, people reach their peak bone mass—the most bone that they will ever have. For 20 or so years, bone gain and bone loss remain approximately balanced in healthy people with good **nutrition**. However, when women enter **menopause**, usually in their mid to late forties, for the first five to seven years bone loss occurs at a rate of 1–5% a year. Men tend to lose less bone, and the loss often begins later in life. Osteoporosis occurs when bone loss continues and bones become so thin and their internal structure is so damaged that they break easily.

Bone remodeling occurs because bone is made primarily of calcium and phosphorous. Calcium is critically involved in muscle contraction, nerve impulse transmission, and many metabolic activities within cells. To remain healthy, the body must keep the level of free calcium ions (Ca^{2+}) within a very narrow concentration range. Besides providing a framework for the body, bone acts as a calcium "bank." When excess calcium is present in the blood, osteoblasts deposit it into bones where it is stored. When too little calcium is present, osteoblasts dissolve calcium from bones and

move it into the blood. This process is controlled mainly by parathyroid hormone (PTH) secreted by the parathyroid glands in the neck. As people age, various conditions cause them to take more calcium out of the "bone bank" than they deposit, and osteoporosis (which literally means porous bones) eventually develops. A person's peak bone mass and the rate at which they lose it in later life affects their risk of developing osteoporosis; the higher the peak bone mass at age 30, the lower the risk of osteoporosis later on.

Doctors divide osteoporosis into three categories or types. Types 1 and 2 are considered primary because they are not caused by other diseases or conditions. Type 3 osteoporosis is sometimes called secondary osteoporosis because it results from taking certain drugs or having other diseases.

- Type 1: This type occurs in women after menopause and results from declining levels of estrogen and other sex hormones in the body. Sometimes called postmenopausal osteoporosis, it is the most common type of the disease. Type 1 may also occur in older men due to low levels of the sex hormone testosterone.
- Type 2: Sometimes called senile osteoporosis, this type of osteoporosis occurs in elderly men as well as elderly women because of decreased bone formation due to aging.
- Type 3: Type 3 osteoporosis is caused by long-term use of certain medications, particularly steroids and drugs given to treat epilepsy; and by such conditions as malnutrition, Klinefelter syndrome, Turner syndrome, thyroid disorders, hemophilia, Marfan syndrome, rheumatoid arthritis, lupus, and lymphoma. Some studies indicate that people receiving chemotherapy for cancer are also at increased risk for this type of osteoporosis.

Risk factors

There are two basic categories of risk factors for osteoporosis. Some of these risk factors can be changed, while others cannot be altered. Risk factors that cannot be changed include:

- Sex. Women have four times the risk of the disease as men, particularly after the menopause.
- Race/ethnicity. Asian and Caucasian women have a higher risk of osteoporosis than African American or Hispanic women. Although their risk is smaller, African-American and Hispanic-American women should still take precautions against osteoporosis. An estimated 10% of African-American women over age 50 have osteoporosis and an additional 30% have low bone density that puts them at risk of developing osteoporosis.
- Body build. Small-boned people of either sex are at greater risk of osteoporosis than people with average or heavy bones.
- Age. Both men and women have an increased risk of osteoporosis as they get older. The highest incidence of the disease is found among those men and women aged 80 or older.
- Genetic factors. A tendency for bones to fracture easily is thought to run in some families.

Risk factors for osteoporosis that people can change include:

- Low sex hormone levels. These can be raised in both men and women by hormone replacement therapy.
- Eating disorders, particularly anorexia.
- Depression. Emotional depression can be treated, most often with a combination of medication and psychotherapy.
- Low intake of calcium and vitamin D. People can change their eating habits and take vitamin or calcium supplements.
- Smoking and alcohol intake. People can quit smoking and drink in moderation.
- Getting the right amount of exercise. Bed rest or inadequate exercise can weaken bones, but so can too much exercise (such as marathon running).
- Medications. People who are taking medications that increase their risk of osteoporosis can ask their doctor about alternatives.

Certain diseases also increase a person's risk of developing osteoporosis:

- hyperthyroidism
- hyperparathyroidism
- celiac disease
- inflammatory bowel disease (IBD)
- cystic fibrosis
- diabetes
- chronic liver disease

Causes and symptoms

The basic cause of osteoporosis is that the loss of bone tissue occurs faster than the production of replacement bone. The increased rate of bone loss can be particularly critical if the person had a low or inadequate peak bone mass to begin with. A low peak bone mass can result from **malnutrition** in childhood; inadequate intake of calcium or vitamin D (necessary for the body to make use of calcium in the diet); an eating

disorder in adolescence, when the body's need for calcium is at its height; or not getting enough **exercise**.

Genetic profile

Osteoporosis results from a complex interaction between genetic and environmental factors throughout life. Evidence suggests that peak bone mass is inherited, but current genetic markers are able to explain only a small proportion of the variation in individual bone mass or fracture risk. As of 2009, no specific mode of inheritance has been identified. Heritability of bone mass has been estimated to account for 60–90% of its variance. Studies have shown reduced bone mass in daughters of osteoporotic women when compared with controls; in men and women who have first-degree relatives with osteoporosis; and in perimenopausal women who have a family history of hip fracture. Body weight in infancy may be a determinant of adult bone mineral area.

Some scientists think that environmental influences during early life interact with the genome to establish the functional level of a variety of metabolic processes involved in skeletal growth.

Many candidate genes exist for osteoporosis, however relatively few have been studied. The first candidate gene to be identified was the vitamin D receptor (VDR) gene, and studies are ongoing as to how much this gene accounts for variance in bone mass. The response of bone mass to dietary supplementation with vitamin D and calcium is known to be dependent, in part, on VDR polymorphisms. Other genes may aid in establishing who would benefit from treatments like **hormone replacement therapy**, bisphosophonates, or exercise. Associations between bone mass and polymorphisms have also been found in the estrogen receptor gene, the interleukin-6 genes, the transforming growth factor beta, and a binding site of the collagen type I alpha1 (COLIA1) gene.

The risk of osteoporosis is greatly determined by peak bone mass, and any gene linked to fractures in the elderly may possibly be associated with low bone mass in children as well.

Symptoms

Osteoporosis can proceed for a long time without any noticeable symptoms. Some older adults simply notice that their height is shrinking. This loss of height is caused by compression of the bones in the spinal column. Sometimes the vertebrae fracture as they come closer together; this type of injury is called a compression fracture and may produce noticeable back pain.

Over many years, a sequence of spinal compression fractures may cause **kyphosis**, the bent-over posture known as dowager's or widow's hump. These fractures rarely require surgery, and they can range from causing minor discomfort to severe painful episodes of backache. In either case, pain generally subsides gradually over one to two months.

Another common symptom of osteoporosis is a fragility fracture. Fragility fractures occur when a person falls from their standing position or a lower height and breaks a bone that would not break in a person with healthy bone. The most common locations of fragility fractures in people with osteoporosis are the wrists, the hips, and the vertebrae in the spine. The patient may experience the pain in various ways; some describe it as sharp while others describe it as dull or nagging. In some cases the pain gets worse when the patient is trying to walk or move around.

Diagnosis

Since osteoporosis can develop undetected for decades until a fracture occurs, early diagnosis is important. Osteoporosis is most likely to be diagnosed following a fragility fracture. The doctor will take a careful history of the patient's risk factors, including a possible family history of easily broken bones as well as a medication history and questions about such lifestyle factors as exercise, diet, **smoking**, and drinking.

Examination

The **physical examination** should include measurement of the patient's height, evaluation of possible loss of height, and assessment for evidence of kyphosis.

Tests

The doctor may order a blood test to rule out a thyroid disorder or to check the levels of sex hormones in the patient's blood.

A bone mineral density test (BMD) is the only way to diagnose osteoporosis and determine risk for future fracture. The painless, noninvasive test measures bone density and helps determine whether medication is needed to help maintain bone mass, prevent further bone loss, and reduce fracture risk. To take this test, the patient lies on an examination table while two x-ray beams of different intensities are aimed at the bones. The result is called a T-score. It is calculated by comparing the patient's bone mineral density to that of a healthy 30-year-old of the same sex and race. A T-score of -1.0 or higher is normal; a score between -1.0 and -2.5 indicates osteopenia; a score below -2.5 indicates osteoporosis.

KEY TERMS

Alendronate—A non-hormonal drug used to treat osteoporosis in postmenopausal women.

Bisphosphonates—Compounds that slow bone loss and increase bone density.

Calcitonin—A naturally occurring hormone made by the thyroid gland that can be used as a drug to treat osteoporosis and Paget's disease of the bone.

Compression fracture—A fracture caused by the collapse of a vertebra in the spinal column, usually caused either by trauma or by weakening of the bone in osteoporosis.

Fragility fracture—A fracture that occurs as a result of a fall from standing height or less. A person with healthy bones would not suffer a broken bone falling from a standing position.

Glucocorticoids—A general class of adrenal cortical hormones that are mainly active in protecting against stress and in protein and carbohydrate metabolism. They are widely used in medicine as anti-inflammatories and immunosuppresives.

Kyphosis—The medical term for curvature of the upper spine. Osteoporosis is a common cause of kyphosis in older adults.

Osteoblast—A type of bone cell that is responsible for bone formation. The number of osteoblasts in a person's body decreases with age.

Osteoclast—A type of bone cell that removes bone tissue.

Osteopenia—The medical name for low bone mass, a condition that often precedes osteoporosis.

Polymorphism—A change in the base pair sequence of DNA that may or may not be associated with a disease.

Resorption—The removal of old bone from the body.

Selective estrogen receptor modulator—A hormonal preparation that offers the beneficial effects of hormone replacement therapy (HRT) without the increased risk of breast and uterine cancer associated with HRT.

T-score—The score on a bone densitometry test, calculated by comparing the patient's bone mineral density to that of a healthy 30-year-old of the same sex and race.

Vertebra (plural, vertebrae)—One of the segments of bone that make up the spinal column.

Several different machines measure bone density. Central machines, such as the dual energy x-ray absorptiometry (DXA or DEXA) and quantitative computed tomography (QCT), measure density in the hip, spine and total body. Peripheral machines, such as radiographic absorptiometry (RA), peripheral dual energy x-ray absorptiometry (pDXA), and peripheral quantitative computed tomography (pQCT), measure density in the finger, wrist, kneecap, shin bone, and heel.

A physician may be able to observe osteoporotic bone in a routine spinal x-ray, however, BMD tests are more accurate and can measure small percentages of lost bone density. In an x-ray, osteoporotic bone appears less dense and the image is less distinct, suggesting weaker bone.

As of 2009, the U.S. Preventive Services Task Force recommends using dual energy x-ray absorptiometry to screen all women 65 years and older and women 60 to 64 years of age who have increased fracture risk. Some physicians also recommend bone density testing at menopause at whatever age it occurs to begin preventive treatment if necessary. The major risk factors are low body weight, low calcium intake, poor health, and a history of osteoporosis in the family.

Some health care organizations recommend considering screening in all men 70 years and older, as well as for men with one of the following risk factors: bone fracture, poor health, or low testosterone levels.

Treatment

Traditional

Drugs

Medications are an important part of treatment for osteoporosis. Various drugs have been shown to be effective in preventing or slowing bone loss and increasing bone mass. These include:

- *Hormone replacement therapy*. For women with postmenopausal osteoporosis, estrogen replacement therapy helps halt bone loss and exerts a modest bone-building effect. Stopping hormone therapy restarts bone loss, so long-term treatment is usually recommended. HRT used to be considered the mainstay of treating osteoporosis in women. But

with newer studies indicating that HRT increases the risk of heart disease and cancer in some women, other medications that work by slowing the process of bone loss or by increasing bone density over time are more widely prescribed as of 2009. Some of these medications have the additional advantage of working well in men with osteoporosis and in people who must take steroid drugs for other health problems.

- *Raloxifene*. One of a class of drugs called selective estrogen receptor modulators (SERMs) that appear to prevent bone loss, raloxifene (Evista) produces small increases in bone mass. It is approved for the prevention and treatment of osteoporosis. Like estrogens, SERMs produce changes in blood lipids that may protect against heart disease, although the effects are not as potent as that of estrogen. Unlike estrogens, SERMs do not appear to stimulate uterine or breast tissue.
- *Alendronate*. One of a class of medications called bisphosphonates, alendronate (Fosamax) may prevent bone loss, increase bone mass, and reduce the risk of fractures. Patients receiving any bisphosphonate, however, should take calcium and vitamin D before and during treatment with a bisphosphonate to lower the risk of side effects from these drugs.
- *Risedronate*. Also from the bisphosphonate family, risedronate (Actonel) has been shown to reduce bone loss, increase bone density, and reduce the risk of fractures.
- *Calcitonin*. A hormone that regulates calcium levels in the blood, calcitonin may prevent bone loss. It is approved for treatment of diagnosed osteoporosis.

Lifestyle changes

Recommended lifestyle changes that can reduce the rate of bone loss include regular exercise, particularly weight-bearing forms of exercise like walking, dancing, treadmill exercises, and jumping. Other measures include quitting smoking, taking supplemental vitamin D and calcium, and watching one's alcohol intake.

Surgery

Unfortunately, surgical treatment for osteoporosis is often necessary. It is usually tied to fractures that result from advanced stages of the disease. For complicated fractures, such as broken hips, hospitalization and a surgical procedure are required. In hip replacement surgery, the broken hip is removed and replaced with a new hip made of plastic, or metal and plastic. Though the surgery itself is usually successful, complications of the hip fracture can be serious. Those individuals have a 5–20% greater risk of dying within the first year following that injury than do others in their age group. A large percentage of those who survive are unable to return to their previous level of activity, and many end up moving from self-care to a supervised living situation or nursing home. Getting early treatment and taking steps to reduce bone loss are vital.

Alternative

Alternative treatments for osteoporosis focus on maintaining or building strong bones. They include nutritional and herbal therapies and homeopathy.

NUTRITIONAL THERAPY. A healthful diet low in fats and animal products and containing whole grains, fresh fruits and vegetables, and calcium-rich foods (such as dairy products, dark-green leafy vegetables, sardines, salmon, and almonds), along with **nutritional supplements** (such as calcium, magnesium, and vitamin D) are important components of nutritional approaches to treating this disease.

Women should also eat more soy products such as tofu, soy burgers, other soy-based products, or miso. Soy beans contain a substance called isoflavones which have estrogen-like activity. Isoflavones may help to increase bone density, alleviate hot flashes and other menopausal symptoms, lower the risk of **cancer**, and even reduce the risk of heart attacks. Natural hormone therapy, such as the use of soy products, is a safer alternative to synthetic estrogenic hormones, which may increase the risk of **breast cancer**.

In addition, women should avoid foods that may accelerate bone loss. They should avoid having too much salt in their diet, not only because salt raises the blood pressure but also because it may contribute to osteoporosis. They should also cut down on coffee, caffeinated sodas, and alcohol. High consumption of these beverages, studies have shown, are associated with accelerated drop in bone density and increase risk of bone fracture in old age. Caffeinated sodas are especially bad for the bones because in addition to containing **caffeine**, they have high amounts of phosphoric acid. Phosphoric acid increases bone resorption, thus decreasing bone density.

HERBAL SUPPLEMENTS. Herbal supplements for osteoporosis emphasize such calcium-containing plants as horsetail (*Equisetum arvense*), oat straw (*Avena sativa*), alfalfa (*Medicago sativa*), licorice (*Glycyrrhiza glabra*), marsh mallow (*Althaea officinalis*), and sourdock (*Rumex crispus*). There are, however, few data from clinical trials to support the use of these herbs.

HOMEOPATHY. Homeopathic remedies for osteoporosis focus on treatments believed to help the body absorb calcium. These remedies may include such substances as *Calcarea carbonica* (calcium carbonate) or *Silica* (flint). Again, there are few data other than isolated case reports regarding the effectiveness of these remedies.

Prognosis

The prognosis for osteoporosis depends on its type and cause; the patient's age, sex, and ethnicity; the presence of other diseases or disorders; and the patient's willingness to follow the doctor's recommendations about medications and lifestyle changes.

People do not die from osteoporosis itself but from complications from bone fractures. These complications can include chronic pain, **pneumonia**, **blood clots** in the deep veins of the leg, or breathing disorders caused by the stooped posture resulting from compression fractures in the spine. The **death** rate within the first six months after a hip fracture is 14 %. Even patients who survive often have a greatly lowered quality of life.

Osteoporosis is likely to continue to be a serious health concern because of the **aging** of the American population. As people continue to live longer, the number of people with Type 2 (age-related) osteoporosis will increase. In addition, people who are at risk for osteoporosis because of sex, race, or a family history of weak bones may not be completely able to prevent the disease even by careful attention to diet and exercise. It is possible that more effective medications to prevent bone loss or restore bone density will be developed.

