Fall Rounds 2020

EBD Rounds - Oral Med

Group 2A-2

D4 - Turner Schmidt

D3 - Madelyn Zastrow

D2 - Carly Schaefer and Audrey Chu

D1 - Ian Soto

Group Leader - Dr. Pelz DMD

Specialty Leader - Dr. Joseph Best DDS, PhD

Patient X

76 yo African-American presents for free denture program.

CC: “I need a new denture, this one is broken.”

Medical Consult indicated due to complex history and extensive medical problem list

Medical Consult

Medical Problems 23

28 Medications

Allergies 7

Medical Problem List

Asthma
B12 deficiency
Esophageal reflux
Esophageal Stricture
Leg cramps
Mitral regurgitation
Spinal Stenosis

Iron Deficiency anemia
Gastric bypass
Abnormal ECG
Colon polyps
Osteoarthritis of knee
Abnormal brain MRI
Osteopenia
Insomnia

Fibromyalgia
Hyperlipidemia
Chronic diarrhea
Thumb osteoarthritis
Herpes Simplex
Ulnar neuropathy
Right hand pain
Numbness and tingling in right hand

Medication List

DenoSumab - osteoporosis
Diazepam - prn
Diclofenac 1% gel - arthritis
Eszopiclone - insomnia
Furosemide - fluid retention
Gabapentin - nerve pain
Hydrocodone-acetaminophen - pain
Isosorbide mononitrate - esophageal spasm
Loperamide - Diarrhea
Morphine - pain
Olopatadine - dry eye

Medication List

Prednisone - asthma, arthritis
Spironolactone - cramps
Tizanidine - muscle spasms
Triamcinolone 0.1% cream - dermatitis
Valacyclovir HCL - herpes simplex
Xarelto - stroke risk

Albuterol, montelukast, spiriva respimat - asthma
Diphenhydramine, fluticasone, loratadine - allergy

Pan

Radiographic findings: WNL, adequate ridge height for predictable denture fabrication

Dental History

History of significant dental treatments from a young age.

Patient has more than 10 year history of full/full complete dentures

Clinical Findings

Patient’s maxillary denture has broken teeth, presented without mandibular denture.

Patient has sufficient ridge and Class I denture relationship.

Specific Findings

Insufficient saliva production

Unrepeatable CR due to patient functional shortcomings

Patient expectations were low due to initial presentation

Patient experience with complete dentures

Diagnosis and Problem List

Diagnosis: Complete edentulism and medication-induced xerostomia

Problem List: edentulism, alveolar ridge resorption, broken denture, missing denture, and tissue pigmentation.

D1 - Basic Science

What is the Anatomy and Physiology of the salivary glands?

Anatomy of the Salivary Glands

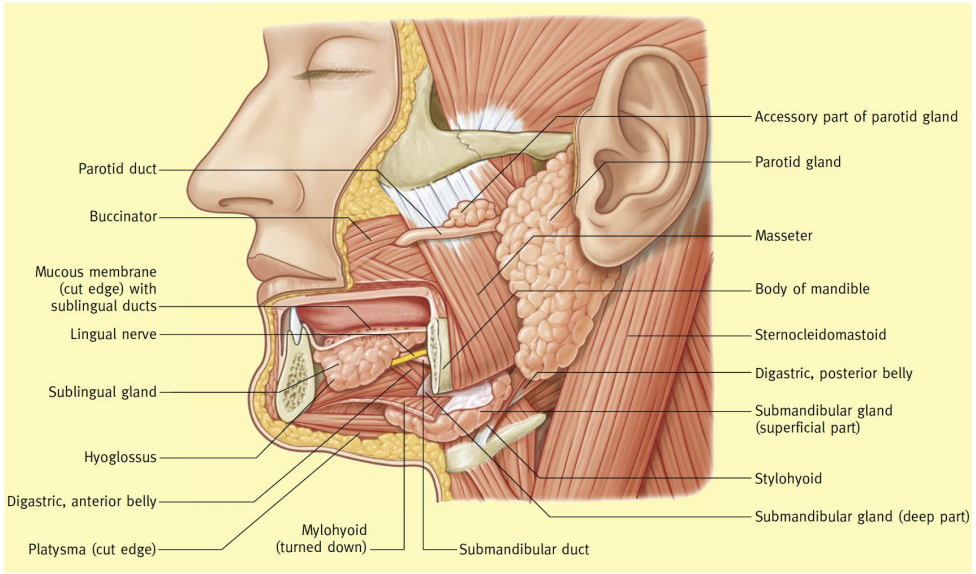
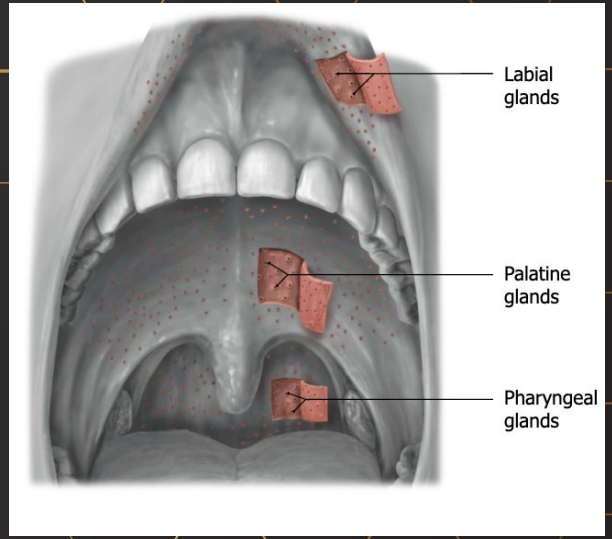


