الاستاذ الدكتور جمال نوري

Oral Medicine Lecture

White and Red Lesions of the Oral Mucosa

(Reference Burket's Oral Medicine Michael Glick, 12ed, 2015)

These lesions include disorders of the oral mucosa that clinically appear either red or white or both in colour. A white appearance of the oral mucosa may be caused by a variety of factors. The oral epithelium may be stimulated to an increased production of keratin (hyperkeratosis), or an abnormal but benign thickening of stratum spinosum (acanthosis). Intra and extracellular accumulation of fluid in the epithelium may also result in clinical whitening of mucosa. Necrosis of the oral epithelium, which may also be perceived as a white lesion, occurs when the oral mucosa is exposed to toxic chemicals. Microbes, particularly fungi, can produce whitish pseudomembranes consisting of sloughed epithelial cells or debris, fungal mycelium, and neutrophils, which are loosely attached to the oral mucosa.
A red lesion of the oral mucosa may develop as the result of atrophic epithelium, characterized by a reduction in the number of epithelial cells or increased vascularization.

These lesions could be associated with and grouped into:

PREMALIGNANT LESIONS
Oral leukoplakia
Erythroplakia
Submucous fibrosis

INFECTIOUS DISEASES
Oral Candidiasis
Hairy Leukoplakia
Syphilitic leukoplakia

IMMUNOPATHOLOGIC DISEASES
Oral Lichen Planus
Lichenoid Reactions
Lupus Erythematosus

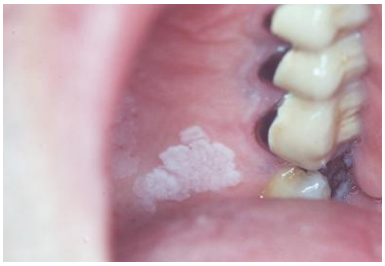
OTHER RED AND WHITE LESIONS
Leukoedema
White Sponge Nevus
Nicotinic stomatitis
Hairy Tongue
Benign Migratory Glossitis (Geographic Tongue)
Epstien pearls

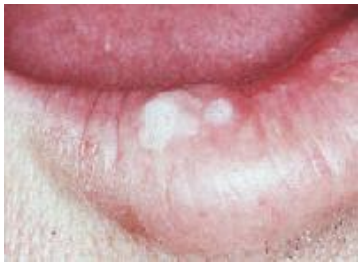
Premalignant Lesions

1-Oral leukoplakia

Oral leukoplakia is defined as a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion. This disorder can be further

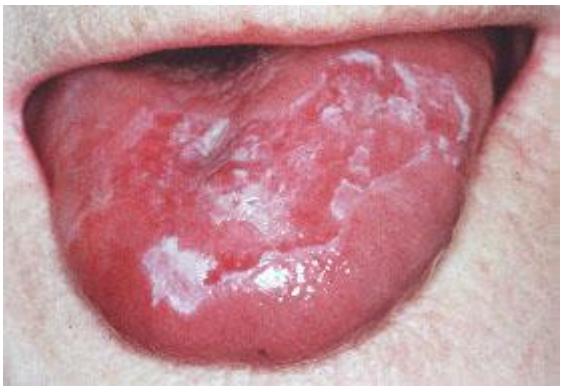
divided into a homogeneous and a non homogeneous type. The typical homogeneous leukoplakia is clinically characterized as a white, well-demarcated plaque with an identical reaction pattern throughout the entire lesion. The lesions are asymptomatic in most patients. There is a lack of a peripheral erythematous zone in homogeneous
Oral leukoplakia


Plaque


verrucous leukoplakia

The nonhomogeneous type of oral leukoplakia may have white patches or plaque intermixed with red tissue. the non homogeneous oral leukoplakia has also been called erythroleukoplakia and speckled leukoplakia.
Both homogeneous and non homogeneous leukoplakias may be encountered in all sites of the oral mucosa. Oral leukoplakias, where the white component is dominated by papillary projections, similar to oral papillomas, are referred to as verrucous or verruciform leukoplakias.
The clinical forms, planner, verruciform, speckeled, snuff and dipper are types of tobacco associated leukopakia.
The floor of the mouth and the lateral borders of the tongue are high-risk sites for malignant transformation.

