

# Adverse Effects of Medications on Oral Health

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# Objectives

- Describe the pathophysiology of various medication-related oral reactions
- Recognize the signs and symptoms associated with medication-related oral reactions
- Identify the populations associated with various offending agents
- Compare the treatment options for medication-related oral reactions

# Medication-related Oral Reactions

- **Stomatitis**
- Burning mouth syndrome
- Glossitis
- Erythema  
Multiforme
- Oral pigmentation
- Tooth discoloration
- Black hairy tongue
- Oral Candidiasis
- Gingival hyperplasia
- **Alterations in salivation**
- **Alterations in taste**
- **Halitosis**
- Angioedema

# Medication-related Stomatitis

- Clinical presentation
  - Aphthous-like ulcers, mucositis, fixed-drug eruption, lichen planus<sup>1,2</sup>
  - Open sores in the mouth
    - Tongue, gum line, buccal membrane
  - Patient complaint of soreness or burning



<http://www.virtualmedicalcentre.com/diseases/oral-mucositis-om/92> 0



<http://www.virtualmedicalcentre.com/diseases/oral-mucositis-om/920>

# Medication-related Stomatitis

- Offending agents<sup>1,2</sup>

Medication	Indication	Patient Population
Aspirin	<ul style="list-style-type: none"> <li>• Heart health</li> <li>• Pain reliever</li> </ul>	<ul style="list-style-type: none"> <li>• &gt;18 years old</li> <li>• Cardiac patients</li> </ul>
NSAIDs (i.e. Ibuprofen, naproxen)	<ul style="list-style-type: none"> <li>• Headache</li> <li>• Pain reliever</li> <li>• Fever reducer</li> </ul>	General population
<b>Chemotherapy</b> (i.e. methotrexate, 5FU, doxorubicin, mercaptopurine, bleomycin)	<ul style="list-style-type: none"> <li>• Breast cancer</li> <li>• Colon cancer</li> <li>• Lung cancer</li> <li>• Prostate cancer</li> </ul>	• Oncology patients
ACE inhibitors (i.e. <b>captopril</b> , enalapril, lisinopril, etc)	<ul style="list-style-type: none"> <li>• Hypertension</li> <li>• Congestive Heart Failure (CHF)</li> </ul>	• High blood pressure and cardiac patients
Alendronate ( <i>Fosamax</i> <sup>®</sup> )	• Osteoporosis	• Women >40 years old
Antibiotics (i.e. tetracyclines)	• Infections, various	• General population

# Medication-related Stomatitis

- Treatment
  - Nonpharmacological
    - Removal of offending agent
    - Good oral hygiene
    - Ice chips
    - Soft, bland diet
    - Cryotherapy
      - Indicated for mucositis
  - Pharmacological<sup>3</sup>
    - Viscous lidocaine
      - Swish and spit 15mL every 3-4 hours
    - Benzocaine 10% - 20%
      - Apply to affected area up to 4 times per day
    - Systemic analgesia if severe (i.e. mucositis)
      - COX2 inhibitors (i.e. Celecoxib)
      - NSAIDs
      - Gabapentin 100 - 600mg PO TID

# Burning Mouth Syndrome

- Clinical presentation<sup>1</sup>
  - Chief complaint of burning or scalding mouth
    - Worsening at the end of the day
  - Associated anxiety
  - Dry mouth



# Burning Mouth Syndrome

- Offending agents<sup>1,3</sup>

Medication	Indication	Patient Population
ACE inhibitors (i.e. captopril, enalapril, lisinopril, etc)	<ul style="list-style-type: none"><li>•Hypertension</li><li>•Congestive Heart Failure (CHF)</li></ul>	<ul style="list-style-type: none"><li>• High blood pressure and cardiac patients</li></ul>
Antiretrovirals (i.e. lamivudine, zidovudine, emtricitabine, etc)	<ul style="list-style-type: none"><li>•Human Immunodeficiency Virus (HIV)</li></ul>	<ul style="list-style-type: none"><li>•HIV/AIDS patients</li></ul>
Cephalosporin antibiotics (i.e. cephalexin, cefdinir, etc)	<ul style="list-style-type: none"><li>•Infections, various</li></ul>	<ul style="list-style-type: none"><li>•General population</li></ul>
Hormone replacement therapy (i.e. estradiol)	<ul style="list-style-type: none"><li>•Menopause</li></ul>	<ul style="list-style-type: none"><li>• Women age 40-60</li></ul>



