

## "Can't Stop the Feeling" and Nothing Helps! Symptomatic Oral Lesions in Adolescence and Adults



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(Photo by A© CORBIS/Corbis via Getty Images)

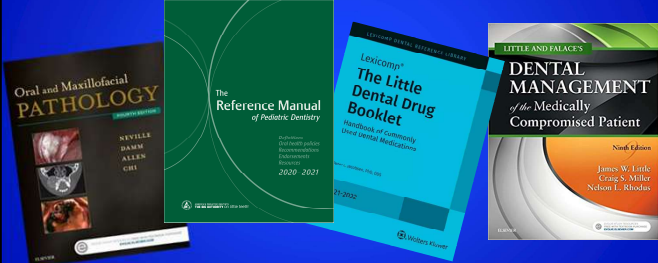
## Course Objectives

- Identify common symptomatic oral lesions, including atypical presentations
- Discover new causes and facts about these common oral conditions
- Learn about the oral diseases associated with post-COVID 19
- Select best treatment options tailored to the individual.



Detail of AI artwork made by Dream by Wombo app  
Image Credits: Natasha Lomas/TechCrunch

## References



## New Diseases That Are a Pain




www.cdc.gov

Coronavirus-19 Infection


## Oral Manifestations in Patients with COVID-19

- Oral lesions are common – 66% have  $\geq 1$  sign/symptom
- Gustatory impairment is most common: 33%
- May be first sign of infection or disease complication (thrombosis)
- Oral lesions had multiple presentations – most symptomatic
- Site: Tongue and lips are most common
- May represent coinfections or secondary manifestations
- Occurrence of oral lesions:
  - Mild cases: developed before or same time as respiratory symptoms
  - Severe cases: developed 7-24 days after symptoms



(Santos, J Dent Res 2020; Silveira, Arch Oral Biol 2022; Farid, Rev Med Virol 2022)

## Oral Manifestations of COVID-19 Infection



- Loss of taste and smell
- Erythema, palatal petechiae, purpura
- Erosions, vesicles, bullae, ulcers
- Bleeding, desquamative gingivitis
- Swollen, chapped lips
- Angioedema and urticarial
- Candidiasis, angular cheilitis
- Pharyngitis
- Xerostomia, sialadenitis
- Glossitis, strawberry tongue
- Cervical lymphadenopathy
- Facial pain/numbness/palsy
- Burning mouth

20YOWF with dysgeusia, swollen, coated tongue, burning mouth, and xerostomia

### Mucocutaneous Conditions Are Common

Adult with chilblains

40YOHF with taste and smell loss, recurrent HSV

60YOM with NUP, glossitis, edema, xerostomia

### Mimickers: Oral Manifestations of COVID-19

- Viral and fungal infections
- Aphthous ulcers
- Allergic reactions
- Autoimmune diseases
- Hematologic disorders
- Neurologic disorders
- Polypharmacy manifestations

[https://www.medicinenet.com/covid\\_19s\\_among\\_wide\\_variety\\_of\\_updated\\_symptoms-news.htm](https://www.medicinenet.com/covid_19s_among_wide_variety_of_updated_symptoms-news.htm)

### “Long Haulers” and COVID-19

- Known as Post COVID Conditions
- Postviral syndrome affects 20% of COVID patients >18y → 4 weeks after infection
- May develop with mild or asymptomatic disease
- Wide age range; F > M
- Late sequelae: Multi-organ complications
- Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a serious, long-term illness that affects many body systems.
- Oral disease has been reported

<https://www.cdc.gov/coronavirus/2019>

### Post-COVID Conditions

Approximately **1 in 5 adults** ages 18+ have a health condition that might be related to their previous COVID-19 illness, such as:

- Neurologic and mental health conditions\*
- Cardiovascular conditions
- Kidney failure
- Respiratory conditions
- Musculoskeletal conditions
- Blood clots and vascular issues

**Talk to your health care provider if you have symptoms after COVID-19**

181JY/MMWR7121 MAY 24, 2022

\*Multi-organ and other stressors via MMWR

### Reactive Infectious Mucocutaneous Eruption

- AKA: RIME
- Definition: Mucositis affecting 2 mucous membrane sites with limited or no cutaneous rash, secondary to respiratory infection
- Caused by multiple viral, bacterial infections
- Occurs 4 days to 12 weeks after COVID-19
- Mimics erythema multiforme, hand-foot-mouth disease, other infections, allergic reactions, autoimmune disease


### Recent Case History

- 65 YO female with sore mouth of recent onset
- Med Hx: COVID-19+ 7 weeks ago; mild to moderate case
- S/S: Painful vesicles and erythema of soft palate, tender tongue with multiple papules
- Pain persisted despite valacyclovir, followed by dexamethasone rinse

DDx: HSV, herpangina, allergic rx

Photo: Dr. Glenda Owen


### Post COVID Case



Acute lingual papillitis and erythema – 2.5 weeks later  
 What is the cause? Post-viral syndrome (RIME), new virus, reactivation of previous virus (EBV, HSV), allergic reaction

### Case History

- 26 YOWM with previous COVID-19 infection 1 year ago; has been vaccinated
- No underlying risk factors for COVID-19
- Extraoral concerns: Brain fog, headaches, fatigue, improved taste and smell impairment
- Oral concerns: Pruritic lips, gingiva, xerostomia, coated, fissured tongue
- Dx: Oral neuropathy and xerostomia probably associated with Post COVID



### Patient management: Team Approach

- NSAIDS
- Gabapentin
- Duloxetine
- Bland oral hygiene products
- Saliva substitutes
- Increase hydration
- Sucking on sugarless candy
- Benadryl®, Lidocaine HCl 2% Viscous, Maalox® 1:1:1 oral susp



### Case History

- ID: Healthy 18 YOWF
- Med Hx: Tested positive for COVID-19 4 weeks ago. She had mild respiratory disease that resolved.
- Denies vaping, tobacco or cannabis use but does drink alcoholic beverages
- S/S: Recent onset collapsed blood filled bullae and scattered macules; enlargement of minor salivary, dry mouth and mucosal sloughing by report.
- Is this associated with COVID-19?