2-Erythroplakia, is defined as a red lesion of the oral mucosa that cannot be



characterized as any other definable lesion. The lesion comprises an eroded red velvety lesion that is frequently observed with distinct not well demarcated borders. Erythroplakia is usually nonsymptomatic, although some patients may experience a burning sensation in conjunction with food intake. Due to the combined appearance of white and red areas, the nonhomogeneous oral leukoplakia has also been called erythroleukoplakia and speckled leukoplakia.
The provisional diagnosis is based on the clinical observation of a white or red patch that is not explained by a definable cause, such as trauma. If trauma is suspected, the cause, such as a sharp tooth cusp or restoration, should be eliminated. If healing does not occur in 2 weeks, biopsy is essential to rule out malignancy.

3- Oral Submucous Fibrosis

is a chronic disease that affects the oral mucosa as well as the pharynx and the upper two-thirds of the esophagus. It appears clinically, paler mucosa, which may comprise white marbling. The most prominent clinical characteristics will appear later in the course of the disease and include fibrotic bands located beneath an atrophic epithelium. Increased fibrosis eventually leads to loss of resilience, which interferes with speech, tongue mobility, and a decreased ability to open the mouth. The atrophic epithelium may cause a smarting sensation and inability to eat hot and spicy food. More than 25% of the patients exhibit also oral leukoplakias. The diagnosis of submucous fibrosis is based on the clinical characteristics and on the patient's report of a habit of betel quid chewing.

INFECTIOUS DISEASES

1-Oral candidiasis

Oral candidiasis is the most prevalent opportunistic infection affecting the oral mucosa. In the vast majority of cases, the lesions are caused by the yeast *Candida albicans*. The pathogenesis is not fully understood, but a number of predisposing factors have the capacity to convert *Candida* from the normal commensal flora (saprophytic stage) to a pathogenic organism (parasitic stage). *C. albicans* is usually a weak pathogen, and candidiasis is said to affect the very young, the very old, and the very sick.1 Most *Candida* infections only affect mucosal linings, but the rare systemic manifestations may have a fatal course.

Oral candidiasis is divided into primary and secondary infections.

The primary infections are restricted to the oral and perioral sites, whereas secondary infections are accompanied by systemic mucocutaneous manifestations.

Clinical Findings

Acute, Pseudomembranous Candidiasis, Moniliasis or Thrush. The acute form of pseudomembranous candidiasis (thrush) is grouped with the primary oral candidiasis and is recognized as the classic *Candida* infection. The infection predominantly affects patients medicated with antibiotics, immunosuppressant drugs, or a disease that suppresses the immune system.

The infection typically presents with loosely attached membranes comprising fungal organisms and cellular debris, which leaves an inflamed, sometimes bleeding area if the pseudomembrane is removed by cotton or scraped by tongue blade.

Erythematous Candidiasis. The erythematous form of candidiasis was previously referred to as atrophic oral candidiasis. An erythematous surface may not just reflect atrophy but can also be explained by increased vascularization.

The lesion has a diffuse border, which helps distinguish it from erythroplakia, which has a sharper demarcation. Erythematous candidiasis may be considered a successor to pseudomembranous candidiasis

Chronic Plaque-Type and Nodular Candidiasis (hyperplastic candidiasis). The chronic plaque type of oral candidiasis replaces the older term, *candidal leukoplakia*. The typical clinical presentation is characterized by a white plaque, which may be indistinguishable from an oral leukoplakia. A positive correlation between oral candidiasis and moderate to severe epithelial dysplasia has been observed, and both

the chronic plaque-type and nodular candidiasis have been associated with malignant transformation, but the probable role of yeasts in oral carcinogenesis is unclear.

