Management of Oral Soft Tissue Conditions and the Use of Medications

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Objectives

- Differential diagnosis of soft tissue conditions
- Describe more common soft tissue conditions
- Diagnosis of soft tissue conditions
- Management strategies of mucosal lesions
  - Treatment
  - Prevention

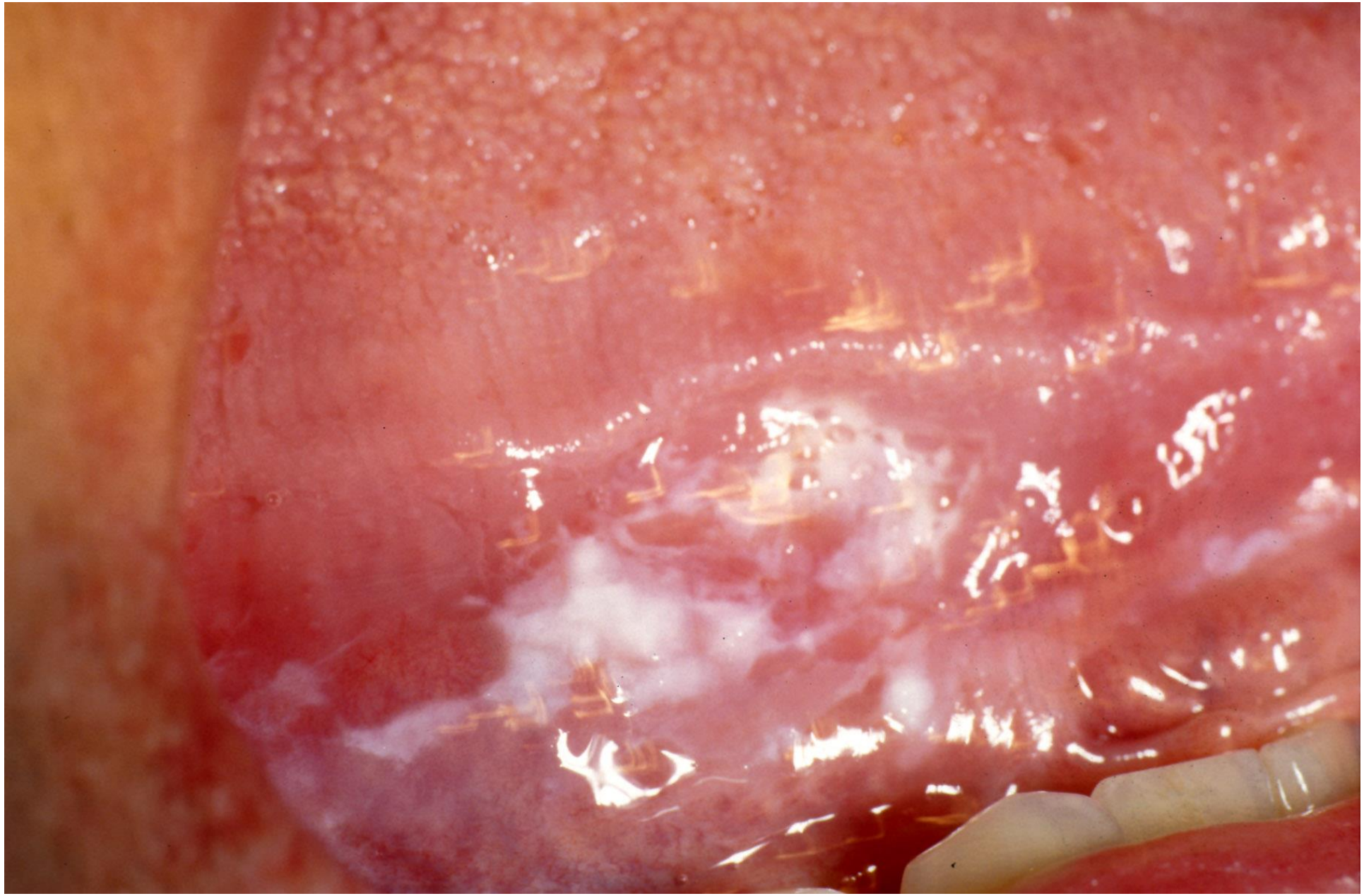
Differential Diagnosis-NIRDS

- Neoplastic
- Infectious
- Reactive
- Developmental
- Systemic

NEOPLASTIC

Leukoplakia- White

- Clinical diagnosis only
- Histologically: hyperplasia, mild, moderate, or severe dysplasia, carcinoma in-situ, invasive carcinoma
- Thin leukoplakia: seldom malignant change
- Thick leukoplakia: 1-7% malignant change
- Granular or verruciform: 4-15% malignant change
- Erythroleukoplakia: 28% malignant change



Neoplastic: Red Lesions

- SCCA

Diagnosis: Incisional vs. Excisional Biopsies

Dysplasia Management – Medical

- Systematic Review: 9 studies met criteria for low bias in prior review
- Three studies were reviewed based adequate study quality.
  - topical bleomycin
  - systemic retinoids
  - systemic lycopene
- No therapeutic recommendations for bleomycin and cis-retinoic acid
- Lycopene (4 and 8 mg) may have some efficacy in patients with risk factors similar to those found in a subcontinental Indian population, for the short-term resolution of oral epithelial dysplasia

