The oral cavity is lined by a membrane composed of stratified squamous epithelium. This epithelium serves as a cover for the oral soft tissues as a barrier to the entry of external pathogenic factors. Depending on the intraoral site, the stratified squamous epithelium may be non-keratinized, orthokeratinized or parakeratinized.

Knowledge of clinical aspects of oral mucosal diseases must be correlated with oral anatomy. E.g. recurrent aphthous stomatitis occurs primarily on the nonkeratinized mucosa, whereas recurrent herpes simplex infections occur almost exclusively on the keratinized mucosa.

In general, oral mucosal lesions could be divided into:

- Oral infections
  - Fungal
  - Bacterial
  - Viral
- Vesiculobullous diseases
- Ulcerative conditions
- White lesions

To better describe the appearances of lesions and communicate these features to others, the clinician should be familiar with the following terms:

*Macule:* Focal area of color change which is not elevated or depressed in relation to its surroundings.
**Papule**: Solid, raised lesion which is less than 5 mm in diameter.

**Nodule**: Solid, raised lesion which is greater than 5 mm in diameter.

**Sessile**: Describing a tumor or growth whose base is the widest part of the lesion.

**Pedunculated**: Describing a tumor or growth whose base is narrower than the widest part of the lesion.

**Papillary**: Describing a tumor or growth exhibiting numerous surface projections.

**Verrucous**: Describing a tumor or growth exhibiting a rough, warty surface.

**Vesicle**: Superficial blister, 5 mm or less in diameter, usually filled with clear fluid.

**Bulla**: Large blister, greater than 5 mm in diameter.

**Pustule**: Blister filled with purulent exudate.

**Ulcer**: Lesion characterized by loss of the surface epithelium and frequently some of the underlying connective tissue. It often appears depressed or excavated.

**Erosion**: Superficial lesion. Often arising secondary to rupture of a vesicle or bulla, that is characterized by partial or total loss of the surface epithelium.

**Fissure**: Narrow, slit like ulceration or groove.

**Plaque**: Lesion that is slightly elevated and is flat on its surface.

**Petechia**: Round, pinpoint area of hemorrhage.

**Ecchymosis**: Nonelevated area of hemorrhage, larger than a petechia.

**Telangiectasia**: Vascular lesion caused by dilatation of a small, superficial blood vessel.

**Cyst**: Pathologic epithelium-lined cavity often filled with liquid or semi-solid contents.

**Microscopical changes of oral mucosa:**

- Divided into epithelial and connective tissue changes

**Epithelial changes:**

**Hyperkeratosis**: refers to an increase in the thickness of stratum cornium, which yields a white appearance of the oral mucosa clinically. This hyperkeratinizations
can occur in keratinized area or abnormally in non-keratinized area. When the nuclei are lost from the surface the conditions is named (hyperorthokeratosis). When remnants of the nuclei persist the condition is named (hyperparakeratosis).

**Hyperplasia:** an increase in the thickness of the epithelium from surface to basal cell layer. An increase in the prickle cell layer is termed (acanthosis).

Epithelial dysplasia (dyskeratosis or epithelial atypia): an abnormal growth pattern of epithelial cells. Generally indicates a premalignant change.

**Acantholysis:** loss of adhesion between the cells of prickle cell layer (spinous cell layer) the cells appear to fall apart, which lead to vesicle formation.

**Connective tissue changes:**
- Inflammatory infiltrate are common, as chronic inflammatory cells infiltration.
- Hyperplasia of connective tissue refers to an increase in the amount of collagen fibers.
- Ductal and glandular distension could be seen in many accessory mucous glands due to pressure and obstruction.

The common oral mucosal infections are caused by viruses, bacteria, and fungi.

**Viral infections**

**The herpes simplex viruses (HSV)**

DNA viruses and the most frequent causes of a viral infection of the mouth. mainly transmitted by droplet spread from saliva or contact with the lesions. Herpes simplex virus (HSV) infections occur in two forms: primary (systemic) and secondary (localized). Both forms are self-limited, but recurrences of the secondary form are common because the virus can remain within ganglionic tissue in a latent state.

