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## MEETING REPORT

# Sjögren's syndrome – managing oral and systemic symptoms via a multi-disciplinary approach*

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## Sjögren's syndrome – a clinical overview

Sjögren's syndrome is a systemic autoimmune exocrinopathy of unknown aetiology that is principally characterized by focal inflammation of the salivary and lacrimal glands. This culminates in clinical symptoms of dryness, particularly in the eyes and mouth (Jonsson, Haga and Gordon, 2001).

Sjögren's syndrome can occur either as a primary disorder (primary SS) or secondary to other well-defined autoimmune diseases including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), progressive systemic sclerosis, and polymyositis (Fox, 1988).

Sjögren's syndrome is estimated to affect up to 4% of the adult population, with 500 000 sufferers in the UK alone (Thomas *et al*, 1998; Arthritis Research Campaign, 2003). Patients with SS are usually female (9:1 female:male gender ratio), with a mean age at diagnosis of 50 years (Bell *et al*, 1999).

Sjögren's syndrome patients often suffer an adverse impact on their emotional and social well being (Bjerrum and Prause, 1990). The condition is characterized by considerable morbidity and discomfort, including symptoms of fatigue, low mood, irritability, headache, and impaired cognitive function (Valtysdottir *et al*, 2000; Connolly, 2001).

Although SS is the second most common connective tissue disease, it remains under-recognized in the clinical setting (Fox, Stern and Michelson, 2000). This is principally because of the variable and often non-specific presentation of the disease. In addition, many patients do not seek immediate help or have been frequently misdiagnosed (Bjerrum and Prause, 1990; Bell *et al*, 1999; Carsons, 2001). Diagnosis has also been hindered by the historic absence of widely accepted diagnostic criteria.

## Clinical presentation

Patients with SS do not always present to their general practitioner with the classic symptoms of xerostomia (dry mouth) and xerophthalmia (dry eyes). Instead they may present with non-specific symptoms such as arthralgia, fatigue, vaginal dryness, pancreatic insufficiency, or extra-glandular complications such as arthritis, Raynaud's phenomenon, thyroid disease, pulmonary disease, or neurological symptoms (Thomas *et al*, 1998; Bell *et al*, 1999; Fleming Cole, Toy and Baker, 2001). As a consequence of the diverse nature of the syndrome, patients may present to a wide range of clinical specialities, including oral medicine, general medicine, ophthalmology, and rheumatology. A typical patient pathway is illustrated in Figure 1.

## Diagnosis

Although SS is not curable at present, early diagnosis and intervention can usually help to minimize some of the sequelae of the condition including gross dental caries and corneal damage and also improve quality of life (Fleming Cole *et al*, 2001).

If untreated, SS can result in a variety of local and systemic complications (e.g. alteration of mucosal and ocular surfaces, breakdown of normal host barriers to infection), and patients may develop extra-glandular problems such as neuropathy, interstitial lung disease, or haematological complications (Jonsson *et al*, 2001). Patients with primary SS who demonstrate hypergammaglobulinaemia have a 44-fold increased risk of developing non-Hodgkin's B-cell lymphoma (Kassan *et al*, 1978) and the presence of anti-Ro/La antibodies in pregnant females can lead to intrauterine death or

*This article was written following the recent Sjögren's Syndrome Special Interest Group (SSSIG) meeting held during the British Society of Rheumatology's (BSR) annual meeting in April, 2003. During the meeting, it was acknowledged that clinicians within the specialty of Oral Medicine were often ideally placed to diagnose and manage patients with Sjögren's syndrome and that there was a need to increase awareness of the condition to prompt timely and effective therapeutic intervention.

