Xerostomia Update:
This course is anything but dry!

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Our Clinician:

Dr. Mark Donaldson BSP, RPH, PHARMD, FASHP, FACHE received his baccalaureate degree from the University of British Columbia and his Doctorate in Clinical Pharmacy from the University of Washington. He completed a residency at Vancouver General Hospital, and has practiced as a clinical pharmacy specialist, clinical coordinator and director of pharmacy services at many healthcare organizations in both Canada and the United States. He is currently the Associate Principal of Clinical Pharmacy Performance Services for Vizient, in Whitefish, Montana.

Dr. Donaldson is a Clinical Professor in the Department of Pharmacy at the University of Montana in Missoula, and Clinical Associate Professor in the School of Dentistry at the Oregon Health & Sciences University in Portland, Oregon. He has a special interest in dental pharmacology and has lectured internationally to both dental and medical practitioners. He has spent the last 22 years focusing on dental pharmacology and dental therapeutics, and is a leader in the field.

Dr. Donaldson has published numerous peer-reviewed works and textbook chapters. He currently serves on the Editorial Board for the Journal Healthcare Executive and the Journal of the American Dental Association, and is a reviewer for over ten other different journals. He is board certified in healthcare management and is the Past-President and current Regent of the American College of Healthcare Executives' Montana Chapter. Dr. Donaldson was named as the 2014 recipient of the Bowl of Hygeia for the state of Montana and is the 2016 recipient of the Dr. Thaddeus V. Weclew Award. This award is conferred by the Academy of General Dentistry upon an individual who has made outstanding contributions to the medical, dental and pharmacy literature. In 2019, Dr. Donaldson was conferred by the Canadian Dental Association (CDA) in Ottawa with the, "Special Friend of Canadian Dentistry Award." This award is given to an individual outside of the dental profession in appreciation for exemplary support or service to Canadian dentistry and/or to the profession as a whole.

Xerostomia Update: This course is anything but dry!

The presence of saliva usually is taken for granted, and it is not required for any life-sustaining functions. Nevertheless, its diminution or absence can cause significant morbidity and a reduction in a patient's perceptions of quality of life. The primary constituents of saliva are water, proteins and electrolytes. These components enhance taste, speech and swallowing and facilitate irrigation, lubrication and protection of the mucous membranes in the upper digestive tract. Additional physiological functions of saliva provide antimicrobial and buffering activities that protect the teeth from dental caries.

Xerostomia is defined as a subjective complaint of dry mouth that may result from a decrease in the production of saliva. Xerostomia is not a disease, but it may be a symptom of various medical conditions, a side effect of a radiation to the head and neck, or a side effect of a wide variety of medications. It may or may not be associated with decreased salivary gland function. Xerostomia is estimated to affect millions of people in the United States and is a common complaint found often among older adults, affecting approximately 20 percent of the elderly. However, xerostomia does not appear to be related to age itself as much as to the potential for elderly to be taking medications that cause xerostomia as a side effect. Studies have found the condition in 17 to 29 percent of sampled populations based on self-reports or measurements of salivary flow rates. Complaints of dry mouth generally are more prevalent in women.

Case Example 1

- 67 y.o. male
- Complaint of "dry mouth" and ill-fitting dentures
- PMHx: Myocardial infarction, depression

Medications:

- Amitriptyline 50mg po qhs
- HCTZ 50mg po qd
- ASA 81mg po qd
- Ramipril 15mg po qd

Case Example 2

- 58 y.o. female
- PMHx: Allergic rhinitis, NKDA
- Medications: OTC Antihistamines

Two-month history of fatigue and general trouble sleeping at night, stating that she wakes up often with a dry mouth and throat. Also states her eyes have been dry, tired and red lately, but she attributes this to her poor sleep patterns. Currently consuming up to seven pints a day of liquids (coffee, tea, water, juice, milk, soda, etc.), and is very distressed by her severe dry mouth.

Questions to Ask:

- Do you need to moisten your mouth frequently or sip liquids often?
- Does your mouth feel dry at mealtime?
- Do you have less saliva than you used to?
- Do you have trouble swallowing?
- Is it difficult to eat dry foods such as crackers or toast?
- Do you suffer from any chronic illness, such as diabetes or hypertension?
- What prescription, OTC medications, dietary supplements are you currently taking?
- How often do you brush your teeth?
- Have you noticed any sores in your mouth or on your lips?
- How much water do you drink throughout the day?

Other Notes or Questions to Ask:

What Xerostomia is . . .

Xerostomia is not a disease it is a symptom. It is defined as dry mouth resulting from reduced or absent saliva flow, but may or may not be associated with decreased salivary gland function. It is not related to age itself as much as the potential for the elderly to be exposed to medications that cause xerostomia as a side effect. Studies have found the condition in 17 to 29 percent of sampled populations based on self-reports or measurements of salivary flow rates.

Definition of Xerostomia

"Xero" = Dry & "Stomia" = Mouth

Xerostomia can be defined as the subjective sensation of oral dryness that may or may not be associated with a reduction in salivary output. It can have profound negative effects on the quality of life

- Subjective complaint of patient.
- Diagnosis based on patient complaint and history.
- Salivary flow can be measured but no normal limits have been established.

Xerostomia: Prevalence

- The reported prevalence of dry mouth varies widely due to the methodological and population differences in various studies.
- Prevalence has been estimated to range from 10% to 38%, with 20% the most commonly reported figure.
- Xerostomia is becoming increasingly common in developed countries where adults are living longer and poly-pharmacy is very common

Gen Dent. 2007;55(4):288-296.
Wed Dent J Suppl 116: 1-70, 1996

What Xerostomia is not. . .

Xerostomia is not hyposalivation. Hyposalivation is a decreased flow of saliva. It may be associated with dehydration, radiation therapy of the salivary gland regions, anxiety, the use of drugs such as atropine and antihistamines, vitamin deficiency, various forms of parotitis, and various syndromes (Sjögren's, Riley-Day, Plummer-Vinson, and Heerfordt's disease). Xerostomia is not a disease it is a symptom.

So what is it about saliva?

A Short Review of Saliva

Production of saliva is by saliva-secreting, oral glandular tissue which begins development at 6 weeks gestation and is completed by about the 12th week of life. The glandular tissue continues to enlarge until birth.

Salivary glands can be classified by major and minor glands. The major salivary glands are the Parotids, found behind the angle of the jaw, below and in front of the ears and; the Submandibular & Sublingual glands found deep in the floor of the mouth.