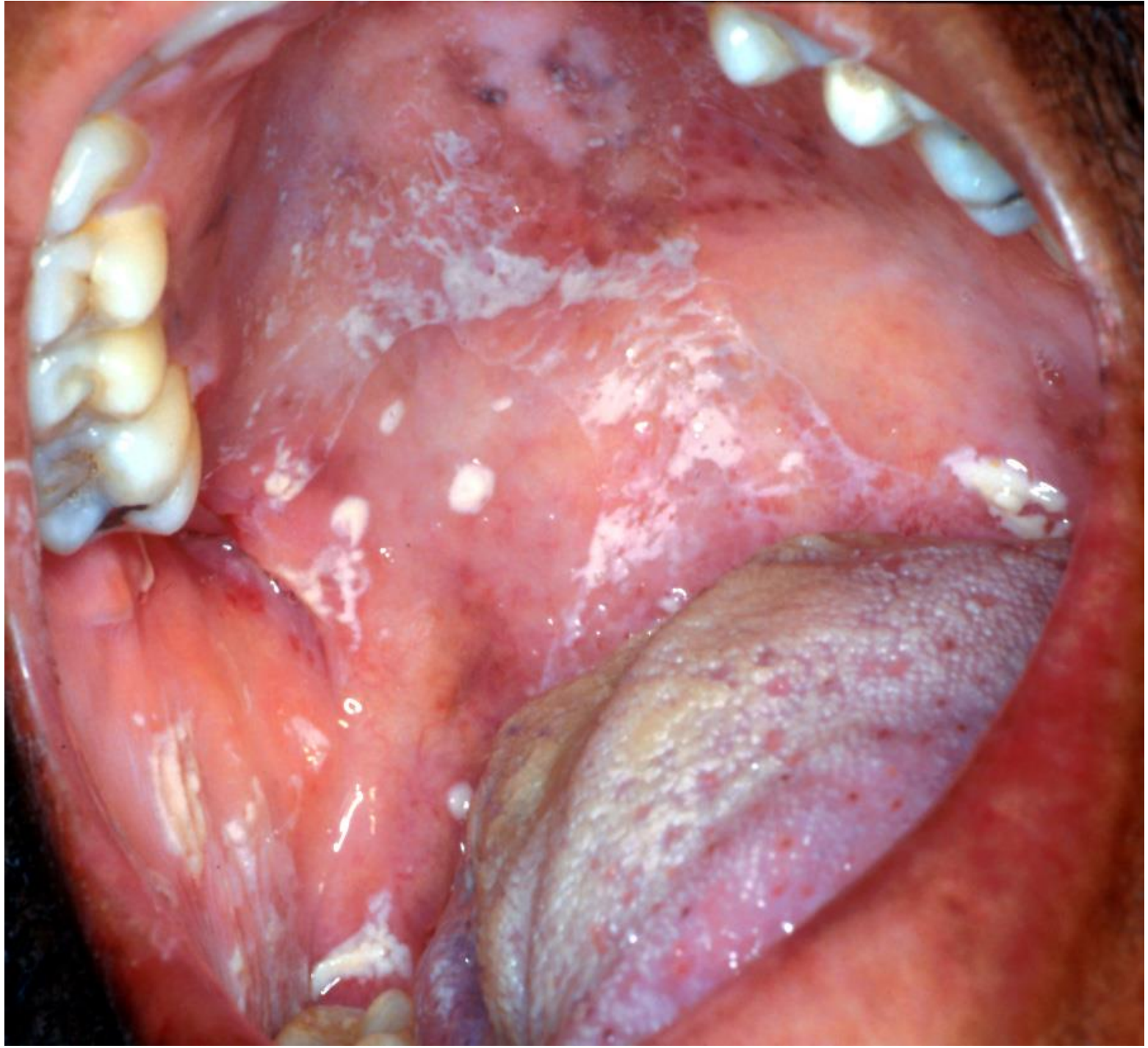
Dysplasia Management – Surgical

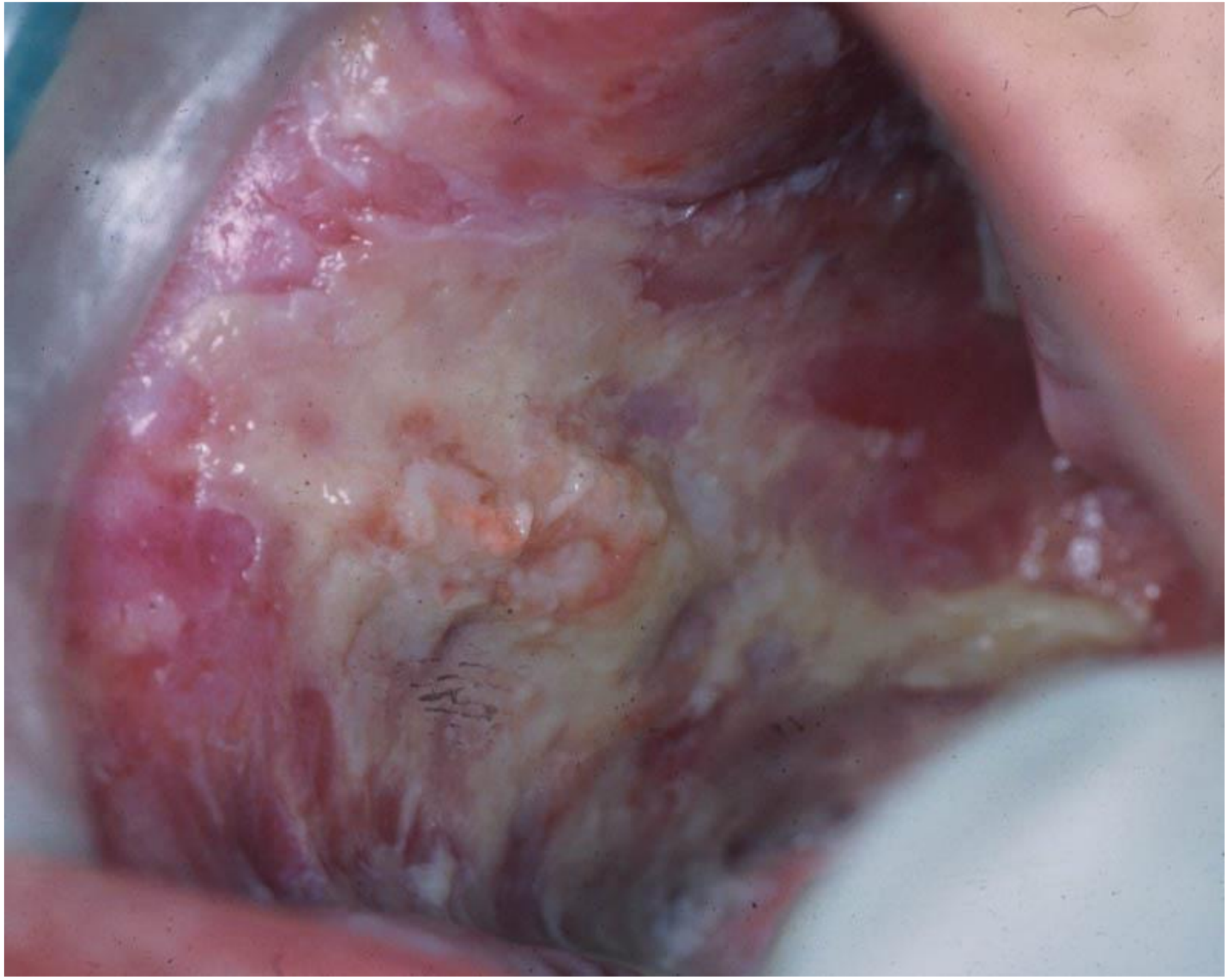
- Lack RCTs that would allow to assess the effectiveness of surgical treatment, including lasers
- In non-RCTs the effectiveness of various surgical modalities in preventing malignant transformation of oral dysplasia have resulted in contradictory outcomes

