THE OFFICIAL PATIENT'S SOURCEBOOK *On*

AUTOIMMUNE DISEASES

A Revised and Updated Directory for the Internet Age

JAMES N. PARKER, M.D.
AND PHILIP M. PARKER, PH.D., EDITORS

A REFERENCE MANUAL FOR SELF-DIRECTED PATIENT RESEARCH

Full Internet Referencing - Essentials and Advanced Studies - Chapter Glossaries

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Dedication

To the healthcare professionals dedicating their time and efforts to the study of autoimmune diseases.

Acknowledgements

The collective knowledge generated from academic and applied research summarized in various references has been critical in the creation of this sourcebook which is best viewed as a comprehensive compilation and collection of information prepared by various official agencies which directly or indirectly are dedicated to autoimmune diseases. All of the *Official Patient's Sourcebooks* draw from various agencies and institutions associated with the United States Department of Health and Human Services, and in particular, the Office of the Secretary of Health and Human Services (OS), the Administration for Children and Families (ACF), the Administration on Aging (AOA), the Agency for Healthcare Research and Quality (AHRQ), the Agency for Toxic Substances and Disease Registry (ATSDR), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Healthcare Financing Administration (HCFA), the Health Resources and Services Administration (HRSA), the Indian Health Service (IHS), the institutions of the National Institutes of Health (NIH), the Program Support Center (PSC), and the Substance Abuse and Mental Health Services Administration (SAMHSA). In addition to these sources, information gathered from the National Library of Medicine, the United States Patent Office, the European Union, and their related organizations has been invaluable in the creation of this sourcebook. Some of the work represented was financially supported by the Research and Development Committee at INSEAD. This support is gratefully acknowledged. Finally, special thanks are owed to Tiffany LaRochelle for her excellent editorial support.

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About ICON Health Publications

In addition to autoimmune diseases, *Official Patient's Sourcebooks* are available for the following related topics:

- The Official Patient's Sourcebook on Behcet's Disease
- The Official Patient's Sourcebook on Crohn's Disease
- The Official Patient's Sourcebook on Immune Thrombocytopenic Purpura
- The Official Patient's Sourcebook on Sjogren's Syndrome

To discover more about ICON Health Publications, simply check with your preferred online booksellers, including Barnes & Noble.com and Amazon.com which currently carry all of our titles. Or, feel free to contact us directly for bulk purchases or institutional discounts:

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INTRODUCTION

Overview

Dr. C. Everett Koop, former U.S. Surgeon General, once said, "The best prescription is knowledge."[1] The Agency for Healthcare Research and Quality (AHRQ) of the National Institutes of Health (NIH) echoes this view and recommends that every patient incorporate education into the treatment process. According to the AHRQ:

> Finding out more about your condition is a good place to start. By contacting groups that support your condition, visiting your local library, and searching on the Internet, you can find good information to help guide your treatment decisions. Some information may be hard to find—especially if you don't know where to look.[2]

As the AHRQ mentions, finding the right information is not an obvious task. Though many physicians and public officials had thought that the emergence of the Internet would do much to assist patients in obtaining reliable information, in March 2001 the National Institutes of Health issued the following warning:

> The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading.[3]

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[1] Quotation from **http://www.drkoop.com**.
[2] The Agency for Healthcare Research and Quality (AHRQ): **http://www.ahcpr.gov/consumer/diaginfo.htm**.
[3] From the NIH, National Cancer Institute (NCI): **http://cancertrials.nci.nih.gov/beyond/evaluating.html**.

Since the late 1990s, physicians have seen a general increase in patient Internet usage rates. Patients frequently enter their doctor's offices with printed Web pages of home remedies in the guise of latest medical research. This scenario is so common that doctors often spend more time dispelling misleading information than guiding patients through sound therapies. *The Official Patient's Sourcebook on Autoimmune Diseases* has been created for patients who have decided to make education and research an integral part of the treatment process. The pages that follow will tell you where and how to look for information covering virtually all topics related to autoimmune diseases, from the essentials to the most advanced areas of research.

The title of this book includes the word "official." This reflects the fact that the sourcebook draws from public, academic, government, and peer-reviewed research. Selected readings from various agencies are reproduced to give you some of the latest official information available to date on autoimmune diseases.

Given patients' increasing sophistication in using the Internet, abundant references to reliable Internet-based resources are provided throughout this sourcebook. Where possible, guidance is provided on how to obtain free-of-charge, primary research results as well as more detailed information via the Internet. E-book and electronic versions of this sourcebook are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). Hard copy users of this sourcebook can type cited Web addresses directly into their browsers to obtain access to the corresponding sites. Since we are working with ICON Health Publications, hard copy *Sourcebooks* are frequently updated and printed on demand to ensure that the information provided is current.

In addition to extensive references accessible via the Internet, every chapter presents a "Vocabulary Builder." Many health guides offer glossaries of technical or uncommon terms in an appendix. In editing this sourcebook, we have decided to place a smaller glossary within each chapter that covers terms used in that chapter. Given the technical nature of some chapters, you may need to revisit many sections. Building one's vocabulary of medical terms in such a gradual manner has been shown to improve the learning process.

We must emphasize that no sourcebook on autoimmune diseases should affirm that a specific diagnostic procedure or treatment discussed in a research study, patent, or doctoral dissertation is "correct" or your best option. This sourcebook is no exception. Each patient is unique. Deciding on

appropriate options is always up to the patient in consultation with their physician and healthcare providers.

Organization

This sourcebook is organized into three parts. Part I explores basic techniques to researching autoimmune diseases (e.g. finding guidelines on diagnosis, treatments, and prognosis), followed by a number of topics, including information on how to get in touch with organizations, associations, or other patient networks dedicated to autoimmune diseases. It also gives you sources of information that can help you find a doctor in your local area specializing in treating autoimmune diseases. Collectively, the material presented in Part I is a complete primer on basic research topics for patients with autoimmune diseases.

Part II moves on to advanced research dedicated to autoimmune diseases. Part II is intended for those willing to invest many hours of hard work and study. It is here that we direct you to the latest scientific and applied research on autoimmune diseases. When possible, contact names, links via the Internet, and summaries are provided. It is in Part II where the vocabulary process becomes important as authors publishing advanced research frequently use highly specialized language. In general, every attempt is made to recommend "free-to-use" options.

Part III provides appendices of useful background reading for all patients with autoimmune diseases or related disorders. The appendices are dedicated to more pragmatic issues faced by many patients with autoimmune diseases. Accessing materials via medical libraries may be the only option for some readers, so a guide is provided for finding local medical libraries which are open to the public. Part III, therefore, focuses on advice that goes beyond the biological and scientific issues facing patients with autoimmune diseases.

Scope

While this sourcebook covers autoimmune diseases, your doctor, research publications, and specialists may refer to your condition using a variety of terms. Therefore, you should understand that autoimmune diseases is often considered a synonym or a condition closely related to the following:

- Anemia - Idiopathic Autoimmune Hemolytic

- Anemia, Autoimmune Hemolytic
- Autoimmune Hemolytic Anemia
- Autoimmune Thrombocytopenic Purpura
- Cold Agglutinin Disease
- Cold Antibody Disease
- Diffuse Thyrotoxic Goiter
- Goitrous Autoimmune Thyroiditis
- Hashimoto's Disease
- Hashimoto's Thyroiditis
- Immune Hemolytic Anemia
- Immune Thrombocytopenic Purpura
- Lupoid Hepatitis
- Lymphadenoid Goiter
- Postinfectious Thrombocytopenia
- Purpura Hemorrhagica Itp
- Struma Lymphomatosa
- Warm Reacting Antibody Disease
- Warm Reactive Antibody
- Werlhof Disease
- Werlhof's Disease

In addition to synonyms and related conditions, physicians may refer to autoimmune diseases using certain coding systems. The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) is the most commonly used system of classification for the world's illnesses. Your physician may use this coding system as an administrative or tracking tool. The following classification is commonly used for autoimmune diseases:[4]

- 283.0 autoimmune hemolytic anemia
- 283.0 autoimmune hemolytic anemias

[4] This list is based on the official version of the World Health Organization's 9th Revision, International Classification of Diseases (ICD-9). According to the National Technical Information Service, "ICD-9CM extensions, interpretations, modifications, addenda, or errata other than those approved by the U.S. Public Health Service and the Health Care Financing Administration are not to be considered official and should not be utilized. Continuous maintenance of the ICD-9-CM is the responsibility of the federal government."

- 287.3 idiopathic thrombocy-topenic purpura (itp)
- 287.3 primary thrombocytopenia
- 288.0 neutropenia

For the purposes of this sourcebook, we have attempted to be as inclusive as possible, looking for official information for all of the synonyms relevant to autoimmune diseases. You may find it useful to refer to synonyms when accessing databases or interacting with healthcare professionals and medical librarians.

Moving Forward

Since the 1980s, the world has seen a proliferation of healthcare guides covering most illnesses. Some are written by patients or their family members. These generally take a layperson's approach to understanding and coping with an illness or disorder. They can be uplifting, encouraging, and highly supportive. Other guides are authored by physicians or other healthcare providers who have a more clinical outlook. Each of these two styles of guide has its purpose and can be quite useful.

As editors, we have chosen a third route. We have chosen to expose you to as many sources of official and peer-reviewed information as practical, for the purpose of educating you about basic and advanced knowledge as recognized by medical science today. You can think of this sourcebook as your personal Internet age reference librarian.

Why "Internet age"? All too often, patients diagnosed with autoimmune diseases will log on to the Internet, type words into a search engine, and receive several Web site listings which are mostly irrelevant or redundant. These patients are left to wonder where the relevant information is, and how to obtain it. Since only the smallest fraction of information dealing with autoimmune diseases is even indexed in search engines, a non-systematic approach often leads to frustration and disappointment. With this sourcebook, we hope to direct you to the information you need that you would not likely find using popular Web directories. Beyond Web listings, in many cases we will reproduce brief summaries or abstracts of available reference materials. These abstracts often contain distilled information on topics of discussion.

While we focus on the more scientific aspects of autoimmune diseases, there is, of course, the emotional side to consider. Later in the sourcebook, we

provide a chapter dedicated to helping you find peer groups and associations that can provide additional support beyond research produced by medical science. We hope that the choices we have made give you the most options available in moving forward. In this way, we wish you the best in your efforts to incorporate this educational approach into your treatment plan.

The Editors

PART I: THE ESSENTIALS

ABOUT PART I

Part I has been edited to give you access to what we feel are "the essentials" on autoimmune diseases. The essentials of a disease typically include the definition or description of the disease, a discussion of who it affects, the signs or symptoms associated with the disease, tests or diagnostic procedures that might be specific to the disease, and treatments for the disease. Your doctor or healthcare provider may have already explained the essentials of autoimmune diseases to you or even given you a pamphlet or brochure describing autoimmune diseases. Now you are searching for more in-depth information. As editors, we have decided, nevertheless, to include a discussion on where to find essential information that can complement what your doctor has already told you. In this section we recommend a process, not a particular Web site or reference book. The process ensures that, as you search the Web, you gain background information in such a way as to maximize your understanding.

CHAPTER 1. THE ESSENTIALS ON AUTOIMMUNE DISEASES: GUIDELINES

Overview

Official agencies, as well as federally-funded institutions supported by national grants, frequently publish a variety of guidelines on autoimmune diseases. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. The great advantage of guidelines over other sources is that they are often written with the patient in mind. Since new guidelines on autoimmune diseases can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

The National Institutes of Health (NIH)[5]

The National Institutes of Health (NIH) is the first place to search for relatively current patient guidelines and fact sheets on autoimmune diseases. Originally founded in 1887, the NIH is one of the world's foremost medical research centers and the federal focal point for medical research in the United States. At any given time, the NIH supports some 35,000 research grants at universities, medical schools, and other research and training institutions, both nationally and internationally. The rosters of those who have conducted research or who have received NIH support over the years include the world's most illustrious scientists and physicians. Among them are 97 scientists who have won the Nobel Prize for achievement in medicine.

[5] Adapted from the NIH: **http://www.nih.gov/about/NIHoverview.html**.

There is no guarantee that any one Institute will have a guideline on a specific disease, though the National Institutes of Health collectively publish over 600 guidelines for both common and rare diseases. The best way to access NIH guidelines is via the Internet. Although the NIH is organized into many different Institutes and Offices, the following is a list of key Web sites where you are most likely to find NIH clinical guidelines and publications dealing with autoimmune diseases and associated conditions:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines available at **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- Centers for Disease Control and Prevention: various fact sheets on infectious diseases at **http://www.cdc.gov/health/diseases.htm**

Among the above, the National Institute of Allergy and Infectious Diseases (NIAID) is particularly noteworthy. The mission of the NIAID is to provide support for scientists conducting research aimed at developing better ways to diagnose, treat, and prevent the many infectious, immunologic and allergic diseases that afflict people worldwide.[6] The NIAID is composed of four extramural divisions: the Division of AIDS; the Division of Allergy, Immunology and Transplantation; the Division of Microbiology and Infectious Diseases; and the Division of Extramural Activities. In addition, NIAID scientists conduct intramural research in laboratories located in Bethesda, Rockville and Frederick, Maryland, and in Hamilton, Montana. The following patient guideline was recently published by the NIAID on autoimmune diseases.

What Are Autoimmune Diseases?[7]

The word "auto" is the Greek word for self. The immune system is a complicated network of cells and cell components (called molecules) that normally work to defend the body and eliminate infections caused by

[6] This paragraph has been adapted from the NIAID: **http://www.niaid.nih.gov/facts/overview.htm**. "Adapted" signifies that a passage has been reproduced exactly or slightly edited for this book.

[7] Adapted from The National Institute of Allergy and Infectious Diseases (NIAID): **http://www.niaid.nih.gov/publications/autoimmune/contents.htm**.

bacteria, viruses, and other invading microbes. If a person has an autoimmune disease, the immune system mistakenly attacks self, targeting the cells, tissues, and organs of a person's own body. A collection of immune system cells and molecules at a target site is broadly referred to as inflammation.

There are many different autoimmune diseases, and they can each affect the body in different ways. For example, the autoimmune reaction is directed against the brain in multiple sclerosis and the gut in Crohn's disease. In other autoimmune diseases such as systemic lupus erythematosus (lupus), affected tissues and organs may vary among individuals with the same disease. One person with lupus may have affected skin and joints whereas another may have affected skin, kidney, and lungs. Ultimately, damage to certain tissues by the immune system may be permanent, as with destruction of insulin-producing cells of the pancreas in Type 1 diabetes mellitus.

Who Is Affected by Autoimmune Diseases?

Many of the autoimmune diseases are rare. As a group, however, autoimmune diseases afflict millions of Americans. Most autoimmune diseases strike women more often than men; in particular, they affect women of working age and during their childbearing years.

Some autoimmune diseases occur more frequently in certain minority populations. For example, lupus is more common in African-American and Hispanic women than in Caucasian women of European ancestry. Rheumatoid arthritis and scleroderma affect a higher percentage of residents in some Native American communities than in the general U.S. population. Thus, the social, economic, and health impact from autoimmune diseases is far-reaching and extends not only to family but also to employers, co-workers, and friends.

What Are the Causes of Autoimmune Diseases?

Are they contagious? No autoimmune disease has ever been shown to be contagious or "catching." Autoimmune diseases do not spread to other people like infections. They are not related to AIDS, nor are they a type of cancer.

Are they inherited? The genes people inherit contribute to their susceptibility for developing an autoimmune disease. Certain diseases such as psoriasis can occur among several members of the same family. This suggests that a specific gene or set of genes predisposes a family member to psoriasis. In addition, individual family members with autoimmune diseases may inherit and share a set of abnormal genes, although they may develop different autoimmune diseases. For example, one first cousin may have lupus, another may have dermatomyositis, and one of their mothers may have rheumatoid arthritis.

Examples of Autoimmune Diseases: (Listed by the Main Target Organ)

Nervous System:

- Multiple sclerosis
- Myasthenia gravis
- Autoimmune neuropathies such as Guillain-Barré
- Autoimmune uveitis

Gastrointestinal System:

- Crohn's Disease
- Ulcerative colitis
- Primary biliary cirrhosis
- Autoimmune hepatitis

Endocrine Glands:

- Type 1 or immune-mediated diabetes mellitus
- Hashimoto's thyroiditis
- Grave's Disease

Blood:

- Autoimmune hemolytic anemia
- Pernicious anemia
- Autoimmune thrombocytopenia
- Autoimmune oophoritis and orchitis
- Autoimmune disease of the adrenal gland

Blood Vessels:

- Temporal arteritis
- Anti-phospholipid syndrome
- Vasculitides such as Wegener's granulomatosis
- Behcet's disease

Multiple Organs Including the Musculoskeletal System:[8]

- Rheumatoid arthritis
- Systemic lupus erythematosus
- Scleroderma
- Polymyositis, dermatomyositis
- Spondyloarthropathies such as ankylosing spondylitis
- Sjogren's syndrome

Skin:

- Psoriasis
- Dermatitis herpetiformis
- Pemphigus vulgaris
- Vitiligo

The development of an autoimmune disease may be influenced by the genes a person inherits together with the way the person's immune system responds to certain triggers or environmental influences.

What Other Factors May Influence the Development of Autoimmune Diseases?

Some autoimmune diseases are known to begin or worsen with certain triggers such as viral infections. Sunlight not only acts as a trigger for lupus but can worsen the course of the disease. It is important to be aware of the factors that can be avoided to help prevent or minimize the amount of damage from the autoimmune disease. Other less understood influences affecting the immune system and the course of autoimmune diseases include aging, chronic stress, hormones, and pregnancy.

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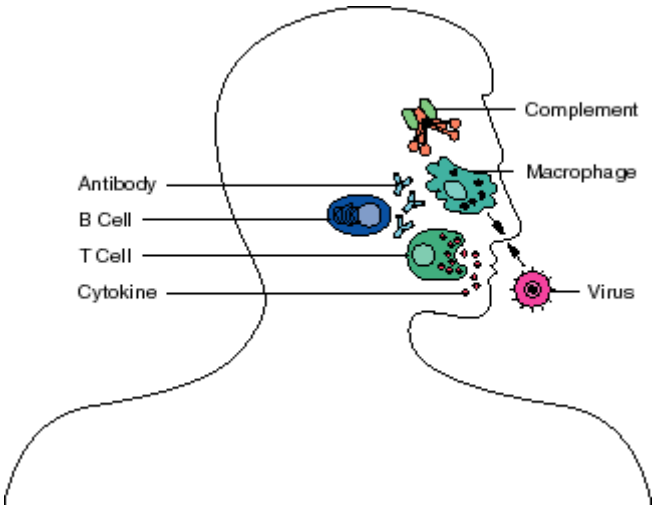
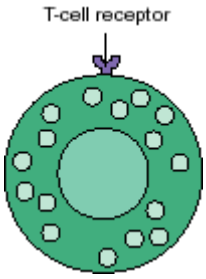
[8] These diseases are also called connective tissue (muscle, skeleton, tendons, fascia, etc.) diseases.

How Does the Immune System Work?

The immune system defends the body from attack by invaders recognized as foreign. It is an extraordinarily complex system that relies on an elaborate and dynamic communications network that exists among the many different kinds of immune system cells that patrol the body. At the heart of the system is the ability to recognize and respond to substances called antigens whether they are infectious agents or part of the body (self antigens).



Cells and molecules of the immune system protect the nose from attack by a virus.



T cell (lymphocyte) with a T-cell receptor on its surface

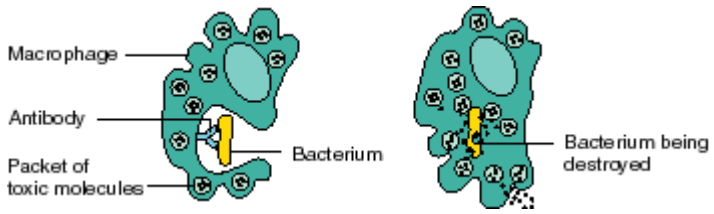
T and B Cells

Most immune system cells are white blood cells, of which there are many types. Lymphocytes are one type of white blood cell, and two major classes of lymphocytes are T cells and B cells. T cells are critical immune system cells that help to destroy infected cells and coordinate the overall immune response. The T cell has a molecule on its surface called the T-cell receptor.

This receptor interacts with molecules called MHC (major histocompatibility complex). MHC molecules are on the surfaces of most other cells of the body and help T cells recognize antigen fragments. B cells are best known for making antibodies. An antibody binds to an antigen and marks the antigen for destruction by other immune system cells. Other types of white blood cells include macrophages and neutrophils.

Macrophages and Neutrophils

Macrophages and neutrophils circulate in the blood and survey the body for foreign substances. When they find foreign antigens, such as bacteria, they engulf and destroy them. Macrophages and neutrophils destroy foreign antigens by making toxic molecules such as reactive oxygen intermediate molecules. If production of these toxic molecules continues unchecked, not only are the foreign antigens destroyed, but tissues surrounding the macrophages and neutrophils are also destroyed. For example, in individuals with the autoimmune disease called Wegener's granulomatosis, overactive macrophages and neutrophils that invade blood vessels produce many toxic molecules and contribute to damage of the blood vessels. In rheumatoid arthritis, reactive oxygen intermediate molecules and other toxic molecules are made by overproductive macrophages and neutrophils invading the joints. The toxic molecules contribute to inflammation, which is observed as warmth and swelling, and participate in damage to the joint.

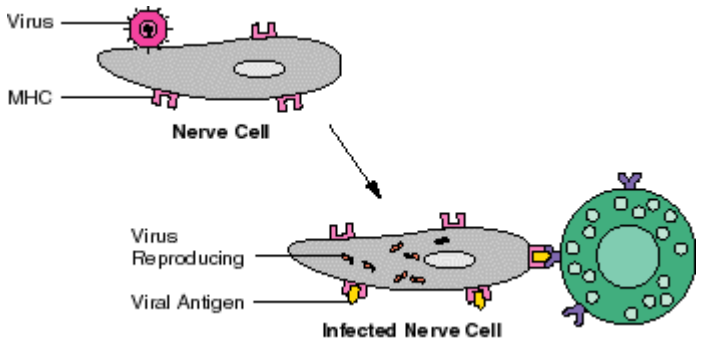


A macrophage engulfing a bacterium and releasing packets of toxic molecules (reactive oxygen intermediates) that break down and destroy the bacterium.

MHC and Co-Stimulatory Molecules

MHC molecules are found on all cell surfaces and are an active part of the body's defense team. For example, when a virus infects a cell, a MHC molecule binds to a piece of a virus (antigen) and displays the antigen on the

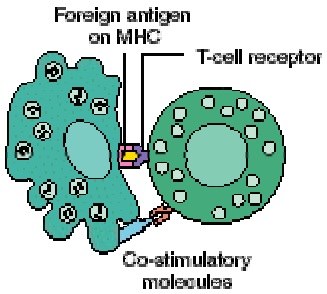
cell's surface. Cells that have the capability of displaying antigen with MHC are called antigen-presenting cells. Each MHC molecule that displays an antigen is recognized by a matching or compatible T-cell receptor. Thus, an antigen-presenting cell is able to communicate with a T cell about what may be occurring inside the cell.



Upper left: a virus attacking a nerve cell. Lower right: a T cell with a T-cell receptor recognizing a piece of a virus (antigen) on the MHC of the infected nerve cell.

However, for the T cell to respond to a foreign antigen on the MHC, another molecule on the antigen-presenting cell must send a second signal to the T cell. A corresponding molecule on the surface of the T cells recognizes the second signal. These two secondary molecules of the antigen-presenting cell and the T cell are called co-stimulatory molecules. There are several different sets of co-stimulatory molecules that can participate in the interaction of antigen-presenting cell with a T cell.

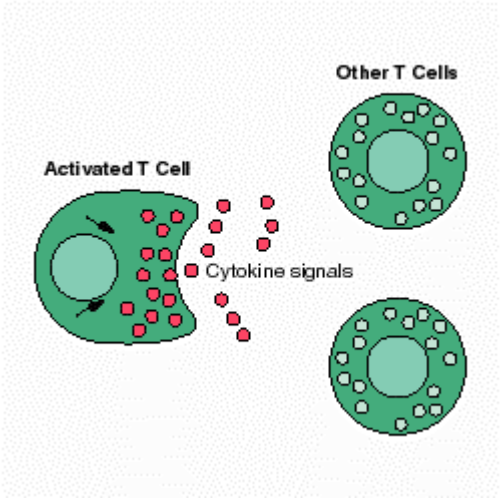
Once the MHC and the T-cell receptor interact, and the co-stimulatory molecules interact, there are several possible paths that the T cell may take. These include T cell activation, tolerance, or T cell death. The subsequent steps depend in part on which co-stimulatory molecules interact and how well they interact. Because these interactions are so critical to the response of the immune system, researchers are intensively studying them to find new therapies that could control or stop the immune system attack on self tissues and organs.



An antigen-presenting cell (for example, a macrophage) with a foreign antigen on its MHC is recognized by a T-cell receptor. In addition, co-stimulatory molecules on the antigen-presenting cell and the T cell interact.

Cytokines and Chemokines

One way T cells can respond after the interaction of the MHC and the T-cell receptor, and the interaction of the co-stimulatory molecules, is to secrete cytokines and chemokines. Cytokines are proteins that may cause surrounding immune system cells to become activated, grow, or die. They also may influence non-immune system tissues. For example, some cytokines may contribute to the thickening of the skin that occurs in people with scleroderma.

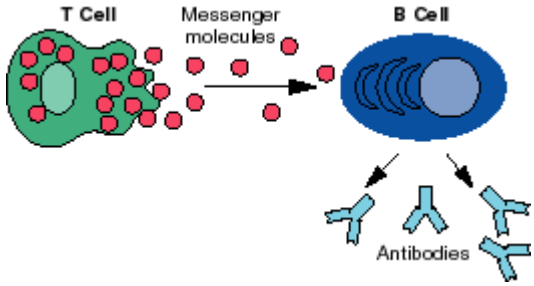


After the antigen-presenting cell and T cell interact through the MHC, T-cell receptor and co-stimumlatory and molecules, the T cell becomes activated, sending cytokine signals to other cells.

Chemokines are small cytokine molecules that attract cells of the immune system. Overproduction of chemokines contributes to the invasion and inflammation of the target organ, which occurs in autoimmune diseases. For example, overproduction of chemokines in the joints of people with rheumatoid arthritis may result in invasion of the joint space by destructive immune system cells such as macrophages, neutrophils, and T cells.

Antibodies

B cells are another critical type of immune system cell. They participate in the removal of foreign antigens from the body by using a surface molecule to bind the antigen or by making specific antibodies that can search out and destroy specific foreign antigens. However, the B cell can only make antibodies when it receives the appropriate command signal from a T cell. Once the T cell signals the B cell with a type of cytokine that acts as a messenger molecule, the B cell is able to produce a unique antibody that targets a particular antigen.



A T cell sends messenger molecules, e.g. cytokines, to the B cell, which allows the B cell to start making antibodies.

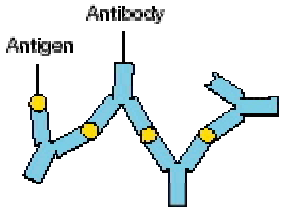
Autoantibodies

In some autoimmune diseases, B cells mistakenly make antibodies against tissues of the body (self antigens) instead of foreign antigens. Occasionally, these autoantibodies either interfere with the normal function of the tissues or initiate destruction of the tissues. People with myasthenia gravis experience muscle weakness because autoantibodies attack a part of the nerve that stimulates muscle movement. In the skin disease pemphigus vulgaris, autoantibodies are misdirected against cells in the skin. The

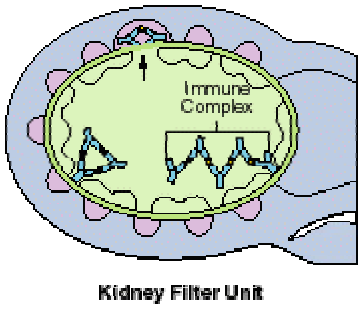
accumulation of antibodies in the skin activates other molecules and cells to break down, resulting in skin blisters.

Immune Complexes and the Complement System

When many antibodies are bound to antigens in the bloodstream, they form a large lattice network called an immune complex. Immune complexes are harmful when they accumulate and initiate inflammation within small blood vessels that nourish tissues. Immune complexes, immune cells, and inflammatory molecules can block blood flow and ultimately destroy organs such as the kidney. This can occur in people with systemic lupus erythematosus.



A large immune complex.



If immune complexes accumulate in the kidney, they may promote movement of other inflammatory cells and molecules into the kidney.

A group of specialized molecules that form the complement system helps to remove immune complexes. The different types of molecules of the complement system, which are found in the bloodstream and on the surfaces

of cells, make immune complexes more soluble. Complement molecules prevent formation and reduce the size of immune complexes so they do not accumulate in the wrong places (organs and tissues of the body). Rarely, some people inherit defective genes for a complement molecule from their parents. Because these individuals cannot make a normal amount or type of complement molecule, their immune systems are unable to prevent immune complexes from being deposited in different tissues and organs. These people develop a disease that is not autoimmune but resembles lupus erythematosus.

Genetic Factors

Genetic factors can affect an individual's immune system and its responses to foreign antigens in several ways. Genes determine the variety of MHC molecules that individuals carry on their cells. Genes also influence the potential array of T-cell receptors present on T cells. In fact, some MHC genes are associated with autoimmune diseases. However, genes are not the only factors involved in determining a person's susceptibility to an autoimmune disease. For example, some individuals who carry disease-associated MHC molecules on their cells will not develop an autoimmune disease.

How Are Autoimmune Diseases Diagnosed?

The diagnosis of an autoimmune disease is based on an individual's symptoms, findings from a physical examination, and results from laboratory tests. Autoimmune diseases can be difficult to diagnose, particularly early in the course of the disease. Symptoms of many autoimmune diseases—such as fatigue—are nonspecific. Laboratory test results may help but are often inadequate to confirm a diagnosis.

If an individual has skeletal symptoms such as joint pain and a positive but nonspecific lab test, she or he may be diagnosed with the confusing name of early or "undifferentiated" connective tissue disease. In this case, a physician may want the patient to return frequently for follow up. The early phase of disease may be a very frustrating time for both the patient and physician. On the other hand, symptoms may be short-lived, and inconclusive laboratory tests may amount to nothing of a serious nature.

In some cases, a specific diagnosis can be made. A diagnosis shortly after onset of a patient's symptoms will allow for early aggressive medical

therapy; and for some diseases, patients will respond completely to treatments if the reason for their symptoms is discovered early in the course of their disease.

Although autoimmune diseases are chronic, the course they take is unpredictable. A doctor cannot foresee what will happen to the patient based on how the disease starts. Patients should be monitored closely by their doctors so environmental factors or triggers that may worsen the disease can be discussed and avoided and new medical therapy can be started as soon as possible. Frequent visits to a doctor are important in order for the physician to manage complex treatment regimens and watch for medication side effects.

How Are Autoimmune Diseases Treated?

Autoimmune diseases are often chronic, requiring lifelong care and monitoring, even when the person may look or feel well. Currently, few autoimmune diseases can be cured or made to "disappear" with treatment. However, many people with these diseases can live normal lives when they receive appropriate medical care.

Physicians most often help patients manage the consequences of inflammation caused by the autoimmune disease. For example, in people with Type 1 diabetes, physicians prescribe insulin to control blood sugar levels so that elevated blood sugar will not damage the kidneys, eyes, blood vessels, and nerves. However, the goal of scientific research is to prevent inflammation from causing destruction of the insulin-producing cells of the pancreas, which are necessary to control blood sugars.

On the other hand, in some diseases such as lupus or rheumatoid arthritis, medication can occasionally slow or stop the immune system's destruction of the kidneys or joints. Medications or therapies that slow or suppress the immune system response in an attempt to stop the inflammation involved in the autoimmune attack are called immunosuppressive medications. These drugs include corticosteroids (prednisone), methotrexate, cyclophosphamide, azathioprine, and cyclosporin. Unfortunately, these medications also suppress the ability of the immune system to fight infection and have other potentially serious side effects.

In some people, a limited number of immuno-suppressive medications may result in disease remission. Remission is the medical term used for

"disappearance" of a disease for a significant amount of time. Even if their disease goes into remission, patients are rarely able to discontinue medications. The possibility that the disease may restart when medication is discontinued must be balanced with the long-term side effects from the immunosuppressive medication.

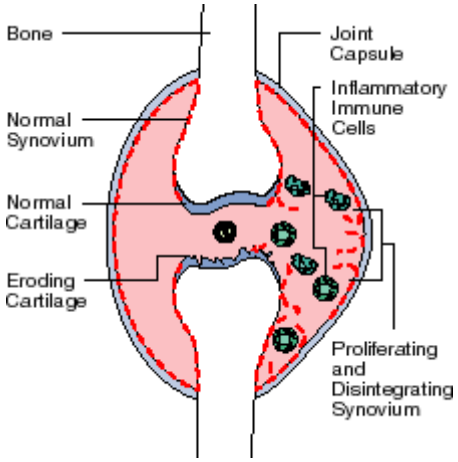
A current goal in caring for patients with autoimmune diseases is to find treatments that produce remissions with fewer side effects. Much research is focused on developing therapies that target various steps in the immune response. New approaches such as therapeutic antibodies against specific T cell molecules may produce fewer long-term side effects than the chemotherapies that now are routinely used.

Ultimately, medical science is striving to design therapies that prevent autoimmune diseases. To this end, a significant amount of time and resources are spent studying the immune system and pathways of inflammation.

What Are Some Examples of Autoimmune Diseases?

Rheumatoid Arthritis

In people with rheumatoid arthritis, the immune system predominantly targets the lining (synovium) that covers various joints. Inflammation of the synovium is usually symmetrical (occurring equally on both sides of the body) and causes pain, swelling, and stiffness of the joints. These features distinguish rheumatoid arthritis from osteoarthritis, which is a more common and degenerative "wear-and-tear" arthritis.



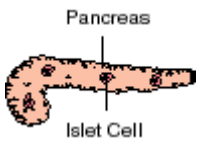
An inflamed joint – the synovium – is attacked by cells and molecules of the immune system.

Currently available therapy focuses on reducing inflammation of the joints with anti-inflammatory or immunosuppresssive medications. Sometimes, the immune system may also target the lung, blood vessels, or eye; occasionally patients may also develop symptoms of other autoimmune diseases such as Sjogren's the inflammation, itching, and scaling. For more severe cases, oral medications are used. Psoriasis is common and may affect more than 2 out of 100 Americans. Psoriasis often runs in families.

Multiple Sclerosis

Multiple sclerosis is a disease in which the immune system targets nerve tissues of the central nervous system. Most commonly, damage to the central nervous system occurs intermittently, allowing a person to lead a fairly normal life. At the other extreme, the symptoms may become constant, resulting in a progressive disease with possible blindness, paralysis, and premature death. Some medications such as beta interferon are helpful to people with the intermittent form of multiple sclerosis.

In young adults, multiple sclerosis is the most common disabling disease of the nervous system. Multiple sclerosis afflicts 1 in 700 people in this country. Researchers continue to search for triggers of the disease.



Immune-Mediated or Type 1 Diabetes Mellitus

Type 1 diabetes mellitus results from autoimmune destruction of the insulin-producing cells of the pancreas. Insulin is required by the body to keep the blood sugar (glucose) level under control. High levels of glucose are responsible for the symptoms and the complications of the disease. However, most of the insulin-producing cells are destroyed before the patient develops symptoms of diabetes. Symptoms include fatigue, frequent urination, increased thirst, and possible sudden confusion.

Type 1 diabetes mellitus is usually diagnosed before the age of 30 and may be diagnosed as early as the first month of life. Together with Type 2 diabetes (not considered an autoimmune disease), diabetes mellitus is the leading cause of kidney damage, loss of eyesight, and leg amputation. Close control of sugar levels decreases the rate at which these events occur. There is a genetic predisposition to Type 1 diabetes, which occurs in 1 out of 800 people in the United States. Among individuals who have a close relative with Type 1 diabetes, those at high risk for developing disease can be identified. Efforts are now under way to evaluate prevention strategies for these family members at risk.

Sunlight is one of the triggers of lupus and can worsen the progression of the disease.

Inflammatory Bowel Diseases

This medical term is used for both Crohn's disease and ulcerative colitis, two diseases in which the immune system attacks the gut (intestine). Patients may have diarrhea, nausea, vomiting, abdominal cramps, and pain that can be difficult to control. Illness in afflicted individuals can result from intestinal inflammation and from side effects of the drugs used for the disease. For example, daily use of high-dose corticosteroid (prednisone) therapy, which is needed to control severe symptoms of Crohn's disease, can predispose patients to infections, bone thinning (osteoporosis), and fractures. For patients with ulcerative colitis, surgical removal of the lower intestine (colon) will eliminate the disease and their increased risk for colon cancer. More than 1 in 500 Americans has some type of inflammatory bowel disease.

Systemic Lupus Erythematosus

Patients with systemic lupus erythematosus most commonly experience profound fatigue, rashes, and joint pains. In severe cases, the immune system may attack and damage several organs such as the kidney, brain, or lung. For many individuals, symptoms and damage from the disease can be controlled with available anti-inflammatory medications. However, if a patient is not closely monitored, the side effects from the medications can be quite serious. Lupus occurs in 1 out of 2,000 Americans and in as many as 1 in 250 young, African-American women.

Psoriasis

Psoriasis is an immune system disorder that affects the skin, and occasionally the eyes, nails, and joints. Psoriasis may affect very small areas of skin or cover the entire body with a buildup of red scales called plaques. The plaques are of different sizes, shapes, and severity and may be painful as well as unattractive. Bacterial infections and pressure or trauma to the skin can aggravate psoriasis. Most treatments focus on topical skin care to relieve the inflammation, itching, and scaling. For more severe cases, oral medications are used. Psoriasis is common and may affect more than 2 out of 100 Americans. Psoriasis often runs in families.

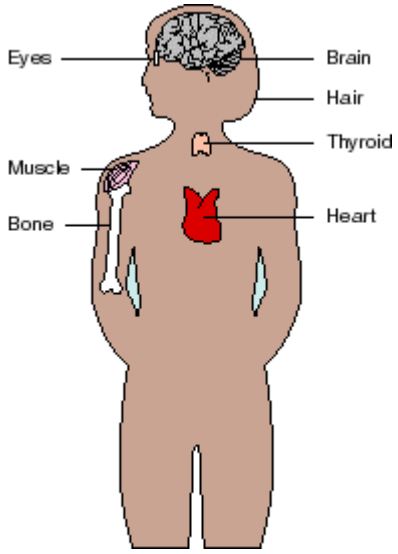
Scleroderma

This autoimmune disease results in thickening of the skin and blood vessels. Almost every patient with scleroderma has Raynaud's, which is a spasm of the blood vessels of the fingers and toes. Symptoms of Raynaud's include increased sensitivity of the fingers and toes to the cold, changes in skin color, pain, and occasionally ulcers of the fingertips or toes. In people with scleroderma, thickening of skin and blood vessels can result in loss of movement and shortness of breath or, more rarely, in kidney, heart, or lung failure. The estimated number of people with any type of scleroderma varies from study to study but may range from 1 to 4 affected individuals for every 10,000 Americans (or as many as 1 out of 2500 individuals).

Autoimmune Thyroid Diseases

Hashimoto's thyroiditis and Grave's disease result from immune system destruction or stimulation of thyroid tissue. Symptoms of low (hypo-) or

overactive (hyper-) thyroid function are nonspecific and can develop slowly or suddenly; these include fatigue, nervousness, cold or heat intolerance, weakness, changes in hair texture or amount, and weight gain or loss. The diagnosis of thyroid disease is readily made with appropriate laboratory tests.



The thyroid gland affect many parts of the body.

The symptoms of hypothyroidism are controlled with replacement thyroid hormone pills; however, complications from over- or under-replacement of the hormone can occur. Treatment of hyperthyroidism requires long-term anti-thyroid drug therapy or destruction of the thyroid gland with radioactive iodine or surgery. Both of these treatment approaches carry certain risks and long-term side effects. Autoimmune thyroid diseases afflict as many as 4 out of 100 women and are frequently found in families where there are other autoimmune diseases.

What Research Is Under Way on Autoimmune Diseases?

The National Institute of Allergy and Infectious Diseases (NIAID) supports research studies on the function of the immune system in various diseases. A basic understanding of the human immune system is central to the understanding of the development of an autoimmune disease (disease pathogenesis). Scientists searching for ways to prevent and treat autoimmune disease are studying disease pathogenesis and investigating new ways to modify the immune system.

Specifically, investigators supported by NIAID are focusing on: 1) studies of the immune system during the progression of an autoimmune disease; 2) analysis of the influence of genetics on autoimmune disease expression and progression; 3) the role of infectious agents in autoimmune diseases; 4) studies of animal models of autoimmune diseases; and 5) the effects of therapeutic intervention on the immune system in an autoimmune disease.

In addition, studies of a specific autoimmune disease such as multiple sclerosis can provide new and additional insights into the pathogenesis of autoimmune diseases affecting other organ systems. Therefore, NIAID also supports studies on specific autoimmune diseases in cooperation with other Institutes of the National Institutes of Health that focus on organ-specific autoimmune diseases.

Resources

National Institutes of Health (NIH) Resources

The following NIH components support medical research and/or provide information on varying aspects of autoimmune diseases:

National Institute of Allergy and Infectious Diseases
Office of Communications
Bldg. 31/Rm. 7A50
31 Center Drive, MSC 2520
Bethesda, MD 20892-2520
(301) 496-5717
http://www.niaid.nih.gov/publications/
and
http://www.niaid.nih.gov/clintrials/default.htm (for clinical trials information)

National Institute of Arthritis and Musculoskeletal and Skin Diseases
Information Clearinghouse/NIH
1 AMS Circle
Bethesda, MD 20892-3675
Fast Facts: (301) 881-2731 (to receive information by fax)
Clearinghouse: (301) 495-4484
http://www.nih.gov/niams/healthinfo/

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
Information Clearinghouse
1 Information Way
Bethesda, MD 20892-3560
Diabetes, Digestive, and Kidney Diseases Information:
(301) 654-3810

NIDDK Information Office (Thyroid Diseases)
Bldg. 31/Rm. 9A04
31 Center Drive
Bethesda, MD 20892-3560
(301) 496-3583
http://www.niddk.nih.gov

National Institute of Neurological Disorders and Stroke
Office of Scientific and Health Reports
P.O. Box 5801
Bethesda, MD 20824
(301) 496-5751
http://www.ninds.nih.gov/

NIH Clinical Center
Patient Recruitment and Referral Center—for specific NIH clinical trials information
4 West Drive, MSC 2655
Quarters 15 D-2
Bethesda, MD 20892-2655
(301) 411-1222
http://clinicalstudies.info.nih.gov/referring_patient.html

Office of Rare Diseases, NIH
Bldg. 31/Rm. 1B03
31 Center Drive
Bethesda, MD 20892
(301) 402-4336
http://rarediseases.info.nih.gov/ord/

Other Resources Sponsored by the Department of Health and Human Services

National Health Information Center
(800) 336-4797 or (301) 565-4167
Health Finder: **http://www.healthfinder.gov**

Combined Health Information Database
http://chid.nih.gov

Private Sector Organizations

The following list is a starting point for additional information on autoimmune diseases. Many of the organizations have extensive educational resources, local chapters, and support groups. The Internet Web site of many organizations can refer you to other disease-oriented groups (for example, the Arthritis Foundation has alink to the Lupus Foundation).

American Autoimmune Related Diseases Association
15475 Gratiot Avenue
Detroit, MI 48205
(800) 598-4668 or (313) 371-8600
http://www.aarda.org/

American Diabetes Association
1660 Duke Street
Alexandria, VA 22314
(800) 232-3472 or (703) 549-1500
http://www.diabetes.org/

American Liver Foundation
1425 Pompton Avenue
Cedar Grove, NJ 07009
(800) 233-0179 and (973) 256-2550

American Thyroid Association Montefiore Medical Center
111 East 210th Street
Bronx, NY 10467
Fax: (718) 882-6085
http://www.thyroid.org/

Arthritis Foundation
1650 Bluegrass Lakes Pkwy.
Alpharetta, GA 30009
(800) 283-7800 or (800) 207-8633
http://www.arthritis.org

Crohn's and Colitis Foundation of America
National Headquarters
386 Park Avenue South, 17th Floor
New York, NY 10016-8804
(800) 932-2423
(800) 343-3637 (Warehouse)
http://www.ccfa.org

Juvenile Diabetes Foundation International
120 Wall Street
New York, NY 10005-4001
(800) JDF-CURE or (800) 533-2873
http://www.jdf.org

Lupus Foundation of America
1300 Piccard Drive, Suite 200
Rockville, MD 20850-4303
(800) 558-0121 and (301) 670-9292
http://www.lupus.org/

Myasthenia Gravis Foundation of America
222 S. Riverside Plaza, Suite 1540
Chicago, IL 60606
(800) 541-5454 or (312) 258-0522
http://www.myasthenia.org/

Myositis Association of America
755 Cantrell Avenue
Suite C
Harrisonburg, VA 22801
(540) 433-7686
http://www.myositis.org

National Adrenal Diseases Foundation
505 Northern Boulevard
Great Neck, NY 11021

(516) 487-4992
http://www.medhelp.org/nadf/

National Alopecia Areata Foundation
710 CStreet, Suite 11
San Rafael, CA 94901-3853
or
P.O. Box 150760
San Rafael, CA 94915-0760
(415) 456-4644
Fax: (415) 456-4274
http://www.alopeciaareata.com

National Multiple Sclerosis Society
733 Third Avenue, 6th Floor
New York, NY 10017-3288
(800) 344-4867 or (212) 986-3240
Fax: (212) 986-7981
http://www.nmss.org
e-mail: **ire@nmss.org**

National Organization for Rare Disorders
P.O. Box 8923
New Fairfield, CT 06812-1783
(800) 999-6673
http://www.rarediseases.org/

National Psoriasis Foundation
6600 SW 92nd Avenue, Suite 300
Portland, OR 97223
(800) 723-9166 or (503) 244-7404
http://www.psoriasis.org

National Sjogren's Syndrome Association
5815 N. Black Canyon Highway, Suite 103
Phoenix, AZ 85015-2200
(602) 433-9844
http://www.sjogrens.org

National Vitiligo Foundation
P.O. Box 6337
Tyler, TX 75703
(903) 531-0074

Fax: (903) 531-9767
http://www.nvfi.org

Sjogren's Syndrome Foundation
333 N. Broadway
Jericho, NY 11753
1-800-4-SJOGRENS or (516) 933-6365
http://www.sjogrens.com

Spondylitis Association of America
P.O. Box 5872
Sherman Oaks, CA 91413
(800) 777-8189 or (888) 777-1594
http://www.spondylitis.org/

The S.L.E. Foundation
149 Madison Avenue, Suite 205
New York, NY 10016
(800) 745-8787
http://www.lupus.org

United Scleroderma Foundation
89 Newbury Street, Suite 201
Danvers, MA 01923
800) 722-HOPE
Fax: (978) 750-9902
http://www.scleroderma.org

Wegener's Foundation
3705 South George Mason Drive, Suite 1813
Falls Church, VA 22041
(703) 931-5852

Wegener's Granulomatosis Support Group
P.O. Box 28660
Kansas City, MO 64188-8668
(800) 277-9474
Fax: (816) 436-8211
http://www.wgsg.org/

More Guideline Sources

The guideline above on autoimmune diseases is only one example of the kind of material that you can find online and free of charge. The remainder of this chapter will direct you to other sources which either publish or can help you find additional guidelines on topics related to autoimmune diseases. Many of the guidelines listed below address topics that may be of particular relevance to your specific situation or of special interest to only some patients with autoimmune diseases. Due to space limitations these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

Topic Pages: MEDLINEplus

For patients wishing to go beyond guidelines published by specific Institutes of the NIH, the National Library of Medicine has created a vast and patient-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages." You can think of a health topic page as a guide to patient guides. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**.

If you do not find topics of interest when browsing health topic pages, then you can choose to use the advanced search utility of MEDLINEplus at **http://www.nlm.nih.gov/medlineplus/advancedsearch.html**. This utility is similar to the NIH Search Utility, with the exception that it only includes material linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on autoimmune diseases and related conditions. One of the advantages of CHID over other sources is that it offers summaries that describe the guidelines available, including contact information and pricing. CHID's general Web site is **http://chid.nih.gov/**. To search this database, go to **http://chid.nih.gov/detail/detail.html**. In particular, you can use the

advanced search options to look up pamphlets, reports, brochures, and information kits. The following was recently posted in this archive:

- **Sjogren's Syndrome and Systemic Lupus Erythematosus**

  Source: Rockville, MD: Lupus Foundation of America. 1999. 6 p.

  Contact: Available from Lupus Foundation of America. 1300 Piccard Drive, Suite 200, Rockville, MD 20850-4303. (800) 558-0121 or (301) 670-9292. Fax (301) 670-9486. Website: www.lupus.org/lupus. Price: Available as part of a package of 21 different lupus related brochures for $3.95 plus shipping and handling.

  Summary: This pamphlet provides people who have Sjogren's syndrome with information on this chronic autoimmune disorder in which the glands that produce tears and saliva do not function correctly. Sjogren's syndrome can occur alone or in association with other autoimmune diseases such as systemic lupus erythematosus (SLE) or rheumatoid arthritis. The disorder is termed primary Sjogren's syndrome when it occurs by itself and secondary Sjogren's syndrome when it is associated with another disease. The pamphlet discusses symptoms, including dryness of the mouth, eyes, and vagina. Other topics are the various laboratory tests and procedures used for diagnosis, as well as laboratory abnormalities associated with the disorder, including the presence of antinuclear antibodies and histocompatibility antigens, elevated erythrocyte sedimentation rate, mild anemia, and low albumin levels. In addition, the pamphlet examines the association between Sjogren's syndrome and SLE, discusses treatment with local and systemic agents that increase lubrication and moisture and with various drugs, comments on the prognosis for people who have Sjogren's syndrome, and provides information on the Lupus Foundation of America.

- **Chronic fatigue and immune dysfunction syndrome physician information packet**

  Source: Charlotte, NC: Chronic Fatigue and Immune Dysfunction Syndrome Association. 1992. 14 items.

  Contact: Available from Chronic Fatigue and Immune Dysfunction Syndrome Association, P.O. Box 220398, Charlotte, NC 28222.

  Summary: This information package includes factual information on chronic fatigue and immune dysfunction syndrome (also known as chronic fatigue syndrome, myalgic encephalomyelitus or M.E., chronic Epstein-Barr virus, and 'yuppie flu'), as well as information on the Chronic Fatigue and Immune Dysfunction Syndrome Association and a sample issue of its journal, the CFIDS Chronicle. Reprints of three journal

articles on the syndrome from other sources are included. The complex illness is characterized by incapacitating fatigue, neurological problems, and a constellation of symptoms that can resemble many disorders, including: mononucleosis, multiple sclerosis, fibromyalgia, AIDS-related complex, Lyme disease, post-polio syndrome, and autoimmune diseases such as lupus.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search their site located at **http://www.guideline.gov** by using the keyword "autoimmune diseases" or synonyms.

Healthfinder™

Healthfinder™ is an additional source sponsored by the U.S. Department of Health and Human Services which offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Primary Immunodeficiency Diseases**

  Summary: Primary immunodeficiency diseases are a group of diseases in which immune system malfunction causes increased susceptibility to infection, autoimmune diseases, and malignancy.

  Source: National Institute of Allergy and Infectious Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=3771

- **Sjögren's Syndrome**

  Summary: General information for the consumer about Sjögren's Syndrome -- a chronic inflammatory autoimmune disorder which may occur by itself or with other autoimmune diseases.

  Source: American Autoimmune Related Diseases Association, Inc.

