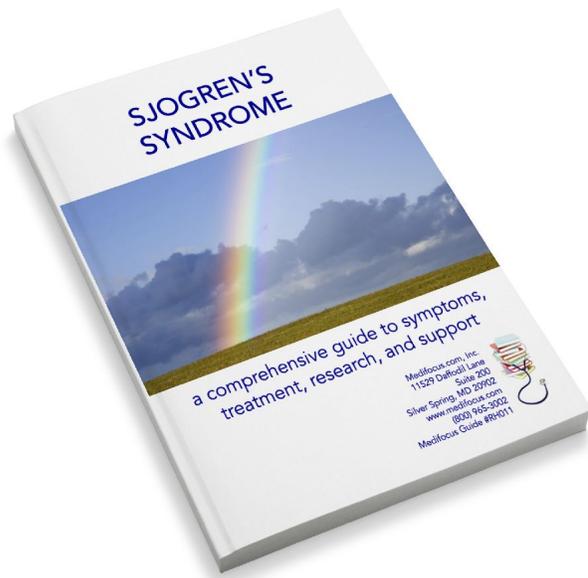


## Preview of the Medifocus Guidebook on: Sjogren's Syndrome

Updated January 11, 2024



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Sjogren's Syndrome**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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# 1 - Background Information

## Introduction

Chronic or life-threatening illnesses can have a devastating impact on both the patient and the family. In today's new world of medicine, many consumers have come to realize that they are the ones who are primarily responsible for their own health care as well as for the health care of their loved ones.

When facing a chronic or life-threatening illness, you need to become an educated consumer in order to make an informed health care decision. Essentially that means finding out everything about the illness - the treatment options, the doctors, and the hospitals - so that you can become an educated health care consumer and make the tough decisions. In the past, consumers would go to a library and read everything available about a particular illness or medical condition. In today's world, many turn to the Internet for their medical information needs.

The first sites visited are usually the well known health "portals" or disease organizations and support groups which contain a general overview of the condition for the layperson. That's a good start but soon all of the basic information is exhausted and the need for more advanced information still exists. What are the latest "cutting-edge" treatment options? What are the results of the most up-to-date clinical trials? Who are the most notable experts? Where are the top-ranked medical institutions and hospitals?

The best source for authoritative medical information in the United States is the National Library of Medicine's medical database called PubMed®, that indexes citations and abstracts (brief summaries) of over 7 million articles from more than 3,800 medical journals published worldwide. PubMed® was developed for medical professionals and is the primary source utilized by health care providers for keeping up with the latest advances in clinical medicine.

A typical PubMed® search for a specific disease or condition, however, usually retrieves hundreds or even thousands of "hits" of journal article citations. That's an avalanche of information that needs to be evaluated and transformed into truly useful knowledge. What are the most relevant journal articles? Which ones apply to your specific situation? Which articles are considered to be the most authoritative - the ones your physician would rely on in making clinical decisions? This is where *Medifocus.com* provides an effective solution.

*Medifocus.com* has developed an extensive library of *MediFocus Guidebooks* covering a wide spectrum of chronic and life threatening diseases. Each *MediFocus Guidebook* is a

high quality, up- to-date digest of "professional-level" medical information consisting of the most relevant citations and abstracts of journal articles published in authoritative, trustworthy medical journals. This information represents the latest advances known to modern medicine for the treatment and management of the condition, including published results from clinical trials. Each *Guidebook* also includes a valuable index of leading authors and medical institutions as well as a directory of disease organizations and support groups. *MediFocus Guidebooks* are reviewed, revised and updated every 4-months to ensure that you receive the latest and most up-to-date information about the specific condition.

## About Your MediFocus Guidebook

### ***Introduction***

Your *MediFocus Guidebook* is a valuable resource that represents a comprehensive synthesis of the most up-to-date, advanced medical information published about the condition in well-respected, trustworthy medical journals. It is the same type of professional-level information used by physicians and other health-care professionals to keep abreast of the latest developments in biomedical research and clinical medicine. The *Guidebook* is intended for patients who have a need for more advanced, in-depth medical information than is generally available to consumers from a variety of other resources. The primary goal of a *MediFocus Guidebook* is to educate patients and their families about their treatment options so that they can make informed health-care decisions and become active participants in the medical decision making process.