# Burning Mouth Syndrome

- Treatment
  - Nonpharmacological
    - Removal of offending agent
    - Good oral hygiene
    - Avoidance of spicy, acidic foods
    - Ice chips
    - Brush with baking soda and water
  - Pharmacological<sup>1</sup>
    - Pilocarpine 5mg TID, MAX dose 30mg/day
    - Alpha-lipoic acid 200-600mg daily
    - Clonazepam 0.5mg BID, target dose of 1mg daily

# Glossitis

- Clinical presentation
  - “Strawberry tongue”
  - Absent papillae
  - Swollen tongue (or patches of swollen tongue)
  - Patient complaints of
    - Soreness
    - Difficulty swallowing, chewing, speaking



# Glossitis

- Offending agents<sup>3</sup>

Medication	Indication	Patient Population
Atorvastatin ( <i>Lipitor</i> ®)	High cholesterol	<ul style="list-style-type: none"> <li>• &gt;30 years old</li> <li>• Overweight</li> <li>• Cardiac patients</li> </ul>
Carbamazepine ( <i>Tegretol</i> ®)	<ul style="list-style-type: none"> <li>• Bipolar disorder</li> <li>• Epilepsy</li> </ul>	<ul style="list-style-type: none"> <li>• General population</li> <li>• Psychiatric patients</li> </ul>
Doxepin	<ul style="list-style-type: none"> <li>• Alcoholism</li> <li>• Anxiety</li> <li>• Depression</li> <li>• Insomnia</li> <li>• Pruritis</li> </ul>	Various
Gold compounds	Rheumatoid arthritis	Various
Xerostomizing medications	--	--

# Glossitis

- Treatment
  - Nonpharmacological
    - Removal of offending agent
    - Good oral hygiene
  - Pharmacological<sup>2</sup>
    - Lidocaine mouth rinse
      - Swish and spit 15mL every 3-4 hours
    - Diphenhydramine (*Benadryl*<sup>®</sup>) mouth rinse
      - Swish and spit 15mL 2-3 times per day
    - Dexamethasone (*Decadron*<sup>®</sup>) mouth rinse
      - Swish and spit 15mL 1-2 times per day

# Erythema Multiforme

- Clinical presentation<sup>1,2</sup>
  - Mucocutaneous inflammation
  - Symmetrical edematous, bullous lesions
  - Ranges from self-limited to life-threatening



# Erythema Multiforme

- Offending agents<sup>1</sup>

Medication	Indication	Patient Population
Antibiotics (Penicillin, amoxicillin, cefdinir, cephalexin, etc)	Infections, various	General population
Allopurinol	Gout	<ul style="list-style-type: none"><li>• Men &gt; Women (3:1)</li><li>• &gt; 40 years old</li></ul>
Carbamazepine ( <i>Tegretol</i> <sup>®</sup> )	<ul style="list-style-type: none"><li>• Bipolar disorder</li><li>• Epilepsy</li></ul>	<ul style="list-style-type: none"><li>• General population</li><li>• Psychiatric patients</li></ul>
<i>Bactrim</i> <sup>®</sup> (Sulfamethoxazole + Trimethoprim)	<ul style="list-style-type: none"><li>• Infection, various</li></ul>	<ul style="list-style-type: none"><li>• Various</li></ul>
NSAIDs (i.e. <b>Diclofenac</b> , ibuprofen, indomethacin)	<ul style="list-style-type: none"><li>• Headache</li><li>• Pain reliever</li><li>• Fever reducer</li></ul>	General population
Phenytoin	Seizure disorder	Various

# Erythema Multiforme

- Treatment
  - Nonpharmacological
    - **Removal of offending agent**
    - Debridement (if lesions are severe)
    - Avoidance of hot, spicy, acidic foods
  - Pharmacological
    - Lidocaine mouth rinse
      - Swish and spit 15mL every 3-4 hours
    - Diphenhydramine (*Benadryl*®) mouth rinse
      - Swish and spit 15mL 2-3 times per day
    - Dexamethasone (*Decadron*®) mouth rinse
      - Swish and spit 15mL 1-2 times per day
    - Chlorhexidine mouth rinse
      - Swish and spit 15mL 2-4 times per day
    - Systemic corticosteroids
      - Dexamethasone taper
      - Prednisone taper
    - Antibiotics
      - Amoxicillin 500mg Q12H

# Oral Pigmentation

- Clinical presentation
  - Often asymptomatic
  - Bluish-gray to yellowish-brown discoloration of the buccal mucosa, tongue, hard palate, gingiva