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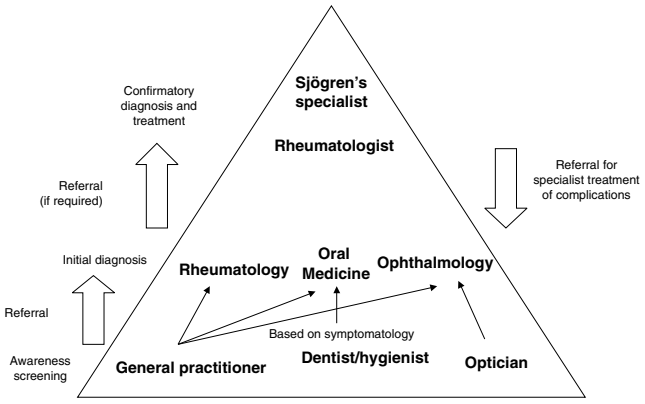


**Figure 1** Typical patient pathway for a Sjögren's syndrome (SS) sufferer; diagrammatic representation of the variety of clinical specialties (including typical referral pathways), involved in the management of patients with SS

**Table 1** EU–USA classification criteria for Sjögren's syndrome

| | |
|---|---|
| I | Symptomatic xerostomia for over 3 months, persistently swollen salivary glands as an adult, or frequent use of liquids to aid in swallowing food |
| II | Symptomatic dry eyes for over 3 months, recurrent 'grittiness', or use of tear substitutes over three times a day |
| III | Objective evidence of ocular involvement as defined by at least one of the following: positive Schirmer's I test or rose Bengal score (or other ocular dye score, e.g. lissamine green) |
| IV | Abnormal minor salivary gland biopsy (focus score ≥1). |
| V | Objective evidence of salivary gland involvement as defined by at least one of the following: unstimulated whole salivary flow ≤1.5 ml in 15 min, parotid sialography showing punctate sialectasis or salivary scintigraphy demonstrating delayed uptake, reduced concentration and/or delayed excretion |
| VI | Antibodies to Ro (SS-A) or La (SS-B), or both |

In general, a diagnosis of primary Sjögren's syndrome is indicated when four of the six criteria are satisfied, provided that either the serological or histological markers are positive.
Exclusion criteria: any patient with past head and neck radiation treatment, hepatitis C infection, AIDS, pre-existing lymphoma, sarcoidosis, graft-*vs*-host disease, or use of drugs known to cause xerostomia.

neonatal heart block in the foetus (Tseng and Buyon, 1997).

The diagnosis of primary SS should be suspected in any patient complaining of dry mouth, gritty eyes, or unexplained lethargy.

As previously stated, the accurate diagnosis of SS has been hampered by the existence of a variety of diagnostic criteria, none of which have gained wide acceptance. With the publication of the EU-USA Consensus Diagnostic Criteria (Vitali, 2003; Table 1) it is hoped that the diagnosis of SS will be more readily facilitated. In general, the presence of any four of the six criteria is indicative of primary SS, provided either the histopathology or serological markers are positive (criteria IV and VI). Furthermore, to avoid the misclassification of asymptomatic patients, an additional definition has been added – namely, three positive results

*Ocular symptoms*

- Have you had daily, persistent, troublesome dry eyes for more then three months?
- Do you have a recurrent sensation of sand or gravel in the eyes?
- Do you use a tear substitute more than three times a day?

*Oral symptoms*

- Have you had a daily feeling of dry mouth for more than three months?
- Have you had recurrently or persistently swollen salivary glands as an adult?
- Do you frequently drink liquids to aid in swallowing dry foods?

**Figure 2** EU screening questions for dry eye and mouth symptoms

from the four objective items (i.e. items III, IV, V and VI).

Figure 2 lists the six screening questions recommended by the EU for identifying symptoms of dry eye and dry mouth.

For patients with RA or other rheumatic diseases, confirmatory diagnosis of secondary SS is derived from positive symptomatology, plus objective evidence of dry eye or dry mouth (the presence of items I or II, plus two from items III, IV, and V).

## Diagnosis – role of the oral medicine specialist

Many referrals from primary care will be directed to oral medicine departments because of either xerostomia or salivary gland swelling. However, not all patients who complain of oral dryness actually have objective evidence of salivary gland hypofunction and these individuals must be appropriately identified. Clinical evidence of salivary hypofunction may include:

- Dry, parchment-like mucosa (Carsons, 2001);
- Lack of salivary pool in mouth floor (Carsons, 2001);
- Thickened saliva (Carsons, 2001);
- Fissures and filiform papillae atrophy (Fleming Cole *et al*, 2001);
- Candidosis (Longman *et al*, 1997);
- Salivary gland swellings (Longman *et al*, 1997);
- Dental caries (Longman *et al*, 1997).

