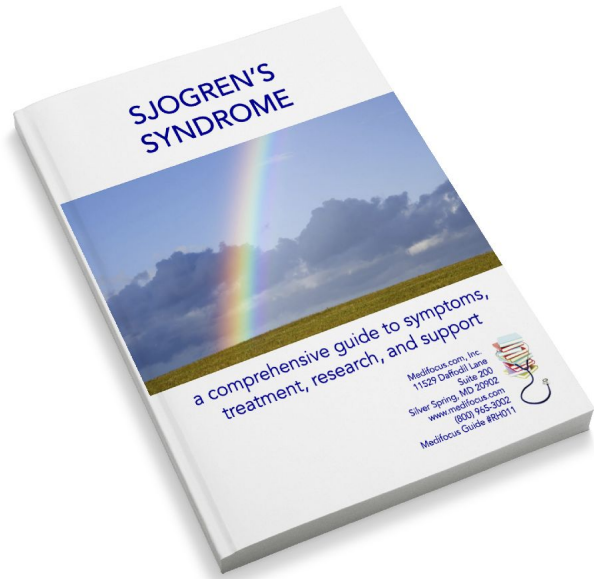


## Preview of the Medifocus Guidebook on: Sjogren's Syndrome

Updated January 5, 2019



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 healthy people seldom give much 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* (T-cells in the majority of cases), *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 a 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 deterioration 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 aspect 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.

## **Major Characteristics of Sjogren's Disease**

The clinical manifestations of Sjogren's syndrome include:

- Dry mouth (*xerostomia*) - caused by reduced saliva production
- Dry eyes (*xerophthalmia*) - caused by reduced production of tears by the lacrimal glands, also called *keratoconjunctiva sicca*
- Extraglandular manifestations

Dryness in Sjogren's syndrome is not generally due to the destruction of the salivary and lacrimal glands. Most biopsy reports show that there is a remnant of the gland but that the tissue in that remnant is inflamed and dysfunctional apparently due to substances that are released in the inflammatory process. This causes a loss of viscosity which increases the friction in areas that the saliva and tears should be lubricating. As a result of the increased friction, the patient experiences chronic inflammation, abrasions of the cornea, (caused by lack of tears), and severe dental problems (caused by lack of saliva).

### **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 we 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*) - these walnut sized glands are located under the lower jaw. These glands 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 our saliva.

#### **Role of Saliva**

Normal salivary function originates in specialized glandular cells called *muscarinic M3 receptor cells* and when they 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

Patients with Sjogren's syndrome who suffer from dry mouth may have several oral-related problems, many of which are described below.

### **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.

Patients with Sjogren's syndrome who suffer from dry eye can develop severe ocular disorders in the absence of sufficient tears including dry, itchy, irritated and/or red eyes. Patients frequently report *photophobia* (aversion to light) and increased ocular irritation, especially at night. See the Guidebook section called *Signs and Symptoms* for further details.

Collectively, dry mouth and dry eyes are the two primary symptoms of Sjogren's syndrome and are known as the *sicca (dry) syndrome*.

### **Extraglandular Involvement in Sjogren's Disease**

In approximately 40% of patients, Sjogren's syndrome progresses beyond the exocrine glands and systemic (*extraglandular*) features develop. In addition to dry mouth and dry eyes, these patients also develop a more systemic form of Sjogren's with the involvement of other organ systems (extraglandular). Symptoms include:

- Cutaneous symptoms - Skin involvement is the most common systemic manifestation of Sjogren's syndrome. Symptoms may include:

- rash
  - itching
  - purpura (the purple color of skin after blood has "leaked" under it)
  - vasculitis (inflammation of the blood vessels)
- 
- Musculoskeletal symptoms such as painful joints
  - Pulmonary symptoms such as a dry cough
  - Hematological symptoms such as *cytopenia* (reduction in the number of cells circulating in the blood)
  - Lymphoproliferative disorders such as *lymphoma* (cancer that starts in the cells of the immune system)

## ***Incidence of Sjogren's Syndrome***

It has been estimated that up to 4 million Americans are afflicted with Sjogren's syndrome and that 1-2% of the population in the United States has been diagnosed with Sjogren's syndrome. However, because the disorder may be difficult to diagnose, the incidence of the disease may be considerably higher. Sjogren's syndrome is a condition that affects primarily women with a female to male ratio of about 24:1, meaning that about 95% of people who suffer from Sjogren's syndrome are women. Symptoms of the disorder most often begin between the ages of 40-60, predominantly in peri/post menopausal women, but are also seen in young women in their 20s and 30s. The average age of onset is 52 years old. The overall prevalence of Sjogren's syndrome in the general population has been estimated to range from 0.5% to 3.0%.

Systemic lupus erythematosus (SLE) shares many features with Sjogren's syndrome and it is believed that a subset of peri/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.

## ***Causes of Sjogren's Syndrome***

Sjogren's syndrome is an autoimmune condition marked by the presence of antinuclear antibodies and rheumatoid factor. Other antibodies (anti-Ro) are associated with extraglandular (outside of the glands) manifestations of Sjogren's syndrome. Organ-specific antibodies are found in approximately 60% of patients with Sjogren's syndrome.

Sjogren's syndrome is associated with chronic stimulation of the immune system, specifically B-cells and T-cells. Histologically (microscopic anatomy of the cells), focal lymphocytic infiltrates (a collection of fluid and cells in the tissue) are located mostly around glandular ducts (salivary and lacrimal ducts) and other exocrine glands (skin, lungs, gastrointestinal tract, and vagina). The infiltrate contains plasma cells, T-cells in most cases, and B-cells in some cases. Eventually, the infiltrate grows and occupies the inner epithelium (inner lining of the gland) that leads to dysfunction and enlargement of the gland as well as degeneration, necrosis, and atrophy.

Although the exact cause of Sjogren's syndrome remains unknown, several theories have been proposed in an attempt to explain the pathophysiology of the disorder. These include:

- Chronic inflammation
- Cellular apoptosis
- Autonomic dysfunction
- Genetic predisposition
- Neurotransmitter abnormality
- Autoimmune response to a viral trigger

### **Chronic Inflammation Theory**

The chronic inflammation theory proposes that Sjogren's syndrome is caused by the continuous infiltration of immune cells (lymphocytes, monocytes, and plasma cells) into the salivary and lacrimal glands, which eventually results in replacement of normal glandular tissue with chronic inflammatory cells, causing progressive dysfunction of the glands with reduced production and secretion of saliva and tears.

Evidence shows that defective glandular tissue seems to be inherently related to the development of antigens which, for unknown reasons, instead of being seen as part of the body, become the focus of an autoimmune attack, bringing on the continued infiltration of lymphocytes. In addition, the attacking cells (B/T-lymphocytes) fail to undergo normal apoptosis (cell death) which results in their proliferation and which may be a factor in prolonging the autoimmune process.

### **Cellular Apoptosis Theory**

The term "apoptosis" refers to death of a cell and is a form of cellular "self-destruction". It has been hypothesized that apoptosis of glandular cells, especially ductal cells, may eventually lead to the glandular dysfunction that is responsible for the classic dry eye and dry mouth symptoms of Sjogren's syndrome. Apoptosis of glandular cells may be triggered by viral infections including:

- Epstein-Barr virus (EBV) infection
- Hepatitis C virus (HCV) infection
- Human Immunodeficiency Virus (HIV) infection

### **Autonomic Dysfunction Theory**

This theory proposes that a dysfunction of the *autonomic nervous system*, the part of the nervous system that controls the production and secretion of saliva and tears, may be a major contributing factor leading to glandular dysfunction and the development of Sjogren's syndrome.

### **Genetic Predisposition Theory**

Proponents of this theory believe that some people who develop Sjogren's syndrome may be genetically predisposed to this disorder. Evidence supporting a genetic predisposition for Sjogren's syndrome has been linked to the *major histocompatibility complex* genes known as *human leukocyte antigens* (HLAs). An increased prevalence of specific HLA genes, including HLAB8, DR3, and DRw52, has been found in patients with primary Sjogren's syndrome.

Genetic evidence has also recently indicated that defective glandular development may predispose an individual to developing epithelial glandular cells that secrete certain immuno-stimulatory agents which are not seen in patients who do not have Sjogren's syndrome.

### **Neurotransmitter Abnormality**

Biopsies of the salivary glands of patients with Sjogren's syndrome have shown that while only 50-60% of glandular tissue is destroyed, the symptoms of dry mouth and dry eye are as severe as if only minimal healthy tissue remained. This puzzle has led some scientists to theorize that some aspect of the immune cells that are produced impair the release of the neurotransmitter acetylcholine and that this may account for the cessation or severe reduction of saliva or tear production, even in the presence of healthy glandular tissue.

### **Autoimmune Response to a Viral Trigger**

Another theory proposes that a trigger, such as a viral infection, may induce an autoimmune T-cell response leading to chronic destruction of epithelial cells, production of inflammatory cells, and the release of chemicals (cytokines, chemokynes) that further stimulate the production of T- and B-cells with the release of autoantibodies. In a subset of these cases, certain B-cell-related factors in the inflamed salivary glands stimulate further production of B-cells which elevates the risk for lymphoma.

Excessive B-cell activation is responsible for many of the extraglandular manifestations of primary Sjogren's syndrome including arthritis, vasculitis, neuropathy, and others. To read more about the role of B-cells in Sjogren's syndrome, please click on the following link:

<http://www.ncbi.nlm.nih.gov/pubmed/19758218>

## ***Signs and Symptoms of Sjogren's Syndrome***

The signs and symptoms of Sjogren's syndrome may be grouped as follows:

- Oral manifestations
- Ocular manifestations
- Systemic manifestations

### **Oral Manifestations**

The major oral manifestation of Sjogren's syndrome is dry mouth (*xerostomia*) resulting in a parched, dry sensation in the mouth and throat. It has been reported that approximately 94% of patients with Sjogren's syndrome experience dry mouth.

Swallowing flushes out the mouth by clearing the oral cavity of saliva, food debris and microorganisms. When this process is interrupted, as occurs in Sjogren's syndrome, there is an increase in many types of microorganisms in the mouth which leads to dental caries (cavities), periodontal disease, and infection.

The mouth may appear moist in the early stages of Sjogren's syndrome, but as the disease progresses, the dryness becomes more pronounced as saliva ceases to pool at the bottom of the mouth and extreme dryness sets in. This may cause the tongue to stick to the roof of the mouth and

as a result affects speech clarity and/or may cause a clicking dimension to speech. Erythema (redness), fissures, and ulcerations may develop with continued dryness.

Other oral manifestations of the disorder may include:

- Tongue
  - dry, red, or painful tongue (*glossodynia*)
  - ulcers on the tongue
  - impaired taste bud function
  - atrophic changes (wasting or diminution) of the taste buds
  - tongue to palate adhesion affecting speaking and eating
- Eating function
  - difficulty chewing and swallowing food, especially dry, crumbly foods such as crackers
  - changes in the ability to taste food (*dysgeusia*)
  - food adhesion to dental surfaces
- Oral mucosa
  - fungal infections such as *chronic erythematous candidiasis* (causes red patches and thinning of mucosa on the palate and inner lining of the cheeks and lips) may affect up to 30% of patients
  - cracked lips with fissures (*cheilitis*)
  - *angular cheilitis* - a painful cracking and soreness that develops at the corners of the mouth
  - fissures of the inner tissue lining the mouth and cheek
- Oral cavity
  - severe dryness
  - burning or tingling sensation in the mouth or soreness
  - unpleasant taste in the mouth
  - halitosis (bad breath)
  - tooth decay -first appears at the gum margins, progressing further into the mouth over time and affects about 70% of Sjogren's patients
  - cavities
  - difficulty anchoring dentures in the gums
  - gum sores due to dentures
  - voice alterations (hoarseness or coarse voice)
- Swelling of the salivary glands (particularly the parotid gland) - this occurs in approximately one third of patients with primary Sjogren's syndrome. It may begin on one side only and develop into bilateral swelling. The enlargement may be chronic or episodic and leads to loss of function of the gland which results in a further decrease of salivary production and

flow rates.

## Ocular Manifestations

The most common ocular feature of Sjogren's syndrome is dry eye, also known as *xerophthalmia* and *keratoconjunctivitis sicca* (KCS). Approximately 65% of patients diagnosed with Sjogren's syndrome complain of dry eyes.

Other ocular manifestations of Sjogren's syndrome include:

- Redness, soreness, burning, or itching eyes
- Foreign body sensation in eyes - sometimes described as "grains of sand in eyes"
- Difficulty tolerating contact lenses
- Photophobia - avoidance of light
- Eye fatigue - particularly when reading or watching television
- Discharge or secretions from the eyes due to abnormal mucus production
- Feeling a film or lack of acuity in the visual field
- Corneal ulceration
- Blurred vision

Some patients have reported that ocular symptoms associated with Sjogren's syndrome are often exacerbated by:

- Low humidity
- Dry climate
- Exposure to cigarette smoke
- Anticholinergic drugs (a class of drugs that block a neurotransmitter called *acetylcholine*)

## Systemic Manifestations

### Sinus Symptoms

Nasal or sinus symptoms are attributable to Sjogren's syndrome in up to 50% of patients who experience atrophy of the mucus lining of the nose. Symptoms include:

- Nasal crusting
- Epistaxis (nose bleeds)
- Perforation of the septum
- Hyposmia (diminished sensitivity to smell)
- Hypogeusia (diminished sensitivity to taste)

### Musculoskeletal Symptoms

Approximately 55% of patients with primary Sjogren's syndrome experience musculoskeletal symptoms including:

- Arthralgia (non-inflammatory joint pain) or arthropathy (diseases of the joint) that occurs in up to 50% of patients
- Arthritis (inflammatory joint pain) is thought to occur in at least 30% of patients and tends to be relapsing, remitting, and tends to occur symmetrically on the right and left sides. Some

patients exhibit signs of arthritis 5-10 years before they are diagnosed with Sjogren's syndrome.

- Myositis - inflammation of muscle tissue
- Myalgia (general term for noninflammatory muscular pain) - up to 20% of patients with Sjogren's syndrome suffer from fibromyalgia
- Muscle weakness

### Fatigue

One of the most debilitating systemic features of Sjogren's syndrome is fatigue which many individuals with Sjogren's syndrome describe as more distressing than any other symptom.

Sleep disorders are also common in patients with Sjogren's syndrome, which may be a factor in fatigue. Patients report that they sleep but do not feel well-rested when they wake up. Some clinicians are of the opinion that the excessive fatigue experienced by these patients may be related to subclinical hypothyroidism which is also associated with Sjogren's syndrome.

Fatigue is not merely a feeling of being "tired" but is more accurately defined as an ever-present lack of vitality that essentially remains unchanged over time. Previous studies have estimated the prevalence of fatigue in patients with primary Sjogren's syndrome to range from 38% to 88%. This contrasts sharply with the prevalence of fatigue in the general population, which has been reported to range from less than 1% to up to 3%. Fatigue in patients with chronic autoimmune disorders, including Sjogren's syndrome, has long been considered as a major contributor to impaired quality of life. Although an association between fatigue and Sjogren's syndrome had been recognized for several decades, the underlying basis or reason for this association is still not well understood.

In a recent study published in *Arthritis Care & Research*, researchers from Greece set out to determine the factors that contribute to fatigue in Sjogren's syndrome using a variety of clinical, laboratory, and psychological tests. The study population consisted of 106 consecutive patients with primary Sjogren's syndrome who were evaluated and followed at two hospitals in Greece. All patients underwent a battery of clinical evaluations, blood tests to measure specific blood components including Sjogren's specific autoantibodies, and a series of self-administered psychological questionnaires designed to measure depression, anxiety, and neuroticism.

The results of the study can be summarized as follows:

- Fatigue was present in 32 of the 106, or 30%, of the subjects with primary Sjogren's syndrome.
- Nearly 80% of the Sjogren's patients with fatigue also experienced joint and/or muscle pain, compared to 54% of the subjects without fatigue.
- A significantly higher proportion (25%) of the Sjogren's patients with fatigue also had fibromyalgia, compared to only 4% without fatigue.
- A significant correlation was also noted between fatigue in Sjogren's syndrome and anxiety, depression, sleep disturbances, and neuroticism.



- Blood test results, measuring various blood components including autoantibodies, did not significantly differ among the Sjogren's patients with or without fatigue.

In summary, this study found a high prevalence of fatigue (30%) among a cohort of 106 patients with primary Sjogren's syndrome. Furthermore, fatigue was also associated with a high likelihood of depression, neuroticism, fibromyalgia, and impaired sleep patterns, all of which contribute to a reduced quality of life. Fatigue and its associated physical and psychological features requires appropriate management through active collaboration between rheumatologists and mental health professionals.

### Cutaneous Symptoms

Estimates of the percentage of Sjogren's syndrome patients who experience skin problems range from 10-40%. *Cutaneous vasculitis* (inflammation of the blood vessels in the skin) is one of the most characteristic extraglandular manifestations of Sjogren's syndrome and is thought to be due to lymphocytic infiltration into the walls of the blood vessels. Typically, small blood vessels are affected more than large ones.

The most common forms of cutaneous vasculitis seen in Sjogren's syndrome patients (typically patients who have anti-Ro and anti-La antibodies) are:

- Palpable or nonpalpable *purpura* (purple spots on the skin after blood "leaks" underneath, similar to a bruise) which can cause raised, red skin lesions
- Urticarial lesions (hives)
- Erythematous micropapules (red spots)

Patients with cutaneous vasculitis also may develop non-vasculitic lesions including:

- *Petechiae* - pinpoint dots
- *Photosensitive cutaneous lesions* - light-sensitive lesions (also seen in patients with systemic lupus erythematosus)
- *Livedo reticularis* - marbled appearance of the skin
- *Lichen planus* - small, itchy pink or purple spots on arm and/or legs
- *Thrombocytopenic purpura* - purple areas on the skin related to a decrease in blood platelets
- *Vitiligo* - white patches on skin due to loss of pigmentation

Cutaneous vasculitis (as well as other forms of vasculitis - see below) is considered to be a significant prognostic indicator with the development of lymphoma and mortality. A large 2004 study of 558 Sjogren's syndrome patients diagnosed with cutaneous involvement reported that 58% of the patients had cutaneous vasculitis and showed a higher incidence of:

- Peripheral neuropathy - damage to the nerves that supply the arms and legs characterized by burning, tingling, numbness and pain
- Raynaud's phenomenon - a circulatory disorder caused by insufficient blood supply to the hands and feet
- Renal (kidney) involvement
- Presence of autoimmune markers such as antinuclear antibodies (ANA) and rheumatoid

factor

- B-cell lymphoma

Other skin problems that may be experienced by patients with Sjogren's syndrome include:

- Dry skin (*xerosis*) - affects up to 55% of patients with Sjogren's syndrome
- Itchy skin
- Burning skin - may be experienced in up to 20% of patients with Sjogren's syndrome
- Skin rashes - may be experienced in up to 10% of patients with Sjogren's syndrome
- Raynaud's phenomenon - may appear many years before the development of symptoms of dry mouth and dry eyes. Estimated to occur in up to 30% of patients, it is usually of minor clinical significance.

### Vasculitis

*Vasculitis* in general refers to inflammation of the blood vessels and is estimated to occur in up to 10% of patients with Sjogren's syndrome. It typically involves small- and medium- blood vessels and ranges from benign (most common) to life-threatening (rare). Risk factors for development of vasculitis include:

- Parotid scintigraphy - Grades III-IV (a diagnostic technique based on the detection of radiation emitted by radioactive substances injected into the body; also called radionuclide scanning), considered an independent prognostic factor of development of vasculitis.
- Low C3 and/or C4 levels in the blood (*hypocomplementemia*).
- *Cryoglobulinemia* (low levels of immunoglobulins that congeal in cold temperatures)
- Anti Ro/La antibodies.

Life-threatening vasculitis, however, is rare and appears to be related to elevated levels of cryoglobulins (abnormal blood proteins) in the blood plasma (*cryoglobulinemia*).

### Pulmonary Symptoms

The most common pulmonary (lung) symptom of Sjogren's syndrome is a dry cough due to xerotrachea (dry, scratchy trachea). Estimates of pulmonary involvement vary widely in the literature and ranges from 9-75% of patients with Sjogren's syndrome (depending upon the diagnostic techniques used) but it is rarely clinically significant. Evidence of pulmonary changes appears on up to 50% of lung scans by some estimates, but they usually remain subclinical (without obvious symptoms). Progression is very slow and typically does not develop into clinically significant pulmonary disease. In one study examining the incidence of pulmonary involvement in patients with Sjogren's syndrome, approximately 87% of patients had some degree abnormal pulmonary function.

Recent studies show that pulmonary involvement is typically at the bronchial or bronchiolar level, but interstitial disease (damage to lung tissue) can occur. Other pulmonary complications which may occur include:

- *Tracheobronchia sicca* - dryness of the tracheal pathways leading to continual dry cough
- *Lymphocytic interstitial pneumonitis* - a syndrome characterized by fever, cough, and shortness of breath with infiltrates of dense interstitial accumulations of lymphocytes and

plasma cells

- *Pulmonary pseudolymphoma* - a benign accumulation of inflammatory lymphoid cells in the lung
- *Alveolitis* - inflammation of the air sacs (alveoli) in the lungs where the exchange of oxygen and carbon dioxide takes place
- Various types of pneumonia, such as *nonspecific interstitial pneumonia*, *organizing pneumonia* (noninfectious inflammation of the bronchioles and surrounding lung tissue), or *usual interstitial pneumonia* (changes in lung tissue indicative of fibrosis or scarring)
- Primary lymphoma of the lung
- Mucosa associated lymphoid tissue (MALT)
- Lung hypersensitivity
- Diffuse interstitial amyloidosis (deposit or accumulation of protein in lung tissue) - not a common development but associated with progressive deterioration and a poor prognosis.

Tracheobronchial sicca and interstitial pneumonitis are the most common lung conditions associated with Sjogren's syndrome.

To read more about interstitial lung disease in primary Sjogren's syndrome, please click on the following link: <http://www.ncbi.nlm.nih.gov/pubmed/19390161>

### *Kidney Involvement*

The prevalence of kidney involvement in people with primary Sjogren's syndrome has been reported to range from 1% to 15%. Studies have shown that the most frequent type of kidney disease that develops in patients with primary Sjogren's syndrome is *tubulointerstitial nephritis* (TIN). TIN is an inflammation of the kidney tubules and intersitium that can lead to reduced kidney function. Most people who develop TIN do not have clinical symptoms but lab testing of urine and blood show electrolyte disturbances, elevated serum creatinine, and low levels of protein in the urine (proteinuria). A definitive diagnosis of TIN can only be established by performing a kidney biopsy. As the disease progresses and if left untreated, TIN can cause chronic kidney failure. At this point, most patients will typically develop hypertension (high blood pressure). The standard treatment for patients with TIN is high-dose steroid therapy and most studies have reported good results with this treatment approach. Due to the risk of chronic kidney failure, most experts recommend screening patients with primary Sjogren's syndrome at least twice a year by means of blood and urine testing to detect any abnormalities in kidney function. These screening tests typically include checking for proteinurea, serum creatinine levels, electrolyte imbalances, urinary pH and osmolality, and the estimated glomerular filtration rate (GFR). If TIN is suspected, a kidney biopsy is usually necessary to establish the diagnosis and, if confirmed, treatment should be initiated with high-dose steroid therapy.

The second most common type of kidney disease that occurs in people with primary Sjogren's syndrome is *membranoproliferative glomerulonephritis* (MPGN) - inflammation of the glomeruli (capillaries) in the kidneys that help to filter waste from the blood. Signs and symptoms of MPGN include hypertension, high levels of protein in the urine, hematuria (blood in the urine), and acute kidney failure. MPGN is a potentially life-threatening condition that requires prompt diagnosis and treatment. This condition is usually treated with steroids, immunosuppressant medications, plasma exchange, rituximab, azathioprine, or mycophenolate mofetyl. Most studies have reported a significant improvement in kidney function in patients with MPGN who are treated with this

protocol.

In summary, kidney disease develops in up to 15% of patients with primary Sjogren's syndrome. The two most common types of kidney disease observed in Sjogren's patients are *tubulointerstitial nephritis* (TIN) and *membranoproliferative glomerulonephritis* (MPGN). The underlying cause of both of these conditions in people with primary Sjogren's syndrome is the infiltration of specialized cells of the immune system (lymphocytes) into the kidneys that clogs the drainage system and, thereby, causes impaired kidney function. Experts recommend that patients with primary Sjogren's syndrome should be screened for kidney disease at least twice each year with laboratory testing of blood and urine. If kidney function is found to be impaired or if electrolyte disturbances are severe, a kidney biopsy is recommended to rule out TIN and MPGN. If either of these conditions is confirmed by kidney biopsy, appropriate treatment should be initiated promptly to prevent chronic kidney failure.

### Gastrointestinal Symptoms

Saliva plays a major role in the initial phases of digestion and reduced amounts or absence of saliva can cause a disruption in the normal function of the gastrointestinal tract. Esophageal dryness is the most common gastrointestinal manifestation of Sjogren's syndrome and is the cause of dysphagia (difficulty swallowing) experienced by many people with Sjogren's syndrome. Other difficulties which patients may experience include:

- Regurgitation of food
- Reflux of gastric acid into the esophagus (neutralizing properties of saliva are lacking)
- Nausea
- Epigastric pain
- Gastritis - irritation of the stomach lining that causes "heartburn"
- Celiac sprue - sensitivity to gluten causing impaired food absorption
- Presence of *Helicobacter pylori* which is associated with MALT lymphoma
- Gastrotracheal reflux - gastric acid refluxes not just to the esophagus but up to the trachea. Continual reflux can lead to abnormal changes in tracheal tissue.

Development of pancreatitis is rare in patients with Sjogren's syndrome; however, laboratory studies may show elevated levels of certain gastric enzymes (e.g., gastrin) and biopsy may show infiltration of lymphocytes into the gastric mucosa.

### Neurologic Symptoms

Approximately 10%-30% of Sjogren's patients (some estimates are as high as 60%) develop neurological symptoms including:

- *Polyneuropathy*- pure or predominantly sensory polyneuropathies cause pain, numbness, tingling, and muscle weakness in the hands, arms, feet, and legs (this is the most common neurologic manifestations of SS)
- *Cranial neuropathy* - most often affecting the trigeminal nerve; may cause a condition called trigeminal neuralgia (intense, sharp pain in the area of the face).
- *Transverse myelitis* - an acute spinal cord disorder causing sudden low back pain, muscle weakness, and abnormal sensations in the lower extremities. This is one of several sclerosis-like syndromes that may occur in a minority (up to 1%) of patients with Sjogren's

syndrome.

- Abnormal nerve conduction
- Motor neuropathy
- Demyelinating neuropathy (neuropathy caused by the destruction of myelin that surrounds the sheath of the nerve cell)
- Myelopathy (conditions affecting the spinal cord)
- Loss of small-diameter nerve fibers

It is sometimes difficult to differentiate between age-related and Sjogren's syndrome-related neurological symptoms, since there is considerable overlap between them. Also, the most common age of onset of Sjogren's syndrome is at a time in life when common aging changes may occur naturally. Thus information is limited regarding specific neurologic symptoms in elderly patients with Sjogren's syndrome.

### Headaches

Although the neurological effects of Sjogren's syndrome have been documented in the medical literature, few studies, however, have evaluated the possible relationship between Sjogren's syndrome and headaches. A study published in 2013 in the *European Journal of Neurology* (Volume 20, pp. 558-563) has shed some light on this issue. In this study, researchers from Norway investigated the prevalence of headaches among 71 patients with primary Sjogren's syndrome and an equal number of age- and sex-matched healthy individuals. All of the study subjects were examined and interviewed by an experienced neurologist and were asked to provide a detailed history of any headache attacks they experienced during the previous 12-months.

In general, the results of this study showed that the overall prevalence of headaches, including migraines, was similar among both groups. Further analysis of the data, however, indicated that the prevalence of chronic tension-type headaches was significantly higher for the patients with primary Sjogren's syndrome (11.3%) than for the group of healthy controls (1.4%). The reason for the higher prevalence of chronic tension-type headaches in the primary Sjogren's disease group remains unknown, however, it is well-recognized that chronic headaches in general have a significant negative impact on quality of life. Although further studies are warranted to prove a definite association between primary Sjogren's syndrome and chronic headaches, Sjogren's patients who suffer from frequent chronic headaches should consult with their healthcare provider to learn about the treatment options that are available to prevent or treat the condition.

### Gynecologic Symptoms

The most common gynecological manifestation of Sjogren's syndrome in women is vaginal dryness which leads to significant general discomfort. It has been estimated that up to 25% of women with Sjogren's syndrome complain of vaginal symptoms but fertility and childbirth do not appear to be affected by the presence of Sjogren's syndrome. *Dyspareunia*, painful intercourse, is thought to affect approximately 40% of premenopausal women and is secondary to insufficient lubrication of the vaginal region.

