

## Systemic features

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### Introduction

In addition to dryness of the eyes and mouth more than one third of patients will have problems affecting other body systems – sometimes referred to as systemic disease. Systemic disease is more common in those patients with the Sjögren's specific antibodies, Ro and La. This article deals with those systemic problems outside the eyes and mouth.

### Systemic disease

#### Dryness

Although dryness of the eyes and mouth are the hallmark of the disease, other secretions may be affected too. Dryness of the nose and nasal passageways is common and irritating for patients. General humidification of the atmosphere helps, but a specific product, such as petroleum jelly smeared around the nostrils, or nozoil (a commercially available oily spray) may be helpful for some. Dry skin is a common complaint. Simple measures usually help with this – such as showering in preference to baths, avoiding soap and using soap substitutes such as E45 wash cream, Dove wash cream etc. instead. You should also use plenty of moisturizing cream such as E45. Sensitivity to sunlight is common and high protection factor suncreams (i.e. SPF30 and above) should be used in the summer months. It is also sensible to protect yourself from excessive sunlight by wearing a wide brimmed hat and long sleeves. Many patients develop an irritating dry cough because of drying up of the secretions in the trachea (windpipe). This is helped by humidification and some patients find pilocarpine (which stimulates natural secretions) helpful.

#### Fatigue and joint symptoms

Tiredness and joint pain are common features and may affect more than half of patients with Sjögren's. The tiredness is often frustrating. Some patients find that hydroxychloroquine improves this symptom a little but in many cases sufferers develop a coping strategy based on adequate rest and planning and pacing activity.

Patients with Sjögren's can develop an inflammatory arthritis where the joints become hot and swollen. This is often intermittent, does not usually cause longterm damage to the joints and in general has a better outlook than the arthritis seen in RA. In most cases intermittent treatment with anti-inflammatory medication is sufficient. Some patients with Sjögren's develop age-related osteoarthritic change in their joints which sometimes is severe enough to warrant surgery. Hydroxychloroquine may be used in patients with inflammatory joint disease.

#### Raynaud's phenomenon

Up to 50% of patients will complain of Raynaud's phenomenon – where the blood flow to the hands and feet is affected, causing severe coldness and colour changes. Firstly it is important to wrap up warm and avoid extremes of temperature. If this alone is insufficient then the Raynaud's may respond to treatment

with Ginkgo Biloba (an over the counter remedy), or failing this Nifedipine (a drug commonly used to treat blood pressure) or other drugs on prescription. The prescription drugs used to treat Raynaud's are on the whole anti-hypertensive drugs and their use may be limited by side effects.

#### Gastrointestinal and liver disease

Many patients complain of symptoms similar to those seen in irritable bowel syndrome (IBS). Symptoms include lower abdominal pain, bloating and change in bowel habit. The mechanism is not fully understood but it may be related to reduced secretions in the wall of the intestine. Some patients benefit from an increase in the fibre content of their diet and anti-spasmodic drugs.

Pancreatitis (inflammation of the pancreas) is a rare complication of Sjögren's Syndrome. It usually presents with upper abdominal pain and often requires specialist treatment.

There is an association between Sjögren's Syndrome and primary biliary cirrhosis. The latter can present with liver function abnormalities and patients often have a specific antimitochondrial autoantibody. The diagnosis is confirmed by liver biopsy and treatment with ursodeoxycholic acid may be helpful.

#### Pregnancy and gynaecological problems

It seems likely that fertility (i.e. the ability to conceive) is normal in patients with Sjögren's Syndrome but that there is an increased risk of miscarriage. The actual risk is difficult to quantify because miscarriage is a common event in any case but at least one study found an increased risk of recurrent miscarriage in women who were positive for either anti-Ro and/or La autoantibodies. These autoantibodies are found in up to 60% of women with Sjögren's Syndrome.