Photo: Dr. Charlie Czerepak and individual

### Case History

*What do we see?*


- Collapsed bullae, purpura in healing stages
- Salivary gland disease

*What are the possible causes?*

- Post COVID-19 due to vasculitis, coagulopathy, and salivary gland disease
- Traumatic purpura
- Effects of binge drinking


*What to do?*

- Refer to PCP for post COVID evaluation



### Post COVID-19 Conditions

- Autonomic nervous system dysfunction
- Fever; tiredness or fatigue
- Difficulty thinking or concentrating ("brain fog")
- Headache; dizziness on standing
- Diminished loss of smell or taste
- Dizziness on standing
- Chest pain; heart palpitations; myocarditis
- Difficulty breathing or shortness of breath; cough
- Joint or muscle pain
- Depression or anxiety
- Symptoms worse after physical or mental activities



<https://www.drugtargetreview.com>

CDC 2023  
 UpToDate 2023  
 Nature 595, 482-483 (2021)


**Pew Research Center**

DECEMBER 12, 2022


At least four-in-ten U.S. adults have faced high levels of psychological distress during COVID-19 pandemic

BY GIANCARLO PASQUINI AND SCOTT KEETER

Higher for young adults (18-29Y): 58%



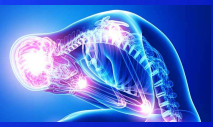
Chloe Zola  
The New York Times



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**Stress-induced Oral Lesions**


- Cheek, tongue biting keratosis
- Ulcers: Factitial lesions, aphthae, herpes
- Superficial mucoceles
- Mucosal sloughing (mouth rinses, vaping)
- Purpura
- Lip sucking habit
- Xerostomia
- Dental erosion
- Bruxism, clenching, tooth fractures, TMD
- Oral disease due to poor hygiene, nutrition



<https://www.apa.org/topics/stress-body>

**Patient History**

- ID 33 YO American-Indian F
- CC: Sensitive teeth and mouth
- Med Hx: Healthy but under stress due to COVID-19 – essential worker and extended family
- S/S: Clenching, masseter tenderness, white shaggy patches on buccal mucosa, tip of tongue, swelling of lip



Bilateral shaggy white patches on buccal mucosa

**Patient History continued**



Scattered white patches on tongue tip



Petechiae, erosions and edema on lip

**Aggressive Lip and Cheek Biting**

**Body-Focused Repetitive Behavior**

- Repetitive, self-directed behavior that damages the skin, hair, or nails.
- Coping mechanism for uncomfortable or anxious situations
- Common habits: hair-pulling, skin-picking, nail-biting
- Tx: Cognitive behavior therapy, medications
- 67% increase in behavior during pandemic (Pathoulas J et al. AAAD, 11-2020 online)



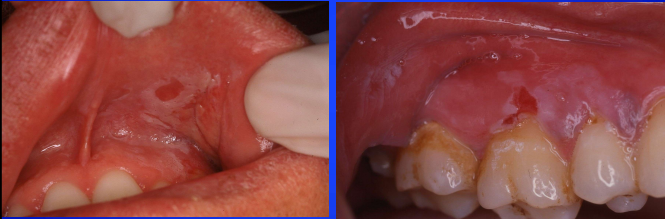
14 YO male with factitial lesions

**Patient History**

- ID: 39YOWF with gum pain
- MHx: Bipolar depression, ADHD, MS, tobacco use, previous cocaine use
- DHx: Periodontal disease
- S/S: Advanced bone loss, exposed bone, gingival recession between #5/6, #27/28
- DDx: Factitial injury, localized NUP, cocaine necrosis





### Oral Cocaine Use? Look for Chemical Burns



❖ Note that you can see mucosal burns from overuse of OTC topical pain relieving gels, mouth rinses, aspirin, whitening agents, and very acidic candy

### Risk Factors: Body-Focused Repetitive Injury

- BFRI is a disease spectrum
- Age: Often starts in adolescence
- Gender: F > M
- Mental health conditions: Depression, anxiety, OCD, substance use disorder, PTSD, ADHD, body dysmorphic disorder
- Family dynamics
- Tx: Gold standard is habit reversal therapy, a form of cognitive behavioral therapy (CBT).



### Patient History

- ID: 76 YO male with well-controlled diabetes, actinic keratosis and actinic cheilitis
- Denies lip biting habit
- Successful businessman; travels 100 days/y
- Duration: unknown but not present at last recall
- S/S: Diffuse, adherent white plaques with submucosal swelling; tender when traumatized





Photo: Dr. Douglas Wilson

### Patient History

- Patients are often unaware of factitial habits
- Stress exacerbates dry mouth
- Lip scar (subepithelial fibrosis and chronic fibrosing sialadenitis are irreversible)
- Tx: Manage actinic cheilitis; sunscreen; increase oral hydration, lubrication; smooth incisal edges; occlusal splint to disrupt habit



### Valuable Resource for You and Patients



**SBIRT**  
SCREENING, BRIEF INTERVENTION,  
AND REFERRAL TO TREATMENT

U.S. Department of Health & Human Services  
**SAMHSA**  
Substance Abuse and Mental Health  
Services Administration

<https://www.samhsa.gov/sbirt>

### Symptomatic Oral Mucosal Lesions

- Red mucosal lesions
- Ulcerative lesions
- White or yellowish mucosal lesions
- Nodular lesions
- Overall prevalence of oral soft tissue lesions = 28%
- NHANES Survey 1988-1994 (JADA 2004)





Illustration from "The poetry of Robert Burns, vol. I", Edinburgh, 1897. Artist: William Brasseay Hole. Sketch accompanies the poem "Address to the toothache".  
<http://scrap.oldschoolillustrations.com/post/71356388853/address-toothache>

### Benign Migratory Glossitis

- Geographic tongue, erythema migrans
- Cause: Unknown; genetic, allergy, hormonal
- Prevalence: 3%; F > M; all ages; in children
- Site: Tongue, especially dorsum; extraglossal
- Duration: Persistent; waxes and wanes
- S/S: Multiple, red annular patches with white scalloped border; loss of filiform papillae; +/- tenderness; +/- fissured tongue; +/- edema
- Concerns: Food restrictions; cosmetic concern

### Benign Migratory Glossitis




Associated with fissured tongue, lateral crenations and burning mouth syndrome

### Benign Migratory Glossitis



- ✓ Early onset may be marker for psoriasis & disease severity
- ✓ Common genetic mutation for severe psoriasis (GPP) and BMG is *IL36RN* (Liang J, et al. Hum Genet 136;241-52; Piccinani B, et al. International J Dermatol 2017)

### Extraglossal Erythema Migrans



81 YOM with incidental finding of the tongue and buccal mucosa  
Complex medical history including recent steroids for gout


### Solitary lesion at high-risk oral cancer site

- ID: 73 YOM with hypertension, HCV, hypothyroidism
- Previous history: cigarettes, marijuana, alcohol
- Diff Dx: Isolated BMG, contact allergy, traumatic erosion, erythroplakia
- Tx: Biopsy atypical BMG – static, solitary, painful