When vaginal dryness develops, it should be treated promptly because it can cause:

- Uncomfortable vaginal itching
- Difficulty in urination

- Urinary tract infections
- Yeast infections

It is thought that vaginal lubrication involves fluid from the bloodstream and from the cervical mucosa that flow through the vaginal wall, and is not related to fluid produced by local glands. When women develop Sjogren's syndrome, lymphocytic inflammatory cells infiltrate the vascular system supplying fluid to the vagina, thereby causing a reduction in vaginal lubrication.

### *Sexual Function in Women with Primary Sjogren's Syndrome*

Primary Sjogren's syndrome (pSS) is an autoimmune disorder that is characterized by dry eyes and dry mouth as well as extraglandular symptoms such as fatigue and arthritis. This syndrome primarily affects women, with a female to male ratio of 9:1. Previous studies have shown that women with pSS often experience vaginal dryness and painful sexual intercourse, however, data on sexual function in women affected by pSS is scarce. A study published in *Rheumatology* in 2015 (Volume 54; pp. 1286-1293) summarized and compared sexual dysfunction, sexual distress, and vaginal complaints in women with pSS to a group of healthy women.

This study, which was conducted in the Netherlands, included 46 women with pSS and 43 age-matched healthy women who served as a control group. All of the participants completed the following two self-administered questionnaires:

- Female Sexual Function Index (FSFI) - An index that measures sexual function by evaluating desire, arousal, orgasm, lubrication, satisfaction, and pain.
- Female Sexual Distress Scale (FSDS) - A scale which measures psychological distress due to sexual dysfunction.

In addition, the European League Against Rheumatism Sjogren's Syndrome Disease Activity Index (ESSDAI) was used to measure extraglandular symptoms of pSS and the Multidimensional Fatigue Inventory (MFI) was used to measure the extent of fatigue in the women who participated in this study.

The researchers reported the following major outcomes of their study:

- Compared to the healthy controls, women with pSS exhibited impaired sexual function as measured on the FSFI. These women had lower scores in the domains of desire, arousal, orgasm, lubrication, and also reported experiencing more pain during intercourse.
- Women with pSS also experienced more sexual distress and were less frequently sexually active compared to the healthy control group.
- Sexual dysfunction in these women correlated significantly with self-reported symptoms of Sjogren's syndrome, depressive symptoms, relationship dissatisfaction, and lower mental quality of life.

In summary, this study found that primary Sjogren's syndrome has a major negative impact on female sexual function. Women with pSS who are experiencing sexual dysfunction are urged to speak with their rheumatologist or gynecologist about these issues. By simply acknowledging and discussing these complaints, doctors can develop a treatment plan to help women with pSS to better cope with their sexual problems.

### Hematologic Abnormalities

Hematologic (blood-related) abnormalities in Sjogren's syndrome are usually asymptomatic and include:

- Elevated sedimentation rate - this is reported in the blood of up to 70% of patients with Sjogren's syndrome.
- Anemia - the number of red blood cells in the bloodstream is lower than normal
- Leukopenia - the number of white blood cells (leukocytes) in the bloodstream is lower than normal
- Autoimmune cytopenia (reduced number of cells circulating in the blood) - this is usually a mild condition but can develop into a serious condition
- Hyper/hypoglobulinemia (elevated or reduced levels of globulins in the blood)

### Lymphoproliferative Disease

Lymphoma develops in approximately 5% of patients diagnosed with Sjogren's syndrome. It has been estimated that patients with primary and secondary Sjogren's syndrome have an approximately 44-fold increased risk for developing lymphoma as compared with healthy, age-matched controls. The most common form of lymphoma associated with Sjogren's syndrome is low or intermediate grade B-cell lymphoma that originates in mucosa-associated lymphoid tissue. Lymphoma occurs more frequently in patients with primary Sjogren's syndrome than secondary Sjogren's syndrome.

It is thought that the chronic stimulation and proliferation of monoclonal B cells in Sjogren's syndrome is related to the transition that takes place from an autoimmune status to the development of non-Hodgkin's lymphoma. Most lymphomas associated with Sjogren's syndrome are characterized as:

- Low- or intermediate-grade malignancy potential
- Localized in extranodal spaces (spaces around the outside of the lymph nodes)

Clinical or laboratory evidence of an emerging lymphoma may include:

- Persistent enlargement of parotid (salivary) glands
- Persistent enlargement of the spleen (splenomegaly)
- Persistent enlargement of lymph nodes (lymphadenopathy)
- Type II mixed monoclonal cryoglobulinemia
- Low levels of complement factors C3 or C4 in the bloodstream
- Inflammation of the blood vessels (vasculitis)

Other lymph-related conditions that may develop with Sjogren's syndrome include:

- Lymphopenia - reduced circulating lymphocytes in the bloodstream
- Waldenstrom's macroglobulinemia - cancer of the B-lymphocytes (a type of white blood cell) which causes overproduction of monoclonal macroglobulins (IgM antibody)
- Lymphadenopathy - enlargement of the lymph glands

### Cardiac Symptoms

Cardiac conditions which may be associated with Sjogren's syndrome include:

- Pericarditis - inflammation of the sac surrounding the heart
- Pulmonary hypertension - high blood pressure in the arteries that supply the lungs
- Orthostatic hypotension - abnormal and sudden changes in blood pressure when changing from sitting or lying to standing).

### Cardiovascular Risk Factors

In a study published in *Arthritis Care & Research* in 2014 (Volume 66, pp. 757-764), a group of investigators from the United Kingdom evaluated and compared the prevalence of cardiovascular risk factors in 543 patients with primary Sjogren's syndrome and 473 healthy control subjects. The overwhelming majority of the subjects included in this study were women. Traditional cardiovascular risk factors that were evaluated included:

- Blood pressure
- Smoking status
- Cholesterol and triglyceride blood levels
- Obesity
- Diabetes
- Family history of cardiovascular disease

The major findings of this study can be summarized as follows:

- Women with primary Sjogren's syndrome had a higher prevalence of hypertension (high blood pressure) and elevated levels of both blood cholesterol and triglycerides compared to the healthy control subjects without Sjogren's syndrome.
- There were no significant differences in the prevalence of either diabetes, obesity, or family history of cardiovascular disease between the two groups of subjects.
- Hypertension was detected in 28% of the Sjogren's syndrome patients compared to 15% of the controls.
- Elevated levels of triglycerides were found in the bloodstream of 21% of the Sjogren's syndrome patients as compared to only 9.5% of the controls.
- No significant differences were found in the blood levels of either total cholesterol, low-density lipoprotein (LDL), or high-density lipoprotein (HDL) between the 2 groups of subjects.

