

Continuing Medical Education

The persistent dry mouth

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While the full extent of individuals in the adult population with a persistent dry mouth is not accurately known, epidemiological data would suggest that it may affect at least 5% of adults. In many instances the diagnosis and attendant problems are not well recognised, or are merely accepted.

Source of saliva

Saliva is produced by the three pairs of major salivary glands, the parotids, submandibulars and sublinguals. In addition, there is a significant contribution from the many minor glands that line the oral cavity (Figure 1).

The nature of saliva from each varies, with a serous secretion from the parotids and a mucous secretion from the sublinguals and minor glands. That from the submandibular is mixed.

Saliva is a complex fluid, varying in composition from moment to moment, under the control of both cholinergic and adrenergic branches of the autonomic nervous system as well as humoral factors (Figure 2). The rationale for this fine control is not well understood.

Functions of saliva

Saliva has numerous functions and these control the environment of the mouth.

Cleansing

By virtue of its water content, saliva cleanses the dentition and mucosa, washing off debris towards the back of the mouth, where it is swallowed.

Lubrication

Mucins lubricate the hard and soft tissues, enabling them to move freely against one another.

Antimicrobials

Saliva contains several antimicrobial systems including secretory-IgA, peroxidase, lysozyme, lactoferrin, histatins and cystatins. Their role is not to sterilise the oral cavity but

collectively to generate a healthy commensal flora.

Mucosal integrity

The hydration of the mucosa is maintained by virtue of the water and mucin content. In addition, there are growth factors in saliva, such as epidermal growth factor, that may also contribute to mucosal integrity.

Buffering

Enamel begins to lose surface calcium and phosphate below pH 5.7. These conditions regularly occur with ingestion of dietary acids or in plaque where carbohydrate is metabolised. The principal buffer in saliva is bicarbonate but there is also a smaller amount of phosphate and protein buffers.

Remineralisation

If the loss of calcium and phosphate from the enamel was an irreversible process, then in a relatively short time the dentition would be seriously eroded or else destroyed by caries. Saliva is supersaturated with calcium and phosphate, with these high concentrations being achieved through binding to peptides, such as statherin and proline-rich-peptides. At neutral pH, these peptides convey the minerals to the enamel surface where they are incorporated back into the hydroxyapatite. Fluoride is also incorporated into the crystal lattice of enamel at this time, which promotes resistance to acid dissolution.

Taste

All substances require to be in solution for tasting.

Digestion

Saliva has long been known to contain amylase that will digest carbohydrates but the importance of this in general digestion is unlikely. There are also several other digestive enzymes in saliva and their role may simply be to break down retained food particles.

Aetiology of salivary hypofunction

Numerous disorders can result in salivary hypofunction, either functional or structural in aetiology.

Functional

► The sensation of a dry mouth is an experience with which many are familiar when anxious but it may be a feature of anxiety neurosis or depression (Figure 3).

➤ While a degree of xerostomia has been recognised to be a side effect of a multitude of medications, this is particularly troublesome with tricyclic antidepressants, antipsychotics, antihistamines and decongestants (Figure 4).

➤ Individuals who are dehydrated rarely present complaining primarily of a dry mouth, although this can be the case in diabetes insipidus or with excessive use of diuretics.

Structural

➤ Aplasia or hypoplasia of the salivary glands is exceedingly rare but results in degrees of dryness according to the extent of the defect.

➤ The salivary glands are sensitive to radiation and are frequently damaged consequent to radiotherapy to the head and neck region. While there is usually some resolution over the subsequent six months, the effects tend to be permanent. The discomfort due to dryness in the mouth may be compounded particularly by mucosal damage as well as loss of taste.

➤ Sjögren's syndrome is an inflammatory exocrinopathy that may co-exist with one of the connective tissue disorders including rheumatoid arthritis, SLE, progressive systemic sclerosis, dermatomyositis and polymyositis (Figures 5 and 60). The exocrine glands are affected by an inflammatory infiltrate, the most prominent being salivary and lacrimal glands (Figures 7-9). However, other exocrine glands may be involved resulting in nasal crusting and dyspareunia. Some individuals develop a lymphoma within the glands (Figure 10).

➤ Patients receiving bone marrow transplant may develop graft-versus-host disease. In the mouth, this presents as ulceration and lichen planus along with a glandular inflammatory infiltrate, to an extent similar in gross appearance to Sjögren's syndrome. Salivary gland swelling and persistent dryness occurs.

