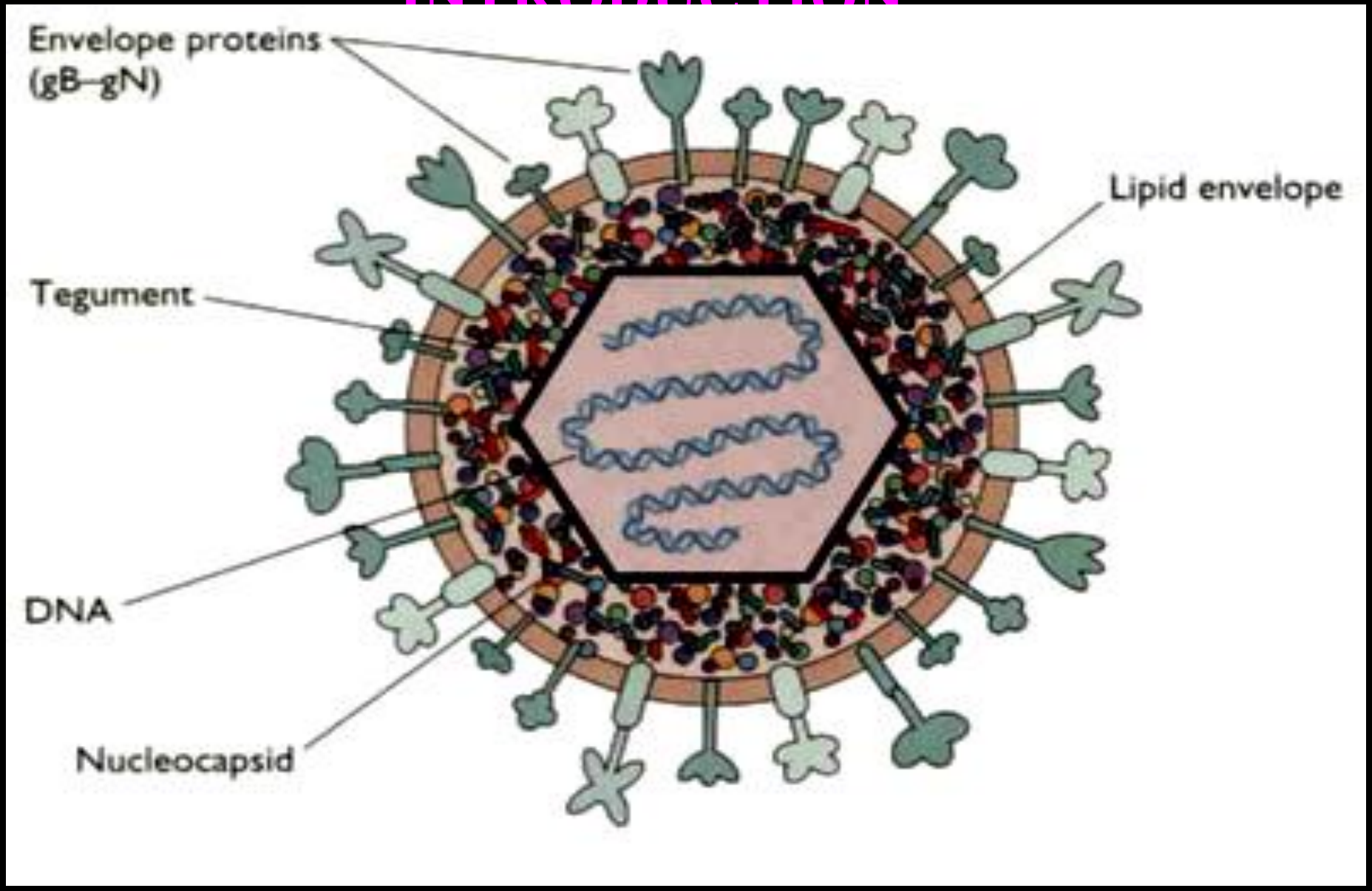
Viral infections of the Oral cavity

DEPARTMENT OF ORAL AND MAXILLOFACIAL PATHOLOGY & ORAL MICROBIOLOGY

INTRODUCTION



- It has been suggested that viraly infected cells produce the nucleic acid characteristic of the virus and that therefore the susceptibility of cells to viral infection may depend upon the availability of suitable nucleic acid within cell to sustain the virus.
- Viruses have long been known to cause certain infectious diseases, and many of them produce a long-lasting immunity against reinfection by the same virus.

The sequelae of the viral infection of the host cell could be

Acute infection : Usually due to lysis of the cell,
Example : Polio virus
Latent invection : with periodic activation,
Example : Herpes virus
Persistent infection : Persistent for many years,
Example : HIV, Hepatitis B
Transformation : Transformation into malignant cells,
Example : subtypes of HPV& retroviruses

CCLASSIFICATION OF MAJOR VIRUS GROUPS AND VIRUS DISEASES

I. RNA viruses

A. Orthomyxovirus
   1. Influenza

B. Paramyxovirus
   1. Measles (rubeola)
   2. Mumps

C. Rhabdovirus
   1. Rabies
   2. Hemorrhagic fever

D. Arenavirus
   1. Lymphocytic choriomeningitis
   2. Lassa fever

E. Calicivirus
F. Coronavirus
    1. Upper respiratory infection
G. Bunyavirus
H. Picornvirus
    1. Poliomyelitis
    2. Coxsackie diseases
    3. Common cold
    4. Foot-and-mouth disease
    5. Encephalomyocarditis
I. Reovirus
J. Togavirus
    1. Rubella
    2. Yellow fever
    3. St. Louis encephalitis
K. Retrovirus (RNA tumor virus)

II. DNA Viruses

A. Herpesvirus
   1. Herpes simplex – 1 & 2
   2. Varicella/herpes zoster – Herpes zoster, Chickenpox
   3. Cytomagalo virus - Cytomegalic inclusion disease
   4. Epstein-Barr virus – infectious mononucleosis, hepatitis

B. Poxvirus
   1. Smallpox
   2. Molluscum contagiosum

C. Adenovirus
   1. Pharyngoconjuctival fever
   2. Epidemic keratoconjunctivitis

D. Parovirus

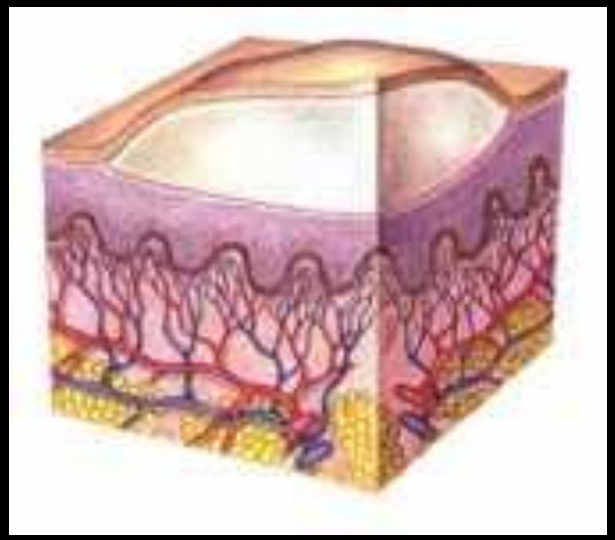
E. Iridovirus

F. Papovavirus
   1. Human warts or papillomas
   2. Tumorigenic viruses in animals.

Terminologies :

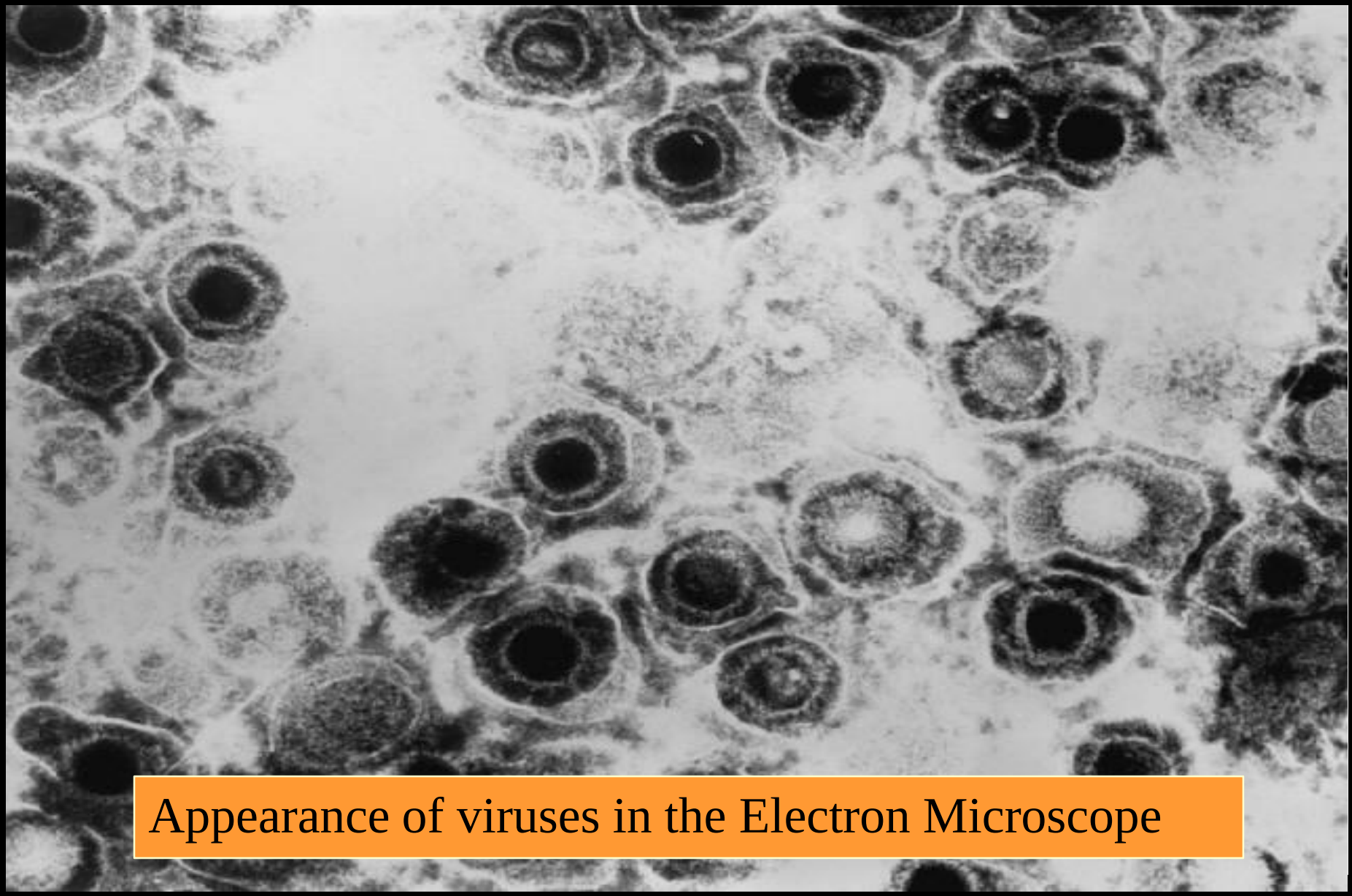
Vesicle – fluid filled blister <1cm
Bulla – Fluid filled blister >1cm
Ulcer – Discontinuity OR breach in the epithelium

Vesicle



Bulla

Ulcer



Appearance of viruses in the Electron Microscope

- There are two immunologically different types of HSV: type 1 and type2.

- They differ antigenically and biologically, but share 50 per cent of the nucleotide sequence. Many types of specific regions exist in both HSV 1 and 2 and are responsible for host immunity. These sub-types can be distinguished serologically or by restriction endonuclease analysis of the DNA.

- The incubation period is 1-26 days and can occur throughout the year. Transmission is mainly through close contact, sharing of glasses, cutlery or crockery etc.

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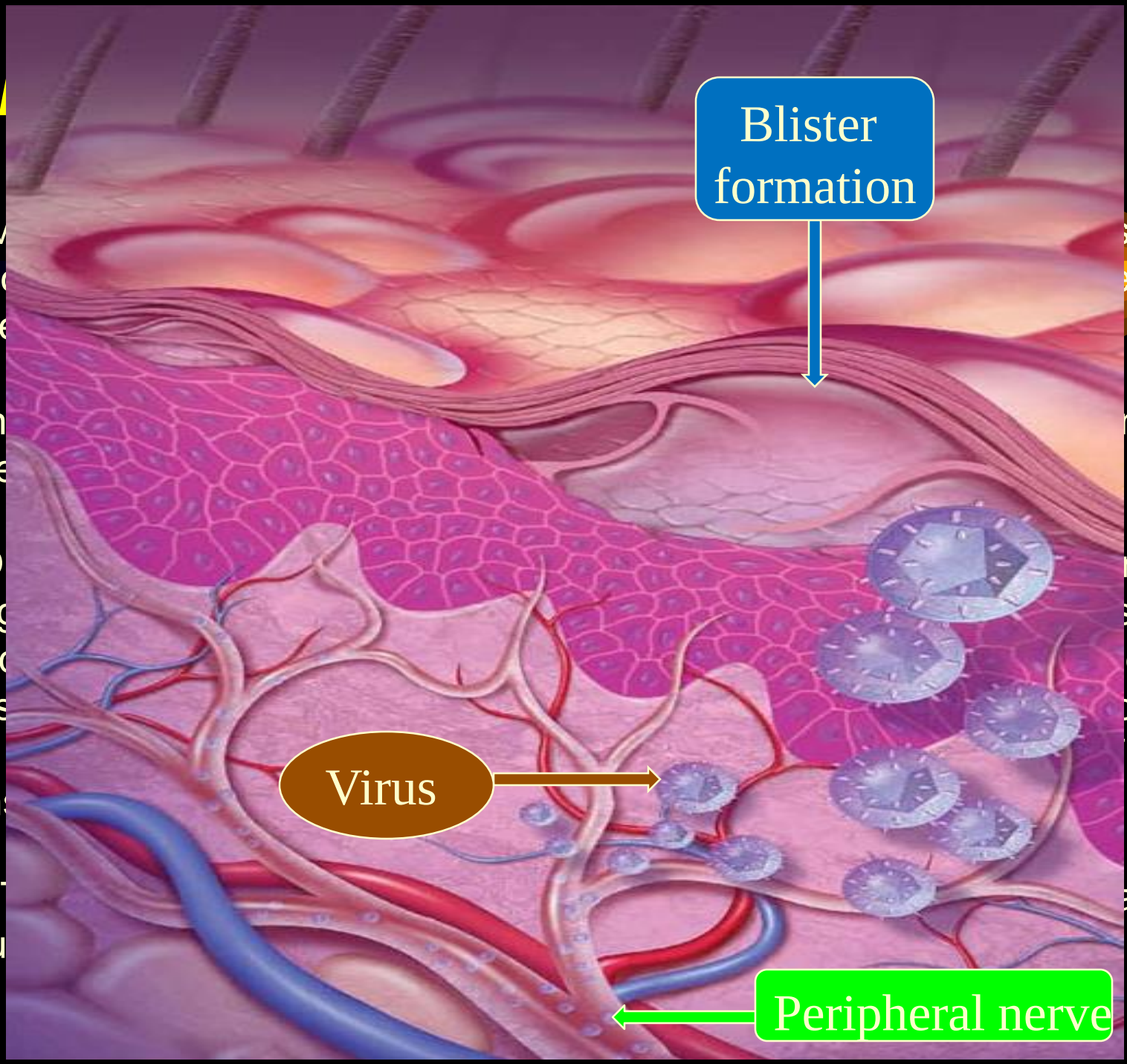


- HSV-1 predominantly affects the face, lips, the oral cavity, and upper body skin; and HSV-2 usually affects the genitals and skin of lower half of the body.

- Primary infection resolves and the virus can no longer be recovered from ganglia but viral DNA can be found in the ganglion cells. Both humoral and cell mediated immunity is responsible for the clinical manifestation, latency, and recurrence of the disease.

- Two types of infection with herpes simplex virus occur. The first is a primary infection in a person who does not have circulating antibodies, and the second is a recurrent infection in persons who have such antibodies.

- It is impossible to differentiate clinically between the lesions of the primary and a recurrent attack, although the primary infection is accompanied more frequently by severe systemic manifestations and is occasionally fatal.

Herpes genitalis

- Caused by HSV-II common in genitals

- Incubation period- it develops 3to6 days after exposure as vesicular lesions that are often preceded by burning and pickling sensation.