Xerostomia: Prevalence

Xerostomia affects 25% of the population and is becoming one of the fastest-growing oral health problems in North America:

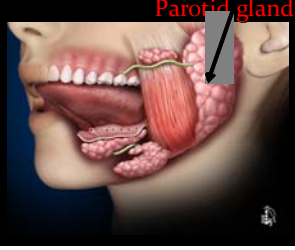
- Medications are the cause of more than 90% of xerostomia cases.
- 32 million Americans today take three or more medications daily.
- Xerostomia was not a great problem in the past because people did not take as many medications as they do today.

Gen Dent. 2007;55(4):288-296.
AGD Impact. 2008;June(Special Report):26-30.

Other Notes or Questions to Ask:

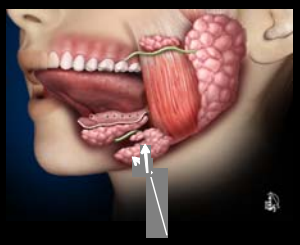
Salivary Gland Classifications
The Major Glands

- **Parotid gland**
  - Largest of the 3 major glands
  - Produces 30% of total saliva output
    - Parotid duct is also known as Stenson's duct
    - Parotid/Stenson's duct exits opposing the maxillary second molar
  - Located anterior but inferior to the external auditory meatus
  - Innervated by sympathetic and parasympathetic divisions
  - Secretes serous type saliva



Salivary Gland Classifications
The Major Glands

- **Submandibular gland**
  - Second largest gland
  - Produces 65-70% of total saliva output
    - The duct is called Wharton's duct which exits on the floor of the mouth opposing the lingual surface of the tongue
  - Innervated by parasympathetic nerve endings and possesses NO sympathetic receptors
  - The parasympathetic fibers arrive through the facial and glossopharyngeal nerves
  - Mixed secretion – mostly serous

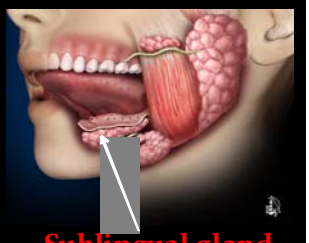


There are Hundreds (600-1000) of other minor salivary glands. The minor salivary glands are found on the lips, buccal mucosa, alveolar mucosa, tongue, and the floor of the mouth. Together, they play a large role
in salivary production.

The major glands secrete saliva intermittently while the minor glands secrete saliva continuously.

Salivary Gland Classifications
The Major Glands

- **Sublingual glands**
  - Smallest of the major glands.
  - Produce less than 5% of total saliva output
    - Saliva delivered via the ducts of Bartholin
  - Innervated by parasympathetic fibers
  - Little or no sympathetic influence
  - Mixed secretion – mostly mucous



Salivary Flow

- **Unstimulated Flow (resting salivary flow? no external stimulus)**
  - Typically 0.2 mL – 0.3 mL per minute
  - Less than 0.1 mL per minute means the person has hyposalivation
- Hyposalivation – not producing enough saliva
- **Stimulated Flow (response to a stimulus, usually taste, chewing, or medication [e.g., at mealtime])**
  - Typically 1.5 mL – 2 mL per minute
  - Less than 0.7 mL per minute is considered hyposalivation

In the UNSTIMULATED state the relative contribution of the major salivary glands is:
1) Submandibular gland=69%
2) Parotid gland=26%
3) Sublingual gland=5%

In the STIMULATED state the relative contribution of the major salivary glands is:
1) Parotid gland=69%
2) Submandibular gland=26%
3) Sublingual gland=5%

Other Notes or Questions to Ask:

Salivary Composition

- 90% of saliva is water.
- 10% is composed of inorganic and organic ions, and cellular components"
  - sodium, potassium, and calcium are positive ions (cations).
  - chloride, bicarbonate, and phosphates are negative ions (anions).
- The cationic and anionic components play an important role in the function of saliva.

Although the sublingual glands and minor salivary glands contribute only about 10% of all saliva, together they produce the majority of mucous and are critical in maintaining the mucin layer over the oral mucosa.

Ptyalism (drooling) may be secondary to salivary hypersecretion caused by either excessive salivary flow, or a salivary flow rate which surpasses the ability to swallow the saliva. Possible surgical treatments for Ptyalism are tympanic neurectomies (eliminating parasympathetic innervation to the Parotid gland) or Parotid duct rerouting. 80-90% of salivary gland stones occur in the Submandibular gland, and of those, 85% occur in Wharton's duct.

As saliva passes through the salivary ducts, cations (sodium and chloride) are reabsorbed into the adjacent blood vessels. In exchange, bicarbonates and potassium are transferred from the blood vessels into the salivary ducts. With stimulated salivary flow saliva passes through the salivary duct very rapidly (a negative result of fast flow). It impedes the exchange of sodium and chloride for potassium and bicarbonate. With unstimulated salivary flow, the saliva has a high content of potassium and bicarbonate (a positive result of slow flow). The quality of unstimulated saliva will change when flow increases because of a stimulus (chewing gum, thinking about lemons, looking at a food you crave).

Salivary glands can also be classified by their type of secretion:

- Serous: very thin and watery (parotid gland and lingual glands of von Ebner).
- Mucous: very thick and viscous (palatine glands posterior lingual glands labial buccal glands).
- Mixed secretions: mixture of the two (Sublingual glands are mostly mucous with some serous while submandibular glands are mostly serous with some mucous and the anterior lingual glands are a mixed secretion still).

Saliva

- The average volume of saliva secreted in a 24 hour period is 1-1.5 liters (approximately 1 mL/minute), most of which is secreted during meals.
- Basal salivary flow rate = 0.001-0.2 mL/minute/gland.
- With stimulation, salivary flow rate increases to 0.18-1.7 ml/min/gland.
- Salivary flow rate from the minor salivary glands is independent of stimulation, constituting 7-8% of total salivary output.
- Flow rates can fluctuate by as much as 50 percent with diurnal rhythms.

The Innervation of Salivary Glands

Both the parasympathetic and sympathetic nervous systems innervate the salivary glands. Parasympathetic stimulation induces more watery secretions, whereas the sympathetic system produces a sparser and more viscous flow. Therefore, a sensation of dryness may occur, for example, during episodes of acute anxiety or stress, which cause changes in salivary composition owing to predominant sympathetic stimulation during such periods.

The parasympathetic nervous system is the primary instigator of salivary secretion. Interruption of parasympathetic innervation to the salivary glands results in atrophy, while interruption of sympathetic innervation results in no significant change in the glands. It was once thought that the sympathetic nervous system antagonizes the parasympathetic nervous system with respect to salivary output, but this is now known not to be true.

