Treatment Considerations with Xerostomia

Evidence Based Dentistry Rounds

Emergency

Group 6

B1

21 October 2020

Rounds Team

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Patient

- 66 year old Caucasian female
- “My teeth are falling apart. I don’t want to lose them, but I just get new cavities all the time and my teeth keep breaking.”
- Patient has history of extensive restorative work and is not limited by finances

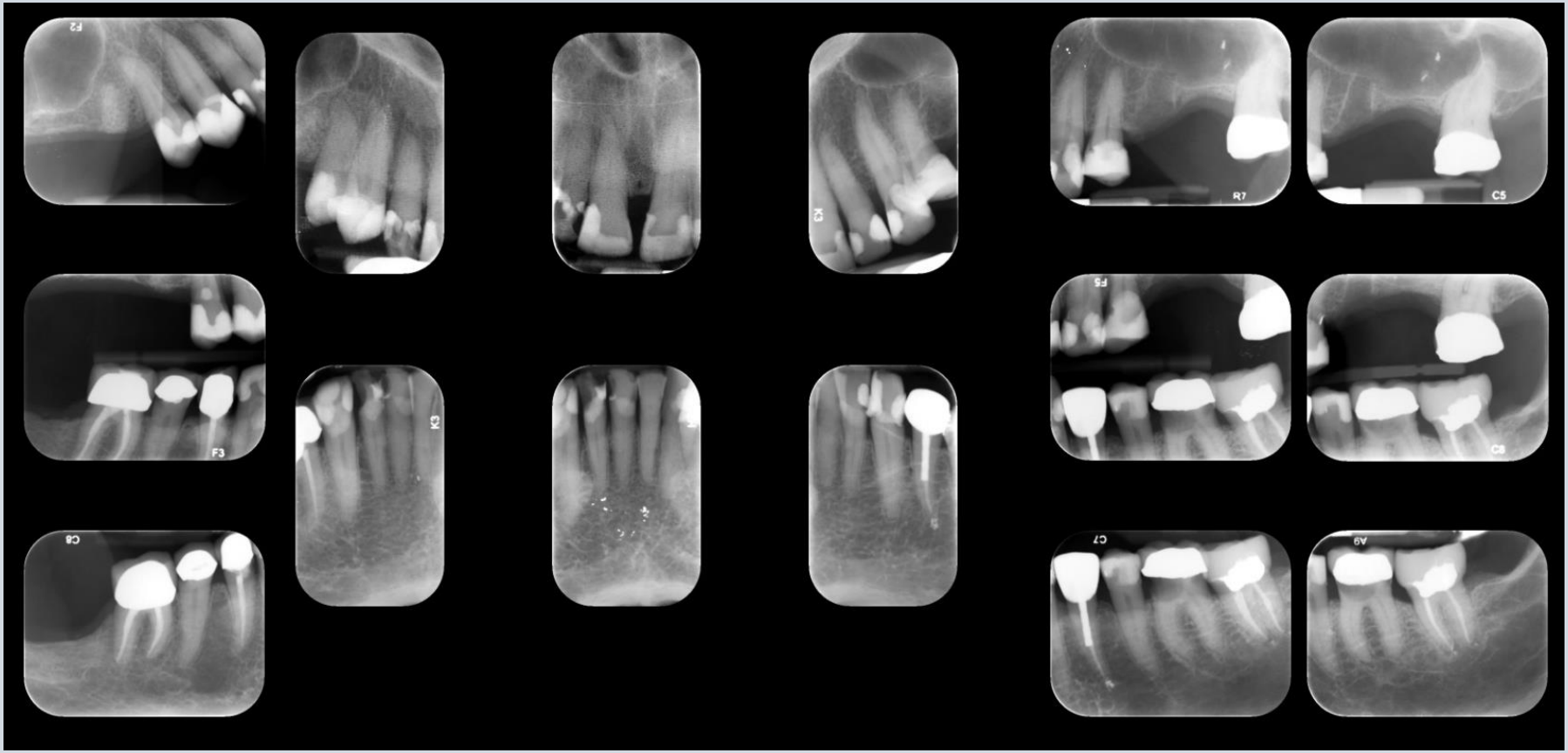
Medical History

- History of double hip replacement
  - Cephalexin for premedication
- Hypertension
  - Patient is prescribed Carvedilol
- Patient sees psychiatrist for depression
  - Prescribed Lexapro and Clonazepam
- Patient also takes a multivitamin, Vitamin B12, Vitamin D, and Zyrtec
- Medical consults were sent out to both the patient's cardiologist and psychiatrist for the medications Carvedilol and Lexapro
  - Both medications have xerostomia as a known side effect
- Patient is slightly xerostomic

