Oral pathology

Dr. Ahlam Thabet

Viral Infection

HERPES SIMPLEX VIRUS

HSV-1 is spread predominantly through infected saliva or active perioral lesions . HSV-2 is adapted best to the genital zones, is transmitted predominantly through sexual contact, and typically involves the genitalia and skin below the waist.

Herpes simplex virus (HSVs) 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.

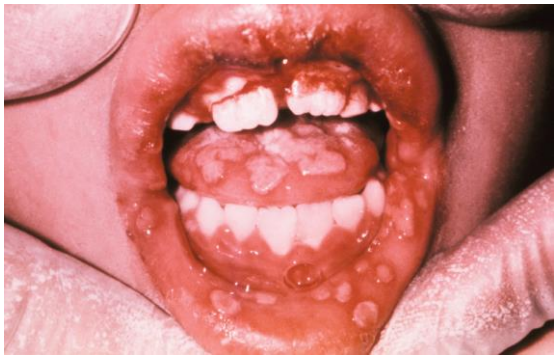
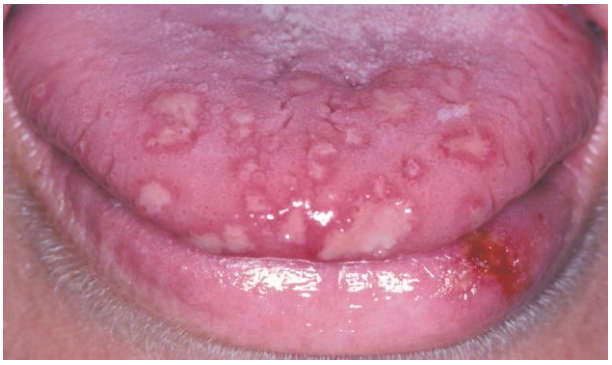
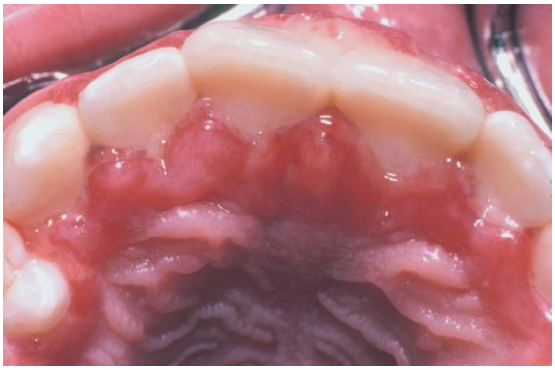
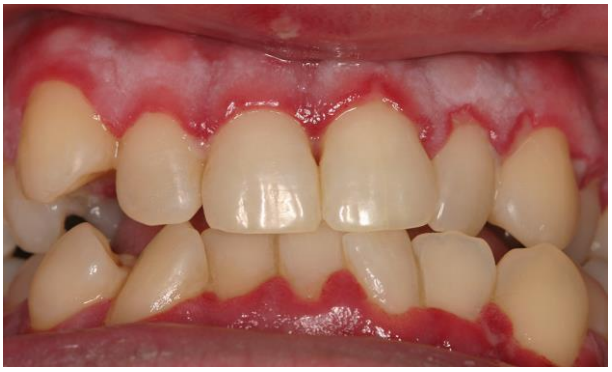
Primary infection refers to initial exposure of an individual without antibodies to the virus. Primary infection with HSV-1 typically occurs at a young age, often is asymptomatic . After primary infection the virus remains in a latent state in trigeminal ganglion.

Recurrent (secondary or recrudescent) infection occurs with reactivation of the virus. Old age, ultraviolet light, physical or emotional stress, fatigue, heat, cold، pregnancy, allergy, trauma, dental treatment, respiratory illnesses, fever, menstruation, systemic diseases, and malignancy have been associated with reactivation.

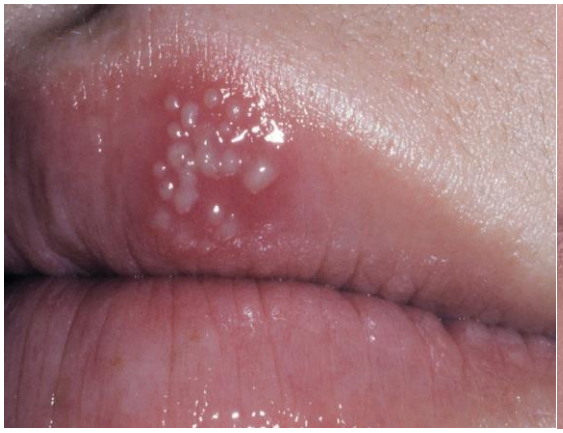
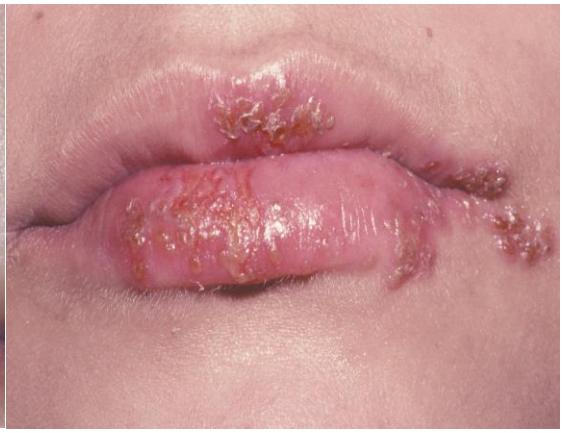
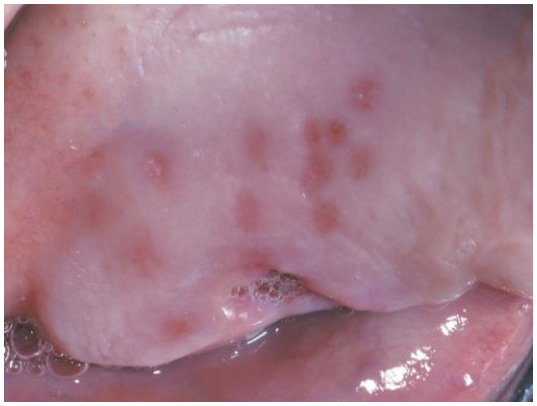
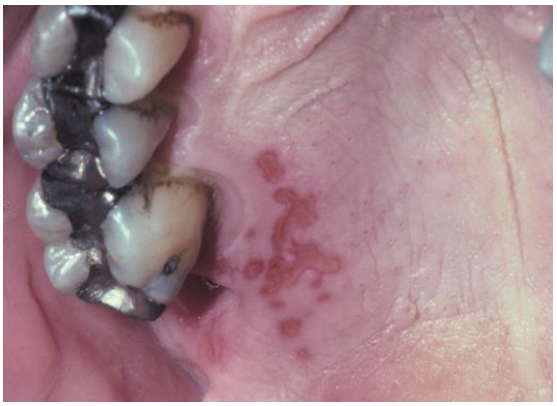
Clinical Features

