

A photograph of a woman with blonde hair, looking distressed. She has several orange, textured patches on her face, likely representing dry mouth or oral discomfort. She is holding a glass of water to her lips.

An approach to the patient with a dry mouth

Key points

- The subjective complaint of xerostomia needs to be differentiated from true salivary hypofunction.
- Salivary hypofunction can significantly reduce quality of life through its adverse effects on taste, mastication, swallowing, cleansing of the mouth, killing of microbes and speech.
- Salivary hypofunction is a substantive risk factor for dental caries, oral mucosal disease and infection, particularly oral candidiasis.
- Patients should be investigated for contributory and underlying causes, which include drugs and rheumatological diseases.
- Patients with salivary hypofunction can be treated with artificial saliva, moisturising gels, sugar-free lozenges or gums and muscarinic drugs (cevimeline, pilocarpine).
- Attention to maintaining and improving oral health is important, and treatment of consequent dental caries is essential.

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Dry mouth is a common and disabling problem. After exclusion of treatable causes, treatment is symptomatic to prevent the consequences of salivary hypofunction, such as tooth decay and infection of the oral mucosa.

Xerostomia, or the subjective feeling of a dry mouth, is a common complaint. It is often a consequence of salivary hypofunction (hyposalivation), in which there is objective evidence of reduced salivary output or qualitative changes in saliva. Typically, patients complain of oral dryness only when salivary secretion is reduced by more than half.¹ As saliva has a crucial role in taste perception, mastication, swallowing, cleansing of the mouth, killing of microbes and speech, abnormalities in saliva production can significantly affect quality of life.

Xerostomia also occurs in patients with no measurable decrease in saliva production. Causes of this 'subjective' xerostomia include burning mouth syndrome (better termed

neuropathic-induced orofacial dysaesthesia) and psychological and psychiatric disorders, such as anxiety and depression.

NORMAL SALIVA PRODUCTION

Under normal physiological conditions, the salivary glands produce 1000 to 1500 mL of saliva daily as an ultrafiltrate from the circulating plasma. Therefore, simple dehydration reduces saliva production. The parotid glands are the major source of serous saliva (60 to 65% of total saliva volume), producing the stimulated salivary flow seen with mastication. Serous saliva is also produced during rest by the submandibular glands. This unstimulated salivary flow is essential for maintenance of oral and dental health. Mucinous saliva is

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produced primarily by minor salivary glands. The quality of saliva depends on the rate of flow. Resting saliva is viscous and acidic, whereas stimulated saliva is hypotonic and alkaline.

SYMPTOMS OF A DRY MOUTH

Several studies have reported discordance between patients' complaints of xerostomia and hyposalivation, with a limited association observed between perceived dry mouth and decreased salivary flow.^{2,3} A South Australian study reported that although dry mouth and hyposalivation had similar prevalence estimates (about 20%), the two conditions occurred together in only 6% of participants.⁴

Symptoms and signs that may accompany hyposalivation include:

- increased thirst and the need to constantly sip or drink water
- difficulty in eating and swallowing dry foods
- difficulty in wearing dentures
- an increased rate of dental caries
- halitosis
- a hoarse voice or the inability to speak continuously
- a constantly sore mouth or throat
- oral candidiasis.

Other symptoms that suggest subjective xerostomia in the absence of hyposalivation include:

- a burning sensation of the tongue
- a feeling of altered quality and viscosity of the saliva
- altered sense of taste (dysgeusia).

CAUSES OF A DRY MOUTH

Causes of xerostomia are summarised in Box 1.⁵

Burning mouth syndrome

A proportion of patients with subjective xerostomia have burning mouth syndrome. This poorly understood syndrome presents in the absence of any identifiable pathology of the oral mucosa or of saliva production and quantity. It has a typical triad of symptoms:

- a burning sensation, particularly

of the tongue

- a feeling of xerostomia or more commonly a sense of an unpleasant alteration in the texture and quality of the saliva
- frequently, dysgeusia.

Best described as an orofacial dysaesthesia, with an element of neuropathic-induced sensory disturbance and associated psychogenic factors, burning mouth syndrome warrants specialist evaluation, for example by a specialist in oral medicine.

Hyposalivation

Drugs

Hyposalivation is a common side effect of many medications (see Box 2).⁶ Most of these medications affect the neural regulation of the saliva, which is controlled by the autonomic nervous system. The sympathetic arm with adrenergic receptors inhibits saliva production, and the parasympathetic arm with cholinergic (specifically muscarinic) receptors stimulates saliva production. Many drugs are innately anticholinergic, thereby limiting or reducing saliva production. Some drugs and common beverages such as caffeine and alcohol also have a diuretic effect, depleting the body's water reserves and so reducing saliva production.

