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ORIGINAL ARTICLE

Investigating the relationship between hyposalivation and mucosal wetness

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BACKGROUND: Mucosal wetness (MW) reflects the layer of residual saliva that covers the oral mucosal surfaces.

OBJECTIVES: The aim of this study was to determine MW at different oral mucosa sites and to investigate the relationship between MW, unstimulated whole salivary flow rates (UWS) and Clinical Oral Dryness Score (CODS).

METHOD: A total of 100 dry mouth patients and 50 healthy subjects participated in the study. MW was sampled with filter paper strips at four sites inside the mouth; anterior hard palate (AHP), buccal mucosa (BUC), anterior tongue (AT), lower lip (LL) and measured with a micro-moisture meter. Reproducibility was assessed by repeated sampling and diurnal variation was examined.

RESULTS: Mucosal wetness in healthy subjects differed according to site and means ± SD were; AHP (11 ± 11.7 μm), BUC (32 ± 14.8 μm), AT (65 ± 17.2 μm), and LL (25 ± 13.5 μm). Dry mouth patients with reduced UWS showed increased CODS. MW at all four sites was significantly reduced ($P < 0.05$) in dry mouth patients compared with the healthy subjects. Reproducibility of MW measurement using the intra-class correlation coefficient showed agreement at different visits within subject. MW of the AT showed a positive correlation with UWS ($P < 0.05$).

CONCLUSION: Mucosal wetness is a reliable measure of oral dryness and had a positive correlation with UWS.
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Keywords: xerostomia; mucosal wetness; salivary secretion

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Introduction

Dry mouth is most commonly caused by alterations in salivary gland function, dehydration, and cognitive alteration. Anxiety or depression and stress can be a cause of both subjective (xerostomia) (Fox *et al*, 1985) and objective (hyposalivation) feelings of dry mouth (Bergdahl and Bergdahl, 2000). It is known that drugs are the most common cause of the dry mouth condition and complaints of xerostomia are a frequent side effect of many drugs (reviewed by Scully, 2003). Hyposalivation is especially known in those drugs used to treat anxiety, depression, and stress but is usually reversible. Salivary gland diseases associated with hyposalivation include primary or secondary Sjögren's syndrome, (Sjögren, 1933; Navazesh *et al*, 1996; Price and Venables, 2002; Kassan and Moutsopoulos, 2004; Atkinson *et al*, 2005), and Sialadenitis, Nodal Osteoarthritis, Xerostomia syndrome (SNOX; Kassimos *et al*, 1995). Sjögren's syndrome affects approximately 0.4% of the population and has a male:female ratio of 1:10 (Fox, 2005). Other conditions and systemic diseases where dry mouth could be a relevant complaint include diabetes, thyroid disorders, connective tissue diseases and graft *vs* host disease (Atkinson and Wu, 1994; Scully, 2003). The prevalence of xerostomia in the general population ranges from 10% to 20% in different published studies (Fox *et al*, 1985; Pujol *et al*, 1998). Prevalence is greater in females and increases with increased medication (Nederfors *et al*, 1997; Schein *et al*, 1999). In the elderly (60 + years) population prevalence is approximately 20% (Ben-Aryeh *et al*, 1985; Nederfors *et al*, 1997; Nayak *et al*, 2004).

As with most symptoms, it has been difficult to quantify dry mouth complaints precisely and reproducibly. To assess oral dryness, investigators have used a variety of methods including questionnaires, visual analogue-scales (VAS), simple functional measures such as observing if a tongue blade adheres to the buccal mucosa or if a patient can chew and swallow dried biscuits without water (Fox, 2005). Dry mouth can also be assessed by measuring the volume of residual saliva on mucosal surfaces using filter paper

and micro-moisture meter and calculating thickness (Disabato-Mordarski and Kleinberg, 1996; Won *et al*, 2001; Lee *et al*, 2002; and Eliasson *et al*, 2005) and more recently mucosal wetness (MW) devices have been used (Kakinoki *et al*, 2004; Takahashi *et al*, 2005).