**Clinical Features**
Primary Herpetic Gingivostomatitis. Primary disease is usually seen in children, although adults who have not been previously exposed to HSV may be affected. The vesicular eruption may appear on the skin, vermilion, and oral mucous membranes. Intraorally, lesions may appear on any mucosal surface. This is in contradistinction to the recurrent form of the disease, in which lesions are confined to the lips, hard palate, and gingiva. The primary lesions are accompanied by fever, arthralgia, malaise, anorexia, headache, and cervical lymphadenopathy. After the systemic primary infection runs its course of about 7 to 10 days, lesions heal without scar formation. By this time, the virus may have migrated to the trigeminal ganglion to reside in a latent form.

Secondary, or Recurrent, Herpes Simplex Infection. Secondary herpes represents the reactivation of latent virus. Patients usually have prodromal symptoms of tingling, burning, or pain in the site at which lesions will appear. Within a matter of hours, multiple fragile and short-lived vesicles appear. These become unroofed and unite to form maplike superficial ulcers. The lesions heal without scarring in 1 to 2 weeks and rarely become secondarily infected. Regionally, most secondary lesions appear on the vermilion and surrounding skin. This type of disease is usually referred to as herpes labialis. Intraoral recurrences are almost always restricted to the hard palate or gingiva.

Herpetic Whitlow. Herpetic whitlow is a primary or a secondary HSV infection involving the finger(s). Before the universal use of examination gloves, this type of infection typically occurred in dental practitioners who had been in physical contact with infected individuals. Contact could result in a vesiculoulcerative eruption on the digit (rather than in the oral region), along with signs and symptoms of primary systemic disease. Pain, redness, and swelling are prominent with herpetic whitlow and can be very pronounced. Vesicles or pustules eventually break and become
ulcers. The duration of herpetic whitlow is protracted and may be as long as 4 to 6 weeks.

**Histopathology.** Microscopically, intraepithelial vesicles containing exudate, inflammatory cells, and characteristic virus-infected epithelial cells are seen. Virus-infected keratinocytes contain one or more nuclear inclusions.

**Treatment:** Symptomatic. In severe cases, systemic aciclovir or valaciclovir.

**Varicella-zoster virus infection**

Primary varicella-zoster virus (VZV) infection is known as chickenpox; secondary or reactivated disease is known as herpes zoster or shingles

Varicella is believed to be transmitted predominantly through the inhalation of contaminated droplets. The condition is very contagious and is known to spread readily from person to person.

**Clinical features**

**chickenpox**

Fever, chills, malaise, and headache may accompany a rash that involves primarily the trunk and head and neck. The rash quickly develops into a vesicular eruption that becomes pustular and eventually ulcerates.

The infection is self-limiting and lasts several weeks. Oral mucous membranes may be involved in primary disease and usually demonstrate multiple shallow ulcers that are preceded by vesicles.

**Herpes zoster**
Zoster is essentially a condition of the older adult population and of individuals who have compromised immune responses. The sensory nerves of the trunk and head and neck are commonly affected. Involvement of various branches of the trigeminal nerve may result in unilateral oral, facial, or ocular lesions. Involvement of facial and auditory nerves produces the Ramsay Hunt syndrome, in which facial paralysis is accompanied by vesicles of the ipsilateral external ear, tinnitus, deafness, and vertigo.

After several days of prodromal symptoms of pain and/or paresthesia in the area of the involved dermatome, a well-delineated unilateral maculopapular rash appears. This may occasionally be accompanied by systemic symptoms. The rash quickly becomes vesicular, pustular, and then ulcerative. Remission usually occurs in several weeks.

**Histopathology:**

Essentially the same as those with HSV

**Treatment:**

For varicella in normal individuals, supportive therapy is generally indicated. However, for immunocompromised patients, more substantial measures are warranted. These include systemically administered acyclovir, vidarabine, and human leukocyte interferon. Corticosteroids generally are contraindicated

**Herpangina**

Herpangina is an acute viral infection caused by Coxsackie type A virus. It is transmitted by contaminated saliva and occasionally through contaminated feces.
**Clinical Features.** Herpangina is usually endemic, with outbreaks occurring typically in summer or early autumn. It is more common in children than in adults. Those infected generally complain of malaise, fever, dysphagia, and sore throat after a short incubation period. Intraorally, a vesicular eruption appears on the soft palate, faucial pillars, and tonsils and persists for 4 to 6 days. A diffuse erythematous pharyngitis is also present. No associated skin lesions are typically seen. Signs and symptoms are usually mild to moderate and generally last less than a week.

**Treatment.** Because herpangina is self-limiting, is mild and of short duration, and causes few complications, treatment usually is not required.

**Hand-Foot-and-Mouth Disease**

HFM disease is a highly contagious viral infection that usually is caused by Coxsackie type A16 or enterovirus 71. The virus is transferred from one individual to another through airborne spread or fecal-oral contamination.

**Clinical Features.** This viral infection typically occurs in epidemic or endemic proportions and predominantly (about 90%) affects children younger than 5 years of age. After a short incubation period, the condition resolves spontaneously in 1 to 2 weeks. Signs and symptoms are usually mild to moderate in intensity and include low-grade fever, malaise, lymphadenopathy, and sore mouth. Pain from oral lesions is often the patient’s chief complaint. Oral lesions begin as vesicles that quickly rupture to become ulcers. Lesions can occur anywhere in the mouth, although the palate, tongue, and buccal mucosa are favored sites, while the lips and gingiva are usually spared. Multiple maculopapular lesions, typically on the feet, toes, hands, and fingers, appear concomitantly with or shortly after the onset of oral lesions. These cutaneous lesions progress to a vesicular state; they eventually become ulcerated.
Histopathology. The vesicles of this condition are found within the epithelium because of obligate viral replication in keratinocytes. Eosinophilic inclusions may be seen within some of the infected epithelial cells.

Treatment. Because of the relatively short duration, generally self-limiting nature, and general lack of virus-specific therapy, treatment for HFM disease is usually symptomatic.

Measles (Rubeola) and German measles (Rubella)

Measles is a highly contagious viral infection caused by a member of the paramyxovirus family of viruses. Typically, oral eruptions consist of early pinpoint elevations over the soft palate that combines with ultimate involvement of the pharynx with bright erythema.

German measles, or rubella, is a contagious disease that is caused by an unrelated virus of the togavirus family. It shares some clinical features with measles, such as fever, respiratory symptoms, and rash. However, these features are very mild and short lived in German measles.

Clinical Features. After an incubation period of 7 to 10 days, prodromal symptoms of fever, malaise, coryza, conjunctivitis, photophobia, and cough develop. In 1 to 2 days, pathognomonic small erythematous macules with white necrotic centers appear in the buccal mucosa, these lesion spots, known as Koplik’s spots. Koplik’s spots generally precede the skin rash by 1 to 2 days. The rash initially affects the head and neck, followed by the trunk, and then the extremities.

Histopathology. Infected epithelial cells, which eventually become necrotic, overlie an inflamed connective tissue that contains dilated vascular channels and a
focal inflammatory response. Lymphocytes are found in a perivascular distribution. In lymphoid tissues, large characteristic multinucleated macrophages, are seen.

**Treatment.** No specific treatment for measles is known. Supportive therapy of bed rest, fluids, adequate diet, and analgesics generally suffices

**Bacterial infections**

**Necrotizing Ulcerative Gingivitis**

Necrotizing ulcerative gingivitis is a relatively rare specific infectious gingival disease of young persons. *Fusobacterium nucleatum*, *Treponema vincentii*, and probably other bacteria play an important role. Predisposing factors are emotional stress, smoking, poor oral hygiene, local trauma, and HIV infection.

**Clinical features.** The characteristic clinical feature is painful necrosis of the interdental papillae and the gingival margins, and the formation of craters covered with a gray pseudomembrane. Spontaneous gingival bleeding, halitosis, and intense salivation are common. Fever, malaise, and lymphadenopathy are less common. Rarely, the lesions may extend beyond the gingiva (necrotizing ulcerative stomatitis).

**Treatment.** Systemic metronidazole and oxygen-releasing agents topically are the best therapy in the acute phase, followed by a mechanical gingival treatment.

**Noma** *(cancrum oris)*

it is characterized by a destructive process of the orofacial tissues. Necrosis of tissue occurs as a consequence of invasion by anaerobic bacteria in a host whose systemic health is significantly compromised.
**Clinical Features.** It typically affects children. The initial lesion of noma is a painful ulceration, usually of the gingiva or buccal mucosa, which spreads rapidly and eventually becomes necrotic. Denudation of involved bone may follow, eventually leading to necrosis and sequestration. Teeth in the affected area may become loose and may exfoliate. Penetration of organisms into the cheek, lip, or palate may also occur, resulting in fetid necrotic lesions.

**Treatment.** Therapy involves treating the underlying predisposing condition, as well as the infection itself. Therefore fluids, electrolytes, and general nutrition are restored, along with the introduction of antibiotics

**Syphilis**

Syphilis is a relatively common sexually transmitted disease Caused by Treponema pallidum.

**Clinical features.** Syphilis may be acquired (common) or congenital (rare). Acquired syphilis is classified as primary, secondary and tertiary. The characteristic lesion in the primary stage is the chancre that appears at the site of inoculation, usually three weeks after the infection. Oral chancre appears in about 5–10% of cases, and clinically presents as a painless ulcer with a smooth surface, raised borders, and an indurated base. Regional lymphadenopathy is a constant finding.

The secondary stage begins 6–8 weeks after the appearance of the chancre, and lasts for 2–10 weeks. Oral lesions are mucous patches (common), macular syphilids, and condylomata lata (rare). Constitutional symptoms and signs (malaise, low-grade fever, headache, lacrimation, sore throat, weight loss, myalgias and multiple arthralgias, generalized lymphadenopathy) as well as cutaneous manifestations
(macular syphilids, papular syphilids, condylomata lata, nail involvement, hair loss, atypical rash, etc.) are constant findings.

Tertiary syphilis begins after a period of 4–7 years. Oral lesions are gumma, atrophic glossitis, and interstitial glossitis. The most common oral lesions in congenital syphilis are a high-arched palate, short mandible, Hutchinson’s teeth, and Moon’s or mulberry molars.

**Histopathology.** The basic tissue response to *T. pallidum* infection consists of a proliferative endarteritis and infiltration of plasma cells. Spirochetes can be demonstrated in the tissues of various lesions of syphilis using silver stains, although they may be scant in tertiary lesions. Gummas may show necrosis and greater numbers of macrophages, resulting in a granulomatous lesion that is similar to other conditions, such as tuberculosis (TB).

**Treatment.** Penicillin is the antibiotic of choice. Erythromycin or cephalosporins are good alternatives.

**Tuberculosis**

Tuberculosis is a chronic, granulomatous, infectious disease that primarily affects the lungs, caused by *Mycobacterium tuberculosis*.

**Clinical features.** The oral lesions are rare, and usually secondary to pulmonary tuberculosis. The tuberculous ulcer is the most common feature. Clinically, the ulcer is painless and irregular, with a thin undermined border and a vegetating surface, usually covered by a gray-yellowish exudate. The surrounding tissues are inflamed and indurated. The dorsum of the tongue is the most commonly affected site, followed by the lip, buccal mucosa, and palate. Osteomyelitis of the jaws, periapical
granuloma, regional lymphadenopathy, and scrofula are less common oral manifestations.

**Histopathology.** The basic microscopic lesion of TB is granulomatous inflammation, in which granulomas show central caseous necrosis. In tissues, M. tuberculosis incites a characteristic macrophage response, in which focal zones of macrophages become surrounded by lymphocytes and fibroblasts. The macrophages develop an abundant eosinophilic cytoplasm, giving them a superficial resemblance to epithelial cells; for this reason, they are frequently called epithelioid cells. Fusion of macrophages results in the appearance of Langerhans giant cells, in which nuclei are distributed around the periphery of the cytoplasm. As the granulomas age, central necrosis occurs; this is usually referred to as caseous necrosis because of the gross cheesy texture of these zones.

A Ziehl-Neelsen or Fite stain must be used to confirm the presence of the organism in the granulomas, because several infectious and noninfectious conditions may produce a similar granulomatous reaction.

**Actinomycosis**

Actinomycosis is a chronic bacterial disease caused by Actinomyces israelii, an anaerobic, gram-positive bacterium. Infection usually appears after trauma, surgery, or previous infection.

**Clinically,** it typically presents as swelling of the mandible that may simulate a pyogenic infection. The lesion may become indurated and eventually may form one or more draining sinuses, leading from the medullary spaces of the mandible to the skin of the neck. The clinical course ranges from acute to chronic. The skin lesions are indurated and are described as having a “woody hard” consistency. Pus draining from the chronic lesion may contain small yellow granules, known as sulfur granules, which represent aggregates of A. israelii organisms. Radiographically, this infection presents as a lucency with irregular and ill-defined margins.
**Histopathology.** A granulomatous inflammatory response with central abscess formation is seen in actinomycosis. At the center of the abscesses, distinctive colonies of gram-positive organisms may be seen. Radiating from the center of the colonies are numerous filaments with clubbed ends.

**Treatment.** Long-term, high-dose penicillin or penicillin analogs are the required antibiotic regimen for actinomycosis.

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**Fungal infections**

**Candidal infection (Candidiasis)**

Candidiasis is the most common oral fungal infection. It is usually caused by Candida albicans. Predisposing factors are local (poor oral hygiene, xerostomia, mucosal damage, dentures, antibiotic mouthwashes) and systemic (broad-spectrum antibiotics, steroids, immunosuppressive drugs, radiation, HIV infection, hematological malignancies, neutropenia, iron-deficiency anemia, cellular immunodeficiency, endocrine disorders).

**Clinical features** Oral candidiasis is classified as primary, consisting of Lesions exclusively on the oral and perioral area, and secondary, consisting of oral lesions of mucocutaneous disease. Primary candidiasis includes five clinical varieties: pseudomembranous (thrush), erythematous, papillary hyperplasia of the palate, and Candida-associated lesions (angular cheilitis, median rhomboid glossitis, denture stomatitis).

**Histopathology:** In acute candidiasis, fungal pseudohyphae are seen penetrating the upper layers of the epithelium at acute angles. Neutrophilic infiltration of the epithelium with superficial microabscess formation is typically seen.

**Treatment:** dealing with predisposing factors + topical and/or systemic antifungals
Human immunodeficiency virus (HIV) infections and AIDS

The oral manifestation of HIV infection are numerous and have been divided into three groups based on the strength of their association with HIV infection.

Group 1-Lesions strongly associated with HIV infections

- Candidiasis
  - Erythematous
  - Hyperplastic
  - Pseudomembranous
- Hairy leukoplakia (EB virus)
- HIV associated periodontal disease
  - HIV gingivitis
  - Necrotizing ulcerative gingivitis
  - HIV associated periodontitis
- Kaposis sarcoma
- Non-Hodgkins lymphoma

Group 2-Lesions less commonly associated with HIV infections

- Atypical ulceration
- Ideopathic thrombocytopenic purpura
- Salivary gland disorders
- Dry mouth, decreased salivary flow rate
- Unilateral or bilateral swelling of major glands
- Viral infection other than (EB virus)
  - Cytomegalo virus
  - Human papilloma virus
- Varicella zoster virus

**Group 3-lesions possibly associated with HIV infection**

- Bacterial infections other than gingivitis/periodontitis
- Fungal infection other than candidiasis
- Melanotic hyperpigmentation
- Neurologic disturbances
- Facial palsy
- Trigeminal neuralgia

**Oral Manifestaton of Aquired immunodyficiency system (AIDS)**

**Persistent generalized lymphadenopathy.**
HIV lymphadenitis may be seen in the HIV scale, later in the course of the disease lymph node biopsies may be necessary to rule out lymphoma

**Oral Candidiasis.**
the most common intra oral manifestation of HIV infection and often is the presenting sign that leads to the initial diagnosis, its presence in a patient infected with HIV is not diagnostic of AIDS but appears to be predictive for the subsequent development of full-blown AIDS in untreated patients with in 2 years
The following four clinical patterns of oral candidiasis are seen;
- Pseudomembranous
- Erythematous
- Hyperplastic
- Angular cheilitis
**HIV-associated periodontal disease.** Three patterns of periodontal disease are associated strongly with HIV infection:

- Linear gingival erythema
- Necrotizing ulcerative gingivitis
- Necrotizing ulcerative periodontitis

Linear gingival erythema initially was termed *HIV*-iated gingivitis but ultimately was noted in association with other disease processes. This unusual pattern of gingivitis appears with a distinctive linear band of erythema that involves the free gingival margin and extends 2 to 3 mm apically.

**Necrotizing ulcerative gingivitis (NUG)**

Refers to ulceration and necrosis of one or more interdental papillae with no loss of periodontal attachment. Necrotizing ulcerative periodontitis (NUP) was previously termed *HIV-associated periodontitis*; however, it has not been seemed to be specific for HIV infection. NUP is characterized by gingival ulceration and necrosis associated with rapidly progressing loss of periodontal attachment. Although severe cases can affect all teeth,

**Herpes simplex virus (HSV).**

Recurrent HSV infections occur in about the same percentage of HIV-infected patients as they do in the immunocompetent population (10% to 15%); however, the lesions are more widespread, occur in an atypical pattern, and may persist for months.

**Varicella-zoster virus (VZV).**
Recurrent VZV infection (herpes zoster) is fairly common in HIV-infected patients, oral involvement often is severe and occasionally leads to bone sequestration and loss of teeth. Associated pain typically is in tense

_Epstein-Barr virus (EBV)._  
Although EBV is thought to be associated with several forms of lymphoma in HIV infected patients, the most common EBV-related lesion in patients with AIDS is oral hairy leukoplakia (OHL). This lesion has a somewhat distinctive (but not diagnostic) pattern of hyperkeratosis and epithelial hyperplasia that is characterized by white mucosal lesions that do not rub off.

_Kaposi's sarcoma (KS)._  
KS is a multifocal neoplasm of vascular endothelial cell origin, KS begins with single or, more frequently. Multiple lesions of the skin or oral mucosa, the trunk, arms, head, and neck are the most commonly involved anatomic sites. Oral lesions are seen in approximately 50% of affected patients and are the initial site of involvement in 20% to 25%. Although any mucosal site may be involved, the hard palate, gingiva, and tongue are affected most frequently the neoplasm mean invade bone and create tooth mobility

_Aphthous ulcerations._  
Lesions that are similar clinically to aphthous ulcerations occur with increased frequency in patients infected with HIV. All three forms (minor, major, and herpetiform) are seen

_Human papillomavirus (HPV)._
HPV is responsible for several facial and oral lesions in immunocompetent patients. The most frequent of which are the verruca vulgaris (*common wart*) and oral squamous papilloma

**Oral squamous cell carcinoma.**
Squamous cell carcinoma of the oral cavity, pharynx, and larynx has been reported in HIV-infected patients.