Prevention

People cannot change such risk factors for osteoporosis as age, sex, and race, but they can eat properly, exercise regularly, and ask their doctor about vitamin D and calcium supplements. Male as well as female adolescents should participate in sports and get adequate calcium in the diet in order to build up a high peak bone mass before midlife. Women who have not yet gone through menopause should get at least 1,000 milligrams (mg) of elemental calcium and a minimum of 800 international units (IU) of vitamin D every day; women who have completed menopause, anyone who must take steroid medications, and all men and women over 65 should aim for 1,500 mg of elemental calcium and at least 800 IU of vitamin D daily.

Other recommendations for lowering the risk of osteoporosis in older adults include:

- Participate in regular weight-bearing exercise, such as walking, jogging, tennis, weight-lifting, and cross-county skiing to strengthen bones.
- Stop smoking.
- Reduce intake of caffeine to not more than three cups a day.
- Limit alcohol intake to not more than two drinks per day.
- Avoid excessive amounts of dietary fiber as it binds to calcium and may interfere with absorption.

Older adults should also try to reduce their risk of falls whether or not they have osteoporosis. There are balance and strength exercises that older adults can practice at home. In addition, such safety measures as wearing properly fitted shoes with non-slip soles, checking one's house for loose rugs, poor lighting, and other hazards, installing grab bars in shower stalls, and keeping a cordless phone within easy reach in case of an accident are all good forms of fall prevention.

Nutrition/Dietetic concerns

Calcium and vitamin D are both essential to building and maintaining strong bones. Dairy products are a good source of these nutrients. Calcium supplements are recommended for many women who have difficulty getting enough calcium in their diet. Recommended dietary allowances (RDAs) and lists of foods that are high in calcium and vitamin D can be found in their individual entries. Fluoride also is needed to develop healthy bones and teeth.

Young people with the eating disorder **anorexia nervosa** are at especially high risk of developing osteoporosis later in life because they have poor, unbalanced **diets**. The menstrual cycle in girls with anorexia is often delayed in starting or if it has started, stops. In addition, people with anorexia almost never get enough calcium to build strong bones during adolescence and they make unusually larger amounts of cortisol, a corticosteroid made by the adrenal gland that causes bone loss. Although the effect of this eating disorder on bones will not be seen until the individual is older, failure to build strong, dense bones during the teen years substantially increases the risk of osteoporosis later.

Health care team roles

Doctors, nurses, physical therapists, radiation technologists, and dietitians all play roles in the process of controlling osteoporosis. Because osteoporosis is treatable but not curable, the main responsibility for controlling the progress of the disease rests with the patient. All of these team members play an important

role in identifying risk of osteoporosis before it strikes and in convincing the patient to take appropriate steps (including lifestyle modification) to minimize the dangers of fracturing major bones.

Caregiver concerns

A survey conducted by the International Osteoporosis Foundation (IOF) in 11 countries showed widespread denial of personal risk by postmenopausal women, lack of discussion about osteoporosis with their primary care physician, and restricted access to diagnosis and treatment before occurrence of the first fracture. The unfortunate result is that osteoporosis is too often underdiagnosed and undertreated in this population group.

Resources

BOOKS

Alexander, Ivy, and Karla A. Knight. *100 Questions & Answers About Osteoporosis and Osteopenia*. Boston: Jones and Bartlett Publishers, 2006.

Bissinger, Margie. *Osteoporosis: An Exercise Guide*. Parsippany, NJ: Workfit Consultants, 2008.

Gueldner, Sarah H., et al. *Osteoporosis: Clinical Guidelines for Prevention, Diagnosis, and Management*. New York: Springer, 2007.

Hoffman, Gretchen. *Osteoporosis*. Tarrytown, NY: Marshall Cavendish Benchmark, 2008.

Nelson, Miriam E., and Sarah Wernick. *Strong Women, Strong Bones*.New York: Perigee Trade, 2006.

PERIODICALS

Ali, T., et al. "Osteoporosis in Inflammatory Bowel Disease." *American Journal of Medicine 122 (July 2009): 599–604*.

Andersen, S. J. "Osteoporosis in the Older Woman." *Clinical Obstetrics and Gynecology* 50 (September 2007): 752–766.

Cabanillas, M. E. "Elderly Patients with non–Hodgkin Lymphoma Who Receive Chemotherapy Are at Higher Risk for Osteoporosis and Fractures." *Leukemia & Lymphoma* 48 (August 2007): 1514–1521.

Carda, S., et al. "Osteoporosis after Stroke: A Review of the Causes and Potential Treatments." *Cerebrovascular Diseases* 28 (June 30, 2009): 191–200.

Ersoy, F. F. "Osteoporosis in the Elderly with Chronic Kidney Disease." *International Urology and Nephrology* 39 (2007): 321–331.

Haas, M. L., and K. Moore. "Osteoporosis: An Invisible, Undertreated, and Neglected Disease of Elderly Men." *Journal of Elder Abuse & Neglect* 19 (2007): 61–73.

Kennel, K. A., and M. T. Drake. "Adverse Effects of Bisphosphonates: Implications for Osteoporosis Management." *Mayo Clinic Proceedings* 84 (July 2009): 632–37.

Madureira, M. M., et al. "Balance Training Program Is Highly Effective in Improving Functional Status and Reducing the Risk of Falls in Elderly Women with Osteoporosis: A Randomized Controlled Trial." *Osteoporosis International* 18 (April 2007): 419–425.

Pigozzi, F., et al. "Bone Mineral Density and Sport: Effect of Physical Activity." *Journal of Sports Medicine and Physical Fitness* 49 (June 2009): 177–83.

Sweet, M. G., et al. "Diagnosis and Treatment of Osteoporosis." *American Family Physician* 79 (February 1, 2009): 193–202.

Troen, B. R. "Osteoporosis in Older People: A Tale of Two Studies (and Three Treatments)." *Journal of the American Geriatric Society* 54 (May 2006): 853–855.

OTHER

3D Health Animations. *Osteoporosis*. http://www.healthscout.com/animation/68/48/main.html

American Family Physician Patient Handout. *Osteoporosis*. http://www.aafp.org/afp/20040301/1207ph.html

Nalamachu, Srinivas, and Shireesha Nalamasu. "Osteoporosis (Primary)." *eMedicine*, September 25, 2008. http://emedicine.medscape.com/article/311331-overview

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). *Osteoporosis Overview*. http://www.niams.nih.gov/Health_Info/Bone/Osteoporosis/default.asp

National Institutes of Health (NIH). *Check Up on Your Bones*. http://www.niams.nih.gov/Health_Info/Bone/Optool/index.asp. This is an interactive website for people of all ages to identify personal risk factors for osteoporosis and suggest possible approaches for reducing risk.

National Osteoporosis Foundation (NOF). *Osteoporosis: What Is It?* http://www.nof.org/osteoporosis/index.htm

ORGANIZATIONS

Arthritis Foundation, P.O. Box 7669, Atlanta, GA, 30357-0669, (800) 283-7800, http://www.arthritis.org/index.php.

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), 1 AMS Circle, Bethesda, MD, 20892-3675, (301) 495-4484, (877) 22-NIAMS, (301) 718-6366, NIAMSinfo@mail.nih.gov, http://www.niams. nih.gov/.

National Osteoporosis Foundation (NOF), 1232 22nd Street N.W., Washington, DC, 20037-1202, (202) 223-2226, (800) 231-4222, http://www.nof.org/.

Osteoporosis Canada, 1090 Don Mills Road, Suite 301, Toronto, Ontario, Canada, M3C 3R6, 416-696-2663, (800) 463-6842 (English), (800) 977-1778 (French), (416) 696-2673, http://www.osteoporosis.ca/.

Jennifer F. Wilson, MS
Tish Davidson, AM
Rebecca J. Frey, PhD

Osteosarcoma *see* **Sarcomas**

Ostomy

Definition

A surgical procedure creating an opening in the body for the discharge of body wastes.

Purpose

Certain diseases of the bowel or urinary tract involve removing all or part of the intestine or bladder. This creates a need for an alternate way for feces or urine to leave the body. To fill that need, an opening is surgically created in the abdomen for body wastes to pass through. The surgical procedure is called an ostomy. The opening that is created at the end of the bowel or ureter is called a stoma, which is pulled through the abdominal wall.

Description

Different types of ostomy are performed depending on how much and what part of the intestines or bladder is removed.

The three most common types of ostomies are:

- colostomy
- ileostomy
- urostomy

Colostomy

A **colostomy** is a when a small portion of the colon (large intestine) is brought to the surface of the abdominal wall to allow stool to be eliminated. A colostomy may be temporary or permanent. A permanent colostomy usually involves the loss of the rectum.

A colostomy might be performed due to **cancer**, **diverticulitis**, imperforate anus, **Hirschsprung's disease**, or trauma to the affected area.

Ileostomy

An ileostomy is an opening created in the small intestine to bypass the colon for stool elimination. The end of the ileum, which is the lowest part of the small intestine, is brought through the abdominal wall to form a stoma.

Ileoanal reservoir surgery is an alternative to a permanent ileostomy. It requires two surgical procedures. The first removes the colon and rectum, and creates a temporary ileostomy. The second procedure creates an internal pouch from a portion of the small intestine to hold stool. This is then attached to the anus. Since the muscle of the rectum is left in place, there is control over bowel movements.

An ileostomy might be performed due to ulcerative **colitis**, **Crohn's disease**, or **familial polyposis**.

Urostomy

A urostomy is a surgical procedure that diverts urine away from a diseased or defective bladder. Among several methods to create the urostomy, the most common method is called an ileal or cecal conduit. Either a section at the end of the small intestine (ileum) or at the beginning of the large intestine (cecum) is relocated surgically to form a stoma for urine to pass out of the body. Other common names for this procedure are ileal loop or colon conduit.

A urostomy may be performed due to **bladder cancer**, spinal cord injuries, malfunction of the bladder, and **birth defects** such as **spina bifida**.

Since colostomy, ileostomy, and usotomy bypass the sphincter muscle, the patient has no voluntary control over bowel movements and must wear an external pouch to catch the discharge.

Preparation

Aftercare

The skin around the stoma, called the peristomal skin, must be protected from direct contact with discharge. The discharge can be irritating to the stoma since it is very high in digestive enzymes. The peristomal skin should be cleansed with plain soap and rinsed with water at each change of the pouch.

The stoma can change in size due to weight gain/loss or several other situations. To ensure proper fit of discharge pouch the stoma should be measured each time supplies are purchased.

Risks

People with ostomies can be prone to certain types of skin infections. Skin irritations or **rashes** around the stoma may be caused by leakage from around the pouch due to an improperly fitted pouch. Correctly fitting the pouch and carefully cleaning the skin around the stoma after each change are the best ways of preventing skin irritation.

Urinary tract infections are common among people who have urostomies. Preventative measures include drinking plenty of fluids, emptying the pouch regularly and using a pouch with an anti-reflux valve to prohibit the discharge from moving back into the stoma.

KEY TERMS

Crohn's disease—A chronic inflammatory disease, primarily involving the small and large intestine, but which can affect other parts of the digestive system as well.

Diverticulitis—Inflammation of the diverticula (small outpouchings) along the wall of the colon, the large intestine.

Familial polyposis—An inherited condition in which several hundred polyps develop in the colon and rectum.

Hirschsprung disease—Hirschsprung disease is a congenital abnormality (birth defect) of the bowel in which there is absence of the ganglia (nerves) in the wall of the bowel. Nerves are missing starting at the anus and extending a variable distance up the bowel. This results in megacolon (massive enlargement of the bowel) above the point where the nerves are missing. (The nerves are needed to assist in the natural movement of the muscles in the lining of the bowels that move bowel contents through.)

Ileum—The lowest part of the small intestine, located beyond the duodenum and jejunum, just before the large intestine (the colon).

Imperforate anus—A congenital malformation (a birth defect) in which the rectum is a blind alley (a cul-de-sac) and there is no anus.

Spina bifida—A birth defect (a congenital malformation) in which there is a bony defect in the vertebral column so that part of the spinal cord, which is normally protected within the vertebral column, is exposed. People with spina bifida can suffer from bladder and bowel incontinence, cognitive (learning) problems and limited mobility.

Normal results

Most ostomy pouches are inconspicuous and can be worn under almost any kind of clothing. There are typically no restrictions of activity, sport, or travel with an ostomy. Certain contact sports would warrant special protection for the stoma.

After recovery from surgery, most people with ostomies can resume a balanced diet.

Ostomy surgery does not generally interfere with a person's sexual or reproductive capacities.

Abnormal results

After an ileostomy, water and electrolyte loss may occur. It may be necessary to drink a significant amount of fluid or fruit juice each day to prevent **dehydration**.

After any type of ostomy surgery digestion and absorbtion of medications may also be affected.

High-fiber foods can cause blockages in the ileum, especially after surgery. Chewing food well helps break fiber into smaller pieces and makes it less likely to accumulate at a narrow point in the bowel. Drinking plenty of fluids can also help.

ORGANIZATIONS

Crohn's and Colitis Foundation of America, 386 Park Avenue South, 17th Floor, New York, NY, 10016, (800)932-2423, info@ccfa.org, http://www.ccfa.org.

International Foundation for Functional Gastrointestinal Disorders, P.O. Box 17864, Milwaukee, WI, 53217-8076, (414)964-1799, (414)964-7176, (888) 964-2001, iffd@iffgd.org, http://www.iffgd.org/.

National Diabetes Information Clearinghouse (NDIC), 1 Information Way, Bethesda, MD, 20892-3560, (703)738-4929, (800)860-8747, ndic@info.niddk.nih.gov, http://diabetes.niddk.nih.gov/.

United Ostomy Association, Inc. (UOA), P.O. Box 512, Northfield, MN, 55057-0512, (800)826-0826, info@ostomy.org, http://www.ostomy.org.

Gary Gilles

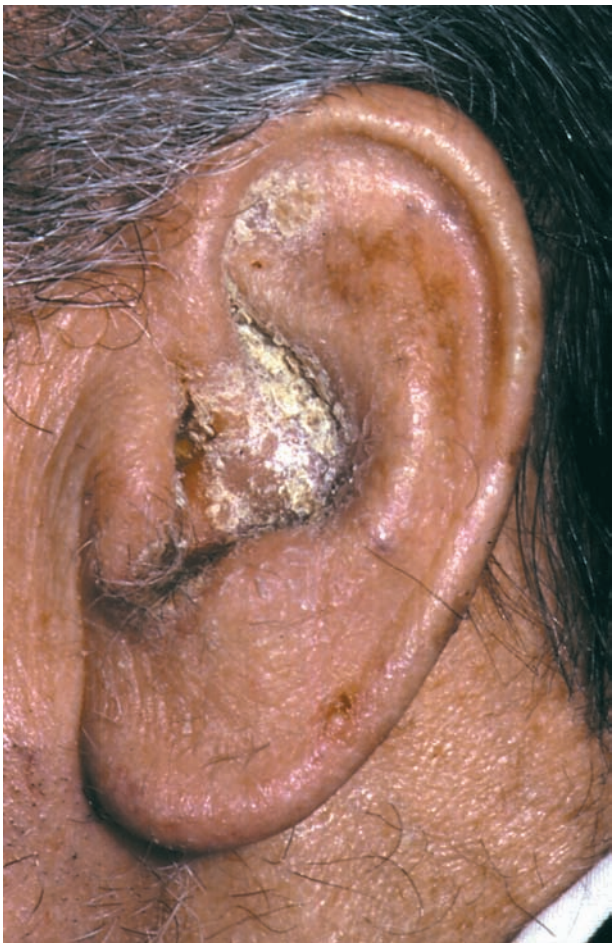
Otitis externa

Definition

Otitis externa refers to an infection of the ear canal, the tube leading from the outside opening of the ear in towards the ear drum.

Description

The external ear canal is a tube approximately 1 in (2.5 cm) in length. It runs from the outside opening of the ear to the start of the middle ear, designated by the ear drum or tympanic membrane. The canal is partly cartilage and partly bone. In early childhood, the first two-thirds of the canal is made of cartilage, and the last one-third is made of bone. By late



A close-up image of the ear of an elderly man suffering from non-infectious otitis externa. The skin in the ear canal and outer ear is scaly. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

childhood, and lasting throughout all of adulthood, this proportion is reversed, so that the first one-third is cartilage, and the last two-thirds is bone. The lining of the ear canal is skin, which is attached directly to the covering of the bone. Glands within the skin of the canal produce a waxy substance called cerumen (popularly called earwax). Cerumen is designed to protect the ear canal, repel water, and keep the ear canal too acidic to allow bacteria to grow.