The Ro and La autoantibodies associated with Sjögren's Syndrome are small enough to cross the placenta and enter the unborn baby's circulation. In the majority of pregnancies this does not cause any harm but in about 5% of cases problems occur. The most common problem is a transient rash in the newborn child. This rash generally lasts about 17 weeks before fading spontaneously. Very rarely the child can be born with congenital heart block (CHB). This is rare, occurring in less than 2% of pregnancies in women with anti Ro or La antibodies and may be detected during pregnancy by ultrasound scanning from about 16 weeks of pregnancy. It is slightly commoner in female children and if the mother has had a previous child with CHB then the risk of a subsequent pregnancy being affected goes up to 12%. More than 70% of the affected children survive but nearly all require pacemakers in the first few months of life.

Vaginal dryness is a frequent problem. KY Jelly may help a little but Replens (a non-hormonal vaginal moisturizer) is more effective – it is not prescribable but can be obtained by mail order or over the counter at the chemists. Another treatment is Sylk, again available via mail order or over the counter at the

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chemists. Some patients benefit from oestrogen containing creams – these are only available on prescription.

### Serositis and respiratory disease

Serositis (inflammation of body cavities) may be seen in 5% of patients and most commonly presents as sharp, pleuritic chest pain which may respond to treatment with anti-inflammatories or steroids. Rarely Sjögren's Syndrome can cause inflammation of the lung itself which requires specific investigation and treatment, often with steroids.

### Renal and urinary tract disease

Renal involvement is uncommon but patients have an increased risk of renal stones. Interstitial cystitis (inflammation of the bladder wall) may cause very troublesome symptoms, such as urinary frequency, and can be difficult to treat. It sometimes responds to treatment with oral cimetidine or bladder instillations. Occasionally low dose steroids are helpful.

### Neurological disease

Neurological disease is rare but can be disabling. The nervous system is complicated and problems can present in many different ways. It is important to remember that some symptoms such as headache are very common in the normal population and do not necessarily imply any serious disease.

A number of different neurological complications have been described in patients with Sjögren's. All are relatively rare, probably affecting less than 5% of patients with Sjögren's. They include conditions such as diffuse sensorimotor neuropathy (damage to the sensory and motor functions of nerves), trigeminal neuralgia (a painful condition affecting the trigeminal nerve which supplies the side of the face), mononeuritis

multiplex (where damage occurs to several peripheral nerves) and autonomic neuropathy which can cause a multitude of symptoms including postural hypotension (low blood pressure on standing up), nocturnal diarrhoea, urinary retention, sweating and dizziness. They are not exclusive to Sjögren's Syndrome and may occur in association with other conditions such as diabetes and rheumatoid arthritis. In some cases investigations such as nerve conduction studies are helpful in confirming a diagnosis. Very rarely patients with Sjögren's can present with a condition which resembles multiple sclerosis.

In some of these conditions hydroxychloroquine is helpful but in others treatment with other agents such as steroids or other immunosuppressant drugs are needed. In many cases specialist advice from a rheumatologist or neurologist will be needed to confirm the diagnosis and guide treatment.

### Thyroid

Thyroid disease may affect up to one fifth of patients with Sjögren's Syndrome and usually presents insidiously with an underactive thyroid. Symptoms are not dissimilar from those of Sjögren's itself and diagnosis is sometimes delayed. Treatment is with thyroxine replacement therapy which is usually lifelong.

### Blood test abnormalities

Blood test abnormalities include high immunoglobulin levels, low white blood count, positive rheumatoid factor, positive ANA and positive Ro and/or La antibodies. The latter are found in 60% of patients with primary Sjögren's and tend to be associated with certain clinical features, including a sun-sensitive rash. Patients with the antibodies tend to be at higher risk of developing systemic disease.