[http://heritageoakdental.com/start/?page\\_id=441](http://heritageoakdental.com/start/?page_id=441)



[http://heritageoakdental.com/start/?page\\_id=441](http://heritageoakdental.com/start/?page_id=441)



# Oral Pigmentation

- Offending agents<sup>1-3</sup>

Medication	Indication	Patient Population
<b>Doxorubicin</b>	<ul style="list-style-type: none"> <li>•Breast cancer</li> <li>•Colon cancer</li> <li>•Lung cancer</li> <li>•Prostate cancer</li> </ul>	•Oncology patients
<b>Minocycline</b>	<ul style="list-style-type: none"> <li>•Infection, various</li> <li>•Acne treatment</li> </ul>	<ul style="list-style-type: none"> <li>• General population</li> <li>• Adolescents</li> </ul>
Phenytoin	Seizure disorder	Various
Quinines (i.e. chloroquine, mefloquine, etc)	Malaria	Travelers
Phenothiazines (i.e. fluphenazine, <b>chlorpromazine</b> , perphenazine, etc)	<ul style="list-style-type: none"> <li>•Schizophrenia</li> <li>•Nausea/Vomiting</li> </ul>	<ul style="list-style-type: none"> <li>• Psychiatric patients</li> <li>• Chemotherapy patients</li> <li>• Other</li> </ul>
<b>Zidovudine</b>	HIV	•HIV patients
Amiodarone	<ul style="list-style-type: none"> <li>•Arrhythmias</li> <li>•Heart failure</li> </ul>	•Cardiac patients
Illicit drugs (i.e. crack, cocaine, heroin)	--	• Drug abusers

# Oral Pigmentation

- Treatment
  - Rule out oral cancers
  - Nonpharmacological
    - Removal of offending agent
    - Laser removal of pigmentation
    - Cryosurgery
    - Abrasion technique

# Tooth Discoloration

- Extrinsic and/or intrinsic discoloration of the tooth
  - Yellow
  - Brown
  - Blue-gray



<http://www.oralanswers.com/2010/09/tetracycline-tooth-staining-cause-treatment-prevention/>

# Tooth Discoloration

- Offending agents

Medication	Indication	Patient Population
Tetracyclines (i. e. <b>minocycline</b> , <b>tetracycline</b> , doxycycline etc)	<ul style="list-style-type: none"><li>•Acne</li><li>•Infection, general</li></ul>	<ul style="list-style-type: none"><li>• Adolescents</li><li>•General population</li></ul>
Ciprofloxacin	<ul style="list-style-type: none"><li>•Infection</li></ul>	General population

# Tooth Discoloration

- Treatment
  - Removal of offending agent
  - External dental cleaning
  - Bleaching

# Black Hairy Tongue

- Clinical presentation
  - Black, hair-like appearance on back of tongue



<http://www.mayoclinic.com/health/medical/IM03891>

# Black Hairy Tongue

- Offending agents<sup>1-3</sup>

Medication	Indication	Patient Population
Broad spectrum antibiotics (i.e. cephalosporins, sulfonamides, tetracyclines)	• Infection	• General
Tricyclic antidepressants (amitriptyline, clomipramine, nortriptyline)	• Depression • Neuralgia	• General population • Patients with chronic pain
Griseofulvin	• Fungal (tinea) infection	• children > adults

# Black Hairy Tongue

- Treatment
  - Nonpharmacological
    - Patient education
      - Good oral hygiene
      - *Smoking cessation*
    - Removal of offending agent
  - Pharmacological<sup>3</sup>
    - Nystatin mouth rinse
      - 4-6mL held in mouth one minute before swallowing
      - Continue use for 2 days after symptoms are gone
    - Fluconazole
      - 100-200mg daily x7-14 days
    - 50% Trichloroacetic acid



# Oral Candidiasis

- Clinical Presentation
  - Whitish, velvety sores in the mouth and on the tongue



# Oral Candidiasis

- Offending agents<sup>1</sup>

Medication	Indication	Patient Population
Antiretrovirals (i.e. lamivudine, zidovudine, emtricitabine, etc)	•Human Immunodeficiency Virus (HIV)	•HIV/AIDS patients
<b>Antibiotics</b> (Penicillin, amoxicillin, cefdinir, cephalexin, etc)	Infections, various	General population
<b>Corticosteroids</b> (dexamethasone, fluticasone, prednisone)	• <b>Asthma</b> •Inflammation	•Various
Chemotherapy agents	•Breast cancer •Colon cancer •Lung cancer •Prostate cancer	•Oncology patients