Causes and symptoms

Bacteria, fungi, and viruses have all been implicated in causing ear infections called otitis externa. The most common cause of otitis externa is bacterial infection. The usual offenders include *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Staphylococcus epidermidis*, and bacteria of the family called Streptococci. Occasionally, fungi may cause otitis externa. These include *Candida* and *Aspergillus*. Two types of viruses, called herpesvirus hominis and varicella-zoster virus, have also been identified as causing otitis externa.

Otitis externa occurs most often in the summer months, when people are frequenting swimming pools and lakes. Continually exposing the ear canal to moisture may cause significant loss of cerumen. The delicate skin of the ear canal, unprotected by cerumen, retains moisture and becomes irritated. Without cerumen, the ear canal stops being appropriately acidic, which allows bacteria the opportunity to multiply. Thus, the warm, moist, dark environment of the ear canal becomes a breeding ground for bacteria.

Other conditions predisposing to otitis externa include the use of cotton swabs to clean the ear canals. This pushes cerumen and normal skin debris back into the ear canal, instead of allowing the ear canal's normal cleaning mechanism to work, which would ordinarily move accumulations of cerumen and debris out of the ear. Also, putting other items into the ear can scratch the canal, making it more susceptible to infection.

The first symptom of otitis externa is often **itching** of the ear canal. Eventually, the ear begins to feel extremely painful. Any touch, movement, or pressure on the outside structure of the ear (auricle) may cause quite severe **pain**. This is because of the way in which the skin lining the ear canal is directly attached to the covering of the underlying bone. If the canal is sufficiently swollen, hearing may become muffled. The canal may appear swollen and red, and there may be evidence of greenish-yellow pus.

In severe cases, otitis externa may have an accompanying **fever**. Often, this indicates that the outside ear structure (auricle) has become infected as well. It will become red and swollen, and there may be enlarged and tender lymph nodes in front of, or behind, the auricle.

A serious and life-threatening otitis externa is called malignant otitis externa. This is an infection which most commonly affects patients who have diabetes, especially the elderly. It can also occur in other patients who have weakened immune systems. In malignant otitis externa, a patient has usually had minor symptoms of otitis externa for some months, with pain and drainage. The causative bacteria is usually *Pseudomonas aeruginosa.* In malignant otitis externa, this bacteria spreads from the external canal into all of the nearby tissues, including the bones of the skull. Swelling and destruction of these tissues may lead to damage of certain nerves, resulting in spasms of the jaw muscles or **paralysis** of the facial muscles. Other, more severe, complications of this very destructive infection include **meningitis**

(swelling and infection of the coverings of the spinal cord and brain), brain infection, or **brain abscess** (the development of a pocket of infection with pus).

Diagnosis

Diagnosis of uncomplicated otitis externa is usually quite simple. The symptoms alone, of ear pain worsened by any touch to the auricle, are characteristic of otitis externa. Attempts to examine the ear canal will usually reveal redness and swelling. It may be impossible (due to pain and swelling) to see much of the ear canal, but this inability itself is diagnostic.

If there is any confusion about the types of organisms causing otitis externa, the canal can be gently swabbed to obtain a specimen. The organisms present in the specimen can then be cultured (allowed to multiply) in a laboratory, and then viewed under a microscope to allow identification of the causative organisms.

If the rare disease malignant otitis externa is suspected, computed tomography scan (CT scan) or **magnetic resonance imaging** (MRI) scans will be performed to determine how widely the infection has spread within bone and tissue. A swab of the external canal will not necessarily reveal the actual causative organism, so some other tissue sample (biopsy) will need to be obtained. The CT or MRI will help the practitioner decide where the most severe focus of infection is located, in order to guide the choice of a biopsy site.

Treatment

Antibiotics which can be applied directly to the skin of the ear canal (**topical antibiotics**) are usually excellent for treatment of otitis externa. These are often combined in a preparation which includes a steroid medication. The steroid helps cut down on the inflammation and swelling within the ear canal. Some practitioners prefer to insert a cotton wick into the ear canal, leaving it there for about 48 hours. The medications are applied directly to the wick, enough times per day to allow the wick to remain continuously saturated. After the wick is removed, the medications are then put directly into the ear canal three to four times each day.

In malignant otitis externa, antibiotics will almost always need to be given through a needle in the vein (intravenously or IV). If the CT or MRI scan reveals that the infection has spread extensively, these IV antibiotics will need to be continued for six to eight weeks. If the infection is in an earlier stage, two weeks of IV antibiotics can be followed by six weeks of antibiotics by mouth.

KEY TERMS

Auricle—The external structure of the ear.

Biopsy—The removal and examination, usually under a microscope, of tissue from the living body. Biopsy is used for diagnosis.

Cerumen—Earwax.

Prognosis

The prognosis is excellent for otitis externa. It is usually easily treated, although it may tend to recur in certain susceptible individuals. Left untreated, malignant otitis externa may spread sufficiently to cause **death**.

Prevention

Keeping the ear dry is an important aspect of prevention of otitis externa. Several drops of a mixture of alcohol and acetic acid can be put into the ear canal after swimming to insure that it dries adequately.

The most serious complications of malignant otitis externa can be avoided by careful attention to early symptoms of ear pain and drainage from the ear canal. Patients with conditions that put them at higher risk for this infection (diabetes, conditions which weakened the immune system) should always report new symptoms immediately.

ORGANIZATIONS

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703)836-4444, http://www.entnet.org.

Rosalyn Carson-DeWitt, MD

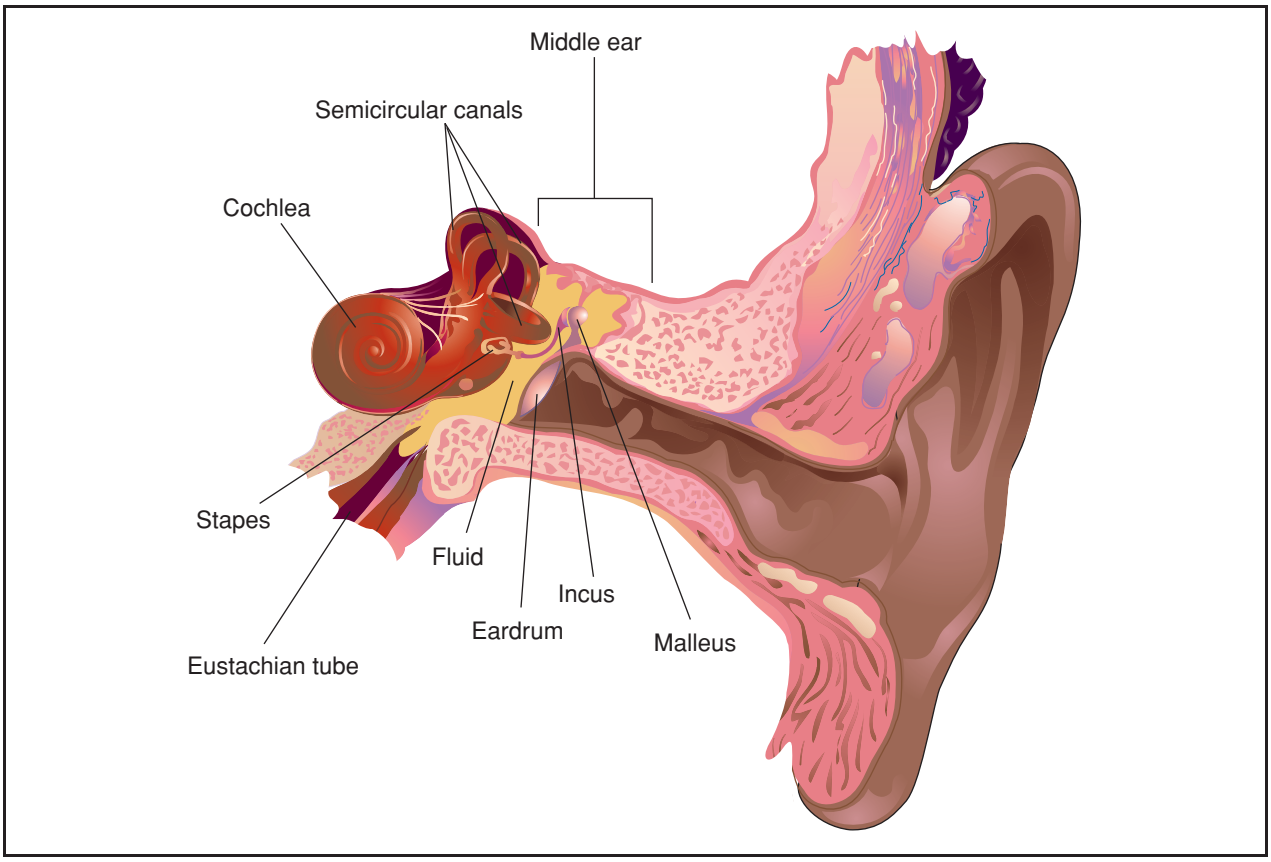
Otitis media

Definition

Otitis media is an infection of the middle ear space, behind the eardrum (tympanic membrane). It is characterized by **pain**, **dizziness**, and partial loss of hearing.

Description

A little knowledge of the basic anatomy of the middle ear will be helpful for understanding the



Otitis media is an ear infection in which fluid accumulates within the middle ear. A common condition occurring in childhood, it is estimated that 85% of all U.S. children will develop otitis media at least once. *(Illustration by Electronic Illustrators Group. Reproduced by permission of Gale, a part of Cengage Learning.)*

development of otitis media. The external ear canal is that tube which leads from the outside opening of the ear to the structure called the tympanic membrane. Behind the tympanic membrane is the space called the middle ear. Within the middle ear are three tiny bones, called ossicles. Sound (in the form of vibration) causes movement in the eardrum, and then the ossicles. The ossicles transmit the sound to a structure within the inner ear, which sends it to the brain for processing.

The nasopharynx is that passageway behind the nose which takes inhaled air into the breathing tubes leading to the lungs. The eustachian tube is a canal which runs between the middle ear and the nasopharynx. One of the functions of the eustachian tube is to keep the air pressure in the middle ear equal to that outside. This allows the eardrum and ossicles to vibrate appropriately, so that hearing is normal.

By age three, almost 85% of all children will have had otitis media at least once. Babies and children between the ages of six months and six years are most likely to develop otitis media. Children at higher risk factors for otitis media include boys, children from poor families, Native Americans, Native Alaskans, children born with **cleft palate** or other defects of the structures of the head and face, and children with **Down syndrome**. Exposure to cigarette smoke significantly increases the risk of otitis media as well as other problems affecting the respiratory system. Also, children who enter daycare at an early age have more upper respiratory infections (URIs or colds), and thus more cases of otitis media. The most usual times of year for otitis media to strike are in winter and early spring (the same times URIs are most common).

Otitis media is an important problem, because it often results in fluid accumulation within the middle ear (effusion). The effusion can last for weeks to months. Effusion within the middle ear can cause significant hearing impairment. When such hearing impairment occurs in a young child, it may interfere with the development of normal speech.

In adults, acute otitis media can lead to such complications as **paralysis** of the facial nerves. Recovery from these complications may take from two weeks to as long as three months.

Causes and symptoms

The first precondition for the development of acute otitis media is exposure to an organism capable of causing the infection. Otitis media can be caused by either viruses or bacteria. Virus infections account for about 15% of cases. The three most common bacterial pathogens are *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis*. About 75% of ear infections caused by *S. pneumoniae* are reported to be penicillin-resistant.

Otitis media may also be caused by other disease organisms, including *Bordetella pertussis*, the causative agent of **whooping cough**, and *Pneumocystis carinii*, which often causes opportunistic infections in patients with **AIDS**.

There are other factors which make the development of an ear infection more likely. Because the eustachian tube has a more horizontal orientation and is considerably shorter in early childhood, material from the nasopharynx (including infection-causing organisms) is better able to reach the middle ear. Children also have a lot of lymph tissue (commonly called the adenoids) in the area of the eustachian tube. These adenoids may enlarge with repeated respiratory tract infections (colds), ultimately blocking the eustachian tubes. When the eustachian tube is blocked, the middle ear is more likely to fill with fluid. This fluid, then, increases the risk of infection, and the risk of **hearing loss** and delayed speech development.

Most cases of acute otitis media occur during the course of a URI. Symptoms include **fever**, ear pain, and problems with hearing. Babies may have difficulty feeding. When significant fluid is present within the middle ear, pain may increase depending on position. Lying down may cause an increase in painful pressure within the middle ear, so that babies may fuss if not held upright. If the fluid build-up behind the eardrum is sufficient, the eardrum may develop a hole (perforate), causing bloody fluid or greenish-yellow pus to drip from the ear. Although pain may be significant leading up to such a perforation, the pain is usually relieved by the reduction of pressure brought on by a perforation.

Recent advances in gene mapping have led to the discovery of genetic factors that increase a child's susceptibility to otitis media. Researchers are hoping to develop molecular diagnostic assays that will help to identify children at risk for severe ear infections.

Diagnosis

Diagnosis is usually made simply by looking at the eardrum through a special lighted instrument called an otoscope. The eardrum will appear red and swollen, and may appear either abnormally drawn inward, or bulging outward. Under normal conditions, the ossicles create a particular pattern on the eardrum, referred to as "landmarks." These landmarks may be obscured. Normally, the light from the otoscope reflects off of the eardrum in a characteristic fashion. This is called the "cone of light." In an infection, this cone of light may be shifted or absent.

A special attachment to the otoscope allows a puff of air to be blown lightly into the ear. Normally, this should cause movement of the eardrum. In an infection, or when there is fluid behind the eardrum, this movement may be decreased or absent.

If fluid or pus is draining from the ear, it can be collected. This sample can then be processed in a laboratory to allow any organisms present to multiply sufficiently (cultured) to permit the organisms to be viewed under a microscope and identified.

Treatment

Medications

Antibiotics are the treatment of choice for acute otitis media (AOM). Different antibiotics are used depending on the type of bacteria most likely to be causing the infection. This decision involves knowledge of the types of antibiotics that have worked on other ear infections occurring within a particular community at a particular time. Options include sulfa-based antibiotics, as well as a variety of **penicillins**, **cephalosporins**, and others. The patient's sensitivity to certain medications, as well as previously demonstrated resistant strains, also contributes to the choice of antibiotic. A 0.3% topical solution of ofloxacin has been recommended as a more effective medication than other oral or **topical antibiotics**.

Some controversy exists regarding whether overuse of antibiotics is actually contributing to the development of bacteria, which may evolve and become able to avoid being killed by antibiotics. Research is being done to try to help determine whether there may be some ear infections that will clear up without antibiotic treatment. In the meantime, the classic treatment of an ear infection continues to involve a seven- to 10-day course of antibiotic medication.

Some medical practitioners prescribe the use of special nosedrops, **decongestants**, or **antihistamines** to improve the functioning of the eustachian tube.

Whether or not antibiotics are used, such pain relievers as Tylenol or Motrin can be very helpful in reducing the pain and inflammation associated with otitis media.

Surgery

In a few rare cases, a surgical perforation to drain the middle ear of pus may be performed. This procedure is called a **myringotomy**. The hole created by the myringotomy generally heals itself in about a week. In 2002 a new minimally invasive procedure was introduced that uses a laser to perform the myringotomy. It can be performed in the doctor's office and heals more rapidly than the standard myringotomy.

Although some doctors have recommended removing the adenoids to prevent recurrent otitis media in young children, recent studies indicate that surgical removal of the adenoids does not appear to offer any advantages over a myringotomy as a preventive measure.

Alternative treatment

Some practitioners believe that **food allergies** may increase the risk of ear infections, and they suggest eliminating suspected food allergens from the diet. The top food allergens are wheat, dairy products, corn, peanuts, citrus fruits, and eggs. Elimination of sugar and sugar products can allow the immune system to work more effectively. A number of herbal treatments have been recommended, including ear drops made with goldenseal (*Hydrastis canadensis*), mullein (*Verbascum thapsus*), **St. John's wort** (*Hypericum perforatum*), and **echinacea** (*Echinacea* spp.). Among the herbs often recommended for oral treatment of otitis media are echinacea and cleavers (*Galium aparine*), or black cohosh (*Cimicifuga racemosa*) and ginkgo (*Ginkgo biloba*). Homeopathic remedies that may be prescribed include aconite (*Acontium napellus*), *Ferrum phosphoricum,* belladonna, chamomile, *Lycopodium,* pulsatilla (*Pulsatilla nigricans*), or silica. **Craniosacral therapy** uses gentle manipulation of the bones of the skull to relieve pressure and improve eustachian tube function.

Prognosis

With treatment, the prognosis for acute otitis media is very good. However, long-lasting accumulations of fluid within the middle ear are a risk both for difficulties with hearing and speech, and for the repeated development of ear infections. Furthermore, without treatment, otitis media can lead to an infection within the nearby mastoid bone, called **mastoiditis**.