### Smokescreen Lesion

- ID: 72 YOWF with diabetes, hypothyroid, and anxiety
- CC: Persistent painful tongue that is nonresponsive to antifungal agents and to DC mouth rinses
- Coincided with Biotin supplement
- Duration: 7 weeks
- Exam: Elongated red and depapillated patch on dorsal tongue, mild tongue coating; lips are red and fissured



### What is the Source of the Pain?



- Note: 25% with BMS have BMG
- Rule out:
  - candidiasis
  - contact allergy/irritation
  - Trauma, habit, referred pain
  - vit B, zinc, iron deficiency
  - medication side effect
  - xerostomia
  - diabetes mellitus, reflux disease
  - Parkinson disease
  - Post COVID condition
  - anxiety, depression

Cause for pain: Biotin caused digestive problems and GERD

### Symptomatic Benign Migratory Glossitis

ID factor; use gentle oral hygiene products; dietary restrictions

Topical coating agents, anesthetics, antihistamines:

- Diphenhydramine liquid 12.5 mg/5ml + aluminum hydroxide, magnesium hydroxide + distilled H<sub>2</sub>O susp (1:2:3 ratio)
- OTC gels, rinses, pain-relievers


Nutritional supplement: Zinc, vitamin B complex, if deficient

Topical steroids +/- antifungals:

- Fluocinonide gel .05% (QID)
- Triamcinolone-Nystatin ointment (QID)

Topical immune suppressants:

- Tacrolimus ointment .1% ointment (BID)



### What is the Evidence?

Summary Review | Published: 28 June 2019

#### What are the best treatments for benign migratory glossitis?

Morteza Banakar


*Evidence-Based Dentistry* 20, 40-41(2019) | Cite this article  
136 Accesses | Metrics



Conclusions: There is substantial heterogeneity in the available studies providing very low-quality evidence for the treatment of symptomatic benign migratory glossitis.


### Transient Lingual Papillitis

- Lesion: Inflamed fungiform papillae
- Cause: Unknown, trauma, allergy/sensitivity, GERD, hormonal, URI, viral infection, BMG
- Gender/Age: F>M; Wide age range
- Site: Dorsal tongue; Anterior, lateral
- 3 types: Single, diffuse or clustered
- S/S: Painful, red or white papules +/- fever, lymphadenopathy, may recur, last 1-7 days
- TX: Topical steroid, anesthetics, coating agent




64YOHM with tender fissured tongue in isolated areas

### Transient Lingual Papillitis



Above: localized type associated with BMG in adult



Below: diffuse type associated with URI in young adult

### Recent Case History

- ID: Healthy 55 YO female
- Hx: Stressed about COVID-19 and her dad just passed away. She started taking sertraline for depression. She is going through menopause and has no other medical issues.
- S/S: 4-6 weeks ago, had sharp isolated pain on two white papules on tongue. One papule turned reddish-brown. Pain is persistent.

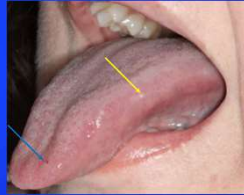



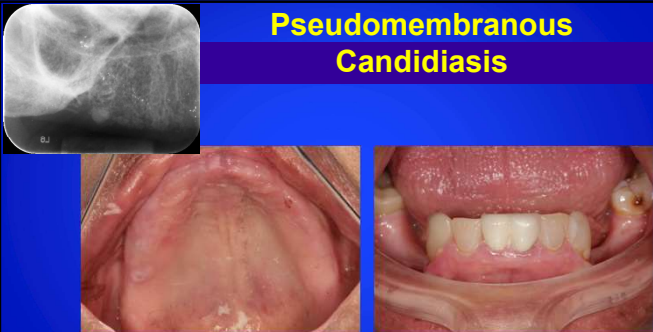
Photo: Dr. Daniel Ho

### Oral Candidiasis



- Cause: *Candida species, Candida albicans*
- New fungus: *Candida auris* – life threatening
- Prevalence: 40 – 60% normal oral inhabitant
- Predisposing factors: ↓ immune status, medications, poor oral hygiene, removable appliances, poor diet, diabetes, dry mouth, CPAP, smoking tobacco & vaping
- Site: Usually multifocal oral involvement
- Types: Pseudomembranous, erythematous, hyperplastic, combination
- S/S: Red or white patches, erosions, burning sensation, taste perversion, sore throat

### Pseudomembranous Candidiasis




Multifocal, nonadherent, cream-colored papules and plaques that wipe off

### Candidiasis & Xerostomia




- ✓ Mimics burning mouth syndrome
- ✓ Concurrent dry mouth, fissured tongue, taste alteration, chapped lips, angular cheilitis

### Candidiasis & Post-inflammatory Pigmentation



➤ Adult with burning mouth and patchy erythema with brown patches on buccal mucosa and soft palate. Note white papules at lip commissures


### Hyperplastic Candidiasis



- ✓ Cigarette smoking is important cause
- ✓ Associated with endocrine disease and/or syndrome in some cases
- ✓ Precancerous condition
- ✓ Mimics leukoplakia, lichen planus, aggressive cheek-biting

### Candida in Dentinal Caries

- Deep dentinal caries harbors fungus
- Contributes to persistent erythematous gingivitis
- Similar appearance as linear gingival erythema
- Candida-streptococcal interactions in biofilm (Koo H, PLoS Pathog 2018;14(12):e1007342)





Patient has substance use disorder & HCV



### Denture Stomatitis

- Controversy as to the specific cause
- Chronic atrophic candidiasis vs. tissue response to multiple microorganisms on the appliance
- Site: Denture-bearing areas
- Factor: Chronic wearing of appliance
- S/S: Usually nontender but may burn; diffuse erythema, petechiae, rarely ulcers
- Part of disease spectrum – papillary hyperplasia
- Mimics: Contact allergy, staph infection



### Appliance Stomatitis

Adolescent after removal of Nance appliance – acrylic button on palate

Affects 1 in 3 adult denture wearers  
Significant biofilm relationship  
NB: Nicotine stomatitis of posterior hard palate (red dots)

### Inflammatory Papillary Hyperplasia Symmetrical Palatal Fibromatosis





ID: 78 YOBF with palatal findings - midline erythema, fine papules  
MHx: Diabetes, hypertension, asthma


ID: 68 YOWM with palatal finding  
Med Hx: Post kidney transplant  
Med: Cyclosporine, prednisone, amlodipine  
Photo: Dr. Sophia Kahn

### Angular Cheilitis

Adolescent



Adult



- ✓ Lip incompetence is a factor
- ✓ Orthodontic appliances
- ✓ Retinoic acids for acne

- ✓ Recurrent lesions cause scarring
- ✓ Extension of hyperplastic candidiasis
- ✓ Secondary staph infection
- ✓ RO: Overclosure (I, VD), vit deficiency

