Dry mouth (xerostomia and hypofunction)

Prof. Mike Brennan - Carolinas Medical Center, USA

Dry Mouth
(Xerostomia and Hypofunction)

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Course objectives

- Define and describe the different causes of dry mouth
- Define and describe how to diagnose dry mouth
- Define and describe oral manifestations of dry mouth
- Describe management strategies for dry mouth

Production of saliva

- Healthy adult produces 1.5 L of saliva in 24 hours
- 3 major pairs of salivary glands
  - Parotid
  - Submandibular
  - Sublingual
- Minor salivary glands
  - Approximately 750
  - Not located in the gingiva or anterior hard palate

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Production of saliva

- Percentage of saliva production
  - Sublingual 5%
  - Parotid 45%
  - Submandibular 45%
  - Minor salivary glands 5%

- The sublingual and minor salivary glands produce the majority of mucous secretions

- Salivary hypofunction
  - UWS: <1.5 ml in 15 min
  - SWS: <10.5 ml in 15 min

Salivary gland physiology

- Acinar cells initially secrete an isotonic fluid (140mEq/L NaCl)
  - Contains 85% of the exocrine salivary proteins

- As saliva passes through ductal tissue, reabsorption of NaCl (and water) follows
  - Results in a hypotonic (20mEq/L NaCl) saliva
  - Ductal cells contribute 15% of remaining salivary proteins

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Salivary gland physiology

- Autonomic control of secretion
  - Parasympathetic stimulation responsible for secretory function
  - Sympathetic stimulation responsible for protein secretion
  - If block parasympathetic innervation, glandular atrophy occurs
  - Blocking sympathetic innervation has little effect on the glands

  Main medications target the parasympathetic system to increase salivary secretion

Salivary gland hypofunction and xerostomia

- Definition
  - Salivary gland hypofunction is a decrease in salivary secretion
    - ≤ 0.1 ml/min for unstimulated whole salivary flow
    - ≤ 0.7 ml/min for stimulated whole salivary flow
  - Xerostomia is defined as the subjective complaint of dry mouth

Causes of hyposalivation

- Proposed mechanisms for hyposalivation include:
  - Neurotransmitter receptor dysfunctions (e.g. medications)
  - Radiation-induced cellular DNA damage
  - Salivary gland parenchymal destruction
  - Immune dysregulation that may interfere with secretory processes
  - Alterations of fluid and electrolytes (dehydration)
  - Combinations of the above
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**Medication-induced xerostomia**

- >1500 medications have been implicated as causing xerostomia
- 80% of the most commonly prescribed medications have been reported to cause xerostomia
- Xerostomic drugs can be found in 42 drug categories and 56 sub-categories
- Med use increases with age
  - > 75% of persons aged ≥ 65 taking at least one prescription medication

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**Medication-induced xerostomia**

- Drugs commonly associated with dry mouth drugs which directly damage salivary glands
  - Anti-neoplastic agents
- Drugs with anticholinergic activity
  - Agents such as atropine and scopolamine
  - Antireflux agents, e.g., proton-pump inhibitors
  - Tricyclic antidepressants
  - Selective serotonin reuptake inhibitors
  - Benzodiazepines
  - Opioids
  - Antihistamines
  - Antipsychotics

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**Medication-induced xerostomia**

- Drugs acting on sympathetic system
  - Drugs with sympathomimetic activity (e.g., ephedrine)
  - Antihypertensive; alpha 1 antagonists (e.g., terazosin and prazosin) and alpha 2 agonists (e.g., clonidine)
  - Beta blockers (e.g., atenolol, propranolol) also change salivary protein levels
- Drugs which deplete fluid
  - Diuretics
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Radiation therapy

- External beam radiation therapy
  (head and neck, mantle, whole body)
  - Conventional RT
  - IMRT
  - 3D-CRT
- Radioiodine therapy (131I)

Xerostomia during and after radiotherapy

![Graph showing prevalence of xerostomia over time for different RT therapies]

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Xerostomia during and after radiotherapy

![Graph showing prevalence of xerostomia over time for different RT therapies]

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**Salivary flow rate during and after radiotherapy**

- Unstim. whole saliva
- Stim. whole saliva

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**Sjögren’s syndrome**

- * > (9:1)
- Age: mid 50’s
- Increased risk of developing lymphoma

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**Revised international criteria for Sjögren's syndrome**

I. Ocular symptoms
II. Oral symptoms
III. Ocular signs
IV. Histopathology
V. Salivary gland involvement
VI. Autoantibodies

*Exclusions: H/O H&N RT, HCV, HIV, GVHD, pre-existing lymphoma, use of anti-cholinergic drugs

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Revised international criteria for Sjögren's syndrome

I. Ocular symptoms
1. Daily, persistent, troublesome dry eyes for >3 months?
2. Recurrent sensation of sand or gravel in eyes?
3. Use tear substitutes >3 times a day?