Serological testing for anti-Ro/La antibodies combined with objective evidence of xerostomia will help to diagnose 70% of the patients with SS. In those cases where this serology is found to be negative, labial salivary gland biopsy should be undertaken (Jonsson *et al*, 2001). This is a simple procedure, but is technique-sensitive and should be performed by an experienced operator to minimize the incidence of complications.

Patients suspected of having SS following such investigations may require referral to a rheumatologist or SS specialist.

## Treatment of Sjögren's syndrome

The treatment goals for SS are to manage symptoms and prevent or limit tissue damage. This may involve both local and systemic management, depending on the clinical features.

In addition to the targeted therapeutic interventions (see below), clinicians should offer general lifestyle advice, including:

- Avoidance of dry, external environments;
- Avoidance of cigarettes;
- The use of sugar-free chewing gum;
- Showering rather than bathing;
- Avoidance of strong soaps, replacing them with aqueous creams or emollients.

Clinicians must explain their diagnosis to the patients, and inform them of patient support groups such as the British Sjögren's Syndrome Association (http://www.bssa.uk.net), or the Sjögren's Syndrome Foundation (http://www.sjögrens.org).

The initial treatment of SS merits the use of simple topical agents that alleviate dryness. The most common treatment for dry eyes is an artificial tear solution (e.g. hypromellose). This type of agent is used as frequently as required, but its efficacy is limited by a short duration of action (Foster *et al*, 1994).

Preservative-free preparations should be used if the drops aggravate symptoms, and if mucous threads are present, mucolytic agents such as acetylcysteine should be administered (Foster *et al*, 1994).

Therapeutic management of xerostomia must address not only symptomatic relief but also be directed towards minimizing the sequelae of this condition. Thus dietary advice, a high standard of oral hygiene and the use of topical fluorides all have important supportive roles to play.

Saliva substitutes (e.g. carboxymethylcellulose sprays) can provide useful relief for dry mouth, but like artificial tear solutions, most formulations have a short duration of action. In general, they also largely fail to effectively replace the protective role of saliva. Saliva replacement gels are usually favoured by patients for providing systematic relief (Al-Hashimi and Taylor, 2001).

Systemic treatment of SS is gaining popularity, because of the introduction of secretagogue agents such as pilocarpine and cevimeline (as yet unavailable in the UK). Secretagogue treatment early in the disease stage can not only palliate symptoms but may also help minimize some of the complications of xerostomia (Vivino, 2001).

Salagen® (pilocarpine hydrochloride) is at present the only systemic treatment licensed in the UK for the treatment of dry eyes and dry mouth associated with SS. It has been shown to be effective in stimulating residual gland function, and significantly reducing the incidence of long-term complications (Papas *et al*, 1997, 1999; Rhodus *et al*, 1998; LeVeque *et al*, 1999; Vivino *et al*, 1999).

Salagen's® efficacy depends on the existence of residual exocrine gland function, and therefore early treatment provides the greatest potential for success. Objective affects such as improvements in salivary flow are generally dose-dependent and are usually observed within 30 min of administration. Subjective improvement, however, may take several weeks to manifest, and in order to aid compliance, patients should be advised to continue treatment for at least 6 weeks before expecting symptomatic improvement (Vivino *et al*, 1999).

Adverse effects such as sweating, urinary frequency, and flushing may be observed, in some patients, although these tend to diminish over time. Anecdotally, it appears helpful to commence with a low dose of 5 mg $day^{-1}$, and advise patients to wait until any adverse effects have subsided before twice-daily dosing is commenced. This strategy should be followed until the usual maintenance dose of 5 mg four-times-daily is attained.

## Conclusion

It is hoped that this article will contribute towards raising awareness of SS. Oral manifestations of SS are a major component of the condition and the specialty of oral medicine is well placed to diagnose and treat these patients.

## Note

Draft guidelines for the management of SS in secondary care are now available. To request a copy please contact info@sjogrensguidelines.co.uk.

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