Cardiovascular risk factors are not routinely evaluated in patients with Sjogren's syndrome as they are for other autoimmune disorders such as rheumatoid arthritis. This study found that patients with primary Sjogren's syndrome were more than 2 times more likely to have hypertension and elevated blood levels of triglycerides compared to age- and sex-matched healthy controls. The study also found that about 70% of the Sjogren's syndrome patients were unaware that they had



high blood pressure and, therefore, were not undergoing treatment for this important cardiovascular risk factor. On the basis of these findings, the investigators noted that doctors should screen patients with primary Sjogren's syndrome for both hypertension and for high triglyceride levels (hypertriglyceridemia) and treat these recognized cardiovascular risk factors when necessary.

### Hepatobiliary Symptoms

Some patients may also develop hepatitis C or a condition called *primary biliary cirrhosis*, a liver disease that slowly destroys the bile ducts and leads to the build-up of bile in the liver and eventual cirrhosis (hardening) of the liver. Typically, however, liver involvement in patients with Sjogren's syndrome is rare (up to 5% of Sjogren's syndrome patients) and when it does occur, it is usually asymptomatic and subclinical (disease has not yet exhibited overt symptoms).

### Psychiatric Symptoms

The most common psychiatric conditions associated with Sjogren's syndrome are:

- Depression
- Anxiety

The high incidence of these conditions has led some researchers to believe that they may be part of Sjogren's syndrome rather than a reaction to the stress. Depression and anxiety also commonly precede the diagnosis of systemic lupus erythematosus as well as other autoimmune conditions. Other symptoms that may develop include subtle changes in cognitive function, memory, and concentration.

### Thyroid Symptoms

Antibodies directed to the thyroid gland can be detected in approximately 50% of people diagnosed with Sjogren's syndrome, while only half of these patients demonstrate abnormalities on thyroid function tests. Various thyroid abnormalities, including *Hashimoto's thyroiditis* (a type of autoimmune thyroid disease) and hypothyroidism (low thyroid function) have been associated with Sjogren's syndrome. It is estimated that approximately 10% of patients with autoimmune thyroid disease may have Sjogren's syndrome.

To read more about thyroid disease and Sjogren's syndrome, please click on the following link:

<http://www.ncbi.nlm.nih.gov/pubmed/17558463>

### Laryngeal Symptoms

Lesions of the vocal cords have been associated with Sjogren's syndrome and can cause hoarseness, which in rare cases may be the first indication of Sjogren's syndrome. Conditions associated with these lesions include:

- Bamboo node - an unusual white or yellow transverse lesion typically located in the middle third of the vocal cord, and most frequently associated with autoimmune diseases.
- Vocal cord nodules

### Otologic Symptoms

Some patients with Sjogren's syndrome demonstrate a mild to moderate sensorineural hearing loss

of high frequency sounds. The connection to Sjogren's syndrome pathology is not well understood.

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 and Psychosocial Considerations in Sjogren's Syndrome**
- **New Developments in Sjogren's Syndrome**
- **Questions to Ask Your Health Care Provider about Sjogren's Syndrome**

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## 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 - 56 Articles
- General Interest Articles - 85 Articles
- Drug Therapy Articles - 8 Articles
- Clinical Trials Articles - 23 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.

## Recent Literature: What Your Doctor Reads

Database: PubMed <January 2014 to January 2019 >

### Review Articles

1.

#### One year in review 2018: Sjogren's syndrome.

**Authors:** Argyropoulou OD; Valentini E; Ferro F; Leone MC; Cafaro G; Bartoloni E; Baldini C  
**Institution:** Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens, Greece. of Pisa, Italy. of Pisa, Italy.  
**Journal:** Clin Exp Rheumatol. 2018 May-Jun;36 Suppl 112(3):14-26. Epub 2018 Jul 18.  
**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=RH011&ID=30156536>

2.

#### Update on Sjogren Syndrome and Other Causes of Sicca in Older Adults.

**Authors:** Baer AN; Walitt B  
**Institution:** Division of Rheumatology, Department of Medicine, Johns Hopkins University School of Medicine, 5200 Eastern Avenue, Suite 4000, Mason Lord Center Tower, Baltimore, MD 21224, USA; National Institute of Dental and Craniofacial Research, National Institutes of Health, 10 Center Drive, Bethesda, MD 20892, USA. Electronic address: alanbaer@jhmi.edu.  
**Journal:** Rheum Dis Clin North Am. 2018 Aug;44(3):419-436. doi: 10.1016/j.rdc.2018.03.002.  
**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=RH011&ID=30001784>

3.

#### The prevalence and relevance of traditional cardiovascular risk factors in primary Sjogren's syndrome.

**Authors:** Bartoloni E; Alunno A; Valentini V; Valentini E; La Paglia GMC; Leone MC; Cafaro G; Marcucci E; Bonifacio AF; Luccioli F; Gerli R  
**Institution:** Rheumatology Unit, University of Perugia, Italy.  
**Journal:** Clin Exp Rheumatol. 2018 May-Jun;36 Suppl 112(3):113-120. Epub 2018 May 30.

**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=RH011&ID=29998823>

4.

### **Cardiovascular Disease in Primary Sjogren's Syndrome.**

**Authors:** Berardicurti O; Ruscitti P; Cipriani P; Ciccia F; Liakouli V; Guggino G; Carubbi F; Di Benedetto P; Triolo G; Giacomelli R

**Institution:** Division of Rheumatology, University of L`Aquila, L`Aquila, Italy.

**Journal:** Rev Recent Clin Trials. 2018;13(3):164-169. doi: 10.2174/1574887113666180315130336.

**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=RH011&ID=29542415>

5.