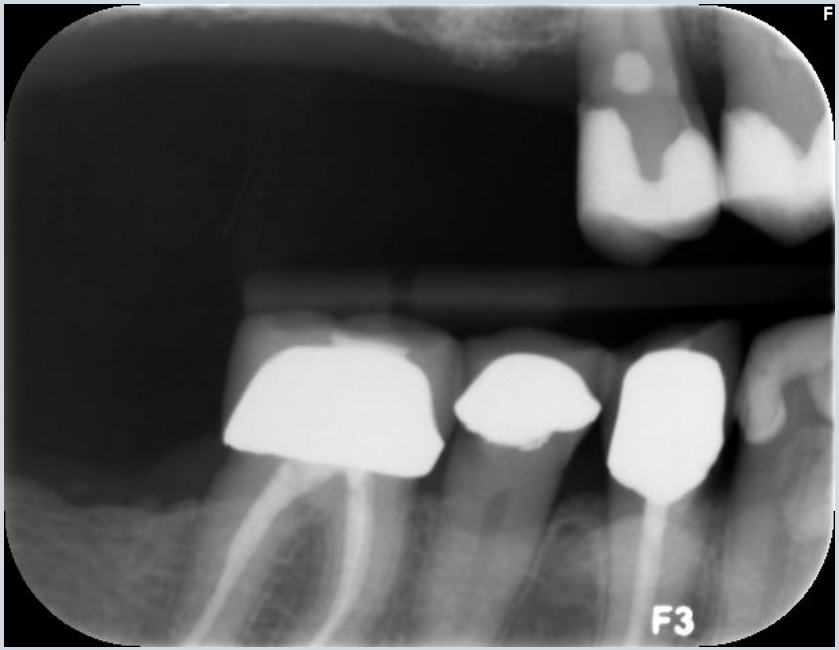
Dental History

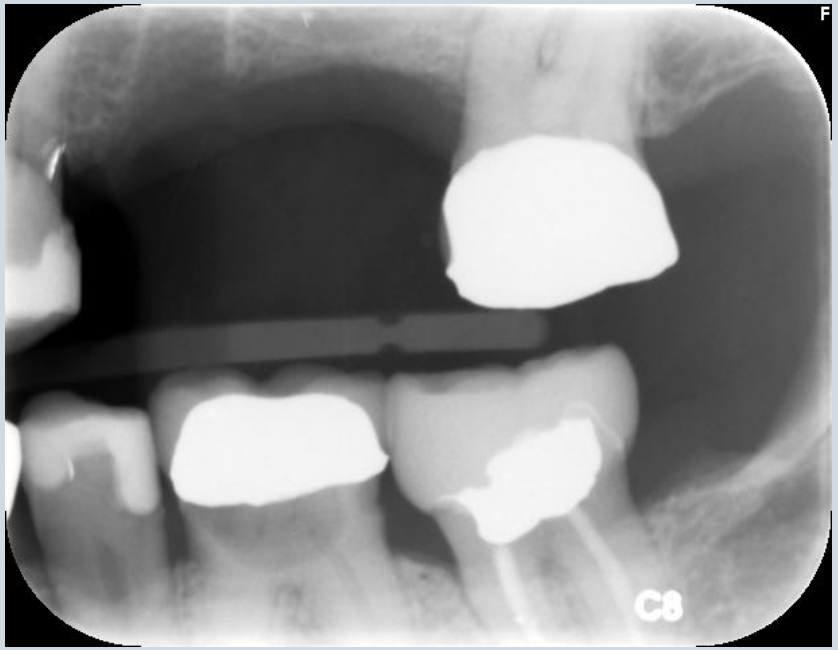
- Missing teeth: #1, 2, 3, 4, 13, 14, 16, 17, 31, 32
- Composite restorations (generalized large restorations): #5, 6, 7, 8, 9, 10, 11, 12, 20, 22, 23, 25, 26, 27
- PFM crown: #15, 19, 21, 28, 29, 30
- Ceramic crown: #18
- RCT: #18, 21, 28, 30
- Patient has history of irregular dental visits