The *Guidebook* production process involves a team of experienced medical research professionals with vast experience in researching the published medical literature. This team approach to the development and production of the *MediFocus Guidebooks* is designed to ensure the accuracy, completeness, and clinical relevance of the information. The *Guidebook* is intended to serve as a basis for a more meaningful discussion between patients and their health-care providers in a joint effort to seek the most appropriate course of treatment for the disease.

### ***Guidebook Organization and Content***

#### **Section 1 - Background Information**

This section provides detailed information about the organization and content of the *Guidebook* including tips and suggestions for conducting additional research about the condition.

#### **Section 2 - The Intelligent Patient Overview**

This section of your *MediFocus Guidebook* represents a detailed overview of the disease or condition specifically written from the patient's perspective. It is designed to satisfy the basic informational needs of consumers and their families who are confronted with the illness and are facing difficult choices. Important aspects which are addressed in "The Intelligent Patient" section include:

- The etiology or cause of the disease
- Signs and symptoms
- How the condition is diagnosed
- The current standard of care for the disease
- Treatment options

- New developments
- Important questions to ask your health care provider

### **Section 3 - Guide to the Medical Literature**

This is a roadmap to important and up-to-date medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest developments and breakthroughs in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new clinical developments, and advances in research. To facilitate your review and analysis of this information, the articles are grouped by specific categories. A typical *MediFocus Guidebook* usually contains one or more of the following article groupings:

- *Review Articles*: Articles included in this category are broad in scope and are intended to provide the reader with a detailed overview of the condition including such important aspects as its cause, diagnosis, treatment, and new advances.
- *General Interest Articles*: These articles are broad in scope and contain supplementary information about the condition that may be of interest to select groups of patients.
- *Drug Therapy*: Articles that provide information about the effectiveness of specific drugs or other biological agents for the treatment of the condition.
- *Surgical Therapy*: Articles that provide information about specific surgical treatments for the condition.
- *Clinical Trials*: Articles in this category summarize studies which compare the safety and efficacy of a new, experimental treatment modality to currently available standard treatments for the condition. In many cases, clinical trials represent the latest advances in the field and may be considered as being on the "cutting edge" of medicine. Some of these experimental treatments may have already been incorporated into clinical practice.

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Article title
- Author Name(s)
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)

- Link to Abstract (brief summary of the actual article)

*Linking to Abstracts:* Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the corresponding URL address that is provided for each cited article. If you purchased a printed copy of a *MediFocus Guidebook*, you can still access the article abstracts online by entering the individual URL address for a particular article into your web browser.

## **Section 4 - Centers of Research**

We've compiled a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of the specific medical condition. The "Centers of Research" directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of the condition.

Inclusion of the names of specific doctors, researchers, hospitals, medical centers, or research institutions in this *Guidebook* does not imply endorsement by Medifocus.com, Inc. or any of its affiliates. Consumers are encouraged to conduct additional research to identify health-care professionals, hospitals, and medical institutions with expertise in providing specific medical advice, guidance, and treatment for this condition.

## **Section 5 - Tips on Finding and Choosing a Doctor**

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver high-level, quality medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it. This section of your *Guidebook* offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

## **Section 6 - Directory of Organizations**

This section of your *Guidebook* is a directory of select disease organizations and support groups that are in the business of helping patients and their families by providing access to information, resources, and services. Many of these organizations can answer your questions, enable you to network with other patients, and help you find a doctor in your geographical area who specializes in managing your condition.

## 2 - The Intelligent Patient Overview

# SJOGREN'S SYNDROME

### Introduction to Sjogren's Syndrome

Most people seldom give thought to "automatic" physiological functions such as saliva production by our salivary glands or tear production by our lacrimal (tear) glands. We take for granted the fact that our salivary glands constantly produce the salivary fluids that keep our mouths moist and clean and that our lacrimal glands continuously produce a slow, steady flow of tears that lubricate our eyes to keep them comfortable and healthy. It is only when the normal physiological production of saliva and tears is disrupted, that we come to realize just how important a role these secretions play in our overall health and well-being.