**Table of treatments for systemic complications**

Product	Uses	Availability
Petroleum Jelly (Vaseline)	Smear around nostrils and over lips	Chemists, supermarkets etc
Nozoil	Spray into dry nostrils	Chemists/pharmacies
E45 wash cream & moisturisers	For showering & moisturising of skin	Chemists, supermarkets etc
Dove wash cream	For showering & moisturising of skin	Chemists, supermarkets etc
High protection factor suncreams (i.e. SPF30 and above)	For sun protection	Chemists, supermarkets etc
Pilocarpine (salagen)	To stimulate secretions	Prescription only medication
Hydroxychloroquine (plaquenil)	Immunomodulatory drug which may help with arthritis & fatigue	Prescription only medication
Ginkgo Biloba	Herbal remedy which may help circulation	Chemists, supermarkets etc
Nifedipine (Adalat)	May improve circulation	Prescription only medication
Anti-hypertensive drugs eg nifedipine, enalapril	May improve circulation	Prescription only medication
Anti-spasmodic drugs (eg mebeverine)	May improve bowel spasm and symptoms of irritable bowel	Prescription only medication
Ursodeoxycholic acid	Used to treat primary biliary cirrhosis	Prescription only medication
KY jelly	May help vaginal dryness	Chemists, supermarkets etc
Replens vaginal moisturiser	May help vaginal dryness	Pharmacies, internet mail-order
Sylk vaginal moisturiser	May help vaginal dryness	Pharmacies, internet mail-order
Steroids (eg prednisolone)	Sometimes used to treat systemic complications in specific circumstances	Prescription only medication

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## Lymphoma

Lymphomas are cancers of the lymphoid system. The incidence of lymphoma is increased in comparison to the general population but it remains rare and probably affects no more than 1 or 2% of patients with Sjögren's Syndrome. In most cases it takes the form of a MALT (mucosal associated lymphoid tissue) lymphoma and usually presents as a localised swelling, often within a salivary gland. In general they respond well to treatment.

## Drugs used to treat systemic disease in Sjögren's Syndrome

With the exception of hydroxychloroquine systemic treatments have been generally disappointing in Sjögren's. Hydroxychloroquine (plaquenil) is an antimalarial drug also used in the treatment of SLE and RA. Many patients find it helps their joint pain and fatigue but unfortunately it does not influence the dryness. It may cause some bloating and nausea when first started but is usually well tolerated. In very rare cases hydroxychloroquine has been reported to cause retinal damage. The Royal College of Ophthalmologists have reviewed the risks associated with hydroxychloroquine and assessed these as very small. They recommend that patients do not exceed a dose of 400mg daily, have a baseline eye test done if any visual impairment is present and then a follow-up eye test annually. They recommend referral to an ophthalmologist only if problems are found on routine eye tests.

Pilocarpine (salagen) is used to stimulate salivary, tear and other secretions. It has already been discussed in the chapters on mouth and eye.

Steroids are only rarely used in patients with Sjögren's Syndrome. They may be useful however in patients with very specific complications such as lung inflammation. Other immunosuppressive drugs e.g. azathioprine, cyclophosphamide should also be reserved for patients with specific complications and require specialist advice and monitoring.

Research into Sjögren's Syndrome is ongoing and in the future new treatments may be developed. Trials of Rituximab, a treatment which reduces B-cell numbers, are currently running in a few centres and have shown some promising early results although it is likely to be some years before this leads to any new treatments.

## Diet and other treatments

No specific diet has been shown to be of benefit in Sjögren's Syndrome. In general patients are advised to eat a healthy diet low in saturated fat (meat and dairy products) and high in polyunsaturated fat (fish and vegetable oils). Glucosamine supplements have recently been shown to have some benefit in patients with osteoarthritis (wear and tear) of the knee. None of the many other commercially available supplements has been shown to have a consistent benefit in patients with Sjögren's Syndrome.

Acupuncture (where fine needles are inserted into specific points on the body) is often helpful for pain but cannot modify the underlying disease. Homeopathy, massage and reflexology have not been shown to help Sjögren's Syndrome although some patients find these treatments relaxing. Osteopathy and chiropractic treatment may have a role in the treatment of mechanical joint pain but are unlikely to influence the outcome in Sjögren's.

## Conclusion

Sjögren's Syndrome is a common autoimmune disease. Many patients have disease in body systems other than the eyes and mouth. It has historically been under-diagnosed and under-treated but public and professional awareness is increasing. Research is ongoing both into the cause of the condition and its treatment.

This information is taken from the Third Edition of the BSSA Advisory Guide.