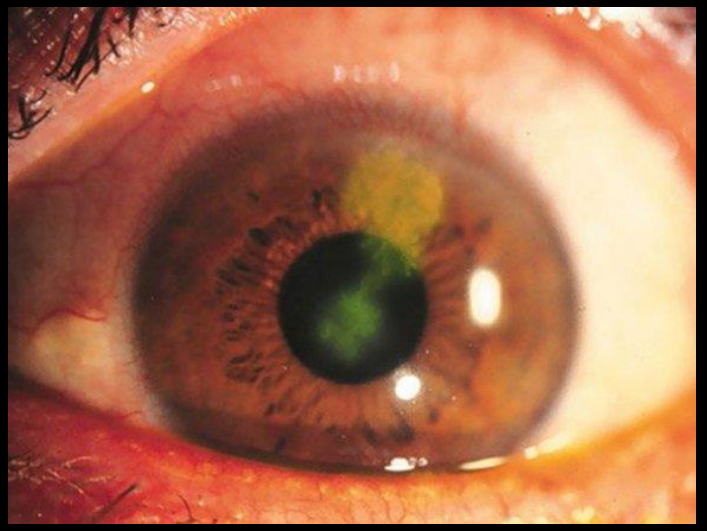
- Symptoms- involved area extremely painful, regional lymphadenopathy, fever, malaise and anorexia may develops.

Herpetic meningoencephalitis

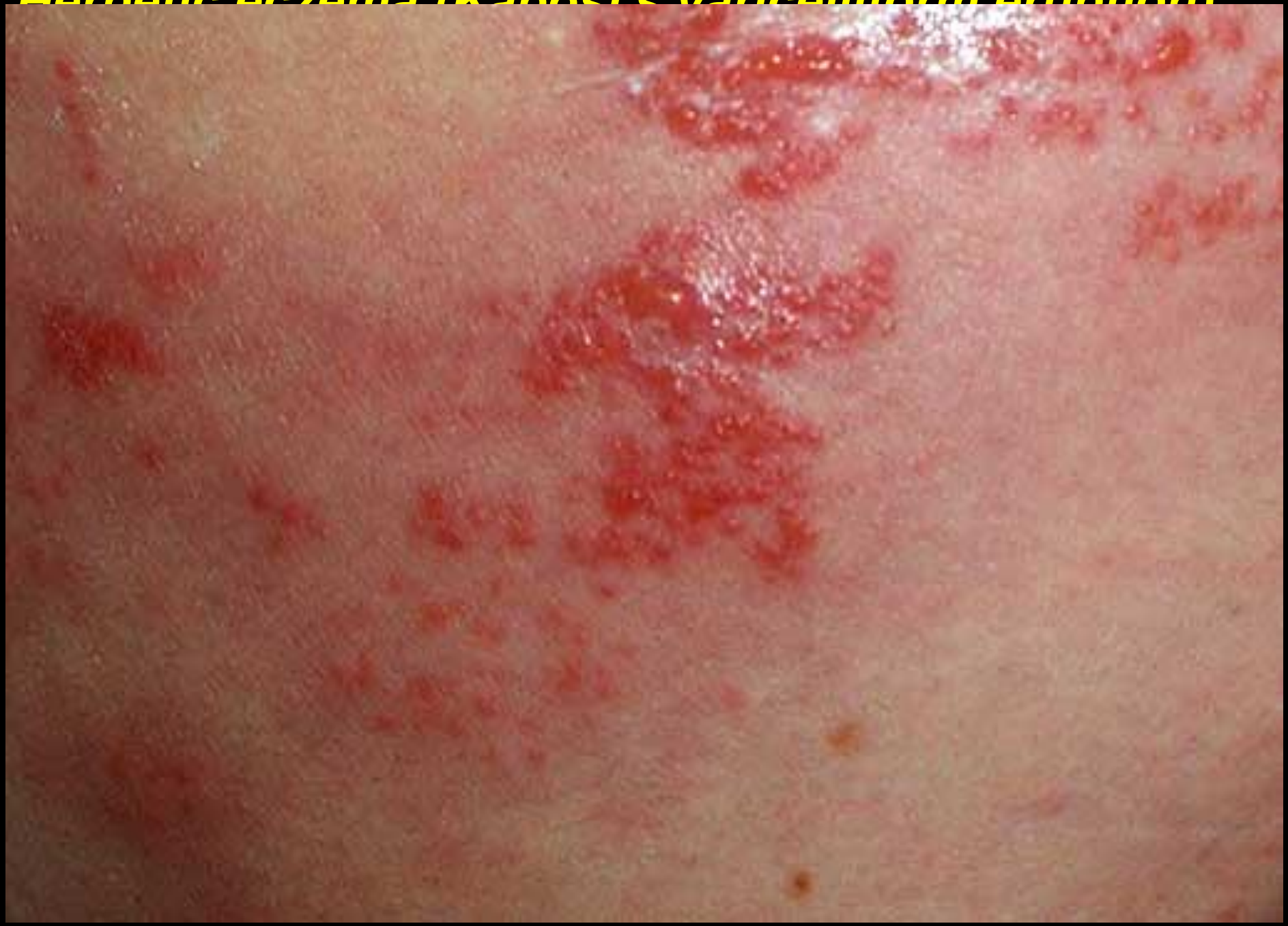
- It is a serious form of this infection, characterized by sudden fever and symptoms of increased intracranial pressure. Paralysis of various muscle groups occurs, while convulsions and even death may ensue.

Herpetic conjunctivitis

- Swelling and congestion of the palpebral conjuctiva although keratitis and corneal ulceration also may occur. Herpetic vesicle of the eyelids are typical but heal rapidly.



Herpetic eczema (Kaposi's varicelliform eruption)



PRIMARY HERPETIC STOMATITIS

Clinical features

- Herpetic stomatitis is a common oral disease transmitted by droplet spread or contact with the lesions.

- It affects children and young adults. It usually occurs after age of six months because of the presence of circulating antibodies in the infant derived from the mother.

- The disease occurring in children is frequently the primary attack and is characterized by the development of fever, irritability, headache, pain upon swallowing, and regional lymphadenopathy.

- Within a few days the mouth becomes painful and the gingival which is intensely inflamed appear erythematous and edematous.

- The lips, tongue, buccal mucosa, palate, pharynx, and tonsils may also be involved.

- The vesicles rupture and form shallow, ragged, extremely painful ulcers covered by a gray membrane and surrounded by an erythematous halo. It is important to recognize that the gingival inflammation precedes the formation of ulcers by several days.

- The ulcers vary considerably in size, ranging from very tiny lesions to lesions measuring several millimeters or even a centimeter in diameter. They heal spontaneously within 7-14 days and leave no scar.

- HSV-1 could be isolated from facial, labial, and oral herpetic lesions for a mean duration of three-and-a-half days, with a range of 2-6 days, after the onset of the lesions, while HSV-2 could be isolated from genital lesions for a mean duration of five-and-a-half days, with a range of 2-14 days, after onset.

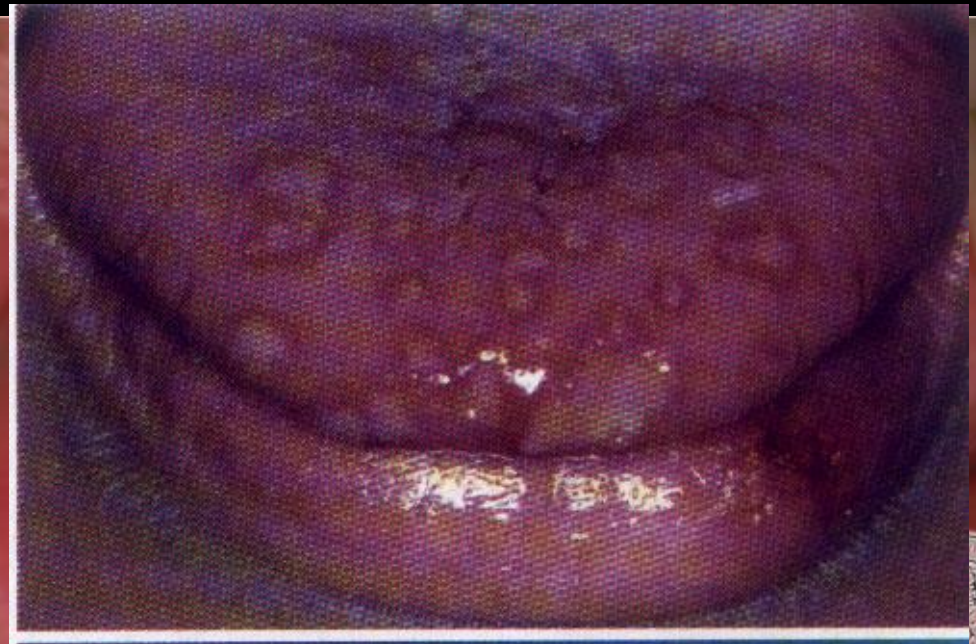
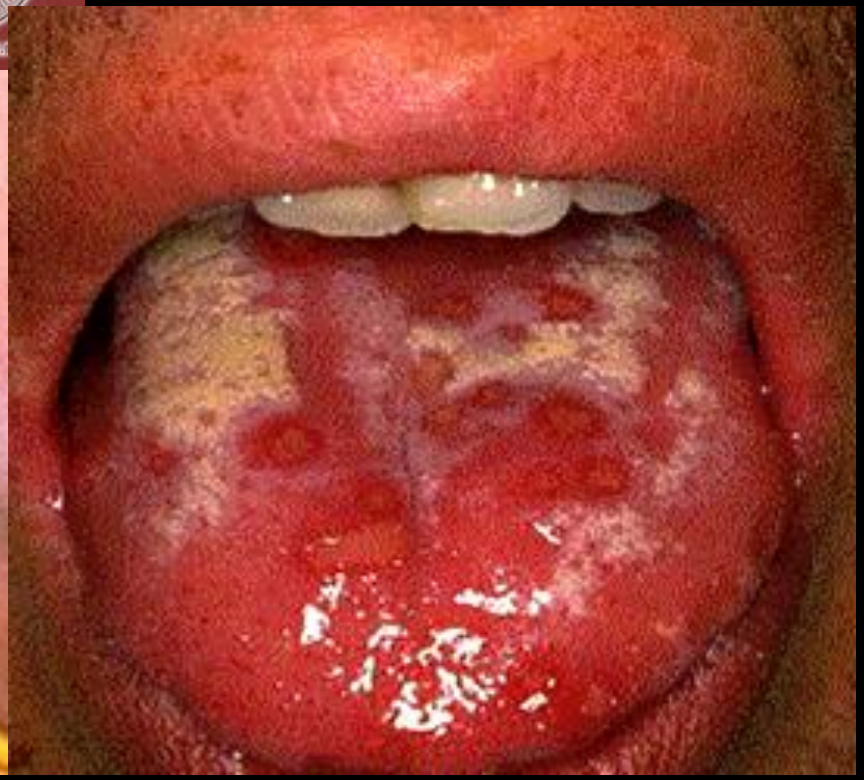


Figure 7-2 • Acute herpetic gingivostomatitis. Numerous coalescing, irregular, and yellowish ulcerations of the dorsal surface o the tongue.



- HSV could survive for two to four hours on environment surfaces such as cloth and plastic as well as on the skin of the hands contaminated by direct contact with labial or oral lesions.

- HSV does not remain latent at the site of the original infection in the skin or oral mucosa. Instead, the virus reaches nerve ganglia supplying the affected areas, presumably along nerve pathways, and remain latent there until reactivated. The usual ganglia involved are the trigeminal for HSV-1 and the lymphosacral for HSV-2. Viral DNA can be demonstrated in these ganglia.

- Unfortunately, this incorporation of viral DNA into host DNA insures a lifelong infection beyond the reach of antibody, cell mediated immune responses or chemotherapy.

Mode of transmission

- Transmission may occur by droplet infection, although direct contact is necessary. There is no animal reservoir for this virus.
- The inoculation period appears to range from 2-20 days with an average of six days before development of lesions.
- Primary herpetic eruptions are commonly associated with pneumonia, meningitis, and the common

Hist

Ballooning degenearion
Of the cell – pale eosinophilic
Cytoplasm, large vesicular
nucleus

Formation of
giant cell-
Multiple nuclei

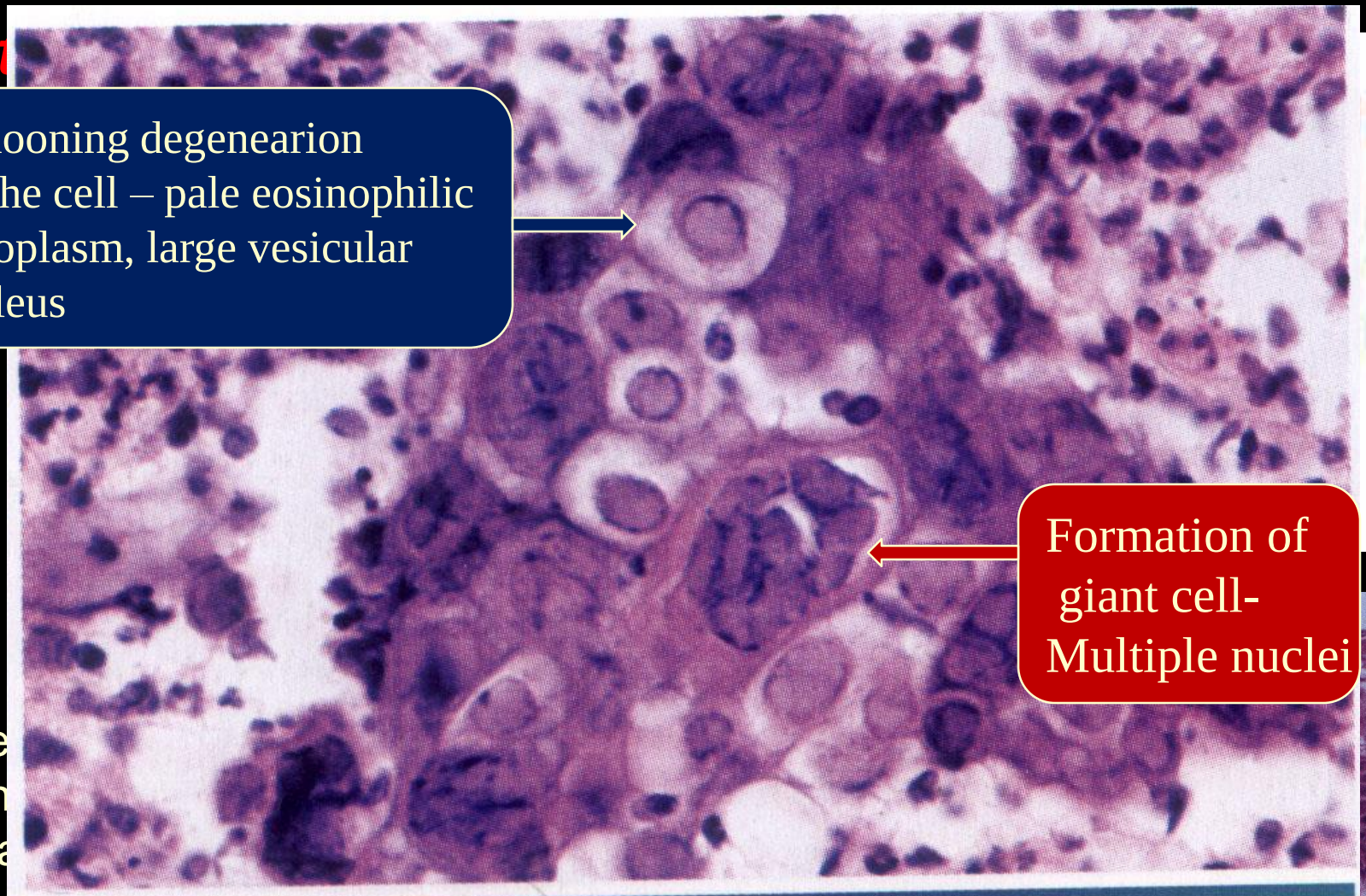


Figure 7-12 • Herpes simplex. Altered epithelial cells exhibiting ballooning degeneration, margination of chromatin, and multinucleation.