Other Notes or Questions to Ask:

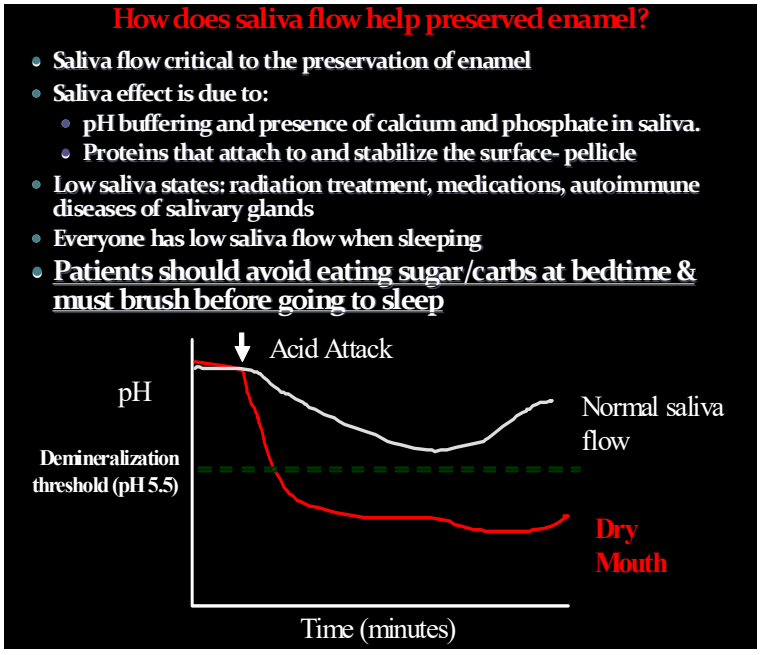
The parasympathetic fibers leave the brain via 3 cranial nerves:

1. Facial (VII) - enter the sublingual and submandibular glands and the minor salivary glands of the mucous membrane of the mouth, pharynx and nasopharynx.
2. Glossopharyngeal (IX) - converge into the parotid gland.
3. Vagus (X).

Parasympathetic cholinergic nerve fibers induce the formation of large amounts of low-protein, serous saliva and as stated above, parasympathetic denervation of the major salivary glands leads to an immediate reduction of salivary secretion. Stimulation by the parasympathetic nervous system results in an abundant, watery saliva with a decrease in amylase concentration in the saliva. Acetylcholine is the active neurotransmitter, binding at muscarinic receptors in the salivary glands. Stimulation by the sympathetic nervous system results in a scant, viscous saliva rich in organic and inorganic solutes with an increase in amylase concentration in the saliva.

The Primary Functions of Saliva:

- Antimicrobial activity.
- Mechanical cleansing action.
- Control of pH.
- Removal of food debris from the oral cavity.
- Lubrication of the oral cavity.
- Remineralization.
- Maintaining the integrity of the oral mucosa.



Salivary hypofunction causes:

- Candidiasis
- Lichen Planus
- Burning Mouth
- Aphthous ulcers
- Xerostomia

The primary constituents of saliva are water, proteins and electrolytes. These components enhance taste, speech and swallowing and facilitate irrigation, lubrication and protection of the mucous membranes in the upper digestive tract. Additional physiological functions of saliva provide antimicrobial and buffering activities that protect the teeth from dental caries.

Other Notes or Questions to Ask:

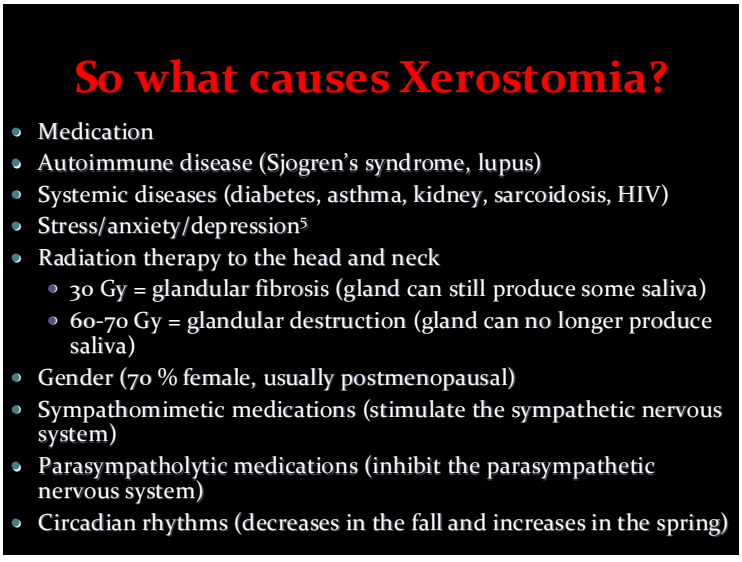
As stated above, saliva possesses many important functions including antimicrobial activity, mechanical cleansing action, control of pH, removal of food debris from the oral cavity, lubrication of the oral cavity, remineralization and maintaining the integrity of the oral mucosa.

Fluoride is also secreted in saliva but unlike the ions in saliva, the fluoride content (level) is not altered whether the salivary flow is simulated or unstimulated.

So What Causes Xerostomia?

Xerostomia is a common and significant side effect of many commonly prescribed drugs. Establishing relative incidence rates for xerostomia for a particular drug, however, is difficult.

As with other side effects, reported rates depend on how the information is accessed (direct vs. open-ended questions), the severity of concomitant adverse reactions, over-reporting for new drug entities, the disorder being treated and the dose of the medication. Nevertheless, the risk for xerostomia increases with the number of drugs being taken. Older people, therefore, are more likely to be affected. In the geriatric population, drug-induced xerostomia has been reported to contribute to difficulty with chewing and swallowing; this may result in avoidance of certain foods. A case of a patient's inability to dissolve a sublingual nitroglycerine tablet owing to lack of saliva has been described in the literature. A variety of drugs that have a wide range of therapeutic activities have been reported to cause xerostomia in 10 percent or more of patients.



Drug-induced hyposalivation also can be an extension of the drug's intended action, as seen with the parasympatholytic agents, such as atropine, or as an anticholinergic side effect with drugs such as tricyclic antidepressants.

When xerostomia is associated with xerophthalmia, also known as "dry eyes," it may represent a chronic autoimmune condition that is recognized as Sjögren's syndrome, which affects predominantly women after the fourth decade of life.