Collins and Dawes (1987) calculated the average surface area of the mouth to be 214.7 cm^2 and calculated the thickness of the salivary film in the mouth to be 44 μm, by dividing the mean residual saliva in the mouth by surface area. The thickness of the salivary film is governed in part by the rheological properties of saliva. It is apparent that the thickness and composition of the salivary film will vary in different parts of the mouth depending upon the position in relation to salivary glands.

The aims of this study were to determine the normal variation of MW at different oral mucosa sites and secondly to determine the relationship between MW, unstimulated whole mouth saliva (UWS) flow rate, Clinical Oral Dryness Score (CODS).

Materials and methods

Study subjects

Samples were collected from a total of 100 patients with a mean age of 62 ± 11 years (range 22–82 years) attending Oral Medicine clinics at Guy's Hospital. They all complained of dry mouth and were divided into five groups according to their diagnosis: primary and secondary Sjögren's syndrome (SS1 & SS2); Drug induced Hyposalivation; non-Sjögren's but presence of sialadenitis, nodular osteoarthritis, SNOX; none of the above.

Fifty healthy age-matched subjects who did not complain of dry mouth were selected as controls and had a mean age of 60 ± 15 years (range 22–83). They were recruited from members of staff and from a residential home for the elderly. All patients and participants were given an explanation and information sheet of the study and all gave their informed consent prior to the procedure. The study was performed under ethical approval of Guy's & St Thomas' Hospitals (Local) Research Committee. Ten healthy volunteers with a mean age ± SD of 35 ± 9.5 years (n = 10) from the 50 controls were used to validate the reproducibility of MW measurements.

Assessment of patients and collection of samples Clinical Oral Dryness Score. The signs of dryness in the mouth were examined using a scoring system (CODS) which is composed of ten features: 1) Mirror sticks to buccal mucosa, 2) Mirror sticks to tongue, 3) Saliva frothy, 4) No saliva pooling in floor of mouth, 5) Tongue shows loss of papillae, 6) Altered gingival architecture/smooth (especially anterior), 7) Glassy appearance to oral mucosa (especially palate), 8) Tongue lobulated/deeply fissured, 9) Cervical caries (more than two teeth), 10) Mucosal debris on palate (excluding under dentures). This technique was validated and the data presented elsewhere (Challacombe *et al*, 2008).

Unstimulated whole mouth saliva flow. Unstimulated whole mouth saliva was collected for 10 min and the subject was asked to spit into a preweighed vessel and not to swallow any saliva. UWS flow rate was calculated and expressed ml min^{-1}, taking 1 g saliva = 1 ml.

Mucosal wetness (MW) measurements. The thickness of residual saliva (oral MW) was measured in dry mouth patients (n = 100) and aged-matched healthy subjects (n = 50) using a filter paper strip (Oraflow Inc, Smithtown, USA) and micro-moisture meter (Periotron® 8000; Oraflow Inc, USA). A filter paper strip with a diameter 7.5 mm covering an area of 44 mm^2 was placed immediately on the mucosa after swallowing and was gently pressed flat with a finger of a gloved hand. After 10 s the paper strip was transferred to the sensors of the micro-moisture meter. Four mucosal sites were measured: anterior hard palate (AHP), buccal (BUC), anterior tongue (AT), and lower lip (LL) (Figure 1). A calibration curve previously constructed using volumes of UWS was used to calculate the volumes (μl) of residual saliva collected from mucosal surfaces and then mucosal thickness (μm) was calculated. For the validation of MW measurements, 10 volunteer subjects were assessed over 10 visits, five morning (9:00–12:00) and five afternoon