Chronic atrophic Candidiasis (Denture Stomatitis). The most prevalent site for denture stomatitis is the denture-bearing palatal mucosa. It is unusual for the mandibular mucosa to be involved. Denture stomatitis is classified into three different types. Type I is localized to minor erythematous sites caused by trauma from the denture. Type II affects a major part of the denture covered mucosa. In addition to the features of type II, type III has a granular mucosa in the central part of the palate. The denture serves as a vehicle that protects the microorganisms from physical influences such as salivary flow. The microflora is complex and contains, in addition to *Candida*, bacteria from several forms, such as *Streptococcus*.

Chronic atrophic candidiasis, Median Rhomboid Glossitis. Median rhomboid glossitis is clinically characterized by an erythematous lesion in the center of the posterior part of the dorsum of the tongue.
As the name indicates, the lesion has an oval configuration. This area of erythema resulting from atrophy of the filiform papillae and the surface may be lobulated. The etiology is not fully clarified, but the lesion frequently shows a mixed bacterial/fungal microflora. Biopsies yield *Candida* hyphea in more than 85% of the lesions. Smokers and denture-wearers have an increased risk of developing median rhomboid glossitis as well as patients using inhalation steroids. Sometimes a concurrent erythematous lesion may be observed in the palatal mucosa (kissing lesions). Median rhomboid glossitis is asymptomatic, and management is restricted to a reduction in predisposing factors. The lesion does not entail any increased risk for malignant transformation.

Angular Cheilitis. Angular cheilitis is infected fissures of the commissures of the mouth, often surrounded by erythema. The lesions are frequently coinfected with both *Candida* and *Staphylococcus aureus*. Vitamin B12, iron deficiencies, and loss of vertical dimension have been associated with this disorder. Atopy has also been associated with the formation of angular cheilitis. Dry skin may promote the development of fissures in the commissures, allowing invasion by the microorganisms. Thirty percent of patients with denture stomatitis also have angular cheilitis.

Oral Candidiasis Associated with HIV. More than 90% of acquired immune deficiency syndrome (AIDS) patients have had oral candidiasis during the course of their HIV infection, and the infection is considered a portent of AIDS development. The most common types of oral candidiasis in conjunction with HIV are pseudomembranous candidiasis, erythematous candidiasis, angular cheilitis, and chronic hyperplastic candidiasis.
Diagnosis by taking **s**mear from the infected area, which comprises epithelial cells, creates opportunities for detection of the yeasts. Material obtained is fixed in isopropyl alcohol and air-dried, then staining with periodic acid–Schiff (PAS). To increase the sensitivity, a second scrape can be transferred to a transport medium followed by cultivation on Sabouraud agar.
In chronic plaque-type and nodular candidiasis, cultivation techniques have to be supplemented by a histopathologic examination. This examination is primarily performed to identify the possible presence of epithelial dysplasia and to identify invading *Candida* organisms by PAS staining.

Management
Before starting antifungal medication, it is necessary to identify any predisposing factor. Local factors are often easy to identify but sometimes not possible to reduce or eradicate.Antifungal drugs have a primary role in such cases. The most commonly used antifungal drugs belong to the groups of polyenes or azoles. Polyenes such as nystatin and amphotericin B while azoles are Ketoconazole , Miconazole, Fluconazole.

2-Hairy Leukoplakia
Hairy leukoplakia (HL) is the second most common HIV associated oral mucosal lesion. HL has been used as a marker of disease activity since the lesion is associated with low CD4+T-lymphocyte counts. The lesion is not pathognomonic for HIV since other immune deficiencies, such as immunosuppressive drugs and cancer chemotherapy, are also associated with HL. HL is strongly associated with Epstein-Barr virus (EBV) and with low levels of CD4+ T lymphocytes. Antiviral medication, which prevents EBV replication, is curative. The disorder is frequently encountered on the lateral borders of the tongue but may also be observed on the dorsum and in the buccal mucosa.The typical clinical appearance is vertical white folds oriented as a palisade along the borders of the tongue. The lesions may also be displayed as white and somewhat elevated plaque, which cannot be scraped off. As HL may present itself in different clinical forms, it is important to always consider this mucosal lesion whenever the border of the tongue is affected by white lesions, particularly in immunocompromised patients. HL is asymptomatic, although symptoms may be present when the lesion is superinfected with *Candida*.
The diagnosis of HL is based on clinical characteristics, a histopathologic examination, and detection of EBV. HL is not related to increased risk of malignant transformation. HL can be treated successfully with antiviral medication.