Radiographs



Radiographs





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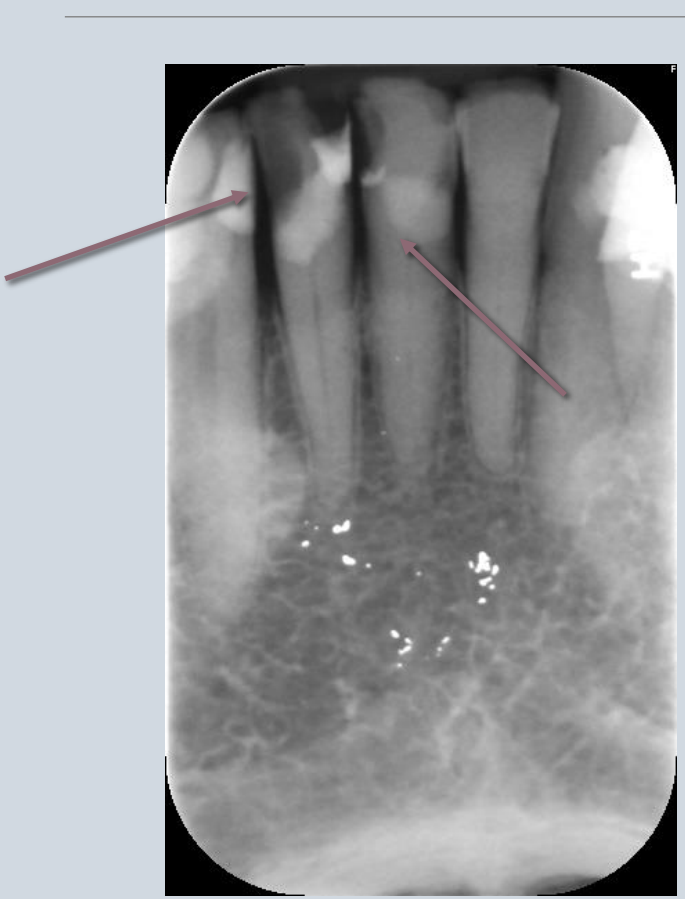
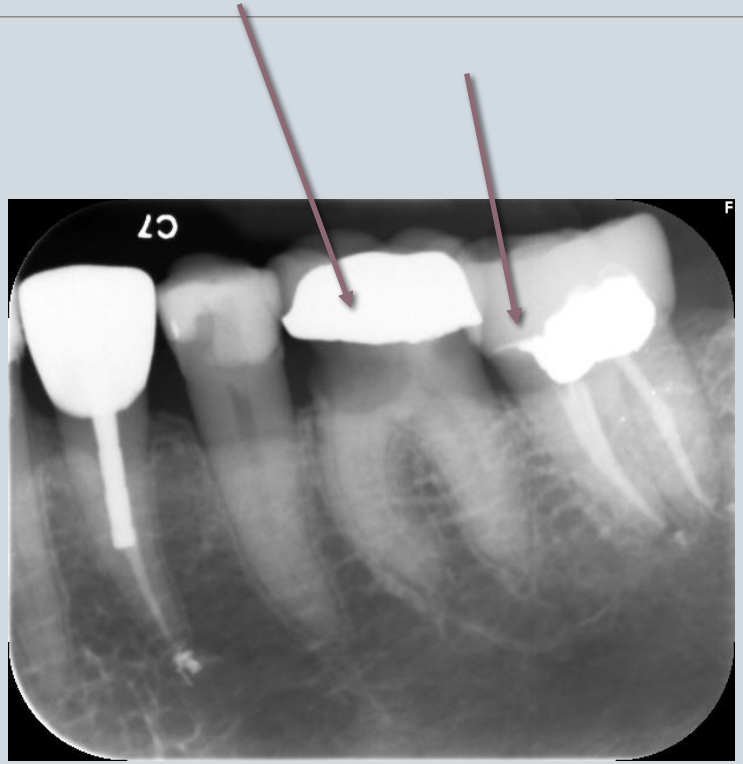


