DRY MOUTH AND SJÖGREN'S SYNDROME: AN OVERVIEW

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ABSTRACT

Dry mouth is a common condition presenting to a GP or general dental practitioner. The most common cause of a dry mouth is related to medication use, however patients with Sjögren's syndrome, a multisystem autoimmune condition, may present to their dentist rather than their GP complaining of dry mouth and dry eyes. This article explores the causes of dry mouth and how a patient can be investigated to find the cause of their dry mouth. An overview of Sjögren's syndrome, the relevant diagnostic criteria, presenting signs and symptoms, investigations and management principles are outlined.

Xerostomia (dry mouth) is extremely common in the UK and affects about 13%[1] of the population. Subjective xerostomia is the term used to describe the feeling of a dry mouth when there is plentiful saliva and the salivary glands are functioning as normal. Objective xerostomia or hyposalivation are the terms used when there is decreased flow of saliva caused by failure of the salivary glands to function as normal.

On average a person can produce 500ml of saliva over a 24 hour period. Saliva production increases considerably during eating producing on average 2ml/min and reduces considerably during the sleeping phase producing on average 0.10ml/min.

KEYWORDS

Dry Mouth, Subjective Xerostomia, Objective Xerostomia, Salivary Hypofunction, Drug Induced Xerostomia, Sjögren's Syndrome, Challacombe Scale, Clinical Oral Dryness Scale

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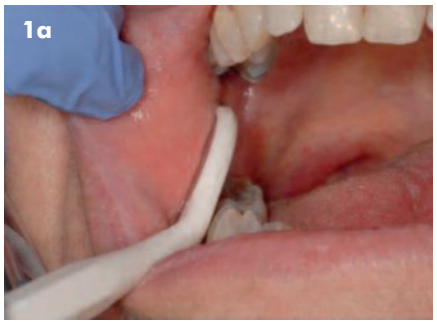
Causes of dry mouth[2,3]

There are many causes of dry mouth (Table 1). Drug-induced xerostomia is the most common cause, and there are more than 1,800 medicines that have dry mouth as a listed side effect.[1,2] The most common medicines include:

- Antidepressants (Tricyclic antidepressants, monoamine oxidases and selective serotonin reuptake inhibitors).
- Antihistamines.
- Antihypertensives (ACE inhibitors, e.g. Ramipril; Beta blockers, e.g. Atenolol, Propranolol).
- Diuretics (Bendroflumethiazide).
- Anti-reflux (Proton pump inhibitors e.g. Omeprazole).
- Anti-cholinergics (Atropine).
- Benzodiazepines (Diazepam).
- Analgesics (Opiates).

TABLE 1
CAUSES OF DRY MOUTH

Type	Causes
Subjective Xerostomia	Mouth breathing Psychological
Objective Xerostomia (Salivary hypofunction)	Iatrogenic • Drug-induced • Irradiation • Smoking Salivary gland disease • Sjögren's syndrome/other connective tissue disease • Sarcoidosis • HIV salivary gland disease • Hepatitis C • Neurological conditions Dehydration • Diabetes and renal failure Physiological • Age Others • Salivary gland developmental anomalies



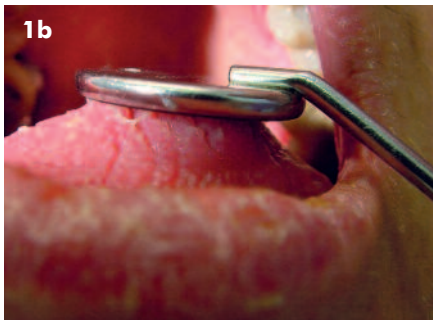


Figure 1a and 1b: Instruments used to examine the oral cavity will stick to the buccal mucosa and tongue