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2576

The NIH Search Utility

After browsing the references listed at the beginning of this chapter, you may want to explore the NIH Search Utility. This allows you to search for documents on over 100 selected Web sites that comprise the NIH-WEB-SPACE. Each of these servers is "crawled" and indexed on an ongoing basis. Your search will produce a list of various documents, all of which will relate in some way to autoimmune diseases. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites that often link to government sites are available to the public. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**
- drkoop.com®: **http://www.drkoop.com/conditions/ency/index.html**
- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Vocabulary Builder

The material in this chapter may have contained a number of unfamiliar words. The following Vocabulary Builder introduces you to terms used in this chapter that have not been covered in the previous chapter:

Abdominal: Pertaining to the abdomen. [EU]

Alopecia: Baldness; absence of the hair from skin areas where it normally is present. [EU]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Antibody: An immunoglobulin molecule that has a specific amino acid sequence by virtue of which it interacts only with the antigen that induced its synthesis in cells of the lymphoid series (especially plasma cells), or with antigen closely related to it. Antibodies are classified according to their ode of action as agglutinins, bacteriolysins, haemolysins, opsonins, precipitins, etc. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Arteritis: Inflammation of an artery. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Biliary: Pertaining to the bile, to the bile ducts, or to the gallbladder. [EU]

Blister: Visible accumulations of fluid within or beneath the epidermis. [NIH]

Chronic: Persisting over a long period of time. [EU]

Cirrhosis: Liver disease characterized pathologically by loss of the normal microscopic lobular architecture, with fibrosis and nodular regeneration. The term is sometimes used to refer to chronic interstitial inflammation of any organ. [EU]

Colitis: Inflammation of the colon. [EU]

Confusion: Disturbed orientation in regard to time, place, or person, sometimes accompanied by disordered consciousness. [EU]

Cyclophosphamide: Precursor of an alkylating nitrogen mustard antineoplastic and immunosuppressive agent that must be activated in the liver to form the active aldophosphamide. It is used in the treatment of lymphomas, leukemias, etc. Its side effect, alopecia, has been made use of in defleecing sheep. Cyclophosphamide may also cause sterility, birth defects, mutations, and cancer. [NIH]

Cytokines: Non-antibody proteins secreted by inflammatory leukocytes and some non-leukocytic cells, that act as intercellular mediators. They differ from classical hormones in that they are produced by a number of tissue or cell types rather than by specialized glands. They generally act locally in a paracrine or autocrine rather than endocrine manner. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dermatitis: Inflammation of the skin. [EU]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Fatigue: The state of weariness following a period of exertion, mental or physical, characterized by a decreased capacity for work and reduced efficiency to respond to stimuli. [NIH]

Gastrointestinal: Pertaining to or communicating with the stomach and intestine, as a gastrointestinal fistula. [EU]

Glucose: D-glucose, a monosaccharide (hexose), C6H12O6, also known as dextrose (q.v.), found in certain foodstuffs, especially fruits, and in the normal blood of all animals. It is the end product of carbohydrate metabolism and is the chief source of energy for living organisms, its utilization being controlled by insulin. Excess glucose is converted to glycogen and stored in the liver and muscles for use as needed and, beyond that, is converted to fat and stored as adipose tissue. Glucose appears in the urine in diabetes mellitus. [EU]

Hematology: A subspecialty of internal medicine concerned with morphology, physiology, and pathology of the blood and blood-forming tissues. [NIH]

Hepatitis: Inflammation of the liver. [EU]

Histocompatibility: The degree of antigenic similarity between the tissues of different individuals, which determines the acceptance or rejection of allografts. [NIH]

Hormones: Chemical substances having a specific regulatory effect on the activity of a certain organ or organs. The term was originally applied to substances secreted by various endocrine glands and transported in the bloodstream to the target organs. It is sometimes extended to include those substances that are not produced by the endocrine glands but that have similar effects. [NIH]

Hyperthyroidism: 1. excessive functional activity of the thyroid gland. 2. the abnormal condition resulting from hyperthyroidism marked by increased metabolic rate, enlargement of the thyroid gland, rapid heart rate, high blood pressure, and various secondary symptoms. [EU]

Hypothyroidism: Deficiency of thyroid activity. In adults, it is most common in women and is characterized by decrease in basal metabolic rate, tiredness and lethargy, sensitivity to cold, and menstrual disturbances. If untreated, it progresses to full-blown myxoedema. In infants, severe hypothyroidism leads to cretinism. In juveniles, the manifestations are intermediate, with less severe mental and developmental retardation and only mild symptoms of the adult form. When due to pituitary deficiency of thyrotropin secretion it is called secondary hypothyroidism. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Iodine: A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

Lubrication: The application of a substance to diminish friction between two surfaces. It may refer to oils, greases, and similar substances for the lubrication of medical equipment but it can be used for the application of substances to tissue to reduce friction, such as lotions for skin and vaginal lubricants. [NIH]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lymphocytic: Pertaining to, characterized by, or of the nature of lymphocytes. [EU]

Methotrexate: An antineoplastic antimetabolite with immunosuppressant properties. It is an inhibitor of dihydrofolate reductase and prevents the formation of tetrahydrofolate, necessary for synthesis of thymidylate, an essential component of DNA. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Mononucleosis: The presence of an abnormally large number of mononuclear leucocytes (monocytes) in the blood. The term is often used alone to refer to infectious mononucleosis. [EU]

Myasthenia: Muscular debility; any constitutional anomaly of muscle. [EU]

Nausea: An unpleasant sensation, vaguely referred to the epigastrium and abdomen, and often culminating in vomiting. [EU]

Nervousness: Excessive excitability and irritability, with mental and physical unrest. [EU]

Neutrophil: Having an affinity for neutral dyes. [EU]

Oophoritis: Inflammation of an ovary. [NIH]

Ophthalmology: A surgical specialty concerned with the structure and function of the eye and the medical and surgical treatment of its defects and diseases. [NIH]

Orchitis: Inflammation of a testis. The disease is marked by pain, swelling, and a feeling of weight. It may occur idiopathically, or it may be associated with conditions such as mumps, gonorrhoea, filarial disease, syphilis, or tuberculosis. [EU]

Osteoarthritis: Noninflammatory degenerative joint disease occurring chiefly in older persons, characterized by degeneration of the articular cartilage, hypertrophy of bone at the margins, and changes in the synovial membrane. It is accompanied by pain and stiffness, particularly after prolonged activity. [EU]

Osteoporosis: Reduction in the amount of bone mass, leading to fractures after minimal trauma. [EU]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the islets of langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Paralysis: Loss or impairment of motor function in a part due to lesion of the neural or muscular mechanism; also by analogy, impairment of sensory function (sensory paralysis). In addition to the types named below, paralysis is further distinguished as traumatic, syphilitic, toxic, etc., according to its cause; or as obturator, ulnar, etc., according to the nerve part, or muscle specially affected. [EU]

Pemphigus: A group of chronic, relapsing, sometimes fatal skin diseases characterized clinically by the development of successive crops of vesicles and bullae, histologically by acantholysis, and immunologically by serum autoantibodies directed against antigens in the intracellular zones of the epidermis. The specific disease is usually indicated by a modifying term; but the term pemphigus is often used alone to designate pemphigus vulgaris. [EU]

Pernicious: Tending to a fatal issue. [EU]

Predisposition: A latent susceptibility to disease which may be activated under certain conditions, as by stress. [EU]

Prednisone: A synthetic anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Psoriasis: A common genetically determined, chronic, inflammatory skin disease characterized by rounded erythematous, dry, scaling patches. The lesions have a predilection for nails, scalp, genitalia, extensor surfaces, and the lumbosacral region. Accelerated epidermopoiesis is considered to be the fundamental pathologic feature in psoriasis. [NIH]

Purpura: Purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues. [NIH]

Radiology: A specialty concerned with the use of x-ray and other forms of radiant energy in the diagnosis and treatment of disease. [NIH]

Receptor: 1. a molecular structure within a cell or on the surface characterized by (1) selective binding of a specific substance and (2) a specific physiologic effect that accompanies the binding, e.g., cell-surface receptors for peptide hormones, neurotransmitters, antigens, complement fragments, and immunoglobulins and cytoplasmic receptors for steroid hormones. 2. a sensory nerve terminal that responds to stimuli of various kinds. [EU]

Remission: A diminution or abatement of the symptoms of a disease; also the period during which such diminution occurs. [EU]

Rheumatoid: Resembling rheumatism. [EU]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Sclerosis: A induration, or hardening; especially hardening of a part from inflammation and in diseases of the interstitial substance. The term is used chiefly for such a hardening of the nervous system due to hyperplasia of the connective tissue or to designate hardening of the blood vessels. [EU]

Sedimentation: The act of causing the deposit of sediment, especially by the use of a centrifugal machine. [EU]

Spondylitis: Inflammation of the vertebrae. [EU]

Systemic: Pertaining to or affecting the body as a whole. [EU]

Systolic: Indicating the maximum arterial pressure during contraction of the

left ventricle of the heart. [EU]

Thrombocytopenia: Decrease in the number of blood platelets. [EU]

Tolerance: 1. the ability to endure unusually large doses of a drug or toxin. 2. acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Topical: Pertaining to a particular surface area, as a topical anti-infective applied to a certain area of the skin and affecting only the area to which it is applied. [EU]

Toxic: Pertaining to, due to, or of the nature of a poison or toxin; manifesting the symptoms of severe infection. [EU]

Transplantation: The grafting of tissues taken from the patient's own body or from another. [EU]

Uveitis: An inflammation of part or all of the uvea, the middle (vascular) tunic of the eye, and commonly involving the other tunics (the sclera and cornea, and the retina). [EU]

Vertigo: An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viruses: Minute infectious agents whose genomes are composed of DNA or RNA, but not both. They are characterized by a lack of independent metabolism and the inability to replicate outside living host cells. [NIH]

Vitiligo: A disorder consisting of areas of macular depigmentation, commonly on extensor aspects of extremities, on the face or neck, and in skin folds. Age of onset is often in young adulthood and the condition tends to progress gradually with lesions enlarging and extending until a quiescent state is reached. [NIH]

CHAPTER 2. SEEKING GUIDANCE

Overview

Some patients are comforted by the knowledge that a number of organizations dedicate their resources to helping people with autoimmune diseases. These associations can become invaluable sources of information and advice. Many associations offer aftercare support, financial assistance, and other important services. Furthermore, healthcare research has shown that support groups often help people to better cope with their conditions.[9] In addition to support groups, your physician can be a valuable source of guidance and support. Therefore, finding a physician that can work with your unique situation is a very important aspect of your care.

In this chapter, we direct you to resources that can help you find patient organizations and medical specialists. We begin by describing how to find associations and peer groups that can help you better understand and cope with autoimmune diseases. The chapter ends with a discussion on how to find a doctor that is right for you.

Associations and Autoimmune Diseases

As mentioned by the Agency for Healthcare Research and Quality, sometimes the emotional side of an illness can be as taxing as the physical side.[10] You may have fears or feel overwhelmed by your situation. Everyone has different ways of dealing with disease or physical injury. Your attitude, your expectations, and how well you cope with your condition can all

[9] Churches, synagogues, and other houses of worship might also have groups that can offer you the social support you need.
[10] This section has been adapted from **http://www.ahcpr.gov/consumer/diaginf5.htm**.

influence your well-being. This is true for both minor conditions and serious illnesses. For example, a study on female breast cancer survivors revealed that women who participated in support groups lived longer and experienced better quality of life when compared with women who did not participate. In the support group, women learned coping skills and had the opportunity to share their feelings with other women in the same situation.

In addition to associations or groups that your doctor might recommend, we suggest that you consider the following list (if there is a fee for an association, you may want to check with your insurance provider to find out if the cost will be covered):

- **American Autoimmune Related Diseases Association, Inc**

  Address: American Autoimmune Related Diseases Association, Inc. Michigan National Bank Building, 15475 Gratiot Avenue, Detroit, MI 48205

  Telephone: (313) 371-8600 Toll-free: (800) 598- 4668

  Fax: (313) 371-6002

  Email: aarda@aol.com

  Web Site: http://www.aarda.org/

  Background: The American Autoimmune Related Diseases Association, Inc. (AARDA) is a national not-for-profit voluntary health agency dedicated to bringing a national focus to autoimmunity, a major cause of serious chronic diseases. The Association was founded for the purposes of supporting research to find a cure for autoimmune diseases and providing services to affected individuals. In addition, the Association's goals include increasing the public's awareness that autoimmunity is the cause of more than 80 serious chronic diseases; bringing national focus and collaborative effort among state and national voluntary health groups that represent autoimmune diseases; and serving as a national advocate for individuals and families affected by the physical, emotional, and financial effects of autoimmune disease. The American Autoimmune Related Diseases Association produces educational and support materials including fact sheets, brochures, pamphlets, and a newsletter entitled 'In Focus.'.

  Relevant area(s) of interest: Autoimmune Diseases, Crohn's Disease

Finding More Associations

There are a number of directories that list additional medical associations that you may find useful. While not all of these directories will provide different information than what is listed above, by consulting all of them, you will have nearly exhausted all sources for patient associations.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about autoimmune diseases. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

DIRLINE

A comprehensive source of information on associations is the DIRLINE database maintained by the National Library of Medicine. The database comprises some 10,000 records of organizations, research centers, and government institutes and associations which primarily focus on health and biomedicine. DIRLINE is available via the Internet at the following Web site: **http://dirline.nlm.nih.gov/**. Simply type in "autoimmune diseases" (or a synonym) or the name of a topic, and the site will list information contained in the database on all relevant organizations.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit your search to "Organizations" and "autoimmune diseases". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." By making these selections and typing in "autoimmune diseases" (or synonyms) into the "For these words:" box, you will only receive results on organizations dealing with autoimmune diseases. You should check back periodically with this database since it is updated every 3 months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by specific diseases. You can access this database at the following Web site: **http://www.rarediseases.org/cgi-bin/nord/searchpage**. Select the option called "Organizational Database (ODB)" and type "autoimmune diseases" (or a synonym) in the search box.

Online Support Groups

In addition to support groups, commercial Internet service providers offer forums and chat rooms for people with different illnesses and conditions. WebMD®, for example, offers such a service at their Web site: **http://boards.webmd.com/roundtable**. These online self-help communities can help you connect with a network of people whose concerns are similar to yours. Online support groups are places where people can talk informally. If you read about a novel approach, consult with your doctor or other healthcare providers, as the treatments or discoveries you hear about may not be scientifically proven to be safe and effective.

Finding Doctors

One of the most important aspects of your treatment will be the relationship between you and your doctor or specialist. All patients with autoimmune diseases must go through the process of selecting a physician. While this process will vary from person to person, the Agency for Healthcare Research and Quality makes a number of suggestions, including the following:[11]

- If you are in a managed care plan, check the plan's list of doctors first.
- Ask doctors or other health professionals who work with doctors, such as hospital nurses, for referrals.
- Call a hospital's doctor referral service, but keep in mind that these services usually refer you to doctors on staff at that particular hospital. The services do not have information on the quality of care that these doctors provide.

[11] This section is adapted from the AHRQ: **www.ahrq.gov/consumer/qntascii/qntdr.htm**.

- Some local medical societies offer lists of member doctors. Again, these lists do not have information on the quality of care that these doctors provide.

Additional steps you can take to locate doctors include the following:

- Check with the associations listed earlier in this chapter.
- Information on doctors in some states is available on the Internet at **http://www.docboard.org**. This Web site is run by "Administrators in Medicine," a group of state medical board directors.
- The American Board of Medical Specialties can tell you if your doctor is board certified. "Certified" means that the doctor has completed a training program in a specialty and has passed an exam, or "board," to assess his or her knowledge, skills, and experience to provide quality patient care in that specialty. Primary care doctors may also be certified as specialists. The AMBS Web site is located at **http://www.abms.org/newsearch.asp**.[12] You can also contact the ABMS by phone at 1-866-ASK-ABMS.
- You can call the American Medical Association (AMA) at 800-665-2882 for information on training, specialties, and board certification for many licensed doctors in the United States. This information also can be found in "Physician Select" at the AMA's Web site: **http://www.ama-assn.org/aps/amahg.htm**.

Finding Specialists

The American Academy of Allergy, Asthma, and Immunology (AAAAI) maintains a Physician Referral System on its Web site (**http://www.aaaai.org/**). The Referral System contains contact information for the organization's 6,000 members, all medical professionals specializing in the treatment of allergies, asthma, or infectious diseases. To use this free service, go to the search form located at **http://www.aaaai.org/scripts/find-a-doc/main.asp** and select the search criteria you would like to use by clicking on the circle to the left of the option. Then type in the information you are looking for such as the physician's location, zip code, name, or specialty. Click the "Search" button. If your query returns information about particular physicians, click on the physician's name for more information.

[12] While board certification is a good measure of a doctor's knowledge, it is possible to receive quality care from doctors who are not board certified.

If the previous sources did not meet your needs, you may want to log on to the Web site of the National Organization for Rare Disorders (NORD) at **http://www.rarediseases.org/**. NORD maintains a database of doctors with expertise in various rare diseases. The Metabolic Information Network (MIN), 800-945-2188, also maintains a database of physicians with expertise in various metabolic diseases.

Selecting Your Doctor[13]

When you have compiled a list of prospective doctors, call each of their offices. First, ask if the doctor accepts your health insurance plan and if he or she is taking new patients. If the doctor is not covered by your plan, ask yourself if you are prepared to pay the extra costs. The next step is to schedule a visit with your chosen physician. During the first visit you will have the opportunity to evaluate your doctor and to find out if you feel comfortable with him or her. Ask yourself, did the doctor:

- Give me a chance to ask questions about autoimmune diseases?
- Really listen to my questions?
- Answer in terms I understood?
- Show respect for me?
- Ask me questions?
- Make me feel comfortable?
- Address the health problem(s) I came with?
- Ask me my preferences about different kinds of treatments for autoimmune diseases?
- Spend enough time with me?

Trust your instincts when deciding if the doctor is right for you. But remember, it might take time for the relationship to develop. It takes more than one visit for you and your doctor to get to know each other.

[13] This section has been adapted from the AHRQ: **www.ahrq.gov/consumer/qntascii/qntdr.htm**.

Working with Your Doctor[14]

Research has shown that patients who have good relationships with their doctors tend to be more satisfied with their care and have better results. Here are some tips to help you and your doctor become partners:

- You know important things about your symptoms and your health history. Tell your doctor what you think he or she needs to know.
- It is important to tell your doctor personal information, even if it makes you feel embarrassed or uncomfortable.
- Bring a "health history" list with you (and keep it up to date).
- Always bring any medications you are currently taking with you to the appointment, or you can bring a list of your medications including dosage and frequency information. Talk about any allergies or reactions you have had to your medications.
- Tell your doctor about any natural or alternative medicines you are taking.
- Bring other medical information, such as x-ray films, test results, and medical records.
- Ask questions. If you don't, your doctor will assume that you understood everything that was said.
- Write down your questions before your visit. List the most important ones first to make sure that they are addressed.
- Consider bringing a friend with you to the appointment to help you ask questions. This person can also help you understand and/or remember the answers.
- Ask your doctor to draw pictures if you think that this would help you understand.
- Take notes. Some doctors do not mind if you bring a tape recorder to help you remember things, but always ask first.
- Let your doctor know if you need more time. If there is not time that day, perhaps you can speak to a nurse or physician assistant on staff or schedule a telephone appointment.
- Take information home. Ask for written instructions. Your doctor may also have brochures and audio and videotapes that can help you.

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[14] This section has been adapted from the AHRQ: **www.ahrq.gov/consumer/qntascii/qntdr.htm**.

- After leaving the doctor's office, take responsibility for your care. If you have questions, call. If your symptoms get worse or if you have problems with your medication, call. If you had tests and do not hear from your doctor, call for your test results. If your doctor recommended that you have certain tests, schedule an appointment to get them done. If your doctor said you should see an additional specialist, make an appointment.

By following these steps, you will enhance the relationship you will have with your physician.

Broader Health-Related Resources

In addition to the references above, the NIH has set up guidance Web sites that can help patients find healthcare professionals. These include:[15]

- Caregivers:
  http://www.nlm.nih.gov/medlineplus/caregivers.html
- Choosing a Doctor or Healthcare Service:
  http://www.nlm.nih.gov/medlineplus/choosingadoctororhealthcareservice.html
- Hospitals and Health Facilities:
  http://www.nlm.nih.gov/medlineplus/healthfacilities.html

Vocabulary Builder

Autoimmunity: Process whereby the immune system reacts against the body's own tissues. Autoimmunity may produce or be caused by autoimmune diseases. [NIH]

Porphyria: A pathological state in man and some lower animals that is often due to genetic factors, is characterized by abnormalities of porphyrin metabolism, and results in the excretion of large quantities of porphyrins in the urine and in extreme sensitivity to light. [EU]

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[15] You can access this information at:
http://www.nlm.nih.gov/medlineplus/healthsystem.html.

CHAPTER 3. CLINICAL TRIALS AND AUTOIMMUNE DISEASES

Overview

Very few medical conditions have a single treatment. The basic treatment guidelines that your physician has discussed with you, or those that you have found using the techniques discussed in Chapter 1, may provide you with all that you will require. For some patients, current treatments can be enhanced with new or innovative techniques currently under investigation. In this chapter, we will describe how clinical trials work and show you how to keep informed of trials concerning autoimmune diseases.

What Is a Clinical Trial?[16]

Clinical trials involve the participation of people in medical research. Most medical research begins with studies in test tubes and on animals. Treatments that show promise in these early studies may then be tried with people. The only sure way to find out whether a new treatment is safe, effective, and better than other treatments for autoimmune diseases is to try it on patients in a clinical trial.

[16] The discussion in this chapter has been adapted from the NIH and the NEI: **www.nei.nih.gov/netrials/ctivr.htm**.

What Kinds of Clinical Trials Are There?

Clinical trials are carried out in three phases:

- **Phase I.** Researchers first conduct Phase I trials with small numbers of patients and healthy volunteers. If the new treatment is a medication, researchers also try to determine how much of it can be given safely.
- **Phase II.** Researchers conduct Phase II trials in small numbers of patients to find out the effect of a new treatment on autoimmune diseases.
- **Phase III.** Finally, researchers conduct Phase III trials to find out how new treatments for autoimmune diseases compare with standard treatments already being used. Phase III trials also help to determine if new treatments have any side effects. These trials--which may involve hundreds, perhaps thousands, of people--can also compare new treatments with no treatment.

How Is a Clinical Trial Conducted?

Various organizations support clinical trials at medical centers, hospitals, universities, and doctors' offices across the United States. The "principal investigator" is the researcher in charge of the study at each facility participating in the clinical trial. Most clinical trial researchers are medical doctors, academic researchers, and specialists. The "clinic coordinator" knows all about how the study works and makes all the arrangements for your visits.

All doctors and researchers who take part in the study on autoimmune diseases carefully follow a detailed treatment plan called a protocol. This plan fully explains how the doctors will treat you in the study. The "protocol" ensures that all patients are treated in the same way, no matter where they receive care.

Clinical trials are controlled. This means that researchers compare the effects of the new treatment with those of the standard treatment. In some cases, when no standard treatment exists, the new treatment is compared with no treatment. Patients who receive the new treatment are in the treatment group. Patients who receive a standard treatment or no treatment are in the "control" group. In some clinical trials, patients in the treatment group get a new medication while those in the control group get a placebo. A placebo is a harmless substance, a "dummy" pill, that has no effect on autoimmune diseases. In other clinical trials, where a new surgery or device (not a

medicine) is being tested, patients in the control group may receive a "sham treatment." This treatment, like a placebo, has no effect on autoimmune diseases and does not harm patients.

Researchers assign patients "randomly" to the treatment or control group. This is like flipping a coin to decide which patients are in each group. If you choose to participate in a clinical trial, you will not know which group you will be appointed to. The chance of any patient getting the new treatment is about 50 percent. You cannot request to receive the new treatment instead of the placebo or sham treatment. Often, you will not know until the study is over whether you have been in the treatment group or the control group. This is called a "masked" study. In some trials, neither doctors nor patients know who is getting which treatment. This is called a "double masked" study. These types of trials help to ensure that the perceptions of the patients or doctors will not affect the study results.

Natural History Studies

Unlike clinical trials in which patient volunteers may receive new treatments, natural history studies provide important information to researchers on how autoimmune diseases develops over time. A natural history study follows patient volunteers to see how factors such as age, sex, race, or family history might make some people more or less at risk for autoimmune diseases. A natural history study may also tell researchers if diet, lifestyle, or occupation affects how a disease or disorder develops and progresses. Results from these studies provide information that helps answer questions such as: How fast will a disease or disorder usually progress? How bad will the condition become? Will treatment be needed?

What Is Expected of Patients in a Clinical Trial?

Not everyone can take part in a clinical trial for a specific disease or disorder. Each study enrolls patients with certain features or eligibility criteria. These criteria may include the type and stage of disease or disorder, as well as, the age and previous treatment history of the patient. You or your doctor can contact the sponsoring organization to find out more about specific clinical trials and their eligibility criteria. If you are interested in joining a clinical trial, your doctor must contact one of the trial's investigators and provide details about your diagnosis and medical history.

If you participate in a clinical trial, you may be required to have a number of medical tests. You may also need to take medications and/or undergo surgery. Depending upon the treatment and the examination procedure, you may be required to receive inpatient hospital care. Or, you may have to return to the medical facility for follow-up examinations. These exams help find out how well the treatment is working. Follow-up studies can take months or years. However, the success of the clinical trial often depends on learning what happens to patients over a long period of time. Only patients who continue to return for follow-up examinations can provide this important long-term information.

Recent Trials on Autoimmune Diseases

The National Institutes of Health and other organizations sponsor trials on various diseases and disorders. Because funding for research goes to the medical areas that show promising research opportunities, it is not possible for the NIH or others to sponsor clinical trials for every disease and disorder at all times. The following lists recent trials dedicated to autoimmune diseases.[17] If the trial listed by the NIH is still recruiting, you may be eligible. If it is no longer recruiting or has been completed, then you can contact the sponsors to learn more about the study and, if published, the results. Further information on the trial is available at the Web site indicated. Please note that some trials may no longer be recruiting patients or are otherwise closed. Before contacting sponsors of a clinical trial, consult with your physician who can help you determine if you might benefit from participation.

- **Autologous Peripheral Blood Stem Cell Transplantation in Patients With Life Threatening Autoimmune Diseases**

  Condition(s): Purpura, Schoenlein-Henoch; Graft Versus Host Disease; Anemia, Hemolytic, Autoimmune; Rheumatoid Arthritis; Churg-Strauss Syndrome; Hypersensitivity Vasculitis; Wegener's Granulomatosis; Systemic Lupus Erythematosus; Giant Cell Arteritis; Pure Red Cell Aplasia; Juvenile Rheumatoid Arthritis; Polyarteritis Nodosa; Autoimmune Thrombocytopenic Purpura; Takayasu Arteritis

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Fairview University Medical Center

  Purpose - Excerpt: Objectives: I. Determine whether there is prompt engraftment after autologous peripheral blood stem cell transplantation using filgrastim (G-CSF) mobilization in patients with life threatening autoimmune diseases. II. Determine the kinetics of T- and B-cell immune

[17] These are listed at **www.ClinicalTrials.gov**.

reconstitution after a combination of timed plasmapheresis, high dose cyclophosphamide and total lymphoid irradiation, and posttransplant immunosuppression with cyclosporine in these patients. III. Determine whether this treatment regimen beneficially influences the clinical course of these patients.

Study Type: Interventional

Contact(s): Minnesota; Fairview University Medical Center, Minneapolis, Minnesota, 55455, United States; Recruiting; Arne Slungaard 612-273-2800. Study chairs or principal investigators: Arne Slungaard, Study Chair; Fairview University Medical Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00006055;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Etanercept Therapy for Sjogren's Syndrome**

  Condition(s): Sjogren's Syndrome

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Dental and Craniofacial Research (NIDCR)

  Purpose - Excerpt: This study will test the effectiveness of etanercept (Enbrel) for treating Sjogren's syndrome-an autoimmune disease that affects the secreting glands. (In autoimmune diseases, the immune system attacks the body's own tissues.) Reduced lacrimal (tear) gland function causes dry eyes with a scratchy sensation, and, in severe cases, vision be may impaired. Reduced salivary gland function causes dry mouth, resulting in greatly increased tooth decay. Dry mouth also makes chewing and swallowing difficult, which may lead to nutrition deficiencies. Sjogren's syndrome can also cause dryness of the skin and of mucous membranes in the nose, throat, airways, and vagina. Patients with Sjogren's syndrome who have had oral and eye examinations under NIDCR's protocol 84-D-0056 may participate in this study. Participants will be randomly assigned to receive either etanercept or placebo (an inactive look-alike substance) by injection under the skin twice a week for 3 months. Patients will be seen for evaluation before treatment begins (baseline) and again at 1, 3, and 4 months. The baseline and 3-month visits include a physical examination, eye examination, saliva collection from salivary glands, blood tests, and evaluation for changes in symptoms and treatment side effects. The 1- and 4-month visits include saliva collection, blood tests, and review of symptoms and treatment side effects. In addition, blood will be drawn every 2 weeks for safety monitoring. Patients will also be surveyed weekly (by telephone or

during the clinic visit) about symptoms and treatment side effects. The Food and Drug Administration has approved Enbrel for treating certain forms of arthritis, which, like Sjogren's syndrome, are autoimmune disorders of the connective tissue. Laboratory studies also indicate that etanercept may be an effective treatment for Sjogren's syndrome.

Phase(s): Phase II

Study Type: Interventional

Contact(s): Maryland; National Institute of Dental And Craniofacial Research (NIDCR), 9000 Rockville Pike Bethesda, Maryland, 20892, United States; Recruiting; Patient Recruitment and Public Liaison Office 1-800-411-1222 prpl@mail.cc.nih.gov; TTY 1-866-411-1010

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00001954;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Immune System Related Kidney Disease**

  Condition(s): Glomerulonephritis; Lupus Nephritis; Membranous Glomerulonephritis; Nephritis; Nephrotic Syndrome

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: Kidney diseases related to the immune system include, nephrotic syndrome, glomerulonephritis, membranous nephropathy, lupus nephritis, and nephritis associated with connective tissue disorders. This study will allow researchers to admit and follow patients suffering from autoimmune diseases of the kidney. It will attempt to provide information about the causes and specific abnormalities associated with autoimmune kidney disease. Patients with kidney disease as a result of their immune system, and patients with diseases of the immune system who may later develop kidney disease, will be potential subjects for this study. Patients will undergo a history and physical examination, and standard laboratory test to more closely understand the causes, signs, symptoms, and responses to medication of these diseases. Based on these evaluations the patients may qualify as candidates for other experimental studies. At any time these patients may be asked to submit blood or urine samples for further research.

  Study Type: Observational

  Contact(s): Maryland; National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 9000 Rockville Pike Bethesda, Maryland,

20892, United States; Recruiting; Patient Recruitment and Public Liaison Office 1-800-411-1222 prpl@mail.cc.nih.gov; TTY 1-866-411-1010

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00001979;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Phase II Study of High-Dose Cyclophosphamide in Patients With Severe Autoimmune Hematologic Disease**

  Condition(s): Anemia, Hemolytic, Autoimmune; Felty Syndrome; Purpura, Thrombocytopenic; Autoimmune Diseases

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Johns Hopkins Oncology Center

  Purpose - Excerpt: Objectives: I. Determine the response rate and 1-year event-free survival in patients with severe autoimmune hematologic disease treated with high-dose cyclophosphamide.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): Maryland; Johns Hopkins Oncology Center, Baltimore, Maryland, 21231, United States; Recruiting; Robert A. Brodsky 410-955-2813. Study chairs or principal investigators: Robert A. Brodsky, Study Chair; Johns Hopkins Oncology Center

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00010387;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Pilot Study of Total Body Irradiation in Combination With Cyclophosphamide, Anti-thymocyte Globulin, and Autologous CD34-Selected Peripheral Blood Stem Cell Transplantation in Children With Refractory Autoimmune Disorders**

  Condition(s): Systemic Sclerosis; Systemic Lupus Erythematosus; Dermatomyositis; Juvenile Rheumatoid Arthritis; Autoimmune Diseases

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Fred Hutchinson Cancer Research Center

  Purpose - Excerpt: Objectives: I. Determine the safety and long term complications of total body irradiation in combination with cyclophosphamide, anti-thymocyte globulin, and autologous CD34-selected peripheral blood stem cell (PBSC) transplantation in children with refractory autoimmune disorders. II. Determine the efficacy of this treatment regimen in these patients. III. Determine the reconstitution of

immunity after autologous CD34-selected PBSC transplantation in these patients. IV. Determine engraftment of autologous CD34-selected PBSC in these patients.

Study Type: Interventional

Contact(s): Washington; Fred Hutchinson Cancer Research Center, Seattle, Washington, 98109, United States; Recruiting; Ann Woolfrey 206-667-4453. Study chairs or principal investigators: Ann Woolfrey, Study Chair; Fred Hutchinson Cancer Research Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00010335;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Positron Emission Tomography (PET) to Locate Areas of White Blood Cell Activity**

  Condition(s): Lupus Erythematosus; Systemic

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

  Purpose - Excerpt: This study will examine whether PET imaging can reveal what is happening in lymph nodes of patients with systemic lupus erythematosus, or lupus, during periods of active disease. Patients may have periods of active disease when they may feel sick with fever, fatigue, and aching or swollen joints. Their blood tests are abnormal and their kidney, lungs or heart may be affected. At other times, the disease is inactive, and patients feel well, their blood is normal, and there is no evidence of organ disease. In lupus, like other autoimmune diseases, the body's immune system attacks it own healthy tissues. Activated lymphocytes (a type of immune cell) lead to the production of antibodies and chemical signals that contribute to the disease process. In animals with lupus, these cells are activated in the lymphoid organs, such as the lymph nodes or spleen. It is not known exactly where these cells are activated in humans. Because some lymph nodes are located deep inside the chest and abdomen; surgery is currently the only way to examining them. PET imaging may provide an alternative, non-invasive, means of obtaining information on lymph node activity in humans. This test uses a radioactive sugar molecule called F18-FDG to find areas of increased cellular activity in the body. (Cells use sugar for fuel, so active cells, such as active lymphocytes, uses more FDG than other body tissues.) This study will determine whether PET can detect these areas of increased activity in lupus during active disease. Patients with active or inactive lupus may be eligible for this study. Candidates are screened with a

history, physical examination, and routine blood and urine tests. Women who are pregnant or breastfeeding may not participate. Participants will undergo PET scanning. On the day of the scan they have a brief medical history and physical examination and a blood sample is drawn to check blood count and look for markers of lymphocyte activation. Then, a small plastic tube (catheter) is placed into a vein in the patient's arm, the FDG is injected through the catheter, and the patient rests for an hour. For the scan, the patient lies flat in a cradle that is moved into the central hole of the doughnut-shaped PET camera, and pictures are taken over the next 2 hours, with the patient lies quietly, without moving the head or arms. After the scan is finished, the patient empties the bladder approximately every hour for 6 hours to excrete the radioactive sugar.

Study Type: Observational

Contact(s): Maryland; National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), 9000 Rockville Pike Bethesda, Maryland, 20892, United States; Recruiting; Patient Recruitment and Public Liaison Office 1-800-411-1222 prpl@mail.cc.nih.gov; TTY 1-866-411-1010

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00029926;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Safety and Efficacy Study of LJP 394 (abetimus sodium) to treat lupus kidney disease**

  Condition(s): Immunologic Diseases; Autoimmune Diseases; Systemic Lupus Erythematosus; Lupus Nephritis; Lupus Glomerulonephritis

  Study Status: This study is currently recruiting patients.

  Sponsor(s): La Jolla Pharmaceutical Company

  Purpose - Excerpt: The purpose of this study is to determine whether LJP 394 (abetimus sodium) is safe and effective in delaying and reducing renal flares in patients with lupus nephritis.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00035308;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Treatment of Multiple Sclerosis with Copaxone and Albuterol**

  Condition(s): Autoimmune Diseases; Multiple Sclerosis

Study Status: This study is currently recruiting patients.

Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

Purpose - Excerpt: The purpose of this study is to determine the effects of Copaxone alone compared to Copaxone plus albuterol in patients with Multiple Sclerosis (MS). MS is thought to be an autoimmune disease of the central nervous system. Certain white blood cells of the immune system become abnormally active and mistakenly attack the myelin of nerve fibers. Myelin is a fatty sheath that surrounds nerve fibers and insulates the nerve like insulation around an electrical wire. Without proper myelin insulation, messages sent between the brain and other parts of the body may be confused or fail completely. Damage to myelin causes the symptoms of MS. The most common form of MS is known as relapsing-remitting (RR), where partial or total recovery occurs after attacks. Four therapies are currently approved for the treatment of MS. These therapies, however, are only moderately effective and can cause undesirable side effects. For this reason, there is a need to find new therapies that have minimal side effects and may stop the disease from getting worse.

Study Type: Interventional

Contact(s): Sandra Cook 617-713-2006 scook@partners.org; Massachusetts; Brigham and Women's Hospital/Harvard Medical School, Boston, Massachusetts, 02115, United States; Recruiting; Sandra Cook 617-713-2006 scook@partners.org. Study chairs or principal investigators: Samia Khoury, Principal Investigator

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00039988;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **Phase II Study of Rituximab in Patients With Immune Thrombocytopenic Purpura**

  Condition(s): Purpura, Thrombocytopenic, Idiopathic

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): UAB Comprehensive Cancer Center

  Purpose - Excerpt: Objectives: I. Determine the response rate and response duration to rituximab in patients with immune thrombocytopenic purpura. II. Evaluate the toxicity associated with this treatment regimen in these patients. III. Evaluate the alteration in antiplatelet antibody with this treatment regimen in these patients.

  Phase(s): Phase II

  Study Type: Interventional

Contact(s): Alabama; University of Alabama Comprehensive Cancer Center, Birmingham, Alabama, 35294, United States; Mansoor Noorali Saleh 205-975-9025. Study chairs or principal investigators: Mansoor Noorali Saleh, Study Chair; UAB Comprehensive Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00005652;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

- **DHEA Treatment for Sjogren's Syndrome**

  Condition(s): Lacrimal Apparatus Disease; Salivary Gland Disease; Sjogren's Syndrome; Xerostomia

  Study Status: This study is completed.

  Sponsor(s): National Institute of Dental and Craniofacial Research (NIDCR)

  Purpose - Excerpt: This study will evaluate the effectiveness of the male hormone dehydroepiandrosterone (DHEA) in treating Sjogren's syndrome. This autoimmune disorder, in which the immune system attacks the salivary glands and tear glands, affects primarily women. Patients' eyes and mouth become drier over time, and can lead to problems such as serious tooth decay and eye irritations. Sex hormones seem to influence the immune response and may help decrease disease severity. DHEA has benefited some patients with two other autoimmune diseases, rheumatoid arthritis and systemic lupus erythematosus. Women 18 to 75 years of age with Sjogren's syndrome may be eligible for this 7-month study. At the initial visit, candidates will have a physical examination, routine blood and urine tests and eye and dental examinations, including a test to measure saliva production for screening purposes and to establish baseline values for participants. Those enrolled in the study will be randomly assigned to take either DHEA or placebo (look-alike tablet with no active ingredient) once a day for 6 months and will be monitored with follow-up visits at months 1, 3, 6 and 7. Physical examination, blood tests and urinalysis will be repeated at months 1, 3, 6 and 7; saliva will be collected at months 3, 6 and 7; and eyes will be examined at 3 and 6 months. Because hormone changes may have both physical and emotional effects, patients will be asked questions about their mood, symptoms and side effects of treatment. It is not known if Sjogren's syndrome is associated with osteoporosis (bone thinning), but since this condition occurs in other autoimmune disorders, patient's bone density will be measured at the first visit, and blood drawn at 3 and 6 months will be tested for various substances associated with changes in

bone density. A 24-hour urine collection at the first visit and later urine tests will also be tested for substances associated with bone thinning.

Phase(s): Phase II

Study Type: Interventional

Contact(s): Maryland; National Institute of Dental And Craniofacial Research (NIDCR), 9000 Rockville Pike Bethesda, Maryland, 20892, United States

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00001598;jsessionid=C1F3E864F97091A5F2D1E5916095D5B1

Benefits and Risks[18]

What Are the Benefits of Participating in a Clinical Trial?

If you are interested in a clinical trial, it is important to realize that your participation can bring many benefits to you and society at large:

- A new treatment could be more effective than the current treatment for autoimmune diseases. Although only half of the participants in a clinical trial receive the experimental treatment, if the new treatment is proved to be more effective and safer than the current treatment, then those patients who did not receive the new treatment during the clinical trial may be among the first to benefit from it when the study is over.
- If the treatment is effective, then it may improve health or prevent diseases or disorders.
- Clinical trial patients receive the highest quality of medical care. Experts watch them closely during the study and may continue to follow them after the study is over.
- People who take part in trials contribute to scientific discoveries that may help other people with autoimmune diseases. In cases where certain diseases or disorders run in families, your participation may lead to better care or prevention for your family members.

[18] This section has been adapted from ClinicalTrials.gov, a service of the National Institutes of Health:
http://www.clinicaltrials.gov/ct/gui/c/a1r/info/whatis?JServSessionIdzone_ct=9jmun6f291.

The Informed Consent

Once you agree to take part in a clinical trial, you will be asked to sign an "informed consent." This document explains a clinical trial's risks and benefits, the researcher's expectations of you, and your rights as a patient.

What Are the Risks?

Clinical trials may involve risks as well as benefits. Whether or not a new treatment will work cannot be known ahead of time. There is always a chance that a new treatment may not work better than a standard treatment. There is also the possibility that it may be harmful. The treatment you receive may cause side effects that are serious enough to require medical attention.

How Is Patient Safety Protected?

Clinical trials can raise fears of the unknown. Understanding the safeguards that protect patients can ease some of these fears. Before a clinical trial begins, researchers must get approval from their hospital's Institutional Review Board (IRB), an advisory group that makes sure a clinical trial is designed to protect patient safety. During a clinical trial, doctors will closely watch you to see if the treatment is working and if you are experiencing any side effects. All the results are carefully recorded and reviewed. In many cases, experts from the Data and Safety Monitoring Committee carefully monitor each clinical trial and can recommend that a study be stopped at any time. You will only be asked to take part in a clinical trial as a volunteer giving informed consent.

What Are a Patient's Rights in a Clinical Trial?

If you are eligible for a clinical trial, you will be given information to help you decide whether or not you want to participate. As a patient, you have the right to:

- Information on all known risks and benefits of the treatments in the study.
- Know how the researchers plan to carry out the study, for how long, and where.
- Know what is expected of you.

- Know any costs involved for you or your insurance provider.
- Know before any of your medical or personal information is shared with other researchers involved in the clinical trial.
- Talk openly with doctors and ask any questions.

After you join a clinical trial, you have the right to:

- Leave the study at any time. Participation is strictly voluntary. However, you should not enroll if you do not plan to complete the study.
- Receive any new information about the new treatment.
- Continue to ask questions and get answers.
- Maintain your privacy. Your name will not appear in any reports based on the study.
- Know whether you participated in the treatment group or the control group (once the study has been completed).

What about Costs?

In some clinical trials, the research facility pays for treatment costs and other associated expenses. You or your insurance provider may have to pay for costs that are considered standard care. These things may include inpatient hospital care, laboratory and other tests, and medical procedures. You also may need to pay for travel between your home and the clinic. You should find out about costs before committing to participation in the trial. If you have health insurance, find out exactly what it will cover. If you don't have health insurance, or if your insurance company will not cover your costs, talk to the clinic staff about other options for covering the cost of your care.

What Should You Ask before Deciding to Join a Clinical Trial?

Questions you should ask when thinking about joining a clinical trial include the following:

- What is the purpose of the clinical trial?
- What are the standard treatments for autoimmune diseases? Why do researchers think the new treatment may be better? What is likely to happen to me with or without the new treatment?
- What tests and treatments will I need? Will I need surgery? Medication? Hospitalization?

- How long will the treatment last? How often will I have to come back for follow-up exams?
- What are the treatment's possible benefits to my condition? What are the short- and long-term risks? What are the possible side effects?
- Will the treatment be uncomfortable? Will it make me feel sick? If so, for how long?
- How will my health be monitored?
- Where will I need to go for the clinical trial? How will I get there?
- How much will it cost to be in the study? What costs are covered by the study? How much will my health insurance cover?
- Will I be able to see my own doctor? Who will be in charge of my care?
- Will taking part in the study affect my daily life? Do I have time to participate?
- How do I feel about taking part in a clinical trial? Are there family members or friends who may benefit from my contributions to new medical knowledge?

Keeping Current on Clinical Trials

Various government agencies maintain databases on trials. The U.S. National Institutes of Health, through the National Library of Medicine, has developed ClinicalTrials.gov to provide patients, family members, and physicians with current information about clinical research across the broadest number of diseases and conditions.

The site was launched in February 2000 and currently contains approximately 5,700 clinical studies in over 59,000 locations worldwide, with most studies being conducted in the United States. ClinicalTrials.gov receives about 2 million hits per month and hosts approximately 5,400 visitors daily. To access this database, simply go to their Web site (**www.clinicaltrials.gov**) and search by "autoimmune diseases" (or synonyms).

While ClinicalTrials.gov is the most comprehensive listing of NIH-supported clinical trials available, not all trials are in the database. The database is updated regularly, so clinical trials are continually being added. The following is a list of specialty databases affiliated with the National Institutes of Health that offer additional information on trials:

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site: **http://clinicalstudies.info.nih.gov/**
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site: **http://www.jhbmc.jhu.edu/studies/index.html**
- For trials on infectious, immune, and allergic diseases, visit the site of the National Institute of Allergy and Infectious Diseases: **http://www.niaid.nih.gov/clintrials/**

General References

The following references describe clinical trials and experimental medical research. They have been selected to ensure that they are likely to be available from your local or online bookseller or university medical library. These references are usually written for healthcare professionals, so you may consider consulting with a librarian or bookseller who might recommend a particular reference. The following includes some of the most readily available references (sorted alphabetically by title; hyperlinks provide rankings, information and reviews at Amazon.com):

- **A Guide to Patient Recruitment : Today's Best Practices & Proven Strategies** by Diana L. Anderson; Paperback - 350 pages (2001), CenterWatch, Inc.; ISBN: 1930624115; **http://www.amazon.com/exec/obidos/ASIN/1930624115/icongroupinterna**
- **A Step-By-Step Guide to Clinical Trials** by Marilyn Mulay, R.N., M.S., OCN; Spiral-bound - 143 pages Spiral edition (2001), Jones & Bartlett Pub; ISBN: 0763715697; **http://www.amazon.com/exec/obidos/ASIN/0763715697/icongroupinterna**
- **The CenterWatch Directory of Drugs in Clinical Trials** by CenterWatch; Paperback - 656 pages (2000), CenterWatch, Inc.; ISBN: 0967302935; **http://www.amazon.com/exec/obidos/ASIN/0967302935/icongroupinterna**
- **The Complete Guide to Informed Consent in Clinical Trials** by Terry Hartnett (Editor); Paperback - 164 pages (2000), PharmSource Information

Services, Inc.; ISBN: 0970153309;
http://www.amazon.com/exec/obidos/ASIN/0970153309/icongroupinterna

- **Dictionary for Clinical Trials** by Simon Day; Paperback - 228 pages (1999), John Wiley & Sons; ISBN: 0471985961;
http://www.amazon.com/exec/obidos/ASIN/0471985961/icongroupinterna
- **Extending Medicare Reimbursement in Clinical Trials** by Institute of Medicine Staff (Editor), et al; Paperback 1st edition (2000), National Academy Press; ISBN: 0309068886;
http://www.amazon.com/exec/obidos/ASIN/0309068886/icongroupinterna
- **Handbook of Clinical Trials** by Marcus Flather (Editor); Paperback (2001), Remedica Pub Ltd; ISBN: 1901346293;
http://www.amazon.com/exec/obidos/ASIN/1901346293/icongroupinterna

Vocabulary Builder

The following vocabulary builder gives definitions of words used in this chapter that have not been defined in previous chapters:

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Albuterol: A racemic mixture with a 1:1 ratio of the r-isomer, levalbuterol, and s-albuterol. It is a short-acting beta2-adrenergic agonist with its main clinical use in asthma. [NIH]

Aplasia: Lack of development of an organ or tissue, or of the cellular products from an organ or tissue. [EU]

Catheter: A tubular, flexible, surgical instrument for withdrawing fluids from (or introducing fluids into) a cavity of the body, especially one for introduction into the bladder through the urethra for the withdraw of urine. [EU]

Hypersensitivity: A state of altered reactivity in which the body reacts with an exaggerated immune response to a foreign substance. Hypersensitivity reactions are classified as immediate or delayed, types I and IV, respectively, in the Gell and Coombs classification (q.v.) of immune responses. [EU]

Invasive: 1. having the quality of invasiveness. 2. involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Kinetic: Pertaining to or producing motion. [EU]

Lacrimal: Pertaining to the tears. [EU]

Membrane: A thin layer of tissue which covers a surface, lines a cavity or

divides a space or organ. [EU]

Mobilization: The process of making a fixed part or stored substance mobile, as by separating a part from surrounding structures to make it accessible for an operative procedure or by causing release into the circulation for body use of a substance stored in the body. [EU]

Nephropathy: Disease of the kidneys. [EU]

Nephrotic: Pertaining to, resembling, or caused by nephrosis. [EU]

Particle: A tiny mass of material. [EU]

Plasmapheresis: Procedure whereby plasma is separated and extracted from anticoagulated whole blood and the red cells retransfused to the donor. Plasmapheresis is also employed for therapeutic use. [NIH]

Reconstitution: 1. a type of regeneration in which a new organ forms by the rearrangement of tissues rather than from new formation at an injured surface. 2. the restoration to original form of a substance previously altered for preservation and storage, as the restoration to a liquid state of blood serum or plasma that has been dried and stored. [EU]

Refractory: Not readily yielding to treatment. [EU]

Tomography: The recording of internal body images at a predetermined plane by means of the tomograph; called also body section roentgenography. [EU]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of mycobacterium. [NIH]

Urinalysis: Examination of urine by chemical, physical, or microscopic means. Routine urinalysis usually includes performing chemical screening tests, determining specific gravity, observing any unusual color or odor, screening for bacteriuria, and examining the sediment microscopically. [NIH]

Vasculitis: Inflammation of a vessel, angiitis. [EU]

Xerostomia: Dryness of the mouth from salivary gland dysfunction, as in Sjögren's syndrome. [EU]

PART II: ADDITIONAL RESOURCES AND ADVANCED MATERIAL

ABOUT PART II

In Part II, we introduce you to additional resources and advanced research on autoimmune diseases. All too often, patients who conduct their own research are overwhelmed by the difficulty in finding and organizing information. The purpose of the following chapters is to provide you an organized and structured format to help you find additional information resources on autoimmune diseases. In Part II, as in Part I, our objective is not to interpret the latest advances on autoimmune diseases or render an opinion. Rather, our goal is to give you access to original research and to increase your awareness of sources you may not have already considered. In this way, you will come across the advanced materials often referred to in pamphlets, books, or other general works. Once again, some of this material is technical in nature, so consultation with a professional familiar with autoimmune diseases is suggested.

CHAPTER 4. STUDIES ON AUTOIMMUNE DISEASES

Overview

Every year, academic studies are published on autoimmune diseases or related conditions. Broadly speaking, there are two types of studies. The first are peer reviewed. Generally, the content of these studies has been reviewed by scientists or physicians. Peer-reviewed studies are typically published in scientific journals and are usually available at medical libraries. The second type of studies is non-peer reviewed. These works include summary articles that do not use or report scientific results. These often appear in the popular press, newsletters, or similar periodicals.

In this chapter, we will show you how to locate peer-reviewed references and studies on autoimmune diseases. We will begin by discussing research that has been summarized and is free to view by the public via the Internet. We then show you how to generate a bibliography on autoimmune diseases and teach you how to keep current on new studies as they are published or undertaken by the scientific community.

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and autoimmune diseases, you will need to use the advanced search options. First, go to **http://chid.nih.gov/index.html**. From there, select the "Detailed Search" option (or go directly to that page with the following hyperlink: **http://chid.nih.gov/detail/detail.html**). The trick in extracting studies is found in the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the

format option "Journal Article." At the top of the search form, select the number of records you would like to see (we recommend 100) and check the box to display "whole records." We recommend that you type in "autoimmune diseases" (or synonyms) into the "For these words:" box. Consider using the option "anywhere in record" to make your search as broad as possible. If you want to limit the search to only a particular field, such as the title of the journal, then select this option in the "Search in these fields" drop box. The following is a sample of what you can expect from this type of search:

- **Giant Cell Myocarditis: Most Fatal of Autoimmune Diseases**

  Source: Seminars in Arthritis and Rheumatism. 30(1): 1-16. August 2000.

  Summary: This journal article provides health professionals with information on the pathogenesis and treatment of giant cell myocarditis (GCM). The article reviews relevant publications from the literature in English on GCM. This rare, frequently fatal inflammatory disorder of cardiac muscle has no known cause. It typically affects young to middle aged adults and is characterized by widespread degeneration and necrosis of myocardial fibers. Congestive heart failure and ventricular tachycardia are common clinical manifestations. GCM occurs primarily in previously healthy adults, although it is frequently associated with various systemic diseases, primarily of autoimmune origin. The inflammatory infiltrate is characterized by the presence of multinucleated giant cells and is distinct from cardiac sarcoidosis. Animal models of GCM are similar to models of other autoimmune disorders such as rheumatoid arthritis. The major distinction to be made, and probably the most difficult, is between GCM and sarcoidosis, a systemic disease defined by the presence of epithelioid granulomas in multiple organs. Initial therapy should be directed toward controlling heart failure, preventing thrombosis, and controlling arrhythmias. The specific therapeutic approach to human myocarditis is inconsistent, in part because of uncertainty as to the severity of the disease, the underlying pathologic process, and the need to tailor therapies accordingly. Nonsteroidal antiinflammatory drugs have been frequently used, but without any observable benefit beyond their analgesic effect. The use of immunosuppressive therapy has not been adequately substantiated in human disease and remains controversial. The poor prognosis improves with cardiac transplantation. The article concludes that the clinical and immunopathogenetic similarities with classical rheumatologic diseases, the differential diagnosis with sarcoidosis and other inflammatory conditions, and the use of standard immunosuppressive medications make GCM a disease process that should be added to the

rheumatologist's expertise. 2 figures, 4 tables, and 119 references. (AA-M).

- **Autoimmune Diseases Affecting the Inner Ear**

  Source: Advances in Otolaryngology-Head and Neck Surgery. Volume 7: 59-77. 1993.

  Summary: Autoimmune inner ear disease is a relatively recently recognized disorder that continues to be difficult to diagnose and treat. This article presents six case reports of individuals with autoimmune inner ear disease, each with a brief comment regarding etiology. The author then describes the pertinent literature and stresses that autoimmune inner ear disease covers a wide spectrum of presentation. Topics include organ-specific autoimmune inner ear disease; diagnostic considerations; pathologic findings; manifestations of disease; Meniere's disease; non-organ-specific autoimmune inner ear disease, including polyarteritis nodosa (PAN), Cogan's syndrome, Wegener's granulomatosis, Behcet's syndrome, relapsing polychondritis, systemic lupus erythematosus (SLE), and rheumatoid arthritis; and treatment options. The author concludes that autoimmune inner ear disease appears now to be recognized as one cause of progressive vestibuloauditory dysfunction. These patients may initially present as having Meniere's disease, with dizziness and vertigo finally culminating in ataxia and oscillopsia, or may have only progressive sensorineural hearing loss seemingly sparing the vestibular sense organs. The clinician should have a high index of suspicion of autoimmune disease, obtain laboratory confirmation, and begin immunosuppressive therapy as soon as possible to preserve function. 89 references. (AA-M).

- **Photopheresis and Autoimmune Diseases**

  Source: Rheumatic Disease Clinics of North America. 26(1): 75-81. February 2000.

  Summary: This journal article provides health professionals with information on the use of photopheresis in the treatment of autoimmune diseases, focusing on reports of treatment trials in systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and scleroderma. Photopheresis, or extracorporeal photochemotherapy, is a procedure in which leukopheresis is combined with the administration of 8 methoxypsoralen either in oral form prior to leukopheresis or by injection of liquid methoxypsoralen into the leukocyte rich cell extract. The patient's peripheral blood is removed and separated by centrifugation into a leukocyte depleted fraction that is returned immediately to the patient and into a leukocyte enriched fraction that is exposed to

ultraviolet light prior to reinfusion. Several case reports and case series have implied effectiveness in the use of photopheresis for the treatment of SLE. Results of an uncontrolled trial of patients with RA who were treated with photopheresis was not considered by the investigators to be a clinical success. Studies of photopheresis in systemic sclerosis have yielded conflicting results. Although several case reports and case series suggest that photopheresis is effective in the treatment of autoimmune diseases, few controlled studies have been conducted to test this hypothesis. After a decade of interest, multiple case reports, open trials, and one controlled study, the role of photopheresis in autoimmune disease remains to be established. Controlled multicenter trials in RA, SLE, and scleroderma may be costly but are clearly needed for proper evaluation of this therapy. 18 references. (AA-M).

- **Hepatitis C-Associated Autoimmune Disorders**

  Source: Rheumatic Disease Clinics of North America. 24(2): 353-374. May 1998.