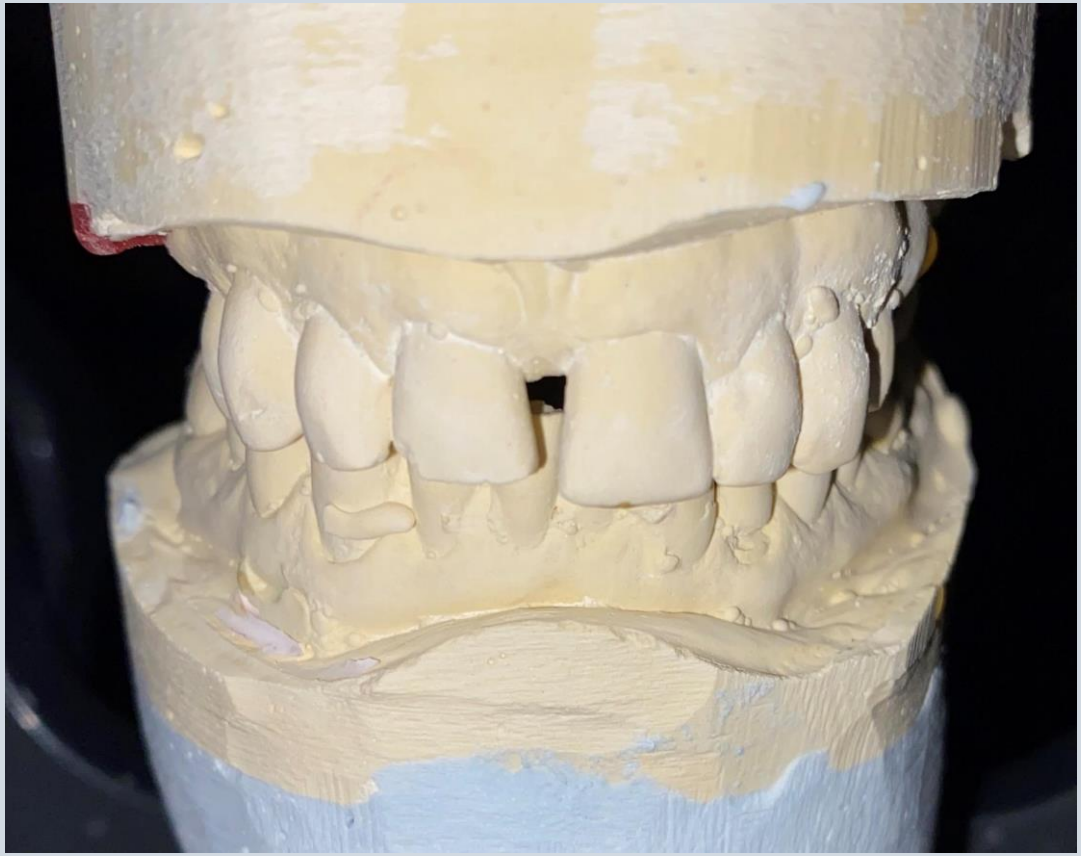


Radiographic Findings

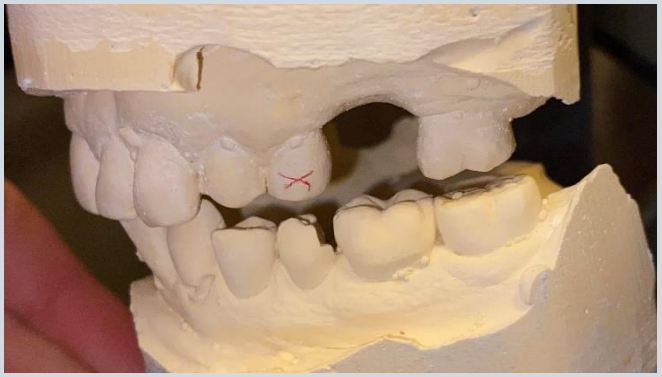
- FMX taken 10/5/2020
- Recurrent decay: #8, 10, 11, 12, 14, 20, 22, 23, 28, 29, 30
- Gross decay: #7, 18, 19, 25, 26

Clinical Findings

- Patient has decreased VDO
- History of extractions
- Clinically visible caries
- Xerostomia
- Heavily restored dentition



Clinical Findings



Specific Findings

- Patient has severe generalized caries that escalated over COVID-19 break
  - 9 new carious lesions between March and August 2020
    - One of which had been restored within the last 12 months
- Patient noted feelings of dry mouth which has coincided with the findings of generalized decay.
- Patient has healthy gingiva with no BOP indicating that the caries may be due external to lack of home care

Periodontal Charting

																MOBILITY
														2		FURCA
				P	P P	P	P	P		P P P	P P	P P		P		PLAQUE
																BOP
				5 5 5	6 6 6	7 7 7	7 7 7	7 7 7	7 7 7	7 7 7	5 5 5	6 6 6		5 5 5		MGJ
				3 3 4	3 3 3	3 3 3	3 2 2	2 2 3	3 3 2	3 2 3	3 2 3	3 2 2		4 3 3		CAL
				3 2 4	3 1 3	3 2 3	3 2 2	2 2 3	3 2 2	3 2 3	3 2 3	3 2 2		2 2 2		P.D.
				0 1 0	0 2 0	0 1 0	0 0 0	0 0 0	0 1 0	0 0 0	0 0 0	0 0 0		2 1 1		FGM
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				0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0		2 1 1		FGM
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				2 2 2	3 1 3	3 1 1	2 1 2	2 1 2	1 1 2	2 1 2	1 2 2	2 2 2		3 3 3		CAL
																MGJ
																BOP
				P P	P P		P	P		P P	P P	P P P				PLAQUE
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																PROGNOSI
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																BOP
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		2 1 3	2 2 3	2 1 3	2 2 2	2 2 2	2 1 2	2 1 2	2 1 2	3 2 3	2 2 2	3 2 2	3 3 3	3 3 2		CAL
		2 1 3	2 2 3	2 1 3	2 2 2	2 2 2	2 1 2	2 1 2	2 1 2	3 2 3	2 2 2	3 2 2	2 2 2	3 3 2		P.D.
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32	31	30	29	28	27	26	25	24	23	22	21	20	19	18	17	
		1 0 0	0 1 1	0 1 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	1 3 1	0 0 0	1 2 1	1 1 1	0 0 0		FGM
		3 1 2	3 2 4	4 2 4	3 1 2	2 1 2	2 1 2	2 1 2	2 1 2	3 2 2	2 1 2	2 1 2	2 2 2	3 3 3		P.D.
		4 1 2	3 3 5	4 3 4	3 1 2	2 1 2	2 1 2	2 1 2	2 1 2	4 5 3	2 1 2	3 3 3	3 3 3	3 3 3		CAL
		6 6 6	5 5 5	4 4 4	4 4 4	4 4 4	4 4 4	4 4 4	3 3 3	4 4 4	4 4 4	5 5 5	5 5 5	3 3 3		MGJ
																BOP
			P	P P	P P	P P	P P	P P	P P	P P	P P	P P				PLAQUE
													1	2		FURCA
																MOBILITY