3-Syphilitic leukoplakia;
It would appear to be a homogenous white patch affecting large areas of the dorsum of the tongue. it is unclear whether this lesion truly reflects syphilis, or more likely a tobacco smoking habit—indeed this was observed by Hutchinson in the 19th century.
An association between tertiary syphilis and oral squamous cell carcinoma—particularly of the tongue—has been suggested for many years. Both clinically- and serologically-based studies have suggested an increased prevalence of syphilis in patient groups with squamous cell carcinoma of the tongue, the association being stronger in males than females. It remains unclear whether any risk of oral squamous cell carcinoma in syphilis is a direct consequence of infection (which seems unlikely) or is the effect of recognized causative factors for oral malignancy, i.e.tobacco, alcohol, and malnourishment.

Immunopathologic Diseases

1-Oral Lichen Planus
Lichenoid reactions represent a family of lesions with different etiologies with a common clinical and histologic appearence. Histopathologic examination does not enable discrimination between different lichenoid reactions but may be used to distinguish lichenoid reactions from other pathologic conditions of the oral mucosa.
Cutaneous lesions may be encountered in approximately 15% of patients with OLP. The classic appearance of skin lesions consists of pruritic erythematous to violaceous

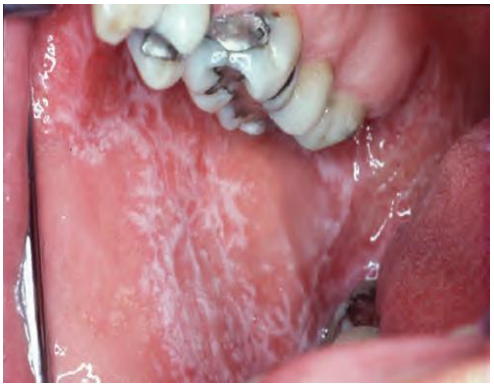
papules that are flat topped that have a predilection for the trunk and flexor surfaces of arms and legs. Lesions appear as;
Lichen planus
Lichenoid contact reactions or drug eruptions
Lichenoid reactions of graft-versus-host disease
(GVHD)

Lichen planus is a mucocutanous lesion affecting the skin as well as the oral mucosa.The oral lesions may be the only site. The etiology of the disease is unknown.OLP may contain both red and white elements and provide, together with the different forms, the basis for the clinical classification of this disorder. The white and red components of the oral lesion can be a part of the following textures:

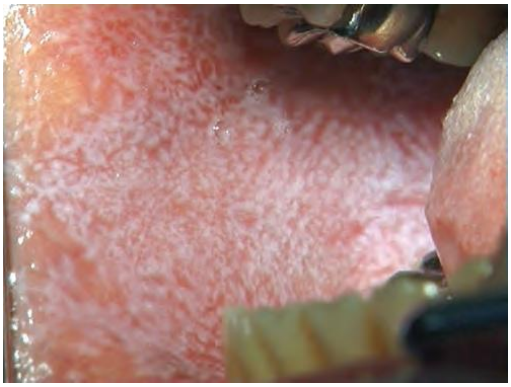
Reticulum and annular
Papules
Plaque-like
Erosive or atrophic (erythematus)
Ulcerative and Bullous
Pigmented LP

To establish a clinical diagnosis of OLP, reticular or popular textures have to be present. If, in addition, plaque-like, bullous, erythematous, or ulcerative areas are present, the OLP lesion is designated clinically. All forms of OLP should be confirmed by a histopathologic examination. Erosive or erythematous OLP is considered to be a premalignant condition. Premalignant conditions are disorders that entail an increased risk of malignant transformation at some site of the oral mucosa; it is a lesion that has an inherent increased risk to develop carcinomas compared with the surrounding tissues.