  Summary: This journal article provides health professionals with information on hepatitis C virus (HCV) infection, HCV-associated immune and autoimmune disorders, and therapeutic strategies and toxicities documented in patients with HCV-associated disorders. The article begins with a discussion of the possible role of the immune system in HCV infection and an explanation of how the HCV infection is diagnosed. This is followed by data on the prevalence of HCV-associated autoimmunity. The article then describes the serologic and clinical correlates of HCV infection to illustrate an emerging picture of autoimmune disease spectra. Correlates include autoantibody formation, cryoglobulinemic manifestation, vasculitis, vascular thrombosis and antiphospholipid antibody syndrome, glomerulonephritis, systemic lupus erythematosus, rheumatoid arthritis, polymyositis, dermatomyositis, Sjogren's syndrome, autoimmune thyroid disease, and autoimmune hepatitis. In addition, the article discusses the treatment of HCV infection with interferon alpha. Although this drug has been shown to reduce cryoglobulins and improve associated proteinuria, vasculitis, and neuropathy, it may have no effect on, precipitate, or exacerbate other autoimmune diseases. The article concludes that further epidemiologic and virologic investigations controlling for HCV risk factors, HCV subtype, human leukocyte antigen genotype, and geographic and environmental variables will be needed to clarify a potential causal relationship for HCV infection in autoimmune disease. 1 figure, 2 tables, and 177 references.

- **Dosing Implications of a Clinical Interaction Between Grapefruit Juice and Cyclosporine and Metabolite Concentrations in Patients With Autoimmune Diseases**

  Source: Journal of Rheumatology. 24(1):49-54; 1997.

  Summary: This journal article for health professionals describes a study that determined the effect of chronic grapefruit juice administration on steady state blood concentrations of cyclosporine and metabolites in patients with autoimmune diseases. Participants were four women and five men with various autoimmune diseases who were stabilized on administration of cyclosporine. They were given either grapefruit juice or water using a randomized crossover design. Whole blood samples were collected before the morning cyclosporine dose and during the 12-hour interdose interval. Cyclosporine concentrations were measured using a relatively specific assay, and total metabolite concentrations were estimated using a nonspecific assay. Results indicate that exposure to grapefruit juice produced significant increases in predose cyclosporine concentrations, total metabolite concentrations, and the area under the cyclosporine and metabolite blood concentration-time curves. One patient developed significant neurological side effects associated with a 68.9 percent and 214 percent increase in predose cyclosporine and metabolite concentrations, respectively, during grapefruit juice co-administration. Results demonstrate that grapefruit juice causes an increase in both parent and metabolite profiles, indicating an alteration in the disposition of cyclosporine and metabolites. This interaction is of potential clinical importance in terms of mechanisms, side effects, and dosing. 51 references, 1 figure, and 3 tables. (AA-M).

- **VIth International Symposium on Sjogren's Syndrome**

  Source: Journal of Rheumatology. 24(Supp. 50):1-54; September 1997.

  Summary: This journal for health professionals presents the proceedings of the Sixth International Symposium on Sjogren's syndrome (SS) in October 1997. Keynote presentations focused on the role of herpes viruses and retroviruses in the etiopathogenesis of SS, apoptosis and autoimmunity, and the diagnostic criteria for SS and the clinical features and disease activity of SS. Other topics included autoantibodies reactive with Ro(SSA) and La(SSB) and pregnancy; the influence of sex hormones on autoimmune diseases, particularly SS; and future directions for SS therapy. In addition, the journal presents abstracts of plenary lectures that focused on the topics of viral and other environmental factors; cytokines and apoptosis; diagnostic criteria, clinical features, and disease activity; antigens, antibodies, and immunoglobulins; hormonal and

neuroendocrine influences; and treatment. Numerous references, 2 figures, and 6 tables.

- **Sex Hormones and Sjogren's Syndrome**

  Source: Journal of Rheumatology. 24(Supp. 50):17-32; September 1997.

  Summary: This journal article for health professionals examines the influence of the sex steroids (androgens, estrogen, and possibly progestins) on autoimmune diseases, particularly Sjogren's syndrome (SS). It reviews the nature, extent, and mechanisms of sex steroid effects on the immune system. The article then explains how sex steroid hormones may promote sex-related variations in the frequency of autoimmune disease and how clarification of these sex differences and endocrine-immune interactions may be used to develop therapeutic strategies for the treatment of autoimmune disorders, especially SS. The article concludes that the research on the interactions between sex steroids and the immune system has significantly increased understanding of the pathogenesis and expression of autoimmune disease. 249 references, 1 figure, and 5 tables.

Federally-Funded Research on Autoimmune Diseases

The U.S. Government supports a variety of research studies relating to autoimmune diseases and associated conditions. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[19] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally-funded biomedical research projects conducted at universities, hospitals, and other institutions. Visit the CRISP Web site at **http://commons.cit.nih.gov/crisp3/CRISP.Generate_Ticket**. You can perform targeted searches by various criteria including geography, date, as well as topics related to autoimmune diseases and related conditions.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally-funded studies use animals or simulated models to explore autoimmune diseases and related conditions. In some cases, therefore, it may

[19] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

be difficult to understand how some basic or fundamental research could eventually translate into medical practice. The following sample is typical of the type of information found when searching the CRISP database for autoimmune diseases:

- **Project Title: Blood from Autoimmune Diseases with Thalidomide Therapy**

  Principal Investigator & Institution: Oliver, Stephen J.; Rockefeller University 66Th and York Ave New York, Ny 10021

  Timing: Fiscal Year 2000; Project Start 1-DEC-1978; Project End 0-NOV-2004

  Summary: This study involves blood specimens drawn from patients with autoimmune diseases who are obtaining thalidomide through their private physicians for treatment of their respective conditions. These blood specimens would be obtained during outpatient visits (between 3 and 5) here at Rockefeller University Hospital and would consist of approximately 10 to 30 cc of EDTA treated blood. The samples will be used for in vitro laboratory work involving plasma cytokine levels and flow cytometry here at Rockefeller. This blood will be provided by the patients on a purely voluntary basis. No diagnostic evaluation or treatment will be provided. Acquiring blood from these individuals will be beneficial to the above named studies by providing additional data on patient immune responses to thalidomide. This data will also help establish potential research projects in related autoimmune diseases to those currently under study in our protocols. Finally, continuing contact with the referring physicians and their patients will also encourage outside cooperation with future study recruitment for these rare diseases.

  Website: http://commons.cit.nih.gov/crisp3/CRISP.Generate_Ticket

- **Project Title: Natural Autoantibody and Autoimmune Diseases**

  Principal Investigator & Institution: Chen, Qing C.; Pathology; Oregon Health & Science University 3181 Sw Sam Jackson Park Rd Portland, or 97201

  Timing: Fiscal Year 2002; Project Start 1-FEB-2002; Project End 1-JAN-2005

  Summary: (provided by applicant): Production of autoantibodies is the hallmark of many autoimmune diseases. To understand how these self-destructive antibodies are controlled, we generated transgenic mice where the majority of B cells express disease-associated anti-DNA antibodies. We have shown that anti-DNA B cells are eliminated by deletion, functional silencing (anergy) and revision of self-reactive

receptors (receptor editing). Paradoxically, although auto reactive B cells are strictly regulated, a substantial proportion of circulating antibodies in normal sera exhibits self- reactivity. Such antibodies, referred as natural autoantibodies (NAA), often have weak reactivity toward conserved cell components such as DNA, nucleoproteins and phospholipids that are also the common targets seen in autoimmune diseases. The function of NAA is presently unknown, as is their relationship to pathologic autoantibodies. Here, we propose two fundamentally different but not mutually exclusive roles of NAA in autoimmunity: 1) they may be a major source of pathological autoantibodies; 2) they may play a central role in maintaining self-tolerance. To test these hypotheses, a new immunoglobulin knock-in mouse model will be generated, where the B cells express a typical NAA. Unlike conventional transgenes, the knock-in gene is able to undergo receptor editing, somatic mutation and isotype switching, all of which are important in development of pathologic antibodies. Using this model, we will define the nature of B cells that produce NAA, and determine whether these B cells will participate in T cell-independent and T cell- dependent antigen responses. Next, by crossing the NAA knock-in mice to an autoimmune-prone background, the relationship between natural and pathologic autoantibodies will be determined, and the molecular mechanisms by which NAA acquire pathogenicity will be explored. Finally, by co-expression of natural autoantibodies and pathologic anti-DNA antibodies in a single animal, we will determine whether NAA can suppress pathologic autoantibody production, and determine whether NAA can alleviate autoimmune diseases. Results from these studies will provide great insight into the etiology of autoimmunity and may lead to new therapeutic strategies for autoimmune diseases.

Website: http://commons.cit.nih.gov/crisp3/CRISP.Generate_Ticket

- **Project Title: Autoimmune Encephalomyelitis and NF-KB**

  Principal Investigator & Institution: Chen, Youhai H.; Associate Professor; Medicine; University of Pennsylvania 3451 Walnut Philadelphia, Pa 19104

  Timing: Fiscal Year 2000; Project Start 0-SEP-1999; Project End 1-JUL-2004

  Summary: Development of autoimmune diseases requires coordinated expression of a number of genes that are involved in the activation, migration and effector functions of inflammatory cells. These include genes that encode costimulatory molecules, cytokines, chemokines, adhesion molecules and inflammatory enzymes. Expression of these genes is regulated by several families of transcription factors that include nuclear factor (NF)-kappaB, activator protein-1 and nuclear factor-IL-6.

These factors, acting either alone or in combination, orchestrate the initiation and progression of autoimmune diseases. The long-term goal of our research is to elucidate the mechanisms of transcription factor regulation of autoimmune diseases. This proposal is based on our recent discovery that NF-kappaB1-deficient mice are resistant to experimental autoimmune encephalomyelitis (EAE), and are unable to develop a strong TH1 or TH2 type response to self-myelin antigens. The goal of this proposal is to elucidate the mechanisms of NF- kappaB1 action in animal models of multiple sclerosis. A major challenge to study the roles of transcription factors in autoimmune diseases is that they are often expressed by a variety of cell types. In the case of NF-kappaB1, it is expressed not only by cells of the immune system, but also by cells of target organs such as brain and spinal cord. The roles of NF-kappaB1 in each of these cell types must be established before a comprehensive understanding of NF-kappaB1 action in autoimmunity can be achieved. We hypothesize that NF-kappaB1 expressed by immune cells and neural cells may play different roles in EAE: NF-kappaB1 expressed by immune cells orchestrates the activation and effector function of inflammatory cells leading to tissue injury, whereas NF-kappaB1 expressed by neural cells protects them from inflammation-induced cell death, presumably by activating anti-apoptotic genes. To test these hypotheses, we will study the roles of NF-kappaB1 in 1) activation of myelin-specific T cells, 2) formation of inflammatory lesions, and 3) death of inflammatory and neural cells in EAE. The roles of NF-kappaB1 expressed by different cell types will be dissected using transgenic adoptive transfer models and bone-marrow chimeric models. Information generated from these studies may not only help elucidate the mechanisms of NF-kappaB1 action in EAE but also aid in developing a general strategy to investigate the roles of transcription factors in autoimmune diseases. Novel strategies targeting NF-kappaB may then be developed to treat or prevent autoimmune diseases.

Website: http://commons.cit.nih.gov/crisp3/CRISP.Generate_Ticket

- **Project Title: CB1-B in T Cell Activation and Tolerance**

  Principal Investigator & Institution: Liu, Yun-Cai; La Jolla Institute for Allergy/Immunolgy Allergy and Immunology San Diego, Ca 92121

  Timing: Fiscal Year 2002; Project Start 1-MAY-2002; Project End 0-APR-2007

  Summary: (provided by applicant): Development of autoimmune diseases is a result of breakdown of self-tolerance in the thymus and/or changes in the activation thresholds of peripheral lymphocytes. Recent genetic studies on Cbl-b gene-targeted mice showed that Cbl-b deficiency

changes the signaling thresholds: Cbl-b deficiency uncouples T cell proliferation, IL-2 production from the co-stimulation of CD28; the gene-targeted mice develop spontaneous autoimmunity or become highly susceptible to exogenous antigen-induced autoimmune diseases. These studies suggest a critical role of Cbl-b in the regulation of T cell activation thresholds and hence in the maintenance of the balance between immunity and tolerance. Our recent demonstration that the RING finger of Cbl, a Cbl-b homologue, can recruit and activate ubiquitin (Ub) conjugation enzyme (Ubc), and that Cbl then facilitates Ub conjugation to the protein tyrosine kinases it associates with, may suggest that Cbl-b could also function as a Ub ligase for Cbl-b-binding proteins. However, the target proteins for Cbl-b-mediated ubiquitination and the link to the induction of autoimmune responses are far from clear. Considering the recent progress on the understanding of Cbl family proteins and on the recent biochemical and genetic data on Cbl-b, we propose the following model regarding the biological function of Cbl-b in T cells: Cbl-b, as both an adaptor protein and a Ub ligase, recruits Ub-loaded Ubc through its RING finger. Cbl-b then helps tag Ub to protein substrates, through a specific interaction of Cbl-b protein interaction domains with its binding partners. Ubiquitination of these target proteins may lead to their downregulation and/or their biological function. Cbl-b-induced ubiquitination events may then change the thresholds of T cells in response to the stimulation of TCR and CD28, which eventually causes the induction and expansion of autoreactive T cells for the subsequent development of autoimmune diseases. We will test this hypothesis by the identification and the functional analysis of intracellular targets for Cbl-b, and as a part of future plan, by the establishment and functional analysis of Cbl-b deficient mice model of autoimmune diabetes. The information generated by the proposed studies will enhance our understanding of the biological function of Cbl-b in physiological T cell tolerance and in pathological autoreactive T cell responses, and will shed light on the development of novel therapeutic approaches to autoimmune diabetes.

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- **Project Title: Congenic Strains: a Model for Gene/Environment Interacti**

  Principal Investigator & Institution: Morel, Laurence M.; Professor; Medicine; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2000; Project Start 0-SEP-1999; Project End 9-SEP-2002

  Summary: It is estimated that upwards of 10 million Americans have some form of autoimmune disorder. It is clear that both genetic and environmental factors contribute to the development and progression of

autoimmune diseases. Recently considerable interest has focused on environmental factors that may contribute to the development of autoimmune disorders. In specific disorders such as systemic lupus erythematosus, women of childbearing age are affected at a rate 9-10 times that of men, and data both from human and animal studies suggest that estrogens can have an adverse impact on the course of the autoimmune process. Several chemicals have been shown to have estrogenic effects, and one mechanism by which environmental toxicants might influence the appearance or severity of autoimmune diseases is by mimicking the effects of estrogen. Heavy metals such has mercury have also been shown to induce systemic autoimmunity in both human and animal models. Epidemiologic and experimental data suggest that a common genetic background confers susceptibility to various autoimmune diseases. In addition, an extensive overlap exists between genomic regions linked to various autoimmune disorders. A panel of 17 murine congenic strains each carrying a genomic region containing an autoimmune susceptibility locus (from the NOD, NZM2410, NZW, and MRL autoimmune-prone strains) have been produced at the University of Florida, and are being used to functionally and genetically characterize these loci. This panel covers 33 percent of the murine genome and 63 percent of the common autoimmune regions. We propose to develop this panel of congenic strains as a model to study gene/environment interactions in autoimmunity. As a proof of principle, we will use 17-betaestradiol, chlordecone, and mercuric chloride as environmental agents (EA). In Specific Aim 1, we will screen the panel to find autoimmune loci showing specific interactions with any of these 3 EA. In Specific Aim 2, these EA/locus interactions will be analyzed by screening cDNA arrays, which will map pathways of genes with altered mRNA levels in response to the expression of the autoimmune locus under that EA exposure. In Specific Aim 3, these insights into the EA/autoimmune locus effector mechanisms will be used to functionally characterize the immunopathology associated with these interactions. The main advantages of the model that we propose to develop are: 1) a great reduction of both genetic and functional complexity, 2) a significant overlap between autoimmune ideases for the genomic regions tested in each strains, and 3) a growing body of genetic and functional data associated with each of the strains.

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- **Project Title: Faseb Summer Conference On Neuroimmunology**

  Principal Investigator & Institution: Benveniste, Etty N.; Professor and Chair; Federation of Amer Soc for Exper Bio for Experimental Biology Bethesda, Md 20814

Timing: Fiscal Year 2002; Project Start 1-AUG-2002; Project End 1-JUL-2003

Summary: (provided by applicant): This application is a request for support for the seventh FASEB Summer Research Conference on Neuroimmunology to be held at the Tucson Omni Resort, Tucson, AZ, August 17-22, 2002. Scientists from a variety of disciplines have become increasingly interested in the dialogue between the immune system and the central nervous system (CNS). Immune activity in the CNS has traditionally been associated with pathological conditions; however, recent evidence suggests that immune-associated cells and other CNS factors have a role in normal physiological conditions. The CNS and the immune system use common factors for their inter- and intra-communications; e.g., cytokines, chemokines and neurotrophic factors. In addition, new information indicates that the, CNS plays an active immunomodulatory role, controlling the immune response in the periphery. Delivery of stable neuropeptide/neurotransmitter analogs and modulation of the corresponding receptors on immune cells offer new avenues for the manipulation of the immune response in vaccination and/or autoimmune diseases. In the past, interest in immune involvement in brain diseases was restricted to autoimmune diseases. It now evident that almost any nerve-related disease involves an immune-associated component as part of its pathogenesis. Examples include Alzheimer's Disease, HIV-1 Associated Dementia, Parkinson's disease and spinal cord injury. On the other hand, several CNS products down regulate peripheral immune reactions, having a beneficial effect on hyper immune pathological conditions such as septic shock and autoimmune diseases. This alters our view of therapeutic approaches currently accepted in the pharmaceutical industry for treatment of CNS degenerative diseases, CNS trauma and peripheral organ autoimmune diseases. At the FASEB meeting in the year 2002, questions to be raised will concern the role of autoimmunity in CNS repair, as well as inflammation and trauma, and how these responses can be manipulated at the cellular and functional levels. Attention will be paid to the role of cytokines/chemokines in the CNS and neurotrophic factors in the immune system, cross-control and cross talk. Issues such as cell trafficking to the CNS and mechanisms triggering the immune response in the CNS will also be discussed. No other platform provides the opportunity for scientific discussion of the field of neuroimmunology where emphasis is placed upon the physiological roles of the immune system in relation to the CNS, as well as to the beneficial rather than detrimental aspects of the immune response in the CNS.

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- **Project Title: Federation of Clinical Immunology Societies Meeting**

  Principal Investigator & Institution: Hafler, David A.; Professor; Clinical Immunology Society 6900 Grove Rd Thorofare, Nj 08086

  Timing: Fiscal Year 2001; Project Start 4-MAY-2001; Project End 3-MAY-2002

  Summary: (Adapted from Applicant's Abstract) The Clinical Immunology Society (CIS) has undertaken the task of arranging a federated meeting for clinical immunology to be held yearly commencing in May 2001. This new meeting plans to provide an opportunity for members of each of the individual clinical immunology societies involved to meet together on a yearly basis. The first Federated meeting will be held in Boston, May 4-7, 2001. We believe that this new meeting will consolidate the field of Clinical Immunology as it reaches maturity, particularly as it relates to the major human autoimmune diseases including multiple sclerosis, rheumatoid arthritis, and juvenile diabetes. Resultant cross-fertilization from this meeting among the disease-centric investigators and members of the biotech and pharmaceutical community is of critical importance with the increasing numbers of therapeutics for treatment of these autoimmune diseases. This meeting reflects the new interdisciplinary nature now necessary for the investigation and treatment of human autoimmune diseases. It will also cover additional immune based diseases including, but not limited to, asthma, immuno-oncology, acquired immunodeficiency, primary immunodeficiency, transplantation tolerance and immuno-dermatology. Another key aspect will be the inclusion of the Immune Tolerance Network annual meeting. This will provide an important opportunity to inform industry about the Immune Tolerance Network and to disseminate new information about science and medicine. The format will be three days on topics of mutual interest to all constituent groups. There will be two major plenary lectures to begin each day, followed by concurrent major symposia on topics of interest to constituent groups. Afternoons will be abstract-driven interspersed with breakout meetings for the constituent societies and presentations by biotech and pharmaceutical firms concerning technologies of interest to the assembled groups. There will be two additional meetings held in conjunction with this meeting. The first of these is a "fellows day" in which plenary and abstract driven talks will be held on the day preceding the main scientific sessions. The second parallel session will be on "science for the non-clinician" which targets the lay societies representing the constituent scientific societies.

  Website: http://commons.cit.nih.gov/crisp3/CRISP.Generate_Ticket

- **Project Title: Genetic Basis of Susceptibility to EAE**

  Principal Investigator & Institution: Kuchroo, Vijay K.; Associate Professor; Brigham and Women's Hospital 75 Francis St Boston, Ma 02115

  Timing: Fiscal Year 2000; Project Start 1-AUG-2000; Project End 1-JUL-2005

  Summary: (Adapted from the Investigator's abstract): To define the factors that control susceptibility to experimental autoimmune encephalomyelitis (EAE), the investigators have performed cellular immunological and genetic analyses of highly susceptible SJL/J and resistant B 10.S mice, both of which are of the same MHC (H-2s) haplotype. In contrast to the SJL mice, the B10. mice show a relatively poor T cell proliferative response to encephalitogenic myelin epitopes and also do not produce significant amounts of proinflammatory Thl cytokines (IFN gamma) in response to the myelin autoantigens. By a genetic approach using microsatellite markers and a backcross of SJL and B 10.S mice, they identified multiple loci that show significant linkage to EAE susceptibility. Some of the same loci have also been identified in other autoimmune diseases, particularly diabetes in NOD mice, thus raising the possibility that the same genetic elements (common "autoimmune gene(s)") may contribute to the susceptibility to multiple autoimmune diseases. To directly study the relationship of susceptibility loci between various autoimmune diseases and the role of EAE-susceptibility loci on T cell response and IFN-y production they propose to: 1) study the NOD congenic mice in which susceptibility loci have been replaced at chromosome 3 (Idd 3, 10, 17, 18) and chromosome 4 (Idd9) with intervals from the resistant B6/B 10 mice for the development of diabetes and EAE, and subphenotypes such as inflammation and cytokine production in the target organ. 2) Define by genome wide scan using microsatellite markers the genetic loci that are linked to differences in IFN-gamma production in the SJL and B10.S mouse strains, and determine whether polymorphism in IL-12 (a potent inducer of IFN-gamma) between the two strains is responsible for the difference. 3) Test the development of EAE, T cell proliferation and cytokine response to myelin antigens in the SJL-B 10.S congenic strains of mice that will be generated by introducing individual EAE-susceptibility loci from the SJL mice into B 10.S and by transferring EAE-resistance loci from B 10.S into the SJL background. These studies will define the cellular and genetic basis for the self tolerance and the congenic approach will lead to the identification of gene(s) within the loci responsible for the disease phenotype. Furthermore, using congenic mice with resistance loci that overlap among multiple autoimmune diseases will further determine

whether genuine "autoimmune alleles" exist that effect multiple autoimmune diseases.

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- **Project Title: Immune Regulation of the B7-H1 Pathway**

  Principal Investigator & Institution: Chen, Lieping; Professor; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

  Timing: Fiscal Year 2002; Project Start 1-JUL-2002; Project End 0-JUN-2007

  Summary: (provided by applicant): We have recently identified B7-H1, a new member of the B7 costimulatory molecule family. Preliminary data from our laboratory demonstrated that B7-H1 engages a receptor of T cells to provide an initial signal for costimulation of T cell growth in vitro and promote cell-mediated and humoral immune responses to antigens in vivo. However, the majority of human cancers examined so far express high levels of B7-H1 and engagement of activated T cells by tumor-associated B7-H1 promotes programmed cell death. The overall goal of our study is to elucidate cellular and molecular mechanisms of B7-H1 in immune regulation and to manipulate this pathway for treatment of autoimmune diseases and cancers. The central hypothesis of this proposal is that B7-H1 regulates T cell responses in autoimmune diseases and cancers in a positive and negative fashion through different receptors. To test this hypothesis, we will use bioinformatics, expression cloning and mass spectrometry techniques to identify the novel receptor of B7-H1. In addition, we will utilize B7-H1 deficient and transgenic mouse models to elucidate immunological functions of B7-H1 in vivo. We will also evaluate the effect of B7-H1 in graft versus host disease (GVHD) models for potential treatment of autoimmune diseases. Finally, we will examine the mechanisms of tumor-associated B7-H1 in evasion of active and adoptive immunity in mouse tumor models. It is anticipated that these studies will provide a foundation for the development of new approaches for the prevention and immunotherapy of autoimmune diseases, transplantation rejection and cancers.

  Website: http://commons.cit.nih.gov/crisp3/CRISP.Generate_Ticket

- **Project Title: Immunoregulatory Circuits in Man**

  Principal Investigator & Institution: Morimoto, Chikao; Associate Professor of Medicine; Dana-Farber Cancer Institute 44 Binney St Boston, Ma 02115

  Timing: Fiscal Year 2000; Project Start 1-JUL-1985; Project End 0-JUN-2003

Summary: (Adapted from Investigator's abstract): Memory CD4 T-cells play a key role in host defense as well as the triggering and maintaining of inflammation. The triggering of the costimulatory signals plays a central role in the generation of effective immune responses. The costimulatory signals can be provided by a number of accessory molecules. Of the costimulatory molecules, CD29/VLA, CD26, and CD27 have been established by this group. CD29/VLA and CD26 are preferentially expressed on CD4 memory T-cells and play an important role in the costimulation, function, and migration of memory T-cells. Much remains to be clarified regarding the complex functions of CD29/VLA and CD26 in signal transduction and the subsequent effects upon T-cell function and cell migration. The major goal of this application is to determine the immunoregulatory circuits in man. The specific aims of this application are: 1) The molecular basis of CD29/VLA in T-cell costimulation, signaling and T-cell function. They will define the structural basis of Cas-L tyrosine phosphorylation and FAK activation and define the role of Cas-L in CD29/VLA-mediated cytokine production and gene expression. Moreover, the role of Cas-L in T-cell migration will be defined. 2) The molecular basis of CD26/DPPIV in T-cell function and costimulation. The role of CD26/DPPIV in T-cell migration, the precise characteristics of the binding of ADA to CD26, and the functional significance of ADA in T-cell activation will be defined. In addition, the structure and function of the ligand of CD26 other than ADA will be defined. 3), The molecular and cellular defects in patients with autoimmune diseases. Analysis of VLA-mediated costimulation in patients with autoimmune diseases will be performed. Moreover, the expression and function, of Cas-L, and FAK as well as the migratory activity of T-cells in autoimmune diseases will be determined. In addition, the level of CD26/DPPIV in serum/plasma and its correlation with clinical complications in autoimmune diseases will be defined. The study will not only provide new insights into understanding of the mechanisms of T-cell activation and migration, but will also provide new insights into understanding the precise molecular mechanisms of immune abnormalities found in various autoimmune diseases and will lead to the development of rational therapy for the manipulation of the abnormalities found in such diseases.

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- **Project Title: Induction of Specific Immune Tolerance**

  Principal Investigator & Institution: Staerz, Uwe D.; Associate Professor; National Jewish Medical & Res Ctr and Research Center Denver, Co 80206

Timing: Fiscal Year 2000; Project Start 5-JUL-1999; Project End 0-JUN-2004

Summary: (Adapted from the Investigator's abstract): The immune system is the major biological defense system responsible for fighting disease. However, immune responses can also be detrimental. In the case of transplantation, although the immune system reacts appropriately, it nevertheless causes harm by destroying the transplanted organs. In autoimmune diseases, the immune system turns against self and attacks otherwise normal tissue. In both situations, it is important to suspend the destructive function of the immune system while maintaining normal immune responses. Presently, in the clinical situation, a general immune suppression is induced, and the patients' defenses against infectious challenges are impaired. Strategies are now being sought that successfully induce specific non-responsiveness (tolerance) without affecting normal immune functions. Important cells of the immune system are T cells. They control many immune responses and also act as effector cells. Their suppression is crucial for the induction of tolerance. Only cells that react with a given organ, e.g. a transplant or a target of an autoimmune disease, should be removed. As different types of cells express tissue-specific antigens, complete tolerance towards a given tissue is best induced by the tissue itself. This should be true for transplant rejections and also autoimmune diseases. It has long been held that the disease mechanisms underlying autoimmune diseases mimic those seen in transplant rejection. Therefore, it should be possible to adapt strategies that induce specific transplantation tolerance to the treatment of autoimmune diseases. The so-called veto-effect (conventional veto) has been shown to efficiently and specifically tolerize T cells. It functions by expression of the co-receptor CD8 on stimulator cells. Based on this original observation, the approach has been expanded toward the development of hybrid antibodies (hAb) that combine a targeting antibody moiety with the functional region of the CD4 or CD9 accessory molecules. The cells coated with these hAbs inhibited the activation of either CD4+ or CD8+ activation in a highly specific fashion. In the current application, it is proposed to examine the function and activity of the CD8 targeting hAb in animal models of organ transplantation.

Website: http://commons.cit.nih.gov/crisp3/CRISP.Generate_Ticket

E-Journals: PubMed Central[20]

PubMed Central (PMC) is a digital archive of life sciences journal literature developed and managed by the National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).[21] Access to this growing archive of e-journals is free and unrestricted.[22] To search, go to **http://www.pubmedcentral.nih.gov/index.html#search**, and type "autoimmune diseases" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for autoimmune diseases in the PubMed Central database:

- **Autologous stem-cell transplantation in refractory autoimmune diseases after in vivo immunoablation and ex vivo depletion of mononuclear cells** by Oliver Rosen, Andreas Thiel, Gero Massenkeil, Falk Hiepe, Thomas Haupl, Hartmut Radtke, Gerd R Burmester, Erika Gromnica-Ihle, Andreas Radbruch, and Renate Arnold; 2000 http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=17815
- **Clustering of non-major histocompatibility complex susceptibility candidate loci in human autoimmune diseases** by Kevin G. Becker, Richard M. Simon, Joan E. Bailey-Wilson, Boris Freidlin, William E. Biddison, Henry F. McFarland, and Jeffrey M. Trent; 1998 August 18 http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=21447
- **High frequency of association of rheumatic/autoimmune diseases and untreated male hypogonadism with severe testicular dysfunction** by F Javier Jimenez-Balderas, Rosario Tapia-Serrano, M Eugenia Fonseca, Jorge Arellano, Arturo Beltran, Patricia Yanez, Adolfo Camargo-Coronel, and Antonio Fraga; 2001 http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=64847
- **Local Nitric Oxide Production in Viral and Autoimmune Diseases of the Central Nervous System** by DC Hooper, ST Ohnishi, R Kean, Y Numagami, B Dietzschold, and H Koprowski; 1995 June 6 http://www.pubmedcentral.nih.gov/articlerender.fcgi?rendertype=abstract&artid=41684

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[20] Adapted from the National Library of Medicine: **http://www.pubmedcentral.nih.gov/about/intro.html**.

[21] With PubMed Central, NCBI is taking the lead in preservation and maintenance of open access to electronic literature, just as NLM has done for decades with printed biomedical literature. PubMed Central aims to become a world-class library of the digital age.

[22] The value of PubMed Central, in addition to its role as an archive, lies the availability of data from diverse sources stored in a common format in a single repository. Many journals already have online publishing operations, and there is a growing tendency to publish material online only, to the exclusion of print.

- **Organ-Specific and Systemic Autoimmune Diseases Originate from Defects in Hematopoietic Stem Cells** by S Ikehara, M Kawamura, F Takao, M Inaba, R Yasumizu, S Than, H Hisha, K Sugiura, Y Koide, TO Yoshida, T Ida, H Imura, and RA Good; 1990 November 1
  http://www.pubmedcentral.nih.gov/articlerender.fcgi?rendertype=abstract&artid=54951
- **Possible Deletion of a Developmentally Regulated Heavy-Chain Variable Region Gene in Autoimmune Diseases** by P Yang, NJ Olsen, KA Siminovitch, T Olee, F Kozin, DA Carson, and PP Chen; 1990 October 15
  http://www.pubmedcentral.nih.gov/articlerender.fcgi?rendertype=abstract&artid=54860
- **Protective Effect of Transforming Growth Factor [beta]1 on Experimental Autoimmune Diseases in Mice** by AP Kuruvilla, R Shah, GM Hochwald, HD Liggitt, MA Palladino, and GJ Thorbecke; 1991 April 1
  http://www.pubmedcentral.nih.gov/articlerender.fcgi?rendertype=abstract&artid=51351

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine. The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign references. It is also free to the public.[23] If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

To generate your own bibliography of studies dealing with autoimmune diseases, simply go to the PubMed Web site at **www.ncbi.nlm.nih.gov/pubmed**. Type "autoimmune diseases" (or synonyms) into the search box, and click "Go." The following is the type of

[23] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

output you can expect from PubMed for "autoimmune diseases" (hyperlinks lead to article summaries):

- **Amicrobial pustulosis associated with autoimmune diseases: healing with zinc supplementation.**
  Author(s): Beneton N, Wolkenstein P, Bagot M, Cosnes A, Wechsler J, Roujeau JC, Revuz J.
  Source: The British Journal of Dermatology. 2000 December; 143(6): 1306-10. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11122040&dopt=Abstract

- **Photopheresis and autoimmune diseases.**
  Author(s): Mayes MD.
  Source: Rheumatic Diseases Clinics of North America. 2000 February; 26(1): 75-81, Viii-Ix. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10680195&dopt=Abstract

Vocabulary Builder

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Analgesic: An agent that alleviates pain without causing loss of consciousness. [EU]

Androgens: A class of sex hormones associated with the development and maintenance of the secondary male sex characteristics, sperm induction, and sexual differentiation. In addition to increasing virility and libido, they also increase nitrogen and water retention and stimulate skeletal growth. [NIH]

Arrhythmia: Any variation from the normal rhythm of the heart beat, including sinus arrhythmia, premature beat, heart block, atrial fibrillation, atrial flutter, pulsus alternans, and paroxysmal tachycardia. [EU]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Ataxia: Failure of muscular coordination; irregularity of muscular action. [EU]

Autoantigens: Endogenous tissue constituents that have the ability to interact with autoantibodies and cause an immune response. [NIH]

Biochemical: Relating to biochemistry; characterized by, produced by, or

involving chemical reactions in living organisms. [EU]

Cardiac: Pertaining to the heart. [EU]

Causal: Pertaining to a cause; directed against a cause. [EU]

Chlordecone: A highly chlorinated polycyclic hydrocarbon insecticide whose large number of chlorine atoms makes it resistant to degradation. It has been shown to be toxic to mammals and causes abnormal cellular changes in laboratory animals. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Dermatology: A medical specialty concerned with the skin, its structure, functions, diseases, and treatment. [NIH]

Dizziness: An imprecise term which may refer to a sense of spatial disorientation, motion of the environment, or lightheadedness. [NIH]

Encephalomyelitis: A general term indicating inflammation of the brain and spinal cord, often used to indicate an infectious process, but also applicable to a variety of autoimmune and toxic-metabolic conditions. There is significant overlap regarding the usage of this term and encephalitis in the literature. [NIH]

Enzyme: A protein molecule that catalyses chemical reactions of other substances without itself being destroyed or altered upon completion of the reactions. Enzymes are classified according to the recommendations of the Nomenclature Committee of the International Union of Biochemistry. Each enzyme is assigned a recommended name and an Enzyme Commission (EC) number. They are divided into six main groups; oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases. [EU]

Epitopes: Sites on an antigen that interact with specific antibodies. [NIH]

Estrogens: A class of sex hormones associated with the development and maintenance of secondary female sex characteristics and control of the cyclical changes in the reproductive cycle. They are also required for pregnancy maintenance and have an anabolic effect on protein metabolism and water retention. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Extracorporeal: Situated or occurring outside the body. [EU]

Fluorescence: The property of emitting radiation while being irradiated.

The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Hepatocytes: The main structural component of the liver. They are specialized epithelial cells that are organized into interconnected plates called lobules. [NIH]

Herpes: Any inflammatory skin disease caused by a herpesvirus and characterized by the formation of clusters of small vesicles. When used alone, the term may refer to herpes simplex or to herpes zoster. [EU]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Hypogonadism: A condition resulting from or characterized by abnormally decreased functional activity of the gonads, with retardation of growth and sexual development. [EU]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Lesion: Any pathological or traumatic discontinuity of tissue or loss of function of a part. [EU]

Lymphoma: Any neoplastic disorder of the lymphoid tissue, the term lymphoma often is used alone to denote malignant lymphoma. [EU]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Myocarditis: Inflammation of the myocardium; inflammation of the muscular walls of the heart. [EU]

Necrosis: The sum of the morphological changes indicative of cell death and caused by the progressive degradative action of enzymes; it may affect groups of cells or part of a structure or an organ. [EU]

Neuropathy: A general term denoting functional disturbances and/or pathological changes in the peripheral nervous system. The etiology may be known e.g. arsenical n., diabetic n., ischemic n., traumatic n.) or unknown. Encephalopathy and myelopathy are corresponding terms relating to involvement of the brain and spinal cord, respectively. The term is also used to designate noninflammatory lesions in the peripheral nervous system, in contrast to inflammatory lesions (neuritis). [EU]

Neurotransmitter: Any of a group of substances that are released on excitation from the axon terminal of a presynaptic neuron of the central or peripheral nervous system and travel across the synaptic cleft to either excite or inhibit the target cell. Among the many substances that have the properties of a neurotransmitter are acetylcholine, norepinephrine, epinephrine, dopamine, glycine, y-aminobutyrate, glutamic acid, substance P, enkephalins, endorphins, and serotonin. [EU]

Nucleoproteins: Proteins conjugated with nucleic acids. [NIH]

Otolaryngology: A surgical specialty concerned with the study and treatment of disorders of the ear, nose, and throat. [NIH]

Pathologic: 1. indicative of or caused by a morbid condition. 2. pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pediatrics: A medical specialty concerned with maintaining health and providing medical care to children from birth to adolescence. [NIH]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Photochemotherapy: Therapy using oral or topical photosensitizing agents with subsequent exposure to light. [NIH]

Plasmacytoma: Any discrete, presumably solitary, mass of neoplastic plasma cells either in bone marrow or various extramedullary sites. [NIH]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Rheumatology: A subspecialty of internal medicine concerned with the study of inflammatory or degenerative processes and metabolic derangement of connective tissue structures which pertain to a variety of musculoskeletal disorders, such as arthritis. [NIH]

Sarcoidosis: An idiopathic systemic inflammatory granulomatous disorder

comprised of epithelioid and multinucleated giant cells with little necrosis. It usually invades the lungs with fibrosis and may also involve lymph nodes, skin, liver, spleen, eyes, phalangeal bones, and parotid glands. [NIH]

Septic: Produced by or due to decomposition by microorganisms; putrefactive. [EU]

Serum: The clear portion of any body fluid; the clear fluid moistening serous membranes. 2. blood serum; the clear liquid that separates from blood on clotting. 3. immune serum; blood serum from an immunized animal used for passive immunization; an antiserum; antitoxin, or antivenin. [EU]

Somatic: 1. pertaining to or characteristic of the soma or body. 2. pertaining to the body wall in contrast to the viscera. [EU]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Substrate: A substance upon which an enzyme acts. [EU]

Tachycardia: Excessive rapidity in the action of the heart; the term is usually applied to a heart rate above 100 per minute and may be qualified as atrial, junctional (nodal), or ventricular, and as paroxysmal. [EU]

Testicular: Pertaining to a testis. [EU]

Thalidomide: A pharmaceutical agent originally introduced as a non-barbiturate hypnotic, but withdrawn from the market because of its known tetratogenic effects. It has been reintroduced and used for a number of immunological and inflammatory disorders. Thalidomide displays immunosuppresive and anti-angiogenic activity. It inhibits release of tumor necrosis factor alpha from monocytes, and modulates other cytokine action. [NIH]

Thrombosis: The formation, development, or presence of a thrombus. [EU]

Transfusion: The introduction of whole blood or blood component directly into the blood stream. [EU]

Transgenes: Genes that are introduced into an organism using gene transfer techniques. [NIH]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Vaccination: The introduction of vaccine into the body for the purpose of inducing immunity. Coined originally to apply to the injection of smallpox vaccine, the term has come to mean any immunizing procedure in which vaccine is injected. [EU]

Vascular: Pertaining to blood vessels or indicative of a copious blood

supply. [EU]

Vestibular: Pertaining to or toward a vestibule. In dental anatomy, used to refer to the tooth surface directed toward the vestibule of the mouth. [EU]

Withdrawal: 1. a pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) a substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

CHAPTER 5. PATENTS ON AUTOIMMUNE DISEASES

Overview

You can learn about innovations relating to autoimmune diseases by reading recent patents and patent applications. Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.[24] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available to patients with autoimmune diseases within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available to patients with autoimmune diseases. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

In this chapter, we show you how to locate information on patents and their inventors. If you find a patent that is particularly interesting to you, contact the inventor or the assignee for further information.

[24]Adapted from The U. S. Patent and Trademark Office:
http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm.

Patents on Autoimmune Diseases

By performing a patent search focusing on autoimmune diseases, you can obtain information such as the title of the invention, the names of the inventor(s), the assignee(s) or the company that owns or controls the patent, a short abstract that summarizes the patent, and a few excerpts from the description of the patent. The abstract of a patent tends to be more technical in nature, while the description is often written for the public. Full patent descriptions contain much more information than is presented here (e.g. claims, references, figures, diagrams, etc.). We will tell you how to obtain this information later in the chapter. The following is an example of the type of information that you can expect to obtain from a patent search on autoimmune diseases:

- **Methimazole derivatives and tautomeric cyclic thiones to treat autoimmune diseases**

  Inventor(s): Kohn; Leonard D. (Bethesda, MD), Curley; Robert W. (Columbus, OH), Rice; John M. (West Chester, OH)

  Assignee(s): Sentron Medical, Inc. (Rockville, MD), The United States of America as represented by the Department of Health and (Washington, DC)

  Patent Number: 6,365,616

  Date filed: August 25, 1999

  Abstract: The present invention provides methods for treating autoimmune diseases in mammals and for preventing or treating transplantation rejection in a transplant recipient. These methods utilize specifically-defined methimazole derivatives and tautomeric cyclic thione compounds, as well as pharmaceutical compositions containing those compounds. These compounds and compositions have been found to be at least as effective as methimazole in terms of pharmaceutical activity, while having less of an adverse affect on thyroid function. They are also more soluble in conventional pharmaceutical vehicles than methimazole. An assay for screening the activity of compounds useful against autoimmune diseases (ability to suppress expression of MHC Class I and II molecules) is also taught.

  Excerpt(s): This invention relates to the treatment of autoimmune diseases and transplantation rejection in mammals. More specifically, the present invention relates to the use of a narrowly-defined group of methimazole derivatives and tautomeric cyclic thiones for the purposes described herein. ... Antigens are presented to the immune system by

antigen presenting cells in the context of Class I or Class II cell surface molecules, for example, CD4.sup.+ helper T-lymphocytes recognize antigens in association with Class II MHC molecules, and CD8.sup.+ cytotoxic lymphocytes (CTL) recognize antigens in association with Class I gene products. It is currently believed that MHC Class I molecules function primarily as the targets of the cellular immune response, while Class II molecules regulate both the humoral and cellular immune response (Klein, J. and Gutze, E., "Major Histocompatibility Complex", Springer Verlag, New York, 1977; Unanue, E. R., Ann. Rev. Immunology, 2:295-428, (1984)). MHC Class I and Class II molecules have been the focus of much study with respect to research in autoimmune diseases because of their roles as mediators or initiators of immune response. MHC Class II antigens have been the primary focus of research in the etiology of autoimmune diseases, whereas MHC Class I antigens have historically been the focus of research in transplantation rejection. ... Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that, like Graves' disease, has a relatively high rate of occurrence. SLE affects predominantly women, the incidence being 1 in 700 among women between the ages of 20 and 60 (Abbus, A. K., Lichtman, A. H., Pober, J. S. (eds), "Cellular and Molecular Immunology", W.B. Saunders Company, Philadelphia, 1991, pp. 360-370). SLE is characterized by the formation of a variety of autoantibodies and by 20 multiple organ system involvement (Stites and Terr, ibid, pp. 438-443). Current therapies for treating SLE involve the use of corticosteroids and cytotoxic drugs, such as cyclophosphamide. Immunosuppressive drugs, such as cyclosporin, FK506 or rapamycin suppress the immune system by reducing T cell numbers and function (Morris, P. J., Curr. Opin. in Immun., 3:748-751 (1991)). While these immunosuppressive therapies alleviate the symptoms of SLE and other autoimmune diseases, they have numerous severe side effects. In fact, extended therapy with these agents may cause greater morbidity than the underlying disease. A link between MHC Class I expression and SLE in animal models has been established. Thus, Class I deficient mice do not develop SLE in the 16/6 ID model (Mozes, et al., Science 261: 91-93 (1993)).

Web site: http://www.delphion.com/details?pn=US06365616__

- **Methods of treating autoimmune diseases with a CD86-specific immunotoxin**

  Inventor(s): De Boer; Mark (Heemskerk, NL), De Gast; G. C. (Utrecht, NL)

  Assignee(s): Innogenetics N.V. (NL)

  Patent Number: 6,346,248

  Date filed: August 12, 1999

  Abstract: A method for treating autoimmune diseases comprising administering to a patient in need of such treatment a therapeutically effective amount of an immunotoxin comprising an anti-human CD86 monoclonal antibody IG10H6D10 as deposited in the ECACC collection under No. 95060210 or a humanized antibody, a single-chain antibody or fragments and specificity of said monoclonal antibody, coupled to a toxin or active fragments thereof wherein the binding of the immunotoxin to CD86 results in the killing of the CD86 expressing cell.

  Excerpt(s): This invention relates to compositions and methods of treating diseases of the immune system. In particular, this invention relates to methods of preventing allograft rejection and methods of treating autoimmune diseases and various malignancies of lymphoid origin. ... The role of the CD80/CD86-CD28 interaction in the chronic activation state of T cells, which have been implicated in autoimmune diseases, has been strongly suggested in various studies. Using immunohistochemical techniques, strong CD80 expression has been found in lesions of autoimmune diseases, such as rheumatoid arthritis and psoriasis. Furthermore, it has been demonstrated that blocking CD80/CD86-CD28 interaction could block autoantibody production and prolongation of life in a murine model of autoimmune disease that closely resembles systemic lupus erythematosus in humans (Finck et al., Science 265:1225 (1994)). ... The problem posed in the present invention may be formulated as providing an alternative method for treating or preventing diseases of the immune system, more particularly for treating or preventing allograft rejection, autoimmune diseases and various malignancies of lymphoid origin.

  Web site: http://www.delphion.com/details?pn=US06346248__

- **Use of recombinant myelin protein for treating T-cell-mediated autoimmune diseases of the peripheral nervous system**

  Inventor(s): Gold; Ralf (Neurologisch Klinik und Polyklinik im Kopfklinikum, Josef-Schneider-Strasse, Wurzburg, DE), Weishaupt; Andreas (Neurologisch Klinik und Polyklinik im Kopfklinikum, Josef-Schneider-Strasse, Wurzburg, DE)

  Assignee(s): none reported

  Patent Number: 6,319,892

  Date filed: March 15, 1999

  Abstract: The present invention relates to the use of recombinant myelin protein for treating T cell-mediated autoimmune diseases of the peripheral nervous system.

  Excerpt(s): This invention relates to the use of recombinant myelin protein for treating T cell-mediated autoimmune diseases of the peripheral nervous system. ... Therefore, it is the object of the present invention to provide a successful and careful method for treating T cell-mediated autoimmune diseases of the peripheral nervous system. ... The presence of neuritic molecules in myelin was proved for the first time by the induction of experimental autoimmune neuritis (EAN) in an animal model where rodents were immunized with homogenates of peripheral nerve tissue (Waksman et al., J. Exp. Med. 102, 213-235 (1955)) or purified P2 protein (Brostoff et al., Nature (New Biol.) 235, 210-217 (1972)). In this animal model for disease of the peripheral nervous system, the immune system is disregulated and autoaggressive T lymphocytes are produced which are specific for structural proteins of the myelin of the peripheral nervous system and result in demyelinization and in inflammation in the peripheral nervous system. This animal model stands in place for the above-mentioned autoimmune diseases of the peripheral nervous system in which an increased T cell number, demyelinization and neuritides occur as well.

  Web site: http://www.delphion.com/details?pn=US06319892__

- **Use of magnesium based products for the treatment or prophylaxis of autoimmune diseases**

  Inventor(s): Valletta; Giampiero (No. 188, Via Campidoglio, 03024 Ceprano (FR)

  Assignee(s): none reported

  Patent Number: 6,248,368

  Date filed: November 21, 1996

  Abstract: Pharmaceutically acceptable compositions suitable for releasing magnesium ions to an organism, such as organic or inorganic magnesium salts or complexes thereof, are used to prevent and to treat neoplastic and autoimmune diseases, whose origin can be attributed to magnesium depletion. For the new therapeutic indications the magnesium based product, preferably magnesium pyrophosphate, is usually administered orally or parenterally, preferably in association with vitamin B.sub.6.

  Excerpt(s): This invention relates to the use of magnesium containing products for the therapy and the prophylaxis of neoplastic and autoimmune diseases. More specifically, this invention relates to the use of magnesium, in the form of magnesium salts or complexes, or in any other form suitable for releasing Mg.sup.++ ions, for the production of drugs to be administered against neoplastic or autoimmune diseases, both for prophylaxis and for therapy purposes. ... According to the current medical opinion, the administration of magnesium would promote the growth of established solid tumours and generally the worsening of autoimmune diseases (see, e.g., J. Durlach, p. 215-216, cited above). Such opinion is based on the finding that erythrocytic magnesium increases when a tumour is under development or when a chronic disease, such as for example hepatic cirrhosis, shows a malignant degeneration, or when an autoimmune disease shows a recrudescence. Furthermore, the erythrocytic magnesium level would decrease when these diseases are under remission. ... Accordingly, the conventional therapies use immunosupressants to treat autoimmune diseases and antineoplastic chemotherapy agents to treat tumoral diseases, i.e. they use drugs aimed at reducing the cell mitotic activity in so far as it is more accelerated. These drugs actually slow down the cell metabolism (thus acting more on the affected cells than on the healthy cells), but they also cause a drastic magnesium depletion throughout the organism.

  Web site: http://www.delphion.com/details?pn=US06248368__

- **Monitoring and/or prognostic of antibody-mediated autoimmune diseases**

  Inventor(s): Newkirk; Marianna M. (Pierrefonds, CA)

  Assignee(s): McGill University (Montreal, CA)

  Patent Number: 6,197,596

  Date filed: December 3, 1998

  Abstract: The present invention relates to a method to determine antibody-mediated autoimmune diseases in a patient, which comprises the steps of: a) determining the amount of clusterin present in a serum, saliva or tissue sample of the patient with an anti-clusterin antibody; b) comparing the amount of clusterin in step a) with normal serum, saliva or tissue sample, wherein a lower than normal amount is indicative of active antibody-mediated autoimmune disease.

  Excerpt(s): The invention relates to the monitoring and/or prognostic of antibody-mediated autoimmune diseases, and treatments thereof. ... It would be highly desirable to be provided with means to monitor antibody-mediated autoimmune diseases. ... One aim of the present invention is to provide means to monitor antibody-mediated autoimmune diseases.

  Web site: http://www.delphion.com/details?pn=US06197596__

- **Characterization and detection of sequences associated with autoimmune diseases**

  Inventor(s): Erlich; Henry A. (Oakland, CA), Horn; Glenn T. (Emeryville, CA)

  Assignee(s): Roche Molecular Systems, Inc. (Pleasanton, CA)

  Patent Number: 6,194,561

  Date filed: November 17, 1987

  Abstract: DNA sequences and corresponding amino acid sequences from the HLA class II beta region of the human genome that are associated with insulin-dependent diabetes mellitus (IDDM) and Pemphigus vulgaris (PV) have been identified. Specifically, marker DNA sequences which detect either directly or indirectly the identity of the codon encoding for the amino acid at position 57 of the DQ.beta. protein sequence are disclosed as well as sequences from the DR.beta. region. These sequences may be used to generate DNA hybridization probes and antibodies for assays to detect a person's susceptibility to autoimmune

diseases, such as IDDM and PV. Such antibodies and peptides encoded by said DNA sequences can be used therapeutically or prophylactically.

Excerpt(s): This invention relates to HLA class II beta genes and proteins associated with autoimmune diseases and methods for their diagnostic detection. Specifically, the autoimmune diseases on which this invention focuses are insulin-dependent diabetes mellitus (IDDM) and Pemphigus vulgaris (PV). ... There is a need in the art for subdivision of the serologic markers HLA DR3, DR4 and DRw6 to obtain more informative and more precisely defined markers for susceptibility to the autoimmune diseases IDDM and PV. Further, there is a need in the art to identify susceptibility conferring haplotypes which are neither DR3, DR4 nor DRw6. ... Susceptibility to other autoimmune diseases may also be related to codon 57 polymorphism. The DRw6 susceptibility to Pemphigus vulgaris is associated with a rare DQ.beta. allele (DQB1.3) which differs from the non-susceptible alleles DQB1.2 and DQB1.1 only by a charge variation at position 57 and is correlated with the Dw9 DRw6 subtype. Similarly, a DP.beta. allele found thus far only in celiac disease patients differs from an allele found in a homozygous typing cell (HTC) by an Ala-Asp substitution at position 57 (Bugawan et al., unpublished). [Celiac disease is a digestive disorder characterized by a malabsorption syndrome affecting both children and adults precipitated by the ingestion of gluten-containing foods; its etiology is unknown but a hereditary factor has been implicated.]Described in Example III is the sequencing of the polymorphic second exon of the DRs1, DR.beta.II and DQ.beta. loci from three PV patients to discern any possible disease association with specific polymorphic class II epitopes. In the DQ.beta. loci, 3 of 4 DR4 haplotypes contained the DQB3.2 allelic sequence variant present on 60-80% of control DR4 haplotypes, and one of the four DR4 haplotypes contained the DQB3.1 allele, present on about 20-40% of control DR4 haplotypes [Erlich, et al., in Schacter et al. (eds): The Molecular Analysis of Histocompatibility Antigens, pp. 93-109 (1987); Arnheim et al., PNAS (USA), (1985) 82:6970-6974; Kim et al., PNAS (USA), (1985) 82:8139-8143]. The two DR5 haplotypes also contained the DQB3.1 allelic sequence variant present on all control DR5 haplotypes. Thus, the distribution of DQ.beta. alleles was essentially the same in patients, and in DR-matched controls. In this small sample, all three patients were DQB3.1/DQB3.2 heterozygotes.