Other Notes or Questions to Ask:

DRUGS ASSOCIATED WITH XEROSTOMIA.*

CATEGORY	GENERIC NAME	TRADE NAME†
Anticholinergic Agents	atropine	Atrohist, Lomotil
	belladonna	Donnatal, Respa-A.R.M.
	benztropine	Cogentin
	oxybutynin	Ditropan
	scopolamine	Transderm Scop
	trihexyphenidyl	Artane
Antidepressant and Antipsychotic Agents		
Selective serotonin-reuptake inhibitors	citalopram	Celexa
	fluoxetine	Prozac
	paroxetine	Paxil
	sertraline	Zoloft
	venlafaxine	Effexor
Tricyclic antidepressant	amitriptyline	(generic)
	desipramine	Norpramin
Heterocyclic antidepressants	imipramine	Tofranil
	haloperidol	Haldol
	mirtazapine	Remeron
Monoamine oxidase inhibitors	pimozide	Orap
Atypical antidepressants	phenelzine	Nardil
	bupropion	Wellbutrin, Zyban
	nefazodone	Serzone
	olanzapine	Zyprexa
Diuretic Agents	chlorothiazide	Diuril
	furosemide	Lasix
	hydrochlorothiazide	HydroDiuril, Dyazide
	triamterene	Dyrenium
Antihypertensive Agents	captopril	Capoten
	clonidine	Catapres
	clonidine/chlorthalidone	Combipres
	enalapril	Vasotec
	guanfacine	Tenex
	lisinopril	Zestril
	methyldopa	Aldomet
Sedative and Anxiolytic Agents	alprazolam	Xanax
	diazepam	Valium
	flurazepam	Dalmane
	temazepam	Restoril
	triazolam	Halcion
Muscle Relaxant Agents	cyclobenzaprine	Flexeril
	orphenadrine	Norflex
	tizanidine	Zanaflex
Analgesic Agents		
Central nervous system/opioids	codeine	(generic)
	meperidine	Demerol
	methadone	Dolophine
	pentazocine	Talwin
	propoxyphene	Darvon
	tramadol	Ultram
Nonsteroidal anti-inflammatory agents	diflunisal	Dolobid
	ibuprofen	Advil, Motrin
	naproxen	Aleve, Naprosyn
	piroxicam	Feldene
Antihistamines	astemizole	Hismanal
	brompheniramine	Dimetane-DX
	chlorpheniramine	Chlor-Trimeton
	diphenhydramine	Benadryl, Dramamine
	loratadine	Claritin
	meclizine	Antivert
Miscellaneous medications		
Anorexiants	diethylpropion	Tenuate
	sibutramine	Merida
Antiacne agent (retinoid)	isotretinoin	Accutane
Anticonvulsant	carbamazepine	Tegretol
Antidysrhythmic	disopyramide	Norpace
Anti-incontinence agent	tolterodine	Detrol
Antiparkinsonian agent	carbidopa/levodopa	Sinemet
Bronchial dilator	ipratropium	Atrovent
Ophthalmic formulation	brimonidine	Alphagan
Smoking cessation agent	nicotine	Nicorette gum, Habitrol

* Drugs listed have been reported to have a xerostomia incidence of 10 percent or more.[31,32]
† For reasons of space, the name and location of each drug's manufacturer are not listed here. A complete list can be requested from the authors as hard copy or an electronic file.

Guggenheimer J, Moore PA. Xerostomia: etiology, recognition and treatment. JADA. 2003 Jan;134(1):61-9.

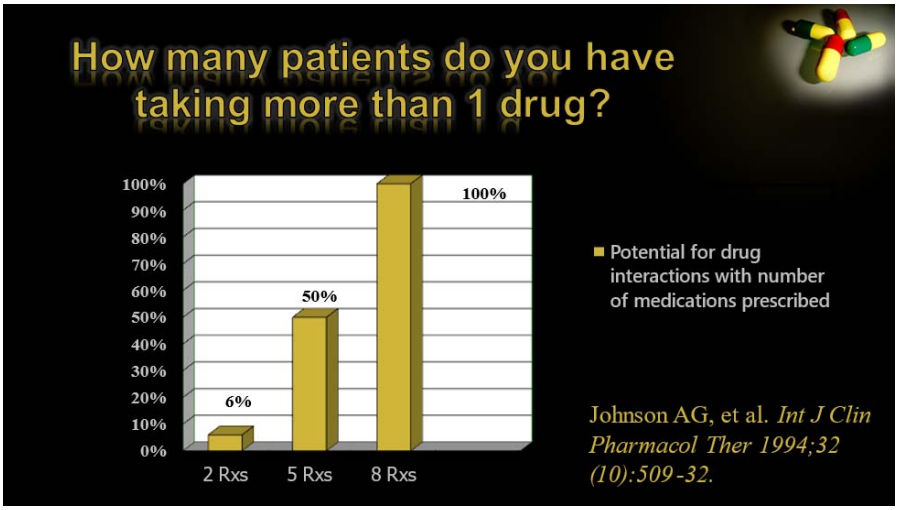
Other Notes or Questions to Ask:

Medications are the cause of more than 90% of xerostomia cases.

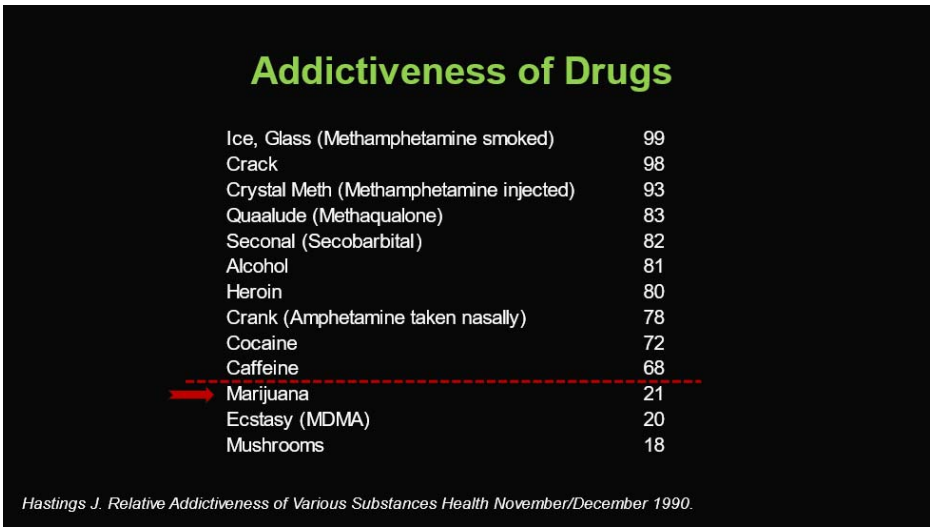
Xerogenic drugs can be found in 42 drug categories and 56 subcategories. More than 400 commonly used drugs can cause xerostomia. The main culprits are antihistamines, antidepressants, anticholinergics, anorexiants, antihypertensives, antipsychotics, anti-Parkinson agents, diuretics and sedatives. Other drug classes that commonly cause xerostomia include antiemetics, antianxiety agents, decongestants, analgesics, antidiarrheals, bronchodilators and skeletal muscle relaxants. These effects are generally not permanent.