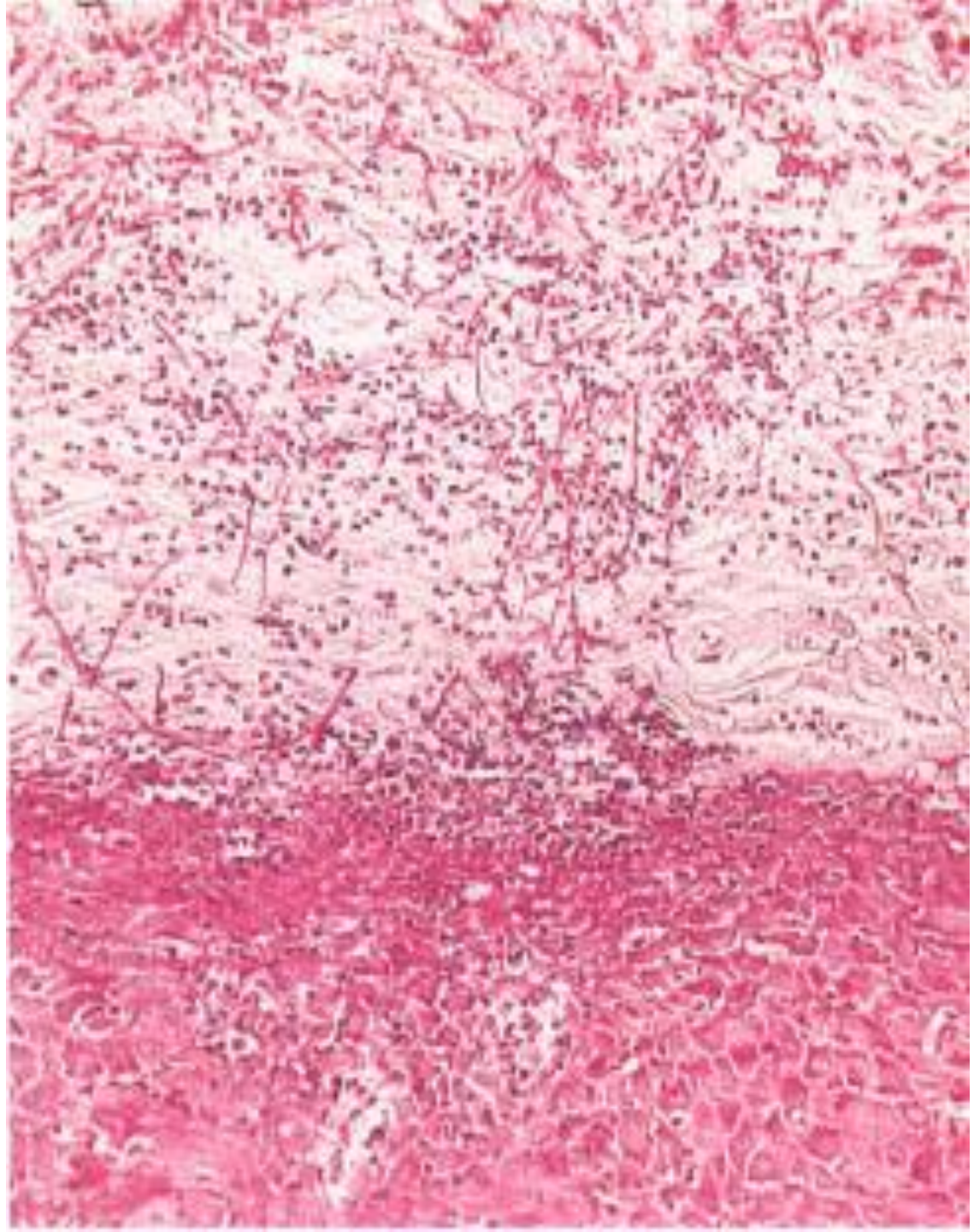
INFECTIOUS

Candidiasis

- Psuedomembranous
- Erythematous
- Hyperplastic
- Angular cheilitis







Soft tissue diagnostic tests

- Fungal
  - Superficial:
    - Smear $\rightarrow$ potassium hydroxide or stained with PAS $\rightarrow$ hyphae
    - Culture
  - Deep fungal: $\rightarrow$ Biopsy

Treatment - Fungal

- Topical
  - 10 mg clotrimazole troches 5x/d for 7-10 days
  - Nystatin rinse- 100,000U/mL swish and spit 5mL 4x/d for 2 weeks
  - Chlorhexidine rinse 10 mL bid
  - Probiotics (reduced oral candida in elderly population- RCT J Dent Res x2)
  - Nystatin/triamcinolone cream- dab on corners of mouth 4x/d
  - Clotrimazole-betamethasone dipropionate (Lotrisone) cream
  - Miconazole (Monistat 7) nitrate vaginal cream 2%
  - Nystatin ointment (thin layer on denture) tid