➤ Salivary glands may be affected for a limited duration by infections such as mumps, leading to temporary dryness. But individuals infected with HIV tend to develop an inflammatory infiltrate, with swelling and tenderness along with xerostomia.

Other

➤ Diabetes mellitus is a disorder that traditionally was considered to cause a persistent dry mouth due to dehydration. While there is no doubt that dryness can be a feature of hyperglycaemia, the consensus now points to the salivary hypofunction being due to autonomic neuropathy, in a similar way to the cardiovascular changes. This would be consistent with the non-inflammatory enlargement (sialosis) that occurs in some diabetics (Figure 11).

➤ Cirrhosis may likewise lead to autonomic neuropathy with a consequential dry mouth along with sialosis but the evidence is as yet less clear (Figure 12).

Problems of salivary hypofunction

➤ The commonest complaint is of a persistent dry mouth (Figures 13-15). This is regularly present throughout the day and usually necessitates taking frequent drinks. Individuals also waken during the night and therefore tend to take a glass of water with them to bed. It is appropriate to exclude those who complain only of being dry at night and first thing in the morning as they are more likely to be snoring or mouth breathing during sleep.

➤ In addition to being dry, some people experience a burning or scalded sensation, which probably reflects the surface changes in the moist lubricating layer of mucin. A drink of water only provides temporary relief. Hot or pungent foods cause discomfort and even standard toothpastes sting. There are other non-salivary causes of a burning mouth that should be excluded in these patients including lichen planus, nutritional deficiencies, allergies, infections, and neurological and psychological disturbances.

➤ During speech, there is effectively mouth breathing. This further aggravates the existing dryness, hindering movement of the oral soft tissues. This necessitates the need for frequent sips of water, which can be particularly inconvenient in many occupations.

➤ With the alteration in salivary composition and quantity, plaque accumulates more readily on the teeth. This initiates an inflammatory reaction in the gums, resulting in gingivitis and periodontal disease. In the longer term there can be gingival recession and eventually tooth loss.

➤ Similarly, dental caries has an increased incidence. In any adult who presents with a significant rise in caries experience it is improbable that their diet has changed markedly or oral hygiene practices have altered. It is far more likely that there is a change in saliva, even in the absence of feeling their mouth to be dry.

➤ With a change in the oral microbial flora, candidiasis is found more commonly. There is frequently denture stomatitis, with the palatal mucosa becoming inflamed or even hyperplastic due to the irritant substances released by candida colonising the fitting surface of dentures. Old or ill-fitting dentures contribute to this.

➤ Dentures normally sit on a thin film of mucin above the mucosa. This enables there to be minor movement during function. In the absence of sufficient lubrication, both complete and partial dentures tend to place undue stress on the underlying mucosa regardless of their mechanical adequacy. Some individuals abandon their dentures or wear them only for 'social occasions'.

► Ascending bacterial infections, up the excretory ducts, are more common in xerostomia. Sialadenitis presents as painful swelling over a parotid or submandibular gland. Thick mucoid material or even pus can be expressed from the duct orifice and, rarely, an abscess may drain through the overlying skin.

► The symptoms of persistent salivary hypofunction might be viewed as being analogous to chronic pain. Discomfort is present all or most of the time and it interferes with their life on a daily basis.

Investigations

The detailed investigation of salivary hypofunction is outwith the scope of this article and it should be appreciated that a number of the procedures do have limited value.

While a careful history is not properly an investigation, most specialists place much weight on the patient's symptoms. Regardless of whether or not the mouth looks dry, the sensation and complaints from an individual are important and might over-ride laboratory results. Another relevant factor is that a number of the investigative procedures have been developed and analysed statistically under research circumstances, using patients who have clearly been diagnosed. In clinical practice, this is not always as straightforward.

Examination of the mouth may reveal no obvious clinical change, with the mucosa appearing moist and healthy despite the patient's complaints (Figure 13). The first visible change in saliva texture is frothiness, with the normally transparent, watery saliva assuming a frothy or a white and frothy appearance (Figure 14). Less commonly the mucosa is patently dry and thick (Figure 15); tenacious mucus may be evident on the posterior pharyngeal wall (Figure 8).

Serology is useful in screening for diabetes mellitus (fasting glucose; glycated haemoglobin), Sjögren's syndrome (ESR; CRP; ANA; ENA; Rheumatoid Factor), HIV infection and sarcoid (ESR; Serum ACE). Further tests may be indicated depending upon the initial results.