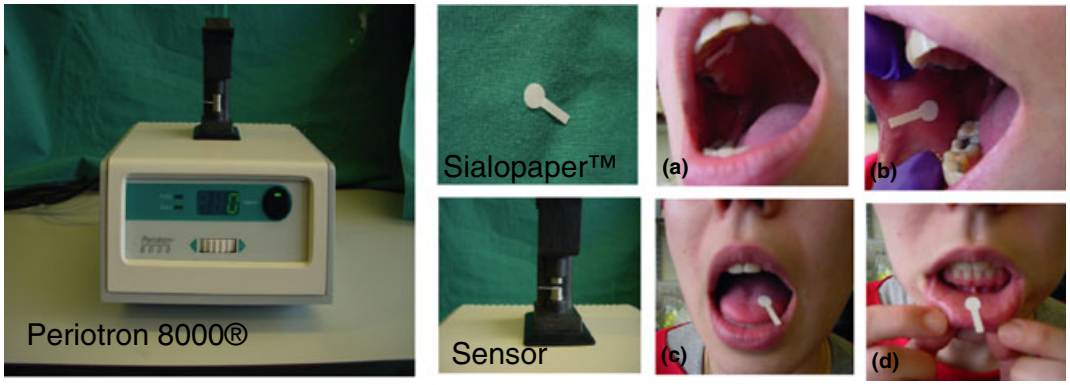

Figure 1 Periotron® 8000 micro-moisture meter, filter paper strip (Sialopaper™) and four mucosal wetness (MW) surfaces inside the mouth, (**a**) anterior hard palate (AHP), (**b**) buccal (BUC), (**c**) anterior tongue (AT), (**d**) lower lip (LL) surfaces on a healthy subjects

(02:00–05:00) visits. UWS flow rate was also measured on each occasion.

Statistics

Statistical analysis was carried out using SPSS computer software version 15.

ANOVA and intra-class correlation coefficient (ICC) were used to validate the MW measurement between and within subjects. For the purpose of analysis, dry mouth patients' data were grouped according to either diagnostic or to UWS flow rate groups. All groups were compared with age-matched controls. Correlations between MW and UWS flow rate were determined using Pearson (parametric) correlation analysis.

Results

Validation of mucosal wetness measurement

Measurement of MW using filter paper strips and the micro-moisture meter showed good reproducibility. Intra-class correlation coefficients (ICC) for MW measurements from the same subjects ($n = 10$) at different visits for AHP, BUC, AT and LL were 0.49, 0.48, 0.58, 0.53 respectively, ($P < 0.02$ for all surfaces). No significant difference was found between morning and afternoon oral MW values for AHP, BUC, AT, and LL (Figure 2) and UWS flow rate.

Mucosal wetness of dry mouth patients and controls

In dry mouth patients, the means ± SD MW of all four surfaces were significantly reduced by approximately 50% compared with age-matched controls (Figure 3) but the trend was the same. That is AHP had the thinnest and AT tongue had the thickest MW among both patients and controls (Figure 3).

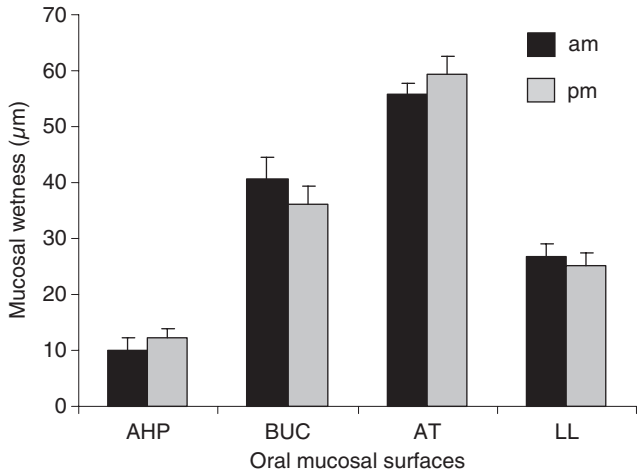

Figure 2 Mean values of mucosal wetness (MW) in μm from four oral surfaces (AHP, BUC, AT, LL) were measured from 10 subjects in the morning (am, light bars) and the afternoon (pm, dark bars) and five visits for each time point of the same subjects. It showed there are no significant ($P < 0.05$) differences in wetness of all the four surfaces between morning and afternoon. Keys: AHP, anterior hard palate; BUC, buccal; AT, anterior tongue; LL, lower lip. Error bars represent SEM