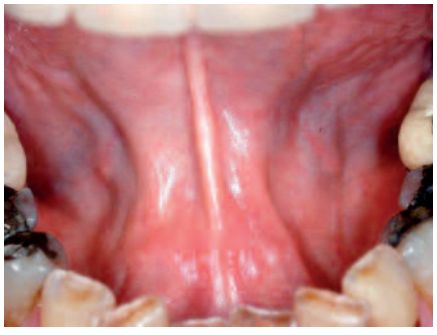


Figure 2: Absence of saliva pooling in the floor of the mouth

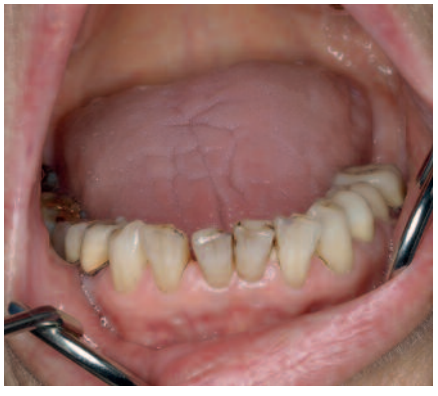


Figure 3: Caries mainly affects the cervical surfaces, cusp tips and incisal edges

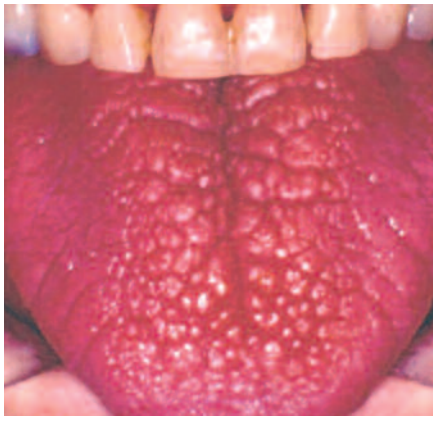


Figure 4: The tongue maybe lobulated, highly fissured, depapillated or atrophic

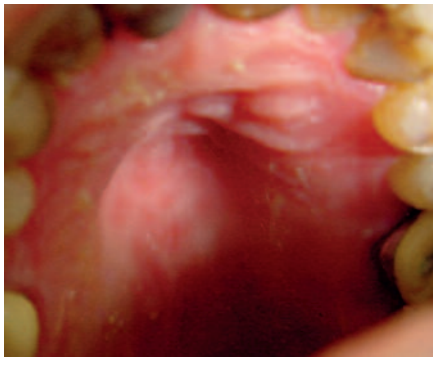


Figure 5: Debris may be present on the palate or under dentures

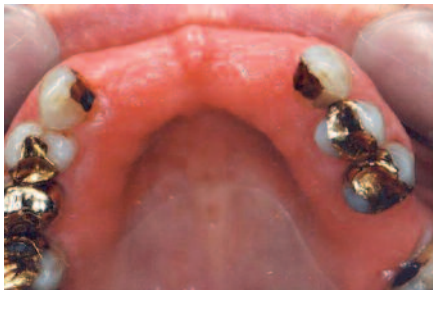


Figure 6: Redness of the mucosa under the denture

Assessment of dry mouth

When a patient presents either to a general dental practitioner (GDP) or a hospital clinic, a thorough history of oral dryness and medical history is crucial for establishing the possible causes of dry mouth. This should be followed by examination and relevant investigations to reach a definitive diagnosis of objective or subjective xerostomia.

The Challacombe dry mouth scale,[4,5] explained in depth in the article by Challacombe and Das on pages 77-79 of this issue, is a useful clinical aid for all dentists in assessing patients presenting with a dry mouth. The purpose of this scale is to be able to identify visually whether patients' have objective xerostomia, i.e. signs of reduced saliva production and to quantify the severity. If the scale for an individual appears to change over time then this will help select the most appropriate interventions (referral to a specialist) and therapy options. It works as an additive score of one to 10; one being the least and 10 being the most severe. Each feature scores one, and symptoms will not necessarily progress in the order shown, however summated scores indicate the likely patient need for treatment of xerostomia. Score changes over time can be used to monitor symptom progression or regression.[5]