Figure 1 The parotid, submandibular and sublingual glands and their relations.



Major Salivary Glands:

Parotid
Submandibular
Sublingual

Minor Salivary Glands:

Buccal, Lingual, Palatal, Incisive, Labial surfaces of the mouth

Figure 1 From Ellis, Harold. "Anatomy of the Salivary Glands." Surgery (Oxford), vol. 30, no. 11, 2012, pp. 569–572., doi:10.1016/j.mpsur.2012.09.008.

Fig. 8.44 Minor Salivary Glands from Schuenke, Michael, et al. Anatomy for Dental Medicine. 2nd ed., Thieme Medical Publishers, 2020

Physiology of Salivary Glands

Protective functions

Mucosal lubrication and growth factors
Lysozyme
Salivary Mucins
IgA
Remineralization

Production of saliva

0.5-1.5 L daily
90% Major Glands
10% Minor Glands

Digestive functions

Salivary Amylase
Breast milk lipids

References

Ellis, Harold. “Anatomy of the Salivary Glands.” Surgery (Oxford), vol. 30, no. 11, 2012, pp. 569–572.

Paula, Fernanda De, et al. “Overview of Human Salivary Glands: Highlights of Morphology and Developing Processes.” The Anatomical Record, vol. 300, no. 7, 2017, pp. 1180–1188.

Schuenke, Michael, et al. Anatomy for Dental Medicine. 2nd ed., Thieme Medical Publishers, 2020, pp. 214-215.

Varga, Gábor. “Physiology of the Salivary Glands.” Surgery (Oxford), vol. 33, no. 12, 2015, pp. 581–586.

D2 - Pathology

What is the etiology and treatment of medication-induced xerostomia?

Xerostomia: the sensation of a dry mouth

- Can occur with reduced salivary flow, but also with normal salivary flow

Etiology

- Salivary secretion is mediated by the parasympathetic nervous system
- Medication-induced xerostomia occurs due to inhibition of the parasympathetic nervous system's activity
    - Parasympatholytics, cholinolytics, anticholinergics = Muscarinic receptor antagonists
    - Prevention of acetylcholine from binding to muscarinic receptor
- Ederly are often affected due to polypharmacy

What is the etiology and treatment of medication-induced xerostomia?

Common classes of medications that cause xerostomia:

- Antihistamines
- Antidepressants
- Antipsychotics
- Sedative agents
- Antihypertensive medications

Treatment

- Topical medications are the first to be recommended
  - Chewing gums, candies, salivary stimulants, and saliva substitutes.
- Sialogogues are not recommended

References

Millsop, Jillian W., et al. "Etiology, Evaluation, and Management of Xerostomia." *Clinics in Dermatology*, Elsevier, 27 June 2017, www.sciencedirect.com/science/article/pii/S0738081X17301062.