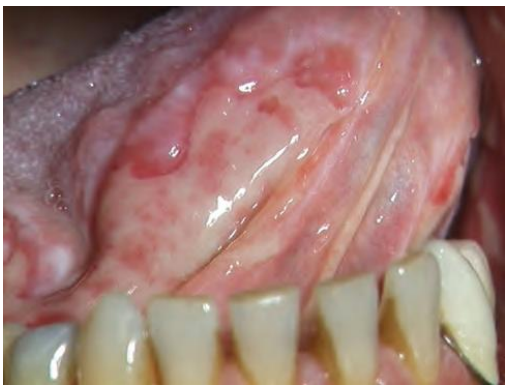
The reticular form of OLP is characterized by fine white lines or striae called wickhams stria. The striae may form a network but can also show annular (circular) patterns. The striae often display a peripheral erythematous zone, which reflects the subepithelial inflammation. Although reticular OLP may be encountered in all regions of the oral mucosa, most frequently this form is observed bilaterally in the buccal mucosa. Plaque-type OLP shows a homogeneous well-demarcated white plaque often, but not always, surrounded by striae. Plaque-type lesions may clinically be very similar to homogeneous oral leukoplakias. The difference between these two mucosal disorders is the simultaneous presence of reticular or papular structures in the case of plaque-like OLP. This form is most often encountered in smokers, and following cessation, the plaque may disappear and convert into the reticular type of OLP. Typically, the reticular, papular, and plaque-like forms of OLP are asymptomatic, although the patient may experience a feeling of roughness. However the erythematous form of OLP, the affected patient complains of a burning pain or sensation in conjunction with food intake.



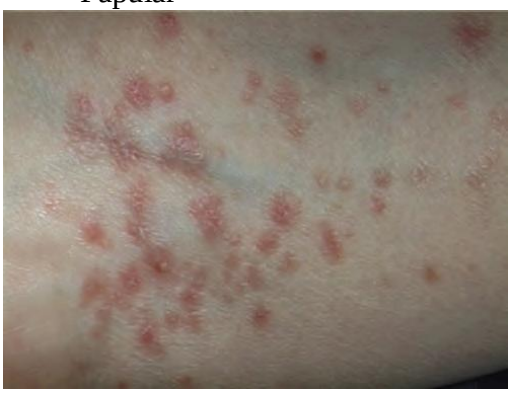
Reticular LP



Papular



Bullous



Skin lesion

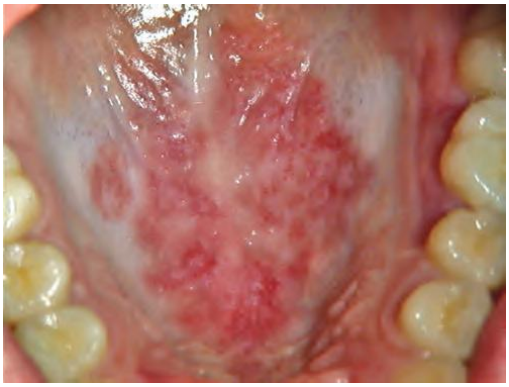
Management

Since the etiology behind OLP is unknown, basic conditions are lacking for development of preventive therapies. Thus, all current treatment strategies are aiming at reducing or eliminating symptoms. Several topical drugs have been suggested, including steroids, calcineurin inhibitors (cyclosporine and tacrolimus), retinoids, and ultraviolet phototherapy. Among these, topical steroids, triamcenolone acetonide (Kenaloge orabase) are widely used and accepted as the primary treatment of choice.
ulcerative areas may be found in close contact with dental materials similar to what is observed in Lichenoid Contact Reactions (LRC). The difference is the extension of the LCR, which is limited to such contacts. When symptomatic ulcerations of this kind are present as part of the OLP lesion, replacement of the dental material, usually amalgams, may convert a symptomatic to a nonsymptomatic lesion.