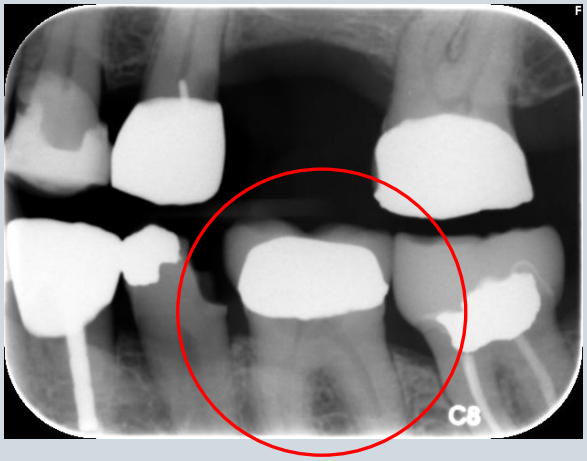
Diagnosis

- Patient was diagnosed with severe generalized caries and xerostomia

Problem List

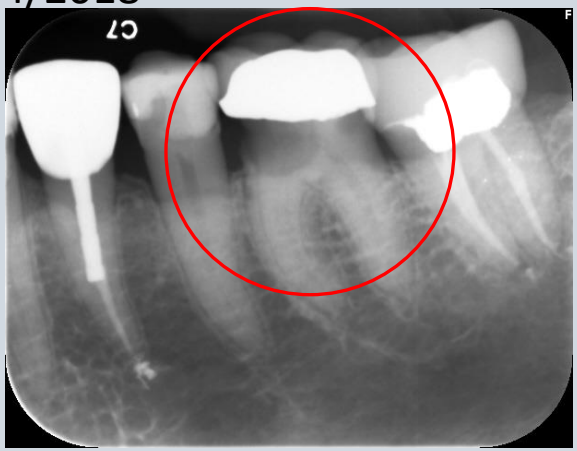
- Generalized rampant caries
- Xerostomia

9/24/2018



9/30/2019

1/27/2020



10/5/2020

Salivary Glands & Their Secretions

Parotid Gland:

Located on each side of the head in front and below the external auditory canal

Largest of the three glands in terms of size

- Responsible for roughly 20% of saliva secreted into the oral cavity

Composed entirely of Serous Acinar Cells that secrete Serous Fluid

Serous Fluid- thin, aqueous, and rich in amylase

- Begins chemical digestion of Carbohydrates in the mouth

Submandibular Gland:

Located in the Submandibular Triangle of the neck posterior to the insertion of the mylohyoid muscle

Responsible for the greatest amount of saliva production and secretion in the oral cavity

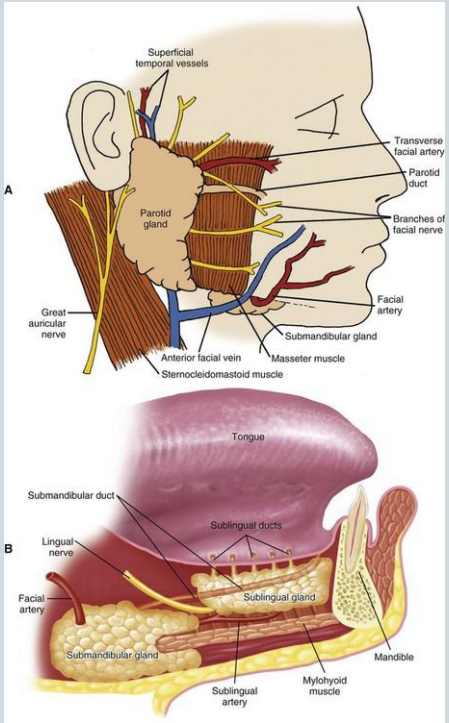
- Roughly 65%

Composed of a mixture of Serous and Mucous Acinar Cells

Mucus- Primarily functions to lubricate the bolus and keep the mouth moist

Sublingual Gland:

- Located on the deep floor of the mouth
- Smallest of the three glands in terms of size and salivary output
  - Approximately 5% or less of total saliva secreted in the oral cavity
- Contains a mixture of Mucous and Serious Acinar cells
  - However, the vast majority of are mucous cells



De Paula, F., Teshima, T., Hsieh, R., Souza, M., Nico, M. and Lourenco, S., 2017. Overview of Human Salivary Glands: Highlights of Morphology and Developing Processes. *The Anatomical Record*, 300(7), pp.1180-1188.