Salivary hypofunction causes changes to the soft and hard tissues of the oral cavity recognisable by a GDP as well as specialist. Examination reveals many common features:

- Instruments used to examine the oral cavity will stick to the buccal mucosa and tongue (Figure 1).
- Saliva will be sparse or frothy and there maybe absence of saliva pooling in the floor of the mouth (Figure 2).
- Due to the changes in saliva composition and volume, the saliva has a reduced buffering capacity, resulting in a lower pH and so patients are more susceptible to dental caries. In addition, when there is a lack of saliva, there are more cariogenic bacteria present (Streptococcus mutans and Lactobacilli) which also contributes to a susceptibility to dental caries. Caries mainly affects the cervical surfaces, cusp tips and incisal edges (Figure 3).
- The tongue maybe lobulated, highly fissured, depapillated or atrophic (Figure 4).
- Debris may be present on the palate or under dentures (Figure 5).
- The gingivae architecture maybe changed with lack of stippling and the oral mucosa may have a more shiny, glassy appearance.
- Patients who wear dentures may present with denture-induced stomatitis from an increase in Candida species and Staphylococci and this will appear as redness of the mucosa under the denture (Figure 6).

All these effects can result in loss of function and patients can experience difficulties in speaking, chewing, swallowing dry foods and wearing dentures.

Sjögren's syndrome

Sjögren's syndrome is a chronic multi-system autoimmune rheumatic disease characterised by mononuclear cell infiltration of the lacrimal and salivary glands causing progressive glandular atrophy and hypofunction of these glands. This results in dry eyes (keratoconjunctivitis sicca) and dry mouth (xerostomia).[6]
The aetiology of Sjögren's syndrome is unknown, but may be triggered by an environmental agent in a background of genetic susceptibility. It is the second most common autoimmune rheumatic disease and it is estimated that half a million people in the UK have Sjögren's syndrome.[7] It most commonly affects middle-aged women and can have two peaks of age on onset. The first peak can occur during the childbearing period (usually mid 30s) and the second peak during the post-menopausal period (usually mid 50s).

Assessment of patients when Sjögren's syndrome is suspected

Patients usually present to their GDP, GP or specialist with symptoms of dry mouth and dry eyes but may also present with symptoms of arthralgia and fatigue (Table 2).

A thorough medical history should be obtained, as patients may have existing rheumatic conditions or other autoimmune disorders. The clinical oral dryness score should be recorded. Investigations are usually performed in a specialist clinic, however it is useful for general dental practitioners to be aware of these and what they entail.

Unstimulated whole saliva flow rate

The patient is sat in a relaxed and upright position and asked to spit gently into a universal pot for 10 minutes. The saliva collected is measured in a graduated syringe.

Stimulated parotid saliva flow rate

The patient is sat in a relaxed and upright position and a special suction cup is attached over the stensens duct opening. A stimulant, such as 2% citric acid, is dropped onto the tongue and saliva is collected into a universal pot over 10 minutes. The saliva collected is measured in a graduated syringe.

Lacrimal flow rate (Schirmer test)

A small strip of filter paper is placed inside the lower eyelid of both eyes and the patient is asked to close their eyes for five minutes. The paper is then removed and the amount of moisture is measured. Less than 5mm wetting of the paper is indicative of dry eyes.

Ocular staining test (Lissamine green dye)

A drop of Lissamine green dye is placed in the eye and the patient is asked to blink twice to spread the stain over the conjunctiva and cornea. The staining is scored using a slit lamp (an optical instrument that provides a magnified image of the tear film and the ocular surface and allows examination of the anterior eye). The Lissamine green dye stains any dessicated and dying cells on the ocular surface.

Tear break up time (TBUT)

To measure TBUT, fluorescein is placed into the patients tear film and the patient is asked not to blink while the tear film is observed using a slit lamp. The TBUT is recorded as the number of seconds that elapse between the last blink and the appearance of the first dry spot in the tear film.

Blood tests

These include ENA, ANA antibodies and rheumatoid factor levels.