2-Lupus Erythematosus (LE)

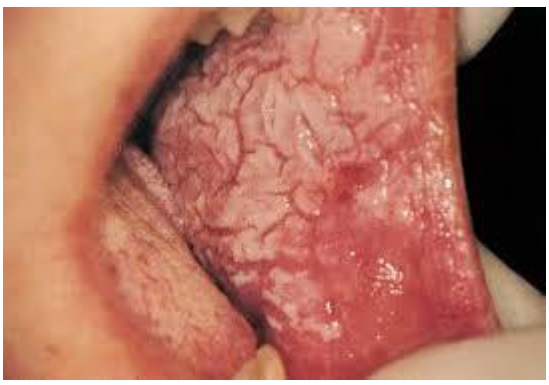
LE represents the classic prototype of an autoimmune disease involving immune complexes. Both the natural and the adaptive parts of the immune system. Environmental factors are of importance as sun exposure, drugs, chemical substances, and hormones which all have been reported to aggravate the disease. The oral lesions observed in Systemic LE and Discoid LE are similar in their characteristics, both clinically and histopathologically. The typical clinical lesion comprises white striae with a radiating orientation, and these may sharply terminate toward the center of the lesions, which has a more erythematous appearance (similar to erythematus LP). The most affected sites are the gingiva, buccal mucosa, tongue, and palate. Lesions in the palatal mucosa can be dominated by erythematous lesions, and white structures may not be observed . Oral mucosa lesions compatible with LE may be the first sign of the disease. . Diff Diagnosis is OLP and Leukoplakia lesions.

The typical DLE diagnosis comprises well-demarcated cutaneous lesions with round or oval erythematous plaques with scales and follicular plugging. These lesions may form butterfly-like rashes over the cheeks and nose known as malar rash.
SLE may also occur in association with other rheumatologic diseases such as secondary Sjogren's syndrome and mixed connective tissue disease.
Diagnosis; Antinuclear antibodies are frequently found in patients with SLE and can be used to indicate a systemic involvement,
Management; The oral lesions may respond to systematic treatment used to alleviate the disease and have to be evaluated first. When symptomatic intraoral lesions are present, topical steroids should be considered to obtain relief of symptoms.



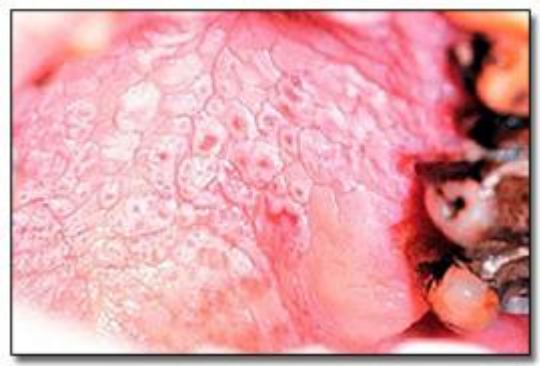
OTHER RED AND WHITE LESIONS

1-Leukoedema. is a generalized white change of oral mucosa which is probably a variation of normal rather than a disease.
The cause is unknown.
It occurs much more commonly in blacks than whites.
Leukoedema is diffuse and symmetrically distributed on the buccal mucosa and may extend onto the labial mucosa.
The appearance is gray-white, opaque, or milky.
It can be smooth to palpation or wrinkled, and it does not rub off.
A characteristic clinical feature is that the white appearance decreases when the buccal mucosa is stretched.
Leukoedema is asymptomatic, and the patient is unaware of its presence.
Leukoedema is diagnosed clinically, and a biopsy is not required.
No treatment is necessary. It is a benign lesion and is not premalignant.



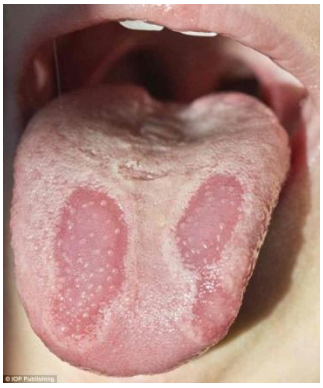
2-White sponge nevus is a genetic disorder, usually congenital or developing in childhood.
The oral mucosa is diffusely white, rough, thickened and folded.
The most common location is the buccal mucosa bilaterally, but other oral mucosal areas may be involved.
Nasal, pharyngeal, and anogenital mucosa may be affected.
The condition is not painful.
Other family members often have the condition.
The clinical features and history are diagnostic.
This condition is benign and requires no treatment.