*Sjogren's syndrome* is a chronic, slowly progressive, inflammatory autoimmune disorder characterized by the infiltration of specialized cells of the immune system called *lymphocytes*, *monocytes*, and *plasma cells* into the *parotid* (salivary) glands and *lacrimal* (tear) glands. These glands are part of a group of *exocrine glands* whose secretions pass into a system of ducts that lead ultimately to the exterior of the body. This chronic lymphocytic infiltration interferes with the normal function of these glands and eventually results in a significant reduction or cessation in the production and secretion of saliva and tears. The condition is named after Henry Sjogren, a Swedish ophthalmologist, who first described the primary clinical features of this disorder in 1933.

Two distinct forms of Sjogren's syndrome have been recognized:

- *Primary Sjogren's syndrome* - defined as dry eye and dry mouth that occurs by itself and is not associated with another autoimmune disorder. Primary Sjogren's syndrome occurs in approximately 50% of cases according to the Sjogren's Foundation of America.
- *Secondary Sjogren's syndrome* - characterized by dry eye and dry mouth that occurs in the presence of another major underlying autoimmune connective tissue disease such as rheumatoid arthritis, systemic lupus erythematosus, or scleroderma.

Sjogren's syndrome is difficult to diagnose since it is comprised of a wide range of symptoms that may not appear concurrently and, as a result, often are treated as individual conditions rather than as a total syndrome. Alternatively, diagnosis may be missed since the individual symptoms of Sjogren's syndrome mimic symptoms related to many other medical conditions. Some studies indicate that many patients with Sjogren's syndrome may suffer for an average of 10 years before they are correctly diagnosed.

While Sjogren's syndrome is a chronic, progressive condition, the progression for most patients is

very slow. Sjogren's syndrome is more benign than other autoimmune diseases and typically is not associated with rapid worsening of symptoms or dramatic changes in condition. Sjogren's syndrome is considered to be more a condition of morbidity (on-going illness) rather than mortality. The most serious complication of Sjogren's syndrome, however, is the increased risk (6.5-fold) of developing non-Hodgkin's lymphoma which is approximately 44 times greater than the risk of the general population, and a 1000-fold increased risk of parotid gland marginal zone lymphoma and diffuse large B-cell and follicular lymphomas. The risk of lymphomas is closely related to B-cell hyperreactivity.

## ***Clinical Features of Sjogren's Syndrome***

The major clinical manifestations of Sjogren's syndrome include:

- *Sicca syndrome* - dry mouth and dry eyes which affect over 90% of patients with Sjogren's syndrome.
- *Glandular enlargement* - Abnormal swelling and enlargement of one or more glands.
- *Extraglandular manifestations* - signs and symptoms of tissue or organ damage due to progressive systemic involvement of the disease.

### **Dry Mouth in Sjogren's Syndrome**

Three pairs of bilateral salivary glands (one pair on each side of the face) are responsible for the production of 90% of the approximately 1.5 liters of saliva that humans produce daily. These glands are:

- *Parotid glands* - these glands are located in front of the ears and extend downward to beneath the earlobes along the border of the lower jaw. They produce up to 70% of the saliva as a result of stimulation (i.e., chewing or eating). This is known as *stimulated saliva*.
- *Submandibular glands* (also called *submaxillary glands*) - these walnut-sized glands are located under the lower jaw. They produce up to 80% of the saliva at rest, also called *unstimulated saliva*.
- *Sublingual glands* - these glands are located beneath the floor of the tongue and also contribute to saliva production.

There are also many tiny salivary glands located in the lips, inner cheek area, and other linings in the mouth and throat that produce the remaining 10% of the saliva.

