

Departments

Clinical Brief

Mix Disease: Diagnosis and Treatment

by V. Kim Kutsch, DMD; Carri Cady, RDH

Medication-induced xerostomia (MIX disease, an acronym first introduced by Edwin Zinman) is becoming a more common problem for Americans. There are many potential causes of xerostomia, or dry mouth, and these causes include loss of saliva production as part of the natural aging process,¹ Sjögren's syndrome,² radiation to the head and neck,³ and medication-induced xerostomia.⁴ There are now about 3,000 prescription medications that list xerostomia as a possible side effect,⁵ but drug companies, by and large, have not included specific labeling to alert the consumer about xerostomia and its increased risk for dental caries.⁶ MIX disease affects people of all ages. The average person has no idea what xerostomia is, so the current drug labeling has little or no significance for them.

Causes of Xerostomia

Xerostomia or dry mouth is a condition where the patient has insufficient saliva flow to maintain oral health. Symptoms may range from irritation, inflammation, and/or recession of the soft tissues to rapid carious destruction of the hard tissues. Other signs and symptoms include candidiasis and burning mouth syndrome. This is a condition becoming more problematic as people are living longer and frequently taking multiple medications. It is not unusual in a healthy patient for saliva to naturally decrease during the aging process. Mouth breathing, particularly when sleeping because the saliva flow decreases, also will lead to dry-mouth symptoms for some patients (Figure 1 [View Figure](#)). Patients with sleep apnea and using a continuous positive airway pressure (CPAP) device may experience xerostomia. Other causes for xerostomia are post-radiation therapy that affects the major salivary glands (Figure 2 [View Figure](#)) and Sjögren's syndrome, which is an autoimmune disease that affects saliva flow (Figure 3 [View Figure](#)). However, the most common cause of xerostomia today is medication-induced (Figure 4 [View Figure](#)).

Drugs Causing MIX Disease

Many drugs list xerostomia as a potential side effect. The most common classes of xerostomic medications include antihistamines, antihypertensives, and methamphetamines, but many drugs commonly contribute to dry mouth, and the multiple-drug combinations that many patients are taking compounds the problem. This condition is prevalent in many senior patients but also is being seen in children taking antihistamines for asthma, antidepressants, and behavioral modification drugs for attention deficit disorder.⁷ It is also common for patients experiencing dry mouth conditions to suck on hard candy to stimulate saliva flow. The continuous exposure to sugar, resulting in continuous periods of acidic pH in the mouth, can have disastrous effects on the dentition of a person with inadequate saliva.

MIX Disease and Dental Caries Risk

A frequent and serious side effect of MIX disease is dental caries.^{8,9} The selection pressure in the biofilm for the acidogenic/aciduric bacteria responsible for caries is not sugar availability but rather protracted periods of low pH.^{10,11} In defense,

the body has several protective mechanisms to maintain a near-neutral pH and maintain the calcium phosphate mineral level in the teeth and to prevent the microbial shift from healthy bacteria to acidogenic/aciduric bacteria.^{12,13} The saliva, however, is the best adaptation for controlling pH as it contains a buffering system that helps to maintain a healthy range of pH in the mouth.¹⁴ For patients with xerostomia or MIX disease, the lack of saliva reduces the body's ability to buffer the acidic conditions, and selection pressure for the acidogenic/aciduric bacteria occurs, which results in dental caries.^{15,16} It is important to note that the cause of dental caries is not a lack of calcium and phosphate mineral or fluoride, but rather an inability for the dental biofilm to maintain neutral pH conditions.¹⁷

Diagnosis of MIX Disease

A good place to start in any caries risk assessment is with a simple validated caries risk assessment form. Ask the patient if they feel that they have a "dry mouth" or are taking medications known to cause xerostomia.¹⁸ (Many patients with xerostomia actually self-diagnose the condition.) Stimulated saliva flow can be measured by having the patient chew on soft wax and spit into a cup for 5 minutes. Average saliva flow should be about 1 mL of saliva created per minute. Less than 0.7 mL of saliva produced per minute is a sign of xerostomia. A review of the medications that the patient is taking will reveal the extent of MIX in the patient's condition.

Treatment Strategies

Recently, Takahashi and Nyvad¹⁹ demonstrated that even bacterial species previously considered commensal are capable of adapting to acidic conditions and becoming causative organisms in dental caries. These include *Streptococcus gordonii*, *S oralis*, *S mitis*, and *S anginosus*, which they termed low-pH, non-mutans streptococci, in addition to the Actinomyces species.¹⁹ Dental caries is now a disease not so much based on which specific bacteria are present, but rather what those bacteria are doing. Their recommendation for treatment strategies included good oral hygiene, effective dietary counseling, and then neutralizing strategies for the biofilm.¹⁹ The goal is not only to help neutralize the biofilm and select for healthy bacteria, but also not to cause the low-pH, non-mutans streptococci and Actinomyces species (commensal) to behave badly. For the patient with MIX disease, important treatment strategies might include a saliva-stimulating drug, use of possible saliva substitutes, staying hydrated, and the importance of plaque control and healthy diets, and the daily use of oral care products that neutralize the mouth and keep the pH within healthy ranges. Effective neutralizing products are available in gels, rinses, sprays, gums with combinations of fluoride, xylitol, and neutralizing and buffering agents.²⁰