Acute herpetic gingivostomatitis (primary herpes) is the most common pattern of symptomatic primary HSV infection، and more than 90% of cases are caused by HSV-1. Most affected individuals are children between the ages of 6 months and 5 years . The onset is abrupt and often accompanied by anterior cervical lymphadenopathy، chills, fever , nausea, anorexia, irritability، and sore mouth lesions.

Initially the affected mucosa develops numerous pinhead vesicles, which rapidly collapse to form numerous small, red lesions. These lesions enlarge slightly and develop central ulceration covered by yellow fibrin ulcerations may coalesce to form larger, shallow, irregular ulcerations . Mild cases usually resolve within 5 to 7 days; severe cases may last 2 weeks.

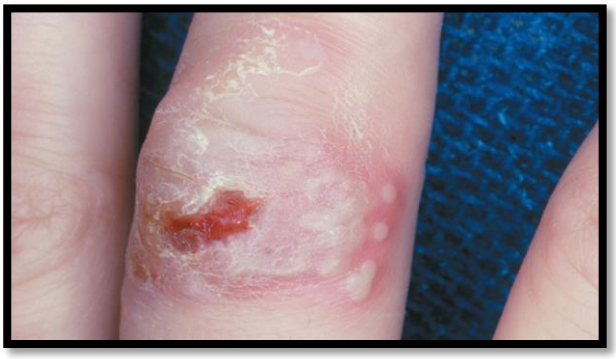





Recurrent herpes simplex infections (secondary herpes) may occur either at the site of primary inoculation or in adjacent areas of surface epithelium supplied by the involved ganglion. The most common site of recurrence for HSV-1 is the vermilion border and adjacent skin of the lips. This is known as herpes labialis (**"cold sore" or "fever blister"**). In some patients, ultraviolet light or trauma can trigger recurrences. Prodromal signs and symptoms (e.g., pain, burning, itching, tingling, localized warmth, and erythema of the involved epithelium) arise 6 to 24 hours before the lesions develop. Multiple small erythematous papules develop and form clusters of fluid-filled vesicles. The vesicles rupture and crust within 2 days. Healing usually occurs within 7 to 10 days. Symptoms are most severe in the first 8 hours.

The lesions begin as 1- to 3-mm vesicles that rapidly collapse to form a cluster of erythematous macules that may coalesce or slightly enlarge . The damaged epithelium is lost, and a central yellowish ulceration develops. Healing occurs within 7 to 10 days. Several less common presentations also exist.

Primary or recurrent HSV infection of the fingers is known as herpetic whitlow (herpetic paronychia) This condition may result from self-inoculation in children with orofacial HSV-1 infection or adults genital HSV-2 infection.Recurrent digital infection may result in paresthesia and permanent scarring.



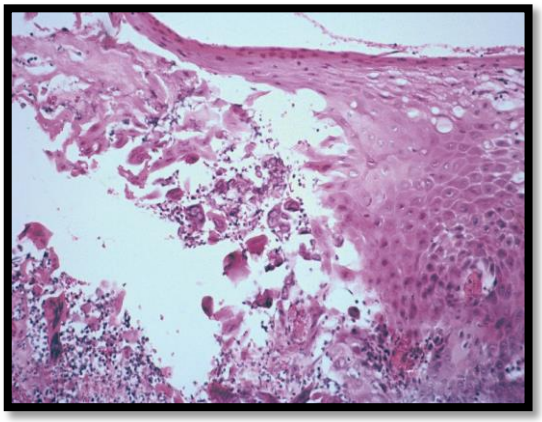
Histopathologic Features:

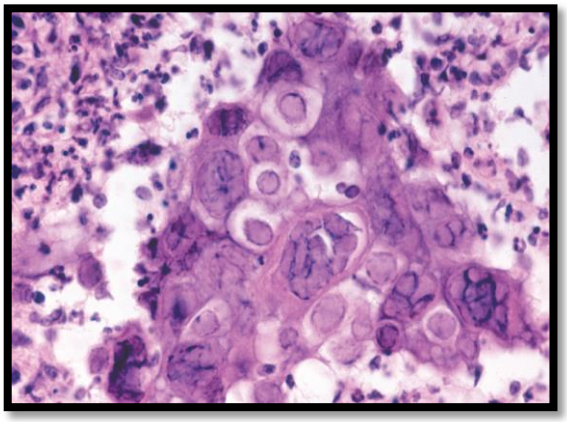
HSV-infected epithelial cells exhibit acantholysis, nuclear clearing, and nuclear enlargement (termed

ballooning degeneration).The acantholytic epithelial cells may be referred to as Tzanck cells. (This term refers to free-floating epithelial cells in any intraepithelial vesicle and is not specific for herpes.) Multinucleated epithelial cells are formed by fusion between adjacent cells .

Treatment and Prognosis:

Symptomatic. In severe cases, systemic aciclovir or valaciclovir. Non-steroidal anti-inflammatory drugs (NSAIDs) used for more immediate pain relief.





VARICELLA (CHICKENPOX):

Varicella (chickenpox) represents primary infection with the varicella-zoster virus (VZV or HHV-3). Secondary or reactivated disease is known as **herpes zoster** .