For decades, great emphasis has been placed on salivary flow rates, using resting or stimulated flows; whole or mixed saliva. Commercial adaptations have been marketed. While these findings are widely published in research papers, there are limitations in their usefulness in routine practice. Values fluctuate for any one individual but more importantly there are not clear dividing lines between health and disease in many instances. What is a putative low value may be consistent with an absence of any disease. Some centres use flow rates to monitor progress in an individual patient.

In addition to salivary volume, there may be compositional changes that lead to symptoms. However, as yet these have not been adopted in routine practice.

Biopsy of the salivary glands can contribute to the diagnosis of Sjögren's syndrome or sarcoid. Usually, several small lobules of minor salivary glands are excised from under the

mucosa inside the lower lip, and the appropriate histology sought (Figure 6).

Straight radiographs are of no value in diagnosing salivary hypofunction - radio-opaque calculi do not cause dryness of the mouth. In sialography, a radio-opaque liquid is infused up to the gland duct from its orifice in the mouth. Radiographs outline the entire ductal system and punctate globules (sialectasis) may be evident as well as ductal strictures and dilatations.

Several tissues in the body accumulate iodide in addition to the thyroid but do not organify it to produce thyroxine. The ducts within the salivary glands accumulate iodide and use of this property is made to assess a parameter of gland function. For scintiscanning, another ion is used (Tc^{99m} -pertechnetate) as it is not retained in the thyroid and causes much less radiation to the patient than do isotopes of iodine but is similarly accumulated in tissues.

Management

An energetic and co-ordinated approach to salivary hypofunction has much to offer for quality of life. Unfortunately this is often overlooked when some more pressing systemic problem is being addressed. Some patients are elderly or infirm due to associated disease and require further support in this area.

The obvious substitute for inadequate saliva is water and xerostomic patients do tend to drink more. Some find that sparkling mineral water affords greater relief. However, there have been many attempts to find saliva substitutes. Glycerine and lemon has long been tried but glycerine is hygroscopic and can result in a feeling of dryness. Most preparations have been based on a slightly viscous solution of carboxymethylcellulose to which have been added buffers, calcium and fluoride. Alternatively, a solution is marketed based on animal mucin; a point to consider with some religious groups or vegetarians. While all of these substitutes offer some immediate relief, so too does water, and a number of centres have largely abandoned using them. A central problem is fluid delivery. Normally saliva is being secreted into the mouth continuously albeit at variable flow rates. To attempt to duplicate this requires frequent applications of whatever substitute is being tried.

For extreme cases of dryness, an oil and water emulsion has been developed as a moisturiser but no commercial preparation is currently available.

In the presence of a residual degree of salivary gland function, it is usually possible to stimulate salivation either with a flavoursome agent in the mouth (a gustatory sialogogue) or pharmacologically (a pharmacological sialogogue). Often individuals have resorted to sucking candles or mints but this will deliver sugar to the teeth for prolonged periods and in already compromised mouths caries will be promoted. An alternative is to recommend the several different sorbitol- or xylitol-containing candies. These are marketed not only for diabetics but also increasingly for people who wish to avoid sucrose. Care must be exercised with taking an excess to avoid osmotic diarrhoea. There is some evidence to suggest that xylitol-containing products actually further suppress the caries process.

Another ideal form of gustatory sialogogue is chewing gum and the sugar-free varieties are especially to be preferred. The action of chewing accompanied by prolonged release of flavour conveniently promotes salivation over significant periods. Chewing sugar-free gums after meals is now a recognised component of a good oral care regimen and may also reduce snacking frequency. For individuals with either complete or partial dentures, there is commercially available a low tack chewing gum (Freudent - Wrigley's) that does not stick to their appliances. Should the standard peppermint or spearmint flavours cause discomfort, the milder fruit flavours may be more acceptable. Recently, a chewing gum has been introduced that contains a casein-derived peptide (Recaldent - Trident) delivering high concentrations of calcium and phosphate with the aim of facilitating remineralisation of the enamel surface. However, this is only available through dental or medical professionals and is more expensive than the more widely available sugar-free chewing gums.

A similar calcium phosphoprotein (Topacal-C5, NuLite) is available as a paste that can be applied by the patients. Regular use of this thrice daily is a further way of protecting the dentition

Several cholinergic drugs have been evaluated to act as pharmacological sialogogues but pilocarpine has remained in use for over 100 years. This is a muscarinic agonist showing some selectivity to secretory acini. A commercial tablet of pilocarpine is unavailable in New Zealand and it has been necessary to develop an alternative preparation. This can be achieved by the pharmacist diluting standard pilocarpine eye drops with water and adding benzoate preservative. The details of this pilocarpine solution are in the Pharmac schedule.