Conclusion

For the patient taking medications that result in xerostomia, it is important to alleviate the immediate discomfort associated with dry mouth and also to educate them about the potential for dental caries and potential loss of their teeth. Practitioners must create individual treatment strategies based on the patient's needs and desires with the goal of creating a healthy pH balance in the mouth. It is incumbent upon the drug manufacturers to clearly label any potential for xerostomia, what that means in lay terms, and the possibility of severe dental caries with the potential for tooth loss.

Disclosure

Dr. Kutsch is the CEO and founder of CariFree/Oral BioTech, and is a stockholder in the company.

REFERENCES

1. Gonsalves WC, Wrightson AS, Henry RG. Common oral conditions in older persons. *Am Fam Physician*. 2008;78(7):845-852.
2. Margaix-Munoz M, Bagan JV, Poveda R, et al. Sjögren's syndrome of the oral cavity, review and update. *Med Oral Path Oral Cir Bucal*. March 20, 2009 (epub ahead of print).
3. Marzi S, Iaccarino G, Pasciuti K, et al. Analysis of salivary flow and dose-volume modeling of complication incidence in patients with head-and-neck cancer receiving intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys*. 2009;15: 73(4): 1252-1259.
4. Gallagher L, Naidoo P. Prescription drugs and their effects on swallowing. *Dysphagia*. December 16, 2008 (epub ahead of print).
5. Oral Biotech. Medications that may cause dry mouth. Available at: <http://www.carifree.com/media/Dry%20Mouth%20Medications.pdf>. Accessed March 2009.
6. Cassolato SF, Turnbull RS. Xerostomia: clinical aspects and treatment. *Gerodontology*. 2003;20(2):64-77.
7. Wu AC, Tantisira L, Li L, et al. Repeatability of response to asthma medications. *J Allergy Clin Immunol*. 2009;23(2): 385-390.
8. Daniels TE. Evaluation, differential diagnosis, and treatment of xerostomia. *J Rheumatol*. 2000;61(6 Suppl):6-10.
9. Marsh PD. Dental plaque as a biofilm and a microbial community-implications for health and disease. *BMC Oral Health*. 2006; 6(Suppl 1):S14.
10. Marsh PD, Bradshaw DJ, McKee AS. Effects of carbohydrate pulses and pH on population shifts within oral microbial communities in vitro. *J Dent Res*. 1989;68: 1298-1302.
11. Alice CL, Harty DWS, Jaques AJ. Stress-responsive proteins are upregulated in *Streptococcus mutans* during acid tolerance. *Microbiol*. 2004;150:1339-1351.
12. Kleinberg I. A mixed-bacteria ecological approach to understanding the role of bacteria in dental caries causation: an alternative to *Streptococcus mutans* and the specific plaque hypothesis. *Crit Rev Oral Biol Med*. 2002;13:108-125.
13. Nascimento MM, Gordan VV, Garvan CW, et al. Correlations of oral bacterial arginine and urea catabolism with caries experience. *Oral Microbial Immunol*. 2009;24(2): 85-89.
14. Wilson M. Microbial Inhabitants of Humans. *Cambridge Press Publishers*. 2005;339-352.
15. Coogan MM, Mackeown JM, Galpin JS, Fatti LP. Microbiological impression of

teeth, saliva and dietary fibre can predict caries activity. *J Dent.* 2008;36(11):892-899.

16. Mungia R, Cano SM, Johnson DA, et al. Interaction of age and specific saliva component output on caries. *Aging Clin Exp Res.* 2008;20(6): 503-508.

17. Featherstone JD. The caries balance: the basis for caries management by risk assessment. *Oral Health Prev Dent.* 2004; 2(Suppl 1):259-264.

18. Fox PC. Xerostomia: recognition and management. *Dent Assist.* 2008;77(5):44-48.

19. Takahashi N, Nyvad B. Caries ecology revisited: microbial dynamics and the caries process. *Caries Res.* 2008;42(6):409-418.

20. Internal data on file. Available at: www.carifree.com. Accessed April 20, 2009.



Figure 1 Gingival recession and inflammation associated with chronic mouth breathing



Figure 2 Xerostomia resulting from head/neck radiation treatment.



Figure 3 Xerostomia resulting from Sjögren's syndrome with rampant dental caries.



Figure 4 Typical appearance of medication-induced xerostomia (MIX disease) with dental caries.

About the Authors



V. Kim Kutsch, DMD
Private Practice
Albany, Oregon

Carri Cady, RDH
Private Practice
Albany, Oregon

[Print article](#)