#### **Role of Saliva**

Normal salivary function originates in specialized glandular cells called *muscarinic M3 receptor cells*, and when these cells are stimulated, saliva is produced. Saliva is a clear watery fluid which is slightly viscous and originates in the salivary glands. The primary component is water (up to

98%) and the remainder is a combination of enzymes, proteins, antibodies, and other substances that perform many important functions including:

- Cleansing and lubricating the oral cavity
- Initiating the breakdown of food for digestion
- Facilitating eating (chewing, swallowing)
- Improving taste
- Removing food debris from the mouth
- Preventing growth and development of viral, bacterial, and fungal infection (anti-microbial protection)
- Controlling the pH level (acid) in the mouth which reduces the development of dental cavities
- Facilitating speech
- Protecting the health of the tongue.

Dry mouth in Sjogren's syndrome, also called *xerostomia*, can cause a multitude of problems, including:

- Difficulty chewing and swallowing dry foods
- Speech difficulties
- Burning sensation in the mouth
- *Halitosis* (bad breath)
- *Oral thrush* - caused by the overgrowth of yeast in the mouth
- Dental problems such as dental caries (cavities) and periodontal disease that can lead to tooth loss.

## **Dry Eyes in Sjogren's Syndrome**

The primary function of tears is to bathe and cleanse the eye, keep it free from dust, and assist in lubrication so that it turns easily in its socket. Tears are produced by the lacrimal glands which are located above the outer corners of each eye. Blinking wipes away the tears by collecting it at the inner corner of the eye where it is carried away via the tear ducts.

Tears are comprised of water as well as other components that protect the surface of the eyes. They contain many elements vital to the health of the eye surface such as epithelial growth factor (regulates cell growth and other functions), fibronectin (protein that supports cellular function), and vitamins. They also contain anti-microbial agents and nourishing substances that help in the mechanical and optical functioning of the eye.

Dry eye associated with Sjogren's syndrome often leads to a condition called *keratoconjunctivitis sicca* (KCS) which causes chronic eye irritation and destruction of the epithelial cells that line the cornea. Signs and symptoms of KCS include:

- Red eyes
- Itchy eyes
- Burning sensation under the eyelids
- *Photosensitivity* - abnormal sensitivity to light

## Sicca Syndrome

In addition to dry mouth and dry eyes, the sicca syndrome in patient's with Sjogren's syndrome can lead to other problems, including:

- Dryness of the airway mucosa that can cause a hoarse voice, *bronchitis* (inflammation of the mucous membranes of the bronchial tubes in the lungs, and *pneumonitis* (inflammation of the walls of the alveoli in the lungs).
- Reduced vaginal secretions that can lead to painful intercourse and impaired sexual function.
- Ear, nose, and skin dryness that causes local irritation, discomfort, and itching.

## Glandular Enlargement

- Swelling of the major salivary glands is a common feature of primary Sjogren's syndrome.
- Enlargement of the parotid gland is noted in about 80% of Sjogren's patients at the time of diagnosis.
- A rapidly enlarging gland in a patient with Sjogren's syndrome may be indicative of the emergence of a malignant B-cell lymphoma such as *Non-Hodgkin's lymphoma* that requires a biopsy to confirm the diagnosis.

## Extraglandular Manifestations

The term "extraglandular manifestations" refers to signs and symptoms of Sjogren's syndrome that develop in tissues and organs beyond the salivary and lacrimal glands that is indicative of the systemic progression of the disease. Extraglandular manifestations of Sjogren's syndrome are relatively common. In one study involving 152 patients with primary Sjogren's syndrome, 71% of the patients were found to have developed systemic features of the disease [*Clinical Medicine*; Volume 14, pages 157-164. 2014].

The extraglandular manifestations of Sjogren's syndrome can occur with or without the classic sicca syndrome symptoms of dry mouth and dry eye and may include:

- *Joint involvement* - joint stiffness, with or without pain, is reported to affect more than 50% of patients with Sjogren's syndrome.
- *Skin lesions* - skin rashes, itching, and cutaneous vasculitis are observed in 8% to 10% of Sjogren's syndrome patients.
- *Raynaud's phenomenon* - discoloration of the fingers and/or toes after to exposure to changes in temperature (hot or cold) or emotional events.
- *Lung involvement* - the most common lung problems noted in patients with Sjogren's syndrome are a dry cough and *rhinosinusitis* (inflammation of the sinuses and nasal cavity).

Less common but more serious lung problems that may develop in some Sjogren's patients include bronchiolitis, COPD, interstitial lung disease, and pneumonia.

- *Peripheral neuropathy* - damage to the peripheral nerves causing weakness, and pain, numbness usually in the hands and feet. Reported to develop in about 65% of patients with Sjogren's syndrome.
- *Kidney involvement* - Less than 3% of patients with Sjogren's syndrome develop kidney problems, the most common of which is *tubulointerstitial nephritis* (injury to the renal tubules and interstitium resulting in decreased kidney function).
- *Low blood counts* - Up to 33% of Sjogren's patients have *cytopenias* (low blood counts) of certain white blood cells and/or platelets that can be detected with routine blood tests. In most cases, however, these cytopenias are mild and produce no symptoms.
- *Lymphomas* - Studies have shown that patients with primary Sjogren's syndrome have a significantly increased risk for developing *non-Hodgkin's lymphoma* and *mucosa-associated lymphoid tissue* (MALT). Predictors for the development of lymphomas include enlarged lymph nodes, parotid gland enlargement, low levels of C4 (a component of the complement cascade), and the presence of cryoglobulins in the blood.

## The Sjogren's Clinical Triad

Many women with Sjogren's syndrome develop a clinical triad of symptoms that consists of dryness, pain, and fatigue. This triad of symptoms has a significant negative impact on quality of life and may also lead to sleep disturbances, depression, and anxiety. Interestingly, Sjogren's patients who experience this triad of symptoms typically have less systemic involvement for reasons that are currently not well understood.

## Epidemiology of Sjogren's Syndrome

Sjogren's syndrome is a condition that overwhelmingly affects women as opposed to men. In fact, over 90% of cases of Sjogren's syndrome occur in women. The condition is relatively rare and has been estimated to affect 0.1% to 0.6% of the general adult population. The mean age at the time of diagnosis of Sjogren's syndrome is 50 years. Although patients with Sjogren's syndrome have a reduced quality of life due to factors such as fatigue, pain, depression, and sleep disturbances, in general, their overall life expectancy is similar to that of the general population in their geographical location. Although data is limited, there appears to be an increased mortality risk in patients with Sjogren's syndrome who develop either non-Hodgkin's lymphoma or more severe systemic involvement.

Systemic lupus erythematosus (SLE) shares many features with Sjogren's syndrome and it is believed that a subset of peri- or post-menopausal women diagnosed with SLE may actually have Sjogren's syndrome. Approximately 30% of patients with rheumatoid arthritis and SLE also suffer from Sjogren's syndrome. In fact, it has been estimated that 50-60% of the cases of Sjogren's syndrome are secondary to another underlying autoimmune disorder such as rheumatoid arthritis,

systemic sclerosis (scleroderma), or SLE.

## **What Causes Sjogren's Syndrome?**

Despite extensive ongoing research over the past several decades, the exact cause of primary Sjogren's syndrome is not yet fully understood. Currently, researchers believe that the condition is the result of a combination of factors involving autoimmune mechanisms, viral infection, and genetic predisposition.

### **Sjogren's Autoantibodies**

Antibodies are part of the host's normal immune system and are produced in response to bacteria and viruses that invade the body and can cause infections. Together with other important components of the immune system, antibodies help fight infections by ridding the body of invading microorganisms. People with certain autoimmune diseases such as lupus, scleroderma, and Sjogren's syndrome produce antibodies that are directed and targeted to specific components, called *antigens*, that are a normal part of their own tissues or organs. These abnormal, self-targeted antibodies are called *autoantibodies* because they are produced in response to and attack an individual's own tissues and/or organs.

Autoantibodies are detected in the blood of many patients with Sjogren's syndrome at the time the condition is diagnosed. The most prevalent types of autoantibodies in Sjogren's syndrome are *antinuclear antibodies* (ANAs), *rheumatoid factor* (RF), *Ro/SSA* (anti-Ro), and *La/SSB* (anti-La). ANAs are found in up to 85% of Sjogren's patients while anti-Ro and anti-La autoantibodies are detected in 33% to 74% of patients. Typically, the presence of autoantibodies is associated with more active systemic disease, including the risk of developing lymphoma.

### **Viral Infections**

Clinically, one of the first signs of Sjogren's syndrome is dry mouth resulting from the decreased production of saliva by the salivary glands. These salivary glands are lined with a thin layer of protective tissue composed of *epithelial cells*. One theory regarding the cause of Sjogren's syndrome proposes that the condition is initiated when a virus infects the salivary gland epithelial cells and triggers the production of autoantibodies that triggers the chronic inflammatory response and lymphocytic infiltration that is a hallmark feature of Sjogren's syndrome. Although this theory accounts for one possible way that Sjogren's syndrome can develop, it should be noted that no single virus has yet been proven to cause the condition.

### **Genetic Predisposition**

This theory proposes that some people who develop primary Sjogren's syndrome may have a genetic predisposition for the disorder. Evidence supporting this theory is derived from studies that have found a link between Sjogren's syndrome and specific *human leukocyte antigens* (HLAs) that are part of the *major histocompatibility complex* (MHC). The MHC is a set of genes that code for the production of cell surface proteins that are essential for the immune system to recognize foreign microorganisms. Specific HLA genetic markers that have been found in some patients with primary Sjogren's syndrome are DR2 and DR3. These two HLA genetic markers have been linked to the production of Sjogren's autoantibodies including anti-Ro and anti-La.

The **Intelligent Patient Overview** in the complete **Medifocus Guidebook on Sjogren's Syndrome** also includes the following additional sections:

- **Diagnosis of Sjogren's Syndrome**
- **Treatment Options for Sjogren's Syndrome**
- **Quality of Life Issues in Sjogren's Syndrome**
- **Questions to Ask Your Healthcare Provider about Sjogren's Syndrome**

To Order the Complete **Guidebook on Sjogren's Syndrome** [Click Here](#)  
Or Call 800-965-3002 (USA) or 301-649-9300 (Outside USA)

## 3 - Guide to the Medical Literature

### Introduction

This section of your *MediFocus Guidebook* is a comprehensive bibliography of important recent medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest advances in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new developments, and advances in research.

To facilitate your review and analysis of this information, the articles in this *MediFocus Guidebook* are grouped in the following categories:

- Review Articles - 53 Articles
- General Interest Articles - 72 Articles
- Drug Therapy Articles - 6 Articles
- Clinical Trials Articles - 19 Articles

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Title of the article
- Name of the authors
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)
- Link to Abstract (brief summary of the actual article)

**Linking to Abstracts:** Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the URI that is provided for each cited article. If you purchased a printed copy of the *MediFocus Guidebook*, you can still access the abstracts online by entering the individual URI for a particular abstract into your computer's web browser.

## 4 - Centers of Research

This section of your *MediFocus Guidebook* is a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition. The *Centers of Research* directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of this disorder.

Use the *Centers of Research* directory to contact, consult, or network with leading experts in the field and to locate a hospital or medical center that can help you.

The following information is provided in the *Centers of Research* directory:

- **Geographic Location**

- United States: the information is divided by individual states listed in alphabetical order. Not all states may be included.
- Other Countries: information is presented for select countries worldwide listed in alphabetical order. Not all countries may be included.

- **Names of Authors**

- Select names of individual authors (doctors, researchers, or other health-care professionals) with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition, who have recently published articles in leading medical journals about the condition.
- E-mail addresses for individual authors, if listed on their specific publications, is also provided.

- **Institutional Affiliations**

- Next to each individual author's name is their **institutional affiliation** (hospital, medical center, or research institution) where the study was conducted as listed in their publication(s).
- In many cases, information about the specific **department** within the medical institution where the individual author was located at the time the study was conducted is also provided.



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