Drug Interactions

- Polypharmacy is the norm especially >65.
- AMA policy survey showed that >20% of acute care hospital admissions for seniors may result directly from adverse drug reactions (ADRs).
- Polypharmacy is used as:
  - complementary therapy
  - co-morbid conditions
  - non-comorbid conditions



Illicit Drug Abuse and Dental Health



Other Notes or Questions to Ask:

Cannabis Respiratory Effects
Generally considered long-term risks
Smoke has same contents as tobacco smoke (i.e., carbon monoxide, bronchial irritants, ↑ tar, ↑ carcinogens)

- 3-4 marijuana cigarettes = 20 tobacco cigarettes
- No filter, deeper inhalation
- Water pipes, vaporizers may increase safety (?)

Cannabis Respiratory Effects
"Smoking both tobacco and marijuana synergistically increases the risk of respiratory symptoms (2.5x) and COPD (3x)"

Cannabis Oral Effects

- Xerostomia
- Periodontal disease – possibly b/c of immunosuppresion, heavy smokers have a 3x increased risk of periodontal disease
- "Cannabis stomatitis" – chronic use may cause inflammation of the oral epithelium (similar to nicotine stomatitis).
- Leukoedema – may progress to leukoplakia
- Increased risk of mouth and neck cancers
- Synergistic risk when combined with tobacco smoking
- Increased prevalence and density of Candida albicans.

Cannabis Respiratory Effects
Generally considered long-term risks. Smoke has same contents as tobacco smoke (i.e., carbon monoxide, bronchial irritants, ↑ tar, ↑ carcinogens). 3-4 marijuana cigarettes = 20 tobacco cigarettes

	Cardiovascular Effects	Respiratory Effects	Xerostomia	Interaction with local anesthesia	Interaction with vasoconstrictors	Interaction with narcotic analgesics
Cannabis	++	+/-	++	-	+	-
Cocaine	++	+	++	+++	+++	+++
Narcotics	++	++	++	-	-	+++
METH	+++	+	+++	-	+++	+++

Dental Considerations: Cocaine

- **Cocaine powder** (cocaine hydrochloride) is made from the leaves of the coca plant, it is separated with alcohol, gasoline, or kersosene
- **Freebase** - a method using ammonia and ether that separates the free-base molecule of cocaine, can be smoked, high potency,↑ toxicity
- **Crack** - a method that converts cocaine hydrochloride into a smokable form using bicarbonate. Results in lower potency than freebase, ↑ impurities

Other Notes or Questions to Ask:

Cocaine Effects
Immediate effects: Within a few minutes a euphoric 'high' feeling occurs which can last for up to 90 mins

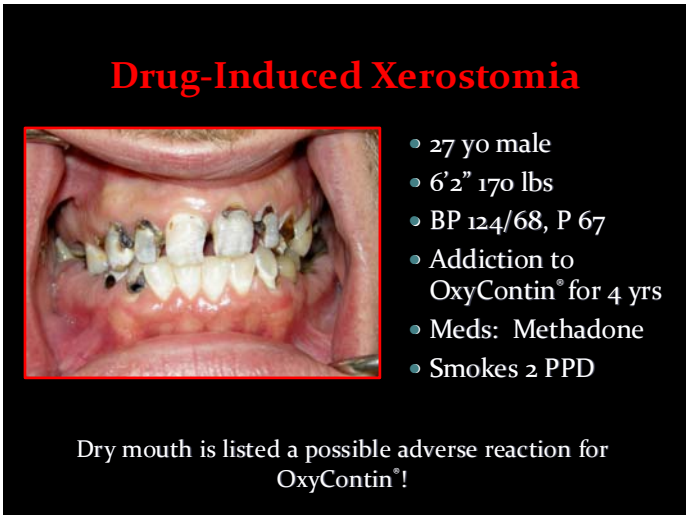
"There's no happy ending to cocaine. You either die, you go to jail, or else you run out."
- Sam Kinison

Cocaine Oral Effects

- Nasal Septum perforation & palatal perforation
- Vasoconstriction → local ischemia
- "Saddle-nose" deformity
- Increased BP
- Local anesthetic toxicity
- Vasoconstrictor toxicity – potentially fatal
- Xerostomia
- Bruxism

Narcotics (heroin and others)

- Xerostomia
- Drug Interactions
- Synergistic with any other narcotic
- Allergic thrombocytopenia
- Quinine
- ↑ risk of endocarditis
- ↑ risk of HIV and Hepatitis
- 40% of IV users exposed to some form of Hepatitis



Methadone Considerations

- Xerostomia
- Increased caries rate with sugar-based formulations
- Consider fluoride supplementation
- Possibly contributes to erosion (↓ pH)
- Same systemic effects as the other opioids

Donaldson M, Goodchild JH, Epstein JB. Sugar content, cariogenicity, and dental concerns with commonly used medications. J Am Dent Assoc 2015;146(2):129-133.

"Meth Mouth"

- The phenomenon is thought to be the result of the ingredients used to make Meth.
- Studies have shown that the ingredients are most likely NOT responsible for the rapid destruction to dentition:
    - Navarro et al. 2001. pH decline from 7.4 to 6.9
    - Critical pH for demineralization of enamel is 5.5
- Current literature suggests that "Meth Mouth" is the result of:
    - Hyposalivation
    - High sugar intake
    - Bruxism
    - Poor oral hygiene

Other Notes or Questions to Ask:

Signs and Symptoms of Xerostomia

- Problems with eating, speaking/swallowing and wearing dentures.
- Dry, crumbly foods, such as cereals and crackers, may be particularly difficult to chew and swallow.
- Denture wearers may have problems with denture retention, denture sores the tongue sticking to the palate.
- Taste disorders (dysgeusia).
- Painful tongue (glossodynia).
- An increased need to drink water, especially at night.

Consequences of Xerostomia

- Xerostomia can lead to markedly increased dental caries.
- Parotid gland enlargement.
- Inflammation and fissuring of the lips (cheilitis).
- Inflammation or ulcers of the tongue and buccal mucosa.
- Oral candidiasis.
- Salivary gland infection (sialadenitis).
- Halitosis.
- Cracking and fissuring of the oral mucosa.

Management of Xerostomia

Symptomatic Treatment:

- Increasing existing saliva flow.
- Replacing lost secretions.
- Control of dental caries.
- Specific measures such as treatment of infections.