Villa, A., Wolff, A., Aframian, D. *et al*. World Workshop on Oral Medicine VI: a Systematic review of medication-induced salivary gland dysfunction: prevalence, diagnosis, and treatment. *Clin Oral Invest* 19, 1563–1580 (2015). https://doi.org/10.1007/s00784-015-1488-2

D2 - Alt Pathology

What is the Etiology, Symptoms, & Treatment of Sjogren Syndrome

Sjogren Syndrome: chronic autoimmune disorder characterized by glandular dysfunction due to lymphocyte infiltration of the exocrine glands.

- Salivary and Lacrimal glands tend to be the most affected

2 Types of Sjogren's Syndrome:

- Primary- absence of other autoimmune disorders
- Secondary - occurs along with other autoimmune disorders

Etiology: currently remains unknown/not fully understood

- Genetic predisposition, hormones, and environmental factors may predispose an individual to developing this disorder.
- Women tend to be affected more than men
- Salivary and lacrimal gland dysfunction results in hyposalivation and decreased tear production

What is the Etiology, Symptoms, & Treatment of Sjogren Syndrome

Hallmark Symptoms of Sjogren's Syndrome are:

- Xerostomia
- Keratoconjunctivita sicca (dry eyes)

Treatment: There is no cure for Sjogren's Syndrome and so treatment is supportive and focused on the patient's symptoms.

- **Sialagogue Drugs:** Pilocarpine and Cevimeline
  - Direct-acting Muscarinic receptor agonists
  - Used to increase salivation when the problem is due to salivary gland dysfunction
    - High affinity for the muscarinic receptors located in the lacrimal and salivary glands
- Cyclosporine- Prescription eye drops used to decrease inflammation of the lacrimal gland
- Artificial tears

References:
Nair JJ, Singh TP. Sjogren's syndrome: Review of the aetiology, Pathophysiology & Potential therapeutic interventions. *J Clin Exp Dent*. 2017;9(4):e584-e589. Published 2017 Apr 1. doi:10.4317/jced.53605

Parisis D, Chivasso C, Perret J, Soyfoo MS, Delporte C. Current State of Knowledge on Primary Sjögren's Syndrome, an Autoimmune Exocrinopathy. *J Clin Med*. 2020;9(7):2299. Published 2020 Jul 20. doi:10.3390/jcm9072299

D3 - PICO

Clinical Question

How do you treat xerostomia?

PICO

- P: Patients with medication induced xerostomia
- I: Maintaining the medications and treating the dry mouth
- C: Changing medications
- O: Affect on quality of life

PICO Formatted Question

In patients with medication induced xerostomia, is changing medications or primarily treating the xerostomia more effective in improving the patients quality of life?

Clinical Bottom Line

Changing medications to treat a patient's xerostomia has not been a common practice. Management of xerostomia may be performed in combination of therapeutic products according to the patient’s concerns, preferences and oral health requirements.

Search Background

- **Date of Search:** 9/20 & 9/21
- **Database(s) Used:** pubmed.gov, The Journal of the American Dental Association and American Dental Association
- **Search Strategy/ Keywords:** Studies containing information about the management and treatment of xerostomia, particularly related to medications if possible
- **MESH terms used**: Xerostomia/therapy, dental caries/prevention and control, life style, artificial substitutes, medications

Article 1: Drug Induced Xerostomia in elderly individuals

- Shetty SR, Bhowmick S, Castelino R, Babu S. Drug induced xerostomia in elderly individuals: An institutional study. *Contemp Clin Dent*. 2012;3(2):173-175. doi:10.4103/0976-237X.96821

- **Study Design:** Cross-Sectional Study

- **Purpose:** Evaluate the Synergistic effects of multiple xerostomia drugs, to determine if such a synergistic effects exists then one of the drugs could be replaced by a counterpart that does not induced xerostomia

Article I Synopsis

- **Methods:** A cross-sectional study involving 60 patients above the age of 60 years were divided into three groups
  - Group A: 20 patients without any systemic disease and long-term medication
  - Group B: 20 patients with intake of a single drug known to cause xerostomia
  - Group C: 20 patients with intake of more than one drug known to cause xerostomia
  - Exclusion criteria: salivary gland aplasia, Sjogren syndrome, sarcoidosis, head and neck radiotherapy, chemotherapy or surgery
  - Unstimulated saliva was collected from each patient using the spit method from 8 am to 2 pm and consumptions of food and beverages, chewing gum, brushing teeth and using any form of tobacco was stopped 2 hours prior
- **Results:**

Study Groups	n	Mean USFR (ml/5min)	Xerostomia Questionnaire	Quality of Life Questionnaire Scores	P Value
Group A	20	1.58 +/- 0.23	2.02 +/- 0.27	75	0.001
Group B	20	0.70 +/- 0.34	6.19 +/- 0.34	50	
Group C	20	0.27 +/- 0.21	8.23 +/- 0.21	29	

Article I Synopsis

- **Conclusion:** The study concluded that synergistic effects of xerostomia-inducing medications were observed in elderly patients taking multiple medications. However, the intensity of xerostomia can be reduced by the substitution of drugs or by change in the manner in which they are taken.