Treatment - Fungal

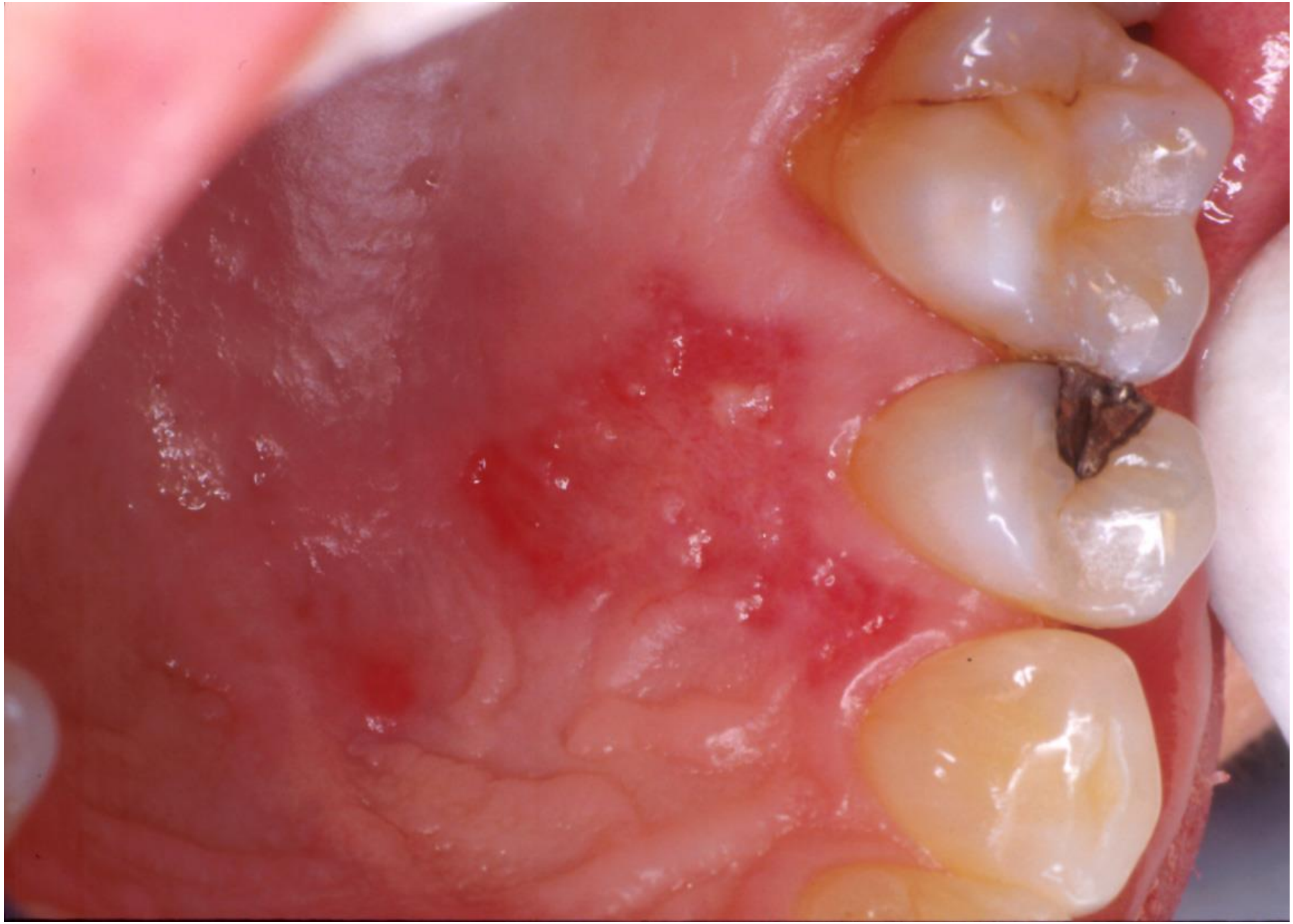
- Systemic
  - Fluconazole
    - 200 mg day 1 followed by 100 mg/d 1-2 weeks
  - Ketoconazole
    - 200 mg/day for 14 days
- Both are potent inhibitors of cytochrome P-450: Check Pharmacology Reference-Drugs.com: 149 major drug interactions-Warfarin, Xanax, Lipitor, Plavix, hydrocodone…

Infectious: Red Lesions

- Fungal
  - Erythematous candidiasis
  - Immunocompromised
  - Histoplasmosis, Coccidioidomycosis, Blastomycosis, Cryptococcus (Solitary painful ulceration of tongue, palate, buccal mucosa)
  - Aspergillosis (sinus, after tooth extraction or endodontic treatment)
  - Mucormycosis (Maxillary sinus infection, swelling of alveolar process and/or palate)
    - Extensive tissue destruction due to preference for small blood vessels: infarction and necrosis disrupts blood flow

Infectious: Red Lesions

- Viral HSV
  - HSV-1 vs. HSV-2
  - Children: Acute herpetic gingivostomatitis-both moveable and attached mucosa
  - Adults: Pharyngotonsillitis- vesicles tonsils and posterior pharynx. Oral mucosa anterior to waldeyer's ring <10% of cases.
  - Most common recurrent site: lip (herpes labialis)



Soft tissue diagnostic tests

- Viral
  - Culture $\rightarrow$ 2-4 days for + ID
  - Cytology $\rightarrow$ Virally damaged epithelial cells
  - Serology $\rightarrow$ Rising titre of antibody
  - DNA in situ hybridization for specific virus identification
- Bacterial
  - Aerobic and anaerobic culture

Infectious: Red Lesions

- Viral VZV
  - Primary infection: chickenpox (oral lesion: palate and buccal mucosa most frequently involved: vesicles.
  - Recurrence: Herpes Zoster
    - 10-20% of older population.
    - One dermatome affected
    - Prodromal pain, fever, malaise 1-4 days before cutaneous/oral lesions.

Treatment- Viral

- Observe/supportive care
  - Immunocompetent patient
  - Maintain hydration and nutrition
- Topical
  - MBX- care with lidocaine (esp. children and elderly)
  - Aquaoral with SPF
  - Penciclovir (Denavir) cream 1%
  - Docosanol (Abreva)

Treatment - Viral

- Systemic
  - Acyclovir caps 200 mg: 2 caps 3x/day for 7 days
  - Valacyclovir 500 mg: 1 g 2x/day for 7-10 days (initial episode)
  - Valacyclovir 500 mg: 4 caps when prodromal symptoms start
  - Valacyclovir 500 mg: 1 cap 2x/day for 3 days

Prevention - Viral

- Systemic
  - Acyclovir caps 200 mg: 2 caps 2x/day
  - Valacyclovir 500 mg: 1 cap daily

REACTIVE

Reactive-White

Reactive lesions

- Focal (frictional) hyperkeratosis
  - Response to low-grade irritation (sharp edge)
  - Buccal mucosa along occlusal line
  - No dysplastic changes

Reactive lesions

- Tobacco pouch keratosis
  - Muccobuccal fold, granular to wrinkled appearance
  - Gingival, periodontal destruction possible
  - 15% chewing tobacco, 60% snuff users
  - Malignant potential
- Nicotine stomatitis
  - Palatal mucosa: elevated papules with red centers are inflammed minor ducts
  - Not pre-malignant. May revert when discontinues smoking

Reactive-Red

Reactive: Red Lesion

- Aphthae
  - Unknown etiology, incidence 20-60%
  - 3 Clinical forms (minor, major, herpetiform)
  - Non-keratinized mucosa
  - Diagnosis by elimination
  - Rule out allergies, hematologic abnormalities, infectious agents, nutritional imbalances, trauma, stress.