Pilocarpine is an invaluable systemic medication for promoting salivation in cases of salivary hypofunction. (It also relieves dry eyes and nasal crusting). It has had a variable reception by some groups although it is widely prescribed in centres throughout the world. Before dismissing pilocarpine as either not efficacious or else causing undue side effects, it must be clearly appreciated that there is a substantial variation in response between individuals. The reason for this is not understood. While one person finds a dose of 2.5 mg taken four times daily produces an increase in moisture, another may require 10 mg each time. Too high a dose for any one individual leads to sweating, nausea and loose bowels. Other less common side effects are bladder urgency and vivid dreaming. Pilocarpine should be used with caution in asthmatics and stopped if wheezing worsens. However, this has not been a common problem and many asthmatics are able to tolerate pilocarpine.

The pilocarpine solution is initially made up as 0.5 mg/1 mL, prescribing 500 mL and labelled to take 5 mL four times daily po. At weekly intervals, the amount can be increased until a beneficial level is established but not one causing side effects. In the long term it has been convenient to use an appropriate dilution as 5 mL is easily measured by patients and small errors in volume tend to be insignificant. Occasionally the last dose of the evening leads to sweating on climbing into a warm bed and for these patients the volume at that time is halved. Pilocarpine does not have a long half-life and some individuals waken in the middle of the night feeling dry. They often benefit from an additional dose taken then.

Recently a new cholinergic drug (Cevimeline) has been released in USA and Japan. It is said to have greater specificity towards the salivary gland muscarinic receptors as well as longer duration of action. However, it is unavailable in New Zealand.

An adequate diet should be palatable, edible, nutritious and non-harmful. As stated above, inadequate saliva makes mastication and, even more so, swallowing difficult. A move towards a more balanced diet can be achieved by not only encouraging drinks with meals but also with the judicious use of vegetable oils and gravy. The flat fish are easier to handle than the thicker more fibrous varieties.

As with sucking candies, there is a greater tendency to consume fruit juices and soft drinks at frequent intervals throughout the day. The former have a connotation of being 'healthy' and in New Zealand are usually labelled as having 'No added sugar'. Perhaps there is no need to add more sugar as the juice is already full of fruit sugar! Fruit juices and soft drinks are pleasant liquids that are both sweet and sour. Their sugar content will promote dental caries and the acid content can result in erosion of the enamel surface - particularly when taken in high quantity by compromised patients (Figure 16). The 'diet' soft drinks are preferred, as they do not contain sugar although the pH remains low. (A pH below 5.7 results in loss of calcium and phosphate from enamel hydroxyapatite and many juices and drinks have pH levels below 4.0). Water or sparkling mineral water is an excellent alternative. Low-fat milk, like cheese, has the benefit of containing the calcium and phosphate casein described above. Edam-style cheese is one of the lower fat content cheeses. Avoidance of excessive caffeine or alcohol are sensible measures to avoid dehydration.

Good oral hygiene is critical, with regular tooth brushing: at least twice a day. Standard soft bristle tooth-brushes are advised along with a fluoride containing toothpaste. For individuals with any compromised dexterity it is possible to obtain sponge sleeves to fit over brush handles to facilitate a grip or else an electric toothbrush. Sometimes the flavour of a toothpaste causes stinging and the selection of one of the children's milder toothpastes may help. For the compromised dentition, it is often decided to advocate the use of very high fluoride content toothpaste (NeutralFluor - Colgate). This is not yet available commercially in New Zealand but medical and dental practitioners are allowed to buy it through Colgate for use by their parents. This is an alternative to adding a separate topical fluoride to what may already be a long list of medications.

Other oral hygiene measures are equally important and regular attendance at their dental surgeon and hygienist should be strongly encouraged. Dentures, either partial or complete, tend to be poorly tolerated and candidiasis of the underlying mucosa also becomes common. Dentures should be removed overnight and stored in a cleanser. Instead of mucosal borne dentures, it is often possible to support a denture on titanium implants fixed into the bone (Figure 17).

Finally, it will be appreciated that an active programme incorporating all of the above measures, as are appropriate, constitutes support for chronic discomfort or pain in addition to the physical benefits.