### Tongue Coating & Dysgeusia

- Not a form of candidiasis
- Mild coating is normal
- Hyposalivation may be concurrent
- May have loss of taste and smell
- Patients with altered taste and coated tongue are concerned about halitosis
- Tx: Gentle brushing of tongue BID and increases oral moisture






Photo: Dr. Glenda Owen

### Strawberry Tongue




- Erythematous tongue with enlarged fungiform papillae
- Scarlet fever
- Kawasaki disease
- COVID-19 infection
- Mimics: erythematous candidiasis



## Oropharyngeal Candidiasis

**Topical Agents:**

- Nystatin suspension 100,000 U/mL
- Clotrimazole troches 10 mg
- Oravig (miconazole) buccal tabs 50 mg




**Systemic Agents:**

- Ketoconazole 200 mg tabs (Not recommended)
- Diflucan, g (fluconazole) 100 mg tabs, 10 mg/mL, 40 mg/mL susp (birth defects rare but ↑ risk for tetralogy of Fallot) *Molgaard-Nielsen, NEJM, Aug 2013*
- Sporanox (itraconazole) 100mg/10mL

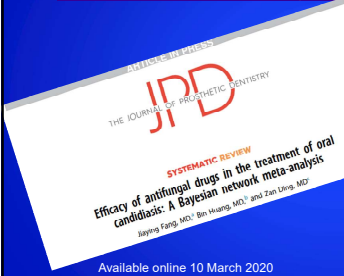
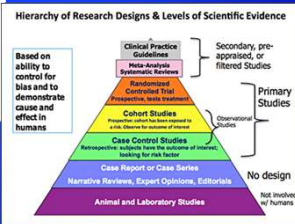
## Miconazole (Oravig): Topical

- Form: Adherent, slowly dissolving 50 mg tablet
- Usual dosage:
  - Adolescents >16 y: 1 tablet for 14 days. Apply to the upper gum region, just above the upper lateral incisor. Alternate sides of mouth.
- Do not use if allergic to milk protein concentrate




2021 Galt Pharmaceuticals

## Recent Meta-analysis: Winner Is Fluconazole


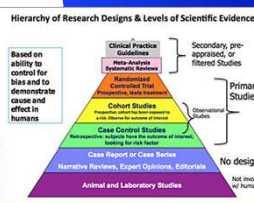



## Denture Sore Mouth

- Topical Antifungal Agents:
  - Nystatin ointment (RX)
  - Clotrimazole cream 1% (RX, OTC)
  - Ketoconazole cream 2% (RX)
  - Miconazole nitrate cream 2% (RX, OTC)
  - Nystatin/triamcinolone ointment (RX)
- Oral moisturizing gel (base of appliance)
- Chlorhexidine oral rinse .12% / OTC mouth rinses
- Clean and/or soak appliances in a cleanser nightly
- Reline or fabricate new prosthesis
- Do not sleep with removable prosthesis in mouth




## Probiotics May Be Beneficial


## Evidence About Probiotics

- Probiotic species:
  - Lactobacillus* spp.
  - Bifidobacterium* spp.
  - Saccharomyces* spp.
- Preventive effect: Candida colonization
- Population: Preterm neonates and elderly
- Systematic reviews:
  - Hu H-J, et al: *Pediatr Neonatol* 2017
  - Ai R, et al: *Arch Oral Biol* 2017




### Oral Erythroplakia

- Red patch that cannot be defined clinically or pathologically as another condition
- Prevalence: Uncommon
- Age/Gender: > 6<sup>th</sup> decade; M = F
- Risk factor: Tobacco and alcohol
- Site: Oral floor, soft palate, buccal mucosa, ventral tongue
- S&S: Soft, velvety or granular red patch +/- white foci; solitary; often tender
- TX: Excision and long-term follow-up; dysplasia in most cases; high malignant transformation rate



- ✓ ID: 65 YOWF who rarely drinks alcohol
- ✓ S/S: Tender, red patch of ventrolateral tongue


### Erythroplakia



Mimics BMG, chronic lingual papulosis, candidiasis, contact allergy

Bouquot, TDJ 2008

### Erythroplakia in Chronic Tobacco-Users




Mimic: thermal burns, traumatic erosions

Note the abrupt margins of both lesions  
Nicotinic stomatitis & prominent leukoedema

### Is This Nicotine Stomatitis Or Erythroplakia?

- ID: 70YO chronic pipe smoker
- Note the sharp transition from hard and soft palate
- Nicotine stomatitis rarely undergoes malignant transformation, but the red pattern of soft palate may mask erythroplakia
- Referral for biopsy is justified



### Sloughing Sore Mouth

- ID: 19 YOWM, college student
- CC: Gums and under tongue burn when eating
- Hx: Healthy but vapes daily
- S/S: Viscous saliva, gingivitis, multifocal areas of white pseudomembrane, swelling of tongue




Photo: Kelly Mansour, DMD

### Sloughing Sore Mouth




DDx:

- ✓ Irritation from oral hygiene products
- ✓ Overuse of mouth rinse
- ✓ Use of e-cigs
- ✓ Pseudomembranous candidiasis

### Vaping and Oral Health?


- Increased risk for caries
- Increased risk for periodontal disease
- Dry mouth
- Mucosal sloughing
- Candidiasis
- Oral erythema and ulcers
- Mucosal burning, irritation
- Beware: drugs placed under tongue cause a similar problem (Suboxone)



Candidiasis and mucosal irritation with sloughing  
Ebersole et al. Tob Induc Dis 2020

### Ulcerative Lesions

- Focal Ulcers of Sudden Onset & Short Duration
- Multifocal Ulcers of Sudden Onset & Short Duration
- Focal Ulcers of Variable Onset & Persistent Duration
- Multifocal Ulcers of Variable Onset & Persistent Duration




Aphthous major

### Aphthous Stomatitis

- Problem: Localized immune dysfunction
- Prevalence: 20% of US population
- Important factors: Immune defect, ↓ mucosal barrier, ↑ antigenic exposure
- Triggers: Trauma, allergies, stress, xerostomia, hormones, GERD, nutritional deficiencies (folic acid, iron, zinc, vit B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, B<sub>12</sub>, D) hematologic abnormalities, smoking cessation, infectious agents
- Genetics: + familial history, specific HLA types, and IL variants

### Genome Wide Analysis for Mouth Ulcers


- Source: UK Biobank and 23andMe meta-analysis
- GWAS: n= 461,106
- Heritability: 8.2%
- 97 genetic variants with mouth ulcers
- Important genetic variants associated with *IL12A* and *IL10*
- Supports role of T cell regulation in etiology of mouth ulcers
- Dudding T et al. Nature Communications 2019