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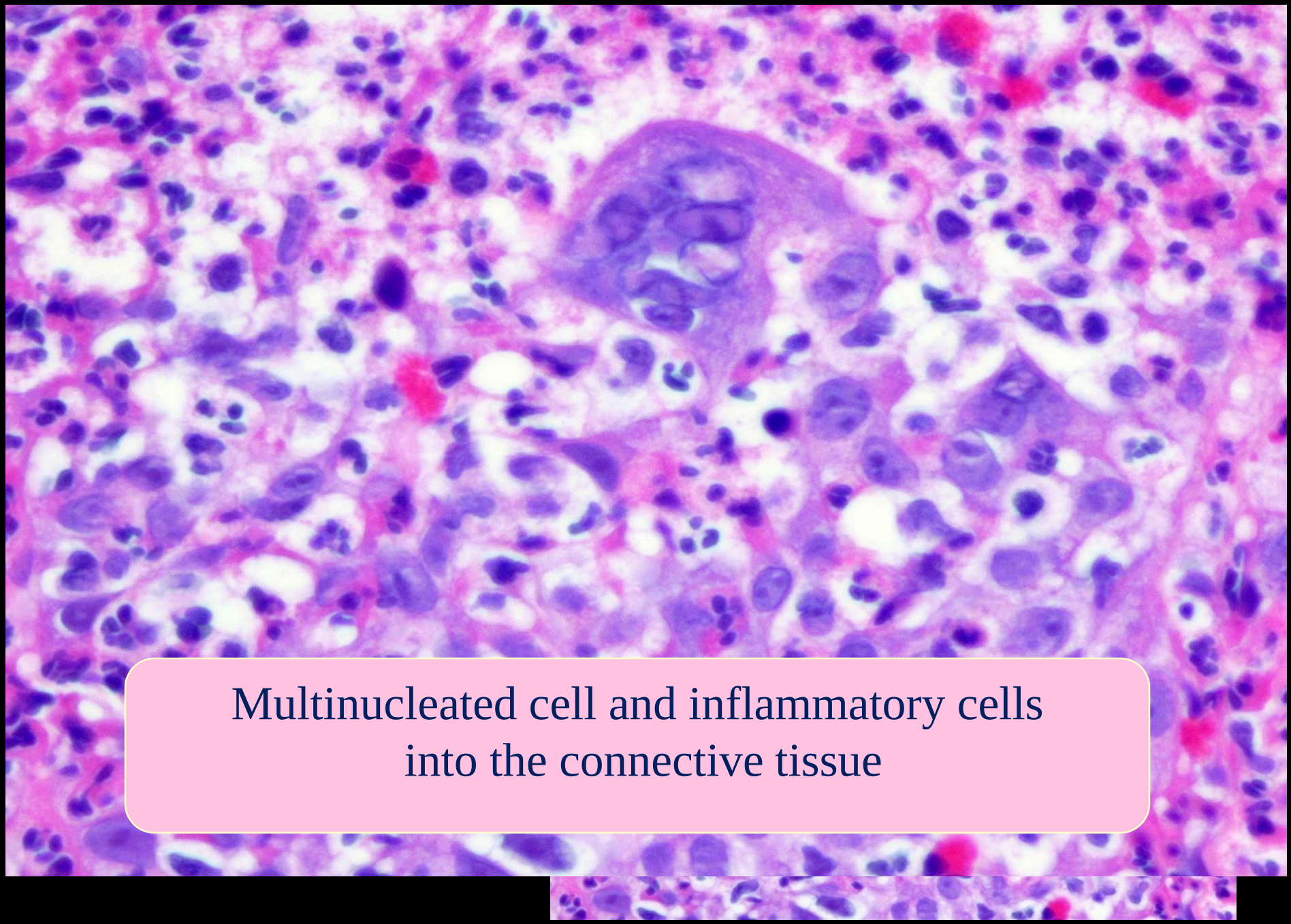
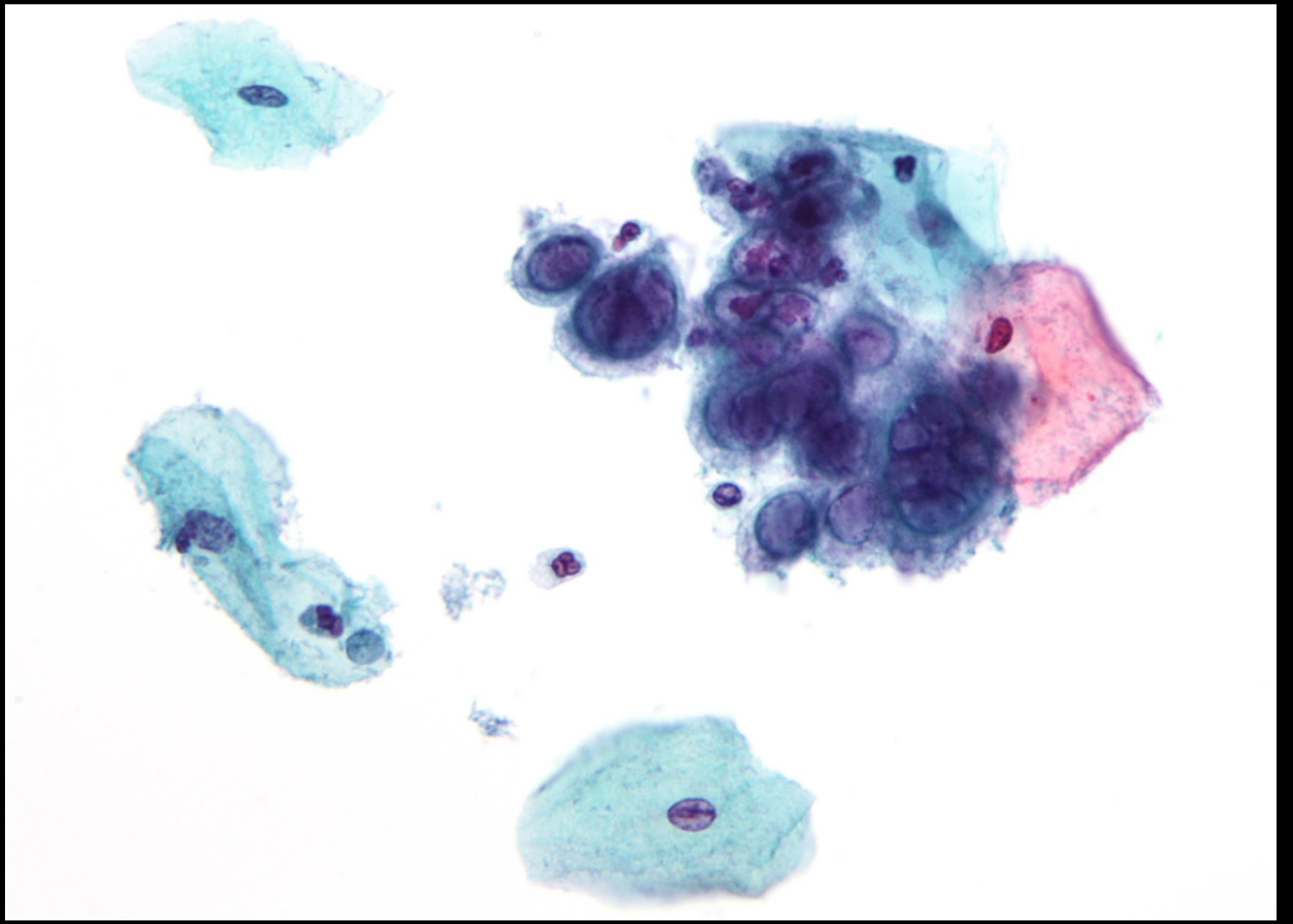

Multinucleated cell and inflammatory cells
into the connective tissue



Differential diagnosis

- Hand-foot and mouth disease- the lesions present on the feet and hand also.
- Herpangina- oropharyngeal and soft palate involvement. It affects children in late summer and early monsoon season on soft palate and facial area with fever and malaise.
- Chronic recurring aphthae- no stomatitis, no general systemic symptoms and lesions are less numerous and more often found in adults.
- Herpes zoster- segmental distribution along the anatomical location of nerve.
- Erythema multiforme- it occurs in young adults, as compared to herpes simplex which occurs in children. Gingivitis is not severe and generally limited to anterior part of the mouth. In erythema multiforme skin lesions are present.
- Bullous lichen planus- it is painful condition characterized by large blister on tongue and cheek with rupture and it undergoes ulceration.

Treatment

- Antiviral drugs have significant impact on the course of the disease, if it is diagnosed early.

- Antibiotic therapy helps in the prevention of secondary infection.

- NSAID and topical anesthetic gel may relieve discomfort considerably.

RECURRENT, OR SECONDARY, HERPETIC LABIALIS AND STOMATITIS

- Recurrent herpetic stomatitis is usually seen in adult patients and manifests itself clinically as an attenuated form of the primary disease.

- Between 80-100 percent of adults in the lower socio-economic levels have HSV-1 and/or HSV-2 circulating antibodies, whereas only 30-50 per cent of adults in the higher socioeconomic levels, including medical, dental, and nursing personnel, have such antibodies. Those without antibodies are at higher risk of contact and infection, especially the latter groups because of the nature of their occupation.

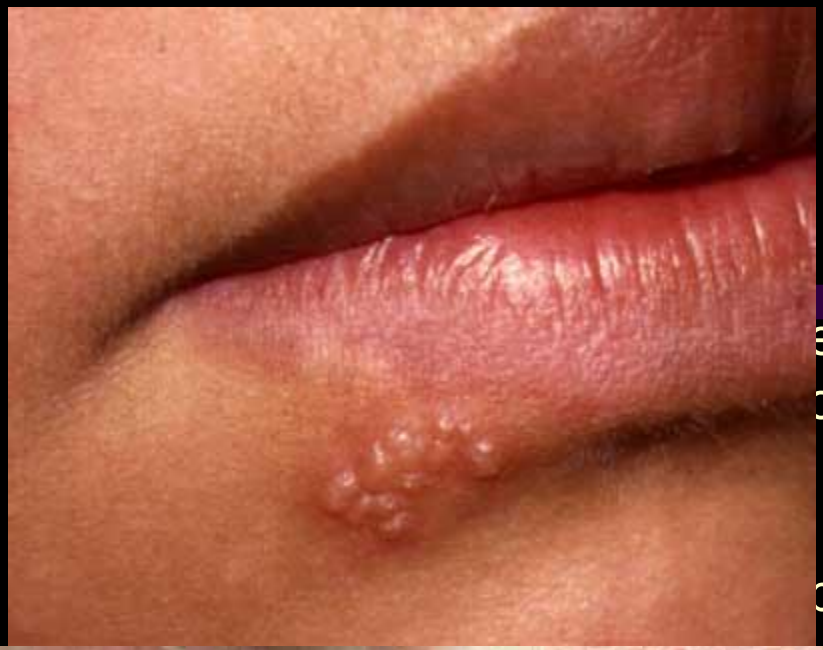
Precipitating factors

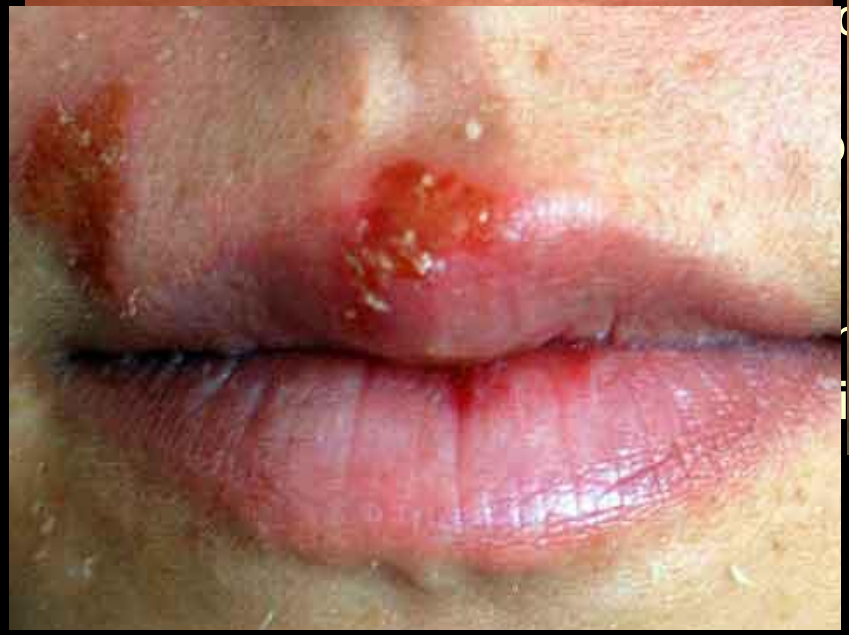
- Trauma, fever, emotional upset and upper respiratory tract infection.
- Sunburns or ultraviolet lamps, fatigue, menstruation and pregnancy.
-
- Allergy and dental extraction

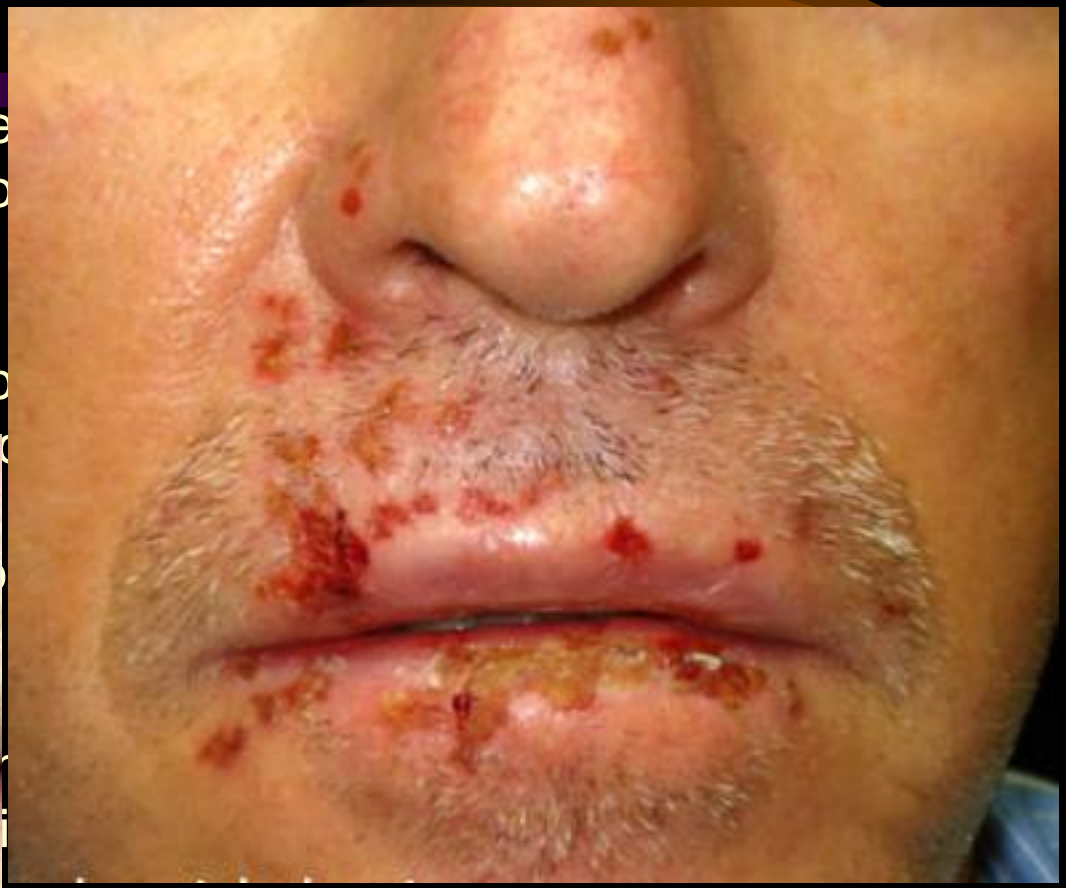
- Surgery involving trigeminal ganglion as it remains latent in trigeminal ganglion.

- The mechanism through which these various precipitating factors elicit an outbreak of lesions is unknown.

- The viruses, once they have been introduced into the body, appear to reside dormantly within regional ganglia, and when reactivation is triggered, spread along the nerves to sites on the oral mucosa and skin where they destroy the epithelial cells and induce the typical inflammatory response with the characteristic lesions of recurrent infection.