# Oral Candidiasis

- Treatment
  - Nonpharmacological
    - Removal of offending agent
    - Good oral hygiene
    - Probiotics (yogurt)
  - Pharmacological
    - 3% hydrogen peroxide rinses
      - Swish and spit 15mL 3-4 times per day
    - Nystatin mouth rinse
      - 4-6mL held in mouth one minute before swallowing
      - Continue use for 2 days after symptoms are gone
    - Fluconazole
      - 100-200mg daily x7-14 days

# Gingival Hyperplasia

- Clinical presentation

- Overgrowth of gums
- Red, swollen gums
- Displaced teeth and plaque depositions predispose patients to gingival hyperplasia



# Gingival Hyperplasia

- Offending agents<sup>1</sup>

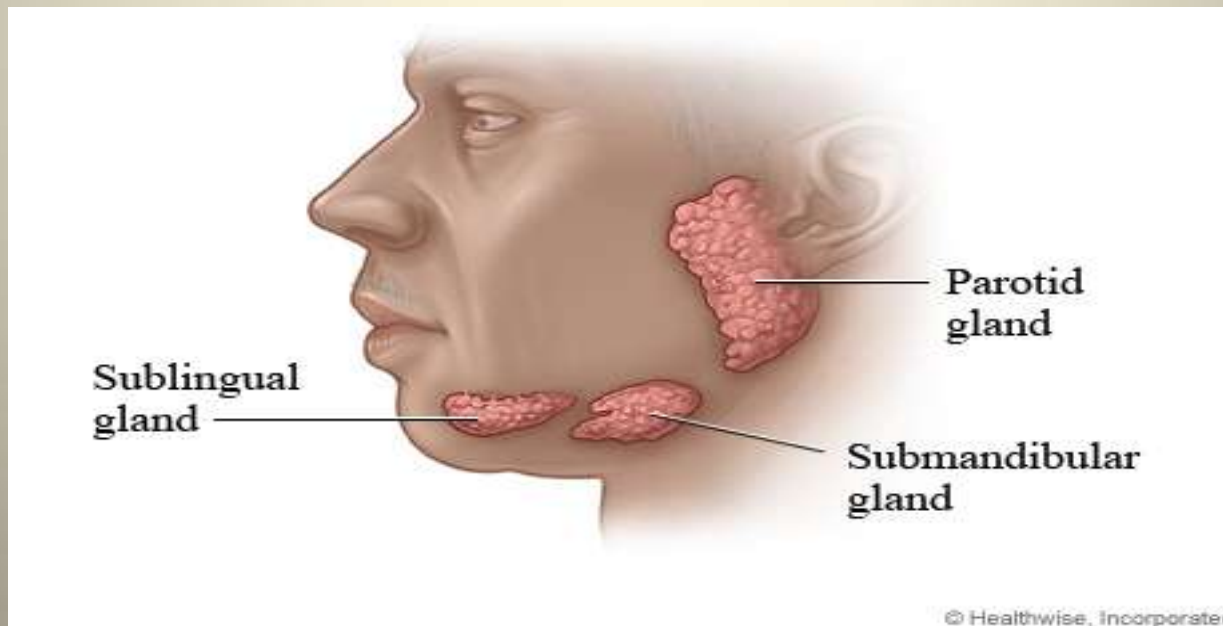
Medication	Indication	Patient population
Anticonvulsants ( <b>phenytoin</b> , valproate, topiramate, phenobarbital)	<ul style="list-style-type: none"><li>•Seizures</li><li>•Bipolar disorder</li></ul>	<ul style="list-style-type: none"><li>•Epileptics</li><li>•Psychiatric patients</li></ul>
<b>Cyclosporin</b>	<ul style="list-style-type: none"><li>•Heart transplant</li><li>•Liver transplant</li><li>•Kidney transplant</li></ul>	<ul style="list-style-type: none"><li>• Transplant patients</li><li>•Surgery patients</li></ul>
Calcium channel blockers ( <b>nifedipine</b> , amlodipine, diltiazem, nicardipine, verapamil)	<ul style="list-style-type: none"><li>•Hypertension</li><li>•Angina</li><li>•Post MI</li></ul>	<ul style="list-style-type: none"><li>•Cardiac patients</li></ul>