60 YOF with recurrent ulcers

### Aphthous Ulcers: Clinical

- Age: 80% before age of 30; rarely <5 yrs
- Site: Nonkeratinized mucosa
- Most common sites: Buccal, labial mucosa
- Duration: 2 days to 6+ weeks
- Variants: Minor (80%), major (10-15%), herpetiform (5-10%); combined variants
- S/S: Recurrent, single or multiple, painful ulcers; sudden onset
- Complication: Scars, nutritional problems, behavioral problems, impact quality of life





Note scarring on lateral tongue from major aphthae

### Aphthous Minor





- Vestibular ulcers mimic a toothache
- Trauma from toothbrushing, other
- Often have more than one ulcer - may coalesce
- Not infectious

### Apthous Major

<p><b>Teen</b></p> 	<p><b>Adult</b></p>  <ul style="list-style-type: none"> <li>✓ Size matters with aphthous ulcers</li> <li>✓ Child: Rule out systemic disease</li> <li>✓ Adult: Medications and xerostomia</li> </ul>
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### Allergens & Aphthous-like Ulcers

- Food: Chocolate, coffee, peanuts, almonds, strawberries, cheese, tomatoes, citrus, wheat, spices – pepper, capsicum, curry
- Irritants: Acidic, carbonated, alcoholic beverages, rough foods, mouth rinses
- Other: Benzoic acid, SLS, cocamidopropyl betaine, cinnamaldehyde, menthol, peppermint, eugenol, Balsam of Peru
- Metals: Nickel, chromium





### Potential Toothpaste Allergens

- Flavors, unspecified
- Sodium lauryl sulfate
- Cocamidopropyl betaine
- Propylene glycol
- Essential oils
- Parabens
- Peppermint, Spearmint, Menthol
- Vitamin E
- Grape extract
- Propolis
- Tea tree oil





Child with ulcer, chapped lips, sloughing, xerostomia  
Otto S, Journal of Clinical & Aesthetic Dermatology, 2010

### You Can Trigger Aphthae Following Dental Treatment


<p><b>Teen</b></p>  <p style="font-size: small; text-align: center;">Herpetiform variant after impression</p>	<p><b>Adult</b></p>  <p style="font-size: small; text-align: center;">Major variant following radiographs</p>
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### Apthous Ulcer and Toothache

	 <ul style="list-style-type: none"> <li>✓ 65 YOF with recurrent oral ulcers</li> <li>✓ Triggers: Sinus infections and dental pain</li> <li>✓ Tx: Nonresponsive to antiviral meds</li> <li>✓ Note cemental tear (arrow)</li> </ul>
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### Medications & Oral Ulcers

<ul style="list-style-type: none"> <li>▪ NSAIDS</li> <li>▪ Propranolol (beta- blockers): HTN</li> <li>▪ Captopril (ACE inhibitors): HTN</li> <li>▪ Alendronate (Fosamax): Osteoporosis</li> <li>▪ Drugs that cause xerostomia</li> </ul>	<ul style="list-style-type: none"> <li>▪ Methotrexate: autoimmune</li> <li>▪ Nicorandil: potassium-channel activators</li> <li>▪ Protease inhibitors, antiretrovirals</li> <li>▪ Everolimus: organ transplant</li> <li>▪ Sirolimus: psoriasis, organ transplant</li> </ul>
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### Aphthae & Systemic Disease

- GERD
- PFAPA
- Behcet disease
- Crohn disease
- Ulcerative colitis
- Celiac disease
- Neutropenia
- Reactive arthritis
- Immunodeficiencies
- Diseases with xerostomia



### RAU: Topical Agents

- Triamcinolone in dental paste 0.1%
- Betamethasone valerate ointment 0.1%
- Dexamethasone elixir, solution 0.5mg/5mL
- Fluocinonide gel, ointment .05%
- Clobetasol gel, ointment .05%
- Chlorhexidine oral rinse .12%



**Treatments for recurrent aphthous ulceration**  
*Clinical Evidence Issue 4 Dec. 2000: p 746-752*  
 Porter S, Scully C. Oral Health. Aphthous ulcers: recurrent.


### Aphthous Stomatitis

**Topical or systemic agents:**

- Dexamethasone elixir, solution 0.5mg/5mL
- Celestone (betamethasone) syrup 0.6mg/5mL
- Triamcinolone 0.1% susp (compounded)
- Doxycycline 100mg, rinse, gel, paste (must be compounded) – 1-3 X/day

**Systemic agents:**

- Prednisone 20mg tabs (20-60mg/day) X 5 d
- Other immunosuppressive agents



### Aphthous Stomatitis: Weak or No Evidence

**Nutritional supplement:**


- Vitamin B<sub>12</sub> 1000 mg (SL, PO)

**Other treatments:**

- Propolis
- Aloe vera
- Low-level laser


**Anesthetics/coating agents**

- Multiple OTC anesthetics and coating agents (be aware of benzocaine in these topicals)



Mucosal burn from overuse of OTC agents

### Inconclusive Evidence



Cochrane Database of Systematic Reviews

**Systemic interventions for recurrent aphthous stomatitis (mouth ulcers) (Review)**

Brocklehurst P, Tickle M, Glennly AM, Lewis MA, Pemberton MN, Taylor J, Walsh T, Riley P, Yates JM

2012


No single treatment was found to be effective and therefore the results remain inconclusive in regard to the best systemic intervention for RAS. This is likely to reflect the poor methodological rigor of trials, and lack of studies for certain drugs, rather than the true effect of the intervention.

### OTC Products for Oral Ulcers: No Evidence




### New Systemic Drug: RAU

- Otezla (apremilast) by Celgene
- Disease-modifying Antirheumatic Drugs
- Indications: psoriatic arthritis, plaque psoriasis, Behcet syndrome, oral ulcers
- Dosage for oral ulcers: 30mg BID, 2-6 wk
- Not approved for pediatric use <18 YO
- Cost: \$3398/mo  
– N Engl J Med 2019



### What Else Should Be on Your Mind?


- Aphthous minor ulcer
- Traumatic/factitial ulcer
- Recurrent HSV infection
- Transient lingual papillitis
- Superficial mucocele
- Systemic diseases
- Hormonal changes



Superficial mucocele


### Recurrent HSV Infection

- Reactivation of HSV-1
- Types: Herpes labialis, facialis, folliculitis, intraoral HSV
- Prevalence: 20-35%
- 20% develop  $\geq 2$  HSL/yr
- Transmission: Direct contact, saliva, inanimate objects
- Risk: UV light, trauma, dental treatment, fever, menses, stress, tooth eruption