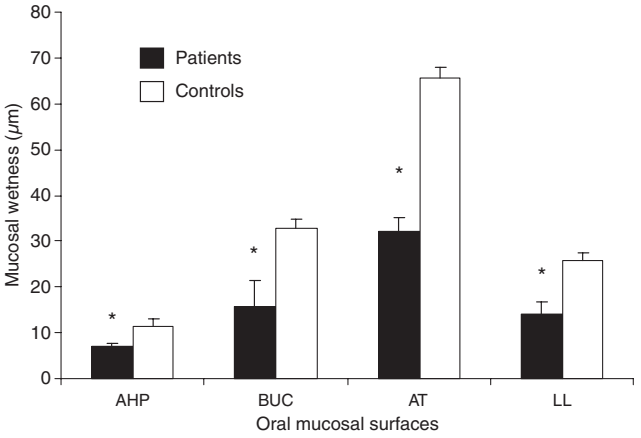

Figure 3 Mean values of mucosal wetness (MW) at four surfaces (AHP, BUC, AT, LL) from dry mouth patients ($n = 100$, dark bars) and healthy subjects as controls ($n = 50$, light bars). There is a significant ($P < 0.05$) reduction in wetness on all mucosal sites from dry mouth patients compared with controls. Keys: AHP, anterior hard palate; BUC, buccal; AT, anterior tongue; LL, lower lip. * = statistically significant ($P < 0.05$). Error bars represent SEM

Correlation between UWS flow and mucosal wetness

Overall UWS flow rate was significantly ($P < 0.05$) directly correlated with MW at all four sites. Pearson correlation coefficients for each site were $r = 0.22$ (AHP), $r = 0.18$ (BUC), $r = 0.4$ (AT), $r = 0.3$ (LL), respectively.

Subjects were grouped according to UWS flow rate as follows: three patient groups with low flow (0–0.1 ml min^{-1}, $n = 57$), moderate flow (0.1–0.2 ml min^{-1}, $n = 25$), high flow ($>$ 0.2 ml min^{-1}, $n = 18$) and a fourth group of controls (mean flow = 0.45 ml min^{-1}, range 0.2–1.0 ml min^{-1}, n = 50). The group with lowest flow ($<$ 0.1 ml min^{-1}) showed a significant ($P < 0.05$) reduction in MW at all four sites (AHP, BUC, AT and LL) compared with controls (Figure 4a). The AHP, BUC and LL mucosal surfaces showed no significant differences between the low and high UWS flow rate patient groups whilst AT showed a significant ($P < 0.05$) reduction in MW between all UWS flow rate patient groups.

In addition, when a patient group ($n = 14$) with UWS flow rate $>$ 0.2–0.3 ml min^{-1} with a mean ± SD (0.24 ± 0.01 ml min^{-1}) was compared with a similar UWS flow rate (mean = 0.26 ± 0.01 ml min^{-1}, $n = 10$) control group there was a significant ($P < 0.05$) reduction in MW at BUC and AT surfaces (Figure 4b). The AHP showed no difference in wetness while the LL showed a significant difference only by a one-tailed t-test ($P < 0.05$). The different flow rate groups of control subjects did not show any statistically significant differences in MW of different oral surfaces.

The relationship between CODS and UWS salivary flow rate

There was inverse correlation between CODS and UWS salivary flow rate of dry mouth patients and healthy subjects (aged-matched controls). Even dry mouth patients with normal UWS flow rates have a significant