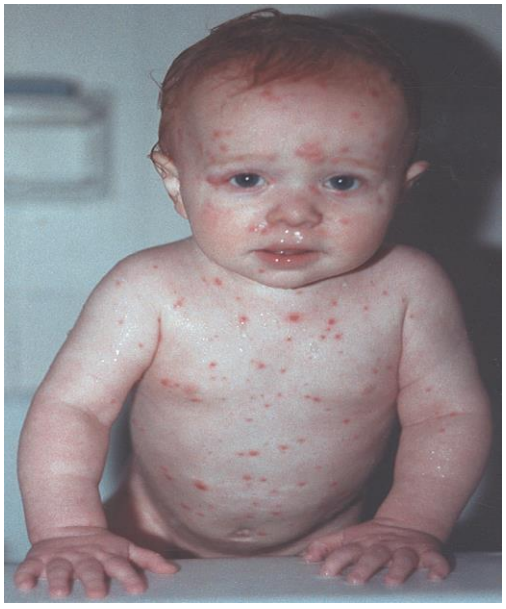
The virus may be spread through air droplets or direct contact with active lesions. In contrast to primary HSV infection, most cases of primary VZV infection are symptomatic.

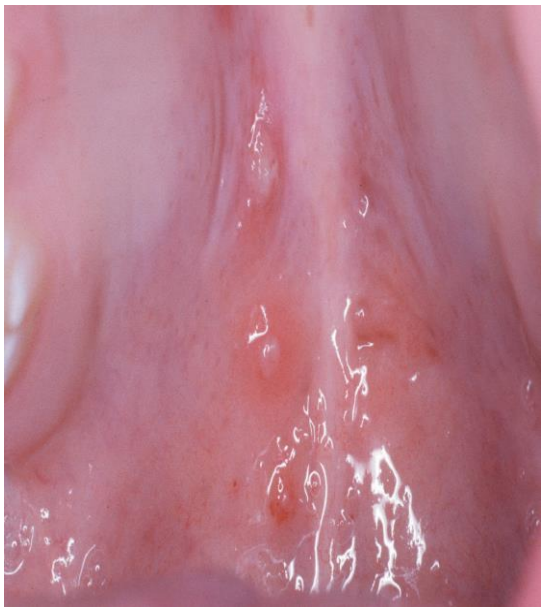
Clinical Features

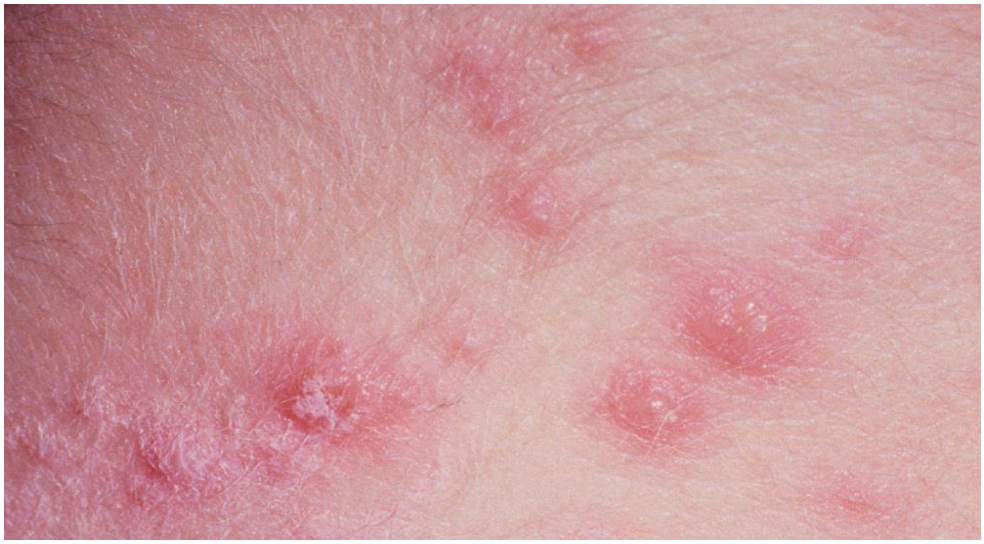
A maculopapular, cutaneous rash with only a small number of lesions, few or no vesicles, low or no fever, and a shortened disease course of approximately 4 to 6 days are characteristic findings. Patients are contagious until no new lesions appear within a 24-hour period.

The symptomatic phase of primary VZV infection usually begins with malaise، pharyngitis, and rhinitis. In older children and adults, additional symptoms (e.g., headache, myalgia, nausea, anorexia، and vomiting) occasionally are seen. This is followed by a characteristic, intensely pruritic exanthem. The rash begins on the face and trunk and spreads to the extremities. Each lesion rapidly progresses through stages of erythema, vesicle، pustule, and hardened crust.

The vesicular stage is the classic presentation. Each vesicle is surrounded by a zone of erythema and has been described as "a **dewdrop on a rose petal**." In contrast to herpes simplex، the lesions typically continue to erupt for 4 or more days.







Perioral and oral manifestations are fairly common and may precede the skin lesions. The vermilion border and palate are involved most often, followed by the buccal mucosa. Occasionally, gingival lesions resemble those noted in primary HSV infection, but distinguishing between the two is not difficult because the lesions of varicella tend to be relatively painless. The lesions begin as 3- to 4-mm‹ white, opaque vesicles that rupture to form 1- to 3-mm ulcerations.

Treatment and Prognosis

Supportive therapy is generally indicated. Warm baths with soap, application of calamine lotion; and systemic antihistamine still are used to relieve pruritus.

Acetaminophen is the preferred antipyretic for childhood cases. Peroral antiviral medications (such as, acyclovir, valacyclovir‹) .

HERPES ZOSTER (SHINGLES)

Herpes zoster develops after reactivation of the virus, with involvement of the distribution of the affected sensory nerve. The prevalence of attacks increases with age, apparently due to age-related decline in cell-mediated immunity. Immunosuppression, HIV infection, treatment with cytotoxic or immunosuppressive , radiation, malignancy, old age, alcohol abuse, stress(emotional or physical), and dental manipulation are additional predisposing factors for reactivation.

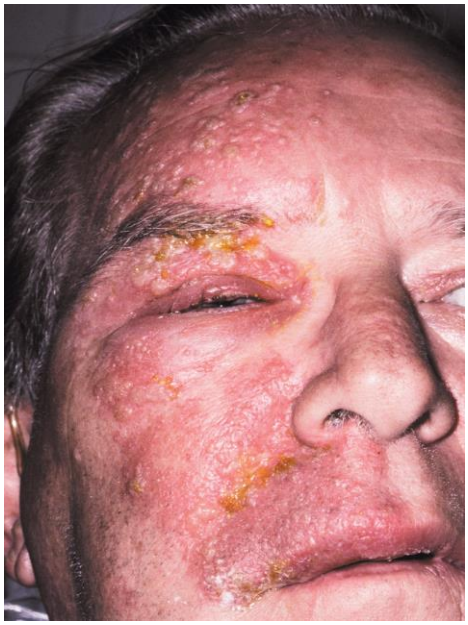
Clinical Features

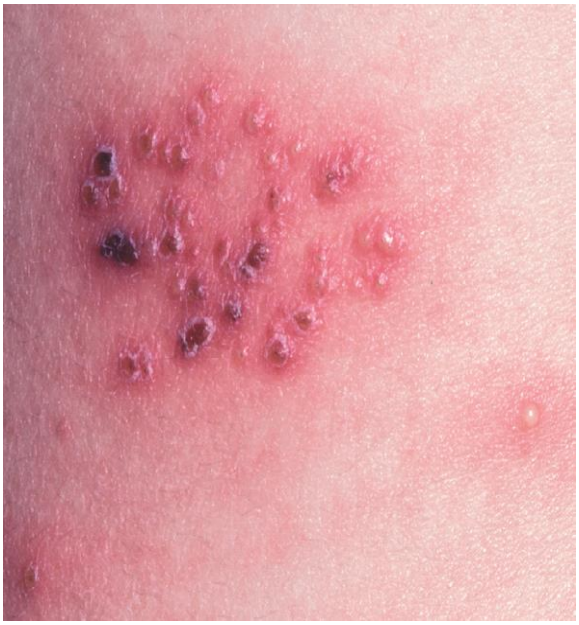
The clinical features of herpes zoster can be grouped into three phases: prodromal , acute, and chronic.

During initial viral replication, ganglionitis develops with resultant neuronal necrosis and severe neuralgia. This inflammatory reaction is responsible for the prodromal pain present in more than 90% of cases. The pain intensifies and has been described as burning, tingling، itching, boring, prickly, or knifelike. and may be accompanied by fever، malaise, and headache.

This prodromal pain normally precedes the acute phase rash by 1 to 4 days and, depending on which dermatome is affected، may masquerade as sensitive teeth, otitis media, migraine headache, myocardial infarction, or appendicitis.

The acute phase begins as the involved skin develops clusters of vesicles set on an erythematous base . Within 3 to 4 days، the vesicles become pustular and ulcerate, with crusts developing after 7 to 10 days. The exanthem typically resolves within 2 to 3 weeks in otherwise healthy individuals. On healing, scarring with hypopigmentation or hyperpigmentation is not unusual.





Infrequently, there is dermatomal pain without development of a rash; this pattern is called **zoster sine herpete**(zoster without rash).

Oral lesions occur with trigeminal nerve involvement and may be present on the movable or bound mucosa. Like varicella, the individual lesions manifest as 1- to 4-mm vesicles or pustules that rupture to form shallow ulcerations . Reactivation of VZV in the geniculate ganglion may cause Ramsay Hunt syndrome. Approximately 15% of patients progress to the chronic phase of herpes zoster (termed **postherpetic neuralgia**), which is characterized by persistent pain after resolution of the rash.

Treatment and Prognosis

Supportive therapy for herpes zoster may include antipruritics. Antiviral medications, such as acyclovir and valacyclovir has been found to accelerate healing of mucocutaneous lesions and reduce pain .

Hand-foot and- mouth disease

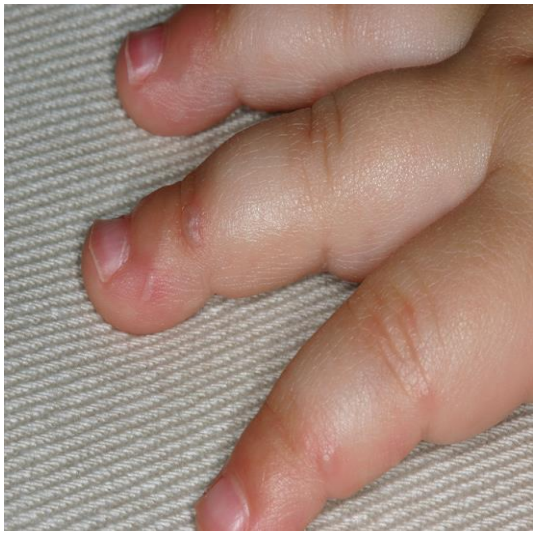
Hand-foot-and-mouth disease is the best-known presentation of enterovirus infection. It is caused by coxsackievirus A16، but also may arise from coxsackie virus A5, A9, or A10.

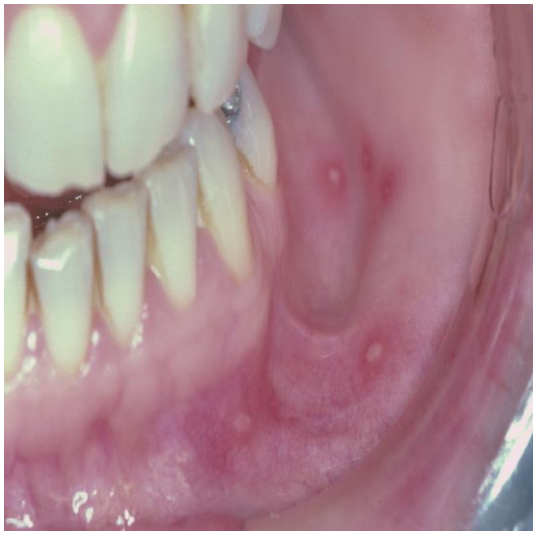
Clinical Features

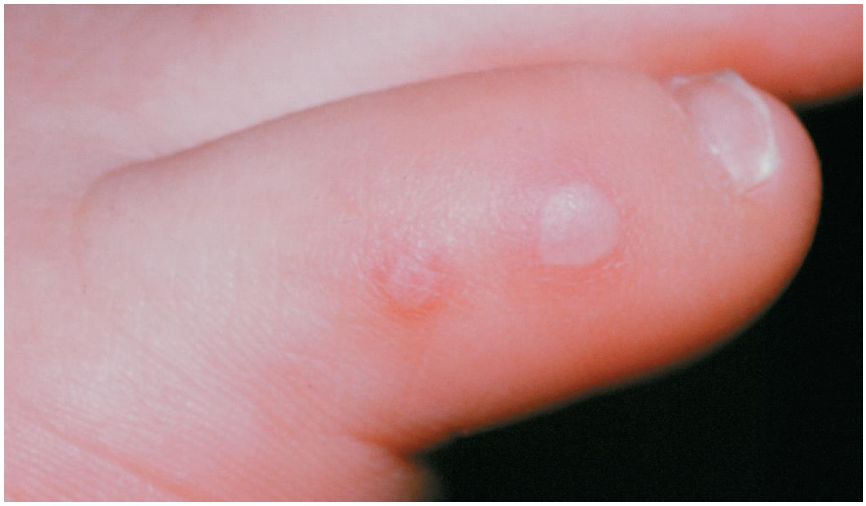
The skin rash and oral lesions typically are associated with flulike symptom (e.g., sore throat, dysphagia, and fever), occasionally accompanied by cough, rhinorrhea, anorexia, vomiting، diarrhea, myalgia, and headache. The name fairly well describes the location of the lesions.

Oral and hand lesions almost always are present. The oral lesions arise without prodromal symptoms and precede the development of the cutaneous lesions. Sore throat and mild fever usually are present also. The cutaneous lesions range from a few to dozens and primarily affect the borders of the palms and soles and the ventral surfaces and sides of the fingers and toes . The cutaneous lesions begin as erythematous macules that develop central vesicles and heal without crusting.

The oral lesions begin as numerous red macules, which form fragile vesicles that rapidly ulcerate and involve anterior regions of the mouth. The number of lesions ranges from 1 to 30. The buccal mucosa, labial mucosa, and tongue are the most common sites. The individual lesions typically measure 2 to 7 mm in diameter but may be larger than 1 cm. The lesions rapidly ulcerate and then typically heal within 1 week.







Treatment and Prognosis

In most instances, enterovirus infections are self-limiting and without significant complications. Therapy is directed toward symptomatic relief;

non-aspirin antipyretics and topical anesthetics, such as dyclonine hydrochloride, often are beneficial.

MEASLES (RUBEOLA):

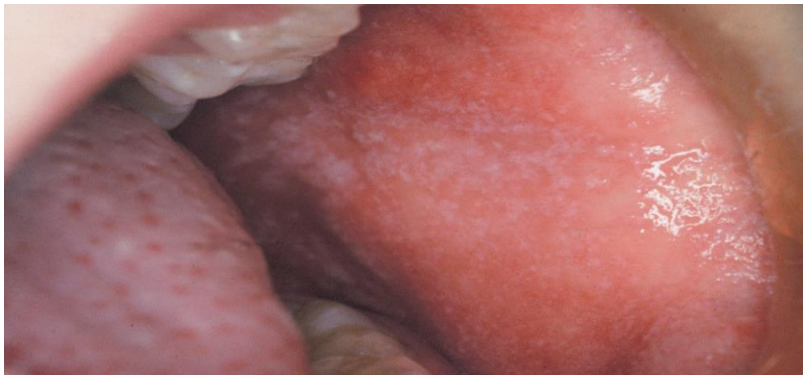
Measles (rubeola) is a highly contagious infection produced by a virus in the family Paramyxoviridae and genus Morbillivirus.

Clinical Features

Most cases of measles arise in late winter or spring and are spread through respiratory droplets. The average incubation period is 14 days, and affected individuals are infectious from 4 days before until 4 days after appearance of the associated rash. The virus is associated with significant lymphoid hyperplasia that often involves the lymph nodes، tonsils, adenoids, and Peyer patches.

There are **three stages** of infection, with each stage lasting 3 days—hence the designation 9-day measles.

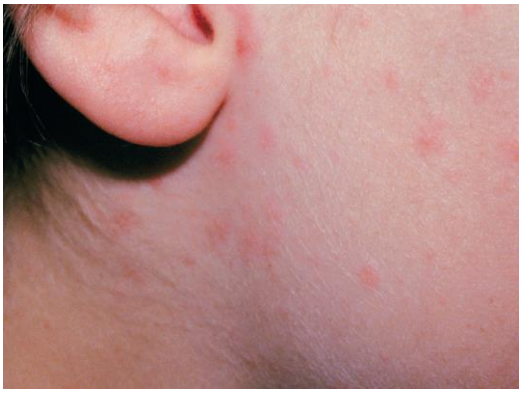
The first 3 days are dominated by the three Cs: coryza (runny nose), cough (typically brassy and uncomfortable), and conjunctivitis (red, watery, and photophobic eyes). Fever typically accompanies these symptoms. During this initial stage, the most distinctive oral manifestation, **Koplik spots**, is seen. These lesions represent foci of epithelial necrosis and appear as numerous small, blue-white macules (or "grains of salt) surrounded by erythema . Typical sites of involvement include the buccal and labial mucosa, and less often the soft palate.



As the second stage begins, the fever continues, the Koplik spots fade, and a maculopapular and erythematous (**morbilliform**)

rash begins. The face is involved first, with eventual downward spread to the trunk and extremities. Ultimately, a diffuse erythematous eruption is formed، which tends to blanch on pressure .

In the third stage, the fever ends. The rash begins to fade،with downward progression and replacement by brown pigmentation. Ultimately, desquamation of the skin is noted in areas previously affected by the rash.

.  

Treatment :

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

Fungal infections

Candidal infection (Candidiasis)

Candidiasis is the most common oral fungal infection. It is usually caused by Candida albicans.

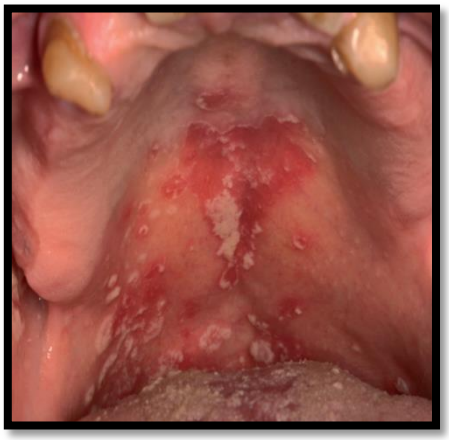
Predisposing factors are **local** (poor oral hygiene, xerostomia،mucosal damage, dentures, antibiotic mouthwashes) and **systemic** (broad-spectrum antibiotics, steroids, immunosuppressive drugs, radiation, HIV infection،hematological malignancies, neutropenia, iron-deficiency anemia, cellular immunodeficiency, endocrine disorders).

Clinical features

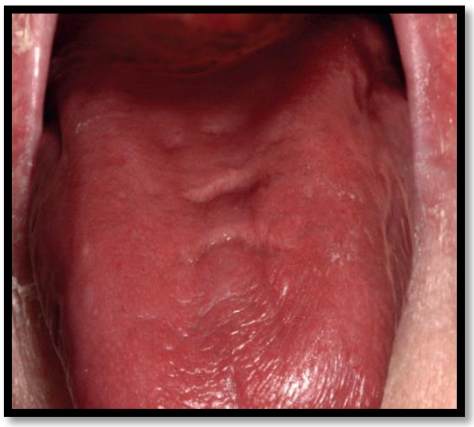
Oral candidiasis is classified as **primary**, consisting of lesions exclusively on the oral and perioral area, and **secondary**, consisting of oral lesions of mucocutaneous disease.

Primary candidiasis includes many clinical varieties:

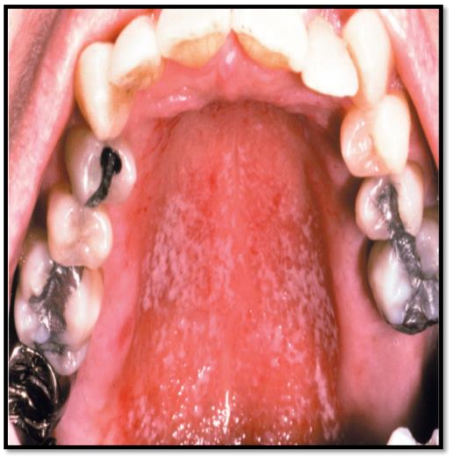
pseudomembranous (thrush) , erythematous(papillary hyperplasia of the palate), Chronic Hyperplastic Candidiasis , and Candida-associated lesions (angular cheilitis, median rhomboid glossitis, denture stomatitis) .



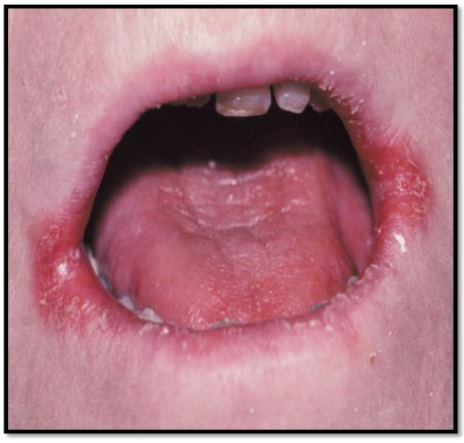
-**Pseudomembranous Candidiasis**



- Erythematous Candidiasis



-Papillary hyperplasia of the palate



- Angular cheilitis

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.

Deep fungal infections

Deep fungal infections are characterized by primary involvement of the lungs. Infections may disseminate from this focus to involve other organs.

Deep fungal infections having a significant incidence of oral involvement include histoplasmosis, coccidioidomycosis, blastomycosis, mucormycosis, and cryptococcosis

Clinical Features: Initial signs and symptoms of deep fungal infection are usually related to lung involvement and include cough, fever, night sweats, weight loss, chest pain, and hemoptysis. The usual oral lesion is ulcerative. Whether single or multiple، lesions are non-healing, indurated, and frequently painful.

Histopathology. The basic inflammatory response in a deep fungal infection is granulomatous. In the presence of these microorganisms, macrophages and multinucleated giant cells dominate the histologic picture

Treatment : Treatment of deep mycotic infection generally consists of antifungals such as ketoconazole, fluconazole, and amphotericin B .

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. the main lesions in each group are listed in table below

Group 1-Lesions strengthly associated with HIV infections

- Candidiasis
  - Erythematous
  - Hyperplastic
  - Pseudomembranous
- Hairy leukoplakia (EB virus)
- HIV associated periodental disease
  - HIV gingivitis
  - Necrotizing ulcerative gingivitis
  - HIV associated periodontitis
  - Necrotizing stomatitis

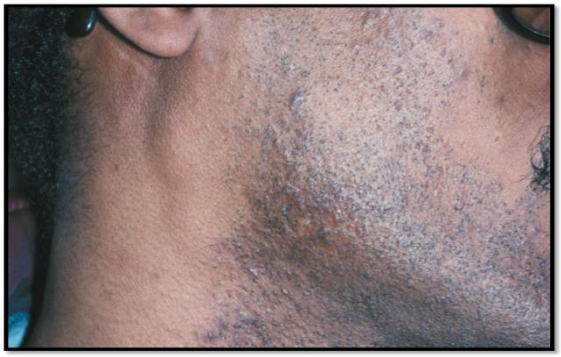
- ❖ Kaposis sarcoma
- ❖ Non-Hodgkins lymphoma

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



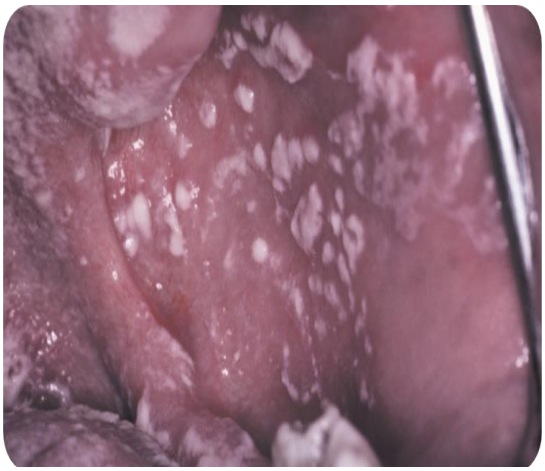
Oral Manifestaton of Aquired immunodyficiency system (AIDS)

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.

Candidiasis.

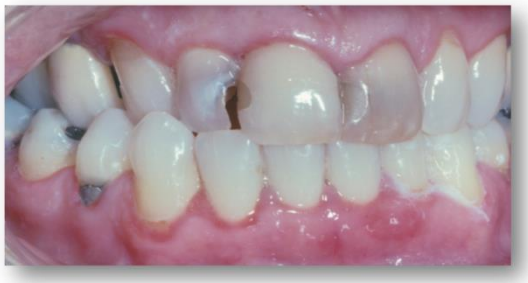
Oral candidiasis is the most common intra oral manifestation of HIV infection and often is the presenting sign that leads to the initial diagnosis, Its presence in a patient infected with HIV is not diagnostic of AIDS but appears to be predictive for the subsequent development of full-blown AIDS in untreated patients with in 2 years.



The following four clinical patterns of oral candidiasis are seen:

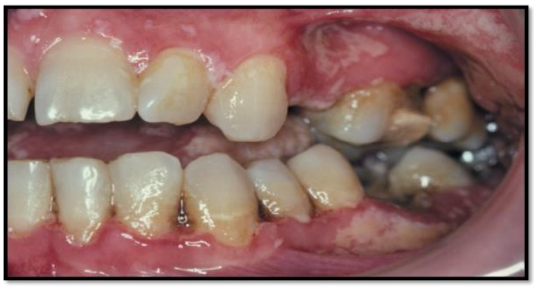
- •Pseudomembranous
- •Erythematous
- •Hyperplastic
- •Angular cheilitis

HIV-associated periodontal disease. Three patterns of periodontal disease are associated strongly with HIV infection:



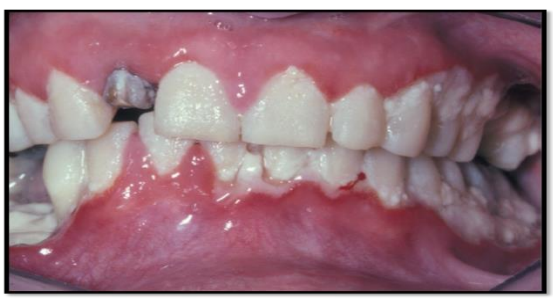
- •Linear gingival erythema
- •Necrotizing ulcerative gingivitis
- •Necrotizing ulcerative periodontitis

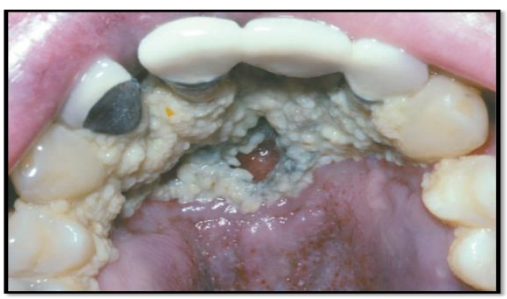
Linear gingival erythema initially was termed HIV" lated gingivitis but ultimately was noted in association with other disease processes. This unusual pattern of gingivitis appears with a distinctive linear band of erythema that involves the free gingival margin and extends 2 to 3 mm apically.

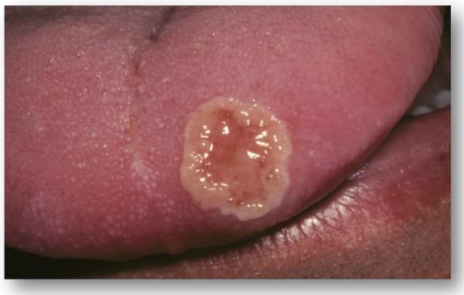


Necrotizing ulcerative gingivitis (NUG)

Refers to ulceration and necrosis of one or more interdental papillae with no loss of periodontal attachment. Necrotizing ulcerative periodontis (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.





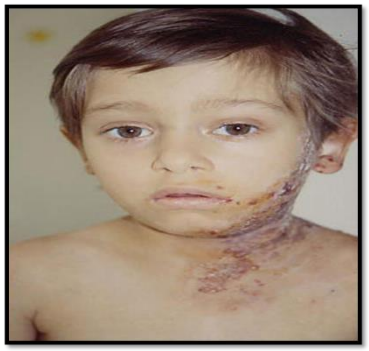


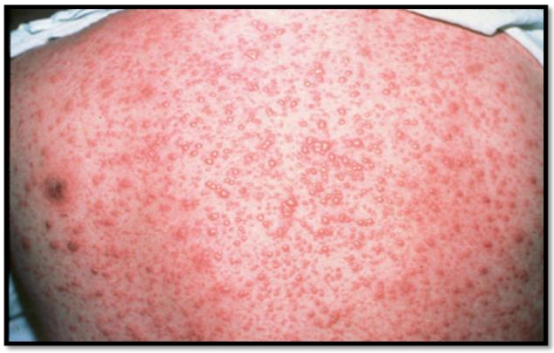
Herpes simplex virus (HSV).

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).

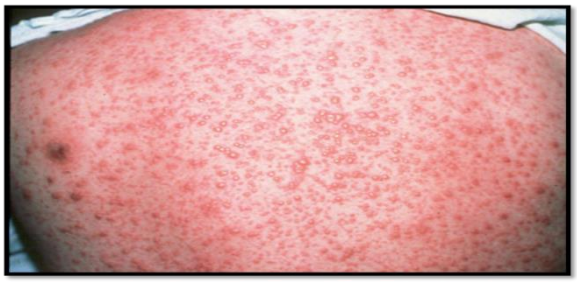
Recurrent VZV infection (herpes zoster) is fairly common in HIV-infected patients، oral involvement often is severe and occasionally leads to bone sequestration and loss of teeth. Associated pain typically is intense.





Epstein-Barr virus (EBV).

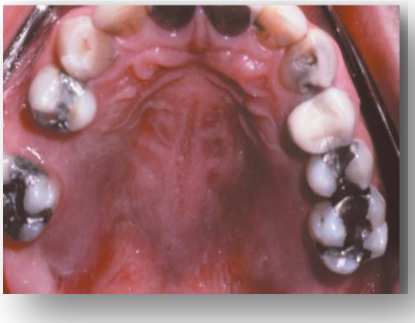
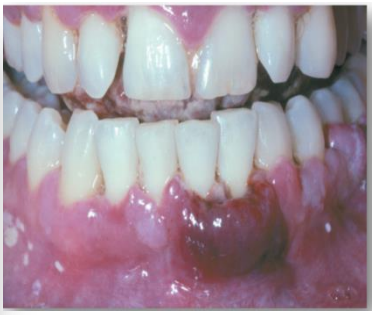
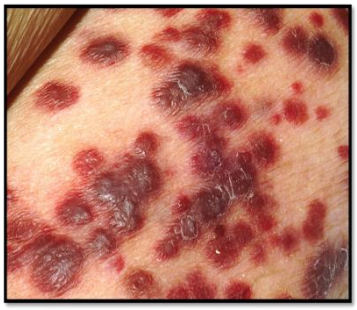
Although EBV is thought to be associated with several forms of lymphoma in HIV infected patients, the most common EBV-related lesion in patients with AIDS is oral hairy leukoplakia (OHL). This lesion has a somewhat distinctive (but not diagnostic)pattern of hyperkeratosis and epithelial hyperplasia that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



Kaposi's sarcoma (KS).

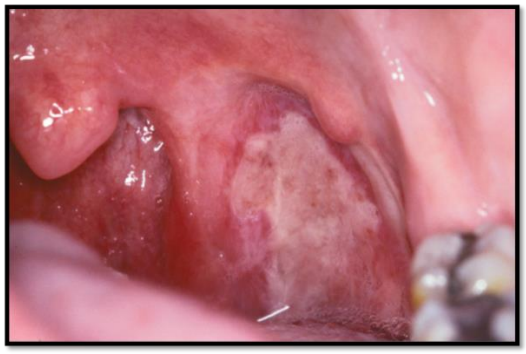
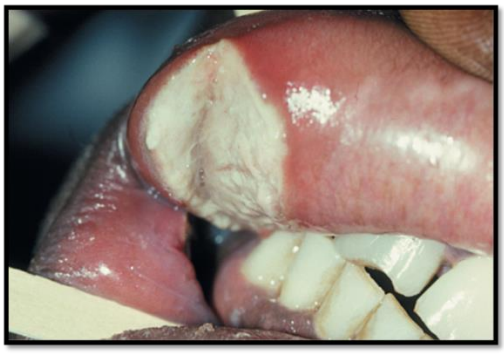
KS is a multifocal neoplasm of vascular endothelial cell origin, KS begins with single or, more frequently. Multiple lesions of the skin or oral mucosa. The trunk, arms, head، and neck are the most commonly involved anatomic sites. Oral lesions are seen in approximately 50% of affected patients and are 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.

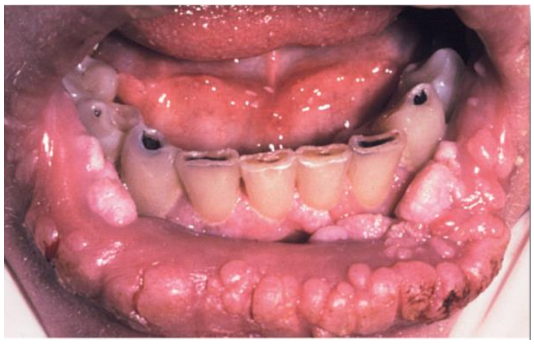
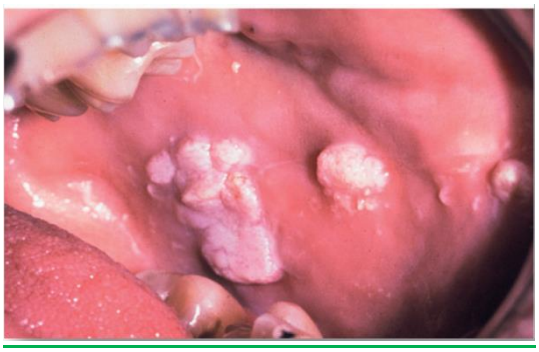
Aphthous ulcerations.

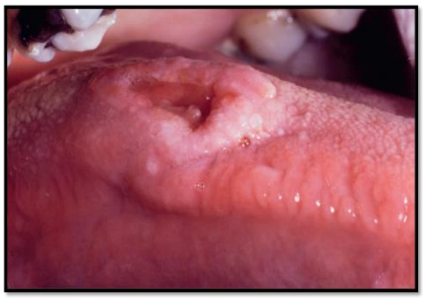
Lesions that are similar clinically to aphthous ulcerations occur with increased frequency in patients infected with HIV. All three forms (minor, major, and herpetiform) are seen.

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.

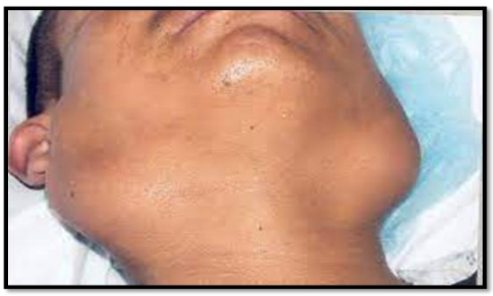


Histoplasmosis.

Histoplasmosis is produced by Histoplasma capsulatum. In healthy patients. The infection typically is subclinical and self-limiting, but clinically evident infections do occur in immunocompromised individuals. Although a number of deep fungal infections are possible in patients with AIDS.

HIV-associated salivary gland disease.

Clinically obvious salivary gland disease is noted in approximately 5% of HIV infected patients, with a greater prevalence noted in children. The main clinical sign is salivary gland enlargement, particularly affecting the parotid. Bilateral involvement is seen in about 60% of the patients with glandular changes and often is associated with cervical lymphadenopathy.



Oral squamous cell carcinoma.

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