Salivary gland ultrasound

An ultrasound of the major salivary glands is useful for assessment of the structure of the glands.

Labial gland biopsy

A labial gland biopsy is usually performed under local anaesthetic. A superficial incision is made on

TABLE 2
COMMON SIGNS & SYMPTOMS OF SJÖGREN'S SYNDROME

Type	Symptom
Glandular	Dry mouth and throat
	Dry eyes – feeling of grit/sand, burning, redness
	Tendency for candidal infection
	Parotid gland enlargement
Extraglandular	Excessive fatigue
	Myalgia and arthralgia
	Peripheral neuropathy
	Polymyopathy
	Lymphopenia
	Thrombocytopenia
	Hypocomplementaemia
	Hypergammaglobulinanaemia
	Cryoglobulinaemia
	Raynauds
	Cutaneous vasculitis
	CNS involvement – memory loss/confusion
	Renal involvement
	Interstitial lung disease (pulmonary fibrosis)
	Hepatobiliary chronic inflammation (primary biliary cirrhosis)

TABLE 3

AMERICAN-EUROPEAN CONSENSUS CRITERIA FOR SJÖGREN'S SYNDROME

In order to make a diagnosis of Sjögren's syndrome, the following criteria must be met:

I. Ocular Symptoms (at least one)
- Symptoms of dry eyes for at least three months
- A foreign body sensation in the eyes
- Use of artificial tears three or more times per day

II. Oral Symptoms (at least one)
- Symptoms of dry mouth for at least three months
- Recurrent or persistently swollen salivary glands
- Need for liquids to swallow dry foods

III. Ocular Signs (at least one)
- Abnormal Schirmer's test, (without anesthesia; ≤5mm/5 minutes)
- Positive vital dye staining of the eye surface

IV. Histopathology
- Lip biopsy showing focal lymphocytic sialoadenitis (focus score ≥1per 4mm2)

V. Oral Signs (at least one)
- Unstimulated whole salivary flow (≤1.5ml in 15minutes)
- Abnormal parotid sialography
- Abnormal salivary scintigraphy

VI. Autoantibodies (at least one)
- Anti-SSA (Ro) or Anti-SSB (La), or both

For a primary Sjögren's syndrome diagnosis:
- Any 4 of the 6 criteria, must include either item IV (Histopathology) or VI (Autoantibodies)
- Any 3 of the 4 objective criteria (III, IV, V, VI)

For a secondary Sjögren's syndrome diagnosis:

In patients with another well-defined major connective tissue disease, the presence of one symptom (I or II) plus two of the three objective criteria (III, IV and V) is indicative of secondary SS.

Exclusion Criteria
- Past head and neck radiation treatment
- Hepatitis C infection
- Acquired immunodeficiency syndrome (AIDS)
- Pre-existing lymphoma
- Sarcoidosis
- Graft versus host disease
- Current use of anticholinergic drugs

Vitali C, et al. Classification criteria for Sjogren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002; 61:554-558.

the labial mucosa of the lower lip. Approximately six minor salivary glands are then collected and the incision is closed with resorbable sutures.

Diagnosing Sjögren's syndrome

The American-European Consensus Group (AECG) criteria (Table 3) were accepted as the gold standard for diagnosing Sjögren's syndrome for more than 10 years.[8] The AECG criteria, which applies to individuals with signs and symptoms that may be suggestive of Sjögren's syndrome, requires the presence of four out of six features, one of which is from the subjective component and three of which are from the objective component.

The features/components are:

Subjective
- Symptomatic dry eyes.
- Symptomatic dry mouth.

Objective
- Positive anti-Ro/anti-La antibodies.
- Positive labial gland biopsy ≥1 focus per 4mm^2.
- Reduced whole salivary flow <0.1ml/min.
- Reduced tear production on Van Bijsterveld Staining or <5mm/5min Schirmer test.