# Gingival Hyperplasia

- Treatment
  - Nonpharmacologic
    - Removal of offending agent
    - Good oral hygiene
      - Plaque control
  - Pharmacologic
    - Cyclosporin-induced gingival hyperplasia
      - Azithromycin 250mg BID on day 1, then 250mg daily x6 days

# Alterations in Salivation

- Clinical presentation
  - Patient complaint (dry mouth, painful salivation)
  - Secondary complications
    - Dental caries, infection, ulcers, dysphagia



# Alterations in Salivation

- Offending agents<sup>1-3</sup>
  - Xerostomia

Medication Class	Indication	Patient population
Antihistamines ( <i>Benadryl</i> ®, <i>Claritin</i> ®, <i>Allegra</i> ®, etc)	<ul style="list-style-type: none"><li>•Allergies</li><li>•Insomnia</li></ul>	<ul style="list-style-type: none"><li>•General population</li></ul>
Antidepressants (SSRIs, TCAs, MAOIs)	<ul style="list-style-type: none"><li>•Depression</li><li>•Neuralgia</li><li>•Insomnia</li></ul>	<ul style="list-style-type: none"><li>•Various</li></ul>
Triptans ( <i>Imitrex</i> ®, conivaptan, zolmitriptan, naratriptan)	<ul style="list-style-type: none"><li>•Migraine headaches</li></ul>	<ul style="list-style-type: none"><li>• &gt;18 years old</li><li>• Female &gt; male</li></ul>
Antihypertensives (Beta-blockers, calcium channel blockers, alpha-agonists)	<ul style="list-style-type: none"><li>•Hypertension</li><li>•Heart disease</li></ul>	Cardiac patients



# Alterations in Salivation

- Offending agents<sup>1</sup>
  - Sialorrhea

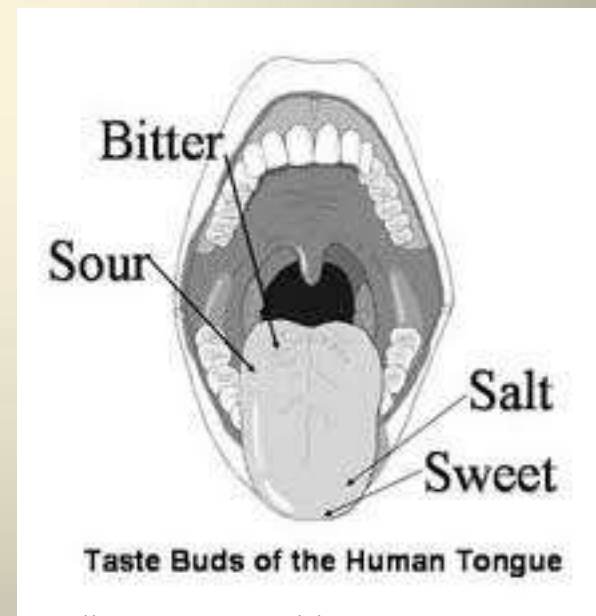
Medication	Indication	Patient Population
Clozapine ( <i>Clozaril</i> ®)	Schizophrenia	Psychiatric patients
Digoxin ( <i>Digitek</i> ®)	•Atrial fibrillation •Heart failure	Cardiac patients
Pilocarpine ( <i>Salagen</i> ®)	•Glaucoma •Xerostomia	•Diabetic patients •Cancer patients
Risperidone ( <i>Risperdal</i> ®)	•Autism •Bipolar disorder •Schizophrenia	•Autistic patients •Psychiatric patients

# Alterations in Salivation

- Treatment
  - Nonpharmacological
    - Removal of offending agent
    - Good oral hygiene
  - Pharmacological
    - Xerostomia
      - Pilocarpine 5mg TID, MAX dose 30mg/day
      - Bethanechol
    - Sialorrhea
      - Atropine drops 1-2 drops as needed
      - Clonidine patch 0.1mg/day patch
        - » Change every 7 days

# Alterations in Taste

- Clinical presentation
  - Patient complaint
    - Loss of taste
    - “Decreased salty taste”
    - Metallic taste