Self-care:

- Be vigilant in minimizing the risks to dental health.
- Conduct a daily mouth exam, checking for red, white or dark patches, ulcers or tooth decay.
- Reported anything unusual to physician or dentist.
- Products containing sodium lauryl sulfate should be avoided (aphthous ulcers or canker sores).
- Sodium fluoride rinses should be held in the mouth for at least one minute before expectorating.
- Fluoride gels can be left in place for 2-3 minutes before expectorating.
- Chlorhexidine rinses can reduce Lactobacillus.
- Dentures should not be worn during sleep and should be kept clean by overnight.
- Acrylic appliances should be soaked in a sodium hypochlorite solution, and metal dentures should be soaked in chlorhexidine.
- Avoid sugary or acidic foods or beverages.
- Avoid irritating foods that are dry, spicy, astringent or excessively hot or cold.
- Tobacco and alcohol intake should be eliminated to control dental caries.
- A cold air humidifier may aid mouth breathers who typically have their worst symptoms at night.

Oral Candidiasis	■ Antifungal rinses: nystatin oral suspension (100,000 units/milliliter), rinse 4 times per day ■ Antifungal ointments: nystatin ointment applied 4 times per day ■ Antifungal lozenges dissolved in mouth 4 times per day, nystatin pastilles (200,000 units), clotrimazole troches (10 mg), nystatin vaginal suppositories ■ Denture antifungal treatment (daily hygiene): soak prosthesis for 30 minutes in benzoic acid, 0.12 percent chlorhexidine or 1 percent sodium hypochlorite
Bacterial Infections	■ Systemic antibiotic therapy for 10 days: amoxicillin with clavulanate (500 mg every 8 hours); clindamycin (300 mg 3 times per day); cephalexin (500 mg every 6 hours) ■ Increase in hydration ■ Salivary stimulation with sugar-free gums, mints, lozenges

Dental Caries	■ Daily use of fluorinated dentifrice (0.05-percent sodium fluoride) ■ Daily use of prescription fluoride gel (1.0-percent sodium fluoride, 0.4-percent stannous fluoride) ■ Application of 0.5-percent sodium fluoride varnish to teeth ■ Dental examinations at least every 6 months and bitewing radiographs every 12 months for early diagnosis
Dry Mouth	■ Oral moisturizers/lubricants, mouthwashes, and sprays ■ Sugar-free gums, mints, lozenges ■ Artificial salivary replacements ■ Prescription sialogogues: pilocarpine (5 mg 3 times per day and at bedtime); cevimeline (30 mg 3 times per day) ■ Lubricants on lips every 2 hours ■ Use of bedside humidifier during sleeping hours
Dysgeusia	■ Drinking of fluids while eating
Dysphagia	■ Careful eating, with fluids ■ Copious use of fluids during meals ■ Avoidance of dry, hard, sticky, and difficult-to-masticate foods

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Over-The-Counter Products

- Saliva substitutes.
- Saliva stimulants.
- Dentrifrices.

Lubricants such as Orajel® or Vaseline® and glycerin swabs on the lips and under dentures may relieve drying, cracking, soreness and mucosal trauma. Saliva stimulants (sialagogues), such as sugarless candies and chewing gum, may be used to stimulate saliva flow when functional salivary glands remain. Patients should be advised to take frequent sips of water throughout the day and to suck on ice chips. Eating foods such as carrots or celery may also help patients with residual salivary gland function.

Saliva Substitutes

- Replacement therapy rather than a cure.
- Artificial saliva or saliva substitutes replace moisture and lubricate the mouth.
- Formulated to mimic natural saliva, but they do not stimulate salivary gland production.
- Available commercially (solutions, sprays, gels and lozenges), but they can be compounded.
- In general, they contain an agent to increase viscosity, such as carboxymethylcellulose or hydroxyethylcellulose, minerals such as calcium and phosphate ions and fluoride, preservatives and flavor.

Other Notes or Questions to Ask:

Saliva Stimulants

- Not appropriate for patients whose salivary gland function has been lost (i.e., radiation treatment) as its effect is to stimulate functional salivary glands.
- Natrol Dry Mouth Relief® utilizes anhydrous crystalline maltose (ACM) to stimulate saliva production.
- ACM shown to increase secretions and significantly improve patient's subjective assessment of symptoms in Sjögren's Syndrome.
- Formulated as lozenges which are to be dissolve in the mouth three times daily.

Dentrifrices

- Used with a toothbrush for cleaning and polishing teeth. Typically contains a mild abrasive, detergent, flavoring agent, fluoride, and binder (i.e., toothpaste).
- Biotene® and Oral Balance® products are antixerostomia dentifrices that contain three salivary enzymes, lactoperoxidase, glucose oxidase and lysozyme, specifically formulated to activate intra-oral bacterial systems.
- Biotene® Dry Mouth Toothpaste
- Biotene® Gentle Mouthwash
- Biotene® Dry Mouth Gum
- Oralbalance® Long-lasting Moisturizing Gel
- Biotene®Dry Mouth Kit

Prescription Products

- Pilocarpine
- Cevimeline
- Anethole trithione
- Yohimbine
- Human interferon alfa (IFN-a)

Pilocarpine (Salagen®)

A cholinergic parasympathomimetic agent with predominantly muscarinic M3 action that causes stimulation of residual functioning exocrine glands. The tablets are indicated for the treatment of symptoms of dry mouth from salivary gland hypofunction caused by Sjögren's syndrome or by radiotherapy for cancer of the head and neck. The time to reach peak concentrations following oral administration is approximately 1.25 hours. The duration of sialogogic effect is about two to three hours.

Other Notes or Questions to Ask:

In clinical studies, pilocarpine at dosages of 5-30 mg, divided into one to four oral daily doses, was shown to significantly decrease dryness of the mouth and eyes compared to artificial saliva or placebo in patients with Sjögren's syndrome and those who developed xerostomia following radiation therapy. Pilocarpine is contraindicate-ed in patients with uncontrolled asthma, narrow-angle glaucoma or iritis. It has a pregnancy risk category C and side effects include increased sweating and GI intolerance, hypotension, rhinitis, diarrhea and visual disturbances. 6-12 weeks of uninterrupted therapy may be necessary before improvement in symptoms is seen. The average wholesale price (AWP) for 30 days of treatment with Salagen® 5 mg QID is $152.64.

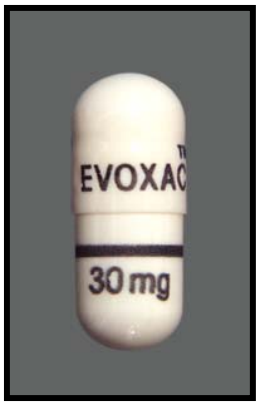
Pilocarpine Eye Drops – Orally??