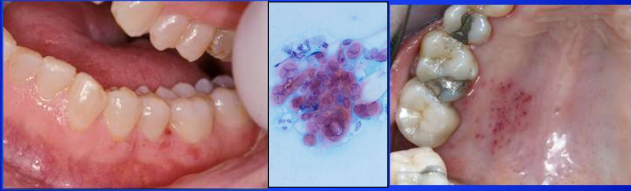


### Recurrent HSV Infection

- Site: Skin, nose, gingiva, vermillion, hard palate
- Duration: 1- 20 days
- Aborted lesions = 25%
- Satellite lesions: 10%
- Bilateral lesions: 10%
- S/S: Recurrent, acute onset, prodromal redness, tender, clustered vesicles, ulcers




### Recurrent HSV & Dental Trauma



- ✓ Trauma from scaling
- ✓ Trauma palatal injection



### Recurrent Zosteriform HSV

- Recurrent HSV – new pattern
- Distribution: Follows an affected nerve; stops at midline
- S/S: Burning, tingling, radiating pain, itchy sensation; painful cluster of vesicles, erosions, ulcers, dysphagia
- Mimics: Herpes zoster, toothache, large mucosal burn
- ID trigger; may be dental treatment
- Tx: Antivirals, palliative



32 YOWF – Radiating painful palatal lesions of sudden onset; feels like multiple toothaches

## Herpes Labialis

- ✓ Labial median fissure
- ✓ Vermilion scarring
- ✓ Trauma-induced Lesion
- ✓ Lip sucking habit
- ✓ Mimics: mucous patch of syphilis


## HSV: New Epidemiologic Facts

- NHANES study, 2015-2016 – ages 14-49
- Overall prevalence: HSV 1 – 48%; HSV 2 – 12%
- Both types higher in ♀ – 51% vs 45% in ♂
- Pediatric prevalence: 14-19 YO – 27%
- Both HSV 1 and 2 down significantly from 1999-2000 study
  - NCHS Data Brief, #304, Feb 2018


## Recurrent Herpetic Infection

### Systemic Agents:

- Sitavig (acyclovir) 50 mg buccal tablets (contains milk protein concentrate)
- Zovirax, g (acyclovir) 400 mg capsules
  - Take 1 capsule 3 times a day X 5 days
- Valtrex, g (valacyclovir) 1 g tablets
  - Take 2 tablets twice daily, 12 hours apart, when symptoms first develop
- Famvir, g (famciclovir) 500 mg tablets
  - Take 3 tablets as a single dose at first sign of infection



## Summary: HSL Prevention



Cochrane Database of Systematic Reviews

Interventions for prevention of herpes simplex labialis (cold sores on the lips) (Review)

Chi CC, Wang SH, Delamere FM, Wojnarowska F, Peters MC, Kanjirath PP 2015

- ✓ The current evidence demonstrates that long-term use of oral antiviral agents can prevent HSL, but the clinical benefit is small.
- ✓ No evidence of an increased risk of adverse events with oral antiviral agents.
- ✓ The evidence on topical antiviral agents and other interventions either showed no efficacy or could not confirm their efficacy in preventing HSL.

## Summary: Herpes Labialis Treatment

Oral Pathology & Medicine

J Oral Pathol Med (2015) 121, 303–308  
© 2015 John Wiley & Sons Ltd. Published by John Wiley & Sons Ltd

**REVIEW ARTICLE**

**Efficacy and safety of nucleoside antiviral drugs for treatment of recurrent herpes labialis: a systematic review and meta-analysis**

Fangman Chen<sup>1\*</sup>, Han Xu<sup>1,2,3\*</sup>, Jiali Liu<sup>1</sup>, Yuan Cui<sup>1</sup>, Xiaobo Luo<sup>1</sup>, Yu Zhou<sup>1</sup>, Qianming Chen<sup>1</sup>, Lu Jiang<sup>1</sup>

<sup>1</sup>State Key Laboratory of Oral Diseases, West China Hospital of Stomatology, Sichuan University, Chengde, Sichuan, China; <sup>2</sup>West China School of Public Health, Sichuan University, Chengde, Sichuan, China


- ✓ Decreased healing time (-0.74 days) – classic lesions (-1.09 days)
- ✓ Decreased time to resolution of pain (-0.38 days) (valacyclovir > acyclovir)
- ✓ Increased percentage of aborted lesions – acyclovir and valacyclovir

## Recurrent Herpetic Infection

- **Topical Antiviral Agents for Lips:**
  - Abreva (docosanol) cream 10% (OTC)
  - Denavir (penciclovir) cream 1%
  - Acyclovir cream 5%
  - Xerese (acyclovir 5%/hydrocortisone 1%) cream

*No evidence for prevention with topicals.*


The CDC 2015 recommends avoidance of topical antivirals, owing to a lack of clinical benefit.





### Treatment Evidence for HSV

- Sunscreen SPF 30 Lip Balm: No evidence
- Nutritional Supplements: No evidence
  - Lysine 1000-3000 mg per day
  - Zinc sulfate 22.5 mg tablets, BID
  - Vitamin C 600 mg or more
- Topical Agents with Supplements: No evidence
  - Zinc oxide cream
  - AverTeaX ointment (Green tea extract + aloe)
- Low level laser therapy: Inconclusive evidence



### New OTC Cold Sore Meds & Devices

Boes H. Nature Scientific Reports (2020) 10:6465



Docosanol 10%  
FDA-approved; not new

Lumiance RED - Cold Sore Treatment - FDA Cleared Light Therapy Laser Device

RELEV Oral Care Treatment  
FASTEST - Multi-Symptom Relief  
Professional Treatment

Benzalkonium chloride, echinacea – for intraoral lesions

AVERTEA Lip Care  
Benzyl alcohol 1.0%, aloe vera, green tea extract

### What Else Should Be on Your Mind?

- Herpes labialis
- Angular cheilitis
- Impetigo
- Median fissure of lips
- Exfoliative cheilitis
- Contact allergy cheilitis
- Candidal cheilitis
- Actinic cheilitis
- Maskne



Impetigo in a child

### Exfoliative Cheilitis

- Cause: Alternating wetness and dryness, fungal and bacterial infection, allergy, factitial injury
- Contributing factors: Eczema, chronic picking or sucking on lips, lipsticks, cosmetics, dry mouth, photosensitivity
- Site: Vermilion and perioral skin
- Duration: Persistent or seasonal condition
- S/S: Recurrent scaling, fissuring, crusting, ulcers; may burn, bleed, or cause swelling; +/- red halo or papules around lips
- Complication: Scarring, infection


### Exfoliative Cheilitis



- ✓ Classic pattern
- ✓ Associated with dry mouth in adult
- ✓ Factitial habit aggravates the condition  
Mimics ulcerated actinic cheilitis