- **Limitations:** The level of evidence is limited and the study does not directly answer the PICO question, more so just infers you can substitute drugs

Article I Selection

- **Reason for selection:** Relates partially to the PICO question
- **Applicability for the patient:** The patient is on 28 medications and this article helps confirm why she has insufficient saliva
- **Implications:** Gives us an idea about how we might move forward with this patient when giving her the new denture or trying to manage her xerostomia

Article I Level of Evidence

- ☐ **1a** – Clinical Practice Guideline, Meta-Analysis, Systematic Review of Randomized Control Trials (RCTs)
- ☐ **1b** – Individual RCT
- ☐ **2a** – Systematic Review of Cohort Studies
- ☐ **2b** – Individual Cohort Study
- ☒ **3** – Cross-sectional Studies, Ecologic Studies, "Outcomes" Research
- ☐ **4a** – Systematic Review of Case Control Studies
- ☐ **4b** – Individual Case Control Study
- ☐ **5** – Case Series, Case Reports
- ☐ **6** – Expert Opinion without explicit critical appraisal, Narrative Review
- ☐ **7** – Animal Research
- ☐ **8** – In Vitro Research

Strength of Recommendation Taxonomy (SORT) For Guidelines and Systematic Reviews

See article **J Evid Base Dent Pract 2007;147-150**

- ☒ **A** – Consistent, good quality patient oriented evidence
- ☐ **B** – Inconsistent or limited quality patient oriented evidence
- ☐ **C** – Consensus, disease oriented evidence, usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening

Article 2: Update knowledge of dry Mouth - A guideline for dentists

- Alsakran Altamimi M. Update knowledge of dry mouth- A guideline for dentists. *Afr Health Sci*. 2014;14(3):736-742. doi:10.4314/ahs.v14i3.33

- **Study Design:** Systematic review

- **Purpose:** Review of the updated literature on dry mouth

Article 2 Synopsis

- **Methods:** A pubmed search was done in the past 10 years using the words: dry mouth, causes, symptoms, treatment and dentistry. A large number of papers were identified and papers not relevant to the issue were removed.

- **Results:** There are no clearly established protocols for the treatment of dry mouth in the literature. Most of the papers identified were systematic reviews, non-systematic reviews and observational studies. The most studied patients were Sjogren's syndrome and irradiated patients. Treatments are focused on the etiology, prevention, symptoms, local salivary stimulation and systemic and topical sialogogues including anticholinesterases and cholinergics.

Article 2 Synopsis

- **Conclusion:** It can be concluded that there is no clear evidence for the treatment of dry mouth and the majority of dental practitioners refer to a specialist. Treatment must be individualized and salivary substitutes along with mechanical stimulation techniques can be applied.

- **Limitations:** The article does not contain quantitative data rather it gives qualifiable data.

Article 2 Selection

- **Reason for selection:** The article gives a good representation of where we are at in the dental field on the treatment of xerostomia, and shows us that more research is needed.

- **Applicability for the patient:** Gives us a good baseline of when to refer the patient out for treatment compared to remedies we can try within the dental clinic.

Levels of Evidence

- ☐ **1a** – Clinical Practice Guideline, Meta-Analysis, Systematic Review of Randomized Control Trials (RCTs)
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Article 3: Efficacy of Artificial Salivary Substitutes in Treatment of Xerostomia: A Systematic Review

- Assery MKA. Efficacy of Artificial Salivary Substitutes in Treatment of Xerostomia: A Systematic Review. *J Pharm Bioallied Sci*. 2019;11(Suppl 1):S1-S12. doi:10.4103/jpbs.JPBS_220_18

- **Study Design:** Systematic Review

- **Purpose:** To provide an artificial saliva used to maintain the health of the oral cavity of patients with severe hyposalivation