Web site: http://www.delphion.com/details?pn=US06194561__

- **Methods for determining genetic predisposition to autoimmune diseases by genotyping apoptotic genes**

  Inventor(s): Jacob; Chaim O. (2110 Beverwil Dr., Los Angeles, CA 90034)

  Assignee(s): none reported

  Patent Number: 6,162,604

  Date filed: April 1, 1999

  Abstract: Genetic markers associated with programmed cell death were characterized and their extent of polymorphism in normal populations was determined allowing for a method for determining genetic predisposition to SLE and other autoimmune diseases by genotyping. The allelic distribution of these gene markers in a large Mexican American SLE cohort and ethnically matched controls was determined. The results were that bcl-2, Fas-L, and IL-10 loci showed significantly different allelic distribution in SLE patients compared with controls, indicating an association between these gens and SLE. The method allows for determining the presence of these alleles. Alone, the presence of each of these alleles is associated with a moderate increase in SLE risk, while the occurrence of these alles together increases the odds of developing SLE by more than 40-fold.

  Excerpt(s): This invention relates generally to methods for determining predisposition to systemic lupus erythematosus (SLE) and other autoimmune diseases by genotyping IL-10, bcl-2, FAS ligand (FAS-L) and other apoptotic genes. More specifically, the bcl-2, Fas-L, and IL-10 loci showed significantly different allelic distribution in SLE patients compared with controls, indicating an association between these genes and SLE. Additionally, further analysis revealed a synergistic effect between susceptibility alleles of the bcl-2 and IL-10 genes in determining disease susceptibility. ... Systemic lupus erythematosus (SLE) is considered to be the prototype of human autoimmune diseases. It is a disorder of generalized autoimmunity characterized by multisystem organ involvement, polyclonal B cell activation, and the production of autoantibodies against nuclear, cytoplasmic, and cell surface antigens. Autoreactive B and T lymphocytes can be found in healthy individuals as well, but their numbers are tightly regulated by a process of programmed cell death (apoptosis), which is crucial in the establishment of self-tolerance. Tolerance to self antigens can fail and can result in autoimmunity if there is a defect in the process of elimination of these cells. ... Several lines of evidence suggest that dysfunctional programmed cell death (apoptosis) might be involved in the pathogenesis of SLE and other autoimmune diseases. It has been postulated that in SLE, dysfunction of apoptosis could result in the inappropriate longevity of

autoreactive B lymphocytes, allowing autoantibody levels to reach pathogenic thresholds and breakdown of self tolerance. Defective apoptosis of autoreactive lymphocytes is an attractive mechanism contributing to SLE, primarily because defects in either the apoptosis-promoting Fas gene or its ligand Fas-L (CD95L) accelerates autoimmunity in mouse strains (MRL-lpr/lpr and C3H-gld/gld, respectively) that exhibit SLE-like diseases. Furthermore, studies reveal links between autoimmunity and several other gene products involved in apoptosis. The bcl-2 gene enhances lymphocyte survival by inhibiting or delaying apoptosis. Transgenic mice overexpressing bcl-2 in their B cells show polyclonal B cell expansion and extended survival in vitro. After a few months, these mice developed an autoimmune syndrome resembling SLE.

Web site: http://www.delphion.com/details?pn=US06162604__

- **Means for treating autoimmune diseases and method for the treatment thereof**

  Inventor(s): Golovistikov; Ivan Nikolaevich (Donbasskaya str, 5, ap. 51, Moscow, RU), Kacharava; Leonid Yazonovich (Mirtskhulava str, 2, ap. 45, Tbilici, GE), Tatarinov; Jury Semyonovich (Moscow, RU), Alikhanov; Khallar Abdumuslimovich (Moscow, RU)

  Assignee(s): Kacharava; Leonid Yazonovich (Tbilici, GE), Golovistikov; Ivan Nikolaevich (Moscow, RU)

  Patent Number: 6,150,326

  Date filed: November 15, 1996

  Abstract: Trophoblastic .beta.-I-glycoprotein (TBG) is used as a means for treating autoimmune diseases showing suppressors immunodeficit.A method of treating of autoimmune diseases comprises the administration of an immune correcting preparation, said preparation being trophoblastic .beta.-I-glycoprotein (TBG), indications with respect to said preparation being determined by testing TBG sensitivity of mononuclear cells (MNCs).

  Excerpt(s): The present invention relates to medicine, more specifically to the use of immune correcting preparations for the treatment of autoimmune diseases. ... Nevertheless the known compound has not been used as a means for treating of autoimmune diseases. ... Nevertheless said work does not disclose the possibility of using TBG for diagnosing a suppressor component and treating autoimmune diseases.

  Web site: http://www.delphion.com/details?pn=US06150326__

- **Therapeutic treatment for autoimmune diseases**

  Inventor(s): Ways; Douglas Kirk (Indianapolis, IN), Wierda; Daniel (Greenfield, IN)

  Assignee(s): Eli Lilly and Company (Indianapolis, IN)

  Patent Number: 6,103,713

  Date filed: February 22, 1999

  Abstract: Methods for inhibiting activation and/or proliferation of T cells and B cells and for treating autoimmune diseases and/or disease manifestations are disclosed, particularly using the isozyme selective PKC inhibitor, (S)-3,4-[N, N'-1,1'-((2"-ethoxy)-3'"(O)-4'"-(N,N-dimethylamino)-butane)-bis-(3,3'-indo ly 1)]-1(H)-pyrrole-2,5-dione and its pharmaceutically acceptable salts.

  Excerpt(s): The present invention is broadly directed to methods for inhibiting T cell or B cell activation, proliferation, and differentiation, especially activation, proliferation, and differentiation events associated with autoimmune diseases, and for inhibiting production of autoimmune antibodies. The present invention is particularly directed to the use of a particular class of isozyme selective Protein Kinase C (PKC) inhibitors for treating autoimmune diseases and disorders accompanied by undesired T cell or B cell reactivity. ... Studies have shown that mouse B-1 B lymphocytes produce many of IgM autoimmune and anti-idiotype antibodies such as cold hemagglutinins, cytosketelal antibodies, and rheumatoid factor (Hayakawa et al., 1984, Proc. Natl. Acad. Sci. U.S.A. 81:2494; Herzenberg et al., 198, Immunological. Rev. 93:81). It has been demonstrated that overexpression of B-1 B lymphocytes in preclinical models such as the New Zealand Black (NZB) and motheaten viable mice strains is associated with autoimmune diseases (Hayakawa et al., 1983, J. Exp. Med. 161:1554; Herzenberg et al., 1986, Immunological. Rev. 93:81). Human B cells corresponding to the mouse B-1 B lymphocyte have also been implicated in the production of a variety of human autoimmune antibodies (Plater-Zyberk et al., 1985. Arth. Rheum. 28: 971). Thus, overexpression or activation of B-1 B lymphocyte-like cells is associated with disease states related to overproduction of IgM and certain autoimmune disorders. ... Presently available treatments for autoimmune diseases and disorders are scarce and not completely effective. There remains a need in the art to develop more ways to treat autoimmune diseases.

  Web site: http://www.delphion.com/details?pn=US06103713__

- **Interleukin-2 stimulated T lymphocyte cell death for the treatment of autoimmune diseases, allergic responses, and graft rejection**

  Inventor(s): Lenardo; Michael J. (Potomac, MD)

  Assignee(s): The United States of America as represented by the Department of Health (Washington, DC)

  Patent Number: 6,083,503

  Date filed: September 15, 1993

  Abstract: A method for the treatment or prevention of autoimmune diseases, allergic or atopic disorders, and graft rejection is provided, comprising inducing the death by apoptosis of a subpopulation of T lymphocytes that is capable of causing such diseases, while leaving substantially unaffected the majority of other T lymphocytes. Cell death is achieved by cycle(s) comprising challenging via immunization these T cells with antigenic substance at short time intervals, or by immunization followed by administering interleukin-2 (IL-2) when these T cells are expressing high levels of IL-2 receptor so as to cause these T cells to undergo apoptosis upon re-immunization with the antigenic peptide or protein. These methods are applicable to the treatment of autoimmune diseases such as, for example, multiple sclerosis, uveitis, arthritis, Type I insulin-dependent diabetes, Hashimoto's thyroiditis, Grave's thyroiditis, autoimmune myocarditis, etc., allergic disorders such as hay fever, extrinsic asthma, or insect bite and sting allergies, food and drug allergies, as well as for the treatment or prevention of graft rejection.

  Excerpt(s): The present invention relates to the treatment and prevention of diseases that are primarily due to T cell immune responses. In particular, it relates to the suppression or elimination of certain autoimmune diseases, graft rejection, and allergic disorders by treatment with interleukin-2 (IL-2) and the specific antigen involved, thus allowing the killing of the subpopulation of T cells that recognizes this specific antigen. In this manner, IL-2 pretreatment sensitizes T cells to undergo programmed cell death following T cell receptor engagement. ... First, there is an emerging set of findings that show that infusion of peptides derived from antigens involved in autoimmune diseases leads to the lessening of severity of such diseases (cf. 73). A variety of studies of the autoimmune disease experimental allergic encephalitis (EAE) shows that it is caused by the activation of T cells by immunization with myelin basic protein (MBP). Interestingly, infusion of peptides derived from the MBP sequence that stimulate the T cells that generate the disease are effective at blocking the disease (60). The discovery disclosed herein provides an explanation for these seemingly paradoxical observations, which is that the T cells are activated and stimulated by IL-2 during

peptide infusion, and then undergo apoptosis when they are re-stimulated by the MBP antigen. Human diseases that have been associated with T cell activation by peptide antigens include multiple sclerosis and autoimmune uveitis (67; 69; 107). It is envisioned that these diseases, and, for example, systemic lupus erythematosus, systemic vasculitis, polymyositis-dermatomyositis, systemic sclerosis (scleroderma), Sjogren's Syndrome, ankylosing spondylitis and related spondyloarthropathies, rheumatic fever, hypersensitivity pneumonitis, allergic bronchopulmonary aspergillosis, inorganic dust pneumoconioses, sarcoidosis, autoimmune hemolytic anemia, immunological platelet disorders, cryopathies such as cryofibrinogenemia, autoimmune polyendocrinopathies, and myasthenia gravis can be approached by therapy which can now be modulated in a rationale way using IL-2 and the relevant peptide to cause apoptosis of the T cells responsible for the disease. The appropriate timing of IL-2 infusion or a repetitive immunization schedule could substantially augment the protective effect of the infused peptides. ... The discovery that interleukin-2 (IL-2) predisposes T lymphocytes to programmed cell death, or apoptosis, allows for a novel method of therapeutic intervention in disease processes in humans and animals primarily caused by the action of T cells (30). In essence, this involves specifically inducing the death of a subpopulation of T lymphocytes that are capable of causing disease, while leaving the majority of T lymphocytes substantially unaffected. This method of intervention contrasts with, and is potentially far superior to, currently used therapeutic methods that cause a general suppression or death of T lymphocytes. Examples of widely-used general immunosuppressive agents are corticosteroids, such as prednisone, which are used to treat autoimmune diseases and allergic conditions, and cyclosporin A, which is used for treating graft rejection (31). These treatments suffer from the drawback of severely compromising immune defenses, leaving the patient vulnerable to infectious diseases. The two key elements of the present process are that: i) only the subset of T cells that reacts with antigens that cause the disease are affected by the treatment; and ii) the T cells affected by the treatment are killed, i.e., they are permanently removed from the repertoire.

Web site: http://www.delphion.com/details?pn=US06083503__

- **Peptides and therapeutic agent for autoimmune diseases containing the same**

  Inventor(s): Yamagata; Nobuyuki (Kawagoe, JP), Ogata; Kenji (Otawara, JP), Wagatsuma; Masako (Higashimurayama, JP), Takanashi; Hitoshi (Tokorozawa, JP)

  Assignee(s): Hoechst Pharmaceuticals & Chemicals K.K. (Tokyo, JP)

  Patent Number: 6,034,064

  Date filed: January 8, 1998

  Abstract: The present invention relates to a peptide having the following amino acid sequence:Ala-Xaa1-Leu-Xaa2-Phe-Xaa3-Xaa4-Xaa5-(Xaa6)n(wherein Xaa1 and Xaa4 each independently represents an amino acid residue which may have an alkyl or heteroalkyl side chain which may be substituted by a hydroxy, amino or guanidyl group;Xaa2 and Xaa6 each independently represents an amino acid residue which may have an alkyl or heteroalkyl side chain which may be substituted by a hydroxyl group;Xaa3 and Xaa5 each independently represents an amino acid residue which may have a hydrophobic side chain; andn stands for 1 or 0), or derivatives thereof; and a modification thereof.The peptide or derivatives thereof according to the present invention is useful as a pharmaceutical composition for the prevention and treatment of autoimmune diseases, rejection reaction attendant on the organ transplantation, inflammation or the like.

  Excerpt(s): The present invention relates to peptides or derivatives thereof. The peptides or derivatives thereof according to the present invention are useful for the antigen non-specific suppressive treatment of abnormally augmented immunoreaction in autoimmune diseases. Having an anti-inflammatory effect, it is also useful for the treatment of the inflammation. ... Autoimmune diseases are induced by the continuous production of an antibody or lymphocyte which reacts with a component of the own tissue. In the autoimmune diseases, described specifically, the break-down of immunologic tolerance heightens immune response to own organic components, which causes the reaction between an autoantibody or autoreactive T cell so produced and an autoantigen or cell corresponding thereto, thereby causing cellular dysfunction or tissue damages. At present, 50 or more types of autoimmune diseases are known and according to the spreading degree of a lesion over the organs, they can be classified into organ specific autoimmune diseases and organ nonspecific autoimmune diseases. ... For the treatment of autoimmune diseases, it is the common practice to administer an immunosuppressant typified by a gluco-steroid preparation, cyclosporin A or FK 506. The treatment using such a preparation is, however, accompanied by the

drawback such as serious side effects, for example, infectious diseases, nephrotoxicity of the drug itself or carcinogenesis, which result from wide spectrum of immunosuppression [Sadao Kashiwazaki, Sogo Rinsho, 43 (9), 1725-1729 (1994)].

Web site: http://www.delphion.com/details?pn=US06034064__

- **12-kDa protein derived from M. Tuberculosis useful for treatment of autoimmune diseases**

  Inventor(s): Ben-Nun; Avraham (Yavne, IL)

  Assignee(s): Yeda Research and Development Co., Ltd. (Rehovot, IL)

  Patent Number: 5,976,543

  Date filed: August 1, 1997

  Abstract: Disclosed is a 12-kDa PPD protein isolated and purified from the purified protein derivative, the major fraction of Mycobacterium tuberculosis that protects mice against the induction of experimental autoimmune encephalomyelitis (EAE), and salts, functional derivatives, analogs and active fractions thereof, and pharmaceutical compositions comprising them for the treatment of autoimmune diseases.

  Excerpt(s): The present invention relates to agents that may be used for the treatment of autoimmune diseases, and more particularly to a protein having a molecular weight of about 12-kDa isolated and purified from the purified protein derivative (PPD), the major fraction of Mycobacterium tuberculosis (Mt) that protects mice against the induction of experimental autoimmune encephalomyelitis (EAE), and to salts, functional derivatives, analogs and active fractions thereof. ... Increasing evidence suggests that infectious agents can affect the development of autoimmune diseases. Viruses have been most often implicated in the etiology of autoimmune diseases, although bacteria may also be involved: streptococcal infection may lead to rheumatic fever and myocarditis, Mycoplasma arthriditis or its toxins can cause arthritis in mice or rats, and arthritis has also been associated with reactivity to mycobacterial antigens, both in humans and rats. However, several reports indicate that viruses and bacteria may also enhance the natural propensity of mice to become resistant to an autoimmune disease. Thus, non-obese diabetic mice infected with lymphocytic choriomeningitis virus become resistant to the development of insulin-dependent diabetes mellitus, and mice infected with lactic dehydrogenase virus are refractory to the development of experimental autoimmune encephalomyelitis (EAE). Similarly, bacteria may also be involved in conferring resistance to autoimmune diseases, as demonstrated in a previous study by the

present inventor (Lehman and Ben-Nun, 1992). ... It should be noted that EAE is the well established and widely accepted animal model for studying the effects of various agents which may be implicated in human autoimmune diseases in general, and particularly multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, insulin-dependent diabetes mellitus and graft-versus-host disease. Thus, an agent found to be capable of eliciting a protective effect against EAE in animals such as mice or rats, is also considered to be an agent capable of eliciting protection against autoimmune diseases in humans.

Web site: http://www.delphion.com/details?pn=US05976543__

- **Methods of treating autoimmune diseases and transplantation rejection**

  Inventor(s): Singer; Dinah S. (6404 Ruffin Rd., Chevy Chase, MD 20815), Kohn; Leonard (9630 Parkwood Dr., Bethesda, MD 20814), Mozes; Edna (51 Hanachi Harishon, Rehovot, IL), Saji; Motoyasu (10228 Rockville Pike, Rockville, MD 20852), Weissman; Jocelyn (3411 Janet Rd., Silver Spring, MD 20906), Napolitano; Giorgio (11315 Commonwealth Dr., Rockville, MD 20852), Ledley; Fred D. (4911 Braesvalley, Houston, TX 77096)

  Assignee(s): none reported

  Patent Number: 5,871,950

  Date filed: June 5, 1995

  Abstract: The present invention provides methods for treating autoimmune diseases in mammals and for preventing or treating transplantation rejection in a transplant recipient. The methods of treatment involve the use of drugs capable of suppressing expression of MHC Class I molecules. In particular the use of the drug methimazole to suppress expression of MHC Class I molecules in the treatment of autoimmune diseases and the prevention or treatment of rejection in a transplant recipient is disclosed. In addition in vivo and in vitro assays are provided for the assessment and development of drugs capable of suppressing MHC Class I molecules.

  Excerpt(s): This invention is in the field of treatment of autoimmune diseases and transplantation rejection in a mammal. More specifically, this invention relates to methods for treating and preventing these diseases using drugs capable of suppressing expression of the major histocompatibility complex (MHC) Class I molecules and to methods for the development or assessment of drugs that are capable of suppressing MHC Class I expression. ... Antigens are presented to the immune system in the context of Class I or Class II cell surface molecules; CD4.sup.+ helper T-lymphocytes recognize antigens in association with Class II

MHC molecules, and CD8.sup.+ cytotoxic lymphocytes (CTL) recognize antigens in association with Class I gene products. It is currently believed that MHC Class I molecules function primarily as the targets of the cellular immune response, whereas the Class II molecules regulate both the humoral and cellular immune response (Klein, J. and Gutze, E., (1977) "Major Histocompatibility Complex" Springer Verlag, N.Y.; Roitt, I. M. (1984) Triangle, (Engl Ed) 23:67-76; Unanue, E. R. (1984) Ann. Rev. Immunology, 2:295-428). MHC Class I and Class II molecules have been the focus of much study with respect to research in autoimmune diseases because of their roles as mediators or initiators of the immune response. MHC-Class II antigens have been the primary focus of research in the etiology of autoimmune diseases, whereas MHC-Class I has historically been the focus of research in transplantation rejection. ... Saji, M. et al. (1992a); Proc. Natl. Acad. Sci. U.S.A. 89:1944-1948 describe hormonal regulation of MHC-class I genes in the rat thyroid cell line, FRTL-5. Treatment of the FRTL-5 cell line with thyroid stimulating hormone (TSH) resulted in decreased transcription of MHC class I DNA and reduced cell surface levels of MHC Class I antigens. Recently, a report by Saji, M. et al., (1992b) J. Clin. Endocrinol. Metab. 75:871-878, demonstrated that agents such as serum, insulin, insulin-like growth factor-I (IGF-1), hydrocortisone and thyroid stimulating thyrotropin receptor autoantibodies from Graves' patients decrease MHC-Class I gene expression in that FRTL-5 cells. In addition, treatment of the FRTL-5 cells with MMI or high doses of iodide resulted in decreased MHC Class I gene expression. The effect of MMI on reduction of MHC Class I expression was shown to be at the level of transcription and was additive with thyroid stimulating hormone and other hormones which normally suppress Class I in these cells. Saji, M. et al. (1992b) J. Clin. Endocrinol. Metab. 75:871-878, suggest a new mechanism by which MMI may act in the thyroid during treatment of Graves' disease; no extrapolation was made to any other autoimmune diseases. Prior to these studies it was known that Rous sarcoma virus, adenoviruses 12 and 2 and certain Gross viruses reduced expression of MHC Class I; however, SV40, Rad LV, and Mo MuLV viruses can increase Class I MHC expression (Singer & Maguire (1990) Crit. Rev. in Immun. 10:235-257).

Web site: http://www.delphion.com/details?pn=US05871950__

- **Pharmaceutical compositions for the treatment of autoimmune diseases comprising the B-oligomer of pertussis toxin or its subunits**

  Inventor(s): Ben-Nun; Avraham (Yavne, IL)

  Assignee(s): Yeda Research and Development Co. Ltd. (Rehovot, IL)

  Patent Number: 5,858,965

  Date filed: July 30, 1997

  Abstract: The invention provides the use of a protein selected from the B-oligomer of pertussis toxin, an individual subunit S2, S3, S4 or S5 thereof, or a combination of the subunits, for the preparation of pharmaceutical compositions comprising them for the treatment of autoimmune diseases.

  Excerpt(s): The present invention is generally in the field of agents that may be used for the treatment of autoimmune diseases, and more particularly relates to pharmaceutical compositions comprising the B-oligomer of pertussis toxin or one of its subunits S2, S3, S4 or S5, or combinations thereof, useful for protection against autoimmune diseases. ... The development of experimental autoimmune encephalomyelitis (EAE), as well as other autoimmune diseases in experimental animals, can be facilitated by injecting Bordetella pertussis concomitantly with inoculation of the autoantigen (Bernard et al., 1992). EAE is a neurological autoimmune disease which can be induced in experimental animals by a single injection of central nervous system (CNS) tissue homogenate or purified myelin antigens such as myelin basic protein (MBP) or proteolipid protein (PLP) in complete Freund's adjuvant (CFA) (Tabira and Kira, 1992). The clinical and pathological features of EAE are reminiscent of multiple sclerosis , and EAE is a well-accepted model for multiple sclerosis. In mice,. consistent elicitation of EAE was shows to be facilitated by administration of B. pertussis at the time of the encephalitogenic challenge (Munoz, 1985). Pertussis toxin (PT) was shown later to be the component of B. pertussis responsible for facilitating disease development, and it is now routinely used in place of B. pertussis for enhancement of autoimmune disease in experimental animals (Munoz, 1995). ... It has now been found in accordance with the present invention that the B-oligomer of pertussis toxin or a subunit S2, S3, S4 or S5 thereof, are able to block the development of EAE in mice. Since EAE is a well-established and widely accepted animal model for the study of autoimmune diseases, these findings indicate that the B-oligomer of pertussis toxin or a subunit S2, S3, S4 or S5 thereof, will be useful for the protection against autoimmune diseases in humans.

  Web site: http://www.delphion.com/details?pn=US05858965__

Patent Applications on Autoimmune Diseases

As of December 2000, U.S. patent applications are open to public viewing.[25] Applications are patent requests which have yet to be granted (the process to achieve a patent can take several years). The following patent applications have been filed since December 2000 relating to autoimmune diseases:

- **Antigen-based heteropolymers and method for treating autoimmune diseases using the same**

  Inventor(s): Taylor, Ronald P.; (Charlottesville, VA), Ferguson, Polly J.; (Charlottesville, VA), Martin, Edward N.; (Charlottesville, VA), Sutherland, William S.; (Charlottesville, VA), Reist, Craig J.; (Charlottesville, VA), Greene, Kirsten; (Charlottesville, VA), Johnson, Cyd; (Charlottesville, VA)

  Correspondence: Pennie and Edmonds; 1155 Avenue of the Americas; New York; NY; 100362711

  Patent Application Number: 20020103343

  Date filed: October 26, 2001

  Abstract: Constructs consisting of antigen-based heteropolymers (AHP's) are provided. The antigen-based heteropolymers comprise at least one monoclonal antibody specific for binding to complement receptor (CR1) site on a human or non-human primate erythrocyte, and the anti-CR1 monoclonal antibody is crosslinked to an antigen specific for a target pathogenic autoantibody. Further provided is a method for treating autoimmune diseases in human or non-human primates using the AHP.

  Excerpt(s): The present invention relates to antigen-based heteropolymers specific for both a specific receptor site on a primate erythrocyte and a target pathogenic autoantibody. The present invention further relates to methods for treating autoimmune diseases using these antigen-based heteropolymers. ... Circulating autoantibodies are responsible for much of the pathogenesis associated with a number of autoimmune diseases including, but not limited to, systemic lupus erythematosus (SLE), autoimmune myocarditis, immune complex mediated kidney disease, rheumatoid arthritis, myasthenia gravis, autoimmune anemias, Sjogren's Syndrome, idiopathic thrombocytopenic purpura, various forms of vasculitis, and at least some of the cellular cytotoxicity accompanying Acquired Immune Deficiency Syndrome (AIDS). ... Another general, non-specific approach involves aggressive immunosuppressive therapy with corticosteroids, and cytotoxic and nonsteroidal anti-inflammatory drugs.

[25] This has been a common practice outside the United States prior to December 2000.

Although in many instances clinical improvements have been obtained, there continues to be significant morbidity and mortality in autoimmune diseases despite these medications.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory antibody combination**

  Inventor(s): Hanna, Nabil ; (Rancho Santa Fe, CA)

  Correspondence: Pillsbury Winthrop LLP; 1600 Tysons Boulevard; Mclean; VA; 22102; US

  Patent Application Number: 20020058029

  Date filed: September 18, 2001

  Abstract: The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory antibody, e.g. an anti-B7.1 or anti-B7.2 or anti-CD40L antibody and at least one B cell depleting antibody, such as CD19, CD20, CD22, CD23, or CD37, wherein such antibodies may be administered separately, or in combination, and in either order, over prolonged periods of time.

  Excerpt(s): This application is related to and claims priority from U.S. Provisional application Ser. No. 60/233,607, filed Sep. 18, 2000, entitled "Combination Therapy for Treatment of Autoimmune Diseases Comprising CD40L Antagonist and Antibodies to B7, CD19, CD20, CD22 or CD23," in the name of Nabil Hanna; and U.S. Provisional application Ser. No. 601257,147, filed Dec. 22, 2000, entitled "Combination Therapy for Treatment of Autoimmune Diseases Using B Cell Depleting/Immunoregulatory Antibody Combination" in the name of Nabil Hanna. ... The present invention provides a novel combination therapy for treatment of autoimmune diseases. Particularly, the invention relates to the combined usage of an immunoregulatory antibody, preferably an antibody that modulates T and/or B cell differentiation, proliferation and/or function and a B cell depleting antibody for autoimmune disease therapy. These antibodies may be administered separately or in combination, and in either order. ... Recently, the use of antibodies for treatment of diseases including cancers, especially non-Hodgkin's lymphoma, leukemias, viral mediated diseases, and autoimmune diseases has gained wide acceptance. In particular, the use of anti-CD20 or anti-CD22 antibodies that possess cell depleting activity for treatment of cancers, e.g., non-Hodgkin's lymphoma and related B cell lymphomas has been reported. Also, the use of B cell depleting antibodies specific to CD19 and CD37 has been reported, among others.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Treatment of B-cell associated diseases such as malignances and autoimmune diseases using a cold anti-CD20 antibody/radiolabeled anti-CD22 antibody combination**

  Inventor(s): White, Christine ; (Rancho Santa Fe, CA)

  Correspondence: Pillsbury Winthrop LLP; 1600 Tysons Boulevard; Mclean; VA; 22102; US

  Patent Application Number: 20020039557

  Date filed: June 20, 2001

  Abstract: Treatment of B-cell associated diseases including autoimmune and B-cell malignancies such as leukemias, lymphomas, using the combination of an anti-CD20 antibody, preferably RITUXAN.RTM. and a radiolabeled anti-CD22 antibody, preferably an .sup.90Y labeled humanized anti-CD22 antibody, is described. These therapeutic regimens provide for enhanced depletion of B cells, and therefore reduce the risk in B cell malignancy treatment of relapse associated with RITUXAN.RTM. and, moreover, provide for prolonged immunosuppression of B-cell immune responses, especially in the context of autoimmune diseases and transplant.

  Excerpt(s): Also, the subject treatment provides for enhanced immunosuppression vis--vis cold CD20 and radiolabeled anti-CD22 therapy alone. This combination therapeutic regimen is useful in the treatment of diseases wherein depletion and/or selective killing, and/or blocking the function of CD20 and CD22 expressing cells is therapeutically beneficial, especially B-cell malignancies, lymphomas, leukemias, and conditions or diseases wherein suppression of B-cell immune function is therapeutically beneficial, e.g., autoimmune diseases, allergic diseases, transplant, and other therapeutic regimens involving administration of antigenic moieties, e.g., protein, cell or gene therapy. Preferably, the therapeutic regimen will comprise the initial administration of RITUXAN.RTM., followed by administration of the radiolabeled anti-CD22 antibody. ... Ligands that specifically bind the CD22 receptor have been reported to have potential application in the treatment of various diseases, especially B-cell lymphomas and autoimmune diseases. In particular, the use of labeled and non-labeled anti-CD22 antibodies for treatment of such diseases has been reported. ... For example, Tedder et al, U.S. Pat. No. 5,484,892, that purportedly bind CD22 with high affinity and block the interaction of CD22 with other ligands. These monoclonal antibodies are disclosed to be useful in

treating autoimmune diseases such as glomerulonephritis, Goodpasture's syndrome, necrotizing vasculitis, lymphadenitis, periarteritis nodosa, systemic lupus erythematosis, arthritis, thrombocytopenia purpura, agranulocytosis, autoimmune hemolytic anemias, and for inhibiting immune reactions against foreign antigens such as fetal antigens during pregnancy, myasthenia gravis, insulin-resistant diabetes, Graves' disease and allergic responses.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Diagnostic Drugs for Autoimmune Diseases**

  Inventor(s): Ozaki, Shoichi; (Kyoto, Jp), Sobajima, Junko; (Osaka, Jp), Uesugi, Hiroko; (Kyoto, Jp), Okazaki, Takahiro; (Kyoto, Jp), Tanaka, Masao; (Kyoto, Jp), Nakao, Kazuwa; (Kyoto, Jp), Yoshida, Michiteru; (Chiba, Jp), Shirakawa, Hitoshi; (Saitama, Jp), Osakada, Fumio; (Hyogo, JP)

  Correspondence: Christopher J. Buntel, Ph.D.; Baker Botts L.L.P.; 910 Louisiana; Houston; TX; 77002; US

  Patent Application Number: 20020009749

  Date filed: June 7, 1999

  Abstract: A diagnostic drug and a diagnostic kit for autoimmune diseases including at least one of a polypeptide selected from an HMG-1 family, a polypeptide selected from an HMG-2 family, a fragment thereof which is reactable with an antibody of an autoimmune disease patient, and a method for detecting an antibody of an autoimmune disease patient using the same are provided.

  Excerpt(s): The present invention relates to a diagnostic drug for and a kit for diagnosing autoimmune diseases, and a method for detecting an antibody of an autoimmune disease patient using high mobility group protein-1 (HMG-1), high mobility group protein-2 (HMG-2), or a fragment of a polypeptide thereof with which the antibody of the autoimmune disease patient reacts. In particular, the present invention relates to a diagnostic drug for and a kit for diagnosing rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, Behet's disease, scleroderma, primary biliary cirrhosis, microscopic polyangiitis/polyarteritis nodosa, ulcerative colitis, Crohn's disease, and autoimmune hepatitis, and a method for detecting an antibody of a patient of any of the above-mentioned diseases, using HMG-1, HMG-2, or a fragment of a polypeptide thereof with which the antibody of such a patient reacts. ... Standard diagnostic methods for ulcerative colitis and Crohn's disease include endoscopy, biopsy, and X-ray examination.

These methods are costly, painful, and time-consuming. Recently, detection of pANCA by indirect immunofluorescence assay has been reported as a serodiagnosis for ulcerative colitis. However, this method is not sufficiently sensitive and tends to have an increased background signal. Serodiagnosis, by which neutrophils and other cells are fixed on a plate with ethanol, has a further disadvantage in that the result depends on the state of the cells and the fixing technique and is not sufficiently reliable. Accordingly, serodiagnosis has not been in general use. Regarding Crohn's disease, even an autoantibody has not been found. As described above, a specific and simple diagnostic method for autoimmune diseases has not been developed. ... Despite these problems, measurement of antinuclear antibodies by indirect immunofluorescence assay is now indispensable to diagnosis of various collagen diseases including systemic lupus erythematosus and understanding of clinical conditions thereat. Needless to say, it is demanded to identify autoantigens of autoimmune diseases other than the antinuclear antibody and to develop a simple and objective method for detecting antibodies using the antigens, with no difference among research facilities.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Treatment of inflammatory and autoimmune diseases**

  Inventor(s): Elliott, Peter J.; (Marlborough, MA), Adams, Julian; (Brookline, MA), Plamondon, Louis; (Watertown, MA)

  Correspondence: Hale and Dorr, LLP; 60 State Street; Boston; MA; 02109

  Patent Application Number: 20010051654

  Date filed: January 26, 2001

  Abstract: This invention is directed to the treatment of inflammatory and autoimmune diseases by administering proteasome inhibitors, ubiquitin pathway inhibitors, agents that interfere with the activation of NF-.kappa.B via the ubiquitin proteasome pathway, or mixtures thereof. The invention is further directed to the treatment of inflammatory and autoimmune diseases by administering an effective combination of a glucocorticoid and a proteasome inhibitor, ubiquitin pathway inhibitor, agent that interferes with the activation of NF-.kappa.B via the ubiquitin proteasome pathway, or mixture thereof. Pharmaceutical compositions comprising a combination of a glucocorticoid and a proteasome inhibitor, ubiquitin pathway inhibitor, agent that interferes with the activation of NF-.kappa.B via the ubiquitin proteasome pathway, or mixture thereof are also contemplated within the scope of the invention.

Excerpt(s): This invention is directed to compositions and methods for treatment of inflammatory and autoimmune diseases. ... This invention is directed to compositions and methods for treatment of inflammatory and autoimmune diseases. All patent applications, patents and literature references cited herein are hereby incorporated by reference in their entirety. In the case of inconsistencies the present disclosure will prevail.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Extracorporeal affinity adsorption methods for the treatment of atherosclerosis, cancer, degenerative and autoimmune diseases**

  Inventor(s): Strahilevitz, Meir ; (Seattle, WA)

  Correspondence: Polster, Lieder, Woodruff; & Lucchesi, L.C.; 763 S. New Ballas Rd.; St. Louis; MO; 63141; US

  Patent Application Number: 20010039392

  Date filed: June 26, 2001

  Abstract: Extracorporeal affinity adsorption treatments which are aimed at the substantial removal of two or more compounds that are etiological in the pathogenesis of diseases in man provide effective therapeutic intervention means for these diseases. The methods are particularly suitable for the treatment of atherosclerosis, cancer, degenerative and autoimmune diseases. Extracorporeal chelation and immunotherapy for atherosclerosis, extracorporeal chelation treatment with on-line regeneration or replacement of chelant, extracorporeal immunotherapy with antibody fragments, and extracorporeal immunoadsorption utilizing antibodies bound to Protein A are also disclosed.

  Excerpt(s): Another objective of the invention is to provide for extracorporeal chelation therapy for cancer, autoimmune diseases and degenerative diseases, such as rheumatoid arthritis.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

Keeping Current

In order to stay informed about patents and patent applications dealing with autoimmune diseases, you can access the U.S. Patent Office archive via the Internet at no cost to you. This archive is available at the following Web address: **http://www.uspto.gov/main/patents.htm**. Under "Services," click on "Search Patents." You will see two broad options: (1) Patent Grants, and (2) Patent Applications. To see a list of granted patents, perform the

following steps: Under "Patent Grants," click "Quick Search." Then, type "autoimmune diseases" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on autoimmune diseases. You can also use this procedure to view pending patent applications concerning autoimmune diseases. Simply go back to **http://www.uspto.gov/main/patents.htm**. Under "Services," click on "Search Patents." Select "Quick Search" under "Patent Applications." Then proceed with the steps listed above.

Vocabulary Builder

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adsorption: The attachment of one substance to the surface of another; the concentration of a gas or a substance in solution in a liquid on a surface in contact with the gas or liquid, resulting in a relatively high concentration of the gas or solution at the surface. [EU]

Agranulocytosis: A symptom complex characterized by marked decrease in the number of granulocytes and by lesions of the throat and other mucous membranes, of the gastrointestinal tract, and of the skin; called also granulocytopenia and Schultz's disease. [EU]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Aspergillosis: Infections with fungi of the genus aspergillus. [NIH]

Atopic: Pertaining to an atopen or to atopy; allergic. [EU]

Biopsy: The removal and examination, usually microscopic, of tissue from the living body, performed to establish precise diagnosis. [EU]

Bordetella: A genus of gram-negative, aerobic bacteria whose cells are minute coccobacilli. It consists of both parasitic and pathogenic species. [NIH]

Bronchopulmonary: Pertaining to the lungs and their air passages; both bronchial and pulmonary. [EU]

Chelation: Combination with a metal in complexes in which the metal is part of a ring. [EU]

Collagen: The protein substance of the white fibres (collagenous fibres) of skin, tendon, bone, cartilage, and all other connective tissue; composed of molecules of tropocollagen (q.v.), it is converted into gelatin by boiling. collagenous pertaining to collagen; forming or producing collagen. [EU]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to

chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cytotoxic: Pertaining to or exhibiting cytotoxicity. [EU]

Encephalitis: Inflammation of the brain. [EU]

Endoscopy: Visual inspection of any cavity of the body by means of an endoscope. [EU]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Gluten: The protein of wheat and other grains which gives to the dough its tough elastic character. [EU]

Haplotypes: The genetic constitution of individuals with respect to one member of a pair of allelic genes, or sets of genes that are closely linked and tend to be inherited together such as those of the major histocompatibility complex. [NIH]

Hemagglutinins: Agents that cause agglutination of red blood cells. They include antibodies, blood group antigens, lectins, autoimmune factors, bacterial, viral, or parasitic blood agglutinins, etc. [NIH]

Hepatic: Pertaining to the liver. [EU]

Heterozygote: An individual having different alleles at one or more loci in homologous chromosome segments. [NIH]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hydrocortisone: The main glucocorticoid secreted by the adrenal cortex. Its synthetic counterpart is used, either as an injection or topically, in the treatment of inflammation, allergy, collagen diseases, asthma, adrenocortical deficiency, shock, and some neoplastic conditions. [NIH]

Hydrophobic: Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

Immunization: The induction of immunity. [EU]

Immunosuppressant: An agent capable of suppressing immune responses. [EU]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Ingestion: The act of taking food, medicines, etc., into the body, by mouth. [EU]

Inorganic: Pertaining to substances not of organic origin. [EU]

Lymphadenitis: Inflammation of the lymph nodes. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malignant: Tending to become progressively worse and to result in death. Having the properties of anaplasia, invasion, and metastasis; said of tumours. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Methimazole: A thioureylene antithyroid agent that inhibits the formation of thyroid hormones by interfering with the incorporation of iodine into tyrosyl residues of thyroglobulin. This is done by interfering with the oxidation of iodide ion and iodotyrosyl groups through inhibition of the peroxidase enzyme. [NIH]

Mobility: Capability of movement, of being moved, or of flowing freely. [EU]

Mycobacterium: An organism of the genus Mycobacterium. [EU]

Mycoplasma: A genus of gram-negative, facultatively anaerobic bacteria bounded by a plasma membrane only. Its organisms are parasites and pathogens, found on the mucous membranes of humans, animals, and birds. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Neuritis: Inflammation of a nerve, a condition attended by pain and tenderness over the nerves, anaesthesia and paraesthesias, paralysis, wasting, and disappearance of the reflexes. In practice, the term is also used to denote noninflammatory lesions of the peripheral nervous system; see neuropathy. [EU]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Prophylaxis: The prevention of disease; preventive treatment. [EU]

Recombinant: 1. a cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Sarcoma: A tumour made up of a substance like the embryonic connective tissue; tissue composed of closely packed cells embedded in a fibrillar or homogeneous substance. Sarcomas are often highly malignant. [EU]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Thyrotropin: A peptide hormone secreted by the anterior pituitary. It promotes the growth of the thyroid gland and stimulates the synthesis of thyroid hormones and the release of thyroxine by the thyroid gland. [NIH]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

Tumour: 1. swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. a new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

CHAPTER 6. BOOKS ON AUTOIMMUNE DISEASES

Overview

This chapter provides bibliographic book references relating to autoimmune diseases. You have many options to locate books on autoimmune diseases. The simplest method is to go to your local bookseller and inquire about titles that they have in stock or can special order for you. Some patients, however, feel uncomfortable approaching their local booksellers and prefer online sources (e.g. **www.amazon.com** and **www.bn.com**). In addition to online booksellers, excellent sources for book titles on autoimmune diseases include the Combined Health Information Database and the National Library of Medicine. Once you have found a title that interests you, visit your local public or medical library to see if it is available for loan.

Book Summaries: Federal Agencies

The Combined Health Information Database collects various book abstracts from a variety of healthcare institutions and federal agencies. To access these summaries, go to **http://chid.nih.gov/detail/detail.html**. You will need to use the "Detailed Search" option. To find book summaries, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer. For the format option, select "Monograph/Book." Now type "autoimmune diseases" (or synonyms) into the "For these words:" box. You will only receive results on books. You should check back periodically with this database which is updated every 3 months. The following is a typical result when searching for books on autoimmune diseases:

- **Primary and Secondary Preventive Nutrition**

  Source: Totowa, NJ, Humana Press, 465 p., 2001.

  Contact: Humana Press Inc., 999 Riverview Drive, Suite 208, Totowa, NJ 07512. (973) 256-1699. FAX: (973) 256-8341. Internet/Email: http://humanapress.com; humana@humanapr.com.

  Summary: Primary and Secondary Preventive Nutrition synthesizes information on what is known about the benefits of nutritional strategies for the primary and secondary prevention of disease and the promotion of health. Definitive data on the value of specific diets and supplements are largely confined to classical nutritional deficiencies and limited areas of overindulgence or underindulgence. The major objective of this text is to highlight and critically review the key recent research findings that are topical issues for health care professionals and their clients, faculty and students of nutritional sciences, and educated consumers who also seek a reliable source of nutritional information. Specific chapters in the text are devoted to (1) an historical perspective of preventive nutrition, (2) vitamin supplements and cancer risk, (3) soy and cancer prevention, (4) micronutrients as intermediate biomarkers in chemotherapy and enhancement for cancer treatments, (5) health effects of trans fatty acids, (6) antioxidant vitamins and atherosclerosis, (7) oxidative stress and antioxidants in type 2 diabetes, (8) effects of hyperhomocysteinemia and diabetes on cardiovascular disease, (9) genetic and environmental influences on obesity, (10) obesity and insulin resistance in childhood and adolescence, (11) prevention of childhood obesity, (12) obesity and chronic disease, (13) meal replacement products and fat substitutes in weight control and maintenance, (14) role of long-chain polyunsaturated fatty acids in infant growth and development, (15) vitamin A-related childhood blindness and mortality, (16) polyunsaturated fatty acids and autoimmune diseases, (17) role of nutrition and dietary supplement interventions in osteoarthritis, (18) calcium requirements during treatment of osteoporosis in women, (19) preventive nutrition issues in ethnic and socioeconomic groups in the United States, (20) micronutrient deficiencies, (21) alcohol, (22) health claims for foods and dietary supplements in the United States and Japan, (23) incorporating preventive nutrition into medical school curricula, and (24) preventive nutrition throughout the life cycle.

- **Disease Prevention: Health Facts**

  Source: Santa Cruz, CA, ETR Associates, 90 p., 1994.

  Contact: ETR Associates, P.O. Box 1830, Santa Cruz, CA 95061. (800) 321-4407.

Summary: Disease Prevention: Health Facts, a book in the Health Facts series, presents issues of concern surrounding disease prevention. Its purpose is to provide background information for educators as they teach young people about health. Section one, Influences on Health and Disease, discusses the definition of disease; what risk means; and primary, secondary, and tertiary prevention. Section two, Infectious Disease, highlights the infection cycle, natural defenses, and the immune response. It discusses the importance of immunization and the diseases prevented by immunization, including (1) diphtheria, (2) tetanus, (3) pertussis, (4) influenza, (5) pneumococcal pneumonia, (6) measles, (7) rubella, (8) mumps, and (9) hepatitis B. Section three, Lifestyle Choices and Chronic Disease, lists the components of a healthy lifestyle and explains how lifestyle can help prevent certain chronic diseases such as heart disease, cancer, stroke and chronic obstructive pulmonary disease. Section four, Other Noninfectious Diseases, discusses heredity, environment, autoimmune diseases, and diseases with unknown causes. Autoimmune diseases include multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus. Section five, Mental Illness, explains the four general categories of mental illness: (1) Schizophrenia, (2) mood disorders, (3) borderline personality disorder, and (4) anxiety disorders. Categories of practitioners who can provide help for people with mental illness include (1) psychiatrists, (2) clinical psychologists, (3) clinical or psychiatric social workers, (4) psychiatric nurses, (5) mental health counselors, and (6) marriage and family counselors. A glossary and list of resources are provided.

- **Diseases of the Oral Mucosa and the Lips**

  Source: Orlando, FL: W.B. Saunders Company. 1993. 389 p.

  Contact: Available from W.B. Saunders Company. Order Fulfillment, 6277 Sea Harbor Drive, Orlando, FL 32887-4430. (800) 545-2522 (individuals) or (800) 782-4479 (schools); Fax (800) 874-6418 or (407) 352-3445; http://www.wbsaunders.com. Price: $99.00 plus shipping and handling. ISBN: 0721640397.

  Summary: This book is a clinically oriented atlas and text covering the symptoms and diseases of the oral mucosa and perioral skin. The authors focus on the essential aspects of each illness, concentrating on the clinical features that are important in the differential diagnosis. The authors include not only diseases confined to the oral mucosa but also those oral problems that may be signs of accompanying cutaneous (skin) or systemic diseases. Sixty-seven chapters are presented in three sections: the normal oral mucosa, general aspects of oral pathology, and diseases of the oral mucosa and the lips. Specific topics are inflammation of the

lips, acquired diseases of the tongue, gingival hyperplasia, enlargement of the parotid gland, aphthous ulcers (stomatitis), pyostomatitis vegetans, disorders of pigmentation, urticaria and angioedema, psoriasis, Reiter's syndrome, lichen planus, graft-versus-host disease, rosacea, perioral dermatitis, erythema multiforme, acute febrile neutrophilic dermatosis (Sweet's syndrome), vesicular and bullous autoimmune diseases, desquamative gingivitis, necrotizing sialometaplasia, oral mucosal hemorrhage, viral diseases, bacterial diseases, fungal diseases, protozoal and parasitic diseases, mechanical damage, trauma, allergic and toxic contact stomatitis, occupational diseases of the oral mucosa, drug reactions and side effects, morphea and scleroderma, lichen sclerosus et atrophicus, dermatomyositis, lupus erythematosus, Sjogren's syndrome, polyarteritis nodosa, giant cell arteritis, plasma cell gingivitis, oral submucous fibrosis, halitosis, xerostomia, sialorrhea, self-induced mucosal injuries, benign granulomatous processes, malignant granulomatoses, heterotopias and congenital malformations, genodermatoses and congenital syndromes, benign and malignant tumors, actinic keratosis, leukoplakia, paraneoplastic disorders, and oral signs of hematologic, nutritional, metabolic, and endocrine disorders. Each chapter includes full-color photographs and references are provided in individual sections. A subject index concludes the volume. (AA-M).