Sjögren's syndrome

Sjögren's syndrome (autoimmune exocrinopathy) is a chronic autoimmune disorder characterised by lymphocytic infiltration of all exocrine glands, with destruction of the acini. It is more common in middle-aged women, particularly those of northern European ancestry. Sjögren's syndrome was previously classified as primary or as secondary to other autoimmune diseases, particularly the mixed connective tissue diseases, rheumatoid arthritis, systemic lupus erythematosus (SLE) and scleroderma.

The major presenting complaint is increasing dryness of the eyes and mouth, but the nose, throat, trachea and vagina may also be affected. Enlargement of the parotid or other major salivary glands is

1. CAUSES OF XEROSTOMIA⁵

Psychological and psychiatric disorders

- Anxiety
- Depression

Burning mouth syndrome

Hyposalivation

- Medications and other drugs
- Rheumatological diseases
 - Sjögren's syndrome
 - Rheumatoid arthritis
 - Systemic lupus erythematosus
 - Scleroderma
- Immune-mediated conditions
 - Sarcoidosis
 - Primary biliary cirrhosis
- Endocrine disorders
 - Diabetes mellitus
 - Diabetes insipidus
- Radiotherapy (> 50 Gy) encompassing one or more major salivary glands, especially the parotid glands
- Metabolic and nutritional disorders
 - Dehydration
- Infections (viral)
 - HIV infection
 - Hepatitis C
 - Cytomegalovirus (and other herpes infections)
- Renal disease (end-stage)
- Congenital
 - Prader-Willi syndrome
 - Congenital rubella
 - Lacrimo-auriculo-dento-digital (LADD) syndrome
 - Complete agenesis of salivary glands

seen in two-thirds of patients with primary Sjögren's syndrome but is not common when the syndrome is associated with other immune-mediated conditions. Systemic manifestations are seen in one-third of patients and include arthralgia, arthritis, Raynaud's phenomenon and vasculitis. Lymphoma (particularly extranodal, low-grade marginal zone B cell lymphoma) is a known complication of Sjögren's syndrome.⁷

2. DRUGS THAT COMMONLY CAUSE SALIVARY HYPOFUNCTION⁶

- Alpha blockers: clonidine, prazosin
- Angiotensin–converting enzyme inhibitors: captopril, lisinopril
- Anticholinergics: atropine, hyoscine, tolterodine
- Antihistamines: loratadine, fexofenadine, diphenhydramine
- Antiparkinsonian agents: levodopa–carbidopa
- Antipsychotics: clozapine, risperidone
- Benzodiazepines: alprazolam
- Beta blockers: atenolol, propranolol
- Calcium channel blockers: nifedipine, verapamil
- Central analgesics: hydromorphone, methadone, morphine
- Decongestants: pseudoephedrine
- Diuretics: frusemide, hydrochlorothiazide
- H₂ receptor antagonists: cimetidine, ranitidine
- Monoamine oxidase inhibitors: moclobemide, phenelzine
- Muscle relaxants: baclofen
- Nonbenzodiazepine hypnotics: zopiclone
- Selective noradrenaline reuptake inhibitors: reboxetine
- Tricyclic antidepressants: amitriptyline, clomipramine

Sarcoidosis

Sarcoidosis is a chronic granulomatous multisystem disease of unknown aetiology that involves the lungs and lymph nodes. Sarcoidosis can, albeit rarely, present with xerostomia associated with true hyposalivation, and investigation for this condition is warranted in patients presenting with xerostomia or reduced saliva. The minor salivary glands can also be involved in sarcoidosis.⁸ Heerfordt's syndrome is a very infrequent presentation of systemic sarcoidosis characterised by swelling of the parotid glands, uveitis and facial nerve palsy.

Endocrine disorders

The most common endocrine disorders that can cause dry mouth include diabetes mellitus, hypothyroidism and diabetes insipidus. Diabetes mellitus can have two major adverse effects on saliva production: diabetes-induced neuropathy of the parasympathetic nervous supply results in reduced saliva and, indirectly, the diuresis associated with diabetes (also seen with diabetes insipidus) can also impair saliva production. Reduced saliva production combined with the immunosuppression associated with diabetes mellitus can result in persistent oral *Candida* infection, which can present with treatment-refractory fissuring of the corners of the lips (angular cheilitis), atrophic candidiasis or severe denture-related stomatitis.