Prevention

Although otitis media seems somewhat inevitable in childhood, some measures can be taken to decrease the chance of repeated infections and fluid accumulation. **Breastfeeding** provides some protection against URIs, which in turn protects against the development of otitis media. If a child is bottle-fed, parents should be advised to feed him or her upright, rather than allowing the baby to lie down with the bottle. General good hygiene practices (especially handwashing) help to decrease the number of upper respiratory infections in a household or daycare center.

The use of pacifiers should be avoided or limited. They may act as fomites (inanimate object that can transmit infectious organisms), particularly in a daycare setting. In children who are more susceptible to otitis media, pacifier use can increase by as much as 50% the number of ear infections experienced.

Two vaccines can prevent otitis media associated with certain strains of bacteria. One is designed to prevent **meningitis** and other diseases, including otitis media, that result from infection with *Haemophilus influenzae* type B. Another is a vaccine against *Streptococcus pneumoniae*, a very common cause of otitis media. Children who are at high risk or have had severe or chronic infections may be good candidates for these vaccines; in fact, a recent consensus report among pediatricians recommended routine administration of the pneumococcal conjugate vaccine to children younger than two years, as well as those at high risk for AOM. Parents should consult a health care provider concerning the advisability of this treatment.

Another vaccine that appears to lower the risk of AOM in children is the intranasal vaccine that was recently introduced for preventing **influenza**. Although the flu vaccine was not developed to prevent AOM directly, one team of researchers found that children who were given the vaccine before the start of flu season were 43% less likely to develop AOM than children who were not vaccinated.

As of early 2003, there is no vaccine effective against *M. catarrhalis*. Researchers are working on developing such a vaccine, as well as a tribacterial vaccine that would be effective against all three pathogens that commonly cause otitis media.

A nutrition-based approach to preventive treatment is undergoing clinical trials. This treatment involves giving children a dietary supplement of lemon-flavored cod liver oil plus a multivitamin formula containing

KEY TERMS

Adenoid—A collection of lymph tissue located in the nasopharynx.

Effusion—A collection of fluid which has leaked out into some body cavity or tissue.

Eustachian tube—A small tube which runs between the middle ear space and the nasopharynx.

Fomite—An inanimate object that can transmit infectious organisms.

Myringotomy—A surgical procedure performed to drain an infected middle ear. A newer type of myringotomy uses a laser instead of a scalpel.

Nasopharynx—The part of the airway into which the nose leads.

Ossicles—Tiny bones located within the middle ear which are responsible for conveying the vibrations of sound through to the inner ear.

Perforation—A hole.

Topical—Referring to a medication applied to the skin or outward surface of the body. Ear drops are one type of topical medication.

selenium. The pilot study found that children receiving the supplement had fewer cases of otitis media, and that those who did develop it recovered with a shorter course of antibiotic treatment than children who were not receiving the supplement.

After a child has completed treatment for otitis media, a return visit to the practitioner should be scheduled. This visit should occur after the antibiotic has been completed, and allows the practitioner to evaluate the patient for the persistent presence of fluid within the middle ear. In children who have a problem with recurrent otitis media, a small daily dose of an antibiotic may prevent repeated full attacks of otitis media. In children who have persistent fluid, a procedure to place tiny tubes within the eardrum may help equalize pressure between the middle ear and the outside, thus preventing further fluid accumulation.

Resources

BOOKS

Shin, Jennifer, Christopher Hartnick, and Gregory Randolph, eds. *Evidence–Based Otolaryngology*. New York: Springer, 2010.

PERIODICALS

Abes, G., N. Espallardo, M. Tong, et al. "A Systematic Review of the Effectiveness of Ofloxacin Otic Solution for the Treatment of Suppurative Otitis Media." *ORL* 65 (March-April 2003): 106–116.

Bucknam, J. A., and P. C. Weber. "Laser Assisted Myringotomy for Otitis Media with Effusion in Children." *ORL-Head and Neck Nursing* 20 (Summer 2002): 11-13.

Cripps, A. W., and J. Kyd. "Bacterial Otitis Media: Current Vaccine Development Strategies." *Immunology and Cell Biology* 81 (February 2003): 46–51.

Decherd, M. E., R. W. Deskin, J. L. Rowen, and M. B. Brindley. "*Bordetella pertussis* Causing Otitis Media: A Case Report." *Laryngoscope* 113 (February 2003): 226–227.

Goodwin, J. H., and J. C. Post. "The Genetics of Otitis Media." *Current Allergy and Asthma Reports* 2 (July 2002): 304-308.

Hoberman, A., C. D. Marchant, S. L. Kaplan, and S. Feldman. "Treatment of Acute Otitis Media Consensus Recommendations." *Clinical Pediatrics* 41 (July-August 2002): 373-390.

Linday, L. A., J. N. Dolitsky, R. D. Shindledecker, and C. E. Pippinger. "Lemon-Flavored Cod Liver Oil and a Multivitamin-Mineral Supplement for the Secondary Prevention of Otitis Media in Young Children: Pilot Research." *Annals of Otology, Rhinology, and Laryngology* 111 (July 2002): 642-652.

Marchisio, P., R. Cavagna, B. Maspes, et al. "Efficacy of Intranasal Virosomal Influenza Vaccine in the Prevention of Recurrent Acute Otitis Media in Children." *Clinical Infectious Diseases* 35 (July 15, 2002): 168-174.

Mattila, P. S., V. P. Joki-Erkkila, T. Kilpi, et al. "Prevention of Otitis Media by Adenoidectomy in Children Younger Than 2 Years." *Archives of Otolaryngology—Head and Neck Surgery* 129 (February 2003): 163–168.

Menger, D. J., and R. G. van den Berg. "*Pneumocystis carinii* Infection of the Middle Ear and External Auditory Canal. Report of a Case and Review of the Literature." *ORL* 65 (January-February 2003): 49–51.

Redaelli de Zinis, L. O., P. Gamba, and C. Balzanelli. "Acute Otitis Media and Facial Nerve Paralysis in Adults." *Otology and Neurotology* 24 (January 2003): 113–117.

Weiner, R., and P. J. Collison. "Middle Ear Pathogens in Otitis-Prone Children." *South Dakota Journal of Medicine* 56 (March 2003): 103–107.

ORGANIZATIONS

American Academy of Otolaryngology—Head and Neck Surgery, 1650 Diagonal Road, Alexandria, VA, 22314-2857, (703)836-4444, http://www.entnet.org.

American Academy of Pediatrics (AAP), 141 Northwest Point Boulevard, Elk Grove Village, IL, 60007-1098, (847)434-4000, (847)424-8000, kidsdocs@aap.org, http://www.aap.org.

American Osteopathic Association (AOA), 142 East Ontario Street, Chicago, IL, 60611, (312)202-8000, (312)202-8200, (800)621-1773, info@osteotech.org, http://www.osteopathic.org/.

Rosalyn Carson-DeWitt, MD
Rebecca J. Frey, PhD

Otosclerosis

Definition

Otosclerosis is an excessive growth in the bones of the middle ear which interferes with the transmission of sound.

Description

The middle ear consists of the eardrum and a chamber which contains three bones called the hammer, the anvil, and the stirrup (or stapes). Sound waves passing through the ear cause the ear drum to vibrate. This vibration is transmitted to the inner ear by the three bones. In the inner ear, the vibrations are changed into impulses which are carried by the nerves, to the brain. If excessive bone growth interferes with the stapes ability to vibrate and transmit sound waves, **hearing loss** will result.

Otosclerosis is classified as a conductive disorder because it involves the bones of the ear. These bones conduct the sound to the nerve. If a person has hearing loss classified as neural, the nerve conducting the impulses to the brain is involved.

Otosclerosis is a common hereditary condition. About 10% of the Caucasion population has some form of otosclerosis, however, it is rare among other ethnic backgrounds. Women are more likely than men to suffer from otosclerosis. It is the most common cause of conductive hearing loss between the ages of 15–50, but if the bony growth affects only the hammer or anvil, there are no symptoms and the condition goes undetected. Disease affecting the stapes is also associated with progressive hearing loss.

Causes and symptoms

Otosclerosis is hereditary. Acquired illness and accidents have no relationship to its development.

The primary symptom of otosclerosis is loss of hearing. In addition, many people experience **tinnitus** (noice originating inside the ear). The amount of tinnitus is not necessarily related to the kind or severity of hearing loss.

Diagnosis

Hearing loss due to otosclerosis is usually first noticed in the late teens or early twenties. Hearing loss usually occurs in the low frequencies first, followed by high frequencies, then middle frequencies. Extensive hearing tests will confirm the diagnosis.

KEY TERMS

Tinnitus—Tinnitus is noise originating in the ear, not in the environment. The noise can range from faint ringing to roaring.

Treatment

People with otosclerosis often benefit from a properly fitted hearing aid.

The surgical replacement of the stapes has become a common procedure to improve conductive hearing problems. During this operation, called a **stapedectomy**, the stapes is removed and replaced with an artificial device. The operation is performed under **local anesthesia** and is usually an outpatient procedure. Surgery is done on only one ear at a time, with a one year wait between procedures. The degree of hearing improvement reaches its maximum about four months after the surgery. More than 80% of these procedures successfully improve or restore hearing.

Prognosis

People with otosclerosis almost never become totally deaf, and will usually be able to hear with a hearing aid or with surgery plus a hearing aid. In older people, the tendency for additional hearing loss is diminished due to the hardening of the bones.

Prevention

Otosclerosis cannot be prevented.

ORGANIZATIONS

American Tinnitus Association, P.O. Box 5, Portland, OR, 97207-0005, (503)248-0024, (503)248-0024, (800)634-8978, tinnitus@ata.org, http://www.ata.org/.

Hearing Loss Association of America, 7910 Woodmont Ave., Suite 1200, Behtesda, MD, 20814, (301)657-2248, http://www.hearingloss.org.

National Association of the Deaf, 8630 Fenton St, #820, Silver Spring, MD, 20910, (301)587-1788, (301)587-1791, http://www.nad.org.

Self Help for Hard of Hearing People, Inc. , 7910 Woodmont Ave., Suite 1200 , Bethesda, MD, 20814, (301)657-2248, http://www.shhh.org.

Dorothy Elinor Stonely

Otoscopic examination *see* **Ear exam with an otoscope**

Ototoxicity

Definition

Ototoxicity is damage to the hearing or balance functions of the ear by drugs or chemicals.

Description

Ototoxicity is drug or chemical damage to the inner ear. This section of the ear contains both the hearing mechanism and the vestibulocochlear nerve, the nerve that sends hearing and balance information to the brain. Because of this, ototoxic drugs may cause lack of hearing, and loss of sense of balance.

The extent of ototoxicity varies with the drug, the dose, and other conditions. In some cases, there is full recovery after the drug has been discontinued. In other cases, the extent of damage is limited, and may even be too small to be noticed. This may occur in high-frequency **hearing loss**, where the damage to the ear makes it difficult to hear high pitched musical notes, but does not affect the ability to hear the spoken word, or carry on a conversation. In extreme cases, there may be permanent and complete deafness.

Although ototoxicity is undesirable, the ear damage can actually be used to help people with **Ménière's disease**. This is a disease of no known cause that is marked by sudden episodes of **dizziness** and vertigo. Other symptoms include a feeling of "fullness" in the ears, roaring in the ears, and ringing in the ears. While most people with this condition can be controlled with medication, about 10% require surgery. However, use of some ototoxic drugs can actually improve this condition, while causing less damage to the hearing mechanism than traditional treatments.

Causes and symptoms

Many drugs can cause ototoxicity.

Antibiotics

- amikacin (Amikin)
- streptomycin
- neomycin
- gentamicin (Garamycin)
- erythromycin (E-Mycin, Eryc)
- kanamycin (Kantrex)
- tobramycin (Nebcin)
- netilmycin (Netromycin)
- vancomycin (Vancocin)

Anti-cancer drugs

- cisplatin (Platinol AQ)
- bleomycin (Blenoxane)
- vincristine (Oncovin)

Diuretics

- acetazolamide (Diamox)
- furosemide (Lasix)
- bumetanide (Bumex)
- ethacrynic acid (Edecrine)

A number of other drugs and chemicals may also cause ototoxicity. **Aspirin** overdose causes ringing in the ears. The **antimalarial drugs** quinine and chloroquine may also cause ear damage. Among the environmental chemicals that can cause ear damage are tin, lead, mercury, carbon monoxide, and carbon disulfide. This list is not complete, and many other drugs and chemicals, such as industrial solvents, may cause ear problems.

Diagnosis

Ototoxicity often goes undiagnosed. This occurs when the hearing loss is slight, or when it is restricted to the higher frequencies. Patients may notice a change in their hearing, but it may not be significant enough to report.

In other cases, the loss of hearing may be very significant, or the ototoxicity may take the form of ringing in the ears, or other sensations.

When physicians are administering medications that are known to cause hearing loss, it is often recommended that the patient receive regular hearing tests. By monitoring hearing on a regular basis, it may be possible to discontinue the medication, or reduce the dose so that no further damage is done.

Ototoxicity that causes loss of balance may be even more difficult to diagnose. These changes may take place gradually, over time, and may be confused with the effects of the condition the drugs are meant to treat. If ototoxicity is suspected, **balance tests** are available, including a platform balance test, and a rotary chair. These, and other tests, determine how a patient responds to motion and changes in body position.

Treatment

There are no current treatments to reverse the effects of ototoxicity.

People who suffer permanent hearing loss may elect to use **hearing aids**, or, when appropriate, receive a cochlear implant. For those who have balance

KEY TERMS

Antibiotic—Drugs that kill or inhibit the growth of bacteria.

Cochlea—A division of the inner ear.

Diuretic—A drug that increases water loss through increased urination.

Ménière's disease—A disorder of the membranous labyrinth of the inner ear that is marked by recurrent attacks of dizziness, tinnitus, and deafness—also called Ménière's syndrome. It is named after Prosper Ménière (1799–1862), a French physician who was among the first people to study diseases of the ear, nose, and throat.

Tinnitus—Ringing sounds in the ears.

problems, **physical therapy** may often be helpful. Physical therapists can help people with balance problems learn to rely more on vision and the sensations from muscles to achieve balance.

Prognosis

The prognosis depends on the drugs that caused the ototoxicity, and their dose.

The aminoglycoside **antibiotics**, gentamicin, kanamycin, netilmycin and tobramycin all cause hearing loss to varying degrees. These drugs may be used to treat life-threatening infections that are resistant to other classes of drugs, and so there may be no choice but to use them. Careful dosing can minimize, but not eliminate the risk. It is estimated that the chances of recovery are 10-15%. The hearing loss usually begins at the higher frequencies, and is usually not recognized immediately.

Erythromycin may cause hearing loss that affects all frequencies. This hearing loss usually reverses itself over time.

Aspirin and the non-steroidal anti-inflammatory drugs (NSAIDS) may cause ringing in the ears (**tinnitus**). This stops when the drug is discontinued.

The **diuretics** may cause a hearing loss with a rapid onset. This will usually, but not always, reverse itself when the drugs are stopped.

In some cases, the prognosis is not really clear. Vancomycin appears to cause hearing loss, but this may only occur when vancomycin is used at the same time as other ototoxic drugs, such as gentamicin or erythromycin.

Prevention

Since most ototoxicity occurs when the harmful drugs are used in high doses, careful dose calculations are the best method of prevention. Sometimes it is possible to replace the ototoxic drugs with drugs that have less severe adverse effects.

Resources

BOOKS

Campbell, Kathleen. *Pharmacology and Ototoxicity for Audiologists*.

ORGANIZATIONS

Deafness Research Foundation, 641 Lexington Avenue, Fl 15, New York, NY, 10022-4503, (212)328-9480, (212)328-9484, http://www.drf.org.

EAR Foundation of Arizona, 668 North 44th Street, Suite 300, Phoenix, AZ, 85008 , (602)685-1050, (602)239-5117, melissa@earfoundationaz.com, http://www.earfoundationaz.com.

National Institute on Deafness and Other Communication Disorders, National Institutes of Health, 31 Center Drive, MSC 2320, Bethesda, MD, 20892-2320, (301)496-7243, (301)402-0018, nidcdinfo@nidcd.nih.gov, http://www.nidcd.nih.gov/.

Samuel D. Uretsky, PharmD

Ova & parasites collection *see* **Stool O & P test**

Ovarian cancer

Definition

Ovarian **cancer** is cancer of the ovaries, the egg–releasing and hormone–producing organs of the female reproductive tract. In ovarian cancer, malignant (cancerous) cells divide and multiply in an uncontrolled, abnormal fashion to form a tumor.

Demographics

Ovarian cancer can develop at any age, but is most likely to occur in women who are 50 years or older; most women are diagnosed after **menopause**. More than half the cases of ovarian cancer are among women who are over age 63. Industrialized countries have the highest incidence of ovarian cancer. Caucasian women, especially those of Ashkenazi Jewish descent, are at somewhat higher risk. African–American and Asian women are at a slightly lower risk.