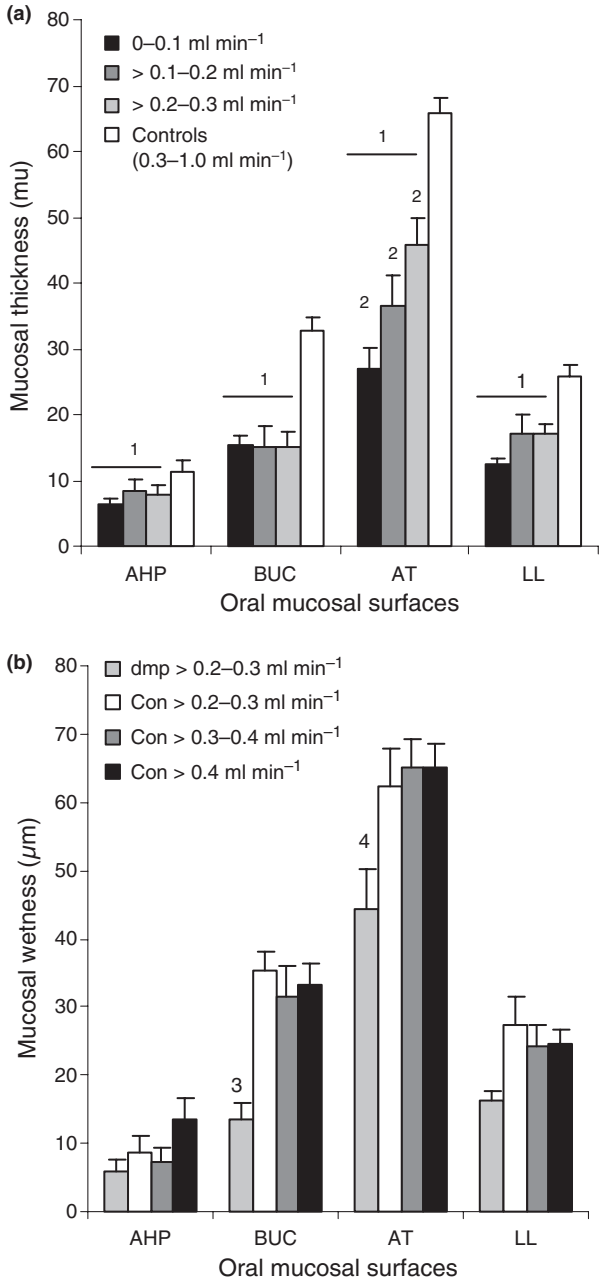

Figure 4 A relationship between mucosal wetness (MW) and unstimulated whole saliva (UWS) flow rate groups. (**a**) Shows four groups of UWS; three groups from dry mouth patients (three groups; 0–0.1, > 0.1–0.2, > 0.2–0.3 ml min^{-1}) and controls (one group > 0.2–1.0 ml min^{-1}, n = 50). All four sites; AHP, BUC, AT, LL in patients with different flow groups were significantly ($P < 0.01$) less than controls. AT shows a statistically significant ($P < 0.05$) increase in MW (μm) with increase in UWS salivary flow. (**b**) The patient group (UWS flow rate > 0.2–0.3 ml min^{-1}) with a mean of 0.24 ± 0.01 ml min^{-1} had a significant reduction in MW at BUC ($P < 0.001$), AT ($P < 0.05$) and were the same at AHP and LL compared with controls of a similar (UWS > 0.2–0.3 ml min^{-1}) flow rate with a mean of 0.26 ± 0.01 ml min^{-1}. Keys: AHP, anterior hard palate; BUC, buccal; AT, anterior tongue; LL, lower lip. [1] = statistically significant different between patients (three groups) and controls. [2] = statistically significant between the three flow rate (0–0.1, > 0.1–0.2, > 0.2–0.3 ml min^{-1}) patient groups at the AT site only. [3] = BUC is statistically significantly different between patient group > 0.2–0.3 ml min^{-1} and controls (three groups). [4] = AT is statistically significantly different between patient group > 0.2 and controls (three groups). Error bars represent SEM

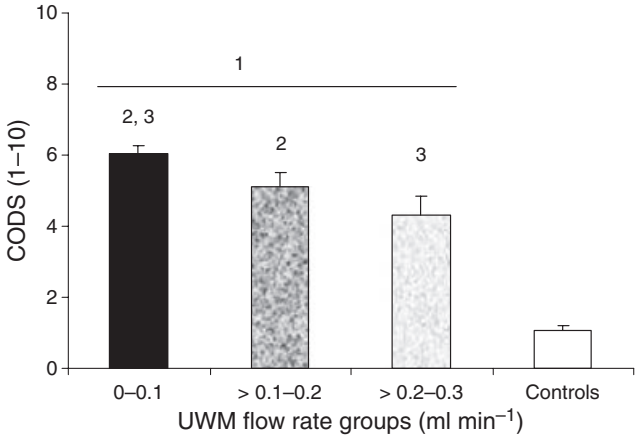

Figure 5 The relationship between Clinical Oral Dryness Score (CODS) and unstimulated whole salivary (UWS) flow rate of dry mouth patients and healthy subjects (aged matched controls). Patients in the lowest UWS flow rate group have the highest CODS. The CODS was significantly ($P < 0.01$) increased in all three patient groups compared with the controls. Keys: [1] = significantly different in all three patient groups compared with the controls. [2] = statistically significant between patient groups 0–0.1 and > 0.1–0.2 ml min^{-1}. [3] = statistically significant between 0–0.1 and > 0.2–0.3 ml min^{-1}. Error bars represent SEM

($P < 0.01$) increase in their CODS compared with the controls (Figure 5).