Metabolic and nutritional causes

A variety of diseases and conditions associated with metabolic or nutritional changes are associated with hyposalivation, including simple dehydration (caused by inadequate fluid intake, excessive exercise or overheating), eating disorders such as anorexia and bulimia, and malnutrition.

Radiation

Profound, often permanent, salivary hypofunction is seen in almost all patients after radiotherapy for malignant head and neck tumours.⁹ Radiation at dosages higher than 50 Gy directed at any of the major salivary glands damages the serous acini, leading to a reduction in output and an increase in viscosity of the saliva within a week. The loss of saliva production is temporary and improves after several months in 8% of patients, but is irreversible in the remaining 92%.

ASSESSMENT OF PATIENTS WITH A DRY MOUTH

History taking

Leading and open questions regarding symptoms and signs can help distinguish xerostomia from salivary hypofunction. Progression in the symptoms of xerostomia or features of hyposalivation in patients

with a history of radiotherapy or systemic conditions associated with hyposalivation may indicate progression of the underlying disease and the need for more aggressive intervention or treatment of the consequences of salivary hypofunction.

Physical examination

Before specifically examining the mouth for signs of hyposalivation, assess the patient's skin for xeroderma and eyes for signs of xerophthalmia, such as a reduced tear meniscus. Palpate the major salivary glands for enlargement. Examine also for any extrastomal signs associated with rheumatoid arthritis, SLE or scleroderma.

On intra-oral examination, check the state of the dentition and the oral mucosa. Frank dental decay of the smooth surfaces or exposed root surfaces of the teeth is generally a sure sign of severe salivary hypofunction. The presence of dry, erythematous and ulcerated lips, dry 'tacky' or 'sticky' oral mucosa or denudation or atrophy of the normal filiform and fungiform papillae of the dorsal tongue are also highly indicative of hyposalivation (Figure 1). The quantity and quality of the saliva should also be assessed, with decreased or absent pooling of saliva on the floor of the mouth or saliva that appears 'frothy' and strings easily being a clear indication of hyposalivation.

The presence of *Candida* infection also suggests there is insufficient saliva to maintain the health of the oral mucosa. *Candida* infection may present as fissuring of the corners of the lips (angular cheilitis), pseudomembranous candidiasis (thrush), markedly erythematous atrophic candidiasis of the palate or dorsal tongue or an unusually red, hyperplastic appearance of the mucosa supporting the dentures.

INVESTIGATIONS

After careful history taking and physical examination, the focus is on objective assessment of salivary flow followed by investigation of the causes and complications of dry mouth.



Figure 1. Atrophy of the dorsal tongue caused by salivary hypofunction.

Assessment of salivary flow rates

The first step is to evaluate the extent of oral dryness and the amount of resting (unstimulated) and stimulated saliva produced. Assessment of salivary flow is a simple bedside examination. For measurement of unstimulated salivary flow, ask the patient to expectorate their saliva into a container every 30 seconds for 15 minutes. An unstimulated saliva flow of less than 1.5 mL in 15 minutes indicates hyposalivation. For measurement of stimulated saliva production, ask the patient to chew some paraffin wax or chewing gum and again expectorate every 30 seconds, for 5 minutes. A stimulated saliva flow of less than 5 mL indicates salivary hypofunction, and further investigations of the cause is warranted.

Imaging

The following imaging tests may help evaluate the function of the salivary glands and diagnose underlying diseases.

Sialography. This invasive procedure was often used before the development of CT scanning. It involves injecting contrast material into the opening of the parotid duct(s) followed by radiography. The changes seen are usually nonspecific and include ductal destruction and sialectasis.

Complications of this method include allergic reaction and rarely parotitis.

Salivary gland scintigraphy. Dynamic evaluation of the function of the major salivary glands is possible by quantitative assessment of the uptake of ^{99m}-technetium pertechnetate. This test is relatively insensitive but highly specific for the diagnosis of Sjögren's syndrome.

Ultrasound and CT scans. These forms of imaging are indicated if there is enlargement or a mass within any of the major salivary glands that cannot be explained. Ultrasound currently has a limited role in the diagnosis of Sjögren's syndrome but is useful as an adjunctive investigation, in addition to its role in assessing salivary gland masses.¹⁰

Laboratory investigations

All patients with a dry mouth should have a full blood count, thyroid function study and measurement of blood glucose, erythrocyte sedimentation rate, C-reactive protein level, rheumatoid factor, antinuclear antibody, anti-SSA (anti-Ro) and anti-SSB (anti-La) antibodies and serum angiotensin-converting enzyme (ACE) levels. If the diagnosis of Sjögren's syndrome is strongly suspected or already established then supplementary investigations should be considered. These include measurement of serum total immunoglobulin and specific IgA, IgM and IgG levels, together with a serum electrophoresis gel (EPG) and immunoelectrophoresis gel (IEPG) to identify any peaks in expression of monoclonal immunoglobulins that may indicate lymphoma. Serological tests for hepatitis C virus and HIV should be performed to exclude these infections.