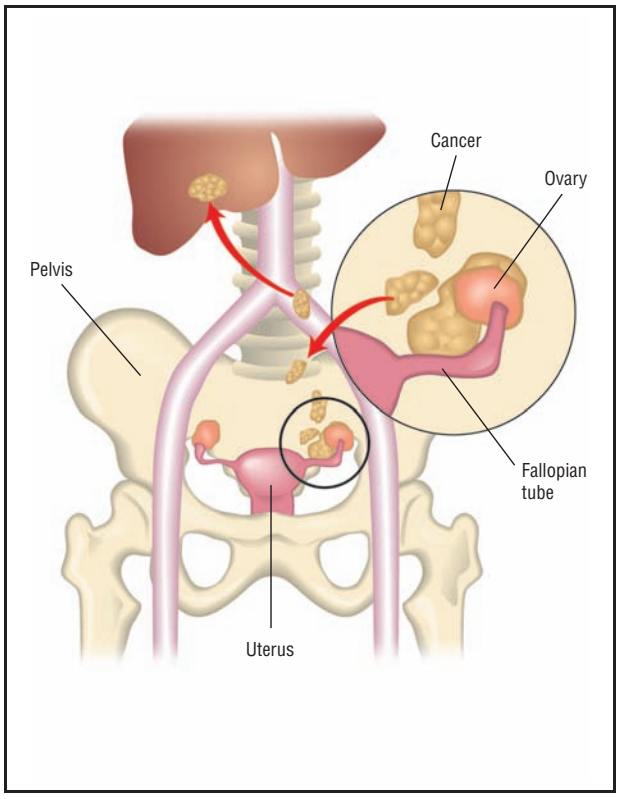


Diagram of the pelvic region with a cancerous growth on the ovary. *(Illustration by PreMediaGlobal. Reproduced by permission of Gale, a part of Cengage Learning.)*

In 2009, ovarian cancer was the eighth most common cancer among women in the United States. It accounted for about 3.3% of all new cancers in American women. However, because of poor early detection, ovarian cancer is the fifth most common cause of cancer **death** among women. About one in 71 American women will develop ovarian cancer during her lifetime, and one in 95 will die from it. Rates are thought to be similar worldwide. The American Cancer Society estimated about 21,550 new cases of ovarian cancer would be diagnosed in the United States in 2009, and the cancer would cause about 14,600 deaths that year.

Description

The ovaries are small, almond–shaped organs located in the pelvic region, one on either side of the uterus. During a woman's childbearing years, the ovaries generally alternate to produce and release one egg each month as part of the normal menstrual cycle. The released egg is shunted into the adjacent fallopian tube and moves downward to the uterus where, if fertilized, it will implant and develop into an embryo, and if unfertilized will be shed along with menstrual blood. The ovaries also secrete the female hormones estrogen and progesterone, which help regulate the menstrual cycle and **pregnancy**, as well as support the development of the secondary female sexual characteristics (i.e., breasts, body shape, and body hair). During pregnancy and when women take certain medications, mainly **oral contraceptives**, the ovaries do not produce eggs.

Types of ovarian tumors

The ovaries contain three main types of cells: epithelial cells, stromal cells, and germ cells. About 90% of all ovarian cancers develop from epithelial cells lining the surface of the ovaries. About 15% of tumors that develop from epithelial cells are considered to be low malignant potential (LMP) tumors. These tumors occur more often in younger women, are more likely to be diagnosed early, and thus have a better prognosis.

Stromal cells are located inside the ovary and produce the hormones estrogen and progesterone. About 5% of ovarian cancers begin in the stromal cells.

Germ cells also are located within the ovary. **Germ cell tumors** develop in the cells that would become eggs (ova). They account for about 2% of ovarian tumors. Many germ cell tumors are benign (noncancerous). These tumors often occur in teenaged girls and young women. The prognosis is good if they are found early, but as with other ovarian cancers, early detection is difficult.

Risk factors

Age is one of the greatest risk factors in developing ovarian cancer, with risk increasing significantly after menopause. Another risk factor is a family or personal history of cancers of the female reproductive tract or breast that are caused by an inherited genetic mutation at the chromosomal sites BRCA1 or BRCA2. Not all women with BRCA1 or BRCA2 mutations will develop ovarian cancer. By age 70, a woman who has the BRCA1 mutation carries about a 40–60% risk of developing ovarian cancer. Women with the genetic mutation BRCA2 have a 15% risk of developing ovarian cancer. However, these gene mutations play a role only in about 5% of all ovarian cancer cases.

Early first menstruation (before age 12) and late menopause also seem to put women at a higher risk of ovarian cancer. The use of talcum powder in the genital

area has been implicated in ovarian cancer in many studies. It may be because talc contains particles of asbestos, a known carcinogen. Female workers exposed to asbestos have a higher–than–normal risk of developing ovarian cancer. Genital deodorant sprays may also present an increased risk; however, not all studies have produced consistent results. Other risk factors include a diet high in saturated fats, treatment with androgens (male hormones), and never having been pregnant (nulliparity). Conversely, having been pregnant, **breastfeeding**, and using oral contraceptives decrease the risk of developing ovarian cancer.

Causes and symptoms

Cells in ovarian tissue normally divide and grow according to controls and instructions by proteins produced by various genes. If certain genes develop changes (mutations), instructions for cellular growth and division may go awry. Abnormal, uncontrolled cell growth may occur, causing cancer. Most of these genetic changes are not inherited. Instead, they are sporadic, still unexplained changes. Most ovarian cancers occur later in life after years of exposure to various environmental factors (e.g., the body's own hormones, asbestos exposure, or **smoking**) that may cause sporadic genetic alterations.

Ovarian cancer often is called a silent killer because it produces few symptoms in its early stages. Most women are unaware they have the disease until it has progressed to advanced stages. Most early symptoms are vague and either abdominal or gastrointestinal in nature. These symptoms may not be properly diagnosed or may recognized as ovarian in nature only after a significant length of time had passed and ovarian cancer has advanced.

The following symptoms are possible indications of ovarian cancer, although these symptoms may also be due to many other causes. Symptoms that persist for two to three weeks or symptoms that are unusual for a particular woman should be evaluated by a doctor.

- digestive symptoms, such as gas, indigestion, constipation, or a feeling of fullness after a light meal
- bloating, distention or cramping
- abdominal or low–back discomfort
- pelvic pressure or frequent urination
- unexplained changes in bowel habits
- nausea or vomiting
- pain or swelling in the abdomen
- loss of appetite (anorexia)
- fatigue
- unexplained weight gain or loss
- pain during intercourse
- vaginal bleeding in post–menopausal women

KEY TERMS

Adjuvant therapy—Treatment involving radiation, chemotherapy (drug treatment), hormone therapy, biotherapeutics, or a combination of any of these given after the primary treatment in order to rid the body of residual microscopic cancer.

Biomarker—A biochemical substance that can be detected in blood samples and indicates the presence of a cancerous tumor.

Estrogen—Any of several steroid hormones, produced mainly in the ovaries, that stimulate the development of the endometrium and the development of female secondary sexual characteristics.

Lymphatic system—A connected network of nodes, or glands that carry lymph throughout the body. Lymph is a fluid that contains the infection–fighting white blood cells that form part of the body's immune system. Because the network goes throughout the body, cancer cells that enter the lymphatic system can travel to and be deposited at any point into the tissues and organs and form new tumors there.

Placebo—A pill or liquid given during the study of a drug or dietary supplement that contains no medication or active ingredient. Usually study participants do not know if they are receiving a pill containing the drug or an identical–appearing placebo.

Diagnosis

In the best–case scenario a woman is diagnosed with ovarian cancer while it is still contained in just one ovary. Early detection can bring five–year survival to about 93%. Unfortunately, about three out of four women have advanced ovarian cancer at the time of diagnosis. Advanced ovarian cancer is at stage III or stage IV, and it has already spread (metastasized) to other organs.) A **physical examination** and **pelvic exam** generally do not reveal early–stage ovarian cancer.

Tests

If ovarian cancer is suspected, several of the following tests and examinations will be necessary to make a definitive diagnosis.

- a complete medical history to assess all risk factors
- a thorough bi–manual pelvic examination
- CA–125 assay
- one or more various imaging procedures
- a lower GI series, or barium enema
- diagnostic laparoscopy for definitive diagnosis

BI–MANUAL PELVIC EXAMINATION. The exam should include palpating (feeling) the following organs for any abnormalities in shape or size: the ovaries, Fallopian tubes, uterus, vagina, bladder, and rectum. Because the ovaries are located deep within the pelvic area, it is unlikely that a manual exam will detect any abnormality while the cancer is still localized. However, a full examination provides the practitioner with a more complete picture. An enlarged ovary does not confirm cancer, as the ovary may be large because of a cyst or **endometriosis**. While women should have an annual **Pap test** to detect **cervical cancer**, this test is ineffective in detecting ovarian cancer.

CA–125 ASSAY. This is a blood test to determine the level of CA–125 (cancer antigen–125), a biomarker or tumor marker. A tumor marker is a measurable protein–based substance given off by the tumor. A series of CA–125 tests may be done to see if the amount of the marker in the blood is stable, increasing, or decreasing. A rising CA–125 level often indicates cancer, while a stable or declining value is more characteristic of a cyst. The CA–125 level should never be used alone to diagnose ovarian cancer. It can be normal in 50% of women with early–stage ovarian cancer. It is elevated in about 80% of women with late–stage ovarian cancer, but in 20% of cases is not elevated. In addition, this is a general biomarker and can be elevated because of a non–ovarian cancer, or from a non–malignant gynecologic conditions such as endometriosis or **ectopic pregnancy**. During menstruation the CA–125 level may be elevated, so the test is best done when the woman is not menstruating period.

IMAGING. Several different imaging techniques are used in evaluating ovarian cancer. Ultrasound uses high–frequency sound waves that create a visual pattern of echoes of the structures at which they are aimed. It often can distinguish between a fluid–filled structure such as a cyst and a solid structure, such as a tumor. Ultrasound is painless and harmless; it is the same technique used to check a developing fetus in the womb. Ultrasound may be done externally through the abdomen and lower pelvic area, or with a transvaginal probe (**transvaginal ultrasound**).

Other painless imaging techniques are computed tomography (CT) and **magnetic resonance imaging** (MRI). Color Doppler analysis provides additional contrast and accuracy in distinguishing masses. These imaging techniques allow better visualization of the internal organs and can detect abnormalities without having to perform surgery.

LOWER GI SERIES. A lower GI series, or **barium enema**, uses a series of x-rays to highlight the colon and rectum. To provide contrast, the patient drinks a chalky liquid containing barium. This test might be done to see if cancer has spread to these areas.

DIAGNOSTIC LAPAROSCOPY. This technique uses a thin hollow lighted instrument inserted through a small incision in abdomen to visualize the organs inside of the abdominal cavity. If the ovary is believed to be malignant, the entire ovary may be removed (**oophorectomy**) and its tissue sent for evaluation to the pathologist, even though only a small piece of the tissue is needed for evaluation. If cancer is present, great care must be taken not to cause the rupture of the malignant tumor, as this could spread cancer cells to adjacent organs. If the cancer is completely contained in the ovary, its removal also functions as the treatment. If the cancer has spread or is suspected to have spread, then a saline solution may be instilled into the cavity and then drawn out again. This technique is called peritoneal lavage. The aspirated fluid will be evaluated for the presence of cancer cells. If peritoneal fluid is present, called **ascites**, a sample of this material will also be drawn and examined for malignant cells. If cancer cells are present in the peritoneum, then treatment will be directed at the abdominal cavity as well.

Treatment

Treatment is based on the stage of cancer at diagnosis and the woman's age.

Clinical staging

Staging is the term used to determine if the cancer is localized or has spread, and if so, how far and to which region(s) of the body. Staging helps define the cancer and will determine the course of suggested treatment. Staging involves examining any tissue samples (biopsies) that have been taken from the ovary, nearby lymph nodes, and any structures where metastasis may be suspected. This may include the diaphragm, lungs, stomach, intestines, and omentum (the tissue covering internal organs), and any fluid, as described above.

The National Cancer Institute Stages uses the Tumor/Node/Metastasis (TNM) system for staging ovarian cancer. Other staging systems such as the International Federation of Gynecology and

Obstetrics (FIGO) staging system also may be used. The TNM staging system is summarized as follows:

- Stage I: Cancer is confined to one or both ovaries.
- Stage II: Cancer is found in one or both ovaries and/or has spread to the uterus, Fallopian tubes, and/or other body parts within the pelvic cavity.
- Stage III: Cancer is found in one or both ovaries and has spread to lymph nodes or other body parts within the abdominal cavity, such as the surfaces of the liver or intestines.
- Stage IV: Cancer is found in one or both ovaries and has spread to other distant organs such as the lungs.

Individual stages are further subdivided. Accurate staging is important in determining a treatment plan.

Surgery

Surgery is done to remove as much of the tumor as possible (called tissue debulking), usually followed by **chemotherapy** and/or radiation (adjuvant therapy) to target cancer cells that have remained in the body without jeopardizing the woman's health. This can be hard to achieve once the cancer has spread. Removal of the ovary is called oophorectomy, and removal of both ovaries is called bilateral oophorectomy. Unless it is very clear that the cancer has not spread, the Fallopian tubes are removed as well (**salpingo–oophorectomy**). Removal of the uterus is called **hysterectomy**.

If a woman is young and wishes to have children, all attempts will be made to spare the uterus. It is crucial that a woman discuss with her surgeon her childbearing plans before surgery. Ovarian cancer spreads easily and often spreads swiftly throughout the reproductive tract, so may be necessary to remove all reproductive organs as well as part of the lining of the peritoneum to provide the woman with the best possible chance of long–term survival. Fertility–sparing surgery can be successful if the ovarian cancer is diagnosed very early.

Side effects of the surgery will depend on the extent of the surgery, but may include **pain** and temporary difficulty with bladder and bowel function, as well as reaction to the loss of hormones produced by the organs removed. A hormone replacement patch may be applied to the woman's skin in the recovery room to help with the transition. An emotional side effect involve the feeling of loss stemming from the removal of reproductive organs.

Chemotherapy

Chemotherapy is used to target cells that have traveled to other organs, and throughout the body via the lymphatic system or the blood stream (metastasized). Chemotherapy drugs are designed to kill cancer cells, but they also harm to healthy cells. Chemotherapy may be administered through a vein in the arm (intravenous, IV), may be taken in tablet form (orally), and/or may be given through a thin tube called a catheter directly into the abdominal cavity (intraperitoneal). IV and oral chemotherapy drugs travel throughout the body; intraperitoneal chemotherapy is localized in the abdominal cavity.

Side effects of chemotherapy vary greatly depending on the drugs used. Currently, chemotherapy drugs are often used in combinations to treat advanced ovarian cancer, and usually the combination includes a platinum–based drug (such as cisplatin) with a taxol agent, such as paclitaxel. Some of the combinations used or being studied include: carboplatin/paclitaxel, cisplatin/paclitaxel, cisplatin/topotecan, and cisplatin/carboplatin. Antineoplastic agents such as topotecan (Hycamtin) or gemcitabine (Gemzar) that interfere with the ability of the tumor cells to reproduce also may be given. The goal of chemotherapy is to maximize effectiveness with minimum of side effects. Side effects include **nausea and vomiting**, **diarrhea**, decreased appetite and resulting weight loss, **fatigue**, headaches, loss of hair, and **numbness and tingling** (parethesia) in the hands or feet. Managing these side effects is an important part of cancer treatment.

After the full course of chemotherapy has been given, the surgeon may perform a "second look" surgery to examine the abdominal cavity again to evaluate the success of treatment.

Radiation

Radiation uses high–energy, highly focused x-rays to target very specific areas of cancer. This is done using a machine that generates an external energy beam. Careful measurements are taken so that the targeted area can be as focused and small as possible. Another form of radiation uses a radioactive liquid that is administered into the abdominal cavity in the same fashion as intraperitoneal chemotherapy. Radiation usually is given on a daily Monday though Friday schedule and for several weeks. Radiation is not painful, but side effects can include skin damage at the area exposed to the external beam and extreme fatigue. Fatigue may hit suddenly around the third week of treatment and may take a while to resolve even after treatments have terminated. Other side

effects may include **nausea**, **vomiting**, diarrhea, loss of appetite, weight loss, and urinary difficulties. For patients with incurable ovarian cancer, radiation may be used to shrink tumor masses to provide pain relief and improve quality of life (**palliative care**).

Following treatment, regular follow–up appointments will be scheduled to monitor for any long–term side effects, relapse, or metastases.

Clinical trials

Clinical trials are human research studies. Their goal is to evaluate the effectiveness of new ways to treat cancer. There are many different designs, and they target different aspects of care. For example, some may investigate the response of different chemotherapy drugs, while another study may compare different types of treatment/chemotherapy combinations.

Research studies often are designed to compare the effectiveness of a new treatment method against the standard method or the effectiveness of a drug against a placebo (an inert substance that would be expected to have no effect on the outcome). Since the research is experimental in nature, there are no guarantees about the outcome. New drugs being used may have harmful, unknown side effects. Some people participate to help further knowledge about their disease. For others, the study may provide a possible treatment that is not yet available otherwise. Although there is no cost to participate, participants have to meet certain criteria before being admitted into the study. It is important to fully understand one's role in the study, and weigh the potential risks versus benefits when deciding whether or not to participate. A list of clinical trials currently enrolling patients can be found at http://clinicaltrials.gov.

Alternative and complementary therapies

The term alternative therapy refers to therapy used instead of conventional treatment. By definition, these treatments have not been scientifically proven or investigated as thoroughly and by the same standards as conventional treatments. The terms complementary or integrative therapy denote practices used in conjunction with rather than instead of conventional treatment. Patients should inform their doctors of any alternative or complementary therapies being used or considered as some alternative and complementary therapies adversely affect the effectiveness of conventional treatments. Some common complementary and alternative medicine therapies include:

- prayer and faith healing
- meditation
- mind/body techniques such as support groups, visualization, guided imagery and hypnosis
- energy work such as Therapeutic Touch and Reiki
- acupuncture and traditional Chinese medicine
- body work such as yoga, massage, and t'ai chi
- vitamin, mineral, and/or herbal supplements
- special diets such as vegetarian, vegan, or macrobiotic

Mind/body techniques along with **meditation**, prayer, **yoga**, t'ai chi, and **acupuncture** have been shown to reduce **stress** levels, and the relaxation provided may help boost the body's immune system. The effectiveness of some other complementary and alternative treatments is being studied by the National Institutes of Health's National Center for Complementary and Alternative Medicine (NCCAM). For a current list of the research studies, recent results and publications, patients can visit the NCCAM web site at http://nccam.nih.gov or call (888) 644-6226.

Coping with cancer treatment

While the cancer may only be in part of the body, it is very much a full mind/body experience. Strategies for coping with the treatment need to address the entire range of the experience. Each woman will have different needs. She might want to create a personal support team of friends. They can provide support by:

- Finding helpful information in the library or on the Internet about clinical trials, new therapies or treatments, different treatment centers, etc.
- Providing transportation to and from appointments. A diagnosis of cancer can be overwhelming. In such a stressful and distracted state it is often hard to remember what a doctor has said, or even to remember the questions to be asked. Having a second set of ears during this stressful time can be helpful.
- Helping with household duties so that the woman can rest after treatments and have more energy to devote to her family.
- Assisting with childcare. Children are very much affected by a parent's cancer diagnosis, whether or not they have been fully informed of what is taking place. For a child to go to a friend's house can provide a sense of normalcy and security.
- Being available to participate in activities and conversations not centering on the cancer. While in the midst of cancer treatments, it is important to talk about non–cancer issues as well and to maintain social relationships and activities.

A woman may wish to join a support group of women with ovarian cancer. This group can provide the environment to talk about the diagnosis, the

treatments, the side effects, and the impact the diagnosis has on her life with others who can empathize. If there is no support group nearby, she may be able to join one on the Internet. Support groups also may exist for caregivers and loved ones.

Prognosis

Prognosis for ovarian cancer depends largely on the stage at which it is first diagnosed. Stage I ovarian cancer has the best survival rate, although ovarian cancer is rarely diagnosed at this stage. The 2009 five–year survival rates for the four stages of ovarian cancer are: stage I, 92.8%; stage II, 78.6%; stage III, 50%; stage IV, 17.5%.

Prevention

Since the cause of ovarian cancer is not known, it is not possible to fully prevent the disease. However, there are ways to reduce one's risks of developing the disease.

Decrease ovulation

Pregnancy temporarily stops ovulation, and multiple pregnancies appear to further reduce the risk of ovarian cancer. The research is not clear as to whether the pregnancy must result in a term delivery to have full benefit. Women who breastfeed their children also appear to have a lower risk of developing the disease. Since oral contraceptives also suppress ovulation, women who take birth-control pills have a lower incidence of ovarian cancer. It appears that the longer a woman takes oral contraceptives, the lower her risk for ovarian cancer. However, since oral contraceptives alter a woman's hormonal status, her risk for other hormonally related cancers may change. The woman should discuss the risks and benefits of oral contraceptives with her health care provider.

Genetic testing

Genetic testing is available that can help determine whether a woman who carries certain genes that increase her risk of breast and ovarian cancer. If a woman tests positive for a BRCA1 or BRCA2 mutation, then she may be able to consider having their ovaries removed as a preventative measure (prophylactic oophorectomy).

Surgery

Procedures such as **tubal ligation** (in which the Fallopian tubes are blocked or tied) and hysterectomy (in which the uterus is removed) appear to reduce the risk of ovarian cancer. However, any removal of the reproductive organs has surgical as well as hormonal side effects.

Screening.

There are no definitive tests or screening procedures as of late 2009 to detect ovarian cancer in its early stages. Women at high risk should consult their physicians about possible regular screenings, which may include transvaginal ultrasound and a blood test for the CA–125 protein. The American Cancer Society recommends annual pelvic examinations for all women after age 40, in order to increase the chances of early detection of both cervical and ovarian cancer.

Early detection remains the key focal point in increasing survival rates for ovarian cancer because the more ovarian cancer has spread, the poorer the chance for survival past one or two years. As women and practitioners become more alert to vague early warning signs and seek out more accurate family histories, earlier awareness may begin to lead to earlier detection and improved survival rates.

Resources

BOOKS

Montz, F. J., Robert E. Bristow, and Paula J. Anastasia. *A Guide to Survivorship for Women with Ovarian Cancer*. Baltimore, MD: Johns Hopkins Press, 2005.

OTHER

"Detailed Guide to Ovarian Cancer." American Cancer Society August 27, 2009 [September 26, 2009]. http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=33

Garcia, Agustin. "Ovarian Cancer." eMedicine.com December 13, 2007. http://emedicine.medscape.com/article/255771-overview (accessed August 31, 2010).

"OncoLink." Abramson cancer Center of the University of Pennsylvania 2009. http://www.oncolink.upenn.edu (accessed August 31, 2010).

"Ovarian Cancer." MedlinePlus September 22, 2009. http://www.nlm.nih.gov/medlineplus/ovariancancer.html (accessed August 31, 2010)

ORGANIZATIONS

American Cancer Society, 1599 Clifton Rd., NE, Atlanta, GA, 30329, (404) 320-3333, (800) ACS-2345, http://www.cancer.org.

Cancer Research and Prevention Foundation, 1600 Duke Street, Suite 500, Alexandria, VA, 22314, (703) 836-4412, (800) 227-2732, info@preventcancer.org, http://www.preventcancer.org.

Gynecologic Cancer Foundation, 230 W. Monroe, Suite 2528, Chicago, IL, 60606, (312) 578-1439, (800) 444-4441, (312) 578-9769, info@thegcf.org, http://www. wcn.org/gcf.

National Cancer Institute Public Inquires Office., 6116 Executive Boulevard, Room 3036A, Bethesda, MD, 20892-8322, (800) 4-CANCER. TTY (800) 332-8615, http://www.cancer.gov.

National Center for Complementary and Alternative Medicine Clearinghouse, P.O. Box 7923, Gaithersburg, MD, 20898, (301) 519-3153. TTY: (866) 464-3615, (888) 644-6226, (866) 464-3616, info@nccam.nih.gov, http://nccam.nih.gov.

Ester Csapo Rastegari, RN, BSN, EdM
Tish Davidson, AM

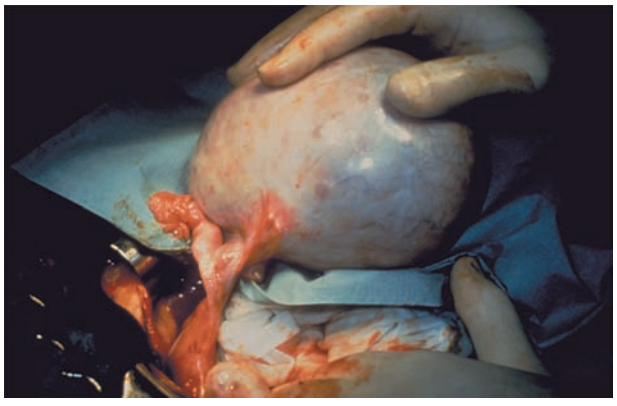
Ovarian cysts

Definition

Ovarian cysts are sacs containing fluid or semisolid material that develop in or on the surface of an ovary.

Description

Ovarian cysts are common, and the vast majority are harmless. Because they cause symptoms that may be the same as ovarian tumors that may be cancerous, ovarian cysts should always be checked out. The most common types of ovarian cysts are follicular and corpus luteum, which are related to the menstrual cycle. Follicular cysts occur when the cyst-like follicle on the ovary in which the egg develops does not burst and release the egg. They are usually small and harmless, disappearing within two to three menstrual cycles. Corpus luteum cysts occur when the corpus luteum—a small, yellow body that secretes hormones—does not dissolve after the egg is released. They usually disappear in a few weeks but can grow to more than 4 in (10 cm) in diameter and may twist the ovary.



An ovarian cyst is being surgically removed from a 25-year-old female patient. *(Custom Medical Stock Photo, Inc. Reproduced by permission.)*

Ovarian cysts can develop at any time in a female's life from infancy to **puberty** to **menopause**, including during **pregnancy**. Follicular cysts occur frequently during the years when a woman is menstruating, and are nonexistent in postmenopausal women or any woman who is not ovulating. Corpus luteum cysts occur occasionally during the menstrual years and during early pregnancy. (Dermoid cysts, which may contain hair, teeth, or skin derived from the outer layer of cells of an embryo, are also occasionally found in the ovary.)

Causes and symptoms

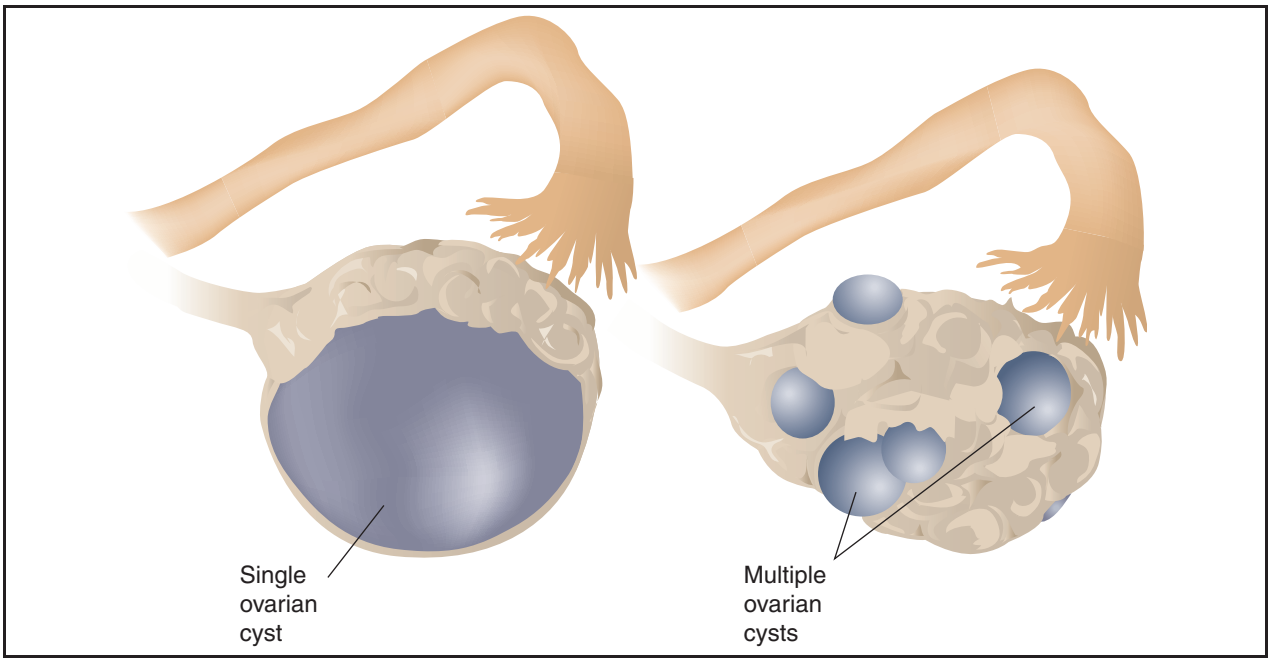
Causes

Follicular cysts are caused by the formation of too much fluid around a developing egg. Corpus luteum cysts are caused by excessive accumulation of blood during the menstrual cycle, hormone therapy, or other types of ovarian tumors.

There is also a condition known as **polycystic ovary syndrome** (PCOS) in which the eggs and follicles are not released from the ovaries and instead form multiple cysts. **Obesity** is linked to this condition, as 50% of women with PCOS are also obese. Hormonal imbalances play a major role in this condition, including high levels of the hormone androgen and low levels of progesterone, the female hormone necessary for egg release. High levels of insulin, the hormone that regulates blood sugar, are often found in women with PCOS. PCOS is also characterized by irregular menstrual periods, **infertility**, and **hirsutism** (excessive hair growth on the body and face). Although PCOS was formerly thought to be an adult-onset condition, more recent research indicates that it begins in childhood, possibly even during fetal development.

PCOS is also known to run in families, which suggests that genetic factors contribute to its development. The specific gene or genes responsible for PCOS have not yet been identified; however, several groups of researchers in different countries have been investigating genetic variations associated with increased risk of type 2 diabetes in order to determine whether the same genetic variations may be involved in PCOS.

In adolescent girls, ovarian cysts may be associated with a genetic disorder known as McCune-Albright syndrome, which is characterized by abnormal bone growth, discoloration of the skin, and early onset of puberty. The ovarian cysts are responsible for the early sexual maturation.



(Illustration by Argosy, Inc. Reproduced by permission of Gale, a part of Cengage Learning.)

As of early 2003, McCune-Albright syndrome is known to be associated with mutations in the GNAS1 gene. The mutation is sporadic, which means that it occurs during the child's development in the womb and that the syndrome is not inherited.

Symptoms

Many ovarian cysts have no symptoms. When the growth is large or there are multiple cysts, the patient may experience any of the following symptoms:

- Fullness or heaviness in the abdomen.
- Pressure on the rectum or bladder.
- Pelvic pain that is a constant dull ache and may spread to the lower back and thighs, occurs shortly before the beginning or end of menstruation, or occurs during intercourse.

Diagnosis

Non-symptomatic ovarian cysts are often felt by a doctor examining the ovaries during a routine **pelvic exam**. Symptomatic ovarian cysts are diagnosed through a pelvic exam and ultrasound. Ultrasonography is a painless test that uses a hand-held wand to send and receive sound waves to create images of the ovaries on a computer screen. The images are photographed for later analysis. It takes about 15 minutes and is usually done in a hospital or a physician's office.

Ovarian cysts can be diagnosed in female fetuses by transabdominal ultrasound during the mother's pregnancy.

Treatment

Watchful waiting

Many follicular and corpus luteum cysts require no treatment and disappear on their own. Often the physician will wait and re-examine the patient in four to six weeks before taking any action. Follicular cysts do not require treatment, but birth-control pills may be taken if the cysts interfere with the patient's daily activities.

Most uncomplicated ovarian cysts in female infants resolve on their own shortly after delivery. Complicated cysts are treated by **laparoscopy** or laparotomy after the baby is born.

Medications

McCune-Albright syndrome is treated with testolactone (Teslac), an anti-estrogen drug that corrects the hormonal imbalance caused by the ovarian cysts.

Long-term management of PCOS has been complicated in the past by lack of a clear understanding of the causes of the disorder. Most commonly, hormonal therapy has been recommended, including estrogen and progesterone and such other hormone-regulating

drugs as ganirelix (Antagon). Birth-control pills have also been prescribed by doctors to regulate the menstrual cycle and to shrink functional cysts.

More recent studies have shown that increasing sensitivity to insulin in women with PCOS leads to improvement in both the hormonal and metabolic symptoms of the disorder. This sensitivity is increased by either weight loss and **exercise** programs or by medications. Metformin (Glucophage), a drug originally developed to treat type 2 diabetes, has been shown to be effective in reducing the symptoms of hyperandrogenism as well as **insulin resistance** in women with PCOS.

Another strategy that is being tried with PCOS is administration of flutamide (Eulexin), a drug normally used to treat **prostate cancer** in men. Preliminary results indicate that the antiandrogenic effects of flutamide benefit patients with PCOS by increasing blood flow to the uterus and ovaries.