Discussion

The findings show that MW differs at different oral surfaces: AHP, BUC, AT and LL. MW follows the same trend in healthy subjects as well as dry mouth patients. In both groups, the wettest surface was AT, followed by BUC, LL then AHP. Our findings are similar to those in previous studies (Disabato-Mordarski and Kleinberg, 1996; Wolff and Kleinberg, 1998; Won *et al*, 2001; Lee *et al*, 2002). Previous studies have also suggested that the percentage contribution of different glandular salivas, in particular parotid saliva, to the total saliva on different oral surfaces varies (Sas and Dawes, 1997). For example, the surface vestibular to the upper right molars appears to have a 50–60% contribution from parotid saliva while the surfaces vestibular or lingual to the lower incisors have only a 5–7% contribution. These differences in composition along with differing densities of minor salivary glands in the submucosae of oral surfaces will also presumably contribute in determining the wetness of the different surfaces measured in this study.

Measurement of MW by filter paper sampling and micro-moisture meter measurement showed good reproducibility and consistency at all four sites. AT and BUC surfaces were very consistent sites while AHP showed variations between individuals. Previously it has been reported that UWS flow rates show a circadian rhythm (Dawes, 1972). However, in this study, neither MW nor UWS flow rate showed a significant difference between samples taken in the morning (9:00–12:00) or in the afternoon (02:00–05:00). This suggests that MW and

UWS flow rate can be measured during the hours of normal clinics.

In dry mouth patients, MW at four sites (AHP, BUC, AT, LL) was significantly reduced by approximately 50% compared with controls. Other studies on subjects with oral dryness have reported similar findings (Wolff and Kleinberg, 1998; Won *et al*, 2001; Lee *et al*, 2002; Eliasson *et al*, 2005). In addition, the distribution pattern of the MW on the four mucosal surfaces was the same in patients and controls. i.e., the AT had the thickest and AHP had the thinnest layers of MW which is in agreement with Lee *et al* (2002). Wolff and Kleinberg (1998) found that the posterior tongue had the thickest layer of MW. Although there appeared to be a decrease in wetness of the AHP in the dry mouth patients compared with controls there was more variation between individuals with means of 7 $\pm$ 7.2 μm and 11 $\pm$ 11.3 μm for patients and controls respectively. In this study, all of the patient groups showed a mean MW of $<$ 10 μm but the normal control group showed a mean thickness of only 11 μm. Others have shown that there was no significant difference in palatal saliva secretion between Sjögren's syndrome patients and healthy controls (Marton *et al*, 2004).

Oral dryness assessed using CODS was significantly increased in all patients complaining of dry mouth. Subjects with lower UWS flow rates showed the highest CODS values. As MW of all surfaces (AHP, AT, BUC, LL) showed a significant decrease with a reduction in UWS flow rate, it can be inferred that CODS and MW also show an inverse relationship. Thus, reduced MW is linked with increased CODS and clinical features of oral dryness. A positive correlation between MW and UWS flow rate has also been previously reported (Wolff and Kleinberg, 1998).The AT showed a different pattern to the other surfaces with a 'stepped' decrease in wetness that mirrored the decrease in UWS flow rate. An explanation for this is that the tongue is the mobile part in the mouth and its fluid coating is derived from all contributions to the whole mouth saliva volume.