Pocket Dentistry, 2020. *Major Salivary Glands*. [image] Retrieved from https://pocketdentistry.com/11-salivary-glands.

Porcheri, C. and Mitsiadis, T., 2019. Physiology, Pathology and Regeneration of Salivary Glands. *Cells*, 8(9), p.976.

How do Salivary Glands Function?

Salivary glands are innervated densely by both branches of the Autonomic Nervous System that ultimately controls the amount of saliva produced

A unique feature of this double innervation is that both Sympathetic and Parasympathetic stimuli increases the amount of Saliva secreted

- The differences between the two stimuli is the composition of the saliva that is secreted upon stimulation

Stimulation of M1 and M3 receptors on acinar cells from the Parasympathetic Nervous system (via acetylcholine) tends to produce a high-flow, fluid rich saliva that can travel through the ductal cells into the mouth

- Remember, 'rest and digest'- parasympathetic input is high at times of resting secretion as well as during digestion in the oral cavity
- The movement of water to form saliva is the result of the movement of a number of ions (Calcium, Sodium, and Chloride) upon stimulation that ultimately allows water to enter the cells via osmosis

Stimulation of Beta-adrenergic receptors on acinar cells via the Sympathetic nervous system tends to produce a low-flow, high protein saliva that has a high mucus content

- Proteins enter saliva via the fusion of secretory granules to acinar cells upon sympathetic stimulation

Reflex pathways also play an important role in the secretion of saliva

- Receptors such as mechanoreceptors are stimulated upon mastication
- Activation of these receptors on the Periodontal Ligament will relay input to salivations centers in the brain and induce the secretion of saliva that will aid in both the moistening of the bolus and chemical digestion of carbohydrates

Olfactory (smell), gustatory(taste), and nociceptors (pain) also increase saliva production upon stimulation and relaying of input via the reflex pathways to the brain

D2 – Pathology

Question: What is xerostomia?

- *Subjective feeling of a dry mouth*
  - Objectively measured by reduced salivary flow (hyposalivation)
- Functions of saliva:
  - Mastication, swallowing, speech
  - Digestion
  - Antibacterial action
  - Buffering
  - Mechanical debridement

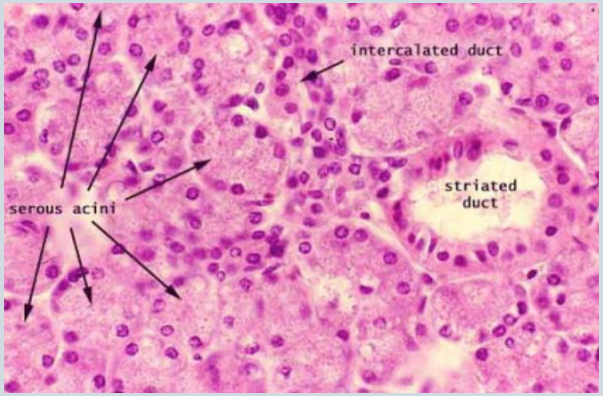
Reference citation(s):
Frydrych AM. Dry mouth: xerostomia and salivary gland hypodunction. Aust Fam Physician. 2016 Jul; 45(7): 488-92.
Rawal Y. Salivary glands. Marquette University School of Dentistry. Oral Biology I. 27 April 2020; 16-50.
Villa A, Connell CL, Abati S. Diagnosis and management of xerostomia and hyposalivation. Ther Clin Risk Manag. 2014 Dec 22; 11: 45-51.

D2 – Pathology

What is xerostomia?

- Secretory cells called acini decrease in volume with age
  - Gradually replaced with adipose tissue and fibrous tissue
  - Results in *hyposalivation*

	Normal Flow	Hyposalivation
Stimulated	1 – 3 mL/min	0.3 – 0.4 mL/min
Unstimulated	< 0.5 mL/min	< 0.1 mL/min



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D2 – Pathology

What is xerostomia?

- Etiology:
  1) Medications
  2) Radiation to the head and neck
  3) Systemic diseases and disorders
- Treatment:
  - Assess underlying cause
  - Alleviate symptoms
  - Stimulate secretions

Reference citation(s):
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D3
PICO

Clinical Question: What are the most effective interventions for xerostomia?

PICO Format

P: Patients with xerostomia

I: Pharmacotherapy

C: Patients receiving no treatment for xerostomia

O: Improvement in treatment outcome

PICO Formatted Question

In patients with xerostomia, is there a difference in treatment prognosis with pharmaceutical interventions?

Clinical Bottom Line

The patient has xerostomia and we want to provide the patient with the most successful treatment, but don’t want the patient’s xerostomia to impinge on the success of her treatment.