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes & Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). The following have been recently listed with online booksellers as relating to autoimmune diseases (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **Autoimmune Aspects of Lung Disease (Respiratory Pharmacology and Pharmacotherapy)** by David A. Isenberg (Editor), Stephen G. Spiro (Editor) (1998); ISBN: 0817657193; http://www.amazon.com/exec/obidos/ASIN/0817657193/icongroupinterna
- **Autoimmune Disease Models: A Guidebook** by Irun R. Cohen (Editor), Ariel Miller (Editor) (1994); ISBN: 0121783308;

http://www.amazon.com/exec/obidos/ASIN/0121783308/icongroupinterna

- **Autoimmune Disease: Aetiopathogenesis, Diagnosis and Treatment: Essays in Honour of the Retirement of Professor Ivan Roitt Frs** by Peter M. Lydyard (Editor), Jonathan Brostoff (Editor) (1994); ISBN: 0632037997; http://www.amazon.com/exec/obidos/ASIN/0632037997/icongroupinterna
- **Autoimmune Diseases: Focus on Sjogren's Syndrome (Ucl Molecular Pathology)** by Isenberg, et al (1994); ISBN: 1872748236; http://www.amazon.com/exec/obidos/ASIN/1872748236/icongroupinterna
- **Autoimmunity** (1994); ISBN: 3540576428; http://www.amazon.com/exec/obidos/ASIN/3540576428/icongroupinterna
- **Auto-Immunity in the Endocrine System** by Robert, VolpE (1981); ISBN: 0387106774; http://www.amazon.com/exec/obidos/ASIN/0387106774/icongroupinterna
- **Autoimmunoregulation and Autoimmune Disease (Concepts in Immunophathology, Vol 4)** by J.M. Cruse, R.E., Jr. Lewis (Editor) (1987); ISBN: 3805544065; http://www.amazon.com/exec/obidos/ASIN/3805544065/icongroupinterna
- **B Cells & Autoantibody Production in Autoimmune Diseases** by Christian Boitard (1996); ISBN: 1570592098; http://www.amazon.com/exec/obidos/ASIN/1570592098/icongroupinterna
- **B Cells and Autoantibody Production in Autoimmune Diseases (Medical Intelligence Unit)** by Christian Boitard (1996); ISBN: 0412101718; http://www.amazon.com/exec/obidos/ASIN/0412101718/icongroupinterna
- **Behcet's Disease: A Contemporary Synopsis** by Gary R. Plotkin, et al (1988); ISBN: 0879933135; http://www.amazon.com/exec/obidos/ASIN/0879933135/icongroupinterna
- **Cellular Aspects of Autoimmunity (Concepts in Immunopathology, Vol 6)** by J.M. Cruse, R.E., Jr. Lewis (Editor) (1988); ISBN: 3805547285; http://www.amazon.com/exec/obidos/ASIN/3805547285/icongroupinterna

- **Ciclosporin in Autoimmune Diseases: 1st International Symposium, Basle, March 18-20, 1985** by Rosemarie Schindler (Editor) (1986); ISBN: 0387156232; http://www.amazon.com/exec/obidos/ASIN/0387156232/icongroupinterna
- **Clinical and Molecular Aspects of Autoimmune Diseases (Concepts in Immunopathology: Series in Immunoregulation Research, Vol. 8)** by Julius M. Cruse, Robert Edwin Lewis (Editor) (1992); ISBN: 3805554028; http://www.amazon.com/exec/obidos/ASIN/3805554028/icongroupinterna
- **Cytokines in Autoimmunity (Medical Intelligence Unit)** by Fionula M. Brennan (Editor), Marc Feldmann (Editor) (1996); ISBN: 0412102714; http://www.amazon.com/exec/obidos/ASIN/0412102714/icongroupinterna
- **Genetic Basis of Autoimmune Disease (Concepts in Immunopathology, Vol 5)** by R.E. Lewis (Editor), Julius M. Cruse (Editor) (1988); ISBN: 3805546351; http://www.amazon.com/exec/obidos/ASIN/3805546351/icongroupinterna
- **Idiotypes and Diseases (Monographs in Allergy, Vol 22)** by M. Zanetti, et al (1987); ISBN: 3805546009; http://www.amazon.com/exec/obidos/ASIN/3805546009/icongroupinterna
- **Immunogenetics of Autoimmune Disease** by Nadir R. Farid (Editor) (1991); ISBN: 0849368987; http://www.amazon.com/exec/obidos/ASIN/0849368987/icongroupinterna
- **Immunogenetics of Autoimmune Diseases** by Nadir R. Farid (Editor) (1991); ISBN: 0849368979; http://www.amazon.com/exec/obidos/ASIN/0849368979/icongroupinterna
- **Immunological Tolerance to Self and Non-Self** by J. R. Battisto (1982); ISBN: 0897661745; http://www.amazon.com/exec/obidos/ASIN/0897661745/icongroupinterna
- **Immunology of Endocrine Diseases (Immunology and Medicine, Vol 3)** by Alan M. McGregor (Editor) (1986); ISBN: 0852009631; http://www.amazon.com/exec/obidos/ASIN/0852009631/icongroupinterna

- **Immunology of Neuromuscular Disease (Immunology and Medicine, Vol 24)** by R. Hohlfeld (Editor) (1994); ISBN: 0792388445; http://www.amazon.com/exec/obidos/ASIN/0792388445/icongroupinterna
- **Immunology of the Male Reproductive System (Immunology Series, No 36)** by Pierluigi E. Bigazzi (Editor) (1987); ISBN: 0824776488; http://www.amazon.com/exec/obidos/ASIN/0824776488/icongroupinterna
- **Immunopharmacology in Autoimmune Diseases and Transplantation** by Hans Erik Rugstad, et al (1992); ISBN: 0306439948; http://www.amazon.com/exec/obidos/ASIN/0306439948/icongroupinterna
- **Immunotherapy of Diabetes and Selected Autoimmune Diseases** by George S. Eisenbarth (Editor) (1989); ISBN: 0849345588; http://www.amazon.com/exec/obidos/ASIN/0849345588/icongroupinterna
- **Microorganisms and Autoimmune Diseases (Infectious Agents and Pathogenesis)** by Herman Friedman (Editor), et al (1996); ISBN: 0306452367; http://www.amazon.com/exec/obidos/ASIN/0306452367/icongroupinterna
- **Monoclonal Antibodies and Peptide Therapy in Autoimmune Diseases** by Jean-Francois Bach (Editor) (1993); ISBN: 082478880X; http://www.amazon.com/exec/obidos/ASIN/082478880X/icongroupinterna
- **Ovarian Autoimmunity: Clinical and Experimental Data (Medical Intelligence Unit)** by Roy Moncayo, Helga E. Moncayo (1995); ISBN: 1570592195; http://www.amazon.com/exec/obidos/ASIN/1570592195/icongroupinterna
- **Perspectives on Autoimmunity** by Irun R. Cohen (Editor) (1988); ISBN: 0849364310; http://www.amazon.com/exec/obidos/ASIN/0849364310/icongroupinterna
- **Rnp Particles, Splicing, and Autoimmune Diseases (Springer Lab Manual)** by Johannes Schenkel (Editor), Johanne Schenkel (1998); ISBN: 3540624481; http://www.amazon.com/exec/obidos/ASIN/3540624481/icongroupinterna

- **Specific Immunotherapy of Chronic Autoimmune Diseases: How to Translate the Experience of the Experimental Models Into Novel Treatment Modalities** (1999); ISBN: 9069842599; http://www.amazon.com/exec/obidos/ASIN/9069842599/icongroupinterna
- **T Cell Vaccination and Autoimmune Disease (Medical Intelligence Unit)** by Jingwu Zhang, Jef Raus (1995); ISBN: 1570592543; http://www.amazon.com/exec/obidos/ASIN/1570592543/icongroupinterna
- **T-Cell Receptor Use in Human Autoimmune Diseases (Annals of the New York Academy of Sciences, Vol 756)** by Mark M. Davis (Editor), Joel Buxbaum (Editor) (1995); ISBN: 0897669150; http://www.amazon.com/exec/obidos/ASIN/0897669150/icongroupinterna
- **The Impact of Biotechnology on Autoimmunity (Medical Science Symposia, Vol 6)** by A. G. Dalgleish (Editor), et al (1994); ISBN: 0792327241; http://www.amazon.com/exec/obidos/ASIN/0792327241/icongroupinterna
- **The Molecular Biology of Autoimmune Disease** (1990); ISBN: 3540517715; http://www.amazon.com/exec/obidos/ASIN/3540517715/icongroupinterna
- **The Molecular Pathology of Autoimmune Diseases** by Constantin A. Bona (1993); ISBN: 3718605554; http://www.amazon.com/exec/obidos/ASIN/3718605554/icongroupinterna
- **The T-Cell Receptor Use in Human Autoimmune Diseases: Proceedings** by Mark M. Davis (Editor), Joel Buxbaum (Editor) (1995); ISBN: 0897669169; http://www.amazon.com/exec/obidos/ASIN/0897669169/icongroupinterna
- **The Thyroid and Autoimmunity: Proceedings of the International Symposium on Thyroid and Autoimmunity, Amsterdam, 19-21 March 1986 (International Con)** by H.A. Drexhage, W.M. Wiersinga (Editor) (1987); ISBN: 0444808299; http://www.amazon.com/exec/obidos/ASIN/0444808299/icongroupinterna
- **Therapy of Autoimmune Diseases (Concepts in Immunopathology, Vol 7)** by J.M. Cruse, R.E. Lewis (Editor) (1989); ISBN: 3805549318;

http://www.amazon.com/exec/obidos/ASIN/3805549318/icongroupinterna

- **Tissue Specificity and Autoimmunity (Molecular Biology, Biochemistry and Biophysics, Vol 16)** by S. Shulman (1974); ISBN: 0387065636; http://www.amazon.com/exec/obidos/ASIN/0387065636/icongroupinterna
- **Viral and Autoimmune Hepatitis: Morphologic and Pathogenetic Aspects of Cell Damage in Hepatitis With Potential Chronicity (Progress in Pathology)** by Hans Peter, Dr. Dienes (1989); ISBN: 0895742802; http://www.amazon.com/exec/obidos/ASIN/0895742802/icongroupinterna

The National Library of Medicine Book Index

The National Library of Medicine at the National Institutes of Health has a massive database of books published on healthcare and biomedicine. Go to the following Internet site, **http://locatorplus.gov/**, and then select "Search LOCATORplus." Once you are in the search area, simply type "autoimmune diseases" (or synonyms) into the search box, and select "books only." From there, results can be sorted by publication date, author, or relevance. The following was recently catalogued by the National Library of Medicine:[26]

- **Autoimmune diseases of the skin: pathogenesis, diagnosis, management.** Author: Michael Hertl (ed.); Year: 2001; Wien; New York: Springer, c2001; ISBN: 3211835989 (alk. paper) http://www.amazon.com/exec/obidos/ASIN/3211835989/icongroupinterna
- **Autoimmune endocrinopathies.** Author: edited by Robert Volpe; Year: 1999; Totowa, N.J.: Humana Press, c1999; ISBN: 0896036804 (alk. paper)

[26] In addition to LOCATORPlus, in collaboration with authors and publishers, the National Center for Biotechnology Information (NCBI) is adapting biomedical books for the Web. The books may be accessed in two ways: (1) by searching directly using any search term or phrase (in the same way as the bibliographic database PubMed), or (2) by following the links to PubMed abstracts. Each PubMed abstract has a "Books" button that displays a facsimile of the abstract in which some phrases are hypertext links. These phrases are also found in the books available at NCBI. Click on hyperlinked results in the list of books in which the phrase is found. Currently, the majority of the links are between the books and PubMed. In the future, more links will be created between the books and other types of information, such as gene and protein sequences and macromolecular structures. See **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books.**

http://www.amazon.com/exec/obidos/ASIN/0896036804/icongroupinterna

- **Autoimmune liver disease: its recent advances: proceedings of the International Symposium of Digestive Diseases Week held in Hiroshima on 29-30, October 1999.** Author: editors, Mikio Nishioka, Seishiro Watanabe, and Keiji Arima; Year: 2000; Amsterdam; New York: Elsevier, 2000; ISBN: 044450527X (alk. paper)
  http://www.amazon.com/exec/obidos/ASIN/044450527X/icongroupinterna
- **Biologic and gene therapy of autoimmune disease.** Author: volume editor, C.G. Fathman; Year: 2000; Basel; New York: Karger, 2000; ISBN: 3805569491 (alk. paper)
  http://www.amazon.com/exec/obidos/ASIN/3805569491/icongroupinterna
- **Case studies on autoimmune diseases and electrically conducting polymers.** Author: Thomas Reiss ... [et al.]; Year: 1998; [Linköping], Sweden: Systems of Innovation Research Program, Linköping University, [1998]
- **Combination treatment in autoimmune diseases.** Author: W.B. Harrison, B.A.C. Dijkmans, eds; Year: 2002; Berlin; New York: Springer-Verlag, 2002; ISBN: 3540430369 (alk. paper)
  http://www.amazon.com/exec/obidos/ASIN/3540430369/icongroupinterna
- **Cytokines and autoimmune diseases.** Author: edited by Vijay K. Kuchroo ... [et al.]; Year: 2002; Totowa, N.J.: Humana Press, c2002; ISBN: 0896038564 (alk. paper)
  http://www.amazon.com/exec/obidos/ASIN/0896038564/icongroupinterna
- **Cytokines and chemokines in autoimmune disease.** Author: Pere Santamaria; Year: 2001; Georgetown, TX: Eurekah.com/Landes Bioscience, c2001; ISBN: 1587060884 (hardcover: alk. paper)
  http://www.amazon.com/exec/obidos/ASIN/1587060884/icongroupinterna
- **Management of autoimmune connective tissue disease.** Author: guest editor, Richard Sontheimer; Year: 2001; Malden, MA: Blackwell Science, c2001
- **Report of the Autoimmune Diseases Coordinating Committee [electronic resource].** Author: National Institute of Allergy and Infectious Diseases (U.S.). Autoimmune Diseases Coordinating Committee; Year: 2000; [Bethesda, Md.: National Institutes of Health, 2000]

- **Specific immunotherapy of chronic autoimmune diseases: how to translate the experience of the experimental models into novel treatment modalities.** Author: edited by W. van Eden ... [et al.]; Year: 1999; Amsterdam: Royal Netherlands Academy of Arts and Sciences, 1999; ISBN: 9069842599
  http://www.amazon.com/exec/obidos/ASIN/9069842599/icongroupinterna
- **Vascular manifestations of systemic autoimmune diseases.** Author: edited by Ronald A. Asherson, Ricard Cervera; associate editors, Steven B. Abramson, Jean-Charles Piette, Douglas A. Triplett; Year: 2001; Boca Raton: CRC Press, c2001; ISBN: 084931335X (alk. paper)
  http://www.amazon.com/exec/obidos/ASIN/084931335X/icongroupinterna

Chapters on Autoimmune Diseases

Frequently, autoimmune diseases will be discussed within a book, perhaps within a specific chapter. In order to find chapters that are specifically dealing with autoimmune diseases, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and autoimmune diseases using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find book chapters, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Book Chapter." By making these selections and typing in "autoimmune diseases" (or synonyms) into the "For these words:" box, you will only receive results on chapters in books. The following is a typical result when searching for book chapters on autoimmune diseases:

- **Veisicular and Bullous Autoimmune Diseases**

  Source: in Bork, K., et al. Diseases of the Oral Mucosa and the Lips. Orlando, FL: W.B. Saunders Company. 1993. p. 71-81.

  Contact: Available from W.B. Saunders Company. Order Fulfillment, 6277 Sea Harbor Drive, Orlando, FL 32887-4430. (800) 545-2522 (individuals) or (800) 782-4479 (schools); Fax (800) 874-6418 or (407) 352-3445; http://www.wbsaunders.com. Price: $99.00 plus shipping and handling. ISBN: 0721640397.

  Summary: This chapter, from a textbook on diseases of the oral mucosa and the lips, discusses vesicular and bullous autoimmune disease. This chapter focuses on pemphigus vulgaris and cicatricial pemphigoid (the

other related disease, erosive lichen planus, is covered in a separate chapter). The chapter covers etiology, clinical features, histopathology, diagnosis, differential diagnosis, and therapy of pemphigus vulgaris, paraneoplastic pemphigus, pemphigus vegetans, pemphigus foliaceus and erythematosus, bullous pemphigoid, and cicatricial pemphigoid. Full-color photographs illustrate the chapter. 16 figures. 23 references. (AA-M).

- **New Horizons in the Treatment of Autoimmune Diseases: Immunoablation and Stem Cell Transplantation**

  Source: in Coggins, C.H.; Hancock, E.W.; Levitt, L.J., eds. Annual Review of Medicine, Volume 51, 2000. Palo Alto, CA: Annual Reviews, Inc. 2000. p. 115-134.

  Contact: Available from Annual Reviews. 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0139. (650) 493-4400. E-mail: science@annurev.org. Website: www.AnnualReviews.org.

  Summary: This chapter provides health professionals with information on the treatment of autoimmune diseases (ADs) with immunosuppression followed by allogeneic or even autologous hemolymphopoietic stem cells (HSCs). The current treatment for severe, relapsing, or refractory AD cases is still not satisfactory. The concept of using intense immunosuppression followed by stem cell transplantation to treat AD is based on encouraging results in experimental animals and from serendipitous cases of patients with both ADs and malignancies who were allotransplanted for the latter. However, rare unexpected relapses despite donor immune engraftment have been reported following HSC transplantation for AD. Autologous transplantation is a more feasible procedure with lower toxicity than allogenic transplantation. The article analyzes the experimental basis for stem cell transplantation in AD and highlights clinical results of HSC transplants in patients with rheumatoid arthritis, juvenile chronic arthritis, systemic lupus erythematous, and systemic sclerosis. The author concludes that although results are encouraging, remissions rather than cures have been obtained. 3 figures and 111 references. (AA-M).

- **Autoimmune Hepatitis: Diagnosis and Treatment**

  Source: in McDonald, J.W.D.; Burroughs, A.K.; Feagan, B.G., eds. Evidence Based Gastroenterology and Hepatology. London, UK: BMJ Publishing Group. 1999. p. 360-371.

  Contact: Available from BMJ Publishing Group. BMA Books, BMA House, Tavistock Square, London WCIH 9JR. Fax 44 (0)20 7383 6402. E-

mail: orders@bmjbooks.com. Website: www.bmjbooks.com. Price: Contact publisher for price.

Summary: Autoimmune hepatitis (AIH) is a self perpetuating, necroinflammatory disease of unknown etiology, which is characterized by a loss of tolerance towards the patient's own liver tissue. The disease may lead to liver cirrhosis (scarring) and liver failure. This chapter on the diagnosis and treatment of autoimmune hepatitis is from a book that emphasizes the approaches of evidence based medicine in gastroenterology (the study of the gastrointestinal tract and gastrointestinal diseases) and hepatology (the study of the liver and liver diseases). The authors note that AIH is a syndrome characterized by a set of epidemiological, laboratory, and clinical features: female predominance (female to male ratio is 4 to 1), overrepresentation of the HLA alleles DR3 and DR4, hypergammaglobulinemia, circulating autoantibodies, response to immunosuppressive therapy, and coexistence of extrahepatic (outside the liver) autoimmune diseases. In the majority of patients, the disease progresses without major symptoms, and the diagnosis is not made until symptoms of severe liver disease are present. Jaundice is present in a large proportion of patients at diagnosis. Patients' complaints include fatigue, anorexia, abdominal pain (10 to 20 percent of patients), and fever (20 percent of patients). Diagnosis requires the assessment of typical clinical and laboratory features; histology confirms disease activity and stage but by itself is not sufficient for diagnosis. Corticosteroids should be administered until remission, incomplete response, treatment failure, or unacceptable adverse effects occur. Remission is defined by the absence of symptoms, resolution of liver inflammation by liver histology, and a normalization of liver enzymes with the exception of AST, which may remain up to twice normal levels. Patients who fail to enter remission after 4 years of conventional treatment are regarded as potential candidates for liver transplantation. Liver transplantation has resulted in excellent long term survival rates that exceed 90 percent after 5 years. 3 figures. 4 tables. 46 references.

- **Association Between Insulin-Dependent Diabetes Mellitus and Other Autoimmune Diseases**

  Source: in LeRoith, D.; Taylor, S.I.; Olefsky, J.M., eds. Diabetes Mellitus: A Fundamental and Clinical Text. Philadelphia, PA: Lippincott-Raven Publishers. 1996. p. 333-339.

  Contact: Available from Lippincott-Raven Publishers. 12107 Insurance Way, Hagerstown, MD 21740-5184. (800) 777-2295. Fax (301) 824-7390. Price: $199.00. ISBN: 0397514565.

Summary: This chapter, from a medical text on diabetes mellitus, investigates the association between insulin-dependent diabetes mellitus (IDDM, or Type 1) and other autoimmune diseases. The authors first review the historical background of this autoimmune pathogenesis. Other topics include the genetics of IDDM, the genetic associations between IDDM and other autoimmune endocrinopathies, clinical relevance (notably to thyroiditis, Addison's disease, atrophic gastritis, and steroidal antibodies), and recommendations for screening. The authors conclude that IDDM often occurs in the context of other autoimmune endocrinopathies. Its most common presentation with other autoimmunity is as part of APS III, which is the constellation of IDDM and autoimmune thyroiditis, sometimes with pernicious anemia, vitiligo, and or hypogonadism. The possible genetic explanations for the association between other endocrinopathies and IDDM remain unclear. Until the issue of genetics has been resolved, the clinician must rely entirely on the recognition of subtle symptoms and a knowledge of serum autoantibody profiles to diagnose and treat polyglandular autoimmunity. 1 figure. 4 tables. 81 references.

General Home References

In addition to references for autoimmune diseases, you may want a general home medical guide that spans all aspects of home healthcare. The following list is a recent sample of such guides (sorted alphabetically by title; hyperlinks provide rankings, information, and reviews at Amazon.com):

- **Epidemic! The World of Infectious Disease** by Rob Desalle (Editor), Paperback – 246 pages, 1st edition (September 1999), New Press; ISBN: 1565845463; **http://www.amazon.com/exec/obidos/ASIN/1565845463/icongroupinterna**
- **Handbook of Diseases**; Paperback **--** 986 pages, 2nd edition (January 15, 2000), Springhouse Pub Co; ISBN: 0874349796; **http://www.amazon.com/exec/obidos/ASIN/0874349796/icongroupinterna**
- **Infectious Disease Secrets** by Robert H. Gates (Editor); Paperback – 400 pages, 1st edition (January 15, 1998), Hanley & Belfus; ISBN: 1560532661; **http://www.amazon.com/exec/obidos/ASIN/1560532661/icongroupinterna**
- **Invisible Enemies: Stories of Infectious Disease** by Jeanette Farrell; Hardcover – 224 pages (April 1998), Farrar, Straus & Giroux (Juv); ISBN: 0374336377; **http://www.amazon.com/exec/obidos/ASIN/0374336377/icongroupinterna**

- **Maneater: And Other True Stories of a Life in Infectious Disease** by Pamela Nagami; Hardcover – 287 pages, 1st edition (November 2001), St. Martin's Press; ISBN: 1580632092; **http://www.amazon.com/exec/obidos/ASIN/1580632092/icongroupinterna**

Vocabulary Builder

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Angioedema: A vascular reaction involving the deep dermis or subcutaneous or submucal tissues, representing localized edema caused by dilatation and increased permeability of the capillaries, and characterized by development of giant wheals. [EU]

Anorexia: Lack or loss of the appetite for food. [EU]

Antioxidant: One of many widely used synthetic or natural substances added to a product to prevent or delay its deterioration by action of oxygen in the air. Rubber, paints, vegetable oils, and prepared foods commonly contain antioxidants. [EU]

Anxiety: The unpleasant emotional state consisting of psychophysiological responses to anticipation of unreal or imagined danger, ostensibly resulting from unrecognized intrapsychic conflict. Physiological concomitants include increased heart rate, altered respiration rate, sweating, trembling, weakness, and fatigue; psychological concomitants include feelings of impending danger, powerlessness, apprehension, and tension. [EU]

Benign: Not malignant; not recurrent; favourable for recovery. [EU]

Bullous: Pertaining to or characterized by bullae. [EU]

Cardiovascular: Pertaining to the heart and blood vessels. [EU]

Contraception: The prevention of conception or impregnation. [EU]

Cutaneous: Pertaining to the skin; dermal; dermic. [EU]

Dermatosis: Any skin disease, especially one not characterized by inflammation. [EU]

Diphtheria: A localized infection of mucous membranes or skin caused by toxigenic strains of corynebacterium diphtheriae. It is characterized by the presence of a pseudomembrane at the site of infection. Diphtheria toxin, produced by C. diphtheriae, can cause myocarditis, polyneuritis, and other systemic toxic effects. [NIH]

Epidemiological: Relating to, or involving epidemiology. [EU]

Febrile: Pertaining to or characterized by fever. [EU]

Fibrosis: The formation of fibrous tissue; fibroid or fibrous degeneration [EU]

Gastritis: Inflammation of the stomach. [EU]

Gingivitis: Inflammation of the gingivae. Gingivitis associated with bony changes is referred to as periodontitis. Called also oulitis and ulitis. [EU]

Halitosis: An offensive, foul breath odor resulting from a variety of causes such as poor oral hygiene, dental or oral infections, or the ingestion of certain foods. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Heredity: 1. the genetic transmission of a particular quality or trait from parent to offspring. 2. the genetic constitution of an individual. [EU]

Hyperhomocysteinemia: An inborn error of methionone metabolism which produces an excess of homocysteine in the blood. It is often caused by a deficiency of cystathionine beta-synthase and is a risk factor for coronary vascular disease. [NIH]

Hyperplasia: The abnormal multiplication or increase in the number of normal cells in normal arrangement in a tissue. [EU]

Incontinence: Inability to control excretory functions, as defecation (faecal i.) or urination (urinary i.). [EU]

Influenza: An acute viral infection involving the respiratory tract. It is marked by inflammation of the nasal mucosa, the pharynx, and conjunctiva, and by headache and severe, often generalized, myalgia. [NIH]

Jaundice: A clinical manifestation of hyperbilirubinemia, consisting of deposition of bile pigments in the skin, resulting in a yellowish staining of the skin and mucous membranes. [NIH]

Keratosis: Any horny growth such as a wart or callus. [NIH]

Malformation: A morphologic defect resulting from an intrinsically abnormal developmental process. [EU]

Menopause: Cessation of menstruation in the human female, occurring usually around the age of 50. [EU]

Micronutrients: Essential dietary elements or organic compounds that are required in only small quantities for normal physiologic processes to occur. [NIH]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Nadir: The lowest point; point of greatest adversity or despair. [EU]

Neuromuscular: Pertaining to muscles and nerves. [EU]

Parasitic: Pertaining to, of the nature of, or caused by a parasite. [EU]

Perioral: Situated or occurring around the mouth. [EU]

Pigmentation: 1. the deposition of colouring matter; the coloration or discoloration of a part by pigment. 2. coloration, especially abnormally increased coloration, by melanin. [EU]

Pneumonia: Inflammation of the lungs with consolidation. [EU]

Psychiatric: Pertaining to or within the purview of psychiatry. [EU]

Rubella: An acute, usually benign, infectious disease caused by a togavirus and most often affecting children and nonimmune young adults, in which the virus enters the respiratory tract via droplet nuclei and spreads to the lymphatic system. It is characterized by a slight cold, sore throat, and fever, followed by enlargement of the postauricular, suboccipital, and cervical lymph nodes, and the appearances of a fine pink rash that begins on the head and spreads to become generalized. Called also German measles, roetln, röteln, and three-day measles, and rubeola in French and Spanish. [EU]

Schizophrenia: A severe emotional disorder of psychotic depth characteristically marked by a retreat from reality with delusion formation, hallucinations, emotional disharmony, and regressive behavior. [NIH]

Sialorrhea: Increased salivary flow. [NIH]

Stomatitis: Inflammation of the oral mucosa, due to local or systemic factors which may involve the buccal and labial mucosa, palate, tongue, floor of the mouth, and the gingivae. [EU]

Tetanus: A disease caused by tetanospasmin, a powerful protein toxin produced by clostridium tetani. Tetanus usually occurs after an acute injury, such as a puncture wound or laceration. Generalized tetanus, the most common form, is characterized by tetanic muscular contractions and hyperreflexia. Localized tetanus presents itself as a mild condition with manifestations restricted to muscles near the wound. It may progress to the generalized form. [NIH]

Urinary: Pertaining to the urine; containing or secreting urine. [EU]

Urticaria: Pathology: a transient condition of the skin, usually caused by an allergic reaction, characterized by pale or reddened irregular, elevated patches and severe itching; hives. [EU]

Vesicular: 1. composed of or relating to small, saclike bodies. 2. pertaining to or made up of vesicles on the skin. [EU]

CHAPTER 7. MULTIMEDIA ON AUTOIMMUNE DISEASES

Overview

Information on autoimmune diseases can come in a variety of formats. Among multimedia sources, video productions, slides, audiotapes, and computer databases are often available. In this chapter, we show you how to keep current on multimedia sources of information on autoimmune diseases. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine. If you see an interesting item, visit your local medical library to check on the availability of the title.

Bibliography: Multimedia on Autoimmune Diseases

The National Library of Medicine is a rich source of information on healthcare-related multimedia productions including slides, computer software, and databases. To access the multimedia database, go to the following Web site: **http://locatorplus.gov/**. Select "Search LOCATORplus." Once in the search area, simply type in autoimmune diseases (or synonyms). Then, in the option box provided below the search box, select "Audiovisuals and Computer Files." From there, you can choose to sort results by publication date, author, or relevance. The following multimedia has been indexed on autoimmune diseases. For more information, follow the hyperlink indicated:

- **Atlas of autoimmune diseases.** Source: Sharad D. Deodhar, Robert M. Nakamura; Year: 1976; Format: Slide; Chicago: American Society of Clinical Pathologists, 1976

- **Autoimmune diseases of the dog associated with the presence of antinuclear antibodies.** Source: by Edward B. Breitschwerdt and Ota Barta, in cooperation with Instructional Resources, School of Veterinary Medicine, LSU, Baton Rouge; Year: 1979; Format: Slide; Baton Rouge, La.: School of Veterinary Medicine, LSU, c1979
- **Autoimmune diseases.** Source: [presented by] Journal of women's health; Year: 1993; Format: Videorecording; Bethesda, MD: BioConferences International, c1993
- **Autoimmune diseases.** Source: Sharad D. Deodhar; Year: 1976; Format: Slide; New York: Medcom, c1976
- **Cold autoimmune hemolytic anemia : introduction.** Source: Mark-Maris; Year: 1982; Format: Videorecording; Buffalo, N.Y.: Mark-Maris, [1982]
- **Diagnostic evaluation of autoimmune disesase.** Source: American Society of Clinical Pathologists; Year: 1979; Format: Videorecording; Chicago: The Society, c1979
- **Immunodiagnostic tests for autoimmune diseases.** Source: Center for Disease Control, Bureau of Laboratories, Laboratory Training & Consultation Division; Year: 1976; Format: Slide; [Atlanta]: The Center, [1976]
- **Interferon regulatory transcription factors : roles in ocular autoimmune diseases and tumor regression.** Source: Medical Arts and Photography Branch; Year: 2001; Format: Videorecording; [Bethesda, Md.: National Institutes of Health, 2001]
- **Irradiation in solid organ transplantation & treatment of autoimmune disease .** Year: 1989; Format: Sound recording; Chicago, IL: Teach'em, [1989]
- **Mechanisms of autoimmune disease.** Source: American Society of Clinical Pathologists; Year: 1979; Format: Videorecording; Chicago: The Society, c1979
- **What is autoimmune disease.** Source: Video Digest, inc; Year: 1972; Format: Motion picture; Cincinnati, Ohio: Video Digest, c1972

CHAPTER 8. PERIODICALS AND NEWS ON AUTOIMMUNE DISEASES

Overview

Keeping up on the news relating to autoimmune diseases can be challenging. Subscribing to targeted periodicals can be an effective way to stay abreast of recent developments on autoimmune diseases. Periodicals include newsletters, magazines, and academic journals.

In this chapter, we suggest a number of news sources and present various periodicals that cover autoimmune diseases beyond and including those which are published by patient associations mentioned earlier. We will first focus on news services, and then on periodicals. News services, press releases, and newsletters generally use more accessible language, so if you do chose to subscribe to one of the more technical periodicals, make sure that it uses language you can easily follow.

News Services & Press Releases

Well before articles show up in newsletters or the popular press, they may appear in the form of a press release or a public relations announcement. One of the simplest ways of tracking press releases on autoimmune diseases is to search the news wires. News wires are used by professional journalists, and have existed since the invention of the telegraph. Today, there are several major "wires" that are used by companies, universities, and other organizations to announce new medical breakthroughs. In the following sample of sources, we will briefly describe how to access each service. These services only post recent news intended for public viewing.

PR Newswire

Perhaps the broadest of the wires is PR Newswire Association, Inc. To access this archive, simply go to **http://www.prnewswire.com**. Below the search box, select the option "The last 30 days." In the search box, type "autoimmune diseases" or synonyms. The search results are shown by order of relevance. When reading these press releases, do not forget that the sponsor of the release may be a company or organization that is trying to sell a particular product or therapy. Their views, therefore, may be biased.

Reuters

The Reuters' Medical News database can be very useful in exploring news archives relating to autoimmune diseases. While some of the listed articles are free to view, others can be purchased for a nominal fee. To access this archive, go to **http://www.reutershealth.com/frame2/arch.html** and search by "autoimmune diseases" (or synonyms). The following was recently listed in this archive for autoimmune diseases:

- **Gene transfer of immunoglobulin-fusion proteins effective against autoimmune diseases**
  Source: Reuters Medical News
  Date: May 15, 2002
  http://www.reuters.gov/archive/2002/05/15/professional/links/20020515scie002.html

The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html.** MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date at **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within their search engine.

Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com**. You can scan the news by industry category or company name.

Internet Wire

Internet Wire is more focused on technology than the other wires. To access this site, go to **http://www.internetwire.com** and use the "Search Archive" option. Type in "autoimmune diseases" (or synonyms). As this service is oriented to technology, you may wish to search for press releases covering diagnostic procedures or tests that you may have read about.

Search Engines

Free-to-view news can also be found in the news section of your favorite search engines (see the health news page at Yahoo: **http://dir.yahoo.com/Health/News_and_Media/,** or use this Web site's general news search page **http://news.yahoo.com/.** Type in "autoimmune diseases" (or synonyms). If you know the name of a company that is relevant to autoimmune diseases, you can go to any stock trading Web site (such as **www.etrade.com**) and search for the company name there. News items across various news sources are reported on indicated hyperlinks.

BBC

Covering news from a more European perspective, the British Broadcasting Corporation (BBC) allows the public free access to their news archive located at **http://www.bbc.co.uk/**. Search by "autoimmune diseases" (or synonyms).

Newsletters on Autoimmune Diseases

Given their focus on current and relevant developments, newsletters are often more useful to patients than academic articles. You can find newsletters using the Combined Health Information Database (CHID). You will need to use the "Detailed Search" option. To access CHID, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Your

investigation must limit the search to "Newsletter" and "autoimmune diseases." Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter." By making these selections and typing in "autoimmune diseases" or synonyms into the "For these words:" box, you will only receive results on newsletters. The following list was generated using the options described above:

- **Infocus**

  Source: Detroit, MI: American Autoimmune Related Diseases Association, Inc. 1994. 12 p. (average).

  Contact: Available from American Autoimmune Related Diseases Association, Inc. 15475 Gratiot Avenue, Detroit, MI 48205. (313) 371-8600 or (800) 598-4668; FAX (313) 371-6002. Price: Free with membership.

  Summary: This newsletter for members of the American Autoimmune Related Diseases Association includes articles on a wide range of autoimmune disorders. A typical issue includes Association news and announcements, research and treatment updates, drug therapies currently being investigated, letters to the editor, specific information about various autoimmune diseases, dietary guidelines, meeting highlights, publication reviews, resource and support group information, and previews of upcoming seminars and programs.

Newsletter Articles

If you choose not to subscribe to a newsletter, you can nevertheless find references to newsletter articles. We recommend that you use the Combined Health Information Database, while limiting your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article."

By making these selections, and typing in "autoimmune diseases" (or synonyms) into the "For these words:" box, you will only receive results on newsletter articles. You should check back periodically with this database as it is updated every 3 months. The following is a typical result when searching for newsletter articles on autoimmune diseases:

- **What Are Autoimmune Diseases?**

  Source: Quarterly: The Journal of the National Pemphigus Foundation. Number 24: 10-11. Winter 2001.

  Contact: Available from National Pemphigus Foundation. P.O. Box 9606, Berkeley, CA 94709-0606. (510) 527-4970. Fax: (510) 527-8497. E-mail: pvnews@aol.com. Website: www.pemphigus.org.

  Summary: This newsletter article uses a question and answer format to provide people who have pemphigus or pemphigoid with information on the causes, diagnosis, genetic basis, and types of autoimmune diseases. These diseases occur when some interruption of the usual immune system process occurs or when some body tissue changes so that it is no longer recognized. The exact mechanisms causing these changes are not completely understood. Genetic predisposition and other factors have a role in initiating the disease process. Types of autoimmunity include organ specific disorders and nonorgan specific types. Organs and tissues frequently affected include the endocrine glands, components of the blood, the connective tissues, skin, muscles, and joints. Diagnosis is based on symptoms, findings from a physical examination, and results from laboratory tests. Although autoimmune diseases are chronic, their course is unpredictable. Therefore, patients should be monitored closely by their doctor. Autoimmune diseases are not contagious, so they cannot be spread to other people like infections.

- **Ear Manifestations of Autoimmune Disorders**

  Source: Infocus. 8(4): 9. December 2000.

  Contact: Available from American Autoimmune Related Diseases Association, Inc. 22100 Gratiot Avenue, East Detroit, MI 48021-2227. (810) 776-3900. Website: www.aarda.org.

  Summary: This newsletter article briefly reviews the ear and hearing manifestations of autoimmune disorders. Autoimmune inner ear problems can occur in conjunction with systemic autoimmune diseases, such as rheumatoid arthritis and lupus. The author stresses that the symptoms of autoimmune changes can often be treated (especially dizziness) and in a number of these cases, hearing can be restored. Approximately two thirds of patients affected by this condition are women, and about 30 percent of these have coexistent systemic autoimmune disease. The author stresses the importance of a careful medical history in the diagnosis and care of these patients. Once the diagnosis of autoimmune inner ear disease is made, the treatment is similar to that of systemic autoimmune diseases. The initial treatment is with steroids; other drugs used include methotrexate. The author notes

that there are side effects and risks of using these medications, but these can be kept to a minimum with proper attention and follow up.

- **Oral Manifestations of Autoimmune Diseases**

  Source: Skin and Allergy News. 31(4): 48. April 2000.

  Contact: Available from Skin and Allergy News. 12230 Wilkins Avenue, Rockville, MD 20852. (301) 816-8796.

  Summary: This brief news report on the oral manifestations of autoimmune diseases is from a newspaper for dermatologists and allergists. The article stresses that oral lesions often are the first indication of autoimmune disorders and other serious underlying diseases. The article discusses the oral manifestations of several diseases, including Behcet's syndrome, inflammatory bowel disease, cheilitis granulomatosa, lupus erythematosus, and Wegener's granulomatosis. For each disease, the article notes the typical oral symptoms, the incidence of such symptoms, and treatment options.

Academic Periodicals covering Autoimmune Diseases

Academic periodicals can be a highly technical yet valuable source of information on autoimmune diseases. We have compiled the following list of periodicals known to publish articles relating to autoimmune diseases and which are currently indexed within the National Library of Medicine's PubMed database (follow hyperlinks to view more information, summaries, etc., for each). In addition to these sources, to keep current on articles written on autoimmune diseases published by any of the periodicals listed below, you can simply follow the hyperlink indicated or go to the following Web site: **www.ncbi.nlm.nih.gov/pubmed**. Type the periodical's name into the search box to find the latest studies published.

If you want complete details about the historical contents of a periodical, you can also visit **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/** you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search." The following is a sample of periodicals which publish articles on autoimmune diseases:

- **Leukemia & Lymphoma. (Leuk Lymphoma)**
  http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi?field=0&regexp=Leukemia+&+Lymphoma&dispmax=20&dispstart=0

- **Rheumatic Diseases Clinics of North America. (Rheum Dis Clin North Am)**
  http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi?field=0&regexp=Rheumatic+Diseases+Clinics+of+North+America&dispmax=20&dispstart=0

- **The British Journal of Dermatology. (Br J Dermatol)**
  http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi?field=0&regexp=The+British+Journal+of+Dermatology&dispmax=20&dispstart=0

- **The Journal of Pediatrics. (J Pediatr)**
  http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi?field=0&regexp=The+Journal+of+Pediatrics&dispmax=20&dispstart=0

- **Transfusion Science. (Transfus Sci)**
  http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi?field=0&regexp=Transfusion+Science&dispmax=20&dispstart=0

Vocabulary Builder

Cheilitis: Inflammation of the lips. It is of various etiologies and degrees of pathology. [NIH]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

Vaccine: A suspension of attenuated or killed microorganisms (bacteria, viruses, or rickettsiae), administered for the prevention, amelioration or treatment of infectious diseases. [EU]

Varicella: Chicken pox. [EU]

CHAPTER 9. PHYSICIAN GUIDELINES AND DATABASES

Overview

Doctors and medical researchers rely on a number of information sources to help patients with their conditions. Many will subscribe to journals or newsletters published by their professional associations or refer to specialized textbooks or clinical guides published for the medical profession. In this chapter, we focus on databases and Internet-based guidelines created or written for this professional audience.

NIH Guidelines

For the more common diseases, The National Institutes of Health publish guidelines that are frequently consulted by physicians. Publications are typically written by one or more of the various NIH Institutes. For physician guidelines, commonly referred to as "clinical" or "professional" guidelines, you can visit the following Institutes:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**

- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/health/diseases.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[27] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[28]

- **Bioethics:** Access to published literature on the ethical, legal and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**

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[27] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[28] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Cancer Information:** Access to caner-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**
- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

While all of the above references may be of interest to physicians who study and treat autoimmune diseases, the following are particularly noteworthy.

The Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to "Brochure/Pamphlet," "Fact Sheet," or "Information Package" and autoimmune diseases using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For the publication date, select "All Years," select your preferred language, and the format option "Fact Sheet." By making these selections and typing "autoimmune diseases" (or synonyms) into the "For these words:" box above, you will only receive

results on fact sheets dealing with autoimmune diseases. The following is a sample result:

- **Fibromyalgia**

  Source: New York, NY: Nidus Information Services. 1997. 8 p.

  Contact: Available from Nidus Information Services, 175 Fifth Avenue, Suite 2338, New York, NY 10010. (212) 260-4268. (800) 334-WELL. (212) 529-2349 (fax).

  Summary: This report for health professionals and individuals with fibromyalgia uses a question-and-answer format to present an overview of fibromyalgia. The symptoms of fibromyalgia are identified. The primary causes of fibromyalgia are outlined, including genetic and biologic factors, chronic sleep disturbance, post-traumatic stress disorder, and hypervigilance. Diagnostic criteria and tests for fibromyalgia are described. Other conditions that exhibit the same symptoms as fibromyalgia are discussed, including chronic fatigue syndrome, Lyme disease, other myalgias, rheumatoid arthritis and other autoimmune diseases, other medical conditions, major depression disorder, and sleep disturbances. Drug and alcohol use and exposure to chemicals and other toxins may also cause some symptoms of fibromyalgia. In addition, the treatment and management of fibromyalgia are reviewed, focusing on exercise, drug therapy, cognitive therapy, stress reduction techniques, and alternative therapies.

- **Questions and Answers About Autoimmunity**

  Source: Bethesda, MD: National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Information Clearinghouse. 2002. 32 p.

  Contact: Available from National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Information Clearinghouse. 1 AMS Circle, Bethesda, MD 20892-3675. (877) 226-4267 toll-free or (301) 495-4484. Fax (301) 718-6366. TTY (301) 565-2966. E-mail: NIAMSInfo@mail.nih.gov. Website: www.niams.nih.gov. Price: 1 to 25 copies free. Order Number: AR-242 QA (booklet), or AR-242L QA (large print fact sheet).

  Summary: This booklet provides people who have an autoimmune disease with information on the causes, diagnosis, and treatment of such diseases. Autoimmune diseases occur when the body attacks its own cells as invaders. Although the cause of autoimmunity is unknown, most scientists believe that genetic and environmental factors are involved. Autoimmunity can affect almost any part of the body, and the problems caused by autoimmunity depend on the tissues targeted. Diagnosis is

based on the medical history, a physical examination, and medical tests. Treatment depends on the type of disease and its symptoms and severity. The goals of treatment are to relieve symptoms, preserve organ function, and target disease mechanisms. The types of doctors who provide treatment for autoimmune diseases vary, and they include rheumatologists, endocrinologists, neurologists, hematologists, gastroenterologists, dermatologists, and nephrologists. Problems that people experience with an autoimmune disease also vary and may be related to self esteem, self care, family relationships, sexual relations, and pregnancy. Research is being conducted to help people with autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, lupus nephritis, vitiligo, type 1 diabetes, multiple sclerosis, and multiple autoimmune diseases. The booklet includes a list of government and other organizations that can provide information about autoimmunity. Appendices provide glossaries of terms and diseases.

- **What Causes Scleroderma?**

  Source: Danvers, MA: Scleroderma Foundation. 2000. 6 p.

  Contact: Available from Scleroderma Foundation. 12 Kent Way, Suite 101, Byfield, MA 01922. (800) 722-4673 or (978) 463-5843. Fax (978) 463-5809. E-mail: sfinfo@scleroderma.org. Website: www.scleroderma.org. Price: Single copy $1.00.

  Summary: This pamphlet for people with scleroderma provides information on clinical and laboratory features of scleroderma that offer clues to the cause of this disease. Almost every patient with scleroderma has a condition known as Raynaud's phenomenon, which is associated with tissue damage and ulceration caused by low blood flow. Most people with scleroderma show evidence of an autoimmune reaction because immune cells, known as T-cells, are found in abnormal numbers in the tissues of patients with scleroderma. Almost all patients with scleroderma develop a fibrotic reaction in the tissues targeted in scleroderma. In addition, a genetic basis for scleroderma has been suggested by the fact that scleroderma occurs among patients whose family members are more likely to have other autoimmune diseases. The brochure uses these features of scleroderma to suggest a possible mechanism by which it occurs. In addition, it presents the mission of the Scleroderma Foundation.

- **What Do These Diseases Have in Common? Autoimmunity**

  Source: Detroit, MI: American Autoimmune Related Diseases Association, Inc. 8 p.

Contact: American Autoimmune Related Diseases Association, Inc. Michigan National Bank Building, 15475 Gratiot Avenue, Detroit, MI 48205. (313) 371-8600.

Summary: This pamphlet presents an overview of autoimmunity, focusing on what autoimmunity is, what causes autoimmunity, and how autoimmunity is treated. In addition, it describes organ-specific and non-organ-specific types of autoimmune disorders, discusses the role of genetics in autoimmune disease, lists autoimmune diseases, and presents facts about the American Autoimmune Related Diseases Association.

The NLM Gateway[29]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing "one-stop searching" for many of NLM's information resources or databases.[30] One target audience for the Gateway is the Internet user who is new to NLM's online resources and does not know what information is available or how best to search for it. This audience may include physicians and other healthcare providers, researchers, librarians, students, and, increasingly, patients, their families, and the public.[31] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "autoimmune diseases" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

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[29] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[30] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

[31] Other users may find the Gateway useful for an overall search of NLM's information resources. Some searchers may locate what they need immediately, while others will utilize the Gateway as an adjunct tool to other NLM search services such as PubMed® and MEDLINEplus®. The Gateway connects users with multiple NLM retrieval systems while also providing a search interface for its own collections. These collections include various types of information that do not logically belong in PubMed, LOCATORplus, or other established NLM retrieval systems (e.g., meeting announcements and pre-1966 journal citations). The Gateway will provide access to the information found in an increasing number of NLM retrieval systems in several phases.

Results Summary

Category	Items Found
Journal Articles	344858
Books / Periodicals / Audio Visual	2564
Consumer Health	293
Meeting Abstracts	3093
Other Collections	100
Total	350908

HSTAT[32]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[33] HSTAT's audience includes healthcare providers, health service researchers, policy makers, insurance companies, consumers, and the information professionals who serve these groups. HSTAT provides access to a wide variety of publications, including clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[34] Simply search by "autoimmune diseases" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[35]

Some patients may wish to have access to a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. To this end, we

[32] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.
[33] The HSTAT URL is **http://hstat.nlm.nih.gov/**.
[34] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.
[35] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

recommend "Coffee Break," a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[36] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[37] This site has new articles every few weeks, so it can be considered an online magazine of sorts, and intended for general background information. You can access the Coffee Break Web site at **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are a few examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Image Engine:** Multimedia electronic medical record system that integrates a wide range of digitized clinical images with textual data stored in the University of Pittsburgh Medical Center's MARS electronic medical record system; see the following Web site: **http://www.cml.upmc.edu/cml/imageengine/imageEngine.html**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.
- **MedWeaver:** Prototype system that allows users to search differential diagnoses for any list of signs and symptoms, to search medical literature, and to explore relevant Web sites; see **http://www.med.virginia.edu/~wmd4n/medweaver.html**.
- **Metaphrase:** Middleware component intended for use by both caregivers and medical records personnel. It converts the informal language generally used by caregivers into terms from formal, controlled vocabularies; see **http://www.lexical.com/Metaphrase.html**.

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[36] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[37] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

The Genome Project and Autoimmune Diseases

With all the discussion in the press about the Human Genome Project, it is only natural that physicians, researchers, and patients want to know about how human genes relate to autoimmune diseases. In the following section, we will discuss databases and references used by physicians and scientists who work in this area.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[38] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

Go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html** to search the database. Type "autoimmune diseases" (or synonyms) in the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. By following these links, especially the link titled "Database Links," you will be exposed to numerous specialized databases that are largely used by the scientific community. These databases are overly technical and seldom used by the general public, but offer an abundance of information. The following is an example of the results you can obtain from the OMIM for autoimmune diseases:

- **Autoimmune Diseases**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?109100

[38] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by the system of the body associated with it. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to re-visit it from time to time. The following systems and associated disorders are addressed:

- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**
- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, Amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, Fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, Spinocerebellar atrophy, Williams syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**
- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Baldness, Cockayne syndrome, Glaucoma, SRY: sex determination, Tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic Fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Nucleotide Sequence Database (Genbank):**
  Web site:
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **Taxonomy:** Organisms in GenBank,
  Web site:
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/**, and then select the database that you would like to search. The databases available are listed in

the drop box next to "Search." In the box next to "for," enter "autoimmune diseases" (or synonyms) and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[39]

This online resource can be quite useful. It has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html** you can also search across syndromes using an alphabetical index**.** You can also search at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[40]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "autoimmune diseases" (or synonyms) into the search box, and review the

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[39] Adapted from the National Library of Medicine: **http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html**.

[40] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html#mission**.

results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms). This database is extremely technical as it was created for specialists. The articles are the results which are the most accessible to non-professionals and often listed under the heading "Citations." The contact names are also accessible to non-professionals.

Specialized References

The following books are specialized references written for professionals interested in autoimmune diseases (sorted alphabetically by title, hyperlinks provide rankings, information, and reviews at Amazon.com):

- **2003 Pocket Book of Infectious Disease Therapy** by John G. Bartlett; 12th edition (June 15, 2003), Lippincott, Williams & Wilkins Publishers; ISBN: 0781738962;
  http://www.amazon.com/exec/obidos/ASIN/0781738962/icongroupinterna
- **Immunology and Evolution of Infectious Disease** by Steven A. Frank; Paperback – 352 pages (August 2002), Princeton University Press; ISBN: 0691095957;
  http://www.amazon.com/exec/obidos/ASIN/0691095957/icongroupinterna
- **Infectious Disease Epidemiology: Theory and Practice** by Kenrad E. Nelson, et al; Hardcover – 600 pages (May 2000), Aspen Publishers, Inc.; ISBN: 083421766X;
  http://www.amazon.com/exec/obidos/ASIN/083421766X/icongroupinterna
- **Infectious Disease Pearls (The Pearls Series)** by Steven A. Sahn (Editor), et al; Paperback – 250 pages (November 1998), Hanley & Belfus; ISBN: 1560532033;
  http://www.amazon.com/exec/obidos/ASIN/1560532033/icongroupinterna
- **Manual of Clinical Problems in Infectious Disease** by Nelson M. Gantz, et al; Spiral-bound -- 523 pages, 4th edition (May 15, 1999), Lippincott Williams & Wilkins Publishers; ISBN: 0781719100;
  http://www.amazon.com/exec/obidos/ASIN/0781719100/icongroupinterna
- **Mims' Pathogenesis of Infectious Disease** by Cedric A. Mims, et al; Paperback **--** 474 pages, 5th edition (January 15, 2001), Academic Press; ISBN: 0124982654;
  http://www.amazon.com/exec/obidos/ASIN/0124982654/icongroupinterna
- **A Practical Approach to Infectious Diseases** by Richard E. Reese, M.D. (Editor), Robert F. Betts, M.D. (Editor); Paperback, 4th edition (September

1996), Little Brown & Co.; ISBN: 0316737216;
http://www.amazon.com/exec/obidos/ASIN/0316737216/icongroupinterna

Vocabulary Builder

Acne: An inflammatory disease of the pilosebaceous unit, the specific type usually being indicated by a modifying term; frequently used alone to designate common acne, or acne vulgaris. [EU]

Bacteriostatic: 1. inhibiting the growth or multiplication of bacteria. 2. an agent that inhibits the growth or multiplication of bacteria. [EU]

Candidiasis: Infection with a fungus of the genus Candida. It is usually a superficial infection of the moist cutaneous areas of the body, and is generally caused by C. albicans; it most commonly involves the skin (dermatocandidiasis), oral mucous membranes (thrush, def. 1), respiratory tract (bronchocandidiasis), and vagina (vaginitis). Rarely there is a systemic infection or endocarditis. Called also moniliasis, candidosis, oidiomycosis, and formerly blastodendriosis. [EU]

Cataract: An opacity, partial or complete, of one or both eyes, on or in the lens or capsule, especially an opacity impairing vision or causing blindness. The many kinds of cataract are classified by their morphology (size, shape, location) or etiology (cause and time of occurrence). [EU]

Conjunctivitis: Inflammation of the conjunctiva, generally consisting of conjunctival hyperaemia associated with a discharge. [EU]

Echinacea: A genus of perennial herbs used topically and internally. It contains echinacoside, glycosides, inulin, isobutyl amides, resin, and sesquiterpenes. [NIH]

Fibroblasts: Connective tissue cells which secrete an extracellular matrix rich in collagen and other macromolecules. [NIH]

Papule: A small circumscribed, superficial, solid elevation of the skin. [EU]

Stimulant: 1. producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. an agent or remedy that produces stimulation. [EU]

Tacrolimus: A macrolide isolated from the culture broth of a strain of Streptomyces tsukubaensis that has strong immunosuppressive activity in vivo and prevents the activation of T-lymphocytes in response to antigenic or mitogenic stimulation in vitro. [NIH]

Ulceration: 1. the formation or development of an ulcer. 2. an ulcer. [EU]

CHAPTER 10. DISSERTATIONS ON AUTOIMMUNE DISEASES

Overview

University researchers are active in studying almost all known diseases. The result of research is often published in the form of Doctoral or Master's dissertations. You should understand, therefore, that applied diagnostic procedures and/or therapies can take many years to develop after the thesis that proposed the new technique or approach was written.

In this chapter, we will give you a bibliography on recent dissertations relating to autoimmune diseases. You can read about these in more detail using the Internet or your local medical library. We will also provide you with information on how to use the Internet to stay current on dissertations.

Dissertations on Autoimmune Diseases

ProQuest Digital Dissertations is the largest archive of academic dissertations available. From this archive, we have compiled the following list covering dissertations devoted to autoimmune diseases. You will see that the information provided includes the dissertation's title, its author, and the author's institution. To read more about the following, simply use the Internet address indicated. The following covers recent dissertations dealing with autoimmune diseases:

- **Clinical and Experimental Studies of Organ-specific Autoimmune Diseases: with Special Reference to Addison's Disease and Autoimmune Hepatitis** by Gebre-medhin, Gennet; Phd from Uppsala Universitet (sweden), 2001, 70 pages
  http://wwwlib.umi.com/dissertations/fullcit/f498337

Keeping Current

As previously mentioned, an effective way to stay current on dissertations dedicated to autoimmune diseases is to use the database called *ProQuest Digital Dissertations* via the Internet, located at the following Web address: **http://wwwlib.umi.com/dissertations.** The site allows you to freely access the last two years of citations and abstracts. Ask your medical librarian if the library has full and unlimited access to this database. From the library, you should be able to do more complete searches than with the limited 2-year access available to the general public.

PART III. APPENDICES

ABOUT PART III

Part III is a collection of appendices on general medical topics which may be of interest to patients with autoimmune diseases and related conditions.

APPENDIX A. RESEARCHING YOUR MEDICATIONS

Overview

There are a number of sources available on new or existing medications which could be prescribed to patients with autoimmune diseases. While a number of hard copy or CD-Rom resources are available to patients and physicians for research purposes, a more flexible method is to use Internet-based databases. In this chapter, we will begin with a general overview of medications. We will then proceed to outline official recommendations on how you should view your medications. You may also want to research medications that you are currently taking for other conditions as they may interact with medications for autoimmune diseases. Research can give you information on the side effects, interactions, and limitations of prescription drugs used in the treatment of autoimmune diseases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

Your Medications: The Basics[41]

The Agency for Health Care Research and Quality has published extremely useful guidelines on how you can best participate in the medication aspects of autoimmune diseases. Taking medicines is not always as simple as swallowing a pill. It can involve many steps and decisions each day. The AHCRQ recommends that patients with autoimmune diseases take part in treatment decisions. Do not be afraid to ask questions and talk about your concerns. By taking a moment to ask questions early, you may avoid problems later. Here are some points to cover each time a new medicine is prescribed**:**

- Ask about all parts of your treatment, including diet changes, exercise, and medicines.
- Ask about the risks and benefits of each medicine or other treatment you might receive.
- Ask how often you or your doctor will check for side effects from a given medication.

Do not hesitate to ask what is important to you about your medicines. You may want a medicine with the fewest side effects, or the fewest doses to take each day. You may care most about cost, or how the medicine might affect how you live or work. Or, you may want the medicine your doctor believes will work the best. Telling your doctor will help him or her select the best treatment for you.

Do not be afraid to "bother" your doctor with your concerns and questions about medications for autoimmune diseases. You can also talk to a nurse or a pharmacist. They can help you better understand your treatment plan. Feel free to bring a friend or family member with you when you visit your doctor. Talking over your options with someone you trust can help you make better choices, especially if you are not feeling well. Specifically, ask your doctor the following:

- The name of the medicine and what it is supposed to do.
- How and when to take the medicine, how much to take, and for how long.
- What food, drinks, other medicines, or activities you should avoid while taking the medicine.
- What side effects the medicine may have, and what to do if they occur.

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[41] This section is adapted from AHCRQ: **http://www.ahcpr.gov/consumer/ncpiebro.htm**.

- If you can get a refill, and how often.
- About any terms or directions you do not understand.
- What to do if you miss a dose.
- If there is written information you can take home (most pharmacies have information sheets on your prescription medicines; some even offer large-print or Spanish versions).

Do not forget to tell your doctor about all the medicines you are currently taking (not just those for autoimmune diseases). This includes prescription medicines and the medicines that you buy over the counter. Then your doctor can avoid giving you a new medicine that may not work well with the medications you take now. When talking to your doctor, you may wish to prepare a list of medicines you currently take, the reason you take them, and how you take them. Be sure to include the following information for each:

- Name of medicine
- Reason taken
- Dosage
- Time(s) of day

Also include any over-the-counter medicines, such as:

- Laxatives
- Diet pills
- Vitamins
- Cold medicine
- Aspirin or other pain, headache, or fever medicine
- Cough medicine
- Allergy relief medicine
- Antacids
- Sleeping pills
- Others (include names)

Learning More about Your Medications

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications your doctor has recommended for autoimmune diseases. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the "U.S. Pharmacopeia (USP)." Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **www.usp.org**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database.[42]

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopoeia (USP). It is important to read the disclaimer by the USP (**http://www.nlm.nih.gov/medlineplus/drugdisclaimer.html**) before using the information provided.

Of course, we as editors cannot be certain as to what medications you are taking. Therefore, we have compiled a list of medications associated with the treatment of autoimmune diseases. Once again, due to space limitations, we only list a sample of medications and provide hyperlinks to ample documentation (e.g. typical dosage, side effects, drug-interaction risks, etc.). The following drugs have been mentioned in the Pharmacopeia and other sources as being potentially applicable to autoimmune diseases:

[42] Though cumbersome, the FDA database can be freely browsed at the following site: **www.fda.gov/cder/da/da.htm**.

Rh O (D) Immune Globulin

- **Systemic - U.S. Brands:** MICRhoGAM; RhoGAM
  http://www.nlm.nih.gov/medlineplus/druginfo/rhodimmunoglobulinsystemic202720.html

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. You may be able to access these sources from your local medical library or your doctor's office.