In 2012 the American College of Rheumatology (ACR) proposed a new criteria by the Sjögren's International Collaborative Clinical Alliance (SICCA) investigators[6] and recommended discarding the terms 'primary Sjögren's syndrome' and 'secondary Sjögren's syndrome.' The SICCA-ACR criteria require two out of three objective features for a diagnosis of Sjögren's syndrome. These components are:
- Positive anti-Ro/anti-La antibodies or Positive Rheumatoid Factor and anti-nuclear antibody titre ≥1;320.
- Positive labial salivary gland biopsy exhibiting focal lymphocytic sialadenitis with a focus score ≥ 1 focus/4mm^2.
- Keratoconjunctivitis sicca with ocular staining score (OSS) >3.

Salivary gland ultrasound is not currently included in either set of criteria but is being used in clinical practice. Currently the European League Against Rheumatism (EULAR) and the American College of Rheumatology are formulating a revised criteria and both the AECG and SICCA-ACR criteria are being used in clinical practice.

The EULAR group has also developed ESSPRI, a simple systemic disease activity index for primary Sjögren's syndrome in which the patient's signs, symptoms and laboratory findings are divided into twelve domains: constitutional, lymphadenopathy, glandular, articular, cutaneous, pulmonary, renal, muscular, peripheral nervous system, cutaneous nervous system, haematological and biological. The index is designed to be used in clinical practice and in clinical trials to indicate the level of disease before and after an intervention.[9,10]

Treatment of dry mouth and management of Sjögren's syndrome

The main aims for treatment of dry mouth are to relieve the symptoms of dryness by replacing or stimulating saliva production, to restore function and to prevent further damage of soft and hard tissues of the oral cavity.

Patients are advised to take regular sips of water throughout the day. Artificial saliva sprays (AS Saliva Orthana), gels (Biotene OralBalance or BioXtra), mouthwashes (Biotene) and lozenges can provide temporary replacement of saliva and can be used throughout the day to provide effective oral lubrication. The patient's own saliva can be stimulated through the use of sugar-free chewing gum, sucking sugar free mints, sialogogues which include saliva stimulating tablets and pilocarpine.

Patients should be advised to follow a diet low in refined carbohydrates and to avoid acidic snacks and drinks. Fluoride toothpastes (Duraphat 500ppm), gels (DalyGel Kam in trays) and alcohol-free fluoride rinses (Dentyl, Fluoriguard, Oral B) can be used daily by the patient for the prevention of dental caries. Duraphat varnish can be professionally applied by the dental team on an intermittent basis.

In addition, it is important to control infection of the oral cavity. Regular intermittent courses (one week in four) of topical antifungals (Nystatin or Miconozole gel) can be prescribed and the use of antibacterial mouthwashes (Chlorhexidine) is recommended.

Patients should be advised to see their dentist and dental hygienist regularly for oral hygiene advice, prevention and treatment of dental caries and periodontal disease.

Patients diagnosed with Sjögren's syndrome must be monitored carefully for potential of development of low grade lymphomas (mucosa-associated lymphoid tissue or MALT type). Management of extraglandular manifestations of the disease may require a multi-disciplinary team approach. For joint pain; paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) can be helpful. If joints are inflamed a short course of corticosteroids can be prescribed. Hydroxychloroquine helps with joint pain and fatigue and is often used as first-line therapy for patients with Sjogren's. Patients with severe or progressive disease may need high-dose corticosteroids and immunosuppressive drugs. Rituximab, which targets and causes depletion of the B cells, the major cell type active in this autoimmune disease, is known to improve salivary function.[11] Despite their proven efficacy in inflammatory arthritis, anti-TNF drugs have not provided any significant benefit in Sjögren's syndrome.[12] More clinical trials are being carried out on the use of biologics for treatment of Sjögren's syndrome and it is hoped that a safe and effective treatment will become available.

In the meantime, patients with xerostomia will continue to be managed with salivary substitutes and sialogogues, which can be prescribed by their general dental practitioner as well as by specialists. They will require regular monitoring by the dental team for the prevention and treatment of dental disease. Patients with Sjögren's syndrome should be closely monitored and managed appropriately.

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