Search Background

- Date(s) of Search: 10/11/2020
- Database(s) Used: PubMed
- Search Strategy/Keywords: Visited PubMed and found a list of MeSH terms relevant to my topic. After doing initial research, I found that pilocarpine was a relatively new and popular pharmacotherapeutic used to treat xerostomia. MeSH terms were inputted and the search results were filtered to results within 5 years to get the most recent research. Articles were also picked based on quality of evidence and reliability.

Search Background

- MESH terms used:
  - Xerostomia
  - Therapeutics
  - Pilocarpine
  - Drug therapy

Article 1 Citation, Introduction

- Citation: Gil-Montoya, J-A et al. “Treatment of xerostomia and hyposalivation in the elderly: A systematic review.” *Medicina oral, patologia oral y cirugia bucal* vol. 21,3 e355-66. 1 May. 2016, doi:10.4317/medoral.20969

- Study Design: Systematic review of RCT

- Study Need / Purpose: The goal of this study was to investigate the latest pharmacological and non-pharmacological treatments for dry mouth in older individuals, regardless of the cause of the problem.

Article 1 Synopsis

Method: The literature was searched in March 2015 using Medline and Embase databases. Clinical trials from 2006 to March 2015 were included in the filtering process. MeSH terms xerostomia or Dry Mouth Syndrome, and Elderly Aged were used. Assessment of article quality and criteria for inclusion were based on PRISMA and the "Oxford Quality Scale." The studies were then divided into 3 categories. The categories were clinical trials testing pilocarpine or cevimeline, clinical trials using non-pharmacological intervention or artificial saliva, and clinical trials using alternatives like acupuncture or elector-stimulation. The initial search yielded a total of 9,275 references and using the selection and quality criteria, 26 trials were deemed acceptable to be used in this review. 14 were related to pharmacological drug treatments, 10 were non-pharmacological, and 2 were alternative treatment.

Results: Based on the results of the randomized control trials used in the review, the effectiveness of different therapeutic interventions used to treat xerostomia aren't effective enough to recommend one treatment over the other, whether pharmacological or not. In xerostomia caused by irradiation or Sjogren's Syndrome, pilocarpine seemed to give the best results whether swallowed, dissolved in the mouth or in mouth rinses. None of the studies examined the adverse effects of pilocarpine probably due to the short follow-up period. In xerostomia caused by medications alone, there were some positive indications for the use of malic acid with fluoride and xylitol to counteract the harmful effects on dental enamel.

Article 1 Synopsis

- Conclusions: Moving forward, more trials must be carried out, with crossover designs, larger sample sizes and long-term monitoring.

- Limitations: Lack of studies that show clinical effectiveness.

Article 1 Selection

- High level of evidence and recently published.
- Our patient has xerostomia and we are looking to treat with pharmacotherapeutics.
- The evidence isn't convincing that pharmacotherapeutics will be clinically effective in treating our patient. None of the treatment options stood out as effective.

Levels 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)

☒	**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 Citation, Introduction

- Citation: Riley, Philip et al. “Pharmacological interventions for preventing dry mouth and salivary gland dysfunction following radiotherapy.” *The Cochrane database of systematic reviews* vol. 7,7 CD012744. 31 Jul. 2017, doi:10.1002/14651858.CD012744

- Study Design: Systematic review of RCT

- Study Need / Purpose: The purpose of this systematic review of RCT was to assess the effects of pharmacological interventions for the prevention of radiation-induced xerostomia.

Article 2 Synopsis

Method: Cochrane Oral Health's Information Specialist searched a large number of databases. Randomized controlled studies were included in the selection process. Participants of all ages, ethnic origins, and genders were included in the evaluation. Pharmacological therapy prescribed prophylactically or during treatment were included. A total of 39 studies were included.

Results: Based on this study, low quality evidence was shown for effective treatment with amifostine compared to placebo or no treatment. Insufficient evidence was shown for effective treatment of pilocarpine compared to placebo or no treatment. Some low-quality evidence suggested that pilocarpine might be associated with an increase in sweating. There is some low-quality evidence to suggest that amifostine can lessen the feeling of dry mouth in radiotherapy patients in the short and medium term.

Article 2 Synopsis

- Conclusions: More research needs to be done with these pharmacotherapeutics in the long term. There was little evidence to suggest any of these pharmacotherapeutics are beneficial in treating the effects of xerostomia.

- Limitations: Lack of studies that show clinical effectiveness. Need more studies looking at pharmacotherapeutic options to treat xerostomia.

Article 2 Selection

- High level of evidence and recently published.
- Our patient has xerostomia and we are looking to treat with pharmacotherapeutics.
- The evidence isn't convincing that pharmacotherapeutics will be clinically effective in treating our patient.