Patients with higher UWS flow rates ($>$ 0.2–0.3 ml min^{-1}) still showed a significant reduction in MW of the BUC and AT surfaces compared with controls with similar UWS flow rates. Others have observed a decrease in labial MW in subjects with a subjective complaint of dry mouth (Niedermeier and Hüber, 1989; Shern *et al*, 1990; Eliasson *et al*, 1996). Therefore, measuring MW is an important investigation in the management of dry mouth patients as it is a direct measure of wetness that can discriminate between normal subjects and dry mouth patients. Our findings suggested that the reduction in MW could be an early sign of dry mouth observed before UWS flow rate is obviously reduced. However, this needs to be substantiated on larger numbers of samples. It may be that this group of patients (UWS $>$ 0.2–0.3 ml min^{-1}) had a more than 50% reduction in their baseline UWS salivary flow rate and consequently had reduced MW. It has been reported that a subject needs at least a 50% reduction in baseline resting (unstimulated) salivary flow rate before dry mouth is experienced and this may coincide with a decrease in oral MW (Dawes, 1987; Wolff and Kleinberg, 1999). It may also be that the patients with higher UWS flows but reduced MW have saliva with altered mucosal co properties as a result of changes in composition. There is evidence of reduced mucin sulphation in Sjögren's syndrome and this may impact on surface coating properties or water retention (Alliende *et al*, 2008). Changed composition could result from a relatively greater reduction in submandibular secretion which might reduce mucin levels in whole mouth saliva, although results from a previous study do not support this idea (Van den Berg *et al*, 2007). It would be interesting to examine the rheological and wetting properties and mucin content of salivas from such patients. When control subjects were divided into UWS flow rate groupings, it is evident that there was little difference in wetness of the oral surfaces with increased UWS flow rate. One might therefore suggesting that above a UWS flow rate of 0.2 ml min^{-1} there is no further significant retention of residual fluid on oral surfaces. If so, then individuals may in fact tolerate reductions in UWS flow without experiencing dryness provided that MW is maintained.

In conclusion, MW can potentially be used as an index of oral dryness. It is a reliable, simple method which can be used at the chair side to measure oral dryness. There is a positive correlation between oral MW and unstimulated salivary flow rate.

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References

Alliende C, Kwon YJ, Brito M *et al* (2008). Reduced sulfation of MUC5b is linked to xerostomia in patients with Sjögren's syndrome. *Ann Rheum Dis* **67**(10)**:** 1480–1487.

Atkinson JC, Wu AJ (1994). Salivary gland dysfunction: causes, symptoms, treatment. *J Am Dent Assoc* **125:** 409–416.

Atkinson JC, Grisius M, Massey W (2005). Salivary hypofunction and xerostomia: diagnosis and treatment. *Dent Clin North Am* **49**(2)**:** 309–326.

Ben-Aryeh H, Miron D, Berdicevsky I, Szargel R, Gutman D (1985). Xerostomia in elderly: prevalence, diagnosis, complications and treatment. *Gerodontology* **4:** 77–82.

Bergdahl M, Bergdahl J (2000). Low unstimulated flow and subjective oral dryness: association with medication, anxiety, depression and stress. *J Dent Res* **79:** 1652–1658.

Challacombe SJ, Osailan SM, Pramanik R *et al* (2008). A clinical score of oral dryness: relation to salivary flow rates *J Dent Res*. http://iadr.confex.com/iadr/2008Toronto/techprogram/abstract_106439.htm.

Collins LMC, Dawes C (1987). The surface area of the adult human mouth and thickness of salivary film covering the teeth and oral mucosa. *J Dent Res* **66**(8)**:** 1300–1302.

Dawes C (1972). Circadian rhythms in human salivary flow rate and composition. *J Physiol* **220**(3)**:** 529–545.

Dawes C (1987). Physiological factors affecting salivary flow rate, oral sugar clearance, and the sensation of dry mouth in man. *J Dent Res* **66:** 648–653.

Disabato-Mordarski T, Kleinberg I (1996). Measurement and comparison of the residual saliva on various oral mucosae and dentition surfaces in humans. *Arch Oral Biol* **41**(7)**:** 655–665.

Eliasson L, Birkhed D, Heyden G, Strömberg N (1996). Studies on human minor salivary gland secretions using the Periotron® method. *Arch Oral Biol* **41:** 1179–1182.

Eliasson L, Almståhl A, Lingström P, Wikström M, Carlén A (2005). Minor gland saliva flow rate and proteins in subjects with hyposalivation due to Sjögren's syndrome and radiation therapy. *Arch Oral Biol* **50:** 293–299.

Fox P (2005) Available at: http://www.symptomresearch.nih.gov/chapter_27/index.htm in Symptom Research (accessed 7 August 2010).