Article 3 Synopsis

- **Methods:** A literature search was conducted in April 2018 in three electronic databases by combining keywords and terms related to the population and intervention of the topic
  - Inclusion criteria:
    - Parallel group and crossover clinical trials, english only, studies on human, studies related to artificial saliva substitutes
  - Exclusion criteria:
    - Review articles, letter to editor, trials related to systemic medication or sialogogues, trials comparing treatments with systemic treatments such as pilocarpine
  - Types of interventions:
    - Oral Moisturizing Jelly, Herbal powder of *Alcea digitata* and *Malva sylvestris*, Immunologically active saliva substitutes, mouthwash and oral sprays, carboxymethylcellulose, oral balance, bioXtra, artificial saliva, etc.

- **Results:** Due to the lack of evidences, it was difficult to conclude the most effective product or intervention. The studies were categorized under:
  - Studies conducted on subjects with drug induced xerostomia
  - Studies conducted on subjects with radiation-induced xerostomia
  - Others

Article 3 Synopsis

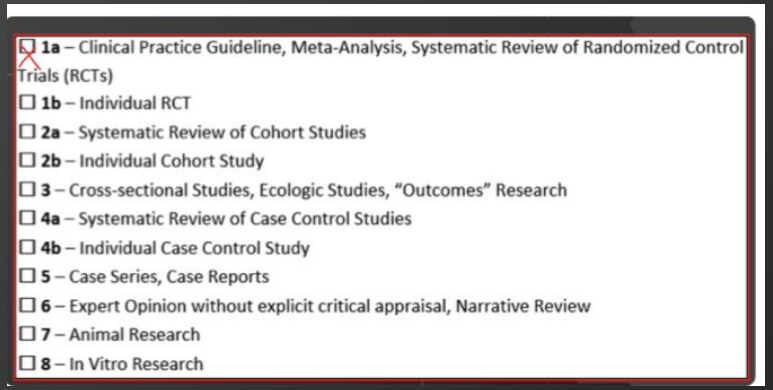
- **Conclusions:** The studies included were carried out on different artificial saliva products and therefore it is challenging to reach a definite conclusion. Although published studies suggest that all tested products reduced signs and symptoms of xerostomia.
  - Herbal products were reported to show more improvement than artificial saliva in radiation-induced
  - Oral Spray and 3% citric acid provided long-lasting effect on drug-induced xerostomia
  - Products that improved dryness and symptoms during swallowing and speaking were OMJ, oral spray and aqueous formulation

- **Limitations:**
  - The review was limited to the last 10 years and to the english language. Also mentioned that the review may be subject to publication bias.
  - Patient satisfaction is an important consideration. Therefore crossover trials, a design that allows more efficiency in determining patient preferences would be appropriate.

Article 3 Selection

- **Reason for selection:** It relates to the PICO question
- **Applicability for the patient:** Patient has many health concerns and changing medications might be hard for her. Supplying her with an artificial saliva substitute could be the best option.
- **Implication:** Treatment for xerostomia needs to be on a case to case basis, comparing one artificial saliva substitute to the next has shown to be difficult.

Levels of evidence



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Conclusion & Advisement to D4

For patients with dry mouth, a systematic and multifactorial management strategy between the dentist, physician and the patient should be used. To start, a detailed health history will facilitate early detection and underlying causes if the problem is not known. Second, collaboration with the physician should include the patient's condition and medication use. Third, preventative measures recommended by the dentist should include salivary stimulants, fluoride interventions, and awareness of increased oral hygiene need. Lastly, the patient needs to stay on top of their oral hygiene and be active in the treatment process too. This multifactorial approach will all help to alleviate symptoms for the patient and prevent dental caries, periodontal disease, halitosis, and candidiasis. It needs to be done on a case to case basis, because not every dry mouth patient will respond the same.

Conclusions - D4

Patients are living longer and are taking more medications.

Medication-induced xerostomia is becoming more common and has significant dental consequences.

More than 3 million new cases of Sjogren's per year worldwide and there is no cure. 90% of these cases are women

Primary and secondary options exist for treating patients suffering from a dry mouth.

Discussion Questions:

In the older population polypharmacy is common. With this in mind which medications have alternatives to prevent xerostomia from occurring in these patients?

What are some ways to increase salivary flow in patients who suffer from medication induced xerostomia?

How likely is it for a patient to experience xerostomia prior to introduction of medications?

Up to 20% of elderly