### **Primary Sjogren's syndrome.**

**Author:** Bowman SJ

**Institution:** Rheumatology Department, Queen Elizabeth Hospital, Edgbaston, Birmingham, UK.

**Journal:** Lupus. 2018 Oct;27(1\_suppl):32-35. doi: 10.1177/0961203318801673.

**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=RH011&ID=30452329>

6.

### **Advances in the diagnosis and treatment of Sjogren's syndrome.**

**Authors:** Chen X; Wu H; Wei W

**Institution:** Institute of Clinical Pharmacology, Anhui Medical University, Hefei, 230032, Anhui, China. Hefei, 230032, Anhui, China. Hefei, 230032, Anhui, China. Anhui, China. wuhuaxun@ahmu.edu.cn. Hefei, 230032, Anhui, China. wuhuaxun@ahmu.edu.cn. Hefei, 230032, Anhui, China. wuhuaxun@ahmu.edu.cn. Anhui, China. wwei@ahmu.edu.cn. Hefei, 230032, Anhui, China. wwei@ahmu.edu.cn. Hefei, 230032, Anhui, China. wwei@ahmu.edu.cn.

**Journal:** Clin Rheumatol. 2018 Jul;37(7):1743-1749. doi: 10.1007/s10067-018-4153-8. Epub 2018 May 26.

**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=RH011&ID=29804149>

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## 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.

## Centers of Research

### United States

#### CA - California

**Name of Author**

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**Institutional Affiliation**

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The **Centers of Research** in the complete **Medifocus Guidebook on Sjogren's Syndrome** includes the following sections:

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- Centers of Research listed for relevant countries outside the United States

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# 5 - Tips on Finding and Choosing a Doctor

## Introduction

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 a high level and quality of 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.

The process of finding and choosing a physician to manage your specific illness or condition is, in some respects, analogous to the process of making a decision about whether or not to invest in a particular stock or mutual fund. After all, you wouldn't invest your hard earned money in a stock or mutual fund without first doing exhaustive research about the stock or fund's past performance, current financial status, and projected future earnings. More than likely you would spend a considerable amount of time and energy doing your own research and consulting with your stock broker before making an informed decision about investing. The same general principle applies to the process of finding and choosing a physician. Although the process requires a considerable investment in terms of both time and energy, the potential payoff can be well worth it--after all, what can be more important than your health and well-being?

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.

## Tips for Finding Physicians

Finding a highly qualified, competent, and compassionate physician to manage your specific illness or condition takes a lot of hard work and energy but is an investment that is well-worth the effort. It is important to keep in mind that you are not looking for just any general physician but rather for a physician who has expertise in the treatment and management of your specific illness or condition. Here are some suggestions for where you can turn to identify and locate physicians who specialize in managing your disorder:

- **Your Doctor** - Your family physician (family medicine or internal medicine specialist) is a good starting point for finding a physician who specializes in your illness. Chances are that your doctor already knows several specialists in your geographic area who specialize in your illness and can recommend several names to you. Your doctor can also provide you with information about their qualifications, training, and hospital affiliations.

The **Tips on Finding and Choosing a Doctor** in the complete **Medifocus Guidebook on Sjogren's Syndrome** includes additional information that will assist you in locating a highly qualified and competent physician to manage your specific illness.

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## 6 - Directory of Organizations

### **American Academy of Ophthalmology**

POB 7424; San Francisco, CA 94120-7424

415.561.8500

[customer\\_service@aao.org](mailto:customer_service@aao.org)

[www.aao.org](http://www.aao.org)

### **American Autoimmune Related Diseases Association**

22100 Gratiot Avenue; E. Detroit, MI 48021

800.598.4668; 586.776.3900

[www.aarda.org](http://www.aarda.org)

### **American College of Rheumatology**

1800 Century Place; Suite 250; Atlanta, GA 30345-4300

404.633.3777

[acr@rheumatology.org](mailto:acr@rheumatology.org)

[www.rheumatology.org](http://www.rheumatology.org)

### **Arthritis Foundation**

POB 7669; Atlanta, GA 30309

800.283.7800

[arthritisfoundation@arthritis.org](mailto:arthritisfoundation@arthritis.org)

[www.arthritis.org](http://www.arthritis.org)

### **British Sjogren's Syndrome Association**

PO Box 10867 Birmingham B16 0ZW UK

01214556532

[office@bssa.uk.net](mailto:office@bssa.uk.net)

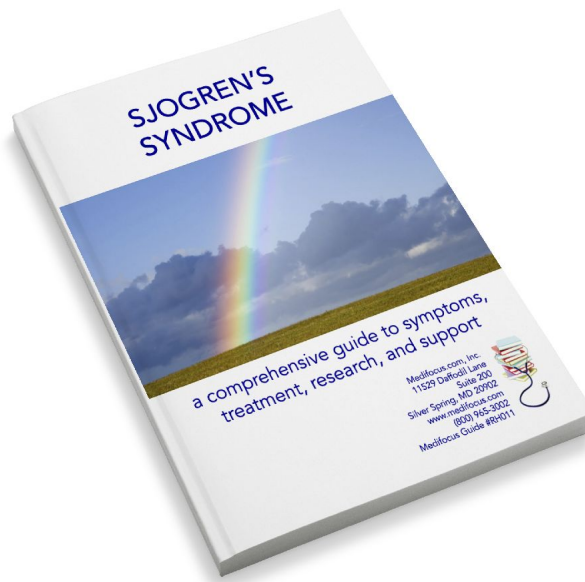
[www.bssa.uk.net/](http://www.bssa.uk.net/)

### **Dry.org**

[dry.org](http://dry.org)

The **Directory of Organizations** in the complete **Medifocus Guidebook on Sjogren's Syndrome** includes a list of selected disease organizations and support groups that are helping people diagnosed with Sjogren's Syndrome.

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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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