Reuters Health Drug Database

The Reuters Health Drug Database can be searched by keyword at the hyperlink: **http://www.reutershealth.com/frame2/drug.html**. The following medications are listed in the Reuters' database as associated with autoimmune diseases (including those with contraindications):[43]

- **Danazol**
  http://www.reutershealth.com/atoz/html/Danazol.htm
- **Mefenamic Acid**
  http://www.reutershealth.com/atoz/html/Mefenamic_Acid.htm

Mosby's GenRx

Mosby's GenRx database (also available on CD-Rom and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Information can be obtained at the following hyperlink: **http://www.genrx.com/Mosby/PhyGenRx/group.html**.

Physicians Desk Reference

The Physicians Desk Reference database (also available in CD-Rom and book format) is a full-text drug database. The database is searchable by brand

[43] Adapted from *A to Z Drug Facts* by Facts and Comparisons.

name, generic name or by indication. It features multiple drug interactions reports. Information can be obtained at the following hyperlink: **http://physician.pdr.net/physician/templates/en/acl/psuser_t.htm**.

Other Web Sites

A number of additional Web sites discuss drug information. As an example, you may like to look at **www.drugs.com** which reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. which allows users to download articles on various drugs and therapeutics for a nominal fee: **http://www.medletter.com/**.

Contraindications and Interactions (Hidden Dangers)

Some of the medications mentioned in the previous discussions can be problematic for patients with autoimmune diseases--not because they are used in the treatment process, but because of contraindications, or side effects. Medications with contraindications are those that could react with drugs used to treat autoimmune diseases or potentially create deleterious side effects in patients with autoimmune diseases. You should ask your physician about any contraindications, especially as these might apply to other medications that you may be taking for common ailments.

Drug-drug interactions occur when two or more drugs react with each other. This drug-drug interaction may cause you to experience an unexpected side effect. Drug interactions may make your medications less effective, cause unexpected side effects, or increase the action of a particular drug. Some drug interactions can even be harmful to you.

Be sure to read the label every time you use a nonprescription or prescription drug, and take the time to learn about drug interactions. These precautions may be critical to your health. You can reduce the risk of potentially harmful drug interactions and side effects with a little bit of knowledge and common sense.

Drug labels contain important information about ingredients, uses, warnings, and directions which you should take the time to read and understand. Labels also include warnings about possible drug interactions. Further, drug labels may change as new information becomes available. This is why it's especially important to read the label every time you use a

medication. When your doctor prescribes a new drug, discuss all over-the-counter and prescription medications, dietary supplements, vitamins, botanicals, minerals and herbals you take as well as the foods you eat. Ask your pharmacist for the package insert for each prescription drug you take. The package insert provides more information about potential drug interactions.

A Final Warning

At some point, you may hear of alternative medications from friends, relatives, or in the news media. Advertisements may suggest that certain alternative drugs can produce positive results for patients with autoimmune diseases. Exercise caution--some of these drugs may have fraudulent claims, and others may actually hurt you. The Food and Drug Administration (FDA) is the official U.S. agency charged with discovering which medications are likely to improve the health of patients with autoimmune diseases. The FDA warns patients to watch out for[44]:

- Secret formulas (real scientists share what they know)
- Amazing breakthroughs or miracle cures (real breakthroughs don't happen very often; when they do, real scientists do not call them amazing or miracles)
- Quick, painless, or guaranteed cures
- If it sounds too good to be true, it probably isn't true.

If you have any questions about any kind of medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

General References

In addition to the resources provided earlier in this chapter, the following general references describe medications (sorted alphabetically by title; hyperlinks provide rankings, information and reviews at Amazon.com):

- **Antimicrobial Pharmacodynamics in Theory and Clinical Practice** by C. H. Nightingale (Editor), et al; Hardcover – 416 pages, 1st edition (January

[44] This section has been adapted from **http://www.fda.gov/opacom/lowlit/medfraud.html**.

15, 2002), Marcel Dekker; ISBN: 0824705610; **http://www.amazon.com/exec/obidos/ASIN/0824705610/icongroupinterna**

- **Antimicrobial Therapy and Vaccines** by Victor L. Yu (Editor), et al; **Hardcover -** 1460 pages, 1st edition (January 15, 1999), Lippincott, Williams & Wilkins; ISBN: 068330061X; **http://www.amazon.com/exec/obidos/ASIN/068330061X/icongroupinterna**
- **Essentials of Antimicrobial Pharmacology: A Guide to Fundamentals for Practice** by Paul H. Axelsen; Paperback – 141 pages, 1st edition (January 15, 2002), Humana Press; ISBN: 0896038424; **http://www.amazon.com/exec/obidos/ASIN/0896038424/icongroupinterna**
- **Macrolide Antibiotics: Chemistry, Biology, and Practice** by Satoshi Omura (Editor); Hardcover – 768 pages, 2nd edition (June 15, 2002), Academic Press; ISBN: 0125264518; **http://www.amazon.com/exec/obidos/ASIN/0125264518/icongroupinterna**
- **Management of Antimicrobials in Infectious Diseases: Impact of Antibiotic Resistance** by Arch G. Mainous, Ph.D. (Editor), et al; Hardcover – 350 pages, 1st edition (January 15, 2001), Humana Press; ISBN: 0896038211; **http://www.amazon.com/exec/obidos/ASIN/0896038211/icongroupinterna**
- **Vaccines** by Stanley A., Md. Plotkin (Editor), et al; Hardcover - 1230 pages, 3rd edition (February 15, 1999), W B Saunders Co.; ISBN: 0721674437; **http://www.amazon.com/exec/obidos/ASIN/0721674437/icongroupinterna**

Vocabulary Builder

The following vocabulary builder gives definitions of words used in this chapter that have not been defined in previous chapters:

Antibiotic: A chemical substance produced by a microorganism which has the capacity, in dilute solutions, to inhibit the growth of or to kill other microorganisms. Antibiotics that are sufficiently nontoxic to the host are used as chemotherapeutic agents in the treatment of infectious diseases of man, animals and plants. [EU]

Danazol: A synthetic steroid with antigonadotropic and anti-estrogenic activities that acts as an anterior pituitary suppressant by inhibiting the pituitary output of gonadotropins. It possesses some androgenic properties. Danazol has been used in the treatment of endometriosis and some benign breast disorders. [NIH]

Mefenamic Acid: A non-steroidal anti-inflammatory agent with analgesic,

anti-inflammatory, and antipyretic properties. It is an inhibitor of cyclooxygenase. [NIH]

Pharmacodynamics: The study of the biochemical and physiological effects of drugs and the mechanisms of their actions, including the correlation of actions and effects of drugs with their chemical structure; also, such effects on the actions of a particular drug or drugs. [EU]

APPENDIX B. RESEARCHING ALTERNATIVE MEDICINE

Overview

Complementary and alternative medicine (CAM) is one of the most contentious aspects of modern medical practice. You may have heard of these treatments on the radio or on television. Maybe you have seen articles written about these treatments in magazines, newspapers, or books. Perhaps your friends or doctor have mentioned alternatives.

In this chapter, we will begin by giving you a broad perspective on complementary and alternative therapies. Next, we will introduce you to official information sources on CAM relating to autoimmune diseases. Finally, at the conclusion of this chapter, we will provide a list of readings on autoimmune diseases from various authors. We will begin, however, with the National Center for Complementary and Alternative Medicine's (NCCAM) overview of complementary and alternative medicine.

What Is CAM?[45]

Complementary and alternative medicine (CAM) covers a broad range of healing philosophies, approaches, and therapies. Generally, it is defined as those treatments and healthcare practices which are not taught in medical schools, used in hospitals, or reimbursed by medical insurance companies. Many CAM therapies are termed "holistic," which generally means that the healthcare practitioner considers the whole person, including physical, mental, emotional, and spiritual health. Some of these therapies are also known as "preventive," which means that the practitioner educates and

[45] Adapted from the NCCAM: **http://nccam.nih.gov/nccam/fcp/faq/index.html#what-is**.

treats the person to prevent health problems from arising, rather than treating symptoms after problems have occurred.

People use CAM treatments and therapies in a variety of ways. Therapies are used alone (often referred to as alternative), in combination with other alternative therapies, or in addition to conventional treatment (sometimes referred to as complementary). Complementary and alternative medicine, or "integrative medicine," includes a broad range of healing philosophies, approaches, and therapies. Some approaches are consistent with physiological principles of Western medicine, while others constitute healing systems with non-Western origins. While some therapies are far outside the realm of accepted Western medical theory and practice, others are becoming established in mainstream medicine.

Complementary and alternative therapies are used in an effort to prevent illness, reduce stress, prevent or reduce side effects and symptoms, or control or cure disease. Some commonly used methods of complementary or alternative therapy include mind/body control interventions such as visualization and relaxation, manual healing including acupressure and massage, homeopathy, vitamins or herbal products, and acupuncture.

What Are the Domains of Alternative Medicine?[46]

The list of CAM practices changes continually. The reason being is that these new practices and therapies are often proved to be safe and effective, and therefore become generally accepted as "mainstream" healthcare practices. Today, CAM practices may be grouped within five major domains: (1) alternative medical systems, (2) mind-body interventions, (3) biologically-based treatments, (4) manipulative and body-based methods, and (5) energy therapies. The individual systems and treatments comprising these categories are too numerous to list in this sourcebook. Thus, only limited examples are provided within each.

Alternative Medical Systems

Alternative medical systems involve complete systems of theory and practice that have evolved independent of, and often prior to, conventional biomedical approaches. Many are traditional systems of medicine that are

[46] Adapted from the NCCAM: **http://nccam.nih.gov/nccam/fcp/classify/index.html**.

practiced by individual cultures throughout the world, including a number of venerable Asian approaches.

Traditional oriental medicine emphasizes the balance or disturbances of qi (pronounced chi) or vital energy in health and disease, respectively. Traditional oriental medicine consists of a group of techniques and methods including acupuncture, herbal medicine, oriental massage, and qi gong (a form of energy therapy). Acupuncture involves stimulating specific anatomic points in the body for therapeutic purposes, usually by puncturing the skin with a thin needle.

Ayurveda is India's traditional system of medicine. Ayurvedic medicine (meaning "science of life") is a comprehensive system of medicine that places equal emphasis on body, mind, and spirit. Ayurveda strives to restore the innate harmony of the individual. Some of the primary Ayurvedic treatments include diet, exercise, meditation, herbs, massage, exposure to sunlight, and controlled breathing.

Other traditional healing systems have been developed by the world's indigenous populations. These populations include Native American, Aboriginal, African, Middle Eastern, Tibetan, and Central and South American cultures. Homeopathy and naturopathy are also examples of complete alternative medicine systems.

Homeopathic medicine is an unconventional Western system that is based on the principle that "like cures like," i.e., that the same substance that in large doses produces the symptoms of an illness, in very minute doses cures it. Homeopathic health practitioners believe that the more dilute the remedy, the greater its potency. Therefore, they use small doses of specially prepared plant extracts and minerals to stimulate the body's defense mechanisms and healing processes in order to treat illness.

Naturopathic medicine is based on the theory that disease is a manifestation of alterations in the processes by which the body naturally heals itself and emphasizes health restoration rather than disease treatment. Naturopathic physicians employ an array of healing practices, including the following: diet and clinical nutrition, homeopathy, acupuncture, herbal medicine, hydrotherapy (the use of water in a range of temperatures and methods of applications), spinal and soft-tissue manipulation, physical therapies (such as those involving electrical currents, ultrasound, and light), therapeutic counseling, and pharmacology.

Mind-Body Interventions

Mind-body interventions employ a variety of techniques designed to facilitate the mind's capacity to affect bodily function and symptoms. Only a select group of mind-body interventions having well-documented theoretical foundations are considered CAM. For example, patient education and cognitive-behavioral approaches are now considered "mainstream." On the other hand, complementary and alternative medicine includes meditation, certain uses of hypnosis, dance, music, and art therapy, as well as prayer and mental healing.

Biological-Based Therapies

This category of CAM includes natural and biological-based practices, interventions, and products, many of which overlap with conventional medicine's use of dietary supplements. This category includes herbal, special dietary, orthomolecular, and individual biological therapies.

Herbal therapy employs an individual herb or a mixture of herbs for healing purposes. An herb is a plant or plant part that produces and contains chemical substances that act upon the body. Special diet therapies, such as those proposed by Drs. Atkins, Ornish, Pritikin, and Weil, are believed to prevent and/or control illness as well as promote health. Orthomolecular therapies aim to treat disease with varying concentrations of chemicals such as magnesium, melatonin, and mega-doses of vitamins. Biological therapies include, for example, the use of laetrile and shark cartilage to treat cancer and the use of bee pollen to treat autoimmune and inflammatory diseases.

Manipulative and Body-Based Methods

This category includes methods that are based on manipulation and/or movement of the body. For example, chiropractors focus on the relationship between structure and function, primarily pertaining to the spine, and how that relationship affects the preservation and restoration of health. Chiropractors use manipulative therapy as an integral treatment tool.

In contrast, osteopaths place particular emphasis on the musculoskeletal system and practice osteopathic manipulation. Osteopaths believe that all of the body's systems work together and that disturbances in one system may have an impact upon function elsewhere in the body. Massage therapists manipulate the soft tissues of the body to normalize those tissues.

Energy Therapies

Energy therapies focus on energy fields originating within the body (biofields) or those from other sources (electromagnetic fields). Biofield therapies are intended to affect energy fields (the existence of which is not yet experimentally proven) that surround and penetrate the human body. Some forms of energy therapy manipulate biofields by applying pressure and/or manipulating the body by placing the hands in or through these fields. Examples include Qi gong, Reiki and Therapeutic Touch.

Qi gong is a component of traditional oriental medicine that combines movement, meditation, and regulation of breathing to enhance the flow of vital energy (qi) in the body, improve blood circulation, and enhance immune function. Reiki, the Japanese word representing Universal Life Energy, is based on the belief that, by channeling spiritual energy through the practitioner, the spirit is healed and, in turn, heals the physical body. Therapeutic Touch is derived from the ancient technique of "laying-on of hands." It is based on the premises that the therapist's healing force affects the patient's recovery and that healing is promoted when the body's energies are in balance. By passing their hands over the patient, these healers identify energy imbalances.

Bioelectromagnetic-based therapies involve the unconventional use of electromagnetic fields to treat illnesses or manage pain. These therapies are often used to treat asthma, cancer, and migraine headaches. Types of electromagnetic fields which are manipulated in these therapies include pulsed fields, magnetic fields, and alternating current or direct current fields.

Can Alternatives Affect My Treatment?

A critical issue in pursuing complementary alternatives mentioned thus far is the risk that these might have undesirable interactions with your medical treatment. It becomes all the more important to speak with your doctor who can offer advice on the use of alternatives. Official sources confirm this view. Though written for women, we find that the National Women's Health Information Center's advice on pursuing alternative medicine is appropriate for patients of both genders and all ages.[47]

[47] Adapted from **http://www.4woman.gov/faq/alternative.htm**.

Is It Okay to Want Both Traditional and Alternative Medicine?

Should you wish to explore non-traditional types of treatment, be sure to discuss all issues concerning treatments and therapies with your healthcare provider, whether a physician or practitioner of complementary and alternative medicine. Competent healthcare management requires knowledge of both conventional and alternative therapies you are taking for the practitioner to have a complete picture of your treatment plan.

The decision to use complementary and alternative treatments is an important one. Consider before selecting an alternative therapy, the safety and effectiveness of the therapy or treatment, the expertise and qualifications of the healthcare practitioner, and the quality of delivery. These topics should be considered when selecting any practitioner or therapy.

Finding CAM References on Autoimmune Diseases

Having read the previous discussion, you may be wondering which complementary or alternative treatments might be appropriate for autoimmune diseases. For the remainder of this chapter, we will direct you to a number of official sources which can assist you in researching studies and publications. Some of these articles are rather technical, so some patience may be required.

The Combined Health Information Database

For a targeted search, The Combined Health Information Database is a bibliographic database produced by health-related agencies of the Federal Government (mostly from the National Institutes of Health). This database is updated four times a year at the end of January, April, July, and October. Check the titles, summaries, and availability of CAM-related information by using the "Simple Search" option at the following Web site: **http://chid.nih.gov/simple/simple.html**. In the drop box at the top, select "Complementary and Alternative Medicine." Then type "autoimmune diseases" (or synonyms) in the second search box. We recommend that you select 100 "documents per page" and to check the "whole records" options. The following was extracted using this technique:

- **Methylsulfonylmenthane: Nutraceutical of the Next Century?**

  Source: Alternative and Complementary Therapies. 5(6): 386-389. December 1999.

Summary: This journal article discusses the potential therapeutic applications of methylsulfonylmethane (MSM). The first part reviews information about MSM's veterinary use, chemical and metabolic properties, metabolic fate, nutritional property, toxicity and side effects, and therapeutic effects in animal studies. The second part reviews clinical research and case reports, and then summarizes the experiences of Drs. S.W. Jacob and R.M. Lawrence, who have used MSM for more than 20 years in a wide variety of applications. Anecdotal evidence from their cases suggest that MSM may offer some benefits for patients with arthritis, other pain and inflammation-related conditions, allergy, asthma, sinusitis, and autoimmune diseases. The article concludes with a brief review of unwarranted claims for MSM; it has 19 references.

- **Bee Products: Properties and Applications**

  Source: Positive Health. Number 25: 41-46. February 1998.

  Summary: This journal article reviews the chemistry, properties, and applications of honey bee products. It describes honey, pollen, propolis, royal jelly, bee venom, and beeswax. According to the author, the usefulness of honey bee products for people is based on the same properties that make these products useful for the bees themselves. The article describes ancient uses, chemical composition, modern applications, nutritional elements, and properties of honey bee products. Possible medicinal properties noted include wound healing (honey), antimicrobial effects (honey, propolis, and royal jelly), dietary supplementation (pollen), treatment of autoimmune diseases (bee venom), and treatment of upper respiratory disorders (beeswax). The author concludes that although honey bee products naturally are intended for the use of bees themselves, bee products may be beneficial to humans. This journal article contains 4 illustrations, 6 tables, and 25 references.

- **Evolution of the Health Benefits of Soy Isoflavones (44249)**

  Source: Proceedings of the Society for Experimental Biology and Medicine. 217: 386-392. 1998.

  Summary: This journal article provides an overview of the health benefits of soy isoflavones. Soy is a major dietary source of the isoflavones genistein and daidzein, which are thought to have beneficial effects. Although soy has been part of the Asian diet for several thousand years, the first recorded growth of soybeans in the West did not occur until the 18th century in botanical gardens in England and France. Ancient Chinese texts discuss the medicinal value of soy, but they favored the black soybean (kuroname) for medicinal purposes over the more familiar

yellow bean grown in the United States. The heavy consumption of soy in southeast Asian populations is associated with lowered rates of certain cancers and cardiovascular disease. Recent experimental evidence suggests that phytochemicals in soy are responsible for its beneficial effects, which also may include the prevention of osteoporosis (thinning of the bones), a hereditary chronic nose-bleed syndrome, and autoimmune diseases. Several mechanisms of action of isoflavones have been proposed, both through estrogen-dependent and estrogen-independent pathways. The article has 5 figures and 75 references. (AA-M).

- **Applications of EDTA Chelation Therapy**

  Source: Alternative Medicine Review. 2(6): 426-432. December 1997.

  Summary: This journal article discusses the use of ethylenediamine tetraacetic acid (EDTA) chelation therapy for the treatment of atherosclerosis and other chronic degenerative diseases. It describes the chelating actions of EDTA, reviews the history of interest in EDTA chelation therapy from the 1950's to the present, and discusses current applications of EDTA chelation therapy. The most common use of EDTA chelation therapy is for the treatment of occlusive vascular disease of the coronary, peripheral, and/or cerebral arteries. This treatment consists of a series of intravenous infusions with EDTA accompanied by vitamins, minerals, and other supplements. The treatment is aimed at removing excessive accumulations of aluminum, iron, copper, and toxic heavy metals, which accelerate oxidative reactions in the body and increase vascular complications. Because of its mechanism of action, EDTA also might be effective in preventing or treating rapid oxidation of low density lipoprotein (LDL) cholesterol, ischemia-reperfusion injuries, arrhythmias, hypertension in the presence of low-level lead accumulation, and congestive cardiomyopathy due to iron overload. Other reports suggest that autoimmune diseases such as rheumatoid arthritis, Wegener's granulomatosis, and scleroderma respond to EDTA chelation therapy. The article has 59 references.

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov**) has created a link to the National Library of Medicine's databases to allow patients to search for articles that specifically relate to autoimmune diseases and complementary medicine. To search the database, go to the following

Web site: **www.nlm.nih.gov/nccam/camonpubmed.html**. Select "CAM on PubMed." Enter "autoimmune diseases" (or synonyms) into the search box. Click "Go." The following references provide information on particular aspects of complementary and alternative medicine (CAM) that are related to autoimmune diseases:

- **Amicrobial pustulosis associated with autoimmune diseases: healing with zinc supplementation.**
  Author(s): Beneton N, Wolkenstein P, Bagot M, Cosnes A, Wechsler J, Roujeau JC, Revuz J.
  Source: The British Journal of Dermatology. 2000 December; 143(6): 1306-10. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11122040&dopt=Abstract

- **Epstein-Barr virus associated diffuse large B-cell lymphoma complicated by autoimmune hemolytic anemia and pure red cell aplasia.**
  Author(s): Katayama H, Takeuchi M, Yoshino T, Munemasa M, Tada A, Soda R, Takahashi K.
  Source: Leukemia & Lymphoma. 2001 July; 42(3): 539-42.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11699422&dopt=Abstract

- **Photopheresis and autoimmune diseases.**
  Author(s): Mayes MD.
  Source: Rheumatic Diseases Clinics of North America. 2000 February; 26(1): 75-81, Viii-Ix. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10680195&dopt=Abstract

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering CAM and related topics. The following is a representative sample:

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**

- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**
- Healthnotes: **http://www.thedacare.org/healthnotes/**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- TPN.com: **http://www.tnp.com/**
- Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WellNet: **http://www.wellnet.ca/herbsa-c.htm**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,,00.html**

The following is a specific Web list relating to autoimmune diseases; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **General Overview**

  Depression
  Source: Integrative Medicine Communications; www.onemedicine.com
  Hyperlink: http://www.drkoop.com/interactivemedicine/ConsConditions/Depressioncc.html

  Diabetes Mellitus
  Source: Integrative Medicine Communications; www.onemedicine.com
  Hyperlink: http://www.drkoop.com/interactivemedicine/ConsConditions/DiabetesMellituscc.html

  Hypothyroidism
  Source: Healthnotes, Inc.; www.healthnotes.com
  Hyperlink: http://www.thedacare.org/healthnotes/Concern/Hypothyroidism.htm

Insomnia
Source: Prima Communications, Inc.
Hyperlink: http://www.personalhealthzone.com/pg000296.html

Lupus
Source: Integrative Medicine Communications;
www.onemedicine.com
Hyperlink:
http://www.drkoop.com/interactivemedicine/ConsConditions/SystemicLupusErythematosuscc.html

Lymphoma
Source: Integrative Medicine Communications;
www.onemedicine.com
Hyperlink:
http://www.drkoop.com/interactivemedicine/ConsConditions/Lymphomacc.html

Systemic Lupus Erythematosus
Source: Healthnotes, Inc.; www.healthnotes.com
Hyperlink:
http://www.thedacare.org/healthnotes/Concern/Lupus.htm

Systemic Lupus Erythematosus
Source: Integrative Medicine Communications;
www.onemedicine.com
Hyperlink:
http://www.drkoop.com/interactivemedicine/ConsConditions/SystemicLupusErythematosuscc.html

Thyroid Inflammation
Source: Integrative Medicine Communications;
www.onemedicine.com
Hyperlink:
http://www.drkoop.com/interactivemedicine/ConsConditions/Thyroiditiscc.html

Thyroiditis
Source: Integrative Medicine Communications;
www.onemedicine.com
Hyperlink:
http://www.drkoop.com/interactivemedicine/ConsConditions/Thyroiditiscc.html

- **Herbs and Supplements**

5-Hydroxytryptophan
Source: Healthnotes, Inc.; www.healthnotes.com
Hyperlink: http://www.thedacare.org/healthnotes/Supp/5-HTP.htm

ALA
Source: Integrative Medicine Communications; www.onemedicine.com
Hyperlink: http://www.drkoop.com/interactivemedicine/ConsSupplements/AlphaLinolenicAcidALAcs.html

Alpha-Linolenic Acid (ALA)
Source: Integrative Medicine Communications; www.onemedicine.com
Hyperlink: http://www.drkoop.com/interactivemedicine/ConsSupplements/AlphaLinolenicAcidALAcs.html

Cyclosporine
Source: Healthnotes, Inc.; www.healthnotes.com
Hyperlink: http://www.thedacare.org/healthnotes/Drug/Cyclosporine.htm

Dehydroepiandrosterone (DHEA)
Source: Healthnotes, Inc.; www.healthnotes.com
Hyperlink: http://www.thedacare.org/healthnotes/Supp/DHEA.htm

Dehydroepiandrosterone (DHEA)
Source: Integrative Medicine Communications; www.onemedicine.com
Hyperlink: http://www.drkoop.com/interactivemedicine/ConsSupplements/DehydroepiandrosteroneDHEAcs.html

DHEA
Source: Integrative Medicine Communications; www.onemedicine.com
Hyperlink: http://www.drkoop.com/interactivemedicine/ConsSupplements/DehydroepiandrosteroneDHEAcs.html

Eicosapentaenoic Acid (EPA)
Source: Integrative Medicine Communications; www.onemedicine.com
Hyperlink: http://www.drkoop.com/interactivemedicine/ConsSupplements/EicosapentaenoicAcidEPAcs.html

EPA
Source: Integrative Medicine Communications; www.onemedicine.com
Hyperlink: http://www.drkoop.com/interactivemedicine/ConsSupplements/EicosapentaenoicAcidEPAcs.html

Glutamine
Source: Integrative Medicine Communications; www.onemedicine.com
Hyperlink: http://www.drkoop.com/interactivemedicine/ConsSupplements/Glutaminecs.html

Melatonin
Source: Prima Communications, Inc.
Hyperlink: http://www.personalhealthzone.com/pg000207.html

Proteolytic Enzymes
Source: Prima Communications, Inc.
Hyperlink: http://www.personalhealthzone.com/pg000132.html

Reishi
Source: Prima Communications, Inc.
Hyperlink: http://www.personalhealthzone.com/pg000229.html

Thyroid Hormones
Source: Healthnotes, Inc.; www.healthnotes.com
Hyperlink:
http://www.thedacare.org/healthnotes/Drug/Thyroid_Hormones.htm

General References

A good place to find general background information on CAM is the National Library of Medicine. It has prepared within the MEDLINEplus system an information topic page dedicated to complementary and alternative medicine. To access this page, go to the MEDLINEplus site at: **www.nlm.nih.gov/medlineplus/alternativemedicine.html.** This Web site provides a general overview of various topics and can lead to a number of general sources. The following additional references describe, in broad terms, alternative and complementary medicine (sorted alphabetically by title; hyperlinks provide rankings, information, and reviews at Amazon.com):

- **Antibiotic Crisis, Antibiotic Alternatives** by Leon Chaitow; Hardcover – 240 pages (October 1998), Thorsons Publishing; ISBN: 0722537727; **http://www.amazon.com/exec/obidos/ASIN/0722537727/icongroupinterna**
- **Natural Alternatives to Antibiotics** by John McKenna; Paperback – 176 pages (November 1998), Avery Penguin Putnam; ISBN: 0895298392; **http://www.amazon.com/exec/obidos/ASIN/0895298392/icongroupinterna**

For additional information on complementary and alternative medicine, ask your doctor or write to:

National Institutes of Health
National Center for Complementary and Alternative Medicine Clearinghouse
P. O. Box 8218
Silver Spring, MD 20907-8218

Vocabulary Builder

The following vocabulary builder gives definitions of words used in this chapter that have not been defined in previous chapters:

Aluminum: A metallic element that has the atomic number 13, atomic symbol Al, and atomic weight 26.98. [NIH]

Arteries: The vessels carrying blood away from the heart. [NIH]

Cardiomyopathy: A general diagnostic term designating primary myocardial disease, often of obscure or unknown etiology. [EU]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cholesterol: The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Glutamine: A non-essential amino acid present abundantly throught the body and is involved in many metabolic processes. It is synthesized from glutamic acid and ammonia. It is the principal carrier of nitrogen in the body and is an important energy source for many cells. [NIH]

Hypertension: Persistently high arterial blood pressure. Various criteria for its threshold have been suggested, ranging from 140 mm. Hg systolic and 90 mm. Hg diastolic to as high as 200 mm. Hg systolic and 110 mm. Hg diastolic. Hypertension may have no known cause (essential or idiopathic h.) or be associated with other primary diseases (secondary h.). [EU]

Insomnia: Inability to sleep; abnormal wakefulness. [EU]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

Isoflavones: 3-Phenylchromones. Isomeric form of flavones in which the benzene group is attached to the 3 position of the benzopyran ring instead of the 2 position. [NIH]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

Propolis: Resinous substance obtained from beehives; contains many

different substances which may have antimicrobial or antimycotic activity topically; its extracts are called propolis resin or balsam. Synonyms: bee bread; hive dross; bee glue. [NIH]

Proteolytic: 1. pertaining to, characterized by, or promoting proteolysis. 2. an enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Reishi: A mushroom, Ganoderma lucidum, of the aphyllophorales order of basidomycetous fungi. It has long been used in traditional Chinese medicine in various forms. Contains sterols, coumarin, mannitol, polysaccharides, and triterpenoids. [NIH]

Reperfusion: Restoration of blood supply to tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. It is primarily a procedure for treating infarction or other ischemia, by enabling viable ischemic tissue to recover, thus limiting further necrosis. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing reperfusion injury. [NIH]

Sinusitis: Inflammation of a sinus. The condition may be purulent or nonpurulent, acute or chronic. Depending on the site of involvement it is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. [EU]

APPENDIX C. RESEARCHING NUTRITION

Overview

Since the time of Hippocrates, doctors have understood the importance of diet and nutrition to patients' health and well-being. Since then, they have accumulated an impressive archive of studies and knowledge dedicated to this subject. Based on their experience, doctors and healthcare providers may recommend particular dietary supplements to patients with autoimmune diseases. Any dietary recommendation is based on a patient's age, body mass, gender, lifestyle, eating habits, food preferences, and health condition. It is therefore likely that different patients with autoimmune diseases may be given different recommendations. Some recommendations may be directly related to autoimmune diseases, while others may be more related to the patient's general health. These recommendations, themselves, may differ from what official sources recommend for the average person.

In this chapter we will begin by briefly reviewing the essentials of diet and nutrition that will broadly frame more detailed discussions of autoimmune diseases. We will then show you how to find studies dedicated specifically to nutrition and autoimmune diseases.

Food and Nutrition: General Principles

What Are Essential Foods?

Food is generally viewed by official sources as consisting of six basic elements: (1) fluids, (2) carbohydrates, (3) protein, (4) fats, (5) vitamins, and (6) minerals. Consuming a combination of these elements is considered to be a healthy diet:

- **Fluids** are essential to human life as 80-percent of the body is composed of water. Water is lost via urination, sweating, diarrhea, vomiting, diuretics (drugs that increase urination), caffeine, and physical exertion.
- **Carbohydrates** are the main source for human energy (thermoregulation) and the bulk of typical diets. They are mostly classified as being either simple or complex. Simple carbohydrates include sugars which are often consumed in the form of cookies, candies, or cakes. Complex carbohydrates consist of starches and dietary fibers. Starches are consumed in the form of pastas, breads, potatoes, rice, and other foods. Soluble fibers can be eaten in the form of certain vegetables, fruits, oats, and legumes. Insoluble fibers include brown rice, whole grains, certain fruits, wheat bran and legumes.
- **Proteins** are eaten to build and repair human tissues. Some foods that are high in protein are also high in fat and calories. Food sources for protein include nuts, meat, fish, cheese, and other dairy products.
- **Fats** are consumed for both energy and the absorption of certain vitamins. There are many types of fats, with many general publications recommending the intake of unsaturated fats or those low in cholesterol.

Vitamins and minerals are fundamental to human health, growth, and, in some cases, disease prevention. Most are consumed in your diet (exceptions being vitamins K and D which are produced by intestinal bacteria and sunlight on the skin, respectively). Each vitamin and mineral plays a different role in health. The following outlines essential vitamins:

- **Vitamin A** is important to the health of your eyes, hair, bones, and skin; sources of vitamin A include foods such as eggs, carrots, and cantaloupe.
- **Vitamin B^1**, also known as thiamine, is important for your nervous system and energy production; food sources for thiamine include meat, peas, fortified cereals, bread, and whole grains.
- **Vitamin B^2**, also known as riboflavin, is important for your nervous system and muscles, but is also involved in the release of proteins from

nutrients; food sources for riboflavin include dairy products, leafy vegetables, meat, and eggs.

- **Vitamin B^3**, also known as niacin, is important for healthy skin and helps the body use energy; food sources for niacin include peas, peanuts, fish, and whole grains
- **Vitamin B^6**, also known as pyridoxine, is important for the regulation of cells in the nervous system and is vital for blood formation; food sources for pyridoxine include bananas, whole grains, meat, and fish.
- **Vitamin B^{12}** is vital for a healthy nervous system and for the growth of red blood cells in bone marrow; food sources for vitamin B^{12} include yeast, milk, fish, eggs, and meat.
- **Vitamin C** allows the body's immune system to fight various diseases, strengthens body tissue, and improves the body's use of iron; food sources for vitamin C include a wide variety of fruits and vegetables.
- **Vitamin D** helps the body absorb calcium which strengthens bones and teeth; food sources for vitamin D include oily fish and dairy products.
- **Vitamin E** can help protect certain organs and tissues from various degenerative diseases; food sources for vitamin E include margarine, vegetables, eggs, and fish.
- **Vitamin K** is essential for bone formation and blood clotting; common food sources for vitamin K include leafy green vegetables.
- **Folic Acid** maintains healthy cells and blood and, when taken by a pregnant woman, can prevent her fetus from developing neural tube defects; food sources for folic acid include nuts, fortified breads, leafy green vegetables, and whole grains.

It should be noted that one can overdose on certain vitamins which become toxic if consumed in excess (e.g. vitamin A, D, E and K).
Like vitamins, minerals are chemicals that are required by the body to remain in good health. Because the human body does not manufacture these chemicals internally, we obtain them from food and other dietary sources. The more important minerals include:

- **Calcium** is needed for healthy bones, teeth, and muscles, but also helps the nervous system function; food sources for calcium include dry beans, peas, eggs, and dairy products.
- **Chromium** is helpful in regulating sugar levels in blood; food sources for chromium include egg yolks, raw sugar, cheese, nuts, beets, whole grains, and meat.

- **Fluoride** is used by the body to help prevent tooth decay and to reinforce bone strength; sources of fluoride include drinking water and certain brands of toothpaste.
- **Iodine** helps regulate the body's use of energy by synthesizing into the hormone thyroxine; food sources include leafy green vegetables, nuts, egg yolks, and red meat.
- **Iron** helps maintain muscles and the formation of red blood cells and certain proteins; food sources for iron include meat, dairy products, eggs, and leafy green vegetables.
- **Magnesium** is important for the production of DNA, as well as for healthy teeth, bones, muscles, and nerves; food sources for magnesium include dried fruit, dark green vegetables, nuts, and seafood.
- **Phosphorous** is used by the body to work with calcium to form bones and teeth; food sources for phosphorous include eggs, meat, cereals, and dairy products.
- **Selenium** primarily helps maintain normal heart and liver functions; food sources for selenium include wholegrain cereals, fish, meat, and dairy products.
- **Zinc** helps wounds heal, the formation of sperm, and encourage rapid growth and energy; food sources include dried beans, shellfish, eggs, and nuts.

The United States government periodically publishes recommended diets and consumption levels of the various elements of food. Again, your doctor may encourage deviations from the average official recommendation based on your specific condition. To learn more about basic dietary guidelines, visit the Web site: **http://www.health.gov/dietaryguidelines/**. Based on these guidelines, many foods are required to list the nutrition levels on the food's packaging. Labeling Requirements are listed at the following site maintained by the Food and Drug Administration: **http://www.cfsan.fda.gov/~dms/lab-cons.html**. When interpreting these requirements, the government recommends that consumers become familiar with the following abbreviations before reading FDA literature:[48]

- **DVs (Daily Values):** A new dietary reference term that will appear on the food label. It is made up of two sets of references, DRVs and RDIs.
- **DRVs (Daily Reference Values):** A set of dietary references that applies to fat, saturated fat, cholesterol, carbohydrate, protein, fiber, sodium, and potassium.

[48] Adapted from the FDA: **http://www.fda.gov/fdac/special/foodlabel/dvs.html**.

- **RDIs (Reference Daily Intakes):** A set of dietary references based on the Recommended Dietary Allowances for essential vitamins and minerals and, in selected groups, protein. The name "RDI" replaces the term "U.S. RDA."
- **RDAs (Recommended Dietary Allowances):** A set of estimated nutrient allowances established by the National Academy of Sciences. It is updated periodically to reflect current scientific knowledge.

What Are Dietary Supplements?[49]

Dietary supplements are widely available through many commercial sources, including health food stores, grocery stores, pharmacies, and by mail. Dietary supplements are provided in many forms including tablets, capsules, powders, gel-tabs, extracts, and liquids. Historically in the United States, the most prevalent type of dietary supplement was a multivitamin/mineral tablet or capsule that was available in pharmacies, either by prescription or "over the counter." Supplements containing strictly herbal preparations were less widely available. Currently in the United States, a wide array of supplement products are available, including vitamin, mineral, other nutrients, and botanical supplements as well as ingredients and extracts of animal and plant origin.

The Office of Dietary Supplements (ODS) of the National Institutes of Health is the official agency of the United States which has the expressed goal of acquiring "new knowledge to help prevent, detect, diagnose, and treat disease and disability, from the rarest genetic disorder to the common cold."[50] According to the ODS, dietary supplements can have an important impact on the prevention and management of disease and on the maintenance of health.[51] The ODS notes that considerable research on the effects of dietary supplements has been conducted in Asia and Europe where

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[49] This discussion has been adapted from the NIH: **http://ods.od.nih.gov/whatare/whatare.html**.

[50] Contact: The Office of Dietary Supplements, National Institutes of Health, Building 31, Room 1B29, 31 Center Drive, MSC 2086, Bethesda, Maryland 20892-2086, Tel: (301) 435-2920, Fax: (301) 480-1845, E-mail: **ods@nih.gov**.

[51] Adapted from **http://ods.od.nih.gov/about/about.html**. The Dietary Supplement Health and Education Act defines dietary supplements as "a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, mineral, amino acid, herb or other botanical; or a dietary substance for use to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of any ingredient described above; and intended for ingestion in the form of a capsule, powder, softgel, or gelcap, and not represented as a conventional food or as a sole item of a meal or the diet."

the use of plant products, in particular, has a long tradition. However, the overwhelming majority of supplements have not been studied scientifically. To explore the role of dietary supplements in the improvement of health care, the ODS plans, organizes, and supports conferences, workshops, and symposia on scientific topics related to dietary supplements. The ODS often works in conjunction with other NIH Institutes and Centers, other government agencies, professional organizations, and public advocacy groups.

To learn more about official information on dietary supplements, visit the ODS site at **http://ods.od.nih.gov/whatare/whatare.html**. Or contact:

The Office of Dietary Supplements
National Institutes of Health
Building 31, Room 1B29
31 Center Drive, MSC 2086
Bethesda, Maryland 20892-2086
Tel: (301) 435-2920
Fax: (301) 480-1845
E-mail: ods@nih.gov

Finding Studies on Autoimmune Diseases

The NIH maintains an office dedicated to patient nutrition and diet. The National Institutes of Health's Office of Dietary Supplements (ODS) offers a searchable bibliographic database called the IBIDS (International Bibliographic Information on Dietary Supplements). The IBIDS contains over 460,000 scientific citations and summaries about dietary supplements and nutrition as well as references to published international, scientific literature on dietary supplements such as vitamins, minerals, and botanicals.[52] IBIDS is available to the public free of charge through the ODS Internet page: **http://ods.od.nih.gov/databases/ibids.html**.

After entering the search area, you have three choices: (1) IBIDS Consumer Database, (2) Full IBIDS Database, or (3) Peer Reviewed Citations Only. We recommend that you start with the Consumer Database. While you may not find references for the topics that are of most interest to you, check back

[52] Adapted from **http://ods.od.nih.gov**. IBIDS is produced by the Office of Dietary Supplements (ODS) at the National Institutes of Health to assist the public, healthcare providers, educators, and researchers in locating credible, scientific information on dietary supplements. IBIDS was developed and will be maintained through an interagency partnership with the Food and Nutrition Information Center of the National Agricultural Library, U.S. Department of Agriculture.

periodically as this database is frequently updated. More studies can be found by searching the Full IBIDS Database. Healthcare professionals and researchers generally use the third option, which lists peer-reviewed citations. In all cases, we suggest that you take advantage of the "Advanced Search" option that allows you to retrieve up to 100 fully explained references in a comprehensive format. Type "autoimmune diseases" (or synonyms) into the search box. To narrow the search, you can also select the "Title" field. The following is a typical result when searching for recently indexed consumer information on autoimmune diseases:

- **Genetic errors that result in diabetes mellitus.**
  Author(s): University of Georgia, Athens.
  Source: Berdanier, C.D. Nutrition-today (USA). (February 1994). volume 29(1) page 17-24. diabetes genetic disorders blood sugar insulin secretion hormone receptors genetic correlation disease control genotype environment interaction viroses autoimmune diseases metabolic disorders pancreas chemical composition overweight calorific value physical activity transferases diet energy glucose soil transport processes poisoning lead side effects nomenclature 0029-666X
  Summary: diabete trouble genetique sucre du sang insuline secretion recepteur d' hormone correlation genetique controle de maladies interaction genotype environnement virose maladie autoimmune trouble du metabolisme pancreas composition chimique surpoids valeur calorique activite physique transferase regime alimentaire energie glucose transport dans le sol intoxication plomb effet secondaire nomenclature

- **Genetic variation and nutrition. 2. Genetic variation, nutrition, and chronic diseases.**
  Author(s): Center for Genetics Nutrition and Health, Washington, DC.
  Source: Simopoulos, A.P. Nutrition-today (USA). (October 1995). volume 30(5) page 194-206. genotype environment interaction overweight carcinomas autoimmune diseases chronic course genetic variation pathogenesis risk hypertension diet families genetic disorders disease control recommended dietary allowances diabetes osteodystrophy 0029-666X
  Summary: interaction genotype environnement surpoids carcinome maladie autoimmune processus chronique variation genetique pathogenese risque hypertension regime alimentaire famille trouble genetique controle de maladies apport alimentaire recommande diabete osteodystrophie

Additional consumer oriented references include:

- **Dietary treatment of arthritis.**
  Source: Nutr-M-D. Van Nuys, Calif. : The Journal. April 1987. volume 13 (4) page 4-5. 0732-0167
- **Evidence of primary beta-cell destruction by T-cells and beta-cell differentiation from pancreatic ductal cells in diabetes associated with active autoimmune chronic pancreatitis.**
  Author(s): Department of Endocrinology and Metabolism, Toranomon Hospital, 2-2-2, Toranomon, Minato-ku, Tokyo 105-8470, Japan.
  Source: Tanaka, S Kobayashi, T Nakanishi, K Okubo, M Murase, T Hashimoto, M Watanabe, G Matsushita, H Endo, Y Yoshizaki, H Kosuge, T Sakamoto, M Takeuchi, K Diabetes-Care. 2001 September; 24(9): 1661-7 0149-5992
- **Mechanisms and functions of vitamin D.**
  Author(s): Department of Biochemistry, University of Wisconsin-Madison 53706, USA.
  Source: DeLuca, H F Zierold, C Nutr-Revolume 1998 February; 56(2 Pt 2): S4-10; discussion S 54-75 0029-6643
- **Nutrition and autoimmune disease.**
  Author(s): University of Texas Health Science Center at San Antonio, USA.
  Source: Fernandes, G Jolly, C A Nutr-Revolume 1998 January; 56(1 Pt 2): S161-9 0029-6643

The following information is typical of that found when using the "Full IBIDS Database" when searching using "autoimmune diseases" (or a synonym):

- **High-dose intravenous IgG therapy in a seven-week-old infant with chronic autoimmune hemolytic anemia.**
  Source: Sasaki, H Akutagawa, H Kuwakado, K Uemura, M Emi, I Am-J-Hematol. 1987 June; 25(2): 215-8 0361-8609
- **Identification and characterization of potential new therapeutic targets in inflammatory and autoimmune diseases.**
  Author(s): Hoechst Marion Roussel, DG Rheumatology, Frankfurt/Main, Germany.
  Source: Mangold, U Dax, C I Saar, K Schwab, W Kirschbaum, B Mullner, S Eur-J-Biochem. 1999 December; 266(3): 1184-91 0014-2956

Federal Resources on Nutrition

In addition to the IBIDS, the United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) provide many sources of information on general nutrition and health. Recommended resources include:

- healthfinder®, HHS's gateway to health information, including diet and nutrition: **http://www.healthfinder.gov/scripts/SearchContext.asp?topic=238&page=0**
- The United States Department of Agriculture's Web site dedicated to nutrition information: **www.nutrition.gov**
- The Food and Drug Administration's Web site for federal food safety information: **www.foodsafety.gov**
- The National Action Plan on Overweight and Obesity sponsored by the United States Surgeon General: **http://www.surgeongeneral.gov/topics/obesity/**
- The Center for Food Safety and Applied Nutrition has an Internet site sponsored by the Food and Drug Administration and the Department of Health and Human Services: **http://vm.cfsan.fda.gov/**
- Center for Nutrition Policy and Promotion sponsored by the United States Department of Agriculture: **http://www.usda.gov/cnpp/**
- Food and Nutrition Information Center, National Agricultural Library sponsored by the United States Department of Agriculture: **http://www.nal.usda.gov/fnic/**
- Food and Nutrition Service sponsored by the United States Department of Agriculture: **http://www.fns.usda.gov/fns/**

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering food and nutrition. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**
- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.thedacare.org/healthnotes/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**

- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,,00.html**

The following is a specific Web list relating to autoimmune diseases; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **Minerals**

  Iodine
  Source: Integrative Medicine Communications; www.onemedicine.com
  Hyperlink:
  http://www.drkoop.com/interactivemedicine/ConsSupplements/Iodinecs.html

  Zinc
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10071,00.html

- **Food and Diet**

  Fish, lean
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/foods_view/0,1523,93,00.html

  Omega-3 fatty acids
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,992,00.html

Omega-6 fatty acids
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,1037,00.html

Vocabulary Builder

The following vocabulary builder defines words used in the references in this chapter that have not been defined in previous chapters:

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carcinoma: A malignant new growth made up of epithelial cells tending to infiltrate the surrounding tissues and give rise to metastases. [EU]

Endocrinology: A subspecialty of internal medicine concerned with the metabolism, physiology, and disorders of the endocrine system. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Niacin: Water-soluble vitamin of the B complex occurring in various animal and plant tissues. Required by the body for the formation of coenzymes NAD and NADP. Has pellagra-curative, vasodilating, and antilipemic properties. [NIH]

Osteodystrophy: Defective bone formation. [EU]

Overdose: 1. to administer an excessive dose. 2. an excessive dose. [EU]

Pancreatitis: Acute or chronic inflammation of the pancreas, which may be asymptomatic or symptomatic, and which is due to autodigestion of a pancreatic tissue by its own enzymes. It is caused most often by alcoholism or biliary tract disease; less commonly it may be associated with hyperlipaemia, hyperparathyroidism, abdominal trauma (accidental or operative injury), vasculitis, or uraemia. [EU]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Potassium: An element that is in the alkali group of metals. It has an atomic symbol K, atomic number 19, and atomic weight 39.10. It is the chief cation in the intracellular fluid of muscle and other cells. Potassium ion is a strong electrolyte and it plays a significant role in the regulation of fluid volume and maintenance of the water-electrolyte balance. [NIH]

Riboflavin: Nutritional factor found in milk, eggs, malted barley, liver, kidney, heart, and leafy vegetables. The richest natural source is yeast. It occurs in the free form only in the retina of the eye, in whey, and in urine; its principal forms in tissues and cells are as FMN and FAD. [NIH]

Secretion: 1. the process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. any substance produced by secretion. [EU]

Selenium: An element with the atomic symbol Se, atomic number 34, and atomic weight 78.96. It is an essential micronutrient for mammals and other animals but is toxic in large amounts. Selenium protects intracellular structures against oxidative damage. It is an essential component of glutathione peroxidase. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

APPENDIX D. FINDING MEDICAL LIBRARIES

Overview

At a medical library you can find medical texts and reference books, consumer health publications, specialty newspapers and magazines, as well as medical journals. In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Before going to the library, highlight the references mentioned in this sourcebook that you find interesting. Focus on those items that are not available via the Internet, and ask the reference librarian for help with your search. He or she may know of additional resources that could be helpful to you. Most importantly, your local public library and medical libraries have Interlibrary Loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. NLM's interlibrary loan services are only available to libraries. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[53]

[53] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries Open to the Public

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries that are generally open to the public and have reference facilities. The following is the NLM's list plus hyperlinks to each library Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located):[54]

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute), **http://www.asmi.org/LIBRARY.HTM**
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos (Community Health Library of Los Gatos), **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**

[54] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** San José PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation), **http://go.sutterhealth.org/comm/resc-library/sac-resources.html**
- **California:** University of California, Davis. Health Sciences Libraries
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System), **http://www.valleycare.com/library.html**
- **California:** Washington Community Health Resource Library (Washington Community Health Resource Library), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.exempla.org/conslib.htm**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**
- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library), **http://hml.org/CHIS/**

- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Northwestern Memorial Hospital, Health Learning Center), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital), **http://www.centralbap.com/education/community/library.htm**
- **Kentucky:** University of Kentucky - Health Information Library (University of Kentucky, Chandler Medical Center, Health Information Library), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital, **http://www.parkviewhospital.org/communit.htm#Library**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital Health Information Library (Western Maine Health), **http://www.wmhcc.com/hil_frame.html**
- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre), **http://www.deerlodge.mb.ca/library/libraryservices.shtml**

- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Md., Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information, **http://www.sladen.hfhs.org/library/consumer/index.html**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center), **http://www.saintpatrick.org/chi/librarydetail.php3?ID=41**

- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**
- **Nevada:** Health Science Library, West Charleston Library (Las Vegas Clark County Library District), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** Saint Francis Health System Patient/Family Resource Center (Saint Francis Health System), **http://www.sfh-tulsa.com/patientfamilycenter/default.asp**

- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System), **http://www.hsls.pitt.edu/chi/hhrcinfo.html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://ww2.mcgill.ca/mghlib/**
- **South Dakota:** Rapid City Regional Hospital - Health Information Center (Rapid City Regional Hospital, Health Information Center), **http://www.rcrh.org/education/LibraryResourcesConsumers.htm**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Texas:** Matustik Family Resource Center (Cook Children's Health Care System), **http://www.cookchildrens.com/Matustik_Library.html**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center), **http://www.swmedctr.com/Home/**

APPENDIX E. YOUR RIGHTS AND INSURANCE

Overview

Any patient with autoimmune diseases faces a series of issues related more to the healthcare industry than to the medical condition itself. This appendix covers two important topics in this regard: your rights and responsibilities as a patient, and how to get the most out of your medical insurance plan.

Your Rights as a Patient

The President's Advisory Commission on Consumer Protection and Quality in the Healthcare Industry has created the following summary of your rights as a patient.[55]

Information Disclosure

Consumers have the right to receive accurate, easily understood information. Some consumers require assistance in making informed decisions about health plans, health professionals, and healthcare facilities. Such information includes:

- ***Health plans.*** Covered benefits, cost-sharing, and procedures for resolving complaints, licensure, certification, and accreditation status, comparable measures of quality and consumer satisfaction, provider network composition, the procedures that govern access to specialists and emergency services, and care management information.

[55]Adapted from Consumer Bill of Rights and Responsibilities: **http://www.hcqualitycommission.gov/press/cbor.html#head1**.

- ***Health professionals.*** Education, board certification, and recertification, years of practice, experience performing certain procedures, and comparable measures of quality and consumer satisfaction.
- ***Healthcare facilities.*** Experience in performing certain procedures and services, accreditation status, comparable measures of quality, worker, and consumer satisfaction, and procedures for resolving complaints.
- ***Consumer assistance programs.*** Programs must be carefully structured to promote consumer confidence and to work cooperatively with health plans, providers, payers, and regulators. Desirable characteristics of such programs are sponsorship that ensures accountability to the interests of consumers and stable, adequate funding.

Choice of Providers and Plans

Consumers have the right to a choice of healthcare providers that is sufficient to ensure access to appropriate high-quality healthcare. To ensure such choice, the Commission recommends the following:

- ***Provider network adequacy.*** All health plan networks should provide access to sufficient numbers and types of providers to assure that all covered services will be accessible without unreasonable delay -- including access to emergency services 24 hours a day and 7 days a week. If a health plan has an insufficient number or type of providers to provide a covered benefit with the appropriate degree of specialization, the plan should ensure that the consumer obtains the benefit outside the network at no greater cost than if the benefit were obtained from participating providers.
- ***Women's health services.*** Women should be able to choose a qualified provider offered by a plan -- such as gynecologists, certified nurse midwives, and other qualified healthcare providers -- for the provision of covered care necessary to provide routine and preventative women's healthcare services.
- ***Access to specialists.*** Consumers with complex or serious medical conditions who require frequent specialty care should have direct access to a qualified specialist of their choice within a plan's network of providers. Authorizations, when required, should be for an adequate number of direct access visits under an approved treatment plan.
- ***Transitional care.*** Consumers who are undergoing a course of treatment for a chronic or disabling condition (or who are in the second or third trimester of a pregnancy) at the time they involuntarily change health

plans or at a time when a provider is terminated by a plan for other than cause should be able to continue seeing their current specialty providers for up to 90 days (or through completion of postpartum care) to allow for transition of care.

- ***Choice of health plans.*** Public and private group purchasers should, wherever feasible, offer consumers a choice of high-quality health insurance plans.

Access to Emergency Services

Consumers have the right to access emergency healthcare services when and where the need arises. Health plans should provide payment when a consumer presents to an emergency department with acute symptoms of sufficient severity--including severe pain--such that a "prudent layperson" could reasonably expect the absence of medical attention to result in placing that consumer's health in serious jeopardy, serious impairment to bodily functions, or serious dysfunction of any bodily organ or part.