Management/prevention of RAS

- Clobetasol (0.05% gel) on lesion immediately when first symptoms occur
- Chlorhexidine start 1-2x/day for 2 weeks and decrease to every other day or every 3rd day
- Vitamin B12 supplement
- Alteration of diet?

Topical steroid by strength

- Ultrapotent
  - Clobetasol 0.05%
  - Halobetasol 0.05%
- Potent
  - Dexamethasone 0.5 mg/5 mL
  - Fluocinonide 0.05%
- Intermediate: Triamcinolone acetonide (Kenalog) 0.1%
- Low: Hydrocortisone 1%
- Gel, Ointment, Cream, Compounded

Topical Steroids

- “for external use only”
- High cost
- Atrophy of mucosa
- Fungal side effects…

Topical Steroids and Fungal Infection: Study Objectives

- **Primary**

  Determine the incidence of oral candidiasis in patients treated with topical steroids for oral lichen planus (OLP)

- **Secondary**

  Determine if different antifungal therapies are more effective than others in preventing the development of clinical fungal infections

Marable DR, Bowers LM, Stout T, Stewart CM, Berg KM, Sankar VS, DeRossi SS, Thoppay JR, Brennan MT. Oral candidiasis following steroid therapy for oral lichen planus. Oral Dis. 2016 Mar;22(2):140-7.

Methods

Multicenter, retrospective chart review of a well-characterized group of Lichen Planus patients

- Carolinas Medical Center (CMC)
- University of Florida College of Dentistry (UF)
- University of Texas Health Science Center at San Antonio (UTHSCSA)
- Georgia Regents University College of Dental Medicine (GRU)

Methods

Inclusion Criteria

- Patients diagnosed with clinical oral lichen planus.
- Patients at CMC, UF, UTHSCSA, and GRU
- Patients treated for lichen planus with topical steroids for at least 2 weeks AND a follow-up visit within 5 weeks of the initiation of daily topical steroids.

Methods

Treatment regimen for oral lichen planus

- Topical Steroid Used: Y/N
- Generic name and % of topical steroid
- Systemic Steroid Used: Y/N
- Antifungal Preventive Therapy Used: Y/N
- Generic name and % (if applicable) of antifungal therapy

Methods

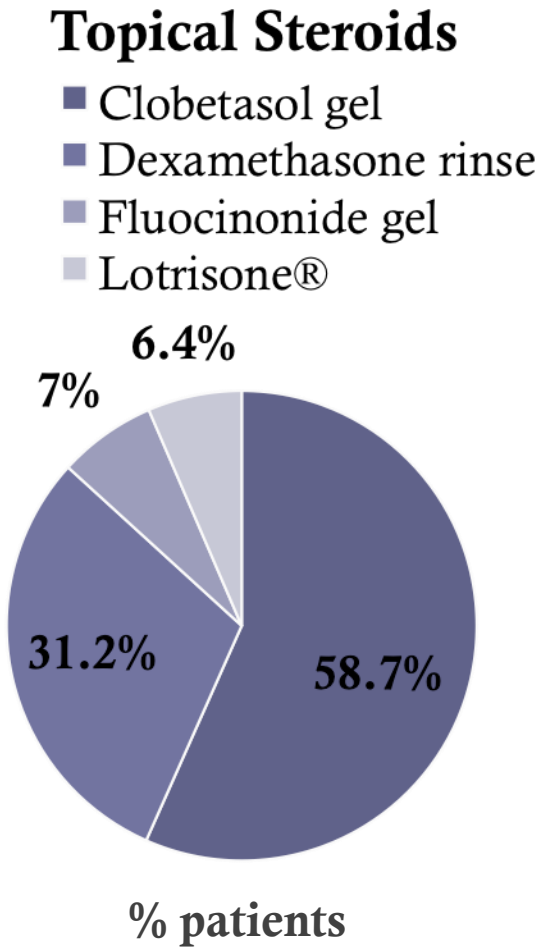
Follow-up Data

- Clinical appearance:
  - Improved/Worsening/No change
- Clinical symptoms (burning/pain):
  - Improved/Worsening/No change
- Oral Fungal Infection? Y/N
  - If yes, describe appearance
- Treatment of oral fungal infection

Results

Topical steroids were used in 303 (96.2%) patients.

Systemic steroids were used in 12 (3.8%).



Results

- Objective improvement
  - Clobetasol
    - 91.1% with clobetasol
    - 81.5% without clobetasol (p=0.02)
  - Use of any preventive antifungal
    - 90.6% with antifungal
    - 80.5% without antifungal (p=0.02)
- Subjective improvement
  - Clotrimazole
    - 94.3% with clotrimazole
    - 85.4% without clotrimazole (p=0.04)

Results

- **Oral fungal infections at follow-up**
  - **Total**: 43 (13.7%) patients

  - No significant difference between sites (p=0.36).
    - CMC - 24/155 (15.5%)
    - UF - 11/67 (16.4%)
    - UTHSCSA - 6/59 (10.2%)
    - GRU - 2/34 (5.9%)

Results

- **Fungal infections at follow-up, by steroid treatment**
  - **Clobetasol** - 32/183 (17.5%), (p=0.02)
  - **Dexamethasone** - 11/98 (11.2%), (p=0.39)
  - **Fluocinonide** - 1/22 (4.6%), (p=0.33)
  - **Lotrisone®** - 4/20 (20%), (p=0.50)

- Preventive antimycotic agents were used in 203 patients and no antimycotic in 111, with fungal infections occurring in 29 (14.3%) and 14 (12.6%), respectively.

Results

- Salivary flow testing was completed in 51 patients of which 10 developed OFI.
- Low stimulated salivary flow group (≤ 0.7 ml/min)
  - 9 (90%) OFI patients
- High stimulated salivary flow (>0.7 ml/min)
  - 1 (10%) OFI patient
- No difference in unstimulated flow

Conclusions

- The incidence of oral fungal infections in OLP patients following steroid therapy was higher than anticipated (13.7%).
- Clobetasol had a significantly higher incidence of fungal infection compared to all other steroid therapies.
- Low saliva is a major risk factor for a fungal infection

Reactive: Red Lesion

- Allergic reaction to systemic drugs
  - Erythema multiforme
  - Lichenoid
  - Lupus erythematous-like eruptions
  - Pemphigus-like lesions

Reactive: Red Lesion

- Erythema Multiforme
  - Immunologically mediated
  - 50% of cases preceding infection or exposure to drug
  - Oral: erythematous patches that develop shallow erosions and ulcerations.
  - Target skin lesions in 50% of cases
  - More severe: erythema multiforme major (Stevens-Johnson syndrome) and Toxic Epidermal Necrolysis (Drug involved)

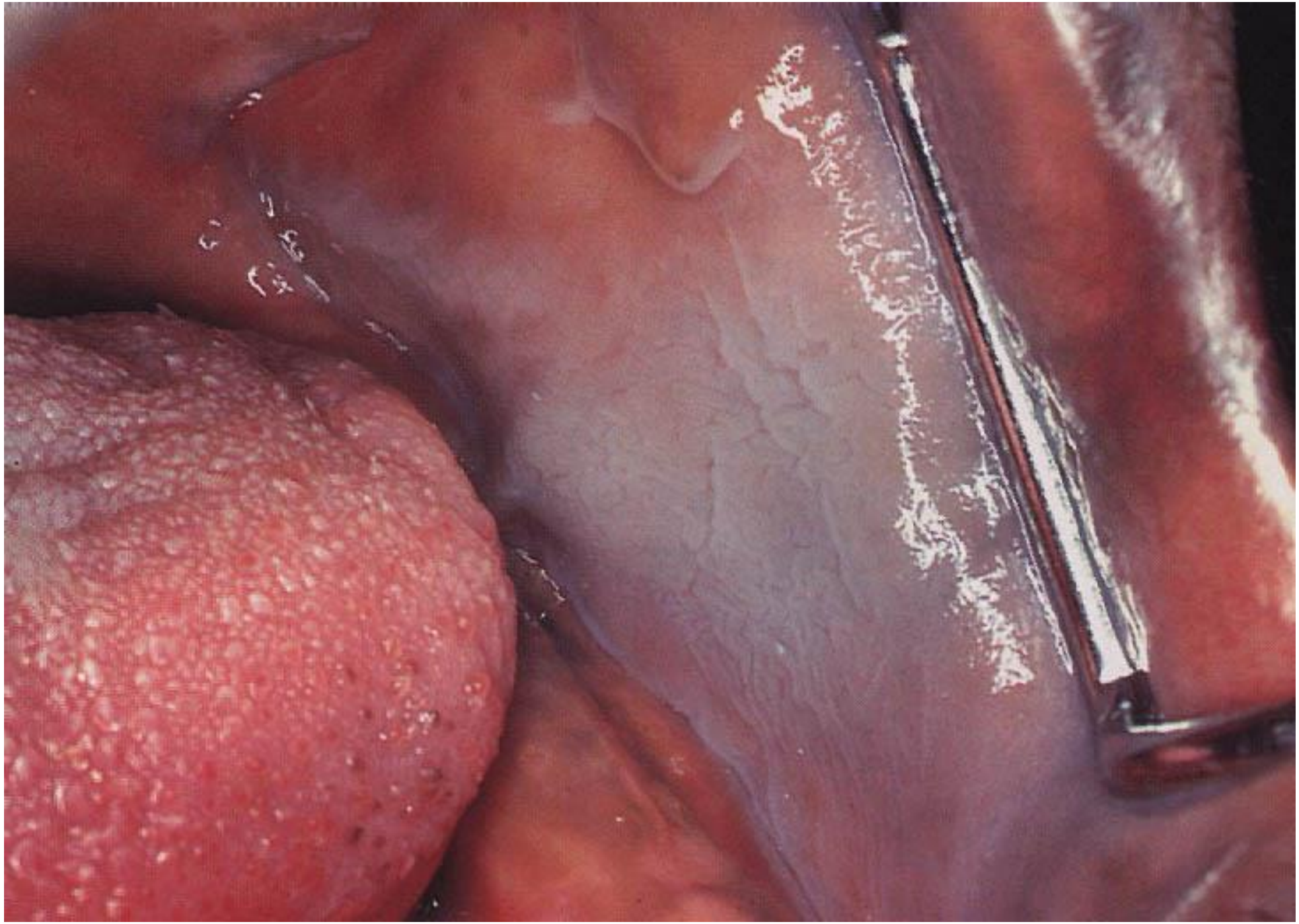
Management – Erythema Multiforme

- Prednisone start of lesions
- Preventive:
  - Acyclovir 400 mg 2x/day
  - Valacyclovir 500-1000 mg /day

DEVELOPMENTAL-White

Hereditary conditions

- Leukoedema
  - Natural variant. Asymptomatic, symmetric gray-white, filmy or milky surface
  - Stretching removes clinical appearance
  - More frequent in African Americans



Fordyce granules

- Sebaceous glands that occur on the oral mucosa. Normal variant
- Found in up to 80% of the population
- Multiple yellowish-white papular lesions.
- Most common buccal mucosa.

Developmental: Red Lesion

- Benign Migratory Glossitis (Geographic Tongue)
  - Red Lesion with white border
  - Usually asymptomatic
  - Moves
  - Diagnosis
    - Elimination
    - Rule out fungal etiology of symptoms

Management of Benign Migratory Glossitis

- Topical Steroids
- Antifungals
- Rule out hematinic deficiencies

SYSTEMIC

Lichen Planus

- The reported prevalence rates of oral lichen planus (OLP) vary from 0.5% to 2.2% of the population
- Often develops between 30-60 years, and it is more frequently seen in women
- Intra-oral: Reticular, plaque-like, erosive, bullous forms, desquamative
- Extra-oral: PPPP: purple, polygonal, pruritic papules- Flexural surfaces, scalp, nails, genitals
- Etiology unknown
- Lichenoid reactions (drugs, amalgam, gold)

Treatment for symptomatic OLP- systematic review

- Topical corticosteroids (+/- topical anti-mycotics) are the first-line treatment for localized lesions
- Insufficient evidence regarding different dosages, formulations or modes of delivery of topical steroids (eg. paste, spray, mouthwash) to make an evidence based recommendation about which is best
- Systemic corticosteroids (+/- topical anti-mycotics) are the first-line treatment only for severe, wide-spread OLP and for lichen planus involving other muco-cutaneous sites (eg.: vaginal/vulval LP) recalcitrant /resistant to topical therapies
- Topical retinoids should be considered only as second line therapy for OLP; systemic retinoids are not recommended
- Topical calcineurin-inhibitors should be considered only as second-line therapy.

Management – Lichen Planus

- Topical steroids
  - Up to 2 weeks followed by 1 week break: repeat if needed
  - Concern of atrophy of mucosa and adrenal suppression with long-term use
- Optimize oral care
- Chlorhexidine with poor plaque control
- Tacrolimus (protopic) 0.1% ointment
  - No a steroid
  - BUT- black box warning

LP malignant transformation

- The alleged annual malignant transformation rate for OLP is between 0.2% and 0.5%
- 10-50X increased risk of SCCA
- 2-4 /100 patients over 10 year follow up
- Patients should be encouraged to avoid or discontinue habits such as excessive tobacco and alcohol use, that are likely to increase the risk of malignant transformation
- Long-term monitoring may be problematic as this is resource intensive. At a minimum, annual monitoring of OLP is recommended

Oral Lichenoid Reactions

- Oral lichenoid contact lesions (OLCL's) are seen in direct topographic relationship to an offending agent
- This reaction is most often attributable to dental restorative materials, most commonly amalgam
- With the removal and replacement of the putative causative material, the majority of such OLCL's resolve within several months
- Patch testing?

Lupus

- Oral lesions approximately 25% of SLE.
- May appear lichenoid, ulcerative or granulomatous. May have more erosive quality.

Pemphigus

- Autoantibodies to desmosomes
- 50% have oral mucosal lesions prior to mucocutaneous lesions. Eventually all have intra-oral lesions.
- Prior to corticosteroids, 60-80% mortality

Pemphigoid

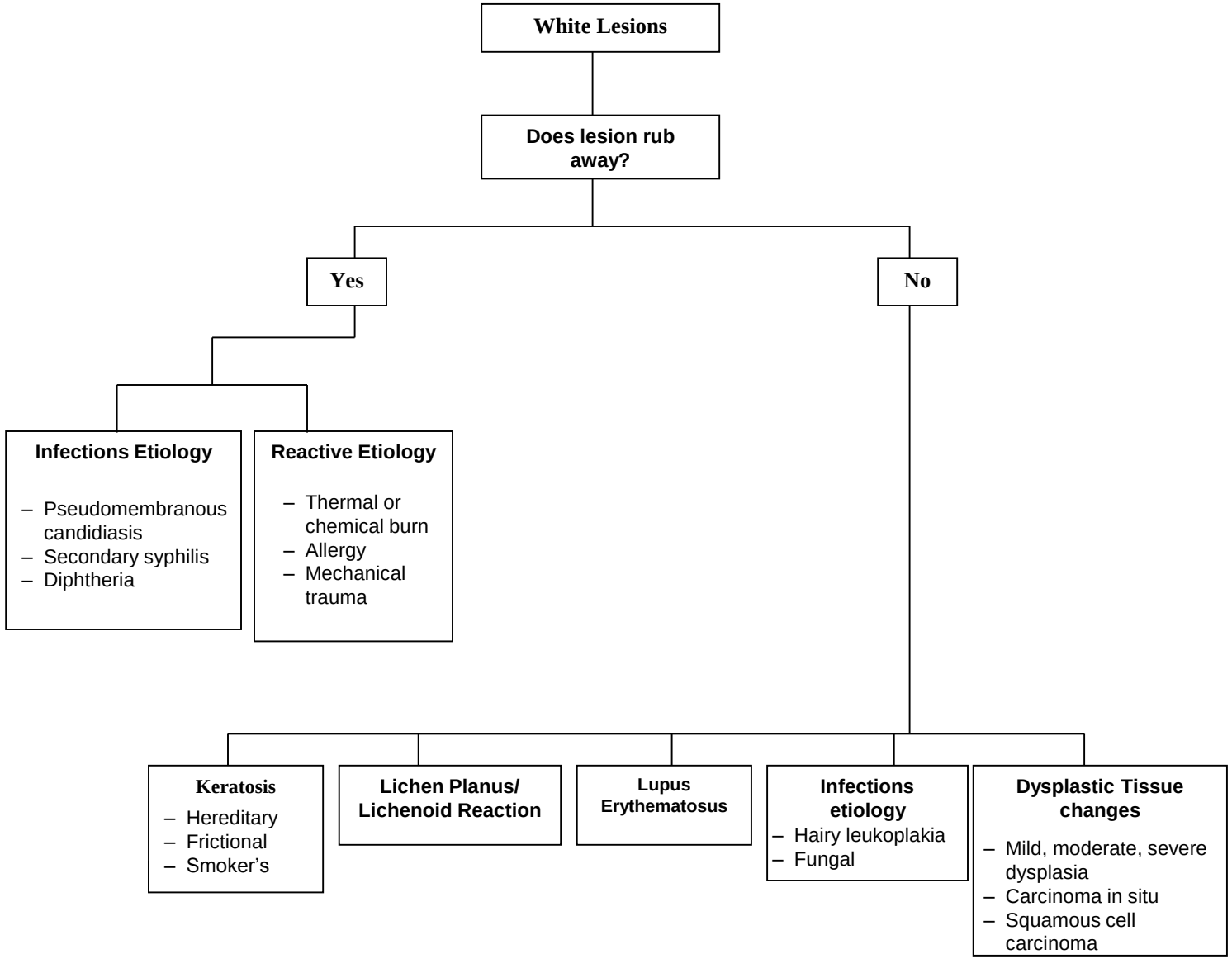
- Autoantibodies to basement membrane
- Average age 60
- Oral lesions most patients. Begin as vesicles or bullae. Painful and persistent if untreated.
- Ocular lesions in 25% of pemphigoid patients with oral lesions

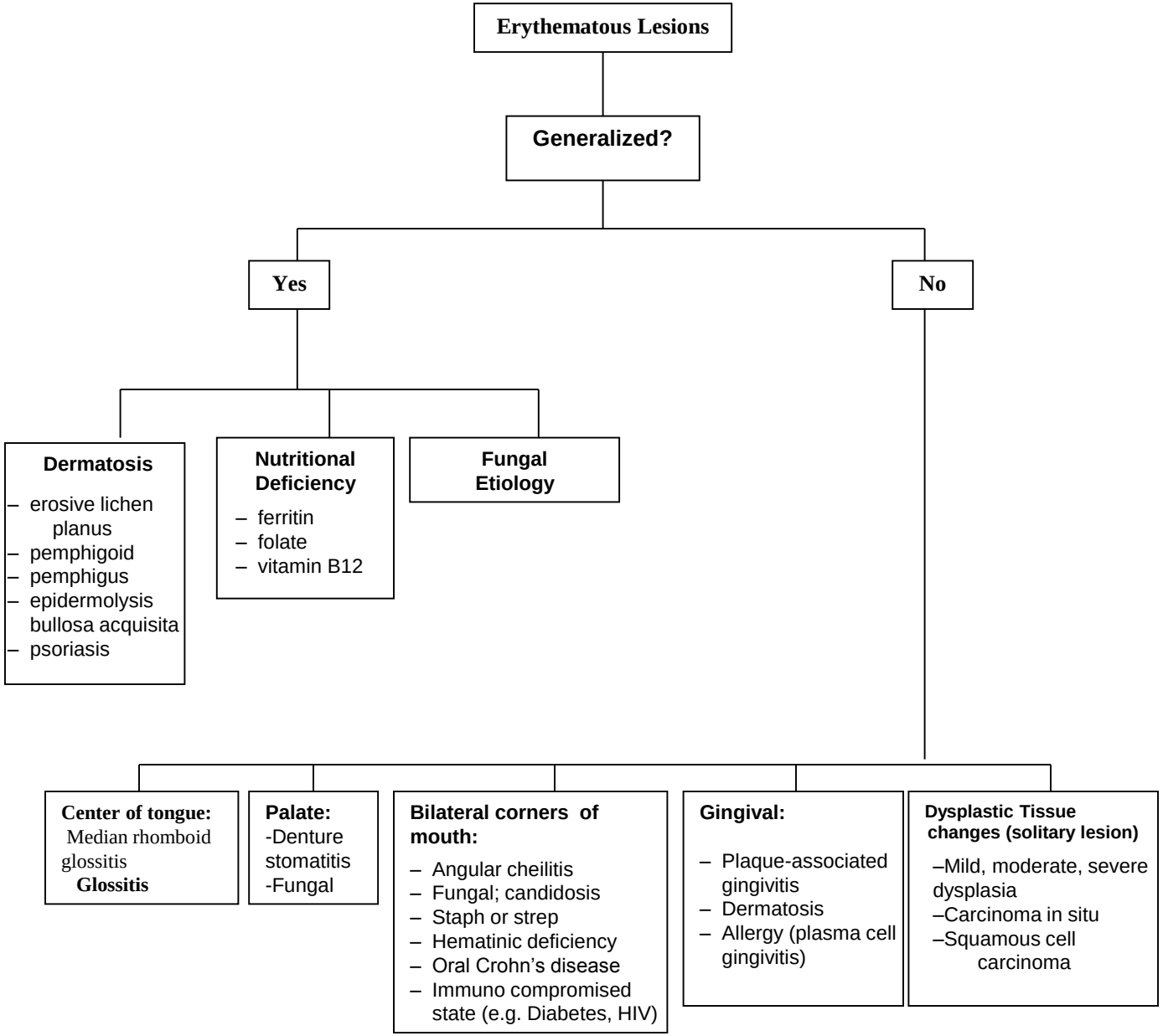
Management - Pemphigoid

- Avoid hard/sharp foods
- Optimal plaque control
- Chlorhexidine
- Topical steroids
- Doxycycline 100 mg daily long-term
- Refractory: dapsone, prednisone

Gingival Differential

- Desquamative Gingivitis
  - Erosive LP (71%)
  - Pemphigoid (14%)
  - Pemphigus (13%)
  - Linear IgA Disease
  - Epidermolysis Bullosa Acquisita
  - Plasma Cell Gingivitis
- Mass on Gingiva (4 Ps)
  - Pyogenic Granuloma
  - Peripheral Ossifying Fibroma
  - Peripheral Giant Cell Granuloma
  - Parulis


White Lesions
Does lesion rub away?
Yes
No
Infections Etiology
– Pseudomembranous candidiasis
– Secondary syphilis
– Diphtheria
Reactive Etiology
– Thermal or chemical burn
– Allergy
– Mechanical trauma
Keratosis
– Hereditary
– Frictional
– Smoker's
Lichen Planus/ Lichenoid Reaction
Lupus Erythematosus
Infections etiology
– Hairy leukoplakia
– Fungal
Dysplastic Tissue changes
– Mild, moderate, severe dysplasia
– Carcinoma in situ
– Squamous cell carcinoma


Erythematous Lesions
Generalized?
Yes
No
Dermatosis
– erosive lichen planus
– pemphigoid
– pemphigus
– epidermolysis bullosa acquisita
– psoriasis
Nutritional Deficiency
– ferritin
– folate
– vitamin B12
Fungal Etiology
Center of tongue:
Median rhomboid glossitis
Glossitis
Palate:
-Denture stomatitis
-Fungal
Bilateral corners of mouth:
– Angular cheilitis
– Fungal; candidosis
– Staph or strep
– Hematinic deficiency
– Oral Crohn's disease
– Immuno compromised state (e.g. Diabetes, HIV)
Gingival:
– Plaque-associated gingivitis
– Dermatosis
– Allergy (plasma cell gingivitis)
Dysplastic Tissue changes (solitary lesion)
–Mild, moderate, severe dysplasia
–Carcinoma in situ
–Squamous cell carcinoma

Management of Oral Lesions

- Acute lesions (i.e. < 2 weeks)
- Chronic lesions (> 2 weeks)
- Long term follow-up of chronic oral lesions
- Transformation of oral lesions to oral cancer

Management of Acute Lesions

- New onset lesions
- CHLORIDE
- Head and neck examination
- Evaluate for etiologic factors
  - Social habit
  - Change in medication or oral care product
  - Parafunctional habits
  - Trauma- sharp areas
- NIRDS

Management of Acute Lesions

- Eliminate potential etiologic factors
- Treat with antifungals if on differential
  - Chlorhexidine 2x/day for 2 weeks
  - Clotrimazole troches 10 mg 5x/d for 7-10 days
  - Nystatin/triamcinolone cream dab corners of mouth 4x/d
  - Probiotic yogurt
  - Fluconazole 200 mg day 1 followed by 100 mg/d one week
  - Nystatin ointment (thin layer on denture) tid
- Return for reassessment in 2 weeks
- Consider incisional biopsy for definitive diagnosis

Questions?

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