Biopsy of a minor salivary gland

Diagnosis of Sjögren's syndrome is based on the finding of dryness of oral and eye mucosa in addition to positive serology for anti-Ro and anti-La antibodies. If the diagnosis is uncertain then biopsy and histopathological examination of a labial minor salivary gland is indicated. The revised American College of Rheumatology criteria for Sjögren's syndrome provide excellent

3. ACR CLASSIFICATION CRITERIA FOR SJÖGREN'S SYNDROME¹¹

Proposed criteria

The classification of Sjögren's syndrome applies to individuals with signs or symptoms suggestive of Sjögren's syndrome that meet at least two of the following three objective features.

1. Laboratory investigations

Positive serum anti-SSA/Ro and/or anti-SSB/La antibodies or positive rheumatoid factor plus ANA titre $\geq 1:320$

2. Histopathological findings of labial minor salivary glands

Labial salivary gland biopsy exhibiting focal lymphocytic sialadenitis with a focus score ≥ 1 focus/4 mm²

3. Ocular findings

Keratoconjunctivitis sicca with an ocular staining score ≥ 3 (assuming that the individual is not currently using daily eye drops for glaucoma and has not had corneal surgery or cosmetic eyelid surgery in the previous five years)

Exclusions

Prior diagnosis of any of the following conditions would exclude a diagnosis of Sjögren's syndrome because of overlapping clinical features or interference with criteria tests:

- history of head and neck radiation
- hepatitis C infection
- AIDS
- sarcoidosis
- amyloidosis
- graft versus host disease
- IgG4-related disease

ABBREVIATIONS: ACR = American College of Rheumatology; ANA = antinuclear antibody.

guidance on the approach to a patient with suspected Sjögren's syndrome (Box 3).¹¹

Fine-needle aspiration biopsy

Patients with established Sjögren's syndrome who present with unilateral major salivary gland enlargement, masses within any salivary gland or lymphadenopathy associated

4. MANAGEMENT OF SALIVARY HYPOFUNCTION

- Artificial saliva
- Oral moisturising gels
- Sugar-free lozenges or gums
- Secretagogue drugs (cevimeline, pilocarpine)
- *Candida* prevention (chlorhexidine)
- *Candida* treatment (nystatin, clotrimazole)
- Referral to a dentist for prevention and management of dental caries

with the major salivary glands merit investigation for non-Hodgkin's lymphoma. Fine-needle aspiration biopsy is readily available. Referral for such investigations should include a direction to consider sending fresh biopsy material for flow cytometry.

MANAGEMENT

For patients with xerostomia alone and no objective findings of salivary hypofunction or disorders of the salivary glands, effective treatment remains a dilemma. Patients with suspected burning mouth syndrome, which has an element of neuropathic-induced sensory disturbance and associated psychogenic factors, warrant referral for evaluation by an appropriate specialist (such as a specialist in oral medicine or oral surgeon).

For patients with hyposalivation, the following strategies are currently recommended to improve quality of life (summarised in Box 4).¹

Patient education

Patients must be warned of the dental consequences of inadequate saliva. They should be encouraged to sip water frequently and to be meticulous about dental hygiene to prevent severe dental decay. They should avoid excessive air-conditioning and consider using a room air-humidifier. Patients also need advice on dietary modifications, with use of noncaloric sugar replacements, avoidance of highly acidic foods

and beverages, regular and frequent consumption of fluoridated water, home use of specific high-dose topical fluoride dentifrices and mouthwashes, and maintenance of adequate hydration.

Dentist and specialist referral

Hyposalivation has a significant impact on the dentition, warranting regular check-ups by the patient's dentist and, in severe cases, assessment by a specialist in oral medicine. Three- to six-monthly dental check-ups, depending on the severity of the salivary hypofunction, are essential for monitoring dental decay, professional cleaning and provision of high-dose topical fluoride treatments. An oral medicine specialist can evaluate the cause of the xerostomia or salivary hypofunction, monitor for complications affecting the dentition, oral mucosa and salivary glands, and provide interventions such as prescription of sialagogues to stimulate saliva production.

