

## Sjögren's Syndrome (SS)

### Introduction:

You probably know someone who has SS; the problem is that they probably don't know they have it. SS is a common yet under-diagnosed condition causing dryness of the mouth and eyes as well as inflammation in other parts of the body. This condition seems to result from the body's immune system attacking the glands that make saliva and tears, causing these glands to swell and/or malfunction.

SS affects about 1% of the general population, which is about as common as rheumatoid arthritis (RA) and 10 times as common as systemic lupus erythematosus (SLE). Even though SS is common, it is not commonly recognized. By the time a patient is diagnosed with SS, an average of 9-11 years has elapsed since the onset of symptoms. This delay is likely due to a combination of factors, including patients blaming their dryness on other factors (medications, allergies, other illnesses, getting older, etc.) and lack of physician awareness of SS.

Roughly 1/2 of patients with this disease have Primary SS, and the remainder has Secondary SS, which is seen along with another rheumatic disease such as RA or SLE. The most common age of onset is between 40 and 60 years of age. As with SLE, women with this condition outnumber men by about 9:1. While an aggravating disease, having SS does not increase one's mortality rate overall, and SS patients can expect normal survival.

### Features of SS:

The key symptoms of SS are due to an impaired ability to make adequate saliva and/or tears. Loss of saliva and subsequent dry mouth may result in difficulty chewing or swallowing food, loss of taste, or accelerated tooth decay. Many individuals note that they cannot eat crackers or other dry foods without water or other liquid to wash it down, and those with SS often find the need to keep a glass of water by their bedside to ease dry mouth symptoms that awaken them from sleep at night. A burning sensation in the mouth may also occur, which may be a sign of yeast infection, a problem SS patients are prone to developing.

Loss of tears and dryness in the eyes may result in the eyes feeling gritty or painful on the surface and those with SS often have the feeling that something is in their eye. These symptoms are often referred to as keratoconjunctivitis sicca (ker`a-to-kon-jungk`ti-vi`tis sik`a). In severe cases, the cornea (surface of the eye) may develop abrasions or ulcers. This complication makes SS patients susceptible to viral or bacterial infections on the surface of the eye. In some individuals, the salivary glands may swell and become uncomfortable. The most common glands that may be noticeably swollen are the parotid (pa-rot`id) glands located on the sides of the cheeks. Other glands less commonly involved are located under the jaw. Infections (such as mumps) and salivary gland stones can cause a similar type of swelling in these glands, but SS can usually be distinguished by the symptoms of dryness in the mouth.

SS may affect many other parts of the body as well. About 1/2 of those with SS have arthritis or at least joint and muscle pain, and nearly 1/2 have hearing loss. Thyroid disease, nerve damage, and irritation of the trachea (windpipe) are also common problems in SS. Other organs occasionally involved include the lungs, liver, brain, bladder, and kidneys. These different parts of the body can become inflamed due to an attack from the immune system much like what we see in patients with SLE (see Systemic Lupus Erythematosus section).

Another problem worth mentioning in SS is the increased risk for developing lymphoma, a cancer of the lymph nodes and blood cells. This occurs in 5% of SS patients, making them 44 times more likely than the general population to develop lymphoma. When this complication occurs, it is seen an average of 7.5 years after the diagnosis of SS is made. The development of lymphoma is the exception to the rule that no excess mortality is seen in SS. For this reason, any enlarged lymph node that remains swollen for more than 4 weeks should be biopsied.

### Diagnosis:

When a patient has symptoms of dry mouth and/or eyes, the next step in deciding whether these symptoms represent SS is to document either the presence of antibodies typical for SS, loss of function of salivary or tear glands, or inflammation of these glands. It is also important to exclude other causes of these symptoms include medications (anti-histamines, certain kinds of anti-depressants), radiation to the head and neck, viral infections, diabetes, and a number of other chronic illnesses.

A physical examination may give certain clues to the diagnosis of SS. About 1/3 of patients will have swollen salivary glands, and many have a lack of normal “pooling” of the saliva under the tongue. In some, the tongue is so dry that it has the appearance of “crocodile skin.” The eyes may appear irritated or red and may show a visible loss of moisture on the surface. Two quick tests that can be done in a few minutes in the office to provide further evidence for SS are the Schirmer’s test and the Rose-Bengal test. The Schirmer’s test involves inserting a strip of paper on each lower eyelid and measuring the tear flow. The Rose-Bengal test consists of a dye that is applied to the surface of the eye to pick up small abrasions of the cornea that are typical for SS. Any of these findings add more evidence to support a SS diagnosis.