II. Oral symptoms
1. Daily feeling of dry mouth for >3 months?
2. Recurrent or persistent swollen salivary glands?
3. Frequently drink liquids to ease swallowing?

Salivary gland biopsy
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Peri-lymphocytic infiltrate

- Infiltrate in minor salivary gland is scored by a focus score
- A focus score of 1 indicates at least 50 lymphocytes are clumped around the ducts
- The focus score in this image is 2

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- No recognizable acinar tissue remains
- Ducts are still present
- Focus score is close to 12

Salivary flow test

- No drinking 1.5 hrs prior to test
- Afterwards patient will spit in the tube for 5-15 min
- Tube is then weighed to determine flow rate based on collection time

Schirmer's test

- Schirmer's test measures lacrimal flow
- When the measure is < 5 ml/5 min = low lacrimal flow

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Extraglandular manifestations

• Dryness of other mucous membranes
• Inflammation of other organ systems
  o Digestive system, kidneys, liver, lungs, thyroid, nervous system, BVs
• Signs/symptoms
  o Fatigue
  o Muscle and joint pain
  o Nausea
  o Difficulty swallowing
  o Heartburn

The end results of the pathologic process in the salivary glands in Sjögren's syndrome are reduction in functional acinar tissue, a loss of secretory output, and symptoms of oral dryness.

Function of saliva

Teeth

Buffer
  Bicarbonate Phosphate Proteins

Protect from demineral.
  Mucins Ca²⁺ Phosphate

Remineral.
  PRPs Statherin Ca²⁺ Phosphate

Lubrication
  Mucins PRG

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Function of saliva

- Food
  - Bolus formation
  - Taste
  - Digestion
    - Mucins
      - Water
    - Gustin
      - Zn^{2+}
      - Water
    - Amylase
      - Protease
      - Lipase
      - DNase
      - RNase

Function of saliva

- Microorganisms
  - Anti-viral
    - Cystatin
    - Mucins
    - ImmunoGI
    - SLPI
  - Anti-fungal
    - Histatins
    - Chromogranin A
    - ImmunoGI
  - Anti-bacterial
    - Cystatins
    - Histatins
    - VEGf
    - SLPI
    - Lysozyme
    - Lactoferrin
    - Calprotectin
    - Lactoperoxidase
    - ImmunoGI
    - Chromogranin A

Function of saliva

- With low saliva one is more prone to develop various problems e.g. with taste or increased infections (viral, bacterial and fungal)
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Clinical features of salivary gland hypofunction

- Oral hard and soft tissue signs
- Salivary signs

Tooth decay in low salivary flow patients

Tooth decay in low salivary flow patients

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Tooth decay in low salivary flow patients

Soft tissue effects of salivary hypofunction

- Mucosal dryness and atrophy
- Increased infections
  - fungal, bacterial
- Loss of papillation or furrowing of tongue

Dry tissues

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Fungal infection

Angular cheilitis

Loss of papillae

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Salivary signs of salivary hypofunction

- Diminished secretions on palpation
- Thicker, opaque, or viscous secretions
- Recurrent salivary gland infection
- Enlarged salivary glands

Thicker, opaque or viscous secretions

Salivary gland infection

Caused by retrograde bacterial infection

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Other clinical features of salivary gland hypofunction
- Difficulties chewing, swallowing and speaking
- Altered or diminished taste acuity
- Compromised nutrition
- Burning sensation

Symptoms of salivary hypofunction
- Dryness when eating meals
- Difficulty swallowing dry foods
- A need to drink fluids when swallowing dry foods
- The impression of too little saliva

Management strategies for salivary hypofunction

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Palliation

- Water
- Water
- Water

+ Saliva stimulation

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Palliation

- Increased humidity
- Oral rinses
- Hydrating emollients
- Saliva stimulation with functional saliva
- OTC vs. prescription products

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Prescription medications

- FDA approved medications for dry mouth
  - Cevimeline (Evoxac\textsuperscript{R}) 30mg TID
  - Pilocarpine (Salagen\textsuperscript{R}) 5 (7.5)mg QID

Patient can try medication once a day and if tolerated increase dosage

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Side effects are common with both pilocarpine and cevimeline due to widespread exocrine stimulation

- Sweating
- Urinary urgency
- Flushing
- GI upset

Often have patient try OTC dry mouth medication first

Management approaches: hard tissues

- Fluoride (sodium f, acidulated phosphate f, stannous f, silver diamine f)
  - OTC
  - Prescription
- Amorphous calcium phosphate (ACP)
- Limit sugar intake
- Oral hygiene
- Frequent dental visits
- Chlorhexidine
- Xylitol artificial sweetener

Management approaches: soft tissues

- Anti-fungals
- Burning sensation
  - Hematinic deficiency (Tx: replacement)
  - Fungal (Tx: anti-fungals)
  - Burning mouth syndrome (Tx: meds)
  - Burning sensation is often due to friction of the mucosa due to the low salivary flow

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A combination of these approaches is often necessary for successful management of xerostomia and the oral manifestations from salivary dysfunction.

Thank You!