3-Nicotine stomatitis is an epithelial thickening lesion of the hard palate caused by



heat from smoking a pipe, cigar, or occasionally cigarettes.
The lesion is white, rough, asymptomatic, and leathery appearing and contains numerous red dots or macules.
The red macules represent inflamed salivary gland duct orifices.
Nicotine stomatitis is not considered a premalignant lesion and does not need to be biopsied.
However, the patient should be encouraged to stop smoking, and the oral mucosa should be evaluated periodically.
The prognosis for nicotine stomatitis is good, but the patient is at increased risk to develop cancer in other locations in the upper aerodigestive tract.

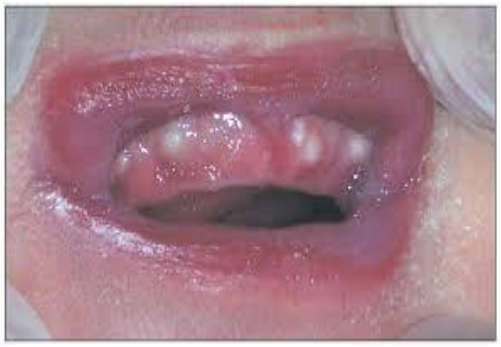
4-Erythema migrans (geographic tongue, benign migratory glossitis)



is a common, harmless lesion that can typically be diagnosed by its clinical features.

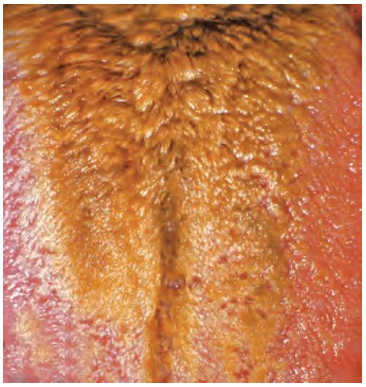
It presents as multiple red patches surrounded by a thickened, irregular, white border.
A lesion will resolve in one area and appear in other areas (migrate).
This condition is usually not painful and requires no treatment.
If the patient complains of pain or burning with the lesions, a diagnosis of candidosis should be considered.
Rarely, lesions of erythema migrans can be found on oral mucosal surfaces other than the tongue.

5-Epstein pearls, also is called gingival cysts of the newborn. Epstein pearls are



whitish-yellow cysts that form on the gums and roof of the mouth in a newborn baby. Epstein pearls occur only in newborns and are very common. They are seen in about 4 out of 5 newborn, Whitish-yellow nodules appear on the gums or the roof of the mouth. They sometimes look like emerging teeth. No treatment is necessary. The condition is harmless. Epstein pearls disappear within 1 to 2 weeks of birth.

Hairy Tongue



The etiology of hairy tongue is unknown in most cases. There are a number of predisposing factors that have been related to this disorder, such as neglected oral hygiene, a shift in the microflora, antibiotics and immunosuppressive drugs, oral candidiasis, excessive alcohol consumption, oral inactivity, and therapeutic radiation. Hairy tongue is also associated with smoking habits. Hairy tongue is characterized by an impaired desquamation of the filiform papilla, which leads to the hairy-like clinical appearance. The elongated papillae have to reach lengths in excess of 3 mm to be classified as “hairy,” although lengths of more than just 15 mm have been reported in hairy tongue. The lesion is commonly found in the posterior one-third of the tongue but may involve the entire dorsum. Hairy tongue may adopt colors from white to

black depending on food constituents and the composition of the oral microflora. Patients with this disorder may experience both physical discomfort and esthetic embarrassment related to the lengths of the filiform papillae. The diagnosis is based on the clinical appearance. The treatment of hairy tongue is focused on reduction or elimination of predisposing factors and removal of the elongated filiform papillae. The patients should be instructed on how to use devices developed to scrape the tongue. The use of food constituents with an abrasive effect may also be used.