Studies of the salivary glands include x-ray studies and salivary gland biopsy. The salivary glands can be imaged with a study known as sialography, which involves injecting dye into the gland through an opening in the cheek and observing inflammation of the ducts in within the gland. Ultrasound, nuclear medicine scans, and magnetic resonance imaging (MRI) have also been used to visualize changes in the glands suggestive of SS. The most specific and accurate study of the salivary glands, however, is a salivary gland biopsy. Most commonly, a small incision is made on the inner lower lip, where small, pea-sized salivary glands are located, and several glands are removed and examined under the microscope for inflammation. This procedure is about 85% accurate in diagnosing SS. While not every patient may need this biopsy to confirm the diagnosis, it is very useful in cases where other evidence has been unclear.

Antibodies seen in SS include the anti-nuclear antibody (ANA) also seen in SLE, the rheumatoid factor (RF) also observed in RA, and some more specific antibodies known as Ro/SSA and La/SSB. While these latter two markers can also be seen in some SLE patients, their presence in a patient who has dry mouth and/or eyes in the absence of other features of SLE strongly supports a diagnosis of SS. On the average, about 70% of SS demonstrate these antibodies; their absence, therefore, does not rule out the diagnosis. In fact, some patients will exhibit none of these antibodies. In these individuals, a salivary gland biopsy or other studies may be most useful if a diagnosis of SS is to be pursued.

While SS may be a difficult illness to evaluate, a combination of these evaluations in the hands of an experienced physician can help determine whether an individual has SS versus a number of other illnesses that can demonstrate the same symptoms. To make matters more complicated, many patients who have SS also have another rheumatic disease such as SLE or RA, and these conditions should be sought in any patient with symptoms suggesting SS.

### **Therapy:**

Treatment of SS consists of measures that are aimed at relieving dry mouth and eye symptoms as well as medications that suppress the inflammation causing the problems in the glands and other parts of the body. In general, the severity of the symptoms, the type of symptoms present, and the extent in the disease in the rest of the body determines what therapy is most appropriate in an individual patient.

Dry mouth symptoms can be treated an approach as simple as extra sips of water. Small, frequent sips rather than large volumes seem to be adequate to relieve symptoms. Over the counter gels and other preparations (Xerolube, Salivart, Oral Balance Gel, Mouth Kote, etc.) are available over the counter and can add moisture to a dry mouth when water isn’t enough. Close attention to good dental care is crucial to prevent cavities. Extra fluoride may be helpful, and if gum is to be chewed, it should be sugar-free to avoid the risk of tooth decay associated with extra sugar. Yeast infections in the mouth also need to be treated when a patient demonstrates a painful or burning sensation in the mouth.

Dry eye symptoms may be treated initially with a variety of over the counter artificial tear preparations or gels (Cellufresh, Refresh Plus, Celluvisc, Lacrilube, etc.). Humidifiers in the home, especially in the bedroom at night, can also help reduce a sensation of dry eyes, and fans should be avoided, as they can further dry the eyes.

Punctal occlusion can add moisture to the eyes in difficult cases. This procedure is typically performed by an eye doctor and involves inserting temporary plugs in the puncta, two tiny opening located on the lower inner eyelids that drain the tears. If the temporary plugs provide relief of symptoms, the puncta can be permanently sealed off with a laser.

A review of a patient’s list of medications should be reviewed, and any non-essential drugs should be discontinued only after a discussion with the prescribing physician. This simple measure may do away with the need for other therapies. Medications focusing on improving flow of saliva and/or tears include pilocarpine (Salagen) and cevimeline (Evxac). These medications both work mostly on the salivary glands and stimulate flow of saliva, and to a lesser extent tears. Both medications must be used consistently for several months before any benefit is seen but may be quite useful at relieving symptoms. Other than excessive sweating, side effects are uncommon and usually mild.

Suppressing the inflammation of SS is an additional challenge. For those with arthritis, salivary gland swelling, and fatigue, hydroxychloroquine (Plaquenil) may be beneficial. This drug is also used for treating mild SLE and RA and has few major side effects, the major complication being a 1 in 1,000 risk of changes in the retina (the back part of the eye) that can be identified by monitoring every 6 to 12 months with an eye doctor. For certain patients, drugs that more powerfully suppress the immune system such as methotrexate or cyclophosphamide may be needed. Because of the side effects of these medications and the need for frequent monitoring, they should be reserved for resistant disease or complications involving other organs (see Medications section or sections on RA or SLE).

Eye drops containing cyclosporine (Restasis) have recently been developed for treating dry eyes in SS and have the advantage of directly suppressing the inflammation in the tear glands as well as on the surface of the cornea. These drops must be administered consistently twice a day for several months if they are to be effective but can produce dramatic results if taken correctly. Another method for treating the inflammation in the salivary glands directly are lozenges containing interferon, a substance produced in the body known to have effects on inflammation. While not expected to be available for a few years, preliminary studies look quite promising.

Only by being aware of SS can this disease be identified and only by being identified can this disease be treated and complications be prevented. Hopefully, the future will hold yet more therapies to reduce debilitating symptoms and potential damage that can result from SS.