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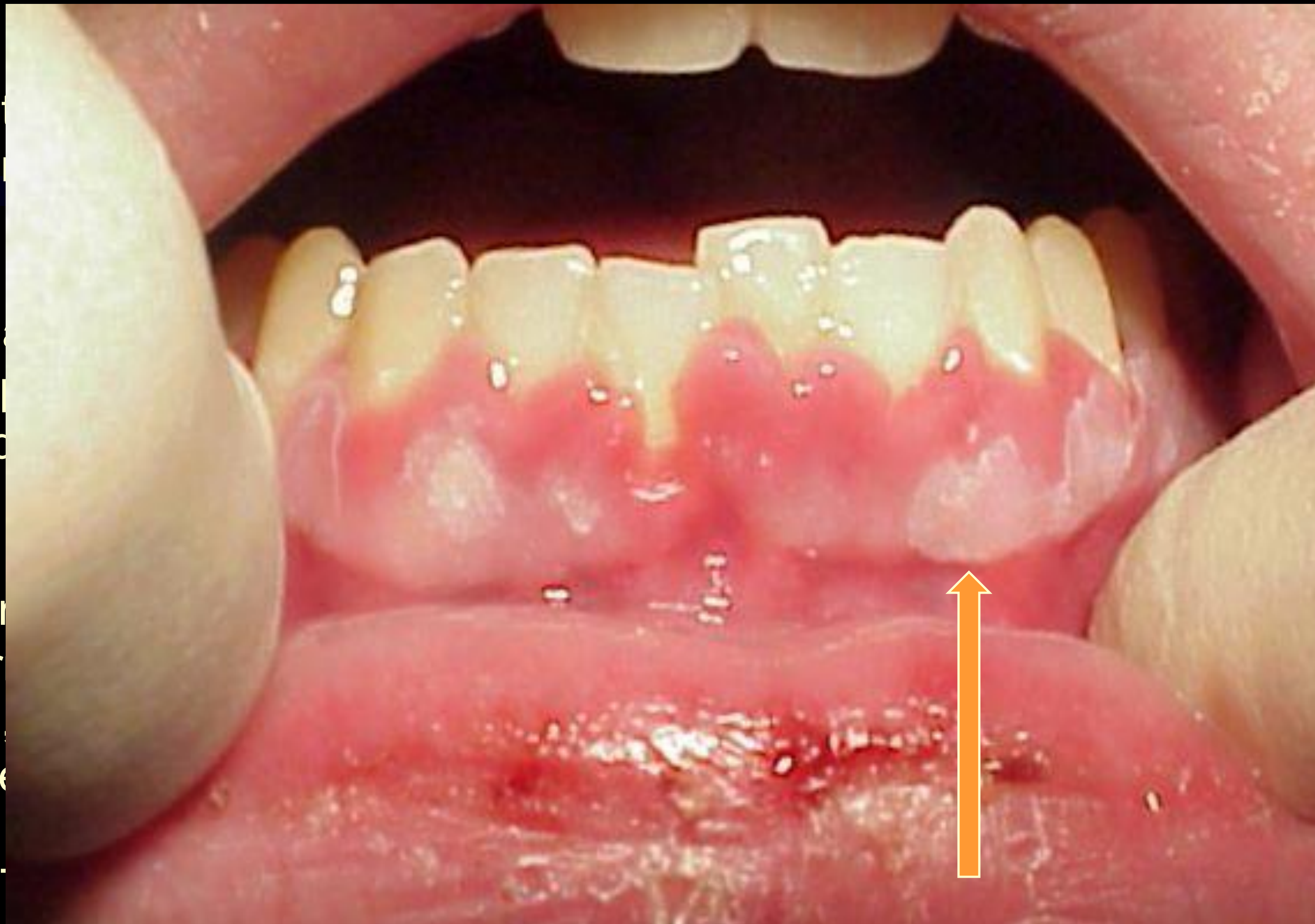

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Histologic features

- Paapanicolaou smear, using fresh scrapings from the base of a vesicle, is a reliable technique for the diagnosis of active herpes simplex infection if herpes zoster/varicella infection is ruled out, since no other conditions produce a similar cytopathic effect.

- Tzank cells, ballooning degeneration, chromatin margination and typical Lipschutz bodies as well as multinucleated giant cells are seen in smears.

Laboratory findings

- Isolation of the herpes simplex virus can be accomplished in the tissue culture, particularly in the early stages of the recurrent infection.

- Current diagnostic methods for herpes viral diagnosis,

a. Viral isolation and identification in various systems, including eggs, and mice, as well as cell culture technique.

b. Immunofluorescent staining of smears, impressions, or cryostat sections with fluorescent-labeled HSV protein or antibody protein.

c. Immunoperoxidase technique which is reportedly far more sensitive than the immunofluorescence technique, is similar in basic principle but does not require fluorescence microscopy.

d. Serologic assays such as the complement fixation assay, radioimmunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA).

Differential diagnosis

- Chronic recurrent aphthae-appear on non keratinized mucosa, usually large.
- Herpangina- generalized symptoms, posterior third of the oral cavity and pharynx are affected, predominately found in infants and young children.
- Herpes zoster- does not recur, has unilateral involvement, differentiation is possible by microbiology and serological testing.
- Chelitis granulomatous- edema appears suddenly without prodromal symptoms and recurrence is absent.
- Benign mucosal pemphigoid- no prodormal symptoms; with progression from erythema to swelling to bister to crusting.
- Allergic contact dermatitis- sudden appearance with allergen proof.

Treatment

Several specific antiviral chemotherapeutic agents are available for use under certain conditions and with certain forms of HSV infection.

1. Acyclovir (9-(2-hydroxyethodymethyl)guanine)
2. Vidarabine (adenine arabinoside)
3. Idoxuridine (5-iodo-2-deoxyuridine)

HERPES ZOSTER

- Herpes zoster is an acute infectious viral disease of an extremely painful and incapacitating nature which is characterized by inflammation of dorsal root ganglia, or extramedullary cranial nerve ganglia, associated with vesicular eruptions of the skin or mucous membranes in areas supplied by the affected sensory nerves.

- The virus causing this disease is the same as that of varicella, or chickenpox.

- It is believed that herpes zoster is caused by reactivation of the latent V-Z virus which had been acquired during a previous attack of chickenpox. In essence, a primary infection by the V-Z virus results clinically in chickenpox, while a recurrent infection results clinically in herpes zoster. The herpes zoster is sporadic in occurrence whereas varicella is seasonal.

Predisposing factors

- The triggering factors initiating the onset of an attack of herpes zoster are varied and may include,

1) Trauma
2) Development of malignancy or tumor involvement of dorsal root ganglia
3)Local X-ray radiation or immunosuppressive therapy.

Clinical features

- Sex -
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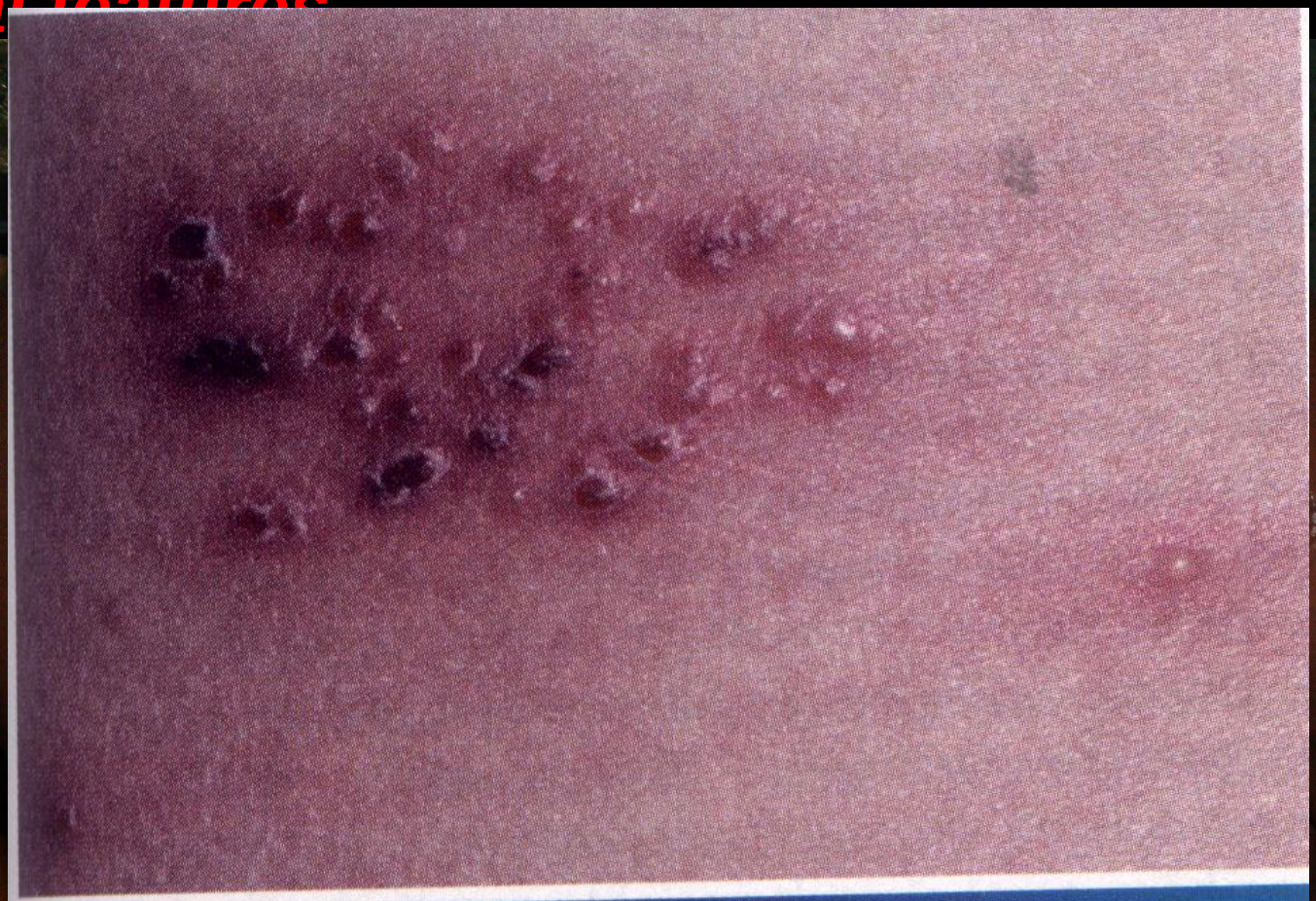
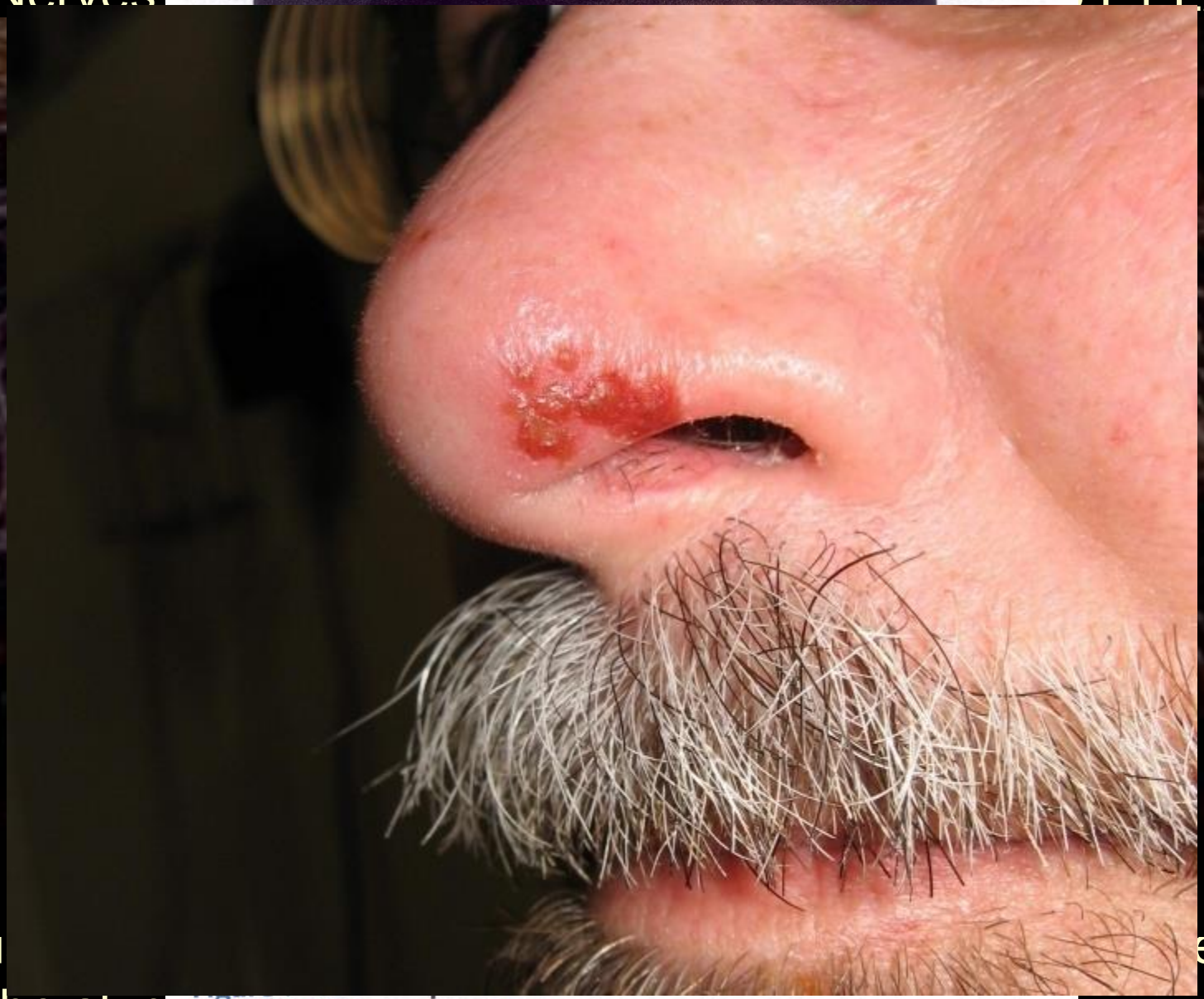
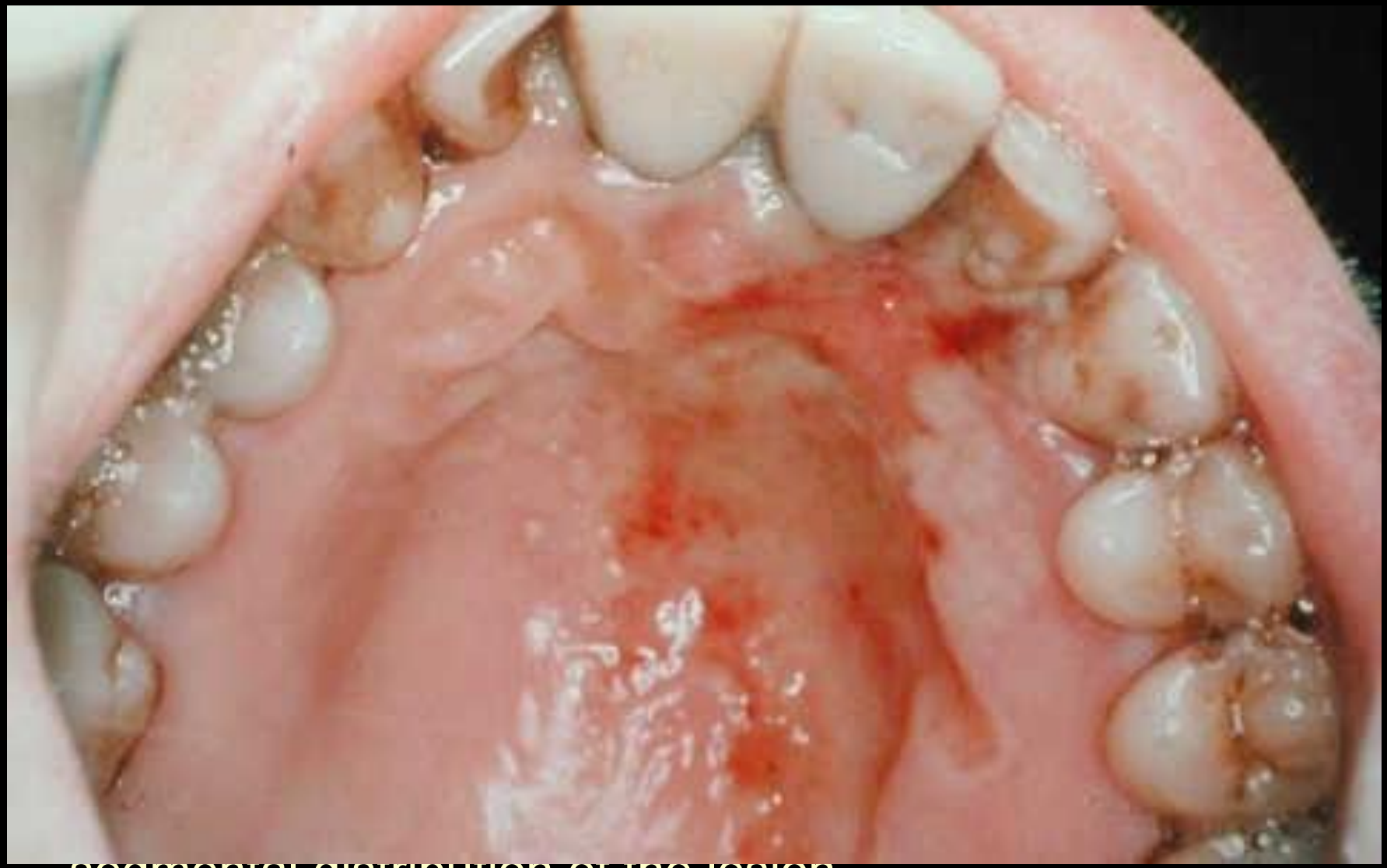


Figure 7-17 ◆ **Herpes zoster.** Cluster of vesicles with surrounding erythema of the skin.