Fox PC, van der Ven PF, Sonies BC, Weiffenbach JM, Baum BJ (1985). Xerostomia: evaluation of a symptom with increasing significance. *J Am Dent Assoc* **110**(4)**:** 519–525.

Kakinoki Y, Nakamura S, Koseki T (2004). The practice of the test of saliva and the point of diagnosis. *Dent Outlook* **103:** 47–52.

Kassan SS, Moutsopoulos HM (2004). Clinical manifestations and early diagnosis of Sjögren's syndrome. *Arch Intern Med* **164:** 1275–1284.

Kassimos DG, Choy EHS, Challacombe SJ, Panayi GS (1995). The prevalence of xerostomia in a population with primary generalized osteoarthritis (PGOA). *Br J Rheumatol* **34:** 132.

Lee SK, Lee SW, Chung SC, Kim YK, Kho HS (2002). Analysis of residual saliva and minor salivary gland secretions in patients with dry mouth. *Arch Oral Biol* **47:** 637–641.

Marton K, Boros I, Fejerdy P, Madlena M (2004). Evaluation of unstimulated flow rates of whole and palatal saliva in healthy patients wearing complete denture and in patients with Sjögren's syndrome. *J Prosthet Dent* **91**(6)**:** 577–581.

Navazesh M, Brightman VJ, Pogoda JM (1996). Relation of medical status, medication, and salivary flow rates in adults of different age. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **81:** 172–176.

Nayak L, Wolff A, Fedele S *et al* (2004). The burden of xerostomia in independent community-dwelling older adults: results from the Saliwell project. *Oral Biosci Med* **1**(4)**:** 283–289.

Nederfors T, Isaksson R, Mornstad H, Dahlof C (1997). Prevalence of perceived symptoms of dry mouth in an adult Swedish population–relation to age, sex and pharmacotherapy. *Community Dent Oral Epidemiol* **25**(3)**:** 211–216.

Niedermeier W, Hüber M (1989). Quantitative studies on the secretory output of the palatine salivary glands. *Dtsch Zahnärztl Z* **44:** 37–40.

Price EJ, Venables PJW (2002). Dry eyes and mouth syndrome—a subgroup of patients presenting with sicca symptoms. *Rheumatology* **41:** 416–422.

Pujol T, Coma M, Pujol M, Postigo P (1998). Prevalence of xerostomia in the general population. *Aten Primaria* **21**(4)**:** 225–228.

Sas R, Dawes C (1997). The intra-oral distribution of unstimulated and chewing gum stimulated parotid saliva. *Arch Oral Biol* **42:** 469–474.

Schein OD, Hochberg MC, Munoz B *et al* (1999). Dry eye and dry mouth in the elderly: a population-based assessment. *Arch Intern Med* **159:** 1359–1363.

Scully C (2003). Drug effects on salivary glands: dry mouth. *Oral Dis* **9**(4)**:** 165–176.

Shern RJ, Fox PC, Cain JL, Li S-H (1990). A method for measuring the flow of saliva from the minor salivary glands. *J Dent Res* **69**(5)**:** 1146–1149.

Sjögren H (1933). Zur Kenntnis der Keratoconjunctivitis sicca (Keratitis filiformis bei Hypofunktion der Tränen-drusen). *Acta Ophthalmol* **11:** 1–151.

Takahashi F, Koji T, Morita O (2005). Oral dryness examinations: use of an oral moisture checking device and a modified cotton method. *Prosthodontic Res Pract* **5:** 26–30.

Van den Berg I, Pijpe J, Vissink A (2007). Salivary gland parameters and clinical data related to the underlying disorder in patients with persisting xerostomia. *Eur J Oral Sci* **115:** 97–102.

Wolff MS, Kleinberg I (1998). Oral mucosa wetness levels in hypo- and normosalivators. *Arch Oral Biol* **43:** 455–462.

Wolff M, Kleinberg I (1999). The effect of ammonium glycopyrrolate (Robinul®-induced xerostomia on oral mucosal wetness and flow of gingival crevicular fluid in humans. *Arch Oral Biol* **44:** 97–102.

Won SH, Kho HS, Kim YK, Chung SC, Lee SW (2001). Analysis of residual saliva and minor salivary gland secretions in patients with dry mouth. *Arch Oral Biol* **46:** 619–624.