Pilocarpine eye drops have been used in patients with Sjögren's syndrome in an effort to reduce the cost of treatment. The eye drops were also used before the availability of the tablets. The gastrointestinal absorption of the solution appears to be similar to that of the tablets, although there have been no specific studies to show this. It is not surprising that the eye drops would work when given orally, since systemic effects have occurred after intraocular administration of pilocarpine solution. The ophthalmic solution has been shown to be as effective as the tablets, and has been equally acceptable. Importantly, the cost can be significantly less.

One study used four drops of 2% pilocarpine solution, swish and swallow, three times daily. In this study, pilocarpine stimulated saliva production in more than 75% of patients. The volume of each dose depends on the concentration of the solution used. Since the usual dose is 5 mg four times per day, the amount of solution used should reflect this same dose. For example, there is 5 mg in each mL of a 0.5% solution. If using a 0.5% solution, a patient would use about eight bottles each month. At $9.00 per bottle, that's $56.00 per month. The cost savings will be greater if more concentrated pilocarpine solutions are used. And although they are not toxic in moderate doses, using a higher concentration also reduces exposure to preservatives in the eye drops. For example, there is 20 mg in each mL of a 2% solution, so only 0.25 mL, or about five drops, is required for each dose. In this case a patient would only use two bottles each month, with a monthly cost of about $20.00 per month.

Remind patients to avoid substances that can exacerbate dry mouth, such as anticholinergic medications, tobacco, and alcohol. Suggest patients use a syringe instead of counting drops to more accurately measure each dose.

Cevimeline (Evoxac®)



Cevimeline is a cholinergic agonist with a high affinity for the muscarinic M3 receptors located on lacrimal and salivary gland epithelium, leading to an increase in exocrine gland secretions including saliva and Xerostomia information for dentists. It is indicated for the treatment of symptoms of dry mouth in patient's with Sjögren's syndrome. It is rapidly absorbed from the gastrointestinal tract, reaching peak concentrations in approximately 90 minutes without food. Its duration of sialogogic effect is unclear. Clinical trials have shown it to be more effective than placebo in relieving symptoms of dry mouth. No clinical trials are available comparing it to pilocarpine.

It is contraindicated in patients with uncontrolled asthma, narrow-angle glaucoma, or iritis. It is pregnancy category C. Excessive sweating and nausea are the most frequently reported adverse effects with cevimeline. Rhinitis, diarrhea and visual disturbances, especially at night, can also occur. The recommended oral dosage is 30 mg TID. The average wholesale price for 30 days of treatment is $118.

Other Notes or Questions to Ask:

Anethole Trithione

Anethole trithione is a bile secretion stimulating drug, or cholagogue. It is available over-the-counter (OTC) in Canada & Germany. It stimulates the parasympathetic nervous system and increases the secretion of acetylcholine, resulting in the stimulation of salivation from serous acinic cells. Anethole trithione has been used for many years in the treatment of chronic xerostomia, but reports differ regarding its efficacy. While some studies report improvements in salivary flow rates in drug-induced xerostomia, trials in patients with Sjögren's syndrome show conflicting results. Side effects reported include abdominal discomfort and flatulence. Dosages of 75 mg three times daily may be effective in treating patients with mild-to-moderate symptoms of xerostomia, but further research is needed to establish its safety and efficacy in this setting.

Yohimbine

Yohimbine is an alpha-2 adrenergic antagonist which indirectly results in an increase of cholinergic activity peripherally.3,30 In one small, randomized, double-blind, crossover study, the effect of yohimbine was compared to that of anethole trithione in 10 patients treated with psychotropic medications. Patients given yohimbine 6 mg three times daily for five days showed significantly increased saliva flow ($p<0.01$) when compared with anethole trithione 25 mg TID.

Human interferon alfa (IFN-a)

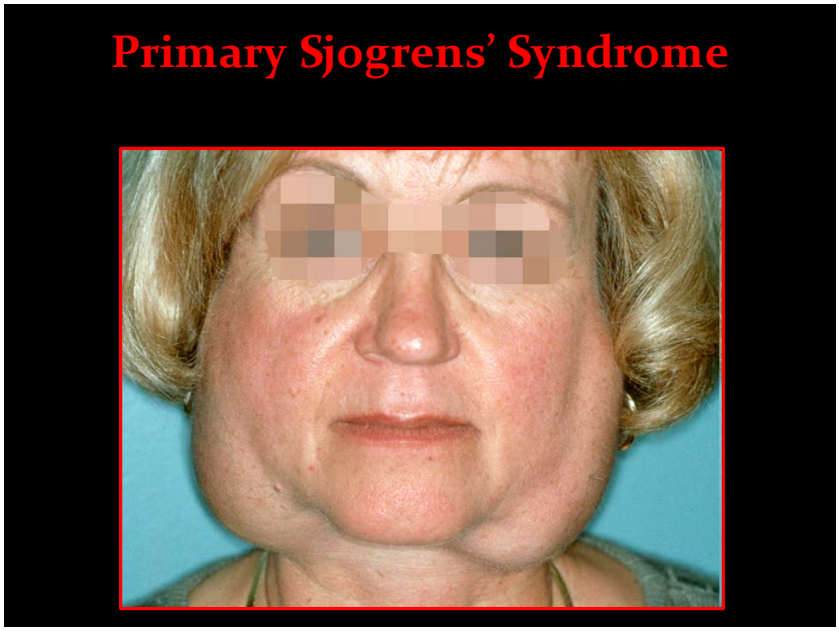
Human interferon alfa (IFN-a) is currently undergoing clinical trials to determine the safety and efficacy of low-dose lozenges in the treatment of salivary gland dysfunction and xerostomia in patients with Sjögren's. In one study, IFN-a lozenges at dosages of 150 IU given TID for 12 weeks resulted in a significant increase in stimulated whole saliva ($p=0.04$) when compared with placebo.

Future Therapies

Development of saliva substitutes based on novel thickening agents in hopes of providing longer retention on the mucosal surface is another area of current research. Substitutes based on linseed polysaccharide (Salinum®, Miwana AB, Gallivare, Sweden) or xanthan gum polysaccharide (Xialine®, Lommerse Pharma BV, Oss, the Netherlands) have been shown to be effective in patients with Sjögren's syndrome. Another area of research includes the production of antimicrobial peptides originally derived by histatins, antifungal proteins naturally occurring in serous salivary glands. Prednisolone irrigation of parotid glands is being investigated as a potential treatment of xerostomia in patients with Sjögren's syndrome. Also look for Neuro-electro-stimulation (NES) of salivary glands (Intraoral electrostimulator).