Surgery

Surgery is usually indicated for patients who have not reached puberty and have an ovarian mass and in postmenopausal patients. Surgery is also indicated if the growth is larger than 4 in (10 cm), complex, growing, persistent, solid and irregularly shaped, on both ovaries, or causes **pain** or other symptoms. Ovarian cysts are curable with surgery but often recur without it.

Surgical options include removal of the cyst or removal of one or both ovaries. More than 90% of benign ovarian cysts can be removed using laparoscopy, a minimally invasive outpatient procedure. In laparoscopic **cystectomy**, the patient receives a general or local anesthetic, then a small incision is made in the abdomen. The laparoscope is inserted into the incision and the cyst or the entire ovary is removed. Laparoscopic cystectomy enables the patient to return to normal activities within two weeks. Surgical cystectomy to remove cysts and/or ovaries is performed under **general anesthesia** in a hospital and requires a stay of five to seven days. After an incision is made in the abdomen, the muscles are separated and the membrane surrounding the abdominal cavity (peritoneum) is opened. Blood vessels to the ovaries are clamped and tied. The cyst is located and removed. The peritoneum is closed, and the abdominal muscles and skin are closed with sutures or clips. Recovery takes four weeks.

A surgical procedure known as ovarian wedge resection appears to improve fertility in women with PCOS who have not responded to drug treatments. In an ovarian wedge resection, the surgeon removes a portion of the polycystic ovary in order to induce ovulation.

KEY TERMS

Corpus luteum—A small, yellow structure that forms in the ovary after an egg has been released.

Cystectomy—Surgical removal of a cyst.

Dermoid—A skin-like benign growth that may appear on the ovary and resemble a cyst.

Endocrine—Internal secretions, usually in the systemic circulation.

Follicular—Relating to one of the round cells in the ovary that contain an ovum.

Hirsutism—A condition marked by excessive hair growth on the face and body.

Functional cyst—A benign cyst that forms on the ovary and resolves on its own without treatment.

McCune-Albright syndrome (MCAS)—A genetic syndrome characterized in girls by the development of ovarian cysts and puberty before the age of eight, together with abnormalities of bone structure and skin pigmentation.

Ovulation—The phase of the female monthly cycle when a developed egg is released from the ovary into the fallopian tube for possible fertilization.

Polycystic ovarian syndrome (PCOS)—A condition in which the eggs are not released from the ovaries and instead form multiple cysts.

Alternative treatment

Alternative treatments for ovarian problems—herbal therapies, **nutrition** and diet, and homeopathy—should be used to supplement, not replace, conventional treatment. General herbal tonics for female reproductive organs that can be taken in tea or tincture (an alcohol-based herbal extract) form include blue cohosh (*Caulophylum thalictroides*) and false unicorn root (*Chamaelirium luteum*). Recommendations to help prevent and treat ovarian cysts include a vegan diet (no dairy or animal products) that includes beets, carrots, dark-green leafy vegetables, and lemons; anitoxidant supplements including zinc and **vitamins** A, E, and C; as well as black currant oil, borage oil, and evening primrose oil (*Oenothera biennis*) supplements. Homeopathic treatments—tablets, powders, and liquids prepared from plant, mineral, and animal extracts—may also be effective in treating ovarian cysts. Castor oil packs can help

reduce inflammation. **Hydrotherapy** applied to the abdomen can help prevent rupture of the cyst and assist its reabsorption.

Prognosis

The prognosis for non-cancerous ovarian cysts is excellent.

Prevention

Ovarian cysts cannot be prevented.

Resources

BOOKS

Beers, Mark H., Robert S. Porter, and Thomas V. Jones, eds. *The Merck Manual of Diagnosis and Therapy*. 18th ed. Whitehouse Station, NJ: Merck Research Laboratories, 2006.

Tredwell, Richard E. *Ovarian Cysts: Symptoms, Causes, and Treatment*. New York: Nova Biomedical Books, 2010.

PERIODICALS

Ajossa, S., S. Guerriero, A. M. Paoletti, et al. "The Antiandrogenic Effect of Flutamide Improves Uterine Perfusion in Women with Polycystic Ovary Syndrome." *Fertility and Sterility* 77 (June 2002): 1136–1140.

de Sanctis, C., R. Lala, P. Matarazzo, et al. "Pubertal Development in Patients with McCune-Albright Syndrome or Pseudohypoparathyroidism." *Journal of Pediatric Endocrinology and Metabolism* 16, Supplement 2 (March 2003): 293–296.

Ehrmann, D. A., P. E. Schwarz, M. Hara, et al. "Relationship of Calpain-10 Genotype to Phenotypic Features of Polycystic Ovary Syndrome." *Journal of Clinical Endocrinology and Metabolism* 87 (April 2002): 1669–1673.

Elkind-Hirsch, K. E., B. W. Webster, C. P. Brown, and M. W. Vernon. "Concurrent Ganirelix and Follitropin Beta Therapy is an Effective and Safe Regimen for Ovulation Induction in Women with Polycystic Ovary Syndrome." *Fertility and Sterility* 79 (March 2003): 603–607.

Franks, S. "Adult Polycystic Ovary Syndrome Begins in Childhood." *Best Practice and Research: Clinical Endocrinology and Metabolism* 16 (June 2002): 263–272.

Kazerooni, T., and M. Dehghan-Kooshkghazi. "Effects of Metformin Therapy on Hyperandrogenism in Women with Polycystic Ovarian Syndrome." *Gynecological Endocrinology* 17 (February 2003): 51–56.

Legro, R. S. "Polycystic Ovary Syndrome. Long-Term Sequelae and Management." *Minerva ginecologica* 54 (April 2002): 97–114.

Marx, T. L., and A. E. Mehta. "Polycystic Ovary Syndrome: Pathogenesis and Treatment Over the Short and Long Term." *Cleveland Clinic Journal of Medicine* 70 (January 2003): 31–33, 36–41, 45.

Mittermayer, C., W. Blaicher, D. Grassauer, et al. "Fetal Ovarian Cysts: Development and Neonatal Outcome." *Ultraschall in der Medizin* 24 (February 2003): 21–26.

Ovalle, F., and R. Azziz. "Insulin Resistance, Polycystic Ovary Syndrome, and Type 2 Diabetes Mellitus." *Fertility and Sterility* 77 (June 2002): 1095–1105.

Vankova, M., J. Vrbikova, M. Hill, et al. "Association of Insulin Gene VNTR Polymorphism with Polycystic Ovary Syndrome." *Annual of the New York Academy of Sciences* 967 (June 2002): 558–565.

Yildirim, M., V. Noyan, M. Bulent Tiras, et al. "Ovarian Wedge Resection by Minilaparatomy in Infertile Patients with Polycystic Ovarian Syndrome: A New Technique." *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 107 (March 26, 2003): 85–87.

ORGANIZATIONS

American College of Obstetricians and Gynecologists (ACOG), P.O. Box 96920, Washington, DC, 20090-6920, (202)638-5577, http://www.acog.org.

American Institute of Ultrasound in Medicine, 14750 Sweitzer Lane, Suite 100, Laurel, MD, 20707-5906, (301)498-4100, (301)498-4450, http://www.aium.org.

Polycystic Ovarian Syndrome Association, P.O. Box 3403, Englewood, CO, 80155-3403, info@pcosupport.org, http://www.pcosupport.org.

Lori De Milto
Rebecca J. Frey, PhD

Ovarian torsion

Definition

Ovarian torsion is the twisting of the ovary due to the influence of another condition or disease. This results in extreme lower abdominal **pain**.

Description

Ovarian torsion occurs infrequently only in females. In can occur in women of all ages, but most women who experience this are younger. Approximately 70-75% of cases occur in women under 30 years old. About 20% of all reported cases are in pregnant women. It is the fifth most common gynecological emergency which can include surgical intervention.

Ovarian torsion usually arises in only one ovary at a time. They can occur in either normal or enlarged ovaries and fallopian tubes, and occasionally they develop in both.

Causes and symptoms

A variety of conditions that can cause torsion of the ovary ranging from changes in normal ovaries to congenital and developmental abnormalities or even a

KEY TERMS

Congenital—Condition present at birth.

Laparoscopy—Endoscope used to observe structures in the abdomen.

Mesosalpinx—A ligament connected to the fallopian tube.

Ovary—Female reproductive gland that contains the ova (eggs).

Tachycardia—Rapidly beating heart.

Torsion—The action of twisting.

disease that affects the tube or ovary. Normal ovaries that experience spasms or changes in the blood vessels in the mesosalpinx can become twisted. For example, if the veins in the mesosalpinx become congested, the ovaries will undergo torsion.

Developmental abnormalities of the fallopian tube such as extremely longer-than-normal tubes or a missing mesosalpinx will cause ovarian torsion. Diseases such as **ovarian cysts** or fibromas, tumor of the ovary or tubes, and trauma to either the ovaries or the tubes will also cause ovarian torsion.

The characteristic symptom of ovarian torsion is the sudden onset of extreme lower abdominal pain that radiates to the back, side and thigh. **Nausea**, **vomiting**, **diarrhea**, and **constipation** can accompany the pain. The patient may also experience tenderness in the lower abdominal area, a mild **fever** and tachycardia.

Diagnosis

The diagnosis of ovarian torsions usually occurs in an emergency room due to the suddenness of extreme pain. Emergency room physicians may consult with another physician specializing in obstetrics and gynecology. Since 20% of ovarian torsions occur in pregnant women, physicians will order a **pregnancy** test. Visualization with an ultrasound and CT scan (computed tomography) will help pinpoint the ovarian structures and allow physicians to diagnose. Diagnosis is often confirmed through **laparoscopy**.

Treatment

Ovarian torsions need to be repaired. This is done through surgery, and for less severe cases laparoscopic surgery is used. Medications such as NSAIDs are given to control pain.

Prognosis

If ovarian torsions are diagnosed and treated early, then the prognosis is favorable. However, if diagnosis is delayed, the torsions can worsen and cut off arterial blood flow into and venous blood flow out of the ovary. This results in necrosis (**death**) of the ovarian tissue. Delayed diagnosis can also result in problems when trying to conceive due to **infertility**.

Prevention

Currently, there are no known methods for prevention of ovarian torsion.

Sally C. McFarlane-Parrott

Ovary and fallopian tube removal *see* **Salpingo-oophorectomy**

Ovary removal *see* **Oophorectomy**

Overactive bladder

Definition

Overactive bladder is the leakage of large amounts of urine at unexpected times, including during sleep.

Description

People who lose urine for no apparent reason while suddenly feeling the need or urge to urinate may have overactive bladder. The condition effects 17 million in the United States. The most common cause of overactive bladder is inappropriate bladder contractions. Medical professionals describe such a bladder as "unstable," "spastic," or "overactive." A doctor might call the condition "reflex incontinence" if it results from overactive nerves controlling the bladder. Having an overactive bladder can mean that the bladder empties during sleep, after drinking a small amount of water, or when touching water or hearing it running (as when someone else is taking a shower or washing dishes). Involuntary actions of bladder muscles can occur because of damage to the nerves of the bladder, to the nervous system (spinal cord and brain), or to muscles themselves. **Multiple sclerosis**, Parkinson's disease, **Alzheimer's disease**, **stroke**, brain tumors, and injury—including injury that occurs during surgery—all can harm bladder nerves or muscles.

KEY TERMS

Alzheimer's disease—A degenerative disorder that affects the brain and causes dementia, especially late in life.

Biofeedback—The use of monitoring devices that display information about the operation of a bodily function, for example, heart rate or blood pressure, that is not normally consciously controlled.

Cystoscopy—The use of a narrow tubular instrument that is passed through the urethra to examine the interior of the urethra and the urinary bladder.

Estrogen—Any of several steroid hormones, produced mainly in the ovaries, that stimulate estrus and the development of female secondary sexual characteristics.

Multiple sclerosis—A serious progressive disease of the central nervous system.

Parkinson's disease—An incurable nervous disorder marked by the symptoms of trembling hands, lifeless face, monotone voice, and a slow, shuffling walk.

Sphincter—A circular band of muscle that surrounds an opening or passage in the body and narrows or closes the opening by contracting.

Urethal—Referring to the tube in humans that carries urine from the bladder out of the body.

Urogynecologist—A physician that deals with women's health, especially with the health of women's reproductive organs and urinary tract.

Urologist—A physician who deals with the study and treatment of disorders of the urinary tract in women and the urogenital system in men.

Causes and symptoms

People with overactive bladder lose urine as soon as they feel a strong need to go to the bathroom. People with overactive bladder may leak urine:

- when they can not get to the bathroom quickly enough
- when they drink even a small amount of liquid
- when they hear or touch running water

People with overactive bladder may also go to the bathroom very often; for example, every two hours during the day and night. They may even wet the bed.

Diagnosis

To diagnose the problem, a doctor will first ask about symptoms and medical history. Other obvious factors that can help define the problem include straining and discomfort, use of drugs, recent surgery, and illness. If the patient's medical history does not define the problem, it will at least suggest which tests are needed. The doctor will physically examine the patient for signs of medical conditions causing the overactive bladder, such as tumors that block the urinary tract, stool impaction, and poor reflexes or sensations, which may be evidence of a nerve-related cause. Overactive bladder is often treated by general or family practicioners but the patient may be referred to a urologist, who specializes in the urinary tract, or a urogynecologist, who focuses on urological problems in women.

Common tests used to diagnose overactive bladder include:

- blood tests to examine blood for levels of various chemicals
- cystoscopy to look for abnormalities in the bladder and lower urinary tract. It works by inserting a small tube into the bladder that has a telescope for the doctor to look through.
- post-void residual (PVR) measurement to see how much urine is left in the bladder after urinating by placing a small soft tube into the bladder or by using ultrasound (sound waves)
- urinalysis to examine urine for signs of infection, blood, or other abnormalities
- urodynamic testing to examine bladder and urethral sphincter function (may involve inserting a small tube into the bladder; x-rays also can be used to see the bladder)

Treatment

Medications can reduce many types of leakage. Some drugs inhibit contractions of an overactive bladder. Others, such as solifenacin succinate (Vesicare), relax muscles, leading to more complete bladder emptying during urination. Some drugs tighten muscles at the bladder neck and urethra, preventing leakage. Among the drugs used are oxybutynin (Ditropan XL), 5-30 mg daily; solifenacin (Vesicare), 5-10 mg a day; darifenacin (Enablex), 3.75-15 mg daily; and tolterodine (Detrol), 2-4 mg daily. A one-month supply of these drugs costs $90-

125. Some medications, especially hormones such as estrogen, are believed to cause muscles involved in urination to function normally. Some of these medications can produce harmful side effects if used for long periods. In particular, estrogen therapy has been associated with an increased risk for cancers of the breast and the lining of the uterus. Patients should talk to their doctor about the risks and benefits of long-term use of medications.

Alternative treatment

Adjusting dietary habits and avoiding acidic and spicy foods, alcohol, **caffeine**, and other bladder irritants can help to prevent urinary leaking. Eat recommended amounts of whole grains, fruits, and vegetables to avoid **constipation**. **Bladder training**, used to treat urge incontinence, can also be a useful treatment tool. The technique involves placing a patient on a toileting schedule. The time interval between urination is then gradually increased until an acceptable time period between bathroom breaks is consistently achieved.

Biofeedback techniques can teach overactive bladder patients to control the urge to urinate. Biofeedback uses sensors to monitor temperature and muscle contractions in the vagina to help overactive bladder patients learn to increase their control over the pelvic muscles.

An infusion, or tea, of horsetail *(Equisetum arvense)*, agrimony *(Agrimonia eupatoria)*, and sweet sumach *(Rhus aromatica)* may be prescribed by an herbalist or naturopath to an overactive bladder. These herbs are natural astringents, and encourage toning of the digestive and urinary tracts. Other herbs, such as urtica, or stinging nettle *(Urtica urens)*, plantain *(Plantago major)*, or maize *(Zea mays)* may be helpful. Homeopathic remedies may include pulsatilla and causticum. Chinese herbalists might recommend golden lock tea, a mixture of several herbs that helps the body retain fluids.

Prognosis

With proper treatment, the prognosis for controlling the disorder is very good. There is no cure for overactive bladder.

Prevention

There are no known preventative measures for overactive bladder.

Resources

BOOKS

Ellsworth, Pamela. *100 Q & A About Overactive Bladder and Urinary Incontinence*. Boston: Jones and Bartlett Publishers, 2005.

Newman, Diane K., and Alan J. Wein. *Overcoming Overactive Bladder: Your Complete Self–Care Guide*. Oakland, CA: New Harbinger Publications, 2004.

PERIODICALS

Perry, Patrick. "On Tour With Debbie Reynolds: The Feisty and Fit Actress Speaks Out About an All-Too-Common Problem—Overactive Bladder." *Saturday Evening Post* (January-February 2003): 26-27.

Radley, Stephen, and Maggi Saunders. "Sex and the Overactive Bladder: Stephen Radley and Maggi Saunders Discuss the Treatment of Patients With an Overactive Bladder in Primary Care." *Primary Health Care* (October 2004): 13-14.

Weiss, Barry D. "Selecting Medications for the Treatment of Urinary Incontinence." *American Family Physician* (January 15, 2005): 315.

Zepf, Bill. "Diagnosis and Management of Overactive Bladder." *American Family Physician* (October 1, 2004): 1386.

ORGANIZATIONS

National Bladder and Bowel Foundation, www.bladderandbowelfoundation.org.

Ken R. Wells

Overhydration

Definition

Overhydration, also called water excess or water intoxication, is a condition in which the body contains too much water.

Description

Overhydration occurs when the body takes in more water than it excretes and its normal **sodium** level is diluted. This can result in digestive problems, behavioral changes, brain damage, seizures, or **coma**. An adult whose heart, kidneys, and pituitary gland are functioning properly would have to drink more than two gallons of water a day to develop water intoxication. This condition is most common in patients whose kidney function is impaired and may occur when doctors, nurses, or other healthcare professionals administer greater amounts of water-producing fluids and medications than the patient's body can excrete. Overhydration is the most common electrolyte imbalance in hospitals, occurring in about 2% of all patients.

Infants seem to be at greater risk for developing overhydration. The Centers for Disease Control and Prevention has declared that babies are especially

susceptible to oral overhydration during the first month of life, when the kidneys' filtering mechanism is too immature to excrete fluid as rapidly as older infants do. Breast milk or formula provide all the fluids a healthy baby needs. Water should be given slowly, sparingly, and only during extremely hot weather. Overhydration, which has been cited as a hazard of infant swimming lessons, occurs whenever a baby drinks too much water, excretes too little fluid, or consumes and retains too much water.

Causes and symptoms

Drinking too much water rarely causes overhydration when the body's systems are working normally. People with heart, kidney, or **liver disease** are more likely to develop overhydration because their kidneys are unable to excrete water normally. It may be necessary for people with these disorders to restrict the amount of water they drink and/or adjust the amount of salt in their **diets**.

Since the brain is the organ most susceptible to overhydration, a change in behavior is usually the first symptom of water intoxication. The patient may become confused, drowsy, or inattentive. Shouting and **delirium** are common. Other symptoms of overhydration may include blurred vision, **muscle cramps** and twitching, **paralysis** on one side of the body, poor coordination, **nausea and vomiting**, rapid breathing, sudden weight gain, and weakness. The patient's complexion is normal or flushed. Blood pressure is sometimes higher than normal, but elevations may not be noticed even when the degree of water intoxication is serious.

Overhydration can cause acidosis (a condition in which blood and body tissues have an abnormally high acid content), anemia, **cyanosis** (a condition that occurs when oxygen levels in the blood drop sharply), hemorrhage, and **shock**. The brain is the organ most vulnerable to the effects of overhydration. If excess fluid levels accumulate gradually, the brain may be able to adapt to them and the patient will have only a few symptoms. If the condition develops rapidly, confusion, seizures, and coma are likely to occur.

Risk factors

Chronic illness, **malnutrition**, a tendency to retain water, and kidney diseases and disorders increase the likelihood of becoming overhydrated. Infants and the elderly seem to be at increased risk for overhydration, as are people with certain mental disorders or **alcoholism**.

Diagnosis

Before treatment can begin, a doctor must determine whether a patient's symptoms are due to overhydration, in which excess water is found within and outside cells, or excess blood volume, in which high sodium levels prevent the body from storing excess water inside the cells. Overhydration is characterized by excess water both within and around the body's cells, while excess blood volume occurs when the body has too much sodium and cannot move water to reservoirs within the cells. In cases of overhydration, symptoms of fluid accumulation do not usually occur. On the other hand, in cases of excess blood volume, fluid tends to accumulate around cells in the lower legs, abdomen, and chest. Overhydration can occur alone or in conjunction with excess blood volume, and differentiating between these two conditions may be difficult.

Treatment

Mild overhydration can generally be corrected by following a doctor's instructions to limit fluid intake. In more serious cases, **diuretics** may be prescribed to increase urination, although these drugs tend to be most effective in the treatment of excess blood volume. Identifying and treating any underlying condition (such as impaired heart or kidney function) is a priority, and fluid restrictions are a critical component of every treatment plan.

In patients with severe neurologic symptoms, fluid imbalances must be corrected without delay. A powerful diuretic and fluids to restore normal sodium concentrations are administered rapidly at first. When the patient has absorbed 50% of the therapeutic substances, blood levels are measured. Therapy is continued at a more moderate pace in order to prevent brain damage as a result of sudden changes in blood chemistry.

Prognosis

Mild water intoxication is usually corrected by drinking less than a quart of water a day for several days. Untreated water intoxication can be fatal, but this outcome is quite rare.

Resources

BOOKS

McPhee, Stephen, and Maxine Papadakis. *Current Medical Diagnosis and Treatment, 2010*, 49th ed. New York: McGraw–Hill Medical, 2009.

PERIODICALS

Berning, Jackie. "Fluids and Hydration." *Clinical Reference Systems* (May 31, 2007).

"Too Much of Water Hast Thou." *Harper's Magazine* (May 2007): 28(3).

ORGANIZATIONS

American College of Sports Medicine (ACSM), 401 West Michigan Street, P.O. Box 1440, Indianapolis, IN, 46202-3233, (317)637-9200, (317)634-7817, http://www.acsm.org.

Maureen Haggerty
Ken R. Wells

Oxycodone *see* **Analgesics, opioid**

Oxygen inhalation therapy *see* **Oxygen/ozone therapy**

Oxygen/ozone therapy

Definition

Oxygen/ozone therapy is a term that describes a number of different practices in which oxygen, ozone, or hydrogen peroxide are administered via gas or water to kill disease microorganisms, improve cellular function, and promote the healing of damaged tissues. The rationale behind bio-oxidative therapies, as they are sometimes known, is the notion that as long as the body's needs for **antioxidants** are met, the use of certain oxidative substances will stimulate the movement of oxygen atoms from the bloodstream to the cells. With higher levels of oxygen in the tissues, bacteria and viruses are killed along with defective tissue cells. The healthy cells survive and multiply more rapidly. The result is a stronger immune system.

Ozone itself is a form of oxygen, O_3, produced when ultraviolet light or an electric spark passes through air or oxygen. It is a toxic gas that creates free radicals, the opposite of what antioxidant **vitamins** do. Oxidation, however, is good when it occurs in harmful foreign organisms that have invaded the body. Ozone inactivates many disease bacteria and viruses.

Purpose

Oxygen and ozone therapies are thought to benefit patients in the following ways:

- stimulating white blood cell production
- killing viruses (ozone and hydrogen peroxide)
- improving the delivery of oxygen from the blood stream to the tissues of the body
- speeding up the breakdown of petrochemicals
- increasing the production of interferon and tumor necrosis factor, thus helping the body to fight infections and cancers
- increasing the efficiency of antioxidant enzymes
- increasing the flexibility and efficiency of the membranes of red blood cells
- speeding up the citric acid cycle, which in turn stimulates the body's basic metabolism

Description

Origins

The various forms of oxygen and ozone therapy have been in use since the late nineteenth century. The earliest recorded use of oxygen to treat a patient was by Dr. J. A. Fontaine in 1879. In the 1950s, hyperbaric oxygen treatment was used by **cancer** researchers. The term "hyperbaric" means that the oxygen is given under pressure higher than normal air pressure. Recently, oxygen therapy has also been touted as a quick purification treatment for mass-market consumers. Oxygen bars can be found in airports and large cities, and provide pure oxygen in 20-minute sessions for approximately $16. While proponents claim that breathing oxygen will purify the body, most medical doctors do not agree. What is more, oxygen can be harmful to people with severe lung diseases, and these people should never self-treat with oxygen.

Ozone has been used since 1856 to disinfect operating rooms in European hospitals, and since 1860 to purify the water supplies of several large German cities. Ozone was not, however, used to treat patients until 1915, when a German doctor named Albert Wolff began to use it to treat skin diseases. During World War I, the German Army used ozone to treat **wounds** and **anaerobic infections**. In the 1950s, several German physicians used ozone to treat cancer alongside mainstream therapeutic methods. It is estimated that as of the late 1990s, about 8,000 practitioners in Germany were using ozone in their practices. This figure includes medical doctors as well as naturopaths and homeopaths.

Hydrogen peroxide is familiar to most people as an over-the-counter preparation that is easily available at supermarkets as well as pharmacies, and is used as an antiseptic for cleansing minor cuts and scrapes. It was first used as an intravenous infusion in 1920 by a British physician in India, T. H. Oliver, to treat a group of 25 Indian patients who were critically ill with **pneumonia**. Oliver's patients had a mortality rate of 48%, compared to the standard mortality rate of 80% for the disease. In the 1920s, a U.S. physician named William Koch experimented with hydrogen

peroxide as a treatment for cancer. He left the United States after a legal battle with the FDA. In the early 1960s, researchers at Baylor University studied the effects of hydrogen peroxide in removing plaque from the arteries as well as its usefulness in treating cancer, but their findings were largely ignored.

Oxygen, ozone, and hydrogen peroxide are used therapeutically in a variety of different ways.

Hyperbaric oxygen therapy (HBO)

Hyperbaric oxygen therapy (HBO) involves putting the patient in a pressurized chamber in which he or she breathes pure oxygen for a period of 90 minutes to two hours. HBO may also be administered by using a tight-fitting mask, similar to the masks used for anesthesia. A nasal catheter may be used for small children.

Ozone therapy

Ozone therapy may be administered in a variety of ways.

- Intramuscular injection: A mixture of oxygen and ozone is injected into the muscles of the buttocks.
- Rectal insufflation: A mixture of oxygen and ozone is introduced into the rectum and absorbed through the intestines.
- Autohemotherapy: Between 10–15 mL of the patient's blood is removed, treated with a mixture of oxygen and ozone and reinjected into the patient.
- Intra-articular injection: Ozone-treated water is injected into the patient's joints to treat arthritis, rheumatism and other joint diseases.
- Ozonated water: Ozone is bubbled through water that is used to cleanse wounds, burns, and skin infections, or to treat the mouth after dental surgery.
- Ozonated oil: Ozone is bubbled through olive or safflower oil, forming a cream that is used to treat fungal infections, insect bites, acne, and skin problems.
- Ozone bagging: Ozone and oxygen are pumped into an airtight bag that surrounds the area to be treated, allowing the body tissues to absorb the mixture.

Hydrogen peroxide

Hydrogen peroxide may be administered intravenously in a 0.03% solution. It is infused slowly into the patient's vein over a period of one to three hours. Treatments are given about once a week for chronic illness but may be given daily for such acute illnesses as pneumonia or **influenza**. A course of intravenous hydrogen peroxide therapy may range from one to 20 treatments, depending on the patient's condition and the type of illness being treated. Injections of 0.03% hydrogen peroxide have also been used to treat rheumatoid and **osteoarthritis**. The solution is injected directly into the inflamed joint.

Hydrogen peroxide is also used externally to treat stiff joints, **psoriasis**, and fungal infections. The patient soaks for a minimum of 20 minutes in a tub of warm water to which one pint of 35% food-grade hydrogen peroxide (a preparation used by the food industry as a disinfectant) has been added.

Preparations

Oxygen is usually delivered to the patient as a gas; ozone as a gas mixed with oxygen or bubbled through oil or water; and hydrogen peroxide as an 0.03% solution for intravenous injection or a 35% solution for external **hydrotherapy**.

Precautions

Patients interested in oxygen/ozone therapies must consult with a physician before receiving treatment. Hyperbaric oxygen treatment should not be given to patients with untreated **pneumothorax**, a condition in which air or gas is present in the cavity surrounding the lungs. Patients with a history of pneumothorax, chest surgery, **emphysema**, middle **ear surgery**, uncontrolled high fevers, upper respitory infections, seizures, or disorders of the red blood cells are not suitable candidates for oxygen/ozone therapy. In addition, patients should be aware that oxygen is highly flammable. If treatments are administered incorrectly or by an unskilled person, there is a risk of fire.

Side effects

Typical side effects of oxygen or ozone therapy can include elevated blood pressure and ear pressure similar to that experienced while flying. Side effects may also include **headache**, **numbness** in the fingers, temporary changes in the lens of the eye, and seizures.

Research and general acceptance

Oxygen/ozone therapies are far more widely accepted in Europe than in the United States. The most intensive research in these therapies is presently being conducted in the former Soviet Union and in Cuba. In the United States, the work of the Baylor researchers was not followed up. In 2000, the Office of Alternative Medicine of the National Institutes of Health (presently the National Center for Complementary and Alternative Medicine, or NCCAM) indicated interest in conducting clinical trials of oxygen/

KEY TERMS

Autohemotherapy—A form of ozone therapy in which a small quantity of the patient's blood is withdrawn, treated with a mixture of ozone and oxygen, and reinfused into the patient.

Hydrogen peroxide—A colorless, unstable compound of hydrogen and oxygen (H_2O_2). An aqueous solution of hydrogen peroxide is used as an antiseptic and bleaching agent.

Hyperbaric oxygen therapy (HBO)—A form of oxygen therapy in which the patient breathes oxygen in a pressurized chamber.

Ozone—A form of oxygen with three atoms in its molecule (O_3), produced by an electric spark or ultraviolet light passing through air or oxygen. Ozone is used therapeutically as a disinfectant and oxidative agent.

ozone therapies; as of 2008, however, these studies have not been carried out.

In 2006, the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), and the Centers for Medicare and Medicaid Services launched a large-scale clinical trial of the effectiveness and safety of long-term, home oxygen therapy for people with **chronic obstructive pulmonary disease** (COPD). The six-year study of about 3,500 people with moderate COPD is being conducted at 14 medical facilities in the United States, including Ohio State University, Los Angeles Biomedical Research Institute, and Duke University.

Recent European research in ozone therapy includes studies in the oxygenation of resting muscles, the treatment of vascular disorders, and the relief of **pain** from herniated lumbar disks. No corresponding studies are being done in the United States as of early 2008.

Resources

BOOKS

Altman, Nathaniel. *The Oxygen Prescription: The Miracle of Oxidative Therapies*. Rochester, VT: Healing Arts Press, 2007.

Harch, Paul G., and Virginia McCullough. *The Oxygen Revolution: Hyperbaric Oxygen Therapy: The Groundbreaking New Treatment for Stroke, Alzheimer's, Parkinson's, Arthritis, Autism, Learning Disabilities and More*. Long Island City, NY: Hatherleigh Press, 2007.

PERIODICALS

Ali, Majid. "The Dysox Model of Respiratory Viral Infections: The Lessons of the 1918 Spanish Flu Pandemic." *Townsend Letter: The Examiner of Alternative Medicine* (December 2006): 138(4).

McMillan, Grant, and Mark Glover. "The Clinical and Economical Potential of Hyperbaric Oxygen Therapy in the Treatment of Diabetic Ulceration and Other Conditions." *International Journal of Lower Extremity Wounds* (September 2007): 130(9).

"Ozone Cure for Slipped Disc." *Times of India* (May 16, 2007).

Senechal, Carole, et al. "Hyperbaric Oxygenation Therapy in the Treatment of Cerebral Palsy: A Review and Comparison to Currently Accepted Therapies." *Journal of American Physicians and Surgeons* (Winter 2007): 109(5).

OTHER

Oxygen Healing Therapies. http://www.oxygenhealingtherapies.com. (Accessed Jan. 4, 2008.)

ORGANIZATIONS

American Institute of Homeopathy, 101 South Whiting Street, Suite 16, Alexandria, VA, 22304, (888)445-9988, admin@homeopathyusa.org, http://www.homeopathyusa.org.

Australian Homeopathic Association, P.O. Box 7108, Toowoomba, Australia, (07)4646 4380, (07)4646 4393, admin@homeopathyoz.org, http://www.homeopathyoz.org.

Council for Homeopathic Certification, PMB 187, 16915 SE 272nd St., Suite 100, Covington, WA, 98042, (815)366-7622, (866)242-3399, http://www.homeopathicdirectory.com.

Homeopathic Medical Council of Canada, 31 Adelaide Street East, Box 605, Toronto, CanadaOntario, M5C 2J8, (416)788-4622, Ontario@HMCC.ca, http://www.hmcc.ca.

Amy Cooper
Ken R. Wells

Oxymetazoline *see* **Decongestants**

Oxytocin *see* **Drugs used in labor**

Ozone therapy *see* **Oxygen/ozone therapy**