Artificial saliva, moisturising gels

Various artificial saliva preparations are available in the form of sprays, liquids and lozenges. These products contain glycerine or carboxymethylcellulose, hydroxypropylcellulose or hydroxyethylcellulose, which approximate but do not replicate the physical and rheological characteristics of saliva. They also lack digestive and antibacterial enzymes. Artificial saliva preparations have a limited duration of action, and some are mildly acidic, potentially demineralising tooth enamel with prolonged use.

An alternative is a sodium bicarbonate rinse, which patients can easily make themselves, consisting of a tablespoon of baking soda dissolved in a litre of water. Patients need to be strongly advised to use this as a rinse only and to spit it out after use to avoid the side effects of ingestion. These include renal impairment and in large doses, metabolic alkalosis, oedema due to sodium overload, hypervolaemic hypernatraemia with hypertension and worsening of congestive heart failure.



Figure 2. Dental caries exacerbated by severe salivary hypofunction.

Prevention of dental caries

Dental caries is a significant complication of hyposalivation, caused by decreased oral irrigation and the inability to rapidly clear foods from the oral cavity (Figure 2). Caries is accelerated by sugar-containing or acidic foods. Patients with a dry mouth tend to drink soft drinks to moisturise the mouth, further increasing their risk of tooth decay because of the high sugar and acid content of these drinks. Low-sugar and diet soft drinks also carry a risk of tooth erosion because of their low pH. Sodium fluoride supplements and good oral hygiene can reduce the risk of dental caries.¹

Management of oral candidiasis

Dentures should be removed for a prolonged period (more than two hours) at least once during the day, and ideally overnight, and soaked in chlorhexidine to help prevent candidiasis. Amphotericin lozenges (requiring a prescription) and miconazole oral gels can be used to treat oral candidiasis. These medications should be used four times daily after meals and at bedtime. Miconazole gel can also be used to line dentures before the patient places them in the mouth. Nystatin, although a popular treatment for oral candidiasis, contains up to 33% sucrose and therefore is not suitable for use in dentate patients with salivary hypofunction.

If patients dislike or are unable to use miconazole or amphotericin lozenges then chlorhexidine mouthwashes (preferably alcohol-free formulations) can also be used

for prevention and treatment of *Candida* infection. Patients should rinse the mouth or gargle with the mouthwash for one minute after meals.

Hydrocortisone–clotrimazole cream is the agent of choice for angular cheilitis. Systemic azole agents such as fluconazole may be indicated for intractable oral candidiasis. However, all azole agents, both systemic and topical, are contraindicated in patients taking warfarin.

Salivary stimulants

Chewing gums, hard lollies and mints are helpful in stimulating salivation, providing patients with some relief particularly over the course of the day. These should be artificially sweetened and/or sugar-free (i.e. free of noncalorific/nonfermentable simple carbohydrate).

Secretagogue drugs

The muscarinic agonists pilocarpine and cevimeline directly increase exocrine gland secretion. These medications are relatively contraindicated in patients with closed-angle glaucoma, congestive heart failure or asthma. Patients require education about these drugs and warnings about their cholinergic side effects (flushing, headache, excessive sweating, diarrhoea and urinary frequency). These drugs should be started at lower doses and then titrated to symptoms. Pilocarpine is available on prescription in Australia but only in the topical form for the treatment of glaucoma. Cevimeline is available from overseas.

Systemic anti-inflammatory and immunosuppressive therapy

There is a role for systemic anti-inflammatory and immunosuppressive therapy in the treatment of dry mouth in Sjögren's syndrome with systemic disease. Studies have shown mixed results for hydroxychloroquine, rituximab, infliximab, cyclosporin and epratuzumab (which has shown promise in the management of Sjögren's syndrome overseas but is not TGA-approved in Australia).¹²

CONCLUSION

Dry mouth is a common and disabling problem often seen in general practice. Xerostomia, or the subjective complaint of oral dryness, needs to be differentiated from salivary hypofunction, an objectively assessed decrease in saliva production or change in saliva quality. Salivary hypofunction substantially increases the risk of dental disease and infections such as oral candidiasis, and also impairs phonation, taste perception, chewing and swallowing and reduces oral comfort.

The most common cause of salivary hypofunction is medication use. Auto-immune diseases such as Sjögren's syndrome and head and neck radiotherapy for malignancy are rare causes but can lead to profound salivary hypofunction. Once treatable causes of salivary hypofunction have been excluded then treatment is conservative, with attention to preventing the sequelae of a dry mouth. Management includes liaison with the patient's dentist and, in severe cases, referral to an oral medicine specialist. **MT**

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