### Exfoliative Cheilitis

- Identify & eliminate the cause
- Avoid medicated, flavored, fragrant lip balm
- Select ointments over balms that are chapsticks
- Simple lubricants:
  - Aquaphor Healing Ointment
  - Vaseline Petroleum Jelly
  - Colorsence Sunforgettable Lip Shine, SPF 35
  - EltaMD UV Lip Balm, SPF 36
- Topical steroids, low potency (short-term only) :
  - Aclovaate (alclometasone) ointment .05%
  - Desonide ointment .05%



### Beware of Mimickers of Chapped Lips

70YOF with angular cheilitis      75 YOM with actinic cheilitis

### Perioral Dermatitis

- Inflammatory disease of the perioral and perinasal area +/- bacteria
- Cause: Idiopathic, topical steroids, toothpastes, heavy creams, cosmetics
- Exacerbated by UV light, heat, wind
- Irritant or allergic contact dermatitis
- S/S: Persistent, pruritic red rash, pustules
- Tx: DC facial products, steroids, change toothpastes; topical antibiotics, topical pimecrolimus, others
- Diff Dx: Adult acne, impetigo, rosacea

Use of mask have aggravated the problem  
Ask about grooming products for mustaches

### Exfoliative Cheilitis and Perioral Dermatitis due to Contact Toothpaste Allergy

Before      After

### Case History

- ID: Healthy 16 YOHM - No history of smoking. Good OH at his last recall
- CC: "Tongue gets whitish (sometimes slightly greenish) buildup." I cannot brush it off with my toothbrush". Metal tongue scraper has not been helpful. What can I do?
- S/S: Mild cream coating, focal elongation of filiform papillae, inflamed fungiform papillae; median fissure. Perioral erythema and dryness. Mild burning.
- Uses antiseptic rinse 3-4X/day – not helpful

Photo: Dr. Katie Gahm


### What is the Problem?

- Vaping, cannabis or alcohol use?
- Stress-induced xerostomia
- Anxiety with a focus on tongue
- Overuse of tongue-scrapper
- Overuse of mouth rinse
- GERD
- Allergies with post-nasal drip
- TX: DC mouth rinse & tongue scrapper, use diluted baking soda rinse, ↑ hydration, Oral Balance gel
- Reassurance is important

### Chemically-Induced Mucositis

- ✓ 46 YO ♂: Gum pain treated with alcohol-containing mouth rinse and then switched to hydrogen peroxide rinse when the sores developed.
- ✓ Cause: Decreased oral moisture, self-medication, misuse of agents
- ✓ S/S: Sudden onset, tender, irregular pattern of sloughing and erosion
- ✓ Site: Nonkeratinized mucosa; often mand mucosa more affected with rinses

### Adverse Events of Mouth Rinses: Systematic Review



- Tooth and mucosal staining
- Mucosal sloughing, desquamation
- Erythema, vesicles, ulcers
- Gingival inflammation
- Dry mouth
- Cracked lips
- Coated tongue, hairy tongue
- Taste disturbances/loss
- Sore mouth, burning sensation
- Oral itching
- Numbness, dysesthesia
- Sore throat
- Hyperkeratosis
- Dental hypersensitivity
- Calculus formation

Tartaglia G, et al. Ther Adv Drug Saf 2019


### Topical Benzocaine Allergy

- ID: 57 YOM
- Med Hx: Depression; allergies to bees, tree pollen, tramadol
- Meds: Wellbutrin, trazodone
- Dental Hx: Periodontal disease, caries, xerostomia
- S/S: Multiple, tender vesicles, erythema, edema of left labial mucosa; sudden onset – 4 h after dental appt



### Multifocal Ulcers of Sudden Onset

- Widespread distribution of acute onset
- Painful, dysphagia
- Duration is usually < 2 weeks
- Vesicles —> ulcers
- Oral +/- skin lesions
- Systemic features
- Cause is often viral
- Most are common diseases



Herpangina


### Primary HSV Infection

- Cause: HSV-1, HSV-2
- Types: Gingivostomatitis, pharyngitis
- 2 age peaks: 6 mo -5yr; early 20s
- Transmission: Direct contact, saliva, sexual
- Symptomatic disease: 12-30% of those infected
- Site: Oropharyngeal, anogenital & cutaneous
- Duration: 7 - 14 days
- S/S: Acute onset, fever, lymphadenopathy, malaise, pain, erythema, vesicles, ulcers, drooling, dysphagia; widespread oral lesions

### Primary HSV Infection




### Primary HSV Infection




Child daycare assistant  
Used rubbing alcohol on the lips for treatment  
Notice the post-inflammatory pigmentation on lips

### Primary HSV infection in Young Adult




- ❖ Adolescents & young adults tend to have increased oropharyngeal involvement
- ❖ Mimics infectious mononucleosis, herpangina, strep pharyngitis

### Primary HSV infection in Young Adult



- ❖ Buccal mucosal ulcers mimic herpetiform aphthous ulcers

### Primary HSV Infection




- Topical Coating Agents: No evidence
  - Benadryl/Maalox susp +/- lidocaine viscous 2%
  - Sucrets (dyclonine) throat lozenges
  - Lip lubricants to prevent adhesions
- Systemic Agents: No evidence except for case series/reports
  - Zovirax, g (acyclovir) 200mg/5mL, caps 400mg
  - Valtrex, g (valacyclovir) tabs 1g
- Nutritional Liquid Supplements and Fluids
- Antimicrobial Agent for 2<sup>nd</sup> Bacterial Infection:
  - Chlorhexidine rinse .12% (after ulcers resolved): No evidence

### ★ Primary HSV: When to Treat?

- Cochrane Review: Retracted review - no evidence
- Early infections - the first 3 days
- Severe cases with extensive skin lesions
- Cases with periorbital or ocular lesions
- Immunosuppressive drugs, steroids
- Individuals who are immunocompromised
- Caution with renal disease, dehydration

### What Else Should Be on Your Mind?

- Primary HSV infection
- Infectious mononucleosis
- Herpangina
- Herpes zoster
- Hand, foot, mouth disease
- Herpetiform aphthae
- Erythema multiforme
- Necrotizing ulcerative gingivitis (NUG)
- COVID-19 infection



NUG

### Necrotizing Gingivitis: Mimicker of HSV

- Painful gingivitis of recent onset
- Microbial cause: Spirochetes, *Prevotella intermedia*
- Predisposition: Smoking, poor OH, viral infections, including COVID-19, HIV, poor nutrition, sleep deprivation and immunosuppression
- Age: Adolescents & young adults
  - ✓ 13 YOF with recent tongue piercing
  - ✓ Painful gingiva of sudden onset
  - ✓ Using OTC toothache gel for pain