Participation in Treatment Decisions

Consumers have the right and responsibility to fully participate in all decisions related to their healthcare. Consumers who are unable to fully participate in treatment decisions have the right to be represented by parents, guardians, family members, or other conservators. Physicians and other health professionals should:

- Provide patients with sufficient information and opportunity to decide among treatment options consistent with the informed consent process.
- Discuss all treatment options with a patient in a culturally competent manner, including the option of no treatment at all.
- Ensure that persons with disabilities have effective communications with members of the health system in making such decisions.
- Discuss all current treatments a consumer may be undergoing.
- Discuss all risks, benefits, and consequences to treatment or nontreatment.
- Give patients the opportunity to refuse treatment and to express preferences about future treatment decisions.

- Discuss the use of advance directives -- both living wills and durable powers of attorney for healthcare -- with patients and their designated family members.
- Abide by the decisions made by their patients and/or their designated representatives consistent with the informed consent process.

Health plans, health providers, and healthcare facilities should:

- Disclose to consumers factors -- such as methods of compensation, ownership of or interest in healthcare facilities, or matters of conscience -- that could influence advice or treatment decisions.
- Assure that provider contracts do not contain any so-called "gag clauses" or other contractual mechanisms that restrict healthcare providers' ability to communicate with and advise patients about medically necessary treatment options.
- Be prohibited from penalizing or seeking retribution against healthcare professionals or other health workers for advocating on behalf of their patients.

Respect and Nondiscrimination

Consumers have the right to considerate, respectful care from all members of the healthcare industry at all times and under all circumstances. An environment of mutual respect is essential to maintain a quality healthcare system. To assure that right, the Commission recommends the following:

- Consumers must not be discriminated against in the delivery of healthcare services consistent with the benefits covered in their policy, or as required by law, based on race, ethnicity, national origin, religion, sex, age, mental or physical disability, sexual orientation, genetic information, or source of payment.
- Consumers eligible for coverage under the terms and conditions of a health plan or program, or as required by law, must not be discriminated against in marketing and enrollment practices based on race, ethnicity, national origin, religion, sex, age, mental or physical disability, sexual orientation, genetic information, or source of payment.

Confidentiality of Health Information

Consumers have the right to communicate with healthcare providers in confidence and to have the confidentiality of their individually identifiable

healthcare information protected. Consumers also have the right to review and copy their own medical records and request amendments to their records.

Complaints and Appeals

Consumers have the right to a fair and efficient process for resolving differences with their health plans, healthcare providers, and the institutions that serve them, including a rigorous system of internal review and an independent system of external review. A free copy of the Patient's Bill of Rights is available from the American Hospital Association.[56]

Patient Responsibilities

Treatment is a two-way street between you and your healthcare providers. To underscore the importance of finance in modern healthcare as well as your responsibility for the financial aspects of your care, the President's Advisory Commission on Consumer Protection and Quality in the Healthcare Industry has proposed that patients understand the following "Consumer Responsibilities."[57] In a healthcare system that protects consumers' rights, it is reasonable to expect and encourage consumers to assume certain responsibilities. Greater individual involvement by the consumer in his or her care increases the likelihood of achieving the best outcome and helps support a quality-oriented, cost-conscious environment. Such responsibilities include:

- Take responsibility for maximizing healthy habits such as exercising, not smoking, and eating a healthy diet.
- Work collaboratively with healthcare providers in developing and carrying out agreed-upon treatment plans.
- Disclose relevant information and clearly communicate wants and needs.
- Use your health insurance plan's internal complaint and appeal processes to address your concerns.
- Avoid knowingly spreading disease.

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[56] To order your free copy of the Patient's Bill of Rights, telephone 312-422-3000 or visit the American Hospital Association's Web site: **http://www.aha.org**. Click on "Resource Center," go to "Search" at bottom of page, and then type in "Patient's Bill of Rights." The Patient's Bill of Rights is also available from Fax on Demand, at 312-422-2020, document number 471124.

[57] Adapted from **http://www.hcqualitycommission.gov/press/cbor.html#head1**.

- Recognize the reality of risks, the limits of the medical science, and the human fallibility of the healthcare professional.
- Be aware of a healthcare provider's obligation to be reasonably efficient and equitable in providing care to other patients and the community.
- Become knowledgeable about your health plan's coverage and options (when available) including all covered benefits, limitations, and exclusions, rules regarding use of network providers, coverage and referral rules, appropriate processes to secure additional information, and the process to appeal coverage decisions.
- Show respect for other patients and health workers.
- Make a good-faith effort to meet financial obligations.
- Abide by administrative and operational procedures of health plans, healthcare providers, and Government health benefit programs.

Choosing an Insurance Plan

There are a number of official government agencies that help consumers understand their healthcare insurance choices.[58] The U.S. Department of Labor, in particular, recommends ten ways to make your health benefits choices work best for you.[59]

1. Your options are important. There are many different types of health benefit plans. Find out which one your employer offers, then check out the plan, or plans, offered. Your employer's human resource office, the health plan administrator, or your union can provide information to help you match your needs and preferences with the available plans. The more information you have, the better your healthcare decisions will be.

2. Reviewing the benefits available. Do the plans offered cover preventive care, well-baby care, vision or dental care? Are there deductibles? Answers to these questions can help determine the out-of-pocket expenses you may face. Matching your needs and those of your family members will result in the best possible benefits. Cheapest may not always be best. Your goal is high quality health benefits.

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[58] More information about quality across programs is provided at the following AHRQ Web site:
http://www.ahrq.gov/consumer/qntascii/qnthplan.htm.

[59] Adapted from the Department of Labor:
http://www.dol.gov/dol/pwba/public/pubs/health/top10-text.html.

3. Look for quality. The quality of healthcare services varies, but quality can be measured. You should consider the quality of healthcare in deciding among the healthcare plans or options available to you. Not all health plans, doctors, hospitals and other providers give the highest quality care. Fortunately, there is quality information you can use right now to help you compare your healthcare choices. Find out how you can measure quality. Consult the U.S. Department of Health and Human Services publication "Your Guide to Choosing Quality Health Care" on the Internet at **www.ahcpr.gov/consumer**.

4. Your plan's summary plan description (SPD) provides a wealth of information. Your health plan administrator can provide you with a copy of your plan's SPD. It outlines your benefits and your legal rights under the Employee Retirement Income Security Act (ERISA), the federal law that protects your health benefits. It should contain information about the coverage of dependents, what services will require a co-pay, and the circumstances under which your employer can change or terminate a health benefits plan. Save the SPD and all other health plan brochures and documents, along with memos or correspondence from your employer relating to health benefits.

5. Assess your benefit coverage as your family status changes. Marriage, divorce, childbirth or adoption, and the death of a spouse are all life events that may signal a need to change your health benefits. You, your spouse and dependent children may be eligible for a special enrollment period under provisions of the Health Insurance Portability and Accountability Act (HIPAA). Even without life-changing events, the information provided by your employer should tell you how you can change benefits or switch plans, if more than one plan is offered. If your spouse's employer also offers a health benefits package, consider coordinating both plans for maximum coverage.

6. Changing jobs and other life events can affect your health benefits. Under the Consolidated Omnibus Budget Reconciliation Act (COBRA), you, your covered spouse, and your dependent children may be eligible to purchase extended health coverage under your employer's plan if you lose your job, change employers, get divorced, or upon occurrence of certain other events. Coverage can range from 18 to 36 months depending on your situation. COBRA applies to most employers with 20 or more workers and requires your plan to notify you of your rights. Most plans require eligible individuals to make their COBRA election within 60 days of the plan's notice. Be sure to follow up with your plan sponsor if you don't receive notice, and make sure you respond within the allotted time.

7. HIPAA can also help if you are changing jobs, particularly if you have a medical condition. HIPAA generally limits pre-existing condition exclusions to a maximum of 12 months (18 months for late enrollees). HIPAA also requires this maximum period to be reduced by the length of time you had prior "creditable coverage." You should receive a certificate documenting your prior creditable coverage from your old plan when coverage ends.

8. Plan for retirement. Before you retire, find out what health benefits, if any, extend to you and your spouse during your retirement years. Consult with your employer's human resources office, your union, the plan administrator, and check your SPD. Make sure there is no conflicting information among these sources about the benefits you will receive or the circumstances under which they can change or be eliminated. With this information in hand, you can make other important choices, like finding out if you are eligible for Medicare and Medigap insurance coverage.

9. Know how to file an appeal if your health benefits claim is denied. Understand how your plan handles grievances and where to make appeals of the plan's decisions. Keep records and copies of correspondence. Check your health benefits package and your SPD to determine who is responsible for handling problems with benefit claims. Contact PWBA for customer service assistance if you are unable to obtain a response to your complaint.

10. You can take steps to improve the quality of the healthcare and the health benefits you receive. Look for and use things like Quality Reports and Accreditation Reports whenever you can. Quality reports may contain consumer ratings -- how satisfied consumers are with the doctors in their plan, for instance-- and clinical performance measures -- how well a healthcare organization prevents and treats illness. Accreditation reports provide information on how accredited organizations meet national standards, and often include clinical performance measures. Look for these quality measures whenever possible. Consult "Your Guide to Choosing Quality Health Care" on the Internet at **www.ahcpr.gov/consumer**.

Medicare and Medicaid

Illness strikes both rich and poor families. For low-income families, Medicaid is available to defer the costs of treatment. The Health Care Financing Administration (HCFA) administers Medicare, the nation's largest health insurance program, which covers 39 million Americans. In the following pages, you will learn the basics about Medicare insurance as well as useful

contact information on how to find more in-depth information about Medicaid.[60]

Who is Eligible for Medicare?

Generally, you are eligible for Medicare if you or your spouse worked for at least 10 years in Medicare-covered employment and you are 65 years old and a citizen or permanent resident of the United States. You might also qualify for coverage if you are under age 65 but have a disability or End-Stage Renal disease (permanent kidney failure requiring dialysis or transplant). Here are some simple guidelines:

You can get Part A at age 65 without having to pay premiums if:

- You are already receiving retirement benefits from Social Security or the Railroad Retirement Board.
- You are eligible to receive Social Security or Railroad benefits but have not yet filed for them.
- You or your spouse had Medicare-covered government employment.

If you are under 65, you can get Part A without having to pay premiums if:

- You have received Social Security or Railroad Retirement Board disability benefit for 24 months.
- You are a kidney dialysis or kidney transplant patient.

Medicare has two parts:

- Part A (Hospital Insurance). Most people do not have to pay for Part A.
- Part B (Medical Insurance). Most people pay monthly for Part B.

Part A (Hospital Insurance)

Helps Pay For: Inpatient hospital care, care in critical access hospitals (small facilities that give limited outpatient and inpatient services to people in rural areas) and skilled nursing facilities, hospice care, and some home healthcare.

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[60] This section has been adapted from the Official U.S. Site for Medicare Information: **http://www.medicare.gov/Basics/Overview.asp**.

Cost: Most people get Part A automatically when they turn age 65. You do not have to pay a monthly payment called a premium for Part A because you or a spouse paid Medicare taxes while you were working.

If you (or your spouse) did not pay Medicare taxes while you were working and you are age 65 or older, you still may be able to buy Part A. If you are not sure you have Part A, look on your red, white, and blue Medicare card. It will show "Hospital Part A" on the lower left corner of the card. You can also call the Social Security Administration toll free at 1-800-772-1213 or call your local Social Security office for more information about buying Part A. If you get benefits from the Railroad Retirement Board, call your local RRB office or 1-800-808-0772. For more information, call your Fiscal Intermediary about Part A bills and services. The phone number for the Fiscal Intermediary office in your area can be obtained from the following Web site: **http://www.medicare.gov/Contacts/home.asp**.

Part B (Medical Insurance)

Helps Pay For: Doctors, services, outpatient hospital care, and some other medical services that Part A does not cover, such as the services of physical and occupational therapists, and some home healthcare. Part B helps pay for covered services and supplies when they are medically necessary.

Cost: As of 2001, you pay the Medicare Part B premium of $50.00 per month. In some cases this amount may be higher if you did not choose Part B when you first became eligible at age 65. The cost of Part B may go up 10% for each 12-month period that you were eligible for Part B but declined coverage, except in special cases. You will have to pay the extra 10% cost for the rest of your life.

Enrolling in Part B is your choice. You can sign up for Part B anytime during a 7-month period that begins 3 months before you turn 65. Visit your local Social Security office, or call the Social Security Administration at 1-800-772-1213 to sign up. If you choose to enroll in Part B, the premium is usually taken out of your monthly Social Security, Railroad Retirement, or Civil Service Retirement payment. If you do not receive any of the above payments, Medicare sends you a bill for your part B premium every 3 months. You should receive your Medicare premium bill in the mail by the 10th of the month. If you do not, call the Social Security Administration at 1-800-772-1213, or your local Social Security office. If you get benefits from the Railroad Retirement Board, call your local RRB office or 1-800-808-0772. For more information, call your Medicare carrier about bills and services. The

phone number for the Medicare carrier in your area can be found at the following Web site: **http://www.medicare.gov/Contacts/home.asp**. You may have choices in how you get your healthcare including the Original Medicare Plan, Medicare Managed Care Plans (like HMOs), and Medicare Private Fee-for-Service Plans.

Medicaid

Medicaid is a joint federal and state program that helps pay medical costs for some people with low incomes and limited resources. Medicaid programs vary from state to state. People on Medicaid may also get coverage for nursing home care and outpatient prescription drugs which are not covered by Medicare. You can find more information about Medicaid on the HCFA.gov Web site at **http://www.hcfa.gov/medicaid/medicaid.htm**.

States also have programs that pay some or all of Medicare's premiums and may also pay Medicare deductibles and coinsurance for certain people who have Medicare and a low income. To qualify, you must have:

- Part A (Hospital Insurance),
- Assets, such as bank accounts, stocks, and bonds that are not more than $4,000 for a single person, or $6,000 for a couple, and
- A monthly income that is below certain limits.

For more information on these programs, look at the Medicare Savings Programs brochure, **http://www.medicare.gov/Library/PDFNavigation/PDFInterim.asp?Language=English&Type=Pub&PubID=10126**. There are also Prescription Drug Assistance Programs available. Find information on these programs which offer discounts or free medications to individuals in need at **http://www.medicare.gov/Prescription/Home.asp**.

NORD's Medication Assistance Programs

Finally, the National Organization for Rare Disorders, Inc. (NORD) administers medication programs sponsored by humanitarian-minded pharmaceutical and biotechnology companies to help uninsured or under-insured individuals secure life-saving or life-sustaining drugs.[61] NORD

[61] Adapted from NORD: **http://www.rarediseases.org/cgi-bin/nord/progserv#patient?id=rPIzL9oD&mv_pc=30**.

programs ensure that certain vital drugs are available "to those individuals whose income is too high to qualify for Medicaid but too low to pay for their prescribed medications." The program has standards for fairness, equity, and unbiased eligibility. It currently covers some 14 programs for nine pharmaceutical companies. NORD also offers early access programs for investigational new drugs (IND) under the approved "Treatment INDs" programs of the Food and Drug Administration (FDA). In these programs, a limited number of individuals can receive investigational drugs that have yet to be approved by the FDA. These programs are generally designed for rare diseases or disorders. For more information, visit **www.rarediseases.org**.

Additional Resources

In addition to the references already listed in this chapter, you may need more information on health insurance, hospitals, or the healthcare system in general. The NIH has set up an excellent guidance Web site that addresses these and other issues. Topics include:[62]

- Health Insurance:
  http://www.nlm.nih.gov/medlineplus/healthinsurance.html
- Health Statistics:
  http://www.nlm.nih.gov/medlineplus/healthstatistics.html
- HMO and Managed Care:
  http://www.nlm.nih.gov/medlineplus/managedcare.html
- Hospice Care: **http://www.nlm.nih.gov/medlineplus/hospicecare.html**
- Medicaid: **http://www.nlm.nih.gov/medlineplus/medicaid.html**
- Medicare: **http://www.nlm.nih.gov/medlineplus/medicare.html**
- Nursing Homes and Long-term Care:
  http://www.nlm.nih.gov/medlineplus/nursinghomes.html
- Patient's Rights, Confidentiality, Informed Consent, Ombudsman Programs, Privacy and Patient Issues:
  http://www.nlm.nih.gov/medlineplus/patientissues.html

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[62] You can access this information at:
http://www.nlm.nih.gov/medlineplus/healthsystem.html.

APPENDIX F. MORE ON THE IMMUNE SYSTEM

Overview[63]

The immune system is a bodywide network of cells and organs that has evolved to defend the body against attacks by "foreign" invaders.

The proper targets of the immune defenses are infectious organisms, including:

- Bacteria such as these streptococci;
- Fungi (this one happens to be the mold from which penicillin is made);
- Parasites, including these worm-like microbes that cause schistosomiasis; and
- Viruses such as this herpes virus.

Markers of Self

At the heart of the immune response is the ability to distinguish between self and non-self.

Every body cell carries distinctive molecules that distinguish it as "self." Normally the body's defenses do not attack tissues that carry a self marker; rather, immune cells coexist peaceably with other body cells in a state known as self-tolerance.

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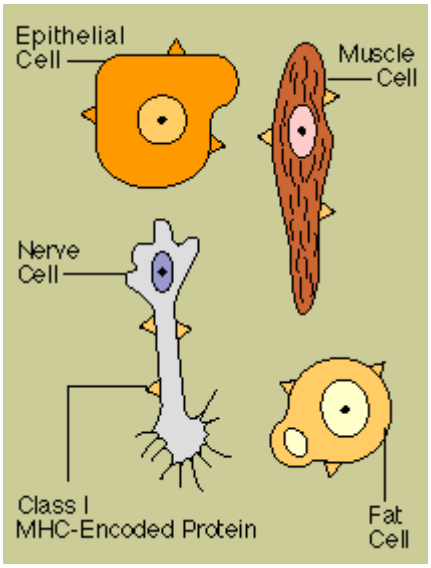
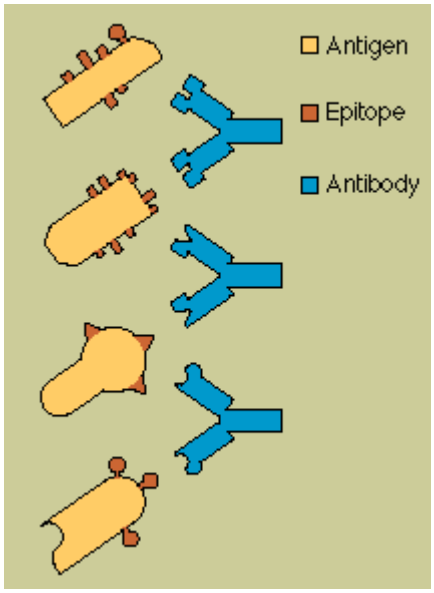
[63] Adapted from the National Institute of Allergy and Infectious Diseases (NIAID): **http://newscenter.cancer.gov/sciencebehind/immune/immune00.htm**.



Markers of Non-Self

Foreign molecules, too, carry distinctive markers, characteristic shapes called epitopes that protrude from their surfaces.

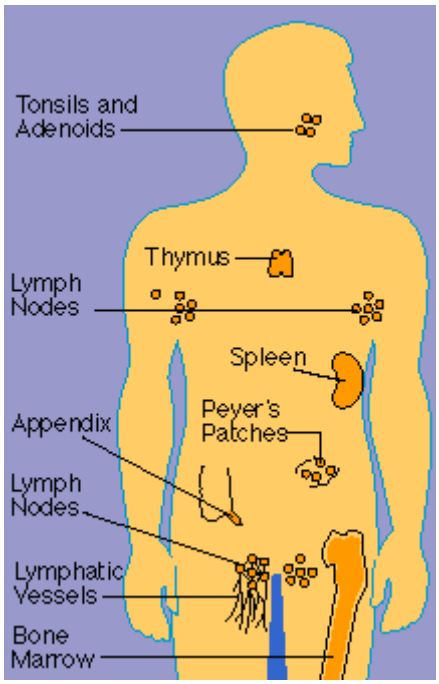


One of the remarkable things about the immune system is its ability to recognize many millions of distinctive non-self molecules, and to respond by producing molecules such as these antibodies—and also cells—that can match and counteract each one of the non-self molecules.

Any substance capable of triggering an immune response is known as an antigen. An antigen can be a bacterium or a virus, or even a portion or product of one of these organisms. Tissues or cells from another individual also act as antigens; that's why transplanted tissues are rejected as foreign.

Organs of the Immune System

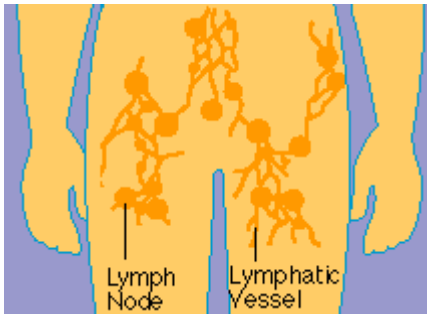
The organs of the immune system are stationed throughout the body.



They are known as lymphoid organs because they are concerned with the growth, development, and deployment of lymphocytes—white blood cells that are key operatives of the immune system.

Lymphatic System

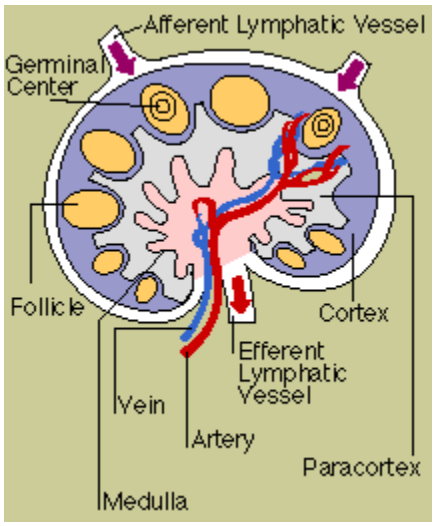
The organs of the immune system are connected with one another and with other organs of the body by a network of lymphatic vessels similar to blood vessels.



Immune cells and foreign particles are conveyed through the lymphatics in lymph, a clear fluid that bathes the body's tissues.

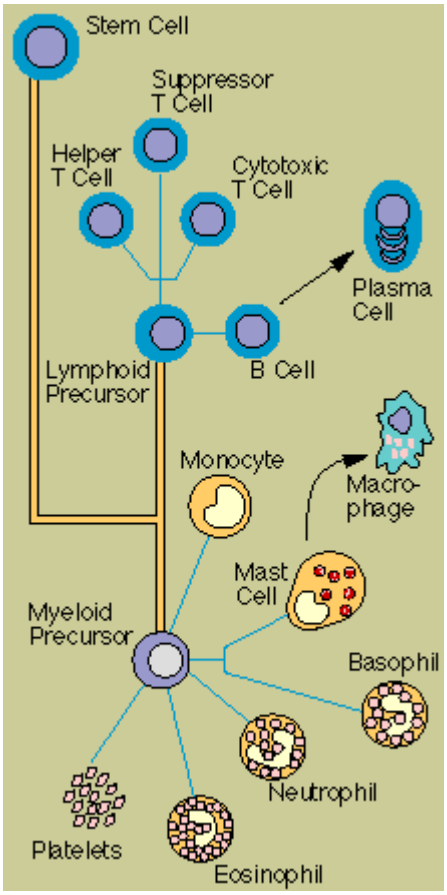
Lymph Node

Lymph nodes are small, bean-shaped structures that are laced throughout the body along the lymphatic routes.



Lymph nodes contain specialized compartments where immune cells congregate, and where they can encounter antigens.

Cells of the Immune System

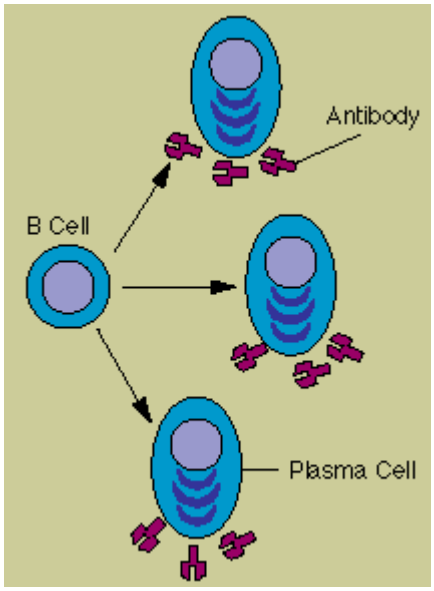


Cells destined to become immune cells, like all blood cells, arise in the bone marrow from so-called stem cells.

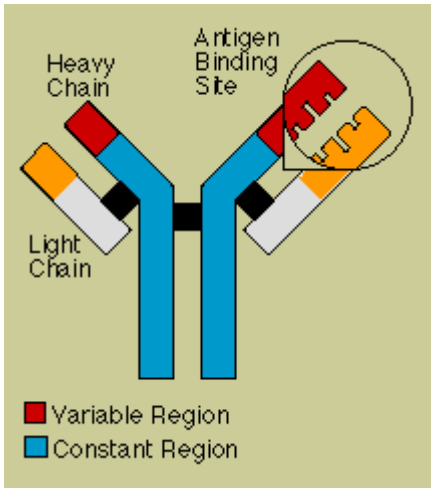
Some develop into myeloid cells, a group typified by the large, cell- and particle- devouring white blood cells known as phagocytes; phagocytes include monocytes, macrophages, and neutrophils. Other myeloid descendants become granule-containing inflammatory cells such as eosinophils and basophils. Lymphoid precursors develop into the small white blood cells called lymphocytes. The two major classes of lymphocytes are B cells and T cells.

B Cells

B cells work chiefly by secreting soluble substances known as antibodies. Each B cell is programmed to make one specific antibody. When a B cell encounters its triggering antigen (along with various accessory cells), it gives rise to many large plasma cells. Each plasma cell is essentially a factory for producing that one specific antibody.



Antibody



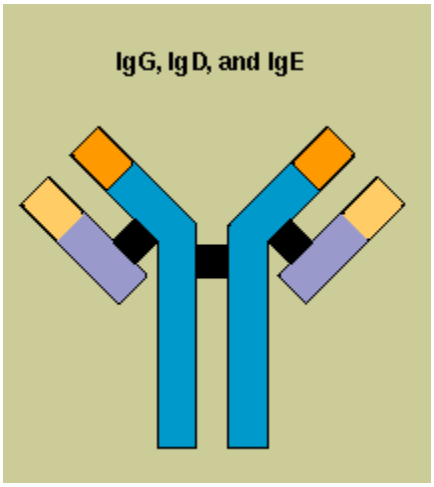
Each antibody is made up of two identical heavy chains and two identical light chains, shaped to form a Y.

The sections that make up the tips of the Y's arms vary greatly from one antibody to another; this is called the variable region. It is these unique contours in the antigen-binding site that allow the antibody to recognize a matching antigen, much as a lock matches a key.

The stem of the Y links the antibody to other participants in the immune defenses. This area is identical in all antibodies of the same class—for instance, all IgEs—and it's called the constant region.

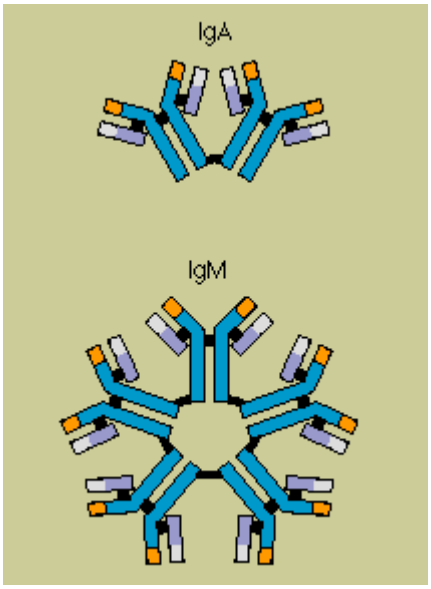
IgG, IgD, and IgE

Antibodies belong to a family of large protein molecules known as immunoglobulins. Scientists have identified nine chemically distinct classes of human immunoglobulins, four kinds of IgG and two kinds of IgA, plus IgM, IgE, and IgD.



Immunoglobulins G, D, and E are similar in appearance. IgG, the major immunoglobulin in the blood, is also able to enter tissue spaces; it works efficiently to coat microorganisms, speeding their uptake by other cells in the immune system. IgD is almost exclusively found inserted into the membrane of B cells, where it somehow regulates the cell's activation. IgE is normally present in only trace amounts, but it is responsible for the symptoms of allergy.

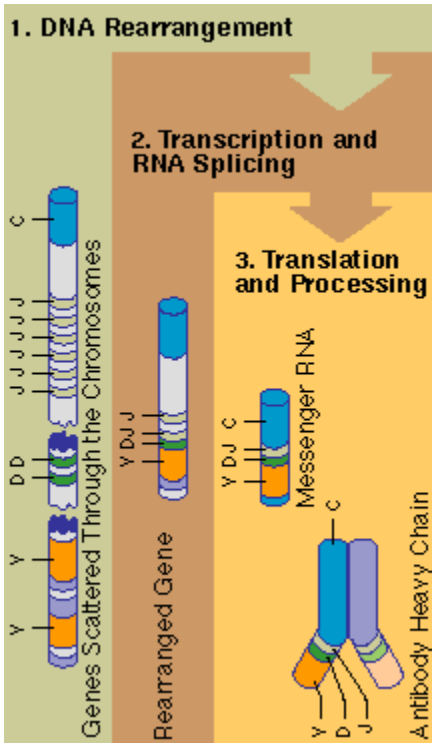
IgA and IgM



IgA—a doublet—concentrates in body fluids such as tears, saliva, and the secretions of the respiratory and gastrointestinal tracts. It is, thus, in a position to guard the entrances to the body.

IgM usually combines in star-shaped clusters. It tends to remain in the bloodstream, where it is very effective in killing bacteria.

Antibody Genes

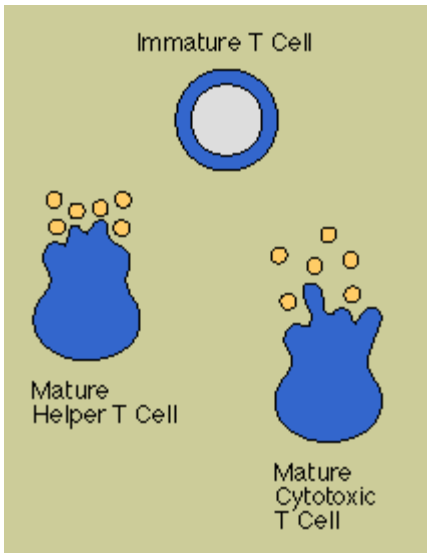


Scientists long wondered how all the genetic information needed to make millions of different antibodies could fit in a limited number of genes.

The answer is that antibody genes are pieced together from widely scattered bits of DNA, and the possible combinations are nearly endless. As this gene forms, it assembles segments that will determine the variable-V, diversity-D, joining-J, and constant-C segments of this antibody molecule, a typical IgM heavy chain.

T Cells

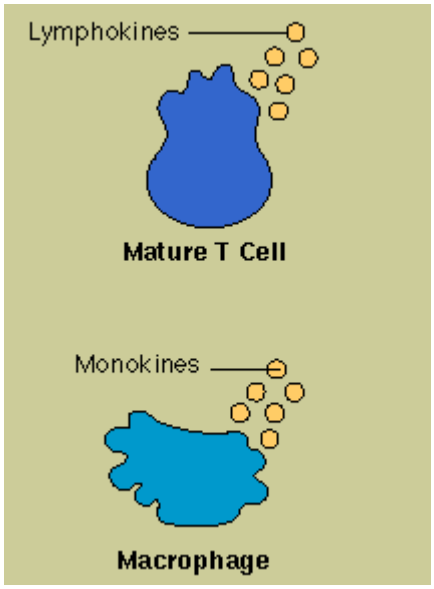
T cells contribute to the immune defenses in two major ways. Some help regulate the complex workings of the immune system, while others are cytotoxic and directly contact infected cells and destroy them.



Chief among the regulatory T cells are "helper/inducer" T cells. They are needed to activate many immune cells, including B cells and other T cells. Another subset of regulatory T cells acts to turn off or suppress immune cells.

Cytotoxic T cells help rid the body of cells that have been infected by viruses as well as cells that have been transformed by cancer. They are also responsible for the rejection of tissue and organ grafts.

Cytokines



Cytokines are diverse and potent chemical messengers secreted by the cells of the immune system—and the chief tool of T cells.

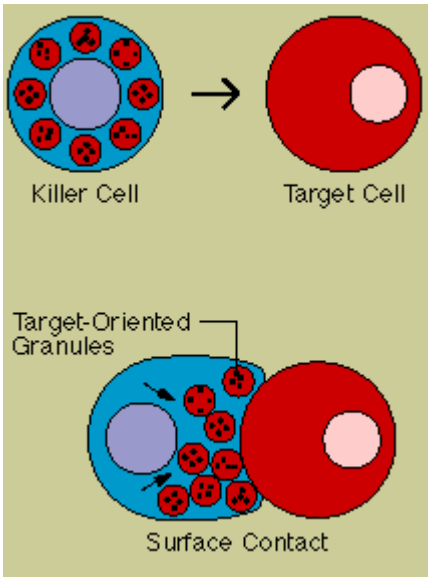
Lymphocytes, including both T cells and B cells, secrete lymphokines, while monocytes and macrophages secrete monokines.

Binding to specific receptors on target cells, cytokines recruit many other cells and substances to the field of action. Cytokines encourage cell growth, promote cell activation, direct cellular traffic, and destroy target cells—including cancer cells. Because they serve as a messenger between white cells, or leukocytes, many cytokines are also known as interleukins.

Natural Killer Cells

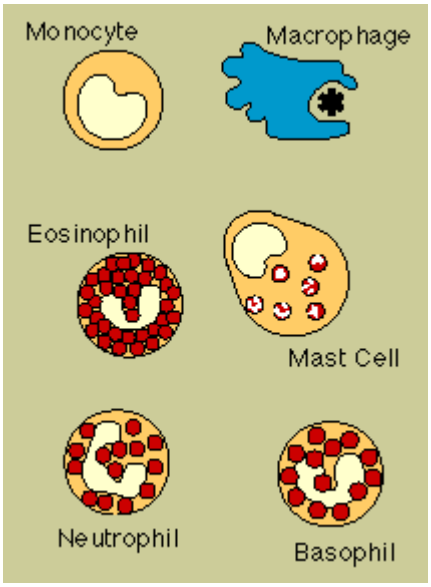
At least two types of lymphocytes are killer cells—cytotoxic T cells and natural killer cells.

To attack, cytotoxic T cells need to recognize a specific antigen, whereas natural killer or NK cells do not. Both types contain granules filled with potent chemicals, and both types kill on contact. The killer binds to its target, aims its weapons, and delivers a burst of lethal chemicals.



Phagocytes and Granulocytes

Phagocytes are large white cells that can engulf and digest foreign invaders.

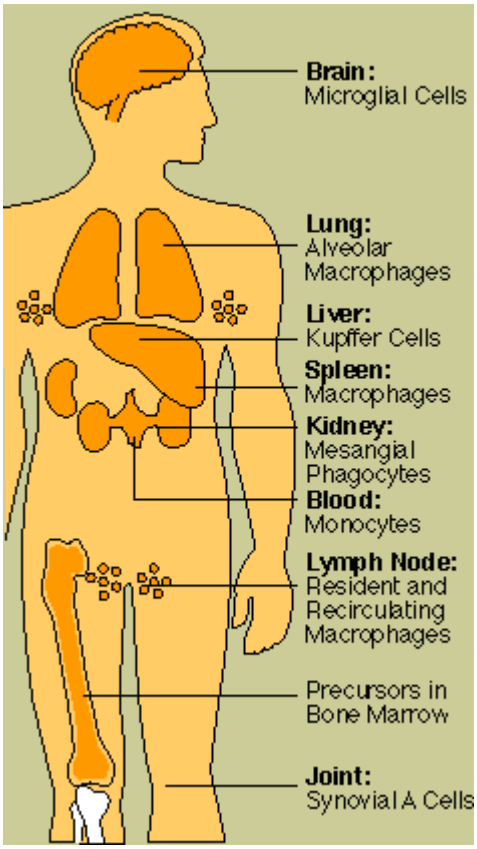


They include monocytes, which circulate in the blood, and macrophages, which are found in tissues throughout the body, as well as neutrophils, cells that circulate in the blood but move into tissues where they are needed. Macrophages are versatile cells; they act as scavengers, they secrete a wide variety of powerful chemicals, and they play an essential role in activating T cells.

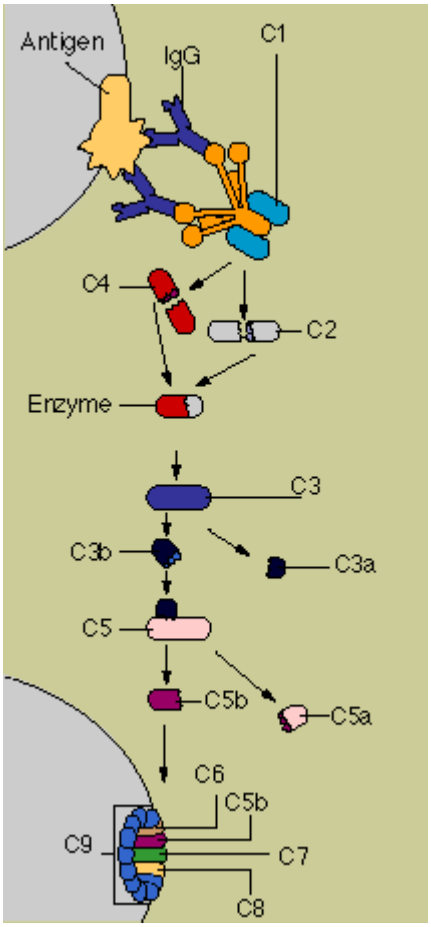
Neutrophils are not only phagocytes but also granulocytes: they contain granules filled with potent chemicals. These chemicals, in addition to destroying microorganisms, play a key role in acute inflammatory reactions. Other types of granulocytes are eosinophils and basophils. Mast cells are granule-containing cells in tissue.

Phagocytes in the Body

Specialized phagocytes are found in organs throughout the body.



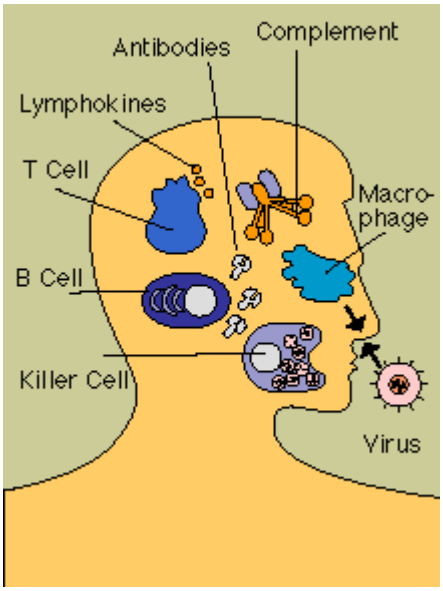
Complement



The complement system consists of a series of proteins that work to "complement" the work of antibodies in destroying bacteria.

Complement proteins circulate in the blood in an inactive form. The so-called "complement cascade" is set off when the first complement molecule, C1, encounters antibody bound to antigen in an antigen-antibody complex. Each of the complement proteins performs its specialized job in turn, acting on the molecule next in line. The end product is a cylinder that punctures the cell membrane and, by allowing fluids and molecules to flow in and out, dooms the target cell.

Mounting an Immune Response



Microbes attempting to get into the body must first get past the skin and mucous membranes, which not only pose a physical barrier but are rich in scavenger cells and IgA antibodies.

Next, they must elude a series of nonspecific defenses—cells and substances that attack all invaders regardless of the epitopes they carry. These include patrolling scavenger cells, complement, and various other enzymes and chemicals.

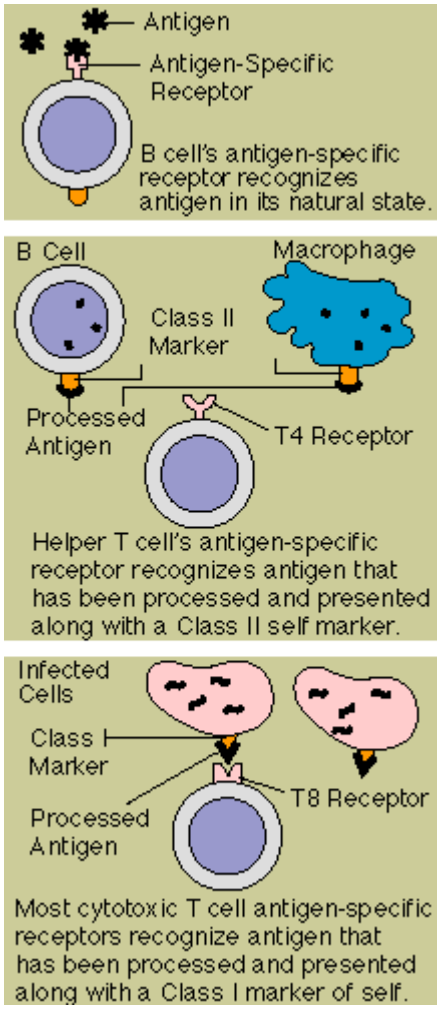
Infectious agents that get past the nonspecific barriers must confront specific weapons tailored just for them. These include both antibodies and cells. Almost all antigens trigger both nonspecific and specific responses.

Antigen Receptors

Both B cells and T cells carry customized receptor molecules that allow them to recognize and respond to their specific targets.

The B cell's antigen-specific receptor is a sample of the antibody it is prepared to manufacture; it recognizes antigen in its natural state.

The T cell receptor system is more complex. A T cell can recognize an antigen only after the antigen is processed and presented to it by a so-called antigen-presenting cell, in combination with a special type of cell marker.

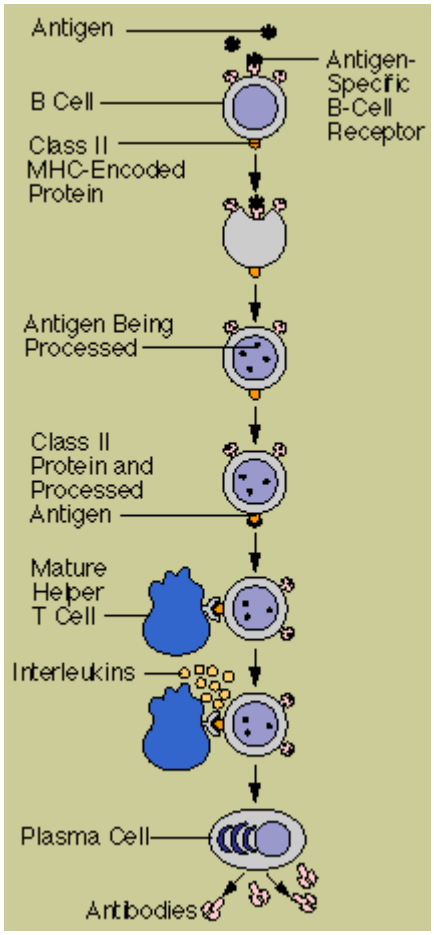


The T4 T cell's receptor looks for an antigen that has been broken down by an immune system cell such as a macrophage or a B cell and combined with a marker, known as a class II protein, carried by immune cells. The T8 T cell's receptor recognizes an antigen fragment produced within the cell, combined with a class I protein; class I proteins are found on virtually all body cells.

This complicated arrangement assures that T cells act only on precise targets and at close range.

Activation of B Cells to Make Antibody

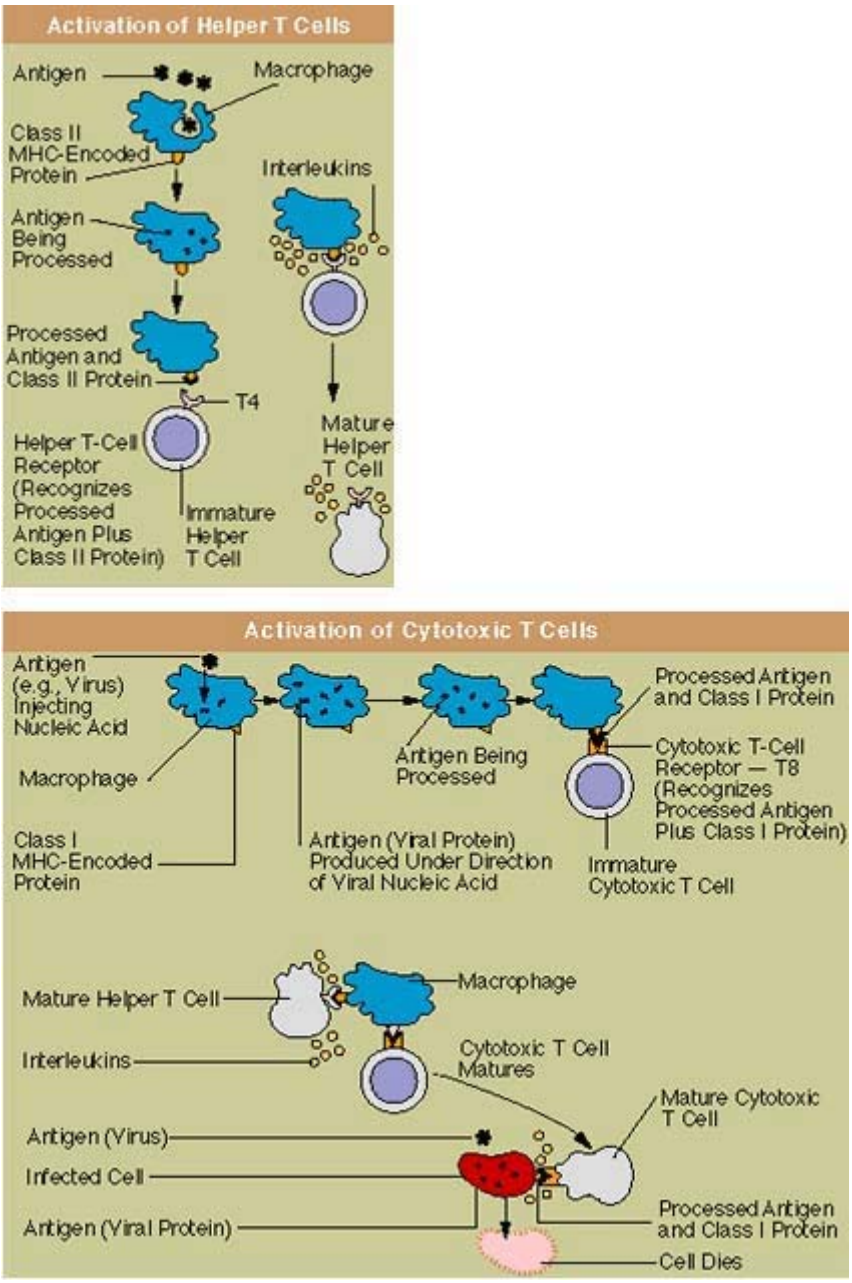
The B cell uses its receptor to bind a matching antigen, which it proceeds to engulf and process. Then it combines a fragment of antigen with its special marker, the class II protein. This combination of antigen and marker is recognized and bound by a T cell carrying a matching receptor. The binding activates the T cell, which then releases lymphokines—interleukins—that transform the B cell into an antibody- secreting plasma cell.



Activation of T Cells: Helper and Cytotoxic

After an antigen-presenting cell such as a macrophage has ingested and processed an antigen, it presents the antigen fragment, along with a class II marker protein, to a matching helper T cell with a T4 receptor.

The binding prompts the macrophage to release interleukins that allow the T cell to mature.

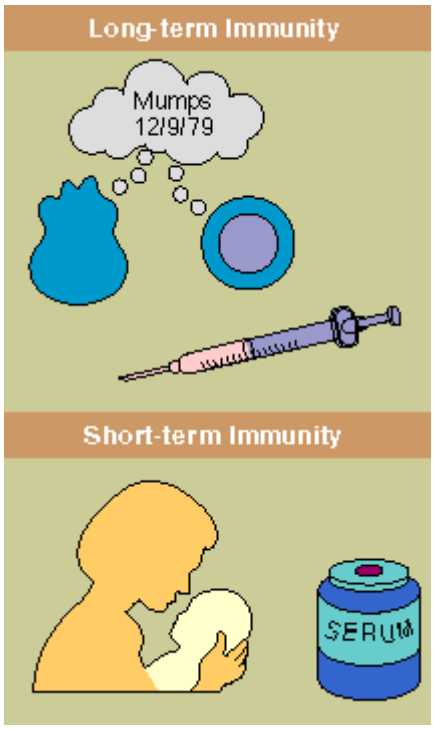


A cytotoxic T cell recognizes antigens such as virus proteins,which are produced within a cell, in combination with a class I self-marker protein. With the cooperation of a helper T cell, the cytotoxic T cell matures. Then, when the mature cytotoxic T cell encounters its specific target antigen combined with a class I marker protein—for instance, on a body cell that has been infected with a virus—it is ready to attack and kill the target cell.

Immunity: Short- and Long-Term Cell Memory

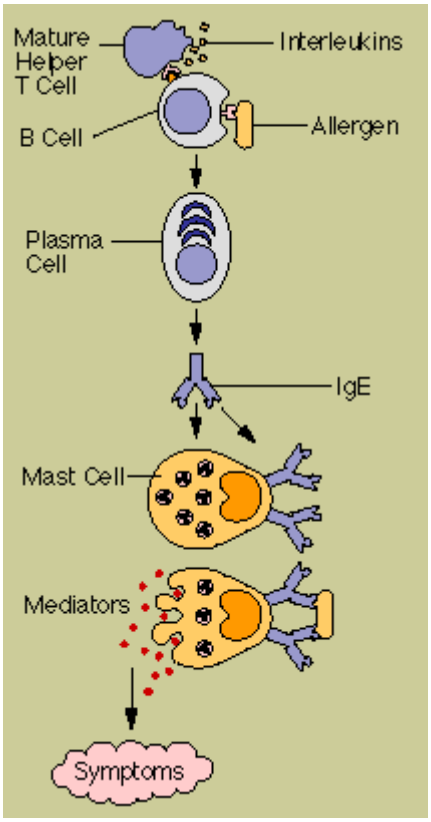
Whenever T cells and B cells are activated, some become "memory" cells.

The next time that an individual encounters that same antigen, the immune system is primed to destroy it quickly. Long-term immunity can be stimulated not only by infection but also by vaccines made from infectious agents that have been inactivated or, more commonly, from minute portions of the microbe.



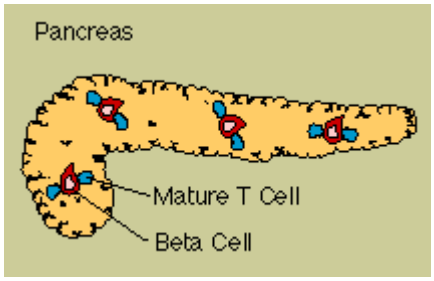
Short-term immunity can be transferred passively from one individual to another via antibody-containing serum; similarly, infants are protected by antibodies they receive from their mothers (primarily before birth).

Disorders of the Immune System: Allergy



When the immune system malfunctions, it can unleash a torrent of disorders and diseases. One of the most familiar is allergy. Allergies such as hay fever and hives are related to the antibody known as IgE. The first time an allergy-prone person is exposed to an allergen—for instance, grass pollen—the individual's B cells make large amounts of grass pollen IgE antibody. These IgE molecules attach to granule-containing cells known as mast cells, which are plentiful in the lungs, skin, tongue, and linings of the nose and gastrointestinal tract. The next time that person encounters grass pollen, the IgE-primed mast cell releases powerful chemicals that cause the wheezing, sneezing, and other symptoms of allergy.

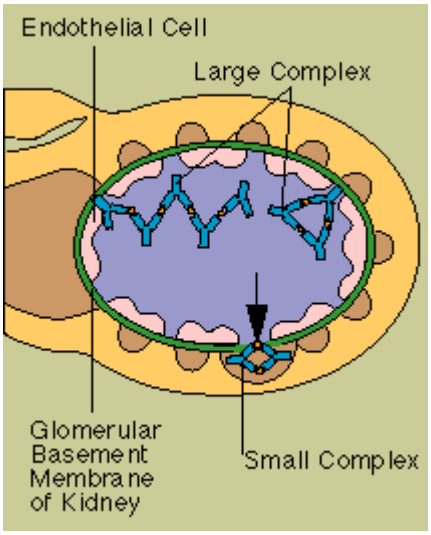
Disorders of the Immune System: Autoimmune Disease



Sometimes the immune system's recognition apparatus breaks down, and the body begins to manufacture antibodies and T cells directed against the body's own cells and organs.

Such cells and autoantibodies, as they are known, contribute to many diseases. For instance, T cells that attack pancreas cells contribute to diabetes, while an autoantibody known as rheumatoid factor is common in persons with rheumatoid arthritis.

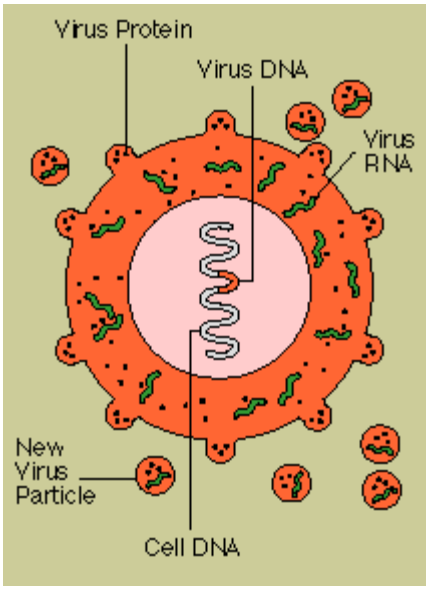
Disorders of the Immune System: Immune Complex Disease



Immune complexes are clusters of interlocking antigens and antibodies. Normally they are rapidly removed from the bloodstream. In some circumstances, however, they continue to circulate, and eventually they

become trapped in and damage the tissues of the kidneys, as seen here, or in the lungs, skin, joints, or blood vessels.

Disorders of the Immune System: AIDS

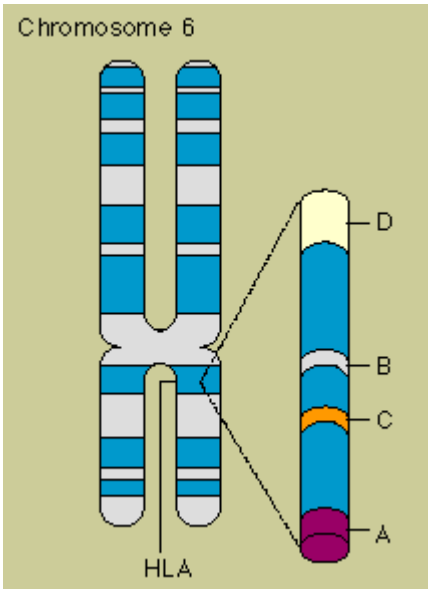


When the immune system is lacking one or more of its components, the result is an immunodeficiency disorder.