- Nerves- L1 L2 and first
- In ment of fir arring and read, neur nse.
- tip of nose ent is more
- F ks to mon eutic neur ation, fibrosi e pain after the skin

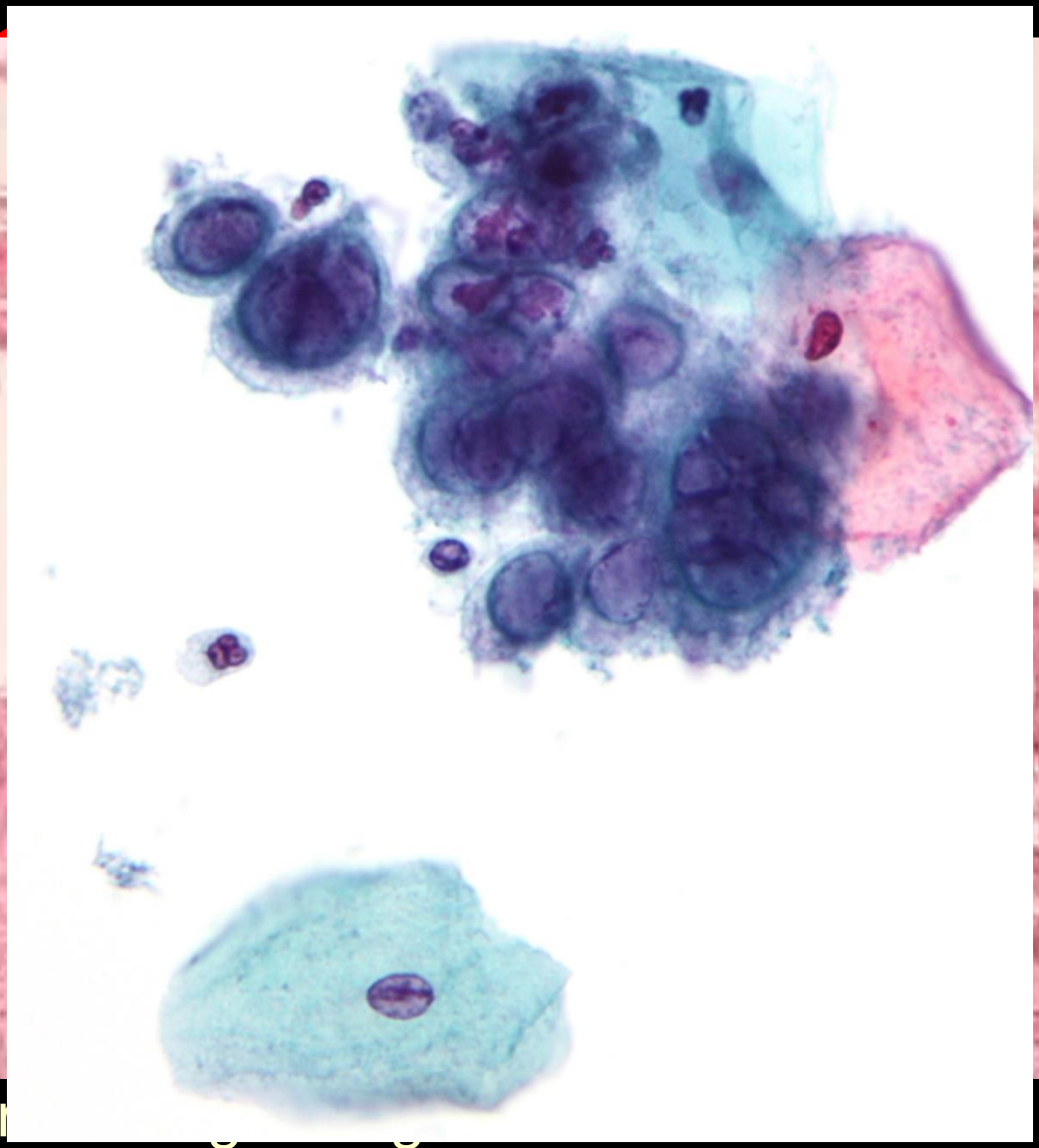


that extend to the midline.



segmental distribution of the lesion.

Diagn



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JAMES-RAMSAY HUNT SYNDROME

- It is zoster infection of geniculate ganglion with involvement of the external ear and oralmucosa.
- The clinical manifestation of it is facial paralysis as well as pain of the external auditory meatus and pinna of the ear.
- In addition, vesicular eruptions occur in the oral cavity and oropharynx with hoarseness, tinnitus, vertigo and occasional other disturbances.

Lab findings

- Cytology
- Viral isolation
- Antibody titre increased

Differential diagnosis

- Recurrent herpes simplex infection-
- Herpangina- acute infection

Management

- Acyclovir-800mg five times daily which is associated with significantly accelerated healing within 48 hrs of the onset of the rash.
- Intralesional steroids and local anesthetic can be used to decrease healing time and to prevent postherpetic neuralgia.
- Topical capsaicin 0.025 percent four times a day has been suggested for temporary relief of neuralgia following herpes zoster infection. Mechanism of action apparently involves the depletion of substance P in the peripheral sensory neurons causing the skin less sensitive.
- Mouth rinsing with tetracycline, three to five times daily, may reduce the pain.

Postherpetic neuralgia

- To control postherpetic neuralgia prednisone 40 to 60 mg daily for 1 to 2 weeks.
- Steroid injection can be given in a patient with age more than 60 years, for the treatment of postherpetic neuralgia.
- Anti depressants like amitriptyline and other tricyclic antidepressant have been used to minimize painful sequelae of this infection.
- Sympathetic nerve block and chemical and surgical neurolysis.

HERPANGINA

- Herpangina is the specific viral infection, caused by Coxsackie group A virus with type-1 through 6,8,10,16 and 22 as well as the other enteroviruses, being isolated at various times.

- Infection occurs through ingestion, direct contact, or through droplet spread. Multiple cases in a single household are common. It occurs in epidemic with highest frequency from June to October.

Clinical features

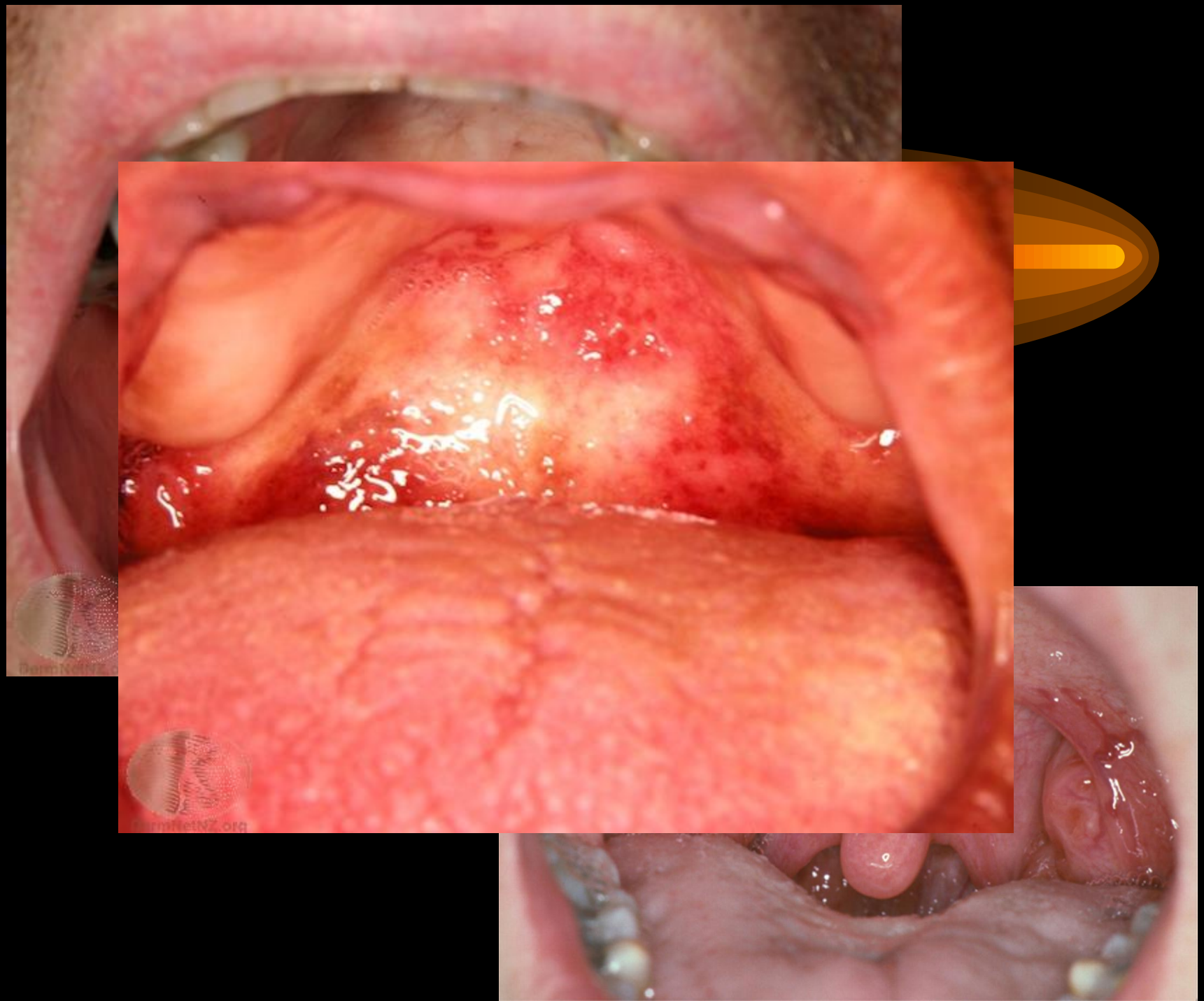
· Age- majority affected is young children aged 3to10 years although older children and adults are only occasionally affected.

· Herpangina is chiefly a summer disease, and many children may actually harbor the virus at this time without exhibiting clinical manifestation of the disease.

· Incubation period- incubation period is 2-10 days.

Generalized symptoms- The clinical manifestations of herpangina are comparatively mild and of short duration. It begins with sore throat, cough, rhinorrhea, low-grade fever, headache, sometimes vomiting, prostration, and abdominal pain.

- Appearance and site - The patients soon exhibit small vesicles with rupture to form crops of ulcers, each showing a gray base and an inflamed periphery on the anterior faucial pillars and sometimes on the hard and soft palates, posterior pharyngeal wall, buccal mucosa and tongue.
- Vesicles preceding the ulcers are small and of short duration. The ulcers do not tend to be extremely painful, although dysphagia may occur.
- Healing- the ulcers do not tend to be extremely painful although dysphagia may occur. The systemic symptoms resolve within few days. Ulcers generally heal within 7-10 days.
- Recurrence- children have been affected several times in one season by infection with different strains of Coxsackie virus. A permanent immunity to the infecting strain usually develops rapidly and most adults have neutralizing antibodies against numerous strains.



Laboratory findings

- The Coxsackie virus can be isolated in sucking mice or hamsters by inoculation of scrapings from the throat lesions or stool specimens of nearly all patients who manifest clinical signs and symptoms of the disease or who have had contact with infected patients.
- Although there are distinct immunologic differences between various strains of herpangina virus, animal inoculation of any type produces the same manifestations-destruction of skeletal muscles followed by death.

Differential between Herpangina and primary HSV

- Herpangina occur in epidemic, HSV does not.
- Clinical manifestation of herpangin is generally milder than HSV infection.
- Lesions of herpangina occur in pharynx and posterior portions of oral mucosa.
- Herpangina does not cause generalized acute marginal gingivitis.
- Lesions of herpangina are smaller than HSV.

Treatment

· No treatment is necessary, since the disease appears to be self limiting and presents few complications.

ACUTE LYMPHONODULAR PHARYNGITIS

- Acute lymphonodular pharyngitis is an acute febrile disease. It is cause by strain of Coxsackie virus 10.
- Delay in recognition of the disease as an entity may have occurred because of the marked resemblance between this and herpangina.

Clinical features

- Age- the disease predominantly affects children and young adults, although older adults are occasionally also involved.
- Site- the lesion appears on uvula, soft palate, anterior pillars and posterior oropharynx.
- Symptoms- the chief complain consists of sore throat, an elevation of temperature varying from 100 to 105 degree Celsius, mild headache and anorexia.
-

Incubation period- it has got 5 days incubation period and course may run for 4to14 days, with local oral lesions resolving within 6to10 days although a residual ring of fading erythema may sometimes be seen for several days. The estimated incubation period of disease is 2-10 days.

•Appearance-it consists of raised, discrete, whitish to yellowish to dark pink solid papules or nodules, surrounded by a narrow zone of erythema. The lesions are not vesicular and do not ulcerate

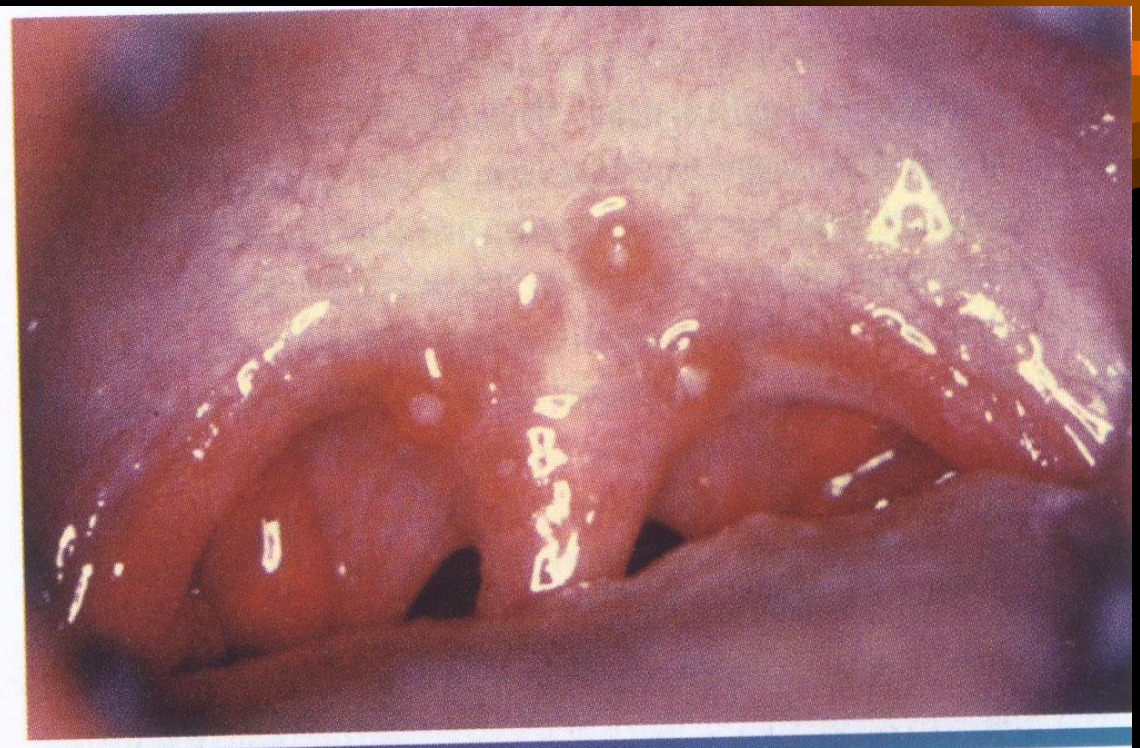
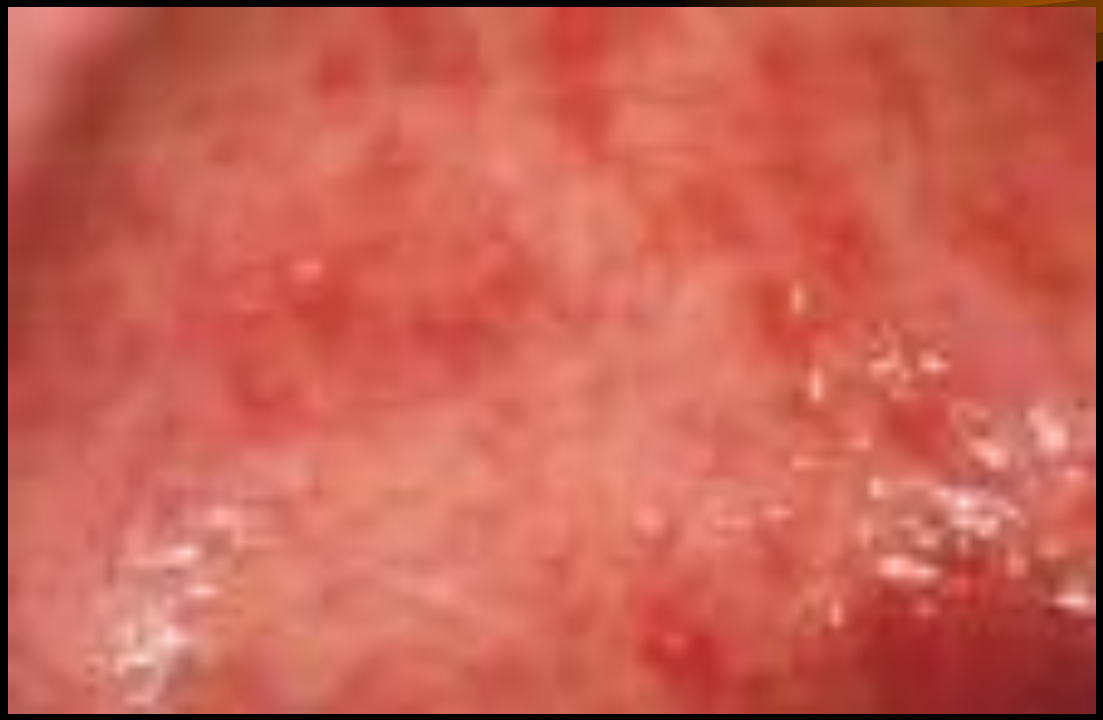


Figure 7-27 • Acute lymphonodular pharyngitis. Numerous dark pink and yellow lymphoid aggregates. (Courtesy of Dr. George Blozis.)



Laboratory findings

- Primary isolation of Coxsackie A10 virus can be established in sucking mice by inoculation of throat swab or fecal material.
- Serologic evidence of infection by this virus is also positive.

Histologic features

- The papules or nodules consist of hyperplastic lymphoid aggregates.
- In some cases the overlying epithelium has shown inclusion of bodies which in some instances were intranuclear but in others, cytoplasmic.

Treatment

No specific treatment is necessary inasmuch as the disease is self-limiting. It has been found that antibiotic therapy is of no benefit.

HAND, FOOT AND MOUTH DISEASE

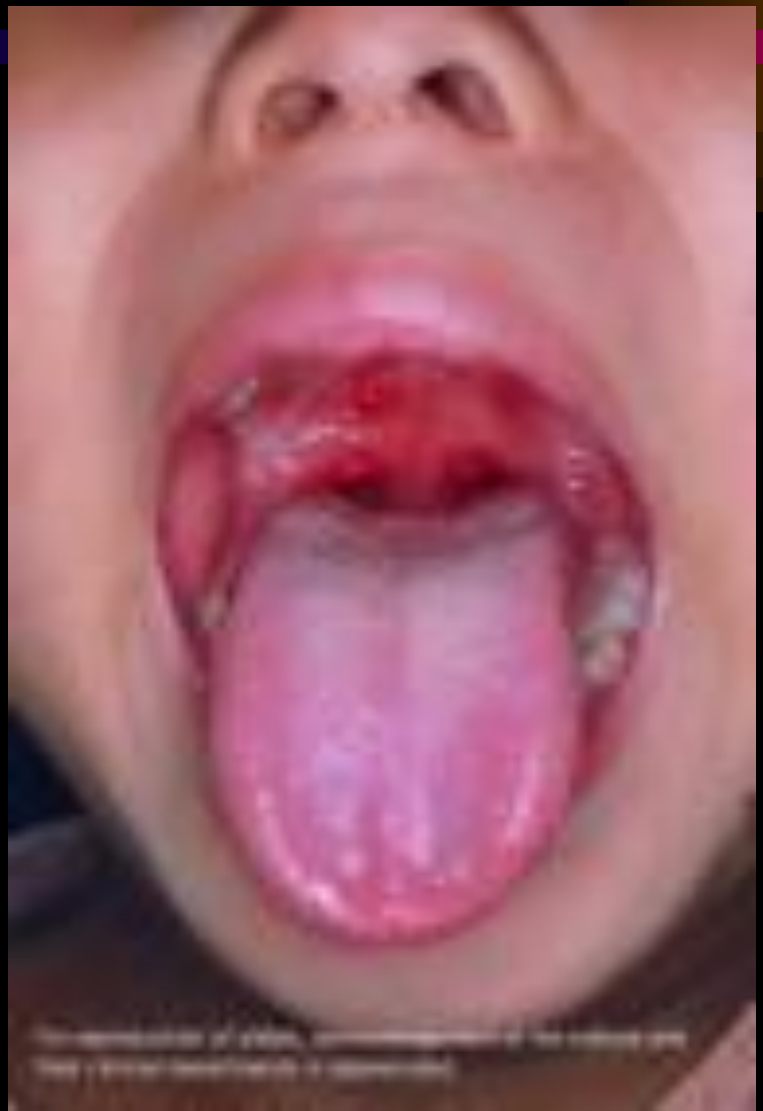
- Hand, foot and mouth disease is an epidemic infection, caused by the enterovirus Coxsackie A16 and has been reported to be cause less frequently by types A5 and A6, and occasionally even by B2, B6 or enterovirus 71.
- Despite the similarity in names, it bears no relationship to foot-and-mouth (Hoof-and-mouth) disease, another viral disease with an animal vector.

Clinical features

- Age- it primarily affects young children between age of 6months and 5years.
- Appearance- it is characterized by the appearance of maculopapular, exanthematous, and vesicular lesions of the skin, particularly involving the hands, feet, legs, arms, and occasionally the buttocks.
- There is anorexia, low-grade fever and sometimes lymphadenopathy, diarrhea and vomiting.

Oral manifestations

- Sites- the most common sites for oral lesions are hard palate, tongue and buccal mucosa.
- Much smaller percentage of patients showing involvement of the lips, gingival and pharynx, including the tonsils.
- Symptoms- a sore mouth with refusal to eat is one of the most common findings in this disease. This is due to small, multiple vesicular and ulcerative oral lesions that are more numerous than seen in herpangina.
- The tongue may also become red and edematous.



Laboratory findings

- Intracytoplasmic viral inclusions can sometimes be demonstrated in vesicular scrapings of the lesions.
- Viral isolates may usually be obtained from vesicular fluid itself.
- There is rise in acute or convalescent serum antibody titer to Coxasackie A16.

Differential diagnosis

- Herpetic gingivostomatitis- entire oral cavity is affected. No hand and feet involvement.
- Varicella zoster infection- segmental distribution along the anatomical location of nerve (unilateral lesions)
- Herpangina- affect children mostly in late summer and early monsoon and lesions are common on soft palate and facial area with fever and malaise.
- Allergic stomatitis- sudden appearance, no prodormal symptoms with itching and noticeable erythema.
- Chichenpox- in addition to intraoral changes, polymorphs exanthema on the entire body and severe lesions.

Management

No specific treatment is necessary since the disease is self limiting and generally regresses within one to two weeks

FOOT-AND-MOUTH DISEASE (APTHOUS FEVER, HOOF-AND-MOUTH DISEASE, EPIZOOTIC STOMATITIS)

It is a viral infection which rarely affects man, but does affect hogs, sheep as well as cattle. Transmission of this disease occurs through infected animals; in human beings, it is usually through milk from infected animals or through the handling of tissues from these animals

Clinical features

- Symptoms- it is manifested by fever, nausea, vomiting, malaise and appearance of ulcerative lesions of oral mucosa and pharynx.
- Sites- development of vesicle on skin also occurs in some cases, usually on the palms of hand s and soles of feet.

Clinical features

- Symptoms- it is manifested by fever, nausea, vomiting, malaise and appearance of ulcerative lesions of oral mucosa and pharynx.
- Sites- development of vesicle on skin also occurs in some cases, usually on the palms of hand s and soles of feet.

Oral manifestations

- Sites- it can occur at any site, but lips, tongue, palate and oropharynx appear to be affected.

Appearance- these lesions being as small vesicles which rapidly rupture, but heal within two weeks.

MEASLES (RUBEOLA, MORBILLI)

- It is an acute, contagious, dermatropic viral infection, primarily affecting children, and occurring man times in epidemic form.
- It is caused by paramyxovirus belongs to the family paramyxoviridae, which is a RNA virus.

Transmission

Spread of disease occurs by direct contact with a person or by droplet infection, the portal of entry being the respiratory tract.

Epidemiology

- Measles has a worldwide distribution but incidence is more in developing countries. The resurgence of measles may be due to failure to immunize infants and young children and failure of vaccination or waning immunity.
- The mortality rate is high among children and adults. It varies from 1-10 percent in developing countries.
- It is contagious from first or second day even before the onset of serious illness or appearance of rash.
- It is transmitted mainly through respiratory secretions and also through direct contact of droplets.
- The incubation period is generally from 8-12 days. It is mainly transmitted in large families, crowded homes and slums.
- It is a self-limiting disease in healthy immune competent children, but morbidity and mortality is high in malnourished and immunocompromised individuals.

Pathogenesis

- Upon invasion of respiratory epithelium it reaches reticuloendothelial system through blood stream and thereby infect skin, respiratory tract, and other organs.
- The invasion of T-lymphocytes and increased levels of suppressive cytokines leads to transient suppression of cellular immunity. Monocyte is mainly infected.
- Symptoms show mainly due to the infection of the entire respiratoryepithelia and the secondary infection with bacteria.
- Viremia develops, but specific antibodies are not developed before the onset of rash. Cellular immunity plays a major role in host defence against measles.

Clinical features

- Incubation period- it is 8 to 10 days.
- Symptoms- it is characterized by the onset of fever, malaise, cough, conjunctivitis, photophobia, lacrimation, and eruptive lesions of the skin and oral mucosa.
- Skin- skin eruptions usually begin on the face, in the hair line and behind the ears, and spread to the neck, chest, back and the extremities. These appear as tiny red macules or papules which enlarge and coalesce to form blotchy, discolored, irregular lesions which blanch upon pressure and gradually fade away in four to five days with a fine desquamation.

Oral manifestations

- Oral lesions are prodromal, frequently occurring two to three days before the cutaneous rash, and are pathognomonic of this disease.
- Site- the most common site is on buccal mucosa.
- Koplik's spot- intra oral lesions are called as Koplik's spots and occur in 97percent of cases. Immune reaction to the virus in the endothelial cells of dermal capillaries plays a role in the development of spots. The spots disappear after the onset of rash.
- Appearance- they are small, irregularly shaped flecks which appear as bluish white specks surrounded by bright red margins. These macular lesions increase in number rapidly and coalesce to form small patches. Palatal and pharyngeal petechiae as well as generalized inflammation, congestion, swelling and focal ulceration of the gingival, palate and throat may also occur.

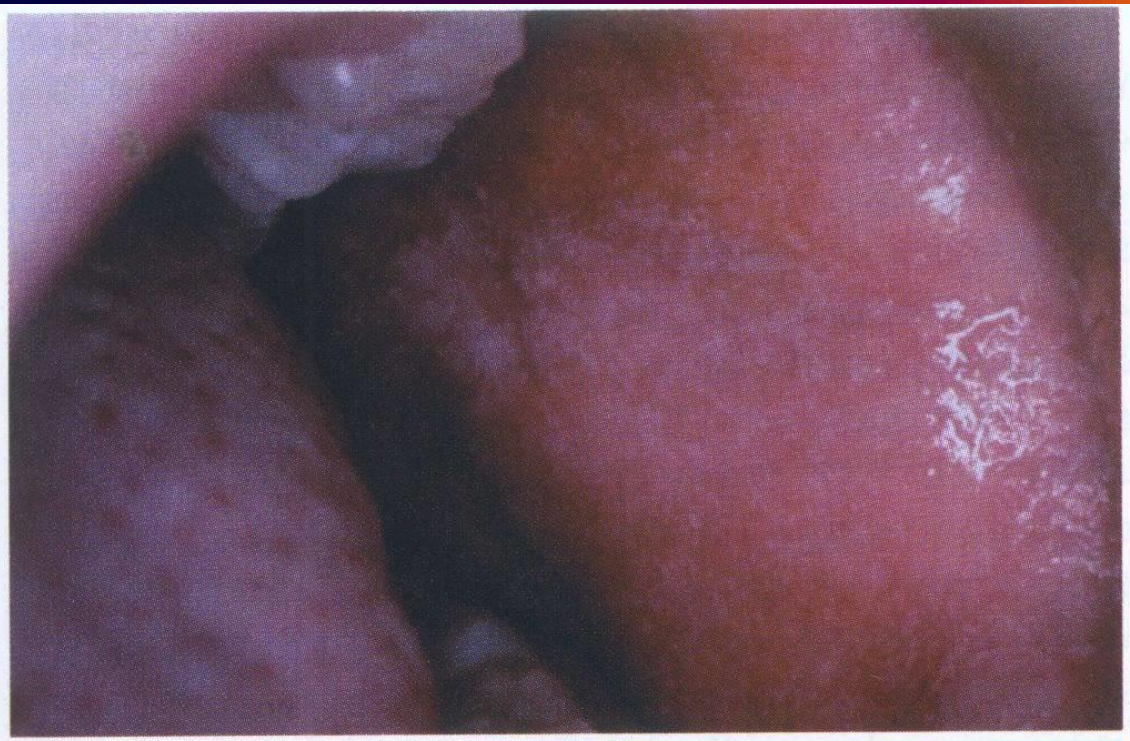


Figure 7-29 • Rubeola. Numerous bluish-white Koplik's spots of buccal mucosa. (Courtesy of Dr. Robert J. Achterberg.)

Complications

- Measles is a disease which lowers the general body resistance and for this reason often leads to complications.
- Bronchial pneumonis
- Encephalitis
- Otitis media
- Noma
- In addition, measles has an immunosuppressive effect through impairment of cell-mediated immunity, so delay in wound healing. It may also cause induction of remission of leukemia and hodgkin's disease. The disease rarely fatal except in the case of secondary complications.

Differential diagnosis

- Smallpox- high fever, monoform exanthema.
- Chickenpox- typical exanthema that follows the intraoral lesion. The diagnosis can be established microscopically (blister swab) and virologically.

Control measures

Measles vaccines are available as single or in combination (MMR).
In asian countries typical in india, the Edmonton Zagrd (EZ strain) 5ml of vaccine is given subcutaneously. Study have suggested that age for vaccination as nine months. A second dose should be given in the form of MMR at 15-18 months for adequate immunity.

Management

- The patient should be isolated, if possible.
- Antiviral drug
- Vitamin-A should be given.

RUBELLA (GERMAN MEASLES)

- Appearance- in, rubella, Koplik's spots do not occur, and the oral mucous membranes are not usually inflamed, although the tonsils may be somewhat swollen and congested and red macules may appear on the palate.
- Complications- complications following this disease are rare except when the disease occurs in women during the first trimester of pregnancy. In such cases, the offspring has a high incidence of congenital defects such as blindness, deafness, and cardiovascular abnormalities, if miscarriage does not occur.

MOLLUSCUM CONTAGIOSUM

· Molluscum contagiosum is a disease cause by a virus of the pox group.

• The lesions which only occur on the skin or mucosal surfaces are often considered tumorlike in nature because of the typical localized epithelial proliferation caused by the virus. The incidence of the condition is not reliably known.

Clinical features

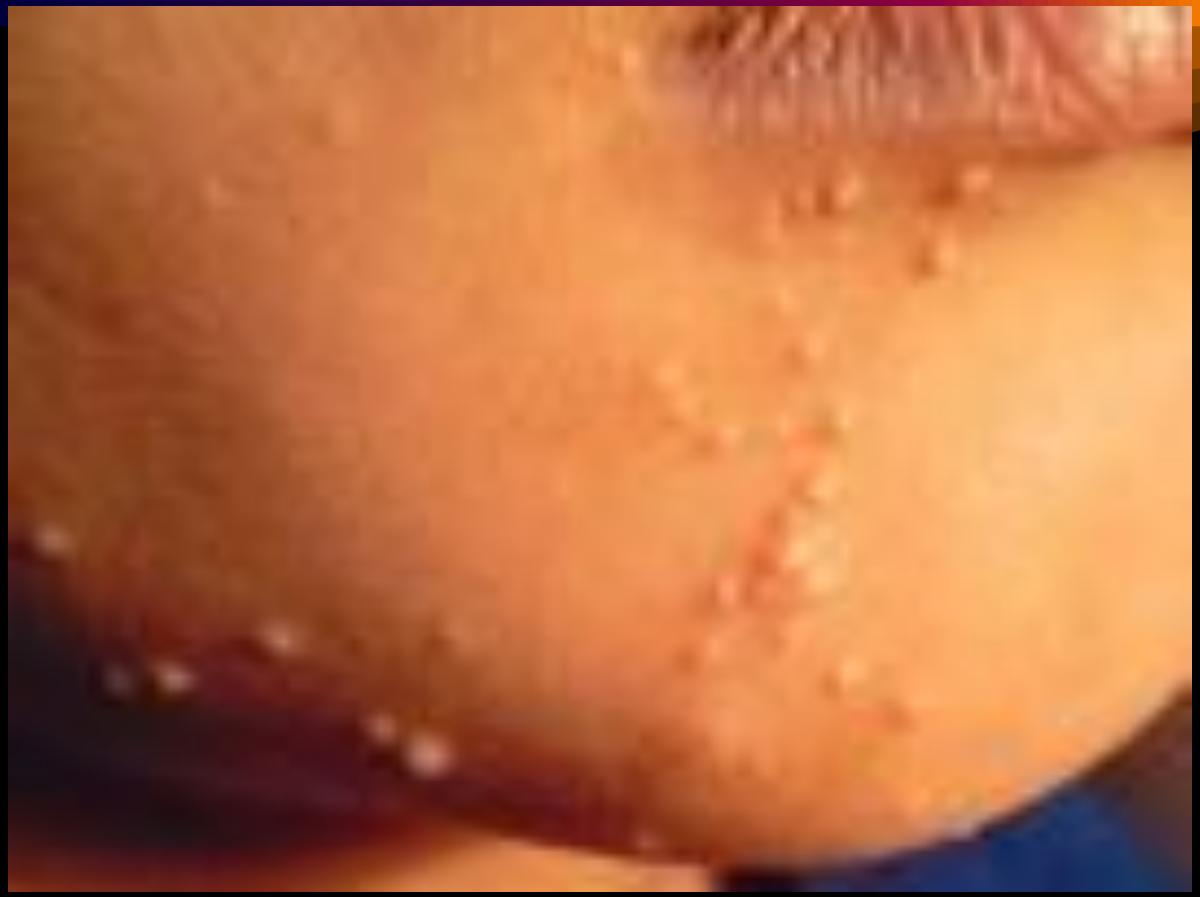
· Age- it more common in children and young adults.
· Transmission and Incubation period- the disease appears to be spread by autoinoculation, by direct contact with an infected individual or by fomites with an incubation period of 14to50 days. The disease can be sexually transmitted and lesions of genitalia and pubo-abdominal area also occur with some frequency
• Appearance- it manifests itself as single, or more frequently, multiple discrete elevated nodules, usually occurring on the arms and legs, trunk and face, particularly the eyelids.

•· Shape and size- these lesions are hemisphere in shape, usually about 5mm in diameter with central umblication which may be keratinized and are normal or slightly red in color.

· HIV-infected individuals are more prone to these lesions. Lineal distribution of these lesions suggests that autoinoculation of virus occurs due to scratching. Lesions in HIV-infected patients are atypical in manifestations. Lesions are multiple and grow to a larger size resembling carcinomas.

· The virus replicates in the stratum spinosum and forms inclusion bodies which are characteristic, and pathognomonic of poxvirus infection called cowdry type A inclusion bodies.

• Healing- most of these lesions heal spontaneously in about 30-60 days and the infection may rarely persist for more than two or three years.



Oral manifestations

- It usually occurs in children, on the face, due to shared sleeping accommodation.
- Mucous membrane involvement particularly oral cavity is not common.
- Most commonly involved sites are lips, tongue and buccal mucosa. Oral lesions are similar to skin lesions.

Histologic features

- The lesion is quite characteristic, showing thickening and down growth of the epithelium with the formation of large eosinohilic intracytoplasmic inclusion bodies known as Henderson-paterson inclusions or simply molluscum bodies, measuring app. 25microns in diameter.
- These bodies characteristically accumulate in the crater formed by the distinctive central umblication of the dome-shaped lesion.

Diagnosis

- Smears are prepared from lesions scrapings or its contents and stained with papstain, giemsastain or gramstain to demonstrate molluscum bodies.

Treatment

The lesions of molluscum contagiosum have been treated by surgical excision or by topical application of a wide variety of drugs such Podophyllin or Cantharidin.

CONDYLOMA ACUMINATUM (VERRUCA ACUMINATA, VENERAL WART)

- Condyloma acuminatum is an infectious disease caused by a virus which belongs to the same group of human papillomaviruses (HPV) as those associated with common and plantar warts, flat warts, cervical flat warts, pityriasis-like lesions in patients with epidermodysplasia verruciformis and juvenile laryngeal papillomals.

Etiology

- Human papilloma viruses are DNA virus belongs to the family papovaviridae.
- More than 50 serotypes of HPV are recognized and they are species specific and have not been propagated in tissue culture or in experimental animals.
- Condyloma acuminatum is caused by HPV type 1, a11, a30, b42, 43, 45, 46b, 51, b54, 55 and 70.
- The virus of anal, genital and presumably oral condyloma acuminatum is HPV-6.

Epidemiology

- It is one of the most common sexually transmitted diseases in the world. Incidence among children and adults is high, but low in early childhood. It reaches its peak between 12-16 years of age then declines sharply to the age of 20 or more.
- Transmission is mainly by close contact with infected persons, autoinoculation, and orogenital sexual practice.

Pathogenesis

- Once inoculated in the epithelium, the virus replicates and is transcribed in the basal cells. Virions are assembled in the reduced and released along with the desquamated cells. This process is associated with the proliferation of all layers except basal cells and produces acanthosis, hyperperakeratosis and hyperorthokeratosis.
- Koilocytes are large vacuolization of cells in and below the granular layer with basophilic inclusion bodies composed of viral particles and eosinophilic inclusions.

Clinical features

- Appearance- This transmissible and autoinoculable viral disease presents as soft pink nodules which proliferate and coalesce rapidly to form diffuse papillomatous clusters of varying size.
- Site- they occur most commonly on the anogenital skin or other warm, moist intertriginous areas.

Oral manifestations

- Appearance and site- Lesions have appeared as small, multiple, white or pink nodules which enlarge, proliferate and coalesce, or as papilomatous, bulbous masses scattered over or diffusely involving the tongue, especially the dorsum, buccal mucosa, palate, gingival or alveolar ridge.

Histologic features

- The papillomatous projections making up the verrucoid lesion generally show a parakeratotic surface with marked underlying acanthosis. Vacuolated cells in the spinous layer are common, as are numerous mitotic figures.
- The epithelial changes are sufficiently disturbing to be mistaken for carcinoma. The supporting connective tissue is usually edematous, with dilated capillaries and a chronic inflammatory cell infiltrate. Intra nuclear viral inclusions in the lesional epithelial cells are also found.

Laboratory investigation

- Virus isolation can be done by staining of viral antigen DNA by hybridization restriction, endo-nuclease analysis and polymerase chain reaction.

Differential diagnosis

- Focal epithelial hyperplasia- in it fine granular surface texture and plaque like shape of enlargement while in case of condyloma there is cauliflower appearance.

Treatment

- Surgical excision is usually used to eradicate the lesions, although topical podophylin has also been used.

CHICKEN POX (VARICELLA)

- It is an acute, ubiquitous, extremely contagious disease usually occurring in children, and is characterized by an exanthematous vesicular rash. It is most common in winter and spring months

Etiology

- Varicella zoster virus is a DNA virus, which causes two distinct lesions known as chickenpox a primary lesion and a reactivated lesion known as herpes zoster.
- Incubation period- it is about two weeks and mode of transmission by airborne droplets or direct contact with infected lesions, with the probable portal of entry being the respiratory tract.

Clinical features

· Prodormal symptoms- it is characterized by headache, nasopharyngitis and anorexia, followed by maculopapular or vesicular eruptions of the skin and low-grade fever.

· Location- these eruptions usually begin on trunk and spread to involve the face and extremities.

· Appearance- they occur in successive crops so that many vesicles in different stage of formation or resorption may be found.

· Healing- the skin eventually ruptures, forming a superficial crust and heals by desquamation.

· Course- the disease runs its clinical course in a week to ten days, seldom leaving any alter effects.

• Secondary infection- occasionally, secondary infection of vesicle results in the formation of pustules which may leave small pitting scar upon healing.

Oral manifestation

- Site- small blister like lesions occasionally involve the oral mucosa chiefly buccal mucosa, tongue, gingival, palate as well as the mucosa of pharynx.
- Appearance- the mucosal lesion, initially a slightly raised vesicles with a surrounding erythema, ruptures soon after formation and forms a small eroded ulcers with red margins, closely resembling aphthous lesion.

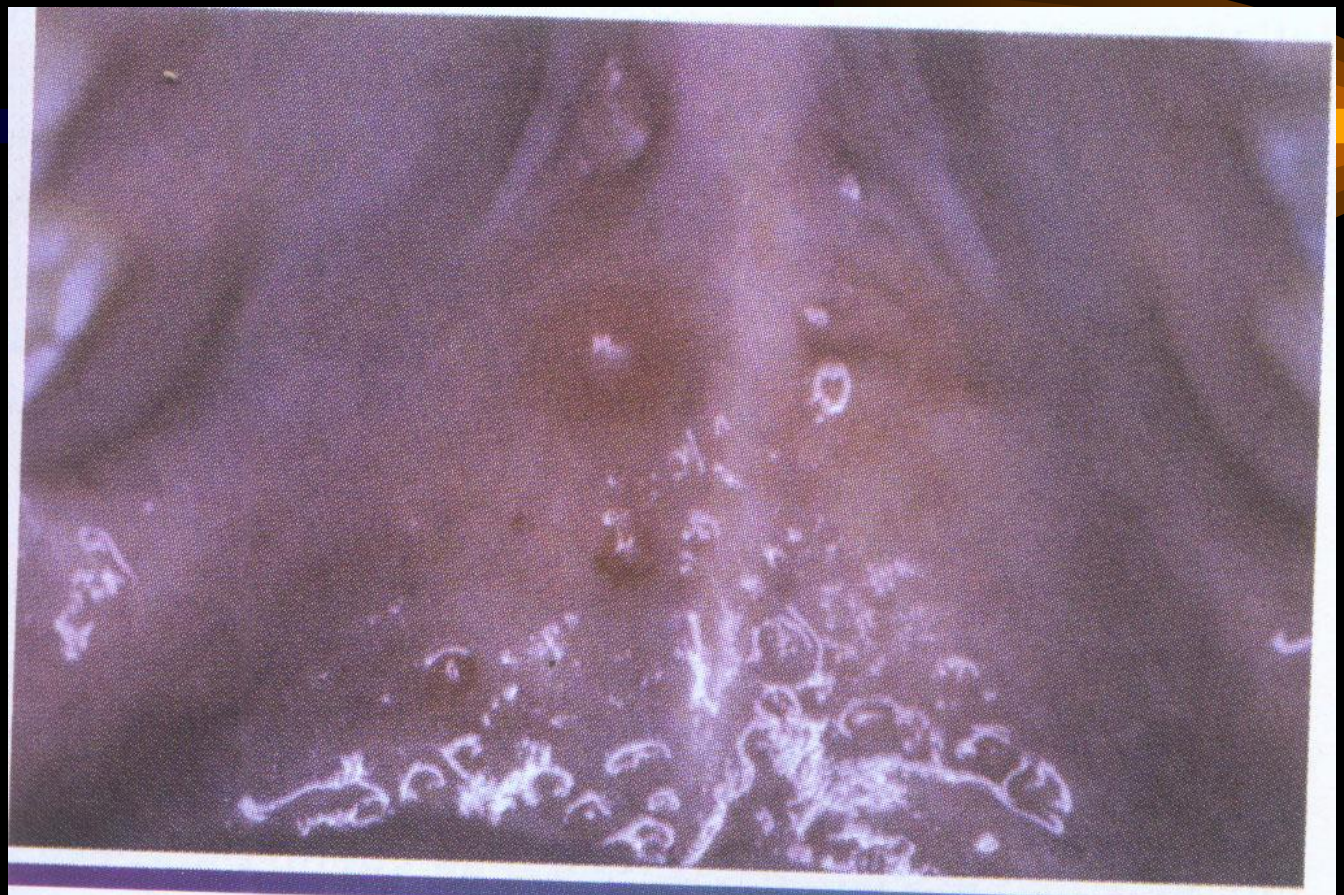


Figure 7-16 ◆ **Varicella.** White opaque vesicles on the hard palate.

Complications

- Secondary infection is common and caused by streptococcus or staphylococcus.
- CNS involvement leads to encephalitis, transverse myelitis, Guillain-Barre syndrome, and Reye's syndrome.
- Other complications include pneumonia, myocarditis, nephritis, arthritis, and bleeding diatheses.
- Renal and hepatic involvement can also occur. Perinatal infections are fatal.

Management

- No treatment is required in majority of the cases.
- As the first sign of secondary infection, a local antiseptic should be applied to the skin.
- If the bacterial infection progresses, appropriate antibiotics should be prescribed

MUMPS (EPIDEMIC PAROTITIS)

- Mumps is an acute contagious viral infection characterized chiefly by unilateral or bilateral swelling of the salivary glands, usually the parotid.
- The submaxillary and sublingual glands are occasionally involved.
- Other than salivary glands it may also involve nerves meninges, pancreas and gonads.
- Although it is disease of childhood, mumps may also affect adults, and in such cases there is a greater tendency

Epidemiology

- Incubation period- 14-18 days with the extreme of one to four weeks. Mumps is transmitted through the respiratory route.
- It can be isolated from the saliva of the infected patients either seven days before the onset of parotitis or nine days after its onset.
- Most cases were unrecognized because of the absence of the parotid swelling.
- As the disease is contagious before the onset of parotitis, isolation of patient is not possible to prevent the infection. Once infected, patients develop a life-long immunity against the disease but recurrence is also reported.

Pathogenesis

- Once transmitted through droplet nuclei or saliva or fomites, it starts replicating in the respiratory epithelium. It spreads to local lymphnodes and subsequently develops viremia. The affected area shows perivascular and interstitial mononuclear cell infiltrates with edema.
- Necrosis of acinar and epithelial ducts cells is seen in salivary glands and in the germinal epithelium of seminiferous tubules.

Clinical features

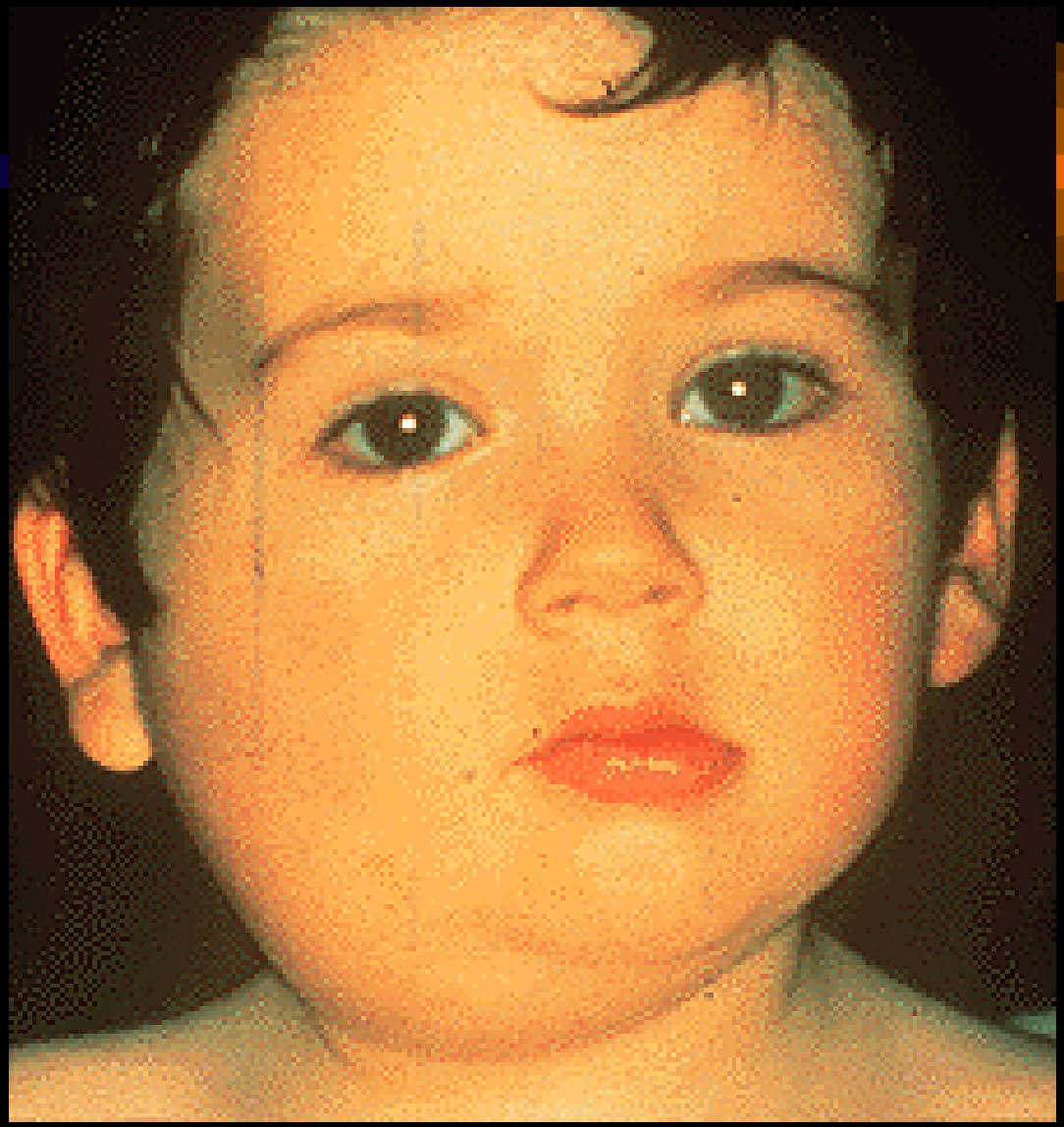
· The disease is usually preceded by the onset of headache, chills, moderate fever, vomiting and pain below the ear. These symptoms are followed by a firm, rubbery or elastic swelling of the salivary glands, frequently elevating the ear, which usually lasts about one week. This salivary gland involvement produces pain upon mastication.

· Bilateral parotid involvement occurs in about 70 percent of the cases. Pain and tenderness may be severe during the rapid phase of parotid enlargement and swelling reaches its maximum in about three days; it remains at its peak for two to three days and then gradually subsides.

· The submandibular gland may also involve separately or in conjunction with the parotid gland.

· The involvement of sublingual gland is rare.

• Presternal edema may be present in a few cases due to pressure on the lymphatics in the neck. Papilla of the opening of the parotid duct on the buccal mucosa is often puffy and reddened.



Diagnosis

- Virus can be isolated from saliva and throat swabs two days before or seven days after the onset of parotitis.
- Diagnosis can be made by demonstration of antibodies to mumps S&V antigens and to the hemagglutination antigen.
- It can also be confirmed by the complement fixation test, hemagglutination inhibition or ELISA, serum amylase is elevated in both parotitis and pancreatitis.

Complications

- Other organs of the body may be affected as a complication of the disease.
- These include the testes, ovaries, pancreas, mammary glands, and occasionally the prostate, epididymis and heart.
- When mumps involve the adult male, orchitis is a great danger. This orchitis is usually unilateral, but occasionally complete sterility results. The involvement of pancreas producing an acute pancreatitis often causes an elevation in serum lipase. Serum amylase is also elevated but this is regardless of pancreatic involvement.
- Meningoencephalitis, deafness and mastitis are also occasional complications.
- The disease though discomforting and often producing an acutly distressing condition, is seldom fatal.

Prognosis

- Overall prognoses is good in uncomplicated cases. Death occurs due to CNS or cardiac involvement.

Treatment

- Treatment is conservative; maintaining hydration and alimentation. Prevention is by means of vaccination.

NON SPECIFIC MUMPS

- There are several nonspecific conditions characterized by enlargement of on eor more of the major salivary glands that are not related etiologically to epidemic parotitis, or true mumps, but yet may produce considerable difficulty in diagnosis and differential separation from true mumps of viral origin.

Classification of parotid swelling

I Neoplastic

II Inflammatory

A. Acute specific virus infections
   1. Mumps
   2. Coxsackie A
   3. ECHO
   4. Lymphocytic choriomeningitis

B. Chronic Specific
   1. Tuberculosis
   2. Actinomycosis
   3. Sarcoidosis

C. Acute suppurative parotitis \

D. ‘Recurrent subacute parotitis and associated pathology

III Hypersensensitivity and drug reactions

IV Metabolic

A. Malnutrition, particularly protein deficiency

B. Associated with alcoholic cirrhosis

C. Diabetes mellitus and disturbed glucose tolerance

V. Miscellaneous

A. Obstruction of duct

1. Direct

a. Papillary trauma

b. Other traumatic stricture

c. Impaction of foreign body (e.g. food particle)

d. Congenital atresia

2. Indirect

B. Pneumopatoritis

C. Functional hypersecretion

- Although not all of these are of specific microbial origin, some of the more common conditions which have clinical and occasional microscopic resemblance to epidemic parotitis, or mumps.

These include,

- chronic nonspecific sialadenitis
- acute postoperative parotitis (surgical mumps, retrograde sialadenitis)
- nutritional mumps
- chemical mumps
- miscellaneous

1. *Chronic nonspecific sialadenitis*

- Nonspecific chronic sialadenitis is an insidious inflammatory disease of major salivary glands characterized by intermittent swelling of the glands which may lead to the development of clinically obvious fibrous masses.
- Most common in adults particularly males.
- Cause- the most frequent cause of chronic sialadenitis is the occurrence of salivary duct calculi (q.v.) with subsequent pyogenic bacterial infection. Any condition which may result in salivary duct occlusion, may result in this form of the disease.
- If the etiologic factor is removed there is generally subsidence of the clinical manifestations of the disease.
- If untreated, the salivary gland may be replace by fibrous tissue, which may be tumor-like in its extent.

s

2. Acute postoperative parotitis

- It is generally believe to be the result of a retrograde infection (one reaching the parotid gland by microorganisms ascending the parotid duct) in debilitated patients suffering from dehydration, suppression of salivary secretion, vomiting and/or mouth-breathing, after a surgical exposure.
- Thus it is feel that xerostomia, or dry mouth is one of the most important factors, since stagnation of salivary flow would allow the ascension of microorganisms through the duct in the gland.
- The microorganisms involved are usually Staphylococcus aureus, Staphylococcus pyogenes, Streptococcus viridans and pneumococci.
- The majority of patients involved are adults of middle age older.

- Bilateral parotid gland involvement is common and the clinical signs and symptoms generally occur between the second and 20th postoperative days. Any type of surgical procedure may be followed by the appearance of this condition.
- The onset of disease is rapid and is frequently accompanied by severe pain and rapid swelling of the parotid gland. The overlying skin may be reddened, and the associated edema may involve the cheek, periorbital area, and the neck.
- Trismus is present, as is a low-grade fever with headache, malaise, and leukocytosis.
- A purulent discharge may be expressed from the parotid duct by digital pressure along the duct toward its orifice.
- Treatment of this condition is generally the administration of antibiotics.

3. Nutritional mumps

- Chronic asymptomatic, bilateral enlargement of the parotid and or submaxillary glands occurring endemically in populations suffering from malnutrition.
- The dietary factors specifically involved have not been identified, but the lesions occur most frequently in patients with multiple signs of nutritional deficiency such as hypoproteinemia, anemia, and angular cheilosis, pellagroid pigmentation of the hands and face, and general underweight.
- A relation to either vitamin A or C deficiency has not been demonstrated.

- The condition is a progressive one, but relatively slow to develop. It appears to be somewhat more common in young and middle-aged adults.
- Histologic studies indicate that salivary gland involvement is essentially non-inflammatory. The enlargement of the salivary glands in the acute phase of the condition is due to hypertrophy of the individual acinar cells, but in chronic phase, to a replacement of normal gland parenchyma with fat. There is apparently little interference with normal salivary gland function.

4. Chemical ‘mumps’

- Bilateral swelling of the salivary glands occasionally accompanies the administration of either inorganic or organic iodine, and this has frequently been referred to as ‘iodine mumps’, this probably represents as iodine idiosyncrasy reaction.
- A similar form of salivary gland swelling has been reported with administration of Triiodothyronine in the treatment of myxedema.

5. Miscellaneous factors

- Salivary gland swelling is common in Sjogren's syndrome, Mikulicz's disease or benign lymphoepithelial lesion, salivary duct calculus, and allergic phenomenon.
- Fibrocystic disease (mucoviscidosis) of the pancreas is a hereditary defect of the secretory mechanism of most of the exocrine glands in the body including the salivary glands.

CYTOMEGALIC INCLUSION DISEASE
(Salivary gland virus disease)

· Salivary gland inclusion disease is a viral infection of interest since routine postmortem examinations have revealed that a considerable proportion of infants who die exhibit this disease, regardless of the case of their death.

· There are no particular signs or symptoms of this disease, although some infants have been reported to have manifested hepatosplenomegaly, hemolytic anaemia, and hemorrhagic tendency.

• It may be an incidental autopsy finding in patients who have died of blood dyscrasias, liver damage, pertussis, purpura, and other diseases.

- Transseptal infection may occur even without visible infection in the mother. In fact, approximately 50 percent of women in the childbearing group are seropositive for complement fixing antibodies to this virus, while approximately 4 percent of pregnant women excrete the virus in the urine.
- There may be some retardatin of mental and motor development.
- Intranuclear and cytoplasmic inclusions in the cells of salivary glands are a constant feature, while similar inclusions frequently occur in the kidneys, liver, pancreas, lungs, adrenals intestine, brain and occasionally other organs.
- The diagnosis is frequently established in living infants by examination of urinary sediment and the demonstration of the inclusion bodies here. These inclusions have a distinctive morphologic appearance and are pathognomonic of the disease.

- According to Cangir and Sullivan, that dissemination of the latent disease may occur in leukemia patients receiving antimetabolite therapy and in organ-transplantation patients or others receiving immunosuppressant drugs and subject to opportunistic infection.
- Other important manifestations of this virus include:
  - Cytomegalovirus mononucleosis, which may be very difficult to distinguish from infectious mononucleosis, since the clinical characteristics of the two may be nearly identical.
  - Its association with Kaposi's sarcoma in the acquired cellular immunodeficiency syndrome (q.v.).

POLIOMYELITIS
(Infantile paralysis)

- Poliomyelitis, at one time, was a very serious viral disease which has been almost totally eliminated particularly the paralyzing form, as a result of the widespread use of the Salk and Sabin vaccines.
- Prior to this, poliomyelitis was of some significance in dentistry because of scattered reports which suggested that the exposed dental pulp might act as a portal of entry into the body for the virus. This no longer appears to be of any significance.

ORAL MANIFESTATIONS OF HIV INFECTIONS

- Acquired immunodeficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV) and is characteriszed by immunosuppression, which leads to a spectrum of clinical manifestations that include opportunistic infections, secondary neoplasms and neurologic manifestations.

Human immunodeficiency virus

- HIV belongs to the retrovirus family, a family of RNA viruses distinguished by possession of a viral reverse transcriptase that transcribes viral RNA into provirus DNA that is integrated into the host-cell genome.
- HIV is subdivided into two distantly related types, HIV-1 and HIV-2. HIV-1 is the predominant worldwide isolate from individuals with AIDS or at high risks for the development of AIDS. HIV-2 is endemic among people in West Africa.

Structure of HIV:

HIV virion:

- The mature HIV virion is a roughly spherical (actually icosahedral) particle with a diameter of 110 nanometers.
- The outer envelope is acquired during virion budding and is studded with 72 spikes formed by the two major viral-envelope glycoproteins (gp120 and gp41).
- The central core contains
  - Four viral proteins (p24 - the major capsid protein, p17- a matrix protein, p9, and p7),
  - Two copies of the HIV RNA genome (to which p7 and p9 are bound), and
  - Three viral enzymes (reverse transcriptase, integrase, and protease) essential for viral replication.

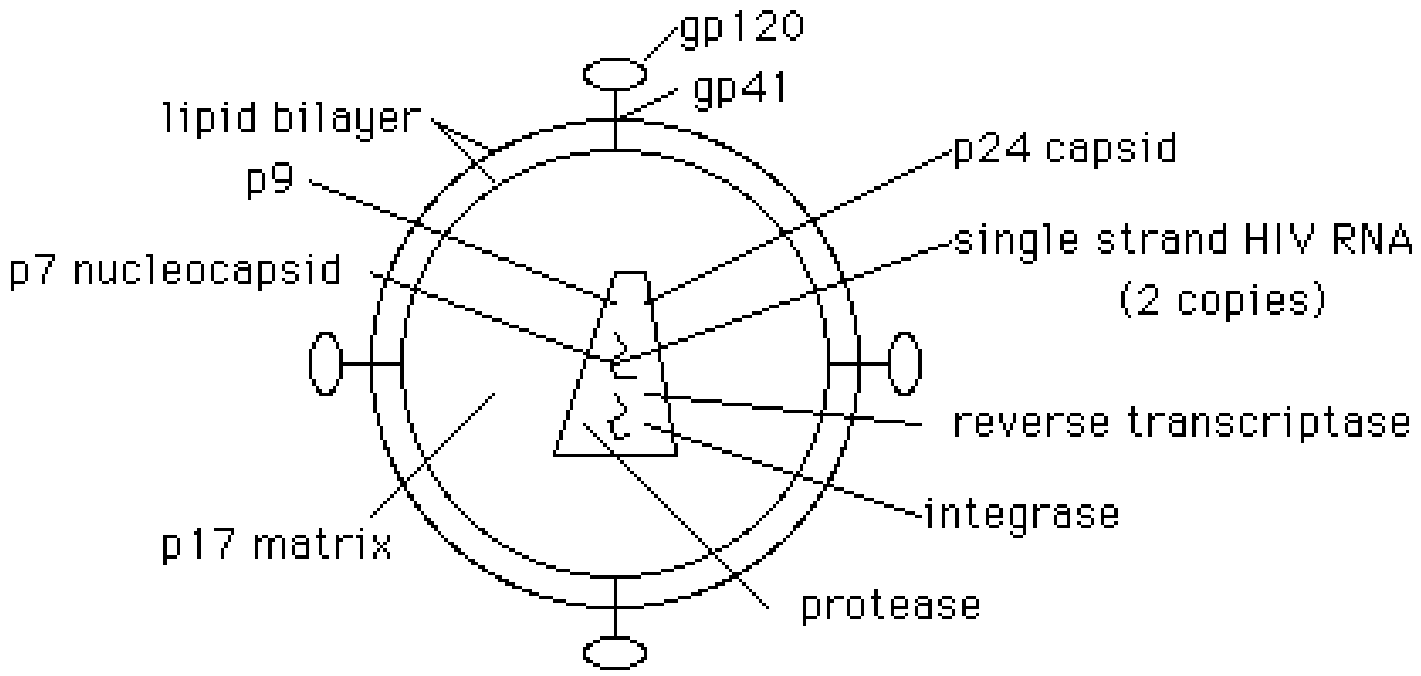


Figure 1. Diagram of mature HIV virion showing envelope proteins (gp120, gp41) in lipid biolayer, core proteins (p24, p17, p9, p7), diploid single-stranded HIV RNA, and viral enzymes (reverse transcriptase integrase, protease) required for replication.

Life cycle of HIV:

- The chief target cells for HIV infection in vitro and in vivo are human CD4 T-lymphocytes and macrophages.
- The CD4 glycoprotein on the surface of these cells serves as a high affinity receptor for HIV.
- An infection is initiated by binding of the virion envelope gp120 to the CD4 receptor on the host cell.
- Recently discovered **coreceptors** (either CCR5 or CXCR4) for HIV-1 must also be present on target cells to facilitate HIV entry. CCR5, a chemotactic cytokine (beta-chemokine) receptor, is a coreceptor for macrophage (M)-tropic strains of HIV; and CXCR4, also a chemokine receptor, is a coreceptor for T-lymphocyte (T)-tropic strains of HIV.

HIV infection is initiated by sequential binding of the viral envelope glycoprotein gp120 to the CD4 receptor and one or the other co receptor and by gp41-mediated fusion of the viral envelope with the cell membrane.

- After uncoating, the viral core and its components - viral RNA, gag gene proteins, and pol gene enzymes - are released into the cytoplasm.
- The viral reverse transcriptase converts the single-strand viral RNA into a first strand DNA copy and, through complex steps, into a viral DNA duplex of two strands. The viral DNA duplex is transported to the cell nucleus where it is inserted (integrated) by the HIV integrase into the host cell genome as covalently linked HIV provirus DNA.
- Once integrated into the host cell genome as provirus DNA, HIV can establish a virus-producing infection or a latent infection depending upon critical host factors, particularly whether the infected cell is in an activated or resting state.

- In a **permissive cellular environment**, the provirus DNA is copied by the host cell RNA polymerase II into viral RNA transcripts that become spliced into messener RNAs for translation into HIV regulatory proteins (Tat, Rev, others) or precursor proteins encoded by the gag, pol, and env genes. The core protein precursor is specifically cleaved by the HIV protease. Once assembled, the HIV core containing HIV RNA (2 copies), core proteins (p24, p17, p9, p7), and pol enzymes (reverse transcriptase, integrase, protease) moves to the cell surface, and acquiring HIV envelope proteins (gp120, gp41) buds through the plasma membrane and is released as infectious virus.
- By contrast, **with a latently infected cell**, the HIV provirus DNA is not expressed as viral RNA, viral proteins, or virions but is replicated as DNA by the host cell DNA polymerase, as are other cellular genes, and is transmitted to progeny cells by cell division.

- As will be noted later, many, perhaps most, of the HIV-infected cells in patients during the asymptomatic period of HIV-infection are latently infected. Without expression or surface adherence of HIV proteins, such latently infected cells are not affected by anti-HIV immune mechanisms.
- Further, a latently infected cell, such as a CD4 T-cell, can be activated by antigens, mitogens, certain cytokines, and other viral gene products to initiate transcription and translation of the HIV provirus DNA and the production and spread of infectious virus.

Natural history of HIV infection:

Primary HIV infection

↓

3-6 weeks

↓

acute HIV syndrome
(Mononucleosis like)
(Plasma viremia)

↓

1-3 months