### Necrotizing Gingivitis: Mimicker of HSV

- Location: Attached gingiva, especially interproximal and marginal gingiva
- S/S: Pain, necrosis, ulceration, bleeding, halitosis, localized or widespread; +/- fever, local lymphadenopathy
- TX: Debridement is critical; chlorhexidine oral rinse; if febrile, amoxicillin and/or metronidazole
- May recur, scarring of papillae




### Age Matters for Oral Lesions




### Lichen Planus

- Cause: T cell-mediated autoimmune disease
- Prevalence: 1% skin and .1-2% oral in adults; F>M
- Site: Oral mucosa, skin, nails, genital region, scalp, eyes, esophagus
- Common sites: Buccal mucosa > gingiva > tongue > labial mucosa > others
- Duration: Persistent; waxes and wanes
- Types: Reticular (plaque), erosive (atrophic, erythematous)
- S/S: Bilateral, symmetrical, red & white patches, ulcers, striations, burning or pain

### Reticular Lichen Planus



### LP: Papular and Short Striae




Note the swollen papilla and red orifice of Stensen's duct and irritation fibroma

### Pigmented Lichen Planus



### Lichen Planus



- Causes: HCV (select populations)
- Acute flare ups: Stress, spicy, salty, acidic, citric foods, dental procedures, systemic illness, heavy alcohol use
- Persistent: Rare remission
- Oral hygiene: critical for gingival disease
- Gingival recession is common
- HPV associated with some cases
- Complications: Candidiasis, periodontal disease, cancer risk – 1%

### Oral Lichen Planus: Plaque-Like Variant?




Controversial variant  
Mimics:

- ✓ Proliferative leukoplakia
- ✓ Chronic hyperplastic candidiasis

### Oral Lichen Planus

- Isolated lesions to single site are uncommon except for gingiva (10%)
- 33% with oral lesions develop skin lesions
- Most common extraoral site for women is genital mucosa (>25%) – vulvovaginal-gingival syndrome
- Mimics: Mucous membrane pemphigoid



Erosive Lichen Planus

### Atrophic or Erosive Oral Lichen Planus




- ✓ Young adult with tender gingival tissues
- ✓ Does not respond to oral hygiene measures
- ✓ Waxes and wanes
- ✓ Gingival lesions may be subtle and mimic toothbrush abrasion

### Erosive Lichen Planus




### Medications: Lichenoid Reaction of Skin & Mouth

- Medications are the most common
  - Antihypertensive agents esp. diuretics (hydrochlorothiazide), beta blockers, ACE inhibitors
  - Sulfonylureas
  - Levothyroxine
  - Sulfasalazine
  - Allopurinol
  - NSAIDs
  - Carbamazepine
  - Some statins
  - Newer drugs eg. biologics such as TNF alpha inhibitor



### Lichenoid Reaction & Superficial Mucocelles: Reaction to Ditropan



NB: Oral lichen planus is exacerbated by salivary gland hypofunction

### Lichenoid Contact Allergy

Allergen: Nicorette chewing gum



Photo: Dr. Glenda Owen

### Lichenoid Contact Reaction to Gold Crowns

Pre-treatment



Post-treatment with topical steroids



Photo: Dr. Stephen Davis


### History is Important



58 YOM with factitial injury from a new electric toothbrush

### Treatment of Lichen Planus

- Betamethasone valerate ointment 0.1%
- Dexamethasone elixir 0.5 mg/5mL
- Fluocinonide gel, ointment .05%
- Temovate (clobetasol) gel, ointment .05%
- Protopic (tacrolimus) ointment .03%, .1% and oral solution (not FDA approved for use)
- Prednisone, dose appropriate
- +/- antifungal treatment
- +/- probiotics?
- Photodynamic therapy?



### Oral Lichen Planus

Other helpful hints:

- May require antifungal agent
- Bland toothpaste
- Soft or extra soft toothbrush
- Professional cleaning every 3-4 months
- Doxycycline 20 mg tabs BID (expert opinion)
- Soft acrylic medication carrier for gingiva
- Annual follow-up is important



## Summary for Pain Management



Cochrane Database of Systematic Reviews

**Interventions for treating oral lichen planus: corticosteroid therapies (Review)**

Lodi G, Manfredi M, Mercadante V, Murphy R, Carrozzo M 2020

- ✓ Evidence suggests the topical corticosteroids may be effective
- ✓ Some evidence that tacrolimus may be more effective, but evidence for negative side effects are inconclusive
- ✓ Reliability of evidence is very low

## Weak Evidence for Oral Erosive Lichen Planus



Cochrane Database of Systematic Reviews

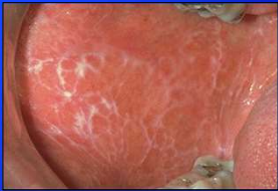
**Interventions for erosive lichen planus affecting mucosal sites (Review)**

Cheng S, Kirtschig G, Cooper S, Thornhill M, Leonardi-Bee J, Murphy R 2015


- ✓ There is no overwhelming evidence for the efficacy of a single treatment, including topical steroids, which are the widely accepted first-line therapy for ELP.
- ✓ With topical corticosteroids, the main side-effects were oral candidiasis and dyspepsia.

## LP & Systemic Associations

- Primary biliary cirrhosis
- Autoimmune chronic active hepatitis
- Lupus erythematosus
- Myasthenia gravis
- Aplastic anemia
- Ulcerative colitis
- Dermatomyositis
- Diabetes mellitus
- Celiac disease
- Multiple sclerosis




## What is the Risk for Cancer?



Oral Oncology 96 (2019) 121–130  
Gastric Site available at ScienceDirect  
**Oral Oncology**  
journal homepage: www.elsevier.com/locate/oraloncology

**Review**  
**Malignant transformation risk of oral lichen planus: A systematic review and comprehensive meta-analysis**  
Miguel Angel González-Moles<sup>a,b,c</sup>, Isabel Ruiz-Ávila<sup>a,b,c</sup>, Lucía González-Ruiz<sup>a</sup>, Ángela Ayén<sup>a</sup>, José Antonio Gil-Montoya<sup>a</sup>, Pablo Ramos-García<sup>a</sup>

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Malignant transformation of lichen planus (1.14%), lichenoid lesion (1.88%), lichenoid reaction (1.71%)  
Malignant transformation risk factors were: tongue localization (RR = 1.82) p = 0.004, presence of atrophic-erosive lesions (RR = 4.09, p < 0.001), tobacco use (RR = 1.98, p = 0.002), alcohol consumption (RR = 2.28, p = 0.02), and hepatitis C virus infection (RR = 4.46, p = 0.053)