Other Notes or Questions to Ask:

In primary Sjögren's syndrome, the disease is limited to the eyes and salivary glands. With secondary Sjögren's syndrome, patients also have an autoimmune or connective tissue disease. It is estimated that 15 percent of patients with rheumatoid arthritis, 25 percent of those with systemic sclerosis and 30 percent of those with systemic lupus erythematosus may develop Sjögren's syndrome. Symptoms comparable with those of Sjögren's syndrome also have been reported to occur with fibromyalgia, chronic fatigue syndrome, Raynaud's phenomenon and other conditions that demonstrate the presence of autoantibodies.



The xerostomia that is associated with primary and secondary Sjögren's syndrome has been attributed to the progressive lymphocytic infiltration that gradually destroys the secretory acini of the major and minor salivary glands. Another explanation for the loss of glandular function may be related to an inhibition of nerve stimuli of the glands. It has been suggested that the reduction in secretions first may affect the minor salivary glands, which can initiate the symptoms of xerostomia.

Slow-release delivery systems for pilocarpine are also being investigated. Vaccination with autoreactive T cells or with T cell receptor peptides is another area of research, as is the possibility of inserting water transporting proteins or aquaporins, in the cell membrane of the ductal cells.

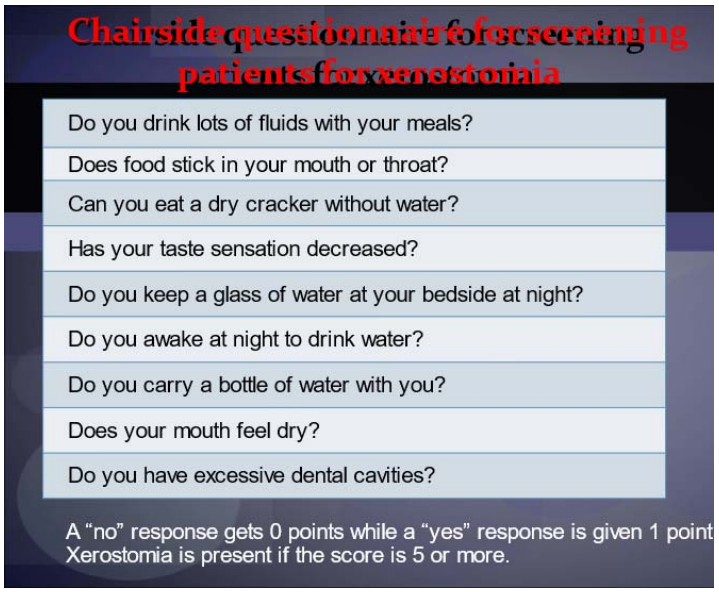
Case Example (Conclusion)

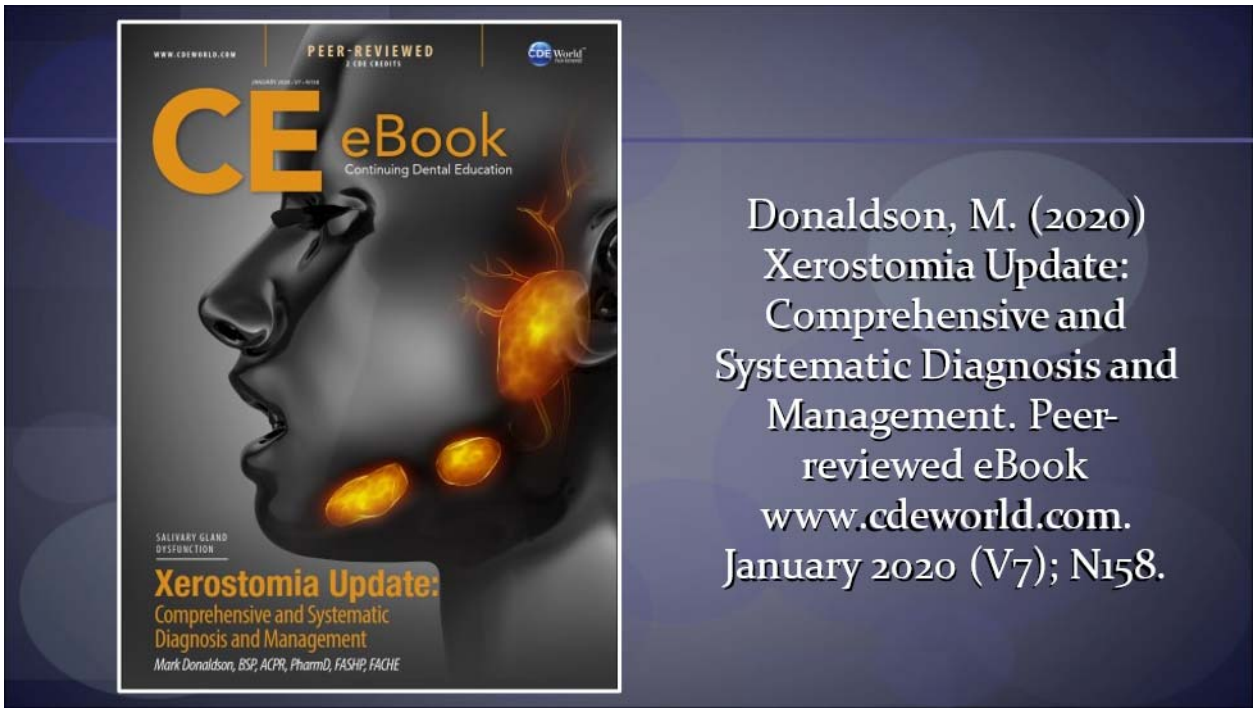
The most common disease causing xerostomia is Sjögren's syndrome, a chronic inflammatory autoimmune disease that occurs predominantly in postmenopausal women. As many as 3% of Americans suffer from Sjögren's, with 90% being women with a mean age at diagnosis of 50 years. It is characterized by lymphocytic infiltration of salivary and lacrimal glands, resulting in xerostomia & xerophthalmia ("sicca complex"). Enlargement of major salivary glands occurs in about one-third of patients with Sjögren's.

There is no cure; the goal of therapy is to manage symptoms: Xerostomia, xerophthalmia, blurred vision, recurrent eye and mouth infections, dysphagia or difficulty swallowing, oral soreness, smell and taste alternations, fissures on the tongue and lips, fatigue, dry nasal passages and throat, constipation and vaginal dryness.

For her allergic rhinitis, a non-sedating antihistamine and avoidance of products containing decongestants. Review self-care measures (with emphasis on minimizing caffeine consumption and smoking). Encourage her to quit smoking. Give advice about good oral hygiene. Encourage adequate fluid intake, avoiding caffeine and sugar-containing products and alcohol. Consider the use of an artificial saliva and/or OTC saliva stimulant.

Other Notes or Questions to Ask:





Other Notes or Questions to Ask: