White Lesions

Actinic (Solar) Cheilitis

Etiology
- Chronic, excessive exposure to solar radiation; ultraviolet spectrum (ranging from 290 to 320 nm) most damaging
- Fair-complexioned people more severely affected than others
- May progress to cutaneous actinic keratosis and/or squamous cell carcinoma

Clinical Presentation
- Vermilion portion of lower lip
- Pale irregularly opaque (keratotic) surface with intervening red (atrophic) zones
- Obfuscated to effaced cutaneous-vermilion border
- More advanced lesions are scaly, crusted and/or indurated.
- Progression to carcinoma often heralded by persistent ulceration or erosion

Microscopic Findings
- Hyperkeratosis
- Epithelial atrophy
- Variable degrees of epithelial dysplasia
- Amphophilic to basophilic change in submucosa (elastosis)
- Telangiectasia

Diagnosis
- Thermal/chemical burn ruled out by history
- Chronic ultraviolet light exposure
- Biopsy findings

Differential Diagnosis
- Exfoliative cheilitis
- Squamous cell carcinoma
**Treatment**

- Prevention of further damage with sunscreens blocking long-wave ultraviolet A (UVA) and short-wave ultraviolet B (UVB) light
- Biopsy of clinically suspicious areas
- CO₂ laser vermilionectomy
- Topical 5-fluorouracil or vermilionectomy for severe disease
- Excision or resection-reconstruction if malignant transformation has occurred

**Prognosis**

- Lifelong follow-up
- Up to 10% develop into squamous cell carcinoma.
- When carcinoma develops, growth tends to be slow and metastasis occurs late; 85 to 90% long-term survival
Candidiasis

Etiology
• Infection with a fungal organism of the Candida species, usually Candida albicans
• Associated with predisposing factors: most commonly, immunosuppression, diabetes mellitus, antibiotic use, or xerostomia (due to lack of protective effects of saliva)

Clinical Presentation
• Acute (thrush)
  • Pseudomembranous
  • Painful white plaques representing fungal colonies on inflamed mucosa
  • Erythematous (acute atrophic): painful red patches caused by acute Candida overgrowth and subsequent stripping of those colonies from mucosa
• Chronic
  • Atrophic (erythematous): painful red patches; organism difficult to identify by culture, smear, and biopsy
  • “Denture-sore mouth”: a form of atrophic candidiasis associated with poorly fitting dentures; mucosa is red and painful on denture-bearing surface
  • Median rhomboid glossitis: a form of hyperplastic candidiasis seen on midline dorsum of tongue anterior to circumvallate papillae
• Perlèche: chronic Candida infection of labial commissures; often co-infected with Staphylococcus aureus
• Hyperplastic/chronic hyperplastic: a form of hyperkeratosis in which Candida has been identified; usually buccal mucosa near commissures; cause and effect not yet proven
• Syndrome associated: chronic candidiasis may be seen in association with endocrinopathies

Diagnosis
• Microscopic evaluation of lesion smears
• Potassium hydroxide preparation to demonstrate hyphae
• Periodic acid–Schiff (PAS) stain
• Culture on proper medium (Sabouraud’s, corn meal, or potato agar)
• Biopsy with PAS, Gomori’s methenamine silver (GMS), or other fungal stain of microscopic sections
**Differential Diagnosis**
- Allergic or irritant contact stomatitis
- Atrophic lichen planus

**Treatment**
- Topical or systemic antifungal agents
  - For immunocompromised patients: routine topical agents after control of infection is achieved, usually with systemic azole agents
  - See “Therapeutics” section
- Correction of predisposing factor, if possible
- Some cases of chronic candidiasis may require prolonged therapy (weeks to months).

**Prognosis**
- Excellent in the immunocompetent host
Exfoliative Cheilitis

Etiology
• Causes may be atopic, contact, factitious, infectious, systemic, or medication induced.

Clinical Presentation
• Usually involves lower lip (in both genders); can involve both lips
• Tender or asymptomatic crusts and impacted scale of vermilion
• Minimal inflammation

Diagnosis
• Clinical appearance
• Nonspecific microscopy results

Differential Diagnosis
• Atopic cheilitis
• Actinic cheilitis
• Contact cheilitis

Treatment
• Determination of cause
• Supportive care
• Topical or intralesional corticosteroids, including lip ointments/pomade (hypoallergenic)
• Topical tacrolimus ointment

Prognosis
• Chronic
• Psychologic support for factitial cheilitis
Fordyce’s Granules

Etiology
• Ectopic sebaceous glands within the oral mucosa and vermilion portion of the lips

Clinical Presentation
• Multiple, scattered, yellowish pink, maculopapular granules
• Buccal mucosa and vermilion of lips predominantly affected
• Asymptomatic
• Increasingly prominent after puberty

Diagnosis
• Bilateral distribution and appearance
• Lack of symptoms
• If biopsy performed, normal sebaceous glands in the absence of hair follicles noted

Differential Diagnosis
• Candidiasis

Treatment
• None
• Reassurance

Prognosis
• Excellent
White Lesions
Geographic Tongue

Etiology
- Unknown; may be familial
- May be related to atopy
- Small percentage associated with cutaneous psoriasis

Clinical Presentation
- May be symptomatic in association with spicy or acidic foods
- Focal red depapillated areas bordered by slightly elevated, yellowish margin
- Dynamic behavior: changes in shape, size, intensity day to day
- Dorsal and lateral tongue surfaces affected predominantly
- Ventral tongue and other areas less often involved
- Often associated with fissured tongue

Diagnosis
- Location and appearance
- Biopsy confirmation usually unnecessary

Differential Diagnosis
- Reiter’s syndrome
- Lichen planus
- Lupus erythematosus
- Candidiasis
- Psoriasis

Treatment
- None, if asymptomatic
- Topical corticosteroids, if symptomatic

Prognosis
- Excellent
- No malignant potential
- May last months to years with periods of remission
Hairy Leukoplakia

Etiology
- Probably due to opportunistic Epstein-Barr virus (EBV) infection of epithelial cells
- Usually in an immunocompromised or immunosuppressed host

Clinical Presentation
- Usually arises on lateral tongue border
- Early lesions are fine, white, vertical streaks with an overall corrugated surface
- Later lesions may be thickened to be plaque-like
- Extensive lesions can involve dorsum of tongue and buccal mucosa
- May serve as a pre-AIDS (acquired immunodeficiency syndrome) sign

Diagnosis
- Incisional biopsy findings show characteristic EBV nuclear inclusions in upper-level keratinocytes

Differential Diagnosis
- Frictional hyperkeratosis
- Lichen planus
- Hyperplastic candidiasis

Treatment
- None necessary; predisposing condition to be investigated
- Can be suppressed with acyclovir for esthetics
- Antiviral acyclovir
- Podophyllin resin topically

Prognosis
- May herald human immunodeficiency virus (HIV) disease in vast majority of cases
- Also may be present after AIDS is established
White Lesions
Hairy Tongue

Etiology
• Generally unknown
• May be related to poor oral hygiene, soft diet, heavy smoking, systemic or topical antibiotic therapy, radiation therapy, xerostomia, or use of oxygenating mouth rinses (H₂O₂, sodium perborate)

Clinical Presentation
• Elongated, hyperkeratotic filiform papillae on tongue dorsum producing a “furred” to “hairy” texture
• Color varies from tan to brownish yellow to black depending upon diet, drugs, chromogenic organisms
• Symptoms usually minimal; may produce gagging or tickling sensation on palate

Diagnosis
• Clinical features
• Culture or cytologic studies not helpful

Treatment
• Physical débridement (brushing with a soft-bristled toothbrush, 5 to 15 strokes, once or twice daily)
• Topical podophyllin (5% in benzoin) followed by débridement
• Elimination of cause, if identified

Prognosis
• Excellent
Leukoedema

Etiology
• Unknown
• Benign; common in general population, with racial clustering in Blacks

Clinical Presentation
• Symmetric, asymptomatic
• Buccal mucosa involved by gray-white, diffuse, milky surface with an opalescent quality
• Wrinkled surface features at rest
• Dissipation of changes with stretching of mucosa

Diagnosis
• Clinical recognition is sufficient.
• Biopsy findings will show marked intracellular edema of spinous layer.
• Individual cells with clear cytoplasm and compact nuclei
• Normal basal cell layer

Differential Diagnosis
• Cheek chewing
• Hereditary benign intraepithelial dyskeratosis
• White sponge nevus
• Lichen planus
• Candidiasis

Treatment
• None necessary; no relation to dysplasia/carcinoma
• Reassurance

Prognosis
• Excellent
White Lesions
Leukoplakia

Etiology

- Essentially unknown, although many cases related to use of tobacco or areca nut in its various formulations
- Other possible factors include nutritional deficiency (iron, vitamin A) and infection (*Candida albicans*, human papillomavirus).

Clinical Presentation

- An idiopathic white (sometimes white-and-red) patch
- Most common on lip, gingiva, buccal mucosa
- Increased risk of dysplasia or carcinoma when occurring on tongue, floor of mouth, vermilion portion of lip
- Clinical subsets include homogeneous, verrucous, speckled, and proliferative verrucous leukoplakia (proliferative form may be multiple and persistent)
- Cases may advance or regress unpredictably—reflective of a dynamic process
- Most occur in the fifth decade and beyond
- Progress to dysplasia or malignancy may occur with little or no change in clinical appearance.

Diagnosis

- Performance of a biopsy is mandatory after elimination of any suspected causative factors
- Multiple biopsies of large lesions are needed to be performed due to microscopic heterogeneity within a single lesion.

Differential Diagnosis

- Other white lesions
  - Frictional keratosis
  - Hyperplastic candidiasis
- Genetic alterations (genodermatoses)
  - White sponge nevus
  - Dyskeratosis
- Burn (thermal/chemical)
- Lichen planus
- Hereditary benign intra-epithelial dyskeratosis

Treatment

- Excision modalities (surgery, laser ablation, cryosurgery)
- Option to observe lesions diagnosed as benign hyperkeratosis or mild dysplasia
• Possibly photodynamic therapy
• Topical cytotoxic drugs (bleomycin) remain experimental.
• Recurrences common following apparent complete excision

**Prognosis**
• Guarded
• Observation with repeat biopsies to be performed

**Prevention**
• Elimination of tobacco use and heavy alcohol consumption
• Recurrences may be reduced by systemic retinoid therapy.
• Possible dietary measures
Lichenoid Drug Eruptions

Etiology
- Hypersensitivity to drugs including sulfasalazine, angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs, β-blockers, gold, antimalarials, sulfonylurea compounds
- Contact hypersensitivity
- Idiopathic reaction to dental restorations including amalgam, composites, gold, other metals

Clinical Presentation
- White striae or papules, as with lichen planus
- Lesions may appear ulcerative with associated tenderness or pain.
- Most often in buccal mucosa and attached gingiva, but any site may be involved

Diagnosis
- Identification and elimination of causative substance
- Biopsy of areas unresponsive to elimination strategy to demonstrate characteristic keratosis and interface inflammation and associated changes
- Patch testing performed to confirm contact allergens

Differential Diagnosis
- Lichen planus
- Leukoplakia
- Dysplasia/carcinoma

Treatment
- Alternative drugs or material to be chosen
- Topical corticosteroid applications
- Topical tacrolimus applications

Prognosis
- Good
- Observation while lesions exist
Lichen Planus

Etiology
• Unknown
• Autoimmune T cell–mediated disease targeting basal keratinocytes (antigen unknown)
• Lichenoid changes associated with galvanism, graft-versus-host disease (GVHD), certain drugs, contact allergens

Clinical Presentation
• Up to 3 to 4% of population have oral lichen planus
• 0.5 to 1% of population have cutaneous lichen planus; 50% also have oral lesions (25% with oral lesions have concomitant skin lesions)
• White females (60%)
• Occurs in fourth to eighth decades
• Variants: reticular (most common oral form); erosive (painful); atrophic, papular, plaque types; bullous (rare)
• Bilateral and often symmetric distribution
• Oral site frequency: buccal mucosa (most frequent), then tongue, then gingiva, then lips (least frequent)
• Skin sites: forearm, shin, scalp, genitalia

Microscopic Findings
• Hyperkeratosis
• Basal keratinocyte necrosis
• Lymphocytes at epithelial-connective tissue interface

Diagnosis
• Examination of oral mucosa, skin, genitalia
• Negative ocular mucosa history; no history of blistering
• Use of drugs, galvanism, GVHD to be ruled out
• Biopsy
• Direct immunofluorescence–fibrinogen and cytoid bodies at interface help confirm

Differential Diagnosis
• Lichenoid drug eruptions
• Lupus erythematosus
• Mucous membrane pemphigoid
• Erythema multiforme
• Contact stomatitis
White Lesions

Treatment of Oral Lichen Planus

- Mild to moderate: topical corticosteroids
- Severe: systemic immunosuppression, chiefly with prednisone
- Corticosteroid-sparing drugs with prednisone
- Topical tacrolimus ointment

Prognosis

- Control, not cure, can be expected.
- Good prognosis; rare malignant transformation (0.5–3%)
- May be cyclic; may last for years/decades
- Tends to be chronic
Morsicatio Buccarum/Labiorum
(Cheek and Lip Chewing)

Etiology
• Chronic, low-grade biting habit

Clinical Presentation
• Shaggy, white, keratotic surface
• Surface often appears granular to macerated
• More uniform keratotic surface may develop over time if habit continues
• Most common sites are lip and buccal mucosa

Microscopic Findings
• Very irregular, fimbriated surface keratin
• Surface bacterial colonization
• No connective tissue changes

Diagnosis
• Presentation
• Biopsy

Differential Diagnosis
• Leukoedema
• Leukoplakia
• Lichen planus
• Lichenoid tissue reactions