# Alterations in Taste

- Offending agents<sup>1,2</sup>

Medication	Taste Alteration	Indication	Patient population
Sulfhydryl compounds (Sulfonamides, sulfonyleureas, etc)	Decreased taste	<ul style="list-style-type: none"> <li>• Infection</li> <li>• Diabetes Mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• General</li> <li>• Diabetics</li> </ul>
Penicillamine	Decreased to total loss of taste	<ul style="list-style-type: none"> <li>• Cystinurea</li> <li>• Rheumatoid arthritis (RA)</li> </ul>	<ul style="list-style-type: none"> <li>• Patients with kidney stones</li> <li>• RA: women &gt; men</li> </ul>
ACE inhibitors ( <b>captopril</b> , enalapril)	Decreased "salty" taste	<ul style="list-style-type: none"> <li>• Hypertension</li> </ul>	Cardiac patients
Griseofulvin	Decreased to total loss of taste	<ul style="list-style-type: none"> <li>• Fungal (tinea) infection</li> </ul>	<ul style="list-style-type: none"> <li>• children &gt; adults</li> </ul>
Proton pump inhibitors ( <i>Protonix</i> <sup>®</sup> , <i>Prevacid</i> <sup>®</sup> , <i>Nexium</i> <sup>®</sup> )	Altered or decreased taste	<ul style="list-style-type: none"> <li>• Heart burn</li> <li>• Reflux disease</li> </ul>	<ul style="list-style-type: none"> <li>• &gt;18 years old</li> <li>• Pregnancy</li> </ul>
Corticosteroids (dexamethasone, fluticasone, prednisone)	Decreased taste	<ul style="list-style-type: none"> <li>• Asthma</li> <li>• Inflammation</li> </ul>	<ul style="list-style-type: none"> <li>• Various</li> </ul>
Chemotherapy agents	Metallic taste > decreased taste	<ul style="list-style-type: none"> <li>• Breast cancer</li> <li>• Colon cancer</li> <li>• Lung cancer</li> <li>• Prostate cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Oncology patients</li> </ul>

# Alterations in Taste

- Treatment
  - Nonpharmacological
    - Removal of offending agent
    - Good oral hygiene
    - Increased water intake with medications
  - Pharmacological treatment
    - Radiation and chemotherapy-induced alterations:
      - Zinc supplementation

# Halitosis

- Clinical presentation
  - Patient complaint of constant foul taste in mouth
  - Secondary causes
    - Dry mouth
    - Infection
    - Excessive alcohol consumption
    - Respiratory infection

# Halitosis

- Offending agents<sup>1</sup>

Medication	Indication	Patient population
Chemotherapy agents	<ul style="list-style-type: none"><li>•Breast cancer</li><li>•Colon cancer</li><li>•Lung cancer</li><li>•Prostate cancer</li></ul>	<ul style="list-style-type: none"><li>•Oncology patients</li></ul>
Disulfiram ( <i>Antabuse</i> ®)	<ul style="list-style-type: none"><li>•Alcoholism</li></ul>	<ul style="list-style-type: none"><li>•Alcoholics</li></ul>
Nitrates	<ul style="list-style-type: none"><li>•Angina</li><li>•Heart disease</li></ul>	Cardiac patients
<b>Xerostomizing medications</b>	--	--

# Halitosis

- Treatment
  - **Good oral hygiene**
  - Tobacco cessation
  - Alcohol cessation
  - Keep a food log



# Angioedema

- Clinical presentation
  - Sudden onset
  - Swelling, redness
    - Lips
    - Throat (pharynx, larynx)
    - Eyelids

# Angioedema

- Offending agents<sup>1,3</sup>

Medication	Indication	Patient Population
NSAIDs (i.e. Ibuprofen, naproxen)	<ul style="list-style-type: none"><li>•Headache</li><li>•Pain reliever</li><li>•Fever reducer</li></ul>	General population
ACE inhibitors (i.e. captopril, enalapril, lisinopril, etc)	<ul style="list-style-type: none"><li>•Hypertension</li><li>•Congestive Heart Failure (CHF)</li></ul>	<ul style="list-style-type: none"><li>• High blood pressure and cardiac patients</li></ul>
Sulphydryl compounds (Sulfonamides, sulfonyleureas, etc)	Decreased taste	<ul style="list-style-type: none"><li>• Infection</li><li>•Diabetes Mellitus</li></ul>

# Angioedema

- Treatment
  - Refer patient to Emergency Department
  - Removal of offending agent
  - Antihistamines
    - *Benadryl*<sup>®</sup>

# Summary

- Most medication-related oral reactions occur within one to two weeks of initiation of therapy<sup>1</sup>
- The most frequent medication-related oral reactions are xerostomia, dysgeusia and stomatitis<sup>1</sup>
- The most common offending agents are chemotherapy agents, antibiotics, antihistamines and psychotropic medications
- First line treatment for most medication-related oral reactions is good oral hygiene

# Questions



# More questions?

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