These can be inherited, acquired through infection, or produced as an inadvertent side effect of drugs such as those used to treat cancer or transplant patients.

AIDS is an immunodeficiency disorder caused by a virus that destroys helper T cells and that is harbored in macrophages as well as helper (T4) T cells. The AIDS virus splices its DNA into the DNA of the cell it infects; the cell is thereafter directed to churn out new viruses.

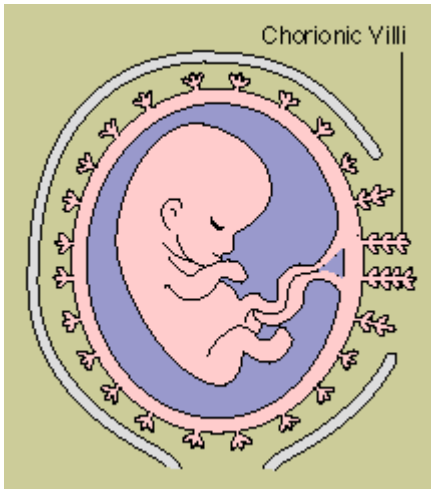
Human Tissue Typing for Organ Transplants



For an organ transplant to "take," it is necessary to minimize the body's drive to rid itself of foreign tissue.

One way is to make sure that the markers of self on the donor's tissue are as similar as possible to those of the recipient. Because tissue typing is usually done on white blood cells, or leukocytes, the markers are referred to as human leukocyte antigens, or HLA. Each cell has a double set of six major antigens, HLA-A, B, and C, and three types of HLA-D. Since each of the antigens exists, in different individuals, in as many as 20 varieties, the number of possible HLA types is about 10,000. The genes that encode the HLA antigens, located on chromosome 6, are the subject of intense research.

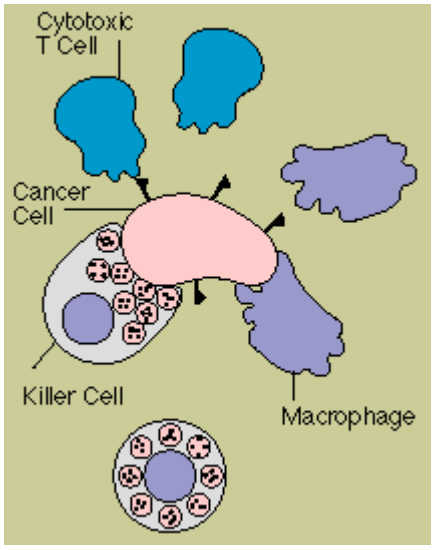
"Privileged" Immunity



A child in the womb carries foreign antigens from the father as well as immunologically compatible self antigens from the mother.

One might expect this condition to trigger a graft rejection,but it does not because the uterus is an "immunologically privileged" site where immune responses are subdued.

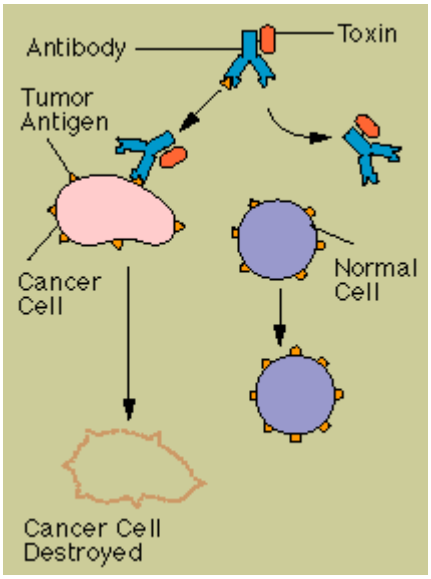
Immunity and Cancer



When normal cells turn into cancer cells, some of the antigens on their surface change.

These new or altered antigens flag immune defenders, including cytotoxic T cells, natural killer cells, and macrophages. According to one theory, patrolling cells of the immune system provide continuing bodywide surveillance, spying out and eliminating cells that undergo malignant transformation. Tumors develop when the surveillance system breaks down or is overwhelmed.

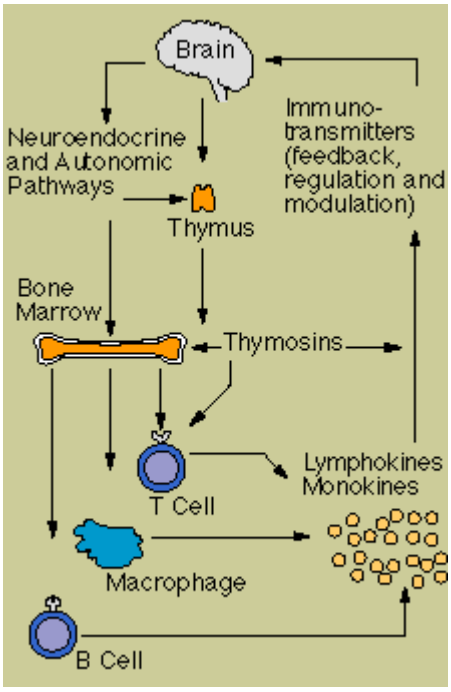
Immunotherapy



A new approach to cancer therapy uses antibodies that have been specially made to recognize specific cancer.

When coupled with natural toxins, drugs, or radioactive substances, the antibodies seek out their target cancer cells and deliver their lethal load. Alternatively, toxins can be linked to a lymphokine and routed to cells equipped with receptors for the lymphokine.

The Immune System and the Nervous System

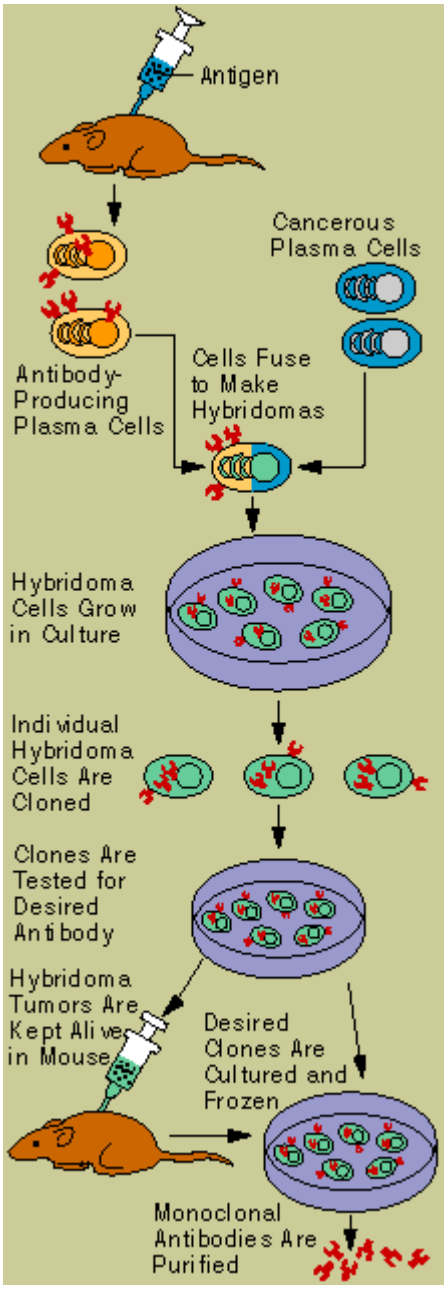


Biological links between the immune system and the central nervous system exist at several levels.

Hormones and other chemicals such as neuropeptides, which convey messages among nerve cells, have been found also to "speak" to cells of the immune system—and some immune cells even manufacture typical neuropeptides. In addition, networks of nerve fibers have been found to connect directly to the lymphoid organs.

The picture that is emerging is of closely interlocked systems facilitating a two-way flow of information. Immune cells, it has been suggested, may function in a sensory capacity, detecting the arrival of foreign invaders and relaying chemical signals to alert the brain. The brain, for its part, may send signals that guide the traffic of cells through the lymphoid organs.

Hybridoma Technology

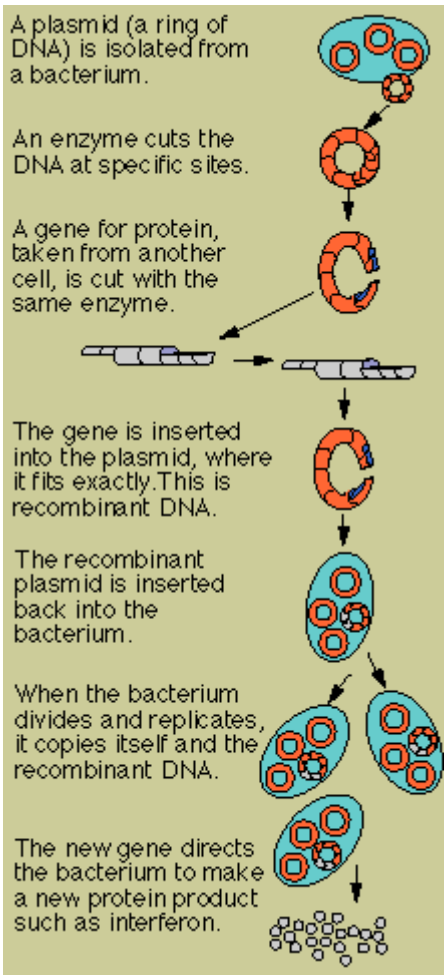


Thanks to a technique known as hybridoma technology, scientists are now able to make quantities of specific antibodies.

A hybridoma can be produced by injecting a specific antigen into a mouse, collecting antibody-producing cells from the mouse's spleen, and fusing them with long-lived cancerous immune cells. Individual hybridoma cells

are cloned and tested to find those that produce the desired antibody. Their many identical daughter clones will secrete, over a long period of time, the made-to-order "monoclonal" antibody.

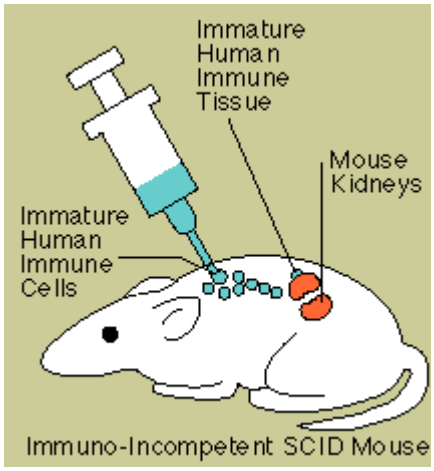
Genetic Engineering



Genetic engineering allows scientists to pluck genes—segments of DNA—from one type of organism and combine them with genes of a second organism.

In this way relatively simple organisms such as bacteria or yeast can be induced to make quantities of human proteins, including interferons and interleukins. They can also manufacture proteins from infectious agents such as the hepatitis virus or the AIDS virus, for use in vaccines.

The SCID-hu Mouse



The SCID mouse, which lacks a functioning immune system of its own, is helpless to fight infection or reject transplanted tissue.

By transplanting immature human immune tissues and/or immune cells into these mice, scientists have created an in vivo model that promises to be of immense value in advancing our understanding of the immune system.

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries and glossaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://www.graylab.ac.uk/omd/**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**
- Terms and Definitions (Office of Rare Diseases): **http://rarediseases.info.nih.gov/ord/glossary_a-e.html**

Beyond these, MEDLINEplus contains a very user-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia Web site address is **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a)** and drkoop.com (**http://www.drkoop.com/**). Topics of interest can be researched by using keywords before continuing elsewhere, as these basic definitions and concepts will be useful in more advanced areas of research. You may choose to print various pages specifically relating to autoimmune diseases and keep them on file. The NIH, in particular, suggests that patients with autoimmune diseases visit the following Web sites in the ADAM Medical Encyclopedia:

- **Basic Guidelines for Autoimmune Diseases**

  Immune hemolytic anemia
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/000576.htm

- **Signs & Symptoms for Autoimmune Diseases**

  Anemia
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/000560.htm

  Dark urine
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/003138.htm

  Enlarged spleen
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/003276.htm

  Fatigue
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/003088.htm

  Joint pain
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/003261.htm

  Joint stiffness
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/003261.htm

  Joint swelling
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/003262.htm

  Pale
  Web site:
  http://www.nlm.nih.gov/medlineplus/ency/article/003244.htm

Rapid heart rate
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003077.htm

Shortness of breath
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003075.htm

Yellow skin color
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003243.htm

- **Diagnostics and Tests for Autoimmune Diseases**

Bilirubin
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003479.htm

Coombs' test, direct
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003344.htm

Hemoglobin
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003645.htm

Red blood cell count
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003644.htm

Reticulocyte count
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003637.htm

Serum haptoglobin
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/003634.htm

- **Surgery and Procedures for Autoimmune Diseases**

Splenectomy
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/002944.htm

- **Background Topics for Autoimmune Diseases**

Antibodies
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/002223.htm

Antibody
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/002223.htm

Bleeding
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/000045.htm

Blood clots
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/001124.htm

Incidence
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/002387.htm

Precipitate
Web site:
http://www.nlm.nih.gov/medlineplus/ency/article/002275.htm

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries and glossaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

AUTOIMMUNE DISEASES GLOSSARY

The following is a complete glossary of terms used in this sourcebook. The definitions are derived from official public sources including the National Institutes of Health [NIH] and the European Union [EU]. After this glossary, we list a number of additional hardbound and electronic glossaries and dictionaries that you may wish to consult.

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Abdominal: Pertaining to the abdomen. [EU]

Acne: An inflammatory disease of the pilosebaceous unit, the specific type usually being indicated by a modifying term; frequently used alone to designate common acne, or acne vulgaris. [EU]

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Adsorption: The attachment of one substance to the surface of another; the concentration of a gas or a substance in solution in a liquid on a surface in contact with the gas or liquid, resulting in a relatively high concentration of the gas or solution at the surface. [EU]

Agranulocytosis: A symptom complex characterized by marked decrease in the number of granulocytes and by lesions of the throat and other mucous membranes, of the gastrointestinal tract, and of the skin; called also granulocytopenia and Schultz's disease. [EU]

Albuterol: A racemic mixture with a 1:1 ratio of the r-isomer, levalbuterol, and s-albuterol. It is a short-acting beta2-adrenergic agonist with its main clinical use in asthma. [NIH]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Allergen: A antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

Alopecia: Baldness; absence of the hair from skin areas where it normally is present. [EU]

Aluminum: A metallic element that has the atomic number 13, atomic symbol Al, and atomic weight 26.98. [NIH]

Analgesic: An agent that alleviates pain without causing loss of consciousness. [EU]

Androgens: A class of sex hormones associated with the development and maintenance of the secondary male sex characteristics, sperm induction, and sexual differentiation. In addition to increasing virility and libido, they also increase nitrogen and water retention and stimulate skeletal growth. [NIH]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Angioedema: A vascular reaction involving the deep dermis or subcutaneous or submucal tissues, representing localized edema caused by dilatation and increased permeability of the capillaries, and characterized by development of giant wheals. [EU]

Anorexia: Lack or loss of the appetite for food. [EU]

Antibiotic: A chemical substance produced by a microorganism which has the capacity, in dilute solutions, to inhibit the growth of or to kill other microorganisms. Antibiotics that are sufficiently nontoxic to the host are used as chemotherapeutic agents in the treatment of infectious diseases of man, animals and plants. [EU]

Antibody: An immunoglobulin molecule that has a specific amino acid sequence by virtue of which it interacts only with the antigen that induced its synthesis in cells of the lymphoid series (especially plasma cells), or with antigen closely related to it. Antibodies are classified according to their ode of action as agglutinins, bacteriolysins, haemolysins, opsonins, precipitins, etc. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antioxidant: One of many widely used synthetic or natural substances added to a product to prevent or delay its deterioration by action of oxygen in the air. Rubber, paints, vegetable oils, and prepared foods commonly contain antioxidants. [EU]

Anxiety: The unpleasant emotional state consisting of psychophysiological responses to anticipation of unreal or imagined danger, ostensibly resulting from unrecognized intrapsychic conflict. Physiological concomitants include increased heart rate, altered respiration rate, sweating, trembling, weakness, and fatigue; psychological concomitants include feelings of impending danger, powerlessness, apprehension, and tension. [EU]

Aplasia: Lack of development of an organ or tissue, or of the cellular products from an organ or tissue. [EU]

Arrhythmia: Any variation from the normal rhythm of the heart beat, including sinus arrhythmia, premature beat, heart block, atrial fibrillation, atrial flutter, pulsus alternans, and paroxysmal tachycardia. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arteritis: Inflammation of an artery. [NIH]

Aspergillosis: Infections with fungi of the genus aspergillus. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Ataxia: Failure of muscular coordination; irregularity of muscular action. [EU]

Atopic: Pertaining to an atopen or to atopy; allergic. [EU]

Autoantigens: Endogenous tissue constituents that have the ability to interact with autoantibodies and cause an immune response. [NIH]

Autoimmunity: Process whereby the immune system reacts against the body's own tissues. Autoimmunity may produce or be caused by autoimmune diseases. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Bacteriostatic: 1. inhibiting the growth or multiplication of bacteria. 2. an agent that inhibits the growth or multiplication of bacteria. [EU]

Basophils: Granular leukocytes characterized by a relatively pale-staining, lobate nucleus and cytoplasm containing coarse dark-staining granules of variable size and stainable by basic dyes. [NIH]

Benign: Not malignant; not recurrent; favourable for recovery. [EU]

Biliary: Pertaining to the bile, to the bile ducts, or to the gallbladder. [EU]

Bilirubin: A bile pigment that is a degradation product of heme. [NIH]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biopsy: The removal and examination, usually microscopic, of tissue from

the living body, performed to establish precise diagnosis. [EU]

Blister: Visible accumulations of fluid within or beneath the epidermis. [NIH]

Bordetella: A genus of gram-negative, aerobic bacteria whose cells are minute coccobacilli. It consists of both parasitic and pathogenic species. [NIH]

Bronchopulmonary: Pertaining to the lungs and their air passages; both bronchial and pulmonary. [EU]

Bullous: Pertaining to or characterized by bullae. [EU]

Candidiasis: Infection with a fungus of the genus Candida. It is usually a superficial infection of the moist cutaneous areas of the body, and is generally caused by C. albicans; it most commonly involves the skin (dermatocandidiasis), oral mucous membranes (thrush, def. 1), respiratory tract (bronchocandidiasis), and vagina (vaginitis). Rarely there is a systemic infection or endocarditis. Called also moniliasis, candidosis, oidiomycosis, and formerly blastodendriosis. [EU]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carcinoma: A malignant new growth made up of epithelial cells tending to infiltrate the surrounding tissues and give rise to metastases. [EU]

Cardiac: Pertaining to the heart. [EU]

Cardiomyopathy: A general diagnostic term designating primary myocardial disease, often of obscure or unknown etiology. [EU]

Cardiovascular: Pertaining to the heart and blood vessels. [EU]

Cataract: An opacity, partial or complete, of one or both eyes, on or in the lens or capsule, especially an opacity impairing vision or causing blindness. The many kinds of cataract are classified by their morphology (size, shape, location) or etiology (cause and time of occurrence). [EU]

Catheter: A tubular, flexible, surgical instrument for withdrawing fluids from (or introducing fluids into) a cavity of the body, especially one for introduction into the bladder through the urethra for the withdraw of urine. [EU]

Causal: Pertaining to a cause; directed against a cause. [EU]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cheilitis: Inflammation of the lips. It is of various etiologies and degrees of

pathology. [NIH]

Chelation: Combination with a metal in complexes in which the metal is part of a ring. [EU]

Chlordecone: A highly chlorinated polycyclic hydrocarbon insecticide whose large number of chlorine atoms makes it resistant to degradation. It has been shown to be toxic to mammals and causes abnormal cellular changes in laboratory animals. [NIH]

Cholesterol: The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

Chronic: Persisting over a long period of time. [EU]

Cirrhosis: Liver disease characterized pathologically by loss of the normal microscopic lobular architecture, with fibrosis and nodular regeneration. The term is sometimes used to refer to chronic interstitial inflammation of any organ. [EU]

Colitis: Inflammation of the colon. [EU]

Collagen: The protein substance of the white fibres (collagenous fibres) of skin, tendon, bone, cartilage, and all other connective tissue; composed of molecules of tropocollagen (q.v.), it is converted into gelatin by boiling. collagenous pertaining to collagen; forming or producing collagen. [EU]

Confusion: Disturbed orientation in regard to time, place, or person, sometimes accompanied by disordered consciousness. [EU]

Conjunctivitis: Inflammation of the conjunctiva, generally consisting of conjunctival hyperaemia associated with a discharge. [EU]

Contraception: The prevention of conception or impregnation. [EU]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Cutaneous: Pertaining to the skin; dermal; dermic. [EU]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyclophosphamide: Precursor of an alkylating nitrogen mustard antineoplastic and immunosuppressive agent that must be activated in the liver to form the active aldophosphamide. It is used in the treatment of lymphomas, leukemias, etc. Its side effect, alopecia, has been made use of in defleecing sheep. Cyclophosphamide may also cause sterility, birth defects, mutations, and cancer. [NIH]

Cytokines: Non-antibody proteins secreted by inflammatory leukocytes and some non-leukocytic cells, that act as intercellular mediators. They differ from classical hormones in that they are produced by a number of tissue or

cell types rather than by specialized glands. They generally act locally in a paracrine or autocrine rather than endocrine manner. [NIH]

Cytotoxic: Pertaining to or exhibiting cytotoxicity. [EU]

Danazol: A synthetic steroid with antigonadotropic and anti-estrogenic activities that acts as an anterior pituitary suppressant by inhibiting the pituitary output of gonadotropins. It possesses some androgenic properties. Danazol has been used in the treatment of endometriosis and some benign breast disorders. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Dermatitis: Inflammation of the skin. [EU]

Dermatology: A medical specialty concerned with the skin, its structure, functions, diseases, and treatment. [NIH]

Dermatosis: Any skin disease, especially one not characterized by inflammation. [EU]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diphtheria: A localized infection of mucous membranes or skin caused by toxigenic strains of corynebacterium diphtheriae. It is characterized by the presence of a pseudomembrane at the site of infection. Diphtheria toxin, produced by C. diphtheriae, can cause myocarditis, polyneuritis, and other systemic toxic effects. [NIH]

Dizziness: An imprecise term which may refer to a sense of spatial disorientation, motion of the environment, or lightheadedness. [NIH]

Echinacea: A genus of perennial herbs used topically and internally. It contains echinacoside, glycosides, inulin, isobutyl amides, resin, and sesquiterpenes. [NIH]

Encephalitis: Inflammation of the brain. [EU]

Encephalomyelitis: A general term indicating inflammation of the brain and spinal cord, often used to indicate an infectious process, but also applicable to a variety of autoimmune and toxic-metabolic conditions. There is significant overlap regarding the usage of this term and encephalitis in the literature. [NIH]

Endocrinology: A subspecialty of internal medicine concerned with the metabolism, physiology, and disorders of the endocrine system. [NIH]

Endoscopy: Visual inspection of any cavity of the body by means of an endoscope. [EU]

Enzyme: A protein molecule that catalyses chemical reactions of other substances without itself being destroyed or altered upon completion of the reactions. Enzymes are classified according to the recommendations of the Nomenclature Committee of the International Union of Biochemistry. Each enzyme is assigned a recommended name and an Enzyme Commission (EC) number. They are divided into six main groups; oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases. [EU]

Eosinophils: Granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are uniform in size and stainable by eosin. [NIH]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epitopes: Sites on an antigen that interact with specific antibodies. [NIH]

Estrogens: A class of sex hormones associated with the development and maintenance of secondary female sex characteristics and control of the cyclical changes in the reproductive cycle. They are also required for pregnancy maintenance and have an anabolic effect on protein metabolism and water retention. [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Extracorporeal: Situated or occurring outside the body. [EU]

Fatigue: The state of weariness following a period of exertion, mental or physical, characterized by a decreased capacity for work and reduced efficiency to respond to stimuli. [NIH]

Febrile: Pertaining to or characterized by fever. [EU]

Fibroblasts: Connective tissue cells which secrete an extracellular matrix rich in collagen and other macromolecules. [NIH]

Fibrosis: The formation of fibrous tissue; fibroid or fibrous degeneration [EU]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and

emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fungistatic: Inhibiting the growth of fungi. [EU]

Gastritis: Inflammation of the stomach. [EU]

Gastrointestinal: Pertaining to or communicating with the stomach and intestine, as a gastrointestinal fistula. [EU]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Gingivitis: Inflammation of the gingivae. Gingivitis associated with bony changes is referred to as periodontitis. Called also oulitis and ulitis. [EU]

Glucose: D-glucose, a monosaccharide (hexose), C6H12O6, also known as dextrose (q.v.), found in certain foodstuffs, especially fruits, and in the normal blood of all animals. It is the end product of carbohydrate metabolism and is the chief source of energy for living organisms, its utilization being controlled by insulin. Excess glucose is converted to glycogen and stored in the liver and muscles for use as needed and, beyond that, is converted to fat and stored as adipose tissue. Glucose appears in the urine in diabetes mellitus. [EU]

Glutamine: A non-essential amino acid present abundantly throught the body and is involved in many metabolic processes. It is synthesized from glutamic acid and ammonia. It is the principal carrier of nitrogen in the body and is an important energy source for many cells. [NIH]

Gluten: The protein of wheat and other grains which gives to the dough its tough elastic character. [EU]

Granule: A small pill made from sucrose. [EU]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Halitosis: An offensive, foul breath odor resulting from a variety of causes such as poor oral hygiene, dental or oral infections, or the ingestion of certain foods. [NIH]

Haplotypes: The genetic constitution of individuals with respect to one member of a pair of allelic genes, or sets of genes that are closely linked and tend to be inherited together such as those of the major histocompatibility complex. [NIH]

Hemagglutinins: Agents that cause agglutination of red blood cells. They include antibodies, blood group antigens, lectins, autoimmune factors,

bacterial, viral, or parasitic blood agglutinins, etc. [NIH]

Hematology: A subspecialty of internal medicine concerned with morphology, physiology, and pathology of the blood and blood-forming tissues. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hepatic: Pertaining to the liver. [EU]

Hepatitis: Inflammation of the liver. [EU]

Hepatocytes: The main structural component of the liver. They are specialized epithelial cells that are organized into interconnected plates called lobules. [NIH]

Heredity: 1. the genetic transmission of a particular quality or trait from parent to offspring. 2. the genetic constitution of an individual. [EU]

Herpes: Any inflammatory skin disease caused by a herpesvirus and characterized by the formation of clusters of small vesicles. When used alone, the term may refer to herpes simplex or to herpes zoster. [EU]

Heterozygote: An individual having different alleles at one or more loci in homologous chromosome segments. [NIH]

Histocompatibility: The degree of antigenic similarity between the tissues of different individuals, which determines the acceptance or rejection of allografts. [NIH]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormones: Chemical substances having a specific regulatory effect on the activity of a certain organ or organs. The term was originally applied to substances secreted by various endocrine glands and transported in the bloodstream to the target organs. It is sometimes extended to include those substances that are not produced by the endocrine glands but that have similar effects. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hydrocortisone: The main glucocorticoid secreted by the adrenal cortex. Its synthetic counterpart is used, either as an injection or topically, in the treatment of inflammation, allergy, collagen diseases, asthma, adrenocortical deficiency, shock, and some neoplastic conditions. [NIH]

Hydrophobic: Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

Hyperhomocysteinemia: An inborn error of methionone metabolism which produces an excess of homocysteine in the blood. It is often caused by a deficiency of cystathionine beta-synthase and is a risk factor for coronary vascular disease. [NIH]

Hyperplasia: The abnormal multiplication or increase in the number of normal cells in normal arrangement in a tissue. [EU]

Hypersensitivity: A state of altered reactivity in which the body reacts with an exaggerated immune response to a foreign substance. Hypersensitivity reactions are classified as immediate or delayed, types I and IV, respectively, in the Gell and Coombs classification (q.v.) of immune responses. [EU]

Hypertension: Persistently high arterial blood pressure. Various criteria for its threshold have been suggested, ranging from 140 mm. Hg systolic and 90 mm. Hg diastolic to as high as 200 mm. Hg systolic and 110 mm. Hg diastolic. Hypertension may have no known cause (essential or idiopathic h.) or be associated with other primary diseases (secondary h.). [EU]

Hyperthyroidism: 1. excessive functional activity of the thyroid gland. 2. the abnormal condition resulting from hyperthyroidism marked by increased metabolic rate, enlargement of the thyroid gland, rapid heart rate, high blood pressure, and various secondary symptoms. [EU]

Hypogonadism: A condition resulting from or characterized by abnormally decreased functional activity of the gonads, with retardation of growth and sexual development. [EU]

Hypothyroidism: Deficiency of thyroid activity. In adults, it is most common in women and is characterized by decrease in basal metabolic rate, tiredness and lethargy, sensitivity to cold, and menstrual disturbances. If untreated, it progresses to full-blown myxoedema. In infants, severe hypothyroidism leads to cretinism. In juveniles, the manifestations are intermediate, with less severe mental and developmental retardation and only mild symptoms of the adult form. When due to pituitary deficiency of thyrotropin secretion it is called secondary hypothyroidism. [EU]

Immunization: The induction of immunity. [EU]

Immunosuppressant: An agent capable of suppressing immune responses. [EU]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Incontinence: Inability to control excretory functions, as defecation (faecal i.) or urination (urinary i.). [EU]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Influenza: An acute viral infection involving the respiratory tract. It is marked by inflammation of the nasal mucosa, the pharynx, and conjunctiva, and by headache and severe, often generalized, myalgia. [NIH]

Ingestion: The act of taking food, medicines, etc., into the body, by mouth. [EU]

Inorganic: Pertaining to substances not of organic origin. [EU]

Insomnia: Inability to sleep; abnormal wakefulness. [EU]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Interferons: Proteins secreted by vertebrate cells in response to a wide variety of inducers. They confer resistance against many different viruses, inhibit proliferation of normal and malignant cells, impede multiplication of intracellular parasites, enhance macrophage and granulocyte phagocytosis, augment natural killer cell activity, and show several other immunomodulatory functions. [NIH]

Interleukins: Soluble factors which stimulate growth-related activities of leukocytes as well as other cell types. They enhance cell proliferation and differentiation, DNA synthesis, secretion of other biologically active molecules and responses to immune and inflammatory stimuli. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Invasive: 1. having the quality of invasiveness. 2. involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Iodine: A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

Ischemia: Deficiency of blood in a part, due to functional constriction or

actual obstruction of a blood vessel. [EU]

Isoflavones: 3-Phenylchromones. Isomeric form of flavones in which the benzene group is attached to the 3 position of the benzopyran ring instead of the 2 position. [NIH]

Jaundice: A clinical manifestation of hyperbilirubinemia, consisting of deposition of bile pigments in the skin, resulting in a yellowish staining of the skin and mucous membranes. [NIH]

Keratosis: Any horny growth such as a wart or callus. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Lacrimal: Pertaining to the tears. [EU]

Lesion: Any pathological or traumatic discontinuity of tissue or loss of function of a part. [EU]

Lethal: Deadly, fatal. [EU]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Lubrication: The application of a substance to diminish friction between two surfaces. It may refer to oils, greases, and similar substances for the lubrication of medical equipment but it can be used for the application of substances to tissue to reduce friction, such as lotions for skin and vaginal lubricants. [NIH]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lymphadenitis: Inflammation of the lymph nodes. [NIH]

Lymphocytic: Pertaining to, characterized by, or of the nature of lymphocytes. [EU]

Lymphokines: Soluble protein factors generated by activated lymphocytes that affect other cells, primarily those involved in cellular immunity. [NIH]

Lymphoma: Any neoplastic disorder of the lymphoid tissue, the term lymphoma often is used alone to denote malignant lymphoma. [EU]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malformation: A morphologic defect resulting from an intrinsically abnormal developmental process. [EU]

Malignant: Tending to become progressively worse and to result in death. Having the properties of anaplasia, invasion, and metastasis; said of

tumours. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Mefenamic Acid: A non-steroidal anti-inflammatory agent with analgesic, anti-inflammatory, and antipyretic properties. It is an inhibitor of cyclooxygenase. [NIH]

Membrane: A thin layer of tissue which covers a surface, lines a cavity or divides a space or organ. [EU]

Menopause: Cessation of menstruation in the human female, occurring usually around the age of 50. [EU]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

Methimazole: A thioureylene antithyroid agent that inhibits the formation of thyroid hormones by interfering with the incorporation of iodine into tyrosyl residues of thyroglobulin. This is done by interfering with the oxidation of iodide ion and iodotyrosyl groups through inhibition of the peroxidase enzyme. [NIH]

Methotrexate: An antineoplastic antimetabolite with immunosuppressant properties. It is an inhibitor of dihydrofolate reductase and prevents the formation of tetrahydrofolate, necessary for synthesis of thymidylate, an essential component of DNA. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Micronutrients: Essential dietary elements or organic compounds that are required in only small quantities for normal physiologic processes to occur. [NIH]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Mobility: Capability of movement, of being moved, or of flowing freely. [EU]

Mobilization: The process of making a fixed part or stored substance mobile, as by separating a part from surrounding structures to make it accessible for an operative procedure or by causing release into the circulation for body use of a substance stored in the body. [EU]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Monocytes: Large, phagocytic mononuclear leukocytes produced in the

vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles. [NIH]

Monokines: Soluble mediators of the immune response that are neither antibodies nor complement. They are produced largely, but not exclusively, by monocytes and macrophages. [NIH]

Mononucleosis: The presence of an abnormally large number of mononuclear leucocytes (monocytes) in the blood. The term is often used alone to refer to infectious mononucleosis. [EU]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Myasthenia: Muscular debility; any constitutional anomaly of muscle. [EU]

Mycobacterium: An organism of the genus Mycobacterium. [EU]

Mycoplasma: A genus of gram-negative, facultatively anaerobic bacteria bounded by a plasma membrane only. Its organisms are parasites and pathogens, found on the mucous membranes of humans, animals, and birds. [NIH]

Myocarditis: Inflammation of the myocardium; inflammation of the muscular walls of the heart. [EU]

Nadir: The lowest point; point of greatest adversity or despair. [EU]

Nausea: An unpleasant sensation, vaguely referred to the epigastrium and abdomen, and often culminating in vomiting. [EU]

Necrosis: The sum of the morphological changes indicative of cell death and caused by the progressive degradative action of enzymes; it may affect groups of cells or part of a structure or an organ. [EU]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

Nephrotic: Pertaining to, resembling, or caused by nephrosis. [EU]

Nervousness: Excessive excitability and irritability, with mental and physical unrest. [EU]

Neuritis: Inflammation of a nerve, a condition attended by pain and tenderness over the nerves, anaesthesia and paraesthesias, paralysis, wasting, and disappearance of the reflexes. In practice, the term is also used to denote noninflammatory lesions of the peripheral nervous system; see neuropathy. [EU]

Neuromuscular: Pertaining to muscles and nerves. [EU]

Neuropathy: A general term denoting functional disturbances and/or

pathological changes in the peripheral nervous system. The etiology may be known e.g. arsenical n., diabetic n., ischemic n., traumatic n.) or unknown. Encephalopathy and myelopathy are corresponding terms relating to involvement of the brain and spinal cord, respectively. The term is also used to designate noninflammatory lesions in the peripheral nervous system, in contrast to inflammatory lesions (neuritis). [EU]

Neuropeptides: Peptides released by neurons as intercellular messengers. Many neuropeptides are also hormones released by non-neuronal cells. [NIH]

Neurotransmitter: Any of a group of substances that are released on excitation from the axon terminal of a presynaptic neuron of the central or peripheral nervous system and travel across the synaptic cleft to either excite or inhibit the target cell. Among the many substances that have the properties of a neurotransmitter are acetylcholine, norepinephrine, epinephrine, dopamine, glycine, y-aminobutyrate, glutamic acid, substance P, enkephalins, endorphins, and serotonin. [EU]

Neutrophil: Having an affinity for neutral dyes. [EU]

Niacin: Water-soluble vitamin of the B complex occurring in various animal and plant tissues. Required by the body for the formation of coenzymes NAD and NADP. Has pellagra-curative, vasodilating, and antilipemic properties. [NIH]

Nucleoproteins: Proteins conjugated with nucleic acids. [NIH]

Ocular: 1. of, pertaining to, or affecting the eye. 2. eyepiece. [EU]

Oophoritis: Inflammation of an ovary. [NIH]

Ophthalmology: A surgical specialty concerned with the structure and function of the eye and the medical and surgical treatment of its defects and diseases. [NIH]

Orchitis: Inflammation of a testis. The disease is marked by pain, swelling, and a feeling of weight. It may occur idiopathically, or it may be associated with conditions such as mumps, gonorrhoea, filarial disease, syphilis, or tuberculosis. [EU]

Osteoarthritis: Noninflammatory degenerative joint disease occurring chiefly in older persons, characterized by degeneration of the articular cartilage, hypertrophy of bone at the margins, and changes in the synovial membrane. It is accompanied by pain and stiffness, particularly after prolonged activity. [EU]

Osteodystrophy: Defective bone formation. [EU]

Osteoporosis: Reduction in the amount of bone mass, leading to fractures after minimal trauma. [EU]

Otolaryngology: A surgical specialty concerned with the study and

treatment of disorders of the ear, nose, and throat. [NIH]

Overdose: 1. to administer an excessive dose. 2. an excessive dose. [EU]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the islets of langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatitis: Acute or chronic inflammation of the pancreas, which may be asymptomatic or symptomatic, and which is due to autodigestion of a pancreatic tissue by its own enzymes. It is caused most often by alcoholism or biliary tract disease; less commonly it may be associated with hyperlipaemia, hyperparathyroidism, abdominal trauma (accidental or operative injury), vasculitis, or uraemia. [EU]

Papule: A small circumscribed, superficial, solid elevation of the skin. [EU]

Paralysis: Loss or impairment of motor function in a part due to lesion of the neural or muscular mechanism; also by analogy, impairment of sensory function (sensory paralysis). In addition to the types named below, paralysis is further distinguished as traumatic, syphilitic, toxic, etc., according to its cause; or as obturator, ulnar, etc., according to the nerve part, or muscle specially affected. [EU]

Parasitic: Pertaining to, of the nature of, or caused by a parasite. [EU]

Particle: A tiny mass of material. [EU]

Pathologic: 1. indicative of or caused by a morbid condition. 2. pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pediatrics: A medical specialty concerned with maintaining health and providing medical care to children from birth to adolescence. [NIH]

Pemphigus: A group of chronic, relapsing, sometimes fatal skin diseases characterized clinically by the development of successive crops of vesicles and bullae, histologically by acantholysis, and immunologically by serum autoantibodies directed against antigens in the intracellular zones of the epidermis. The specific disease is usually indicated by a modifying term; but the term pemphigus is often used alone to designate pemphigus vulgaris. [EU]

Perennial: Lasting through the year of for several years. [EU]

Perioral: Situated or occurring around the mouth. [EU]

Pernicious: Tending to a fatal issue. [EU]

Pharmacodynamics: The study of the biochemical and physiological effects of drugs and the mechanisms of their actions, including the correlation of actions and effects of drugs with their chemical structure; also, such effects on the actions of a particular drug or drugs. [EU]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Photochemotherapy: Therapy using oral or topical photosensitizing agents with subsequent exposure to light. [NIH]

Pigmentation: 1. the deposition of colouring matter; the coloration or discoloration of a part by pigment. 2. coloration, especially abnormally increased coloration, by melanin. [EU]

Plasmacytoma: Any discrete, presumably solitary, mass of neoplastic plasma cells either in bone marrow or various extramedullary sites. [NIH]

Plasmapheresis: Procedure whereby plasma is separated and extracted from anticoagulated whole blood and the red cells retransfused to the donor. Plasmapheresis is also employed for therapeutic use. [NIH]

Pneumonia: Inflammation of the lungs with consolidation. [EU]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Porphyria: A pathological state in man and some lower animals that is often due to genetic factors, is characterized by abnormalities of porphyrin metabolism, and results in the excretion of large quantities of porphyrins in the urine and in extreme sensitivity to light. [EU]

Potassium: An element that is in the alkali group of metals. It has an atomic symbol K, atomic number 19, and atomic weight 39.10. It is the chief cation in the intracellular fluid of muscle and other cells. Potassium ion is a strong electrolyte and it plays a significant role in the regulation of fluid volume and maintenance of the water-electrolyte balance. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance

from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Predisposition: A latent susceptibility to disease which may be activated under certain conditions, as by stress. [EU]

Prednisone: A synthetic anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. [NIH]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Prophylaxis: The prevention of disease; preventive treatment. [EU]

Propolis: Resinous substance obtained from beehives; contains many different substances which may have antimicrobial or antimycotic activity topically; its extracts are called propolis resin or balsam. Synonyms: bee bread; hive dross; bee glue. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Proteolytic: 1. pertaining to, characterized by, or promoting proteolysis. 2. an enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Psoriasis: A common genetically determined, chronic, inflammatory skin disease characterized by rounded erythematous, dry, scaling patches. The lesions have a predilection for nails, scalp, genitalia, extensor surfaces, and the lumbosacral region. Accelerated epidermopoiesis is considered to be the fundamental pathologic feature in psoriasis. [NIH]

Psychiatric: Pertaining to or within the purview of psychiatry. [EU]

Punctures: Incision of tissues for injection of medication or for other diagnostic or therapeutic procedures. Punctures of the skin, for example may be used for diagnostic drainage; of blood vessels for diagnostic imaging procedures. [NIH]

Purpura: Purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues. [NIH]

Radiology: A specialty concerned with the use of x-ray and other forms of radiant energy in the diagnosis and treatment of disease. [NIH]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Receptor: 1. a molecular structure within a cell or on the surface

characterized by (1) selective binding of a specific substance and (2) a specific physiologic effect that accompanies the binding, e.g., cell-surface receptors for peptide hormones, neurotransmitters, antigens, complement fragments, and immunoglobulins and cytoplasmic receptors for steroid hormones. 2. a sensory nerve terminal that responds to stimuli of various kinds. [EU]

Recombinant: 1. a cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Reconstitution: 1. a type of regeneration in which a new organ forms by the rearrangement of tissues rather than from new formation at an injured surface. 2. the restoration to original form of a substance previously altered for preservation and storage, as the restoration to a liquid state of blood serum or plasma that has been dried and stored. [EU]

Refractory: Not readily yielding to treatment. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Reishi: A mushroom, Ganoderma lucidum, of the aphyllophorales order of basidomycetous fungi. It has long been used in traditional Chinese medicine in various forms. Contains sterols, coumarin, mannitol, polysaccharides, and triterpenoids. [NIH]

Remission: A diminution or abatement of the symptoms of a disease; also the period during which such diminution occurs. [EU]

Reperfusion: Restoration of blood supply to tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. It is primarily a procedure for treating infarction or other ischemia, by enabling viable ischemic tissue to recover, thus limiting further necrosis. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing reperfusion injury. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

Rheumatology: A subspecialty of internal medicine concerned with the study of inflammatory or degenerative processes and metabolic derangement of connective tissue structures which pertain to a variety of musculoskeletal disorders, such as arthritis. [NIH]

Riboflavin: Nutritional factor found in milk, eggs, malted barley, liver, kidney, heart, and leafy vegetables. The richest natural source is yeast. It occurs in the free form only in the retina of the eye, in whey, and in urine; its principal forms in tissues and cells are as FMN and FAD. [NIH]

Rubella: An acute, usually benign, infectious disease caused by a togavirus and most often affecting children and nonimmune young adults, in which

the virus enters the respiratory tract via droplet nuclei and spreads to the lymphatic system. It is characterized by a slight cold, sore throat, and fever, followed by enlargement of the postauricular, suboccipital, and cervical lymph nodes, and the appearances of a fine pink rash that begins on the head and spreads to become generalized. Called also German measles, roetln, röteln, and three-day measles, and rubeola in French and Spanish. [EU]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Sarcoidosis: An idiopathic systemic inflammatory granulomatous disorder comprised of epithelioid and multinucleated giant cells with little necrosis. It usually invades the lungs with fibrosis and may also involve lymph nodes, skin, liver, spleen, eyes, phalangeal bones, and parotid glands. [NIH]

Sarcoma: A tumour made up of a substance like the embryonic connective tissue; tissue composed of closely packed cells embedded in a fibrillar or homogeneous substance. Sarcomas are often highly malignant. [EU]

Schizophrenia: A severe emotional disorder of psychotic depth characteristically marked by a retreat from reality with delusion formation, hallucinations, emotional disharmony, and regressive behavior. [NIH]

Sclerosis: A induration, or hardening; especially hardening of a part from inflammation and in diseases of the interstitial substance. The term is used chiefly for such a hardening of the nervous system due to hyperplasia of the connective tissue or to designate hardening of the blood vessels. [EU]

Secretion: 1. the process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. any substance produced by secretion. [EU]

Sedimentation: The act of causing the deposit of sediment, especially by the use of a centrifugal machine. [EU]

Selenium: An element with the atomic symbol Se, atomic number 34, and atomic weight 78.96. It is an essential micronutrient for mammals and other animals but is toxic in large amounts. Selenium protects intracellular structures against oxidative damage. It is an essential component of glutathione peroxidase. [NIH]

Septic: Produced by or due to decomposition by microorganisms; putrefactive. [EU]

Serum: The clear portion of any body fluid; the clear fluid moistening serous membranes. 2. blood serum; the clear liquid that separates from blood on clotting. 3. immune serum; blood serum from an immunized animal used for passive immunization; an antiserum; antitoxin, or antivenin. [EU]

Sialorrhea: Increased salivary flow. [NIH]

Sinusitis: Inflammation of a sinus. The condition may be purulent or nonpurulent, acute or chronic. Depending on the site of involvement it is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. [EU]

Sneezing: Sudden, forceful, involuntary expulsion of air from the nose and mouth caused by irritation to the mucous membranes of the upper respiratory tract. [NIH]

Somatic: 1. pertaining to or characteristic of the soma or body. 2. pertaining to the body wall in contrast to the viscera. [EU]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Spondylitis: Inflammation of the vertebrae. [EU]

Stimulant: 1. producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. an agent or remedy that produces stimulation. [EU]

Stomatitis: Inflammation of the oral mucosa, due to local or systemic factors which may involve the buccal and labial mucosa, palate, tongue, floor of the mouth, and the gingivae. [EU]

Substrate: A substance upon which an enzyme acts. [EU]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Systemic: Pertaining to or affecting the body as a whole. [EU]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Tachycardia: Excessive rapidity in the action of the heart; the term is usually applied to a heart rate above 100 per minute and may be qualified as atrial, junctional (nodal), or ventricular, and as paroxysmal. [EU]

Tacrolimus: A macrolide isolated from the culture broth of a strain of Streptomyces tsukubaensis that has strong immunosuppressive activity in vivo and prevents the activation of T-lymphocytes in response to antigenic or mitogenic stimulation in vitro. [NIH]

Testicular: Pertaining to a testis. [EU]

Tetanus: A disease caused by tetanospasmin, a powerful protein toxin produced by clostridium tetani. Tetanus usually occurs after an acute injury, such as a puncture wound or laceration. Generalized tetanus, the most common form, is characterized by tetanic muscular contractions and hyperreflexia. Localized tetanus presents itself as a mild condition with manifestations restricted to muscles near the wound. It may progress to the generalized form. [NIH]

Thalidomide: A pharmaceutical agent originally introduced as a non-barbiturate hypnotic, but withdrawn from the market because of its known tetratogenic effects. It has been reintroduced and used for a number of immunological and inflammatory disorders. Thalidomide displays immunosuppresive and anti-angiogenic activity. It inhibits release of tumor necrosis factor alpha from monocytes, and modulates other cytokine action. [NIH]

Thermoregulation: Heat regulation. [EU]

Thrombocytopenia: Decrease in the number of blood platelets. [EU]

Thrombosis: The formation, development, or presence of a thrombus. [EU]

Thyrotropin: A peptide hormone secreted by the anterior pituitary. It promotes the growth of the thyroid gland and stimulates the synthesis of thyroid hormones and the release of thyroxine by the thyroid gland. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

Tolerance: 1. the ability to endure unusually large doses of a drug or toxin. 2. acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Tomography: The recording of internal body images at a predetermined plane by means of the tomograph; called also body section roentgenography. [EU]

Topical: Pertaining to a particular surface area, as a topical anti-infective applied to a certain area of the skin and affecting only the area to which it is applied. [EU]

Toxic: Pertaining to, due to, or of the nature of a poison or toxin; manifesting the symptoms of severe infection. [EU]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

Transfusion: The introduction of whole blood or blood component directly into the blood stream. [EU]

Transgenes: Genes that are introduced into an organism using gene transfer techniques. [NIH]

Transplantation: The grafting of tissues taken from the patient's own body or from another. [EU]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of mycobacterium. [NIH]

Tumour: 1. swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. a new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Ulceration: 1. the formation or development of an ulcer. 2. an ulcer. [EU]

Urinalysis: Examination of urine by chemical, physical, or microscopic means. Routine urinalysis usually includes performing chemical screening tests, determining specific gravity, observing any unusual color or odor, screening for bacteriuria, and examining the sediment microscopically. [NIH]

Urinary: Pertaining to the urine; containing or secreting urine. [EU]

Urticaria: Pathology: a transient condition of the skin, usually caused by an allergic reaction, characterized by pale or reddened irregular, elevated patches and severe itching; hives. [EU]

Uterus: The hollow muscular organ in female mammals in which the fertilized ovum normally becomes embedded and in which the developing embryo and fetus is nourished. In the nongravid human, it is a pear-shaped structure; about 3 inches in length, consisting of a body, fundus, isthmus, and cervix. Its cavity opens into the vagina below, and into the uterine tube on either side at the cornu. It is supported by direct attachment to the vagina and by indirect attachment to various other nearby pelvic structures. Called also metra. [EU]

Uveitis: An inflammation of part or all of the uvea, the middle (vascular) tunic of the eye, and commonly involving the other tunics (the sclera and cornea, and the retina). [EU]

Vaccination: The introduction of vaccine into the body for the purpose of inducing immunity. Coined originally to apply to the injection of smallpox vaccine, the term has come to mean any immunizing procedure in which vaccine is injected. [EU]

Vaccine: A suspension of attenuated or killed microorganisms (bacteria, viruses, or rickettsiae), administered for the prevention, amelioration or treatment of infectious diseases. [EU]

Varicella: Chicken pox. [EU]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vasculitis: Inflammation of a vessel, angiitis. [EU]

Ventricular: Pertaining to a ventricle. [EU]

Vertigo: An illusion of movement; a sensation as if the external world were

revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

Vesicular: 1. composed of or relating to small, saclike bodies. 2. pertaining to or made up of vesicles on the skin. [EU]

Vestibular: Pertaining to or toward a vestibule. In dental anatomy, used to refer to the tooth surface directed toward the vestibule of the mouth. [EU]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viruses: Minute infectious agents whose genomes are composed of DNA or RNA, but not both. They are characterized by a lack of independent metabolism and the inability to replicate outside living host cells. [NIH]

Vitiligo: A disorder consisting of areas of macular depigmentation, commonly on extensor aspects of extremities, on the face or neck, and in skin folds. Age of onset is often in young adulthood and the condition tends to progress gradually with lesions enlarging and extending until a quiescent state is reached. [NIH]

Withdrawal: 1. a pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) a substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Xerostomia: Dryness of the mouth from salivary gland dysfunction, as in Sjögren's syndrome. [EU]

General Dictionaries and Glossaries

While the above glossary is essentially complete, the dictionaries listed here cover virtually all aspects of medicine, from basic words and phrases to more advanced terms (sorted alphabetically by title; hyperlinks provide rankings, information and reviews at Amazon.com):

- **Dictionary of Medical Acronymns & Abbreviations** by Stanley Jablonski (Editor), Paperback, 4th edition (2001), Lippincott Williams & Wilkins Publishers, ISBN: 1560534605, **http://www.amazon.com/exec/obidos/ASIN/1560534605/icongroupinterna**
- **Dictionary of Medical Terms : For the Nonmedical Person (Dictionary of Medical Terms for the Nonmedical Person, Ed 4)** by Mikel A. Rothenberg, M.D, et al, Paperback - 544 pages, 4th edition (2000), Barrons Educational

Series, ISBN: 0764112015,
http://www.amazon.com/exec/obidos/ASIN/0764112015/icongroupinterna

- **A Dictionary of the History of Medicine** by A. Sebastian, CD-Rom edition (2001), CRC Press-Parthenon Publishers, ISBN: 185070368X,
http://www.amazon.com/exec/obidos/ASIN/185070368X/icongroupinterna
- **Dorland's Illustrated Medical Dictionary (Standard Version)** by Dorland, et al, Hardcover - 2088 pages, 29th edition (2000), W B Saunders Co, ISBN: 0721662544,
http://www.amazon.com/exec/obidos/ASIN/0721662544/icongroupinterna
- **Dorland's Electronic Medical Dictionary** by Dorland, et al, Software, 29th Book & CD-Rom edition (2000), Harcourt Health Sciences, ISBN: 0721694934,
http://www.amazon.com/exec/obidos/ASIN/0721694934/icongroupinterna
- **Dorland's Pocket Medical Dictionary (Dorland's Pocket Medical Dictionary, 26th Ed)** Hardcover - 912 pages, 26th edition (2001), W B Saunders Co, ISBN: 0721682812,
http://www.amazon.com/exec/obidos/ASIN/0721682812/icongroupinterna/103-4193558-7304618
- **Melloni's Illustrated Medical Dictionary (Melloni's Illustrated Medical Dictionary, 4th Ed)** by Melloni, Hardcover, 4th edition (2001), CRC Press-Parthenon Publishers, ISBN: 85070094X,
http://www.amazon.com/exec/obidos/ASIN/85070094X/icongroupinterna
- **Stedman's Electronic Medical Dictionary Version 5.0 (CD-ROM for Windows and Macintosh, Individual)** by Stedmans, CD-ROM edition (2000), Lippincott Williams & Wilkins Publishers, ISBN: 0781726328,
http://www.amazon.com/exec/obidos/ASIN/0781726328/icongroupinterna
- **Stedman's Medical Dictionary** by Thomas Lathrop Stedman, Hardcover - 2098 pages, 27th edition (2000), Lippincott, Williams & Wilkins, ISBN: 068340007X,
http://www.amazon.com/exec/obidos/ASIN/068340007X/icongroupinterna
- **Tabers Cyclopedic Medical Dictionary (Thumb Index)** by Donald Venes (Editor), et al, Hardcover - 2439 pages, 19th edition (2001), F A Davis Co, ISBN: 0803606540,
http://www.amazon.com/exec/obidos/ASIN/0803606540/icongroupinterna

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