Treatment
• Elimination of hyperfunction habit

Prognosis
• Excellent
Proliferative Verrucous Leukoplakia

Etiology
• Some associated with human papillomavirus types 16 and 18
• Role of tobacco and other risk factors
• Represents a clinicopathologic spectrum of disease
• Multiple lesions develop from hyperkeratosis and/or verrucous hyperplasia to verrucous carcinoma or papillary squamous cell carcinoma

Clinical Presentation
• Slowly progressive and persistent
• Initially a flat hyperkeratotic to warty surface
• Surface may be friable
• Typically multiple and recurrent
• Seen in middle-aged to elderly patients

Diagnosis
• Based upon appearance, clinical course, and microscopic diagnosis (ie, clinical-pathologic correlation)
• Microscopic diagnoses include epithelial hyperplasia, hyperkeratosis, verrucous hyperplasia, “atypical papillary-verrucal proliferation,” verrucous or well-differentiated squamous cell carcinoma

Differential Diagnosis
• Idiopathic leukoplakia
• Oral warts/condyloma
• Verrucous/squamous cell carcinoma

Treatment
• Surgical excision
  • Mucosal stripping or excision for benign lesions
  • Wide excision to resection for advanced lesions
  • Laser ablation for benign/ataypical lesions
  • Systemic retinoids to control keratosis
Prognosis

- Progression to carcinoma frequently occurs, usually many years after initial lesion(s) develops.
- Fair to good prognosis after malignant transformation
- Frequent follow-up visits recommended and surgical intervention as new/recurrent lesions develop
Smokeless Tobacco Keratosis (Snuff Pouch)

Etiology
• Persistent habit of holding ground tobacco within the mucobuccal vestibule

Clinical Presentation
• Usually in men in Western countries
• Powdered snuff use prevalent in Southeast United States often by women
• Mucosal pouch with soft, white, fissured appearance
• Surface may be pumice-like to verrucous
• Leathery surface due to chronic tobacco use over many years

Microscopic Findings
• Hyperkeratosis with parakeratotic “chevron sign” at surface
• Increased vascularity
• Older lesions with hyalinization in submucosa and minor salivary glands
• Epithelial dysplasia and carcinoma may evolve.

Diagnosis
• Clinical appearance
• Biopsy

Differential Diagnosis
• Leukoplakia (idiopathic)
• Mucosal burn (chemical/thermal)

Treatment
• Discontinuation of habit
• If dysplasia is present, stripping of mucosal site

Prognosis
• Generally good with tobacco cessation
• Malignant transformation to squamous cell carcinoma or verru- cous carcinoma occurs but less frequently than does smoking-related carcinoma.
Submucous Fibrosis

Etiology
• Results from direct mucosal contact with a quid containing areca (betel) nut, tobacco, and other ingredients; alkaloids and tannin in the areca nut are liberated by action of slaked lime within the quid, which is wrapped with the betel leaf
• Risk of oral squamous cell carcinoma is increased several-fold

Clinical Presentation
• Early phase: tenderness, vesicles, erythema, burning, melanosis
• Later phase: mucosal rigidity, trismus
• Sites most often affected: buccal mucosa, soft palate
• Leukoplakia of surface with pallor
• Deep scarring, epithelial atrophy in cheeks, soft palate

Microscopic Findings
• Biopsy results show submucosal deposition of dense collagen.
• Epithelial thinning, hyperkeratosis
• Epithelial dysplasia found in up to 15% of cases

Diagnosis
• Appearance
• History

Differential Diagnosis
• Lichen sclerosus

Treatment
• Intralssional corticosteroid placement
• Surgical release of scar bands in latter stages
• Careful follow-up and vigilance for development of squamous cell carcinoma

Prognosis
• Irreversible
• Fair
White Lesions

Both photographs courtesy of Dr. John S. Greenspan.
White Sponge Nevus

Etiology
- Hereditary (autosomal-dominant) disorder of keratinization affecting nonkeratinizing oral, esophageal, and anogenital mucosal epithelium
- Point mutations in the keratin 4 and/or 13 genes

Clinical Presentation
- Asymptomatic
- Deeply folded, thickened, white mucosa
- Buccal mucosa chiefly affected
- No functional impairment
- Increased prominence during second decade

Microscopic Findings
- Parakeratosis, acanthosis, intracellular edema
- Perinuclear condensation of keratin

Diagnosis
- Clinical appearance
- Family history
- Microscopic findings

Differential Diagnosis
- Idiopathic leukoplakia
- Chemical/thermal burn
- Chronic low-grade trauma (morsicatio)

Treatment
- None required
- No malignant potential

Prognosis
- Excellent