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Article 3 Citation, Introduction

- Citation: Li KX, Loshak H. “Pilocarpine for Medication-induced Dry Mouth and Dry Eyes: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines [Internet].” *Ottawa (ON): Canadian Agency for Drugs and Technologies in Health*; 2019 Dec 11.

- Study Design: Systematic review of RCT

- Study Need / Purpose: The purpose of this study was to examine recent literature regarding clinical effectiveness and cost effectiveness of pilocarpine in treating psychoactive medication induced dry mouth and dry eyes.

Article 3 Synopsis

Method: A literature search was carried out by an information specialist on databases including Embase, Cochrane Library, and Medline among others. Literature was limited to publication between January 1, 2009 and November 25, 2019. MeSH terms included xerostomia, pilocarpine, and dry eyes. Studies had to meet a list of inclusion criteria.

Results: The authors of this study were not able to find any studies regarding the clinical effectiveness or cost effectiveness of pilocarpine in treatment of psychoactive medication induced dry mouth and dry eyes.

Article 3 Synopsis

- Conclusions: More studies must be carried out in order to gain knowledge on clinical and cost effectiveness of pilocarpine.

- Limitations: Lack of studies that show clinical effectiveness. More studies need to be carried out on drug induced xerostomia and pharmacotherapeutic treatment.

Article 3 Selection

- High level of evidence and recently published.
- Our patient has xerostomia and we are looking to treat with pharmacotherapeutics.
- The evidence isn't convincing that pharmacotherapeutics will be clinically effective in treating our patient.

Levels of Evidence

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Article 4 Citation, Introduction

- Citation: Tanasiewicz M, Hildebrandt T, Obersztyn I. Xerostomia of Various Etiologies: A Review of the Literature. Adv Clin Exp Med. 2016 Jan-Feb;25(1):199-206. doi: 10.17219/acem/29375. PMID: 26935515.

- Study Design: Narrative review

- Study Need / Purpose: This paper gave some of the main causes, clinical manifestations, evaluation methods, and treatments of xerostomia.

Article 4 Synopsis

Method: Review current literature on xerostomia and its treatment.

Results: In terms of treatment of medication based xerostomia, focus is on eliminating the medications that are the cause. Amifostine has been found to be useful in patients with xerostomia caused by radiation therapy. However, different studies have found conflicting evidence. Some have found very high clinical effectiveness while others have only found placebo type effects depending on the patient. Pilocarpine has been shown to induce saliva secretion through parasympathetic influences. It has an affinity for muscarinic receptors M1 and M3, which lead to increased saliva secretion in peripheral tissues. Pilocarpine is contraindicated in some patients with drug induced xerostomia. Cevimeline is another agent used to treat xerostomia with high affinity for muscarinic receptors M1 and M3. It is effective in treating head and neck radiation patients.

Article 4 Synopsis

- Conclusions: This paper concluded that the treatment of xerostomia whether from head and neck radiation, Sjogren's syndrome, medication, or aging, is long term and demanding. Treatment requires a high level of patient motivation.

- Limitations: This study doesn't offer a very high level of evidence.

Article 4 Selection

- This narrative review was a fairly comprehensive paper from authors in the field of dentistry. Although not a high level of evidence, it gives the etiology, clinical manifestations, evaluation, and treatment of xerostomia. Pharmacotherapy used to treat xerostomia is a relatively new phenomenon, so high levels of evidence advocating for its clinical effectiveness are limited.
- Our patient has xerostomia and we are looking to treat with pharmacotherapeutics.
- The evidence isn't convincing that pharmacotherapeutics will be clinically effective in treating our patient.

Levels of Evidence

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☒	**C** – Consensus, disease oriented evidence, usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening

Conclusions: D3

The available evidence to support the use of pharmacotherapeutics for the treatment of xerostomia as a result of multiple causes is weak at best. All four of the studies came to a similar basic conclusion that pharmacotherapeutics could possibly be beneficial in treating xerostomia, but more extensive research needs to be carried out before definitive recommendations can be given to patients. I would recommend the use of more traditional palliative treatment for this case. Examples of such treatment could include gels, aerosols/sprays, oral rinses, or chewing gums.

Conclusions: D4

- Recommended the patient increase water intake especially during working hours
- Recommended patient purchase sugar-free lozenges containing xylitol for throughout the day
- Referred patient to faculty practice to receive more rapid care in hopes of saving more of her dentition than I would have been able to given the current COVID-19 situation

Discussion Questions

- What is the preferred standard treatment of xerostomia?
- What are the common risk factors that put patients at risk for xerostomia?
- What are the common side effects to the preferred method to treating xerostomia?
- What common pharmaceuticals can cause xerostomia as a side effect?

Discussion Questions

- How does xerostomia affect the overall caries progression in the dentition?
- What is the best pharmaceutical intervention for treatment of xerostomia?
- What are home remedies to recommend to patients with xerostomia?
- What are the long-term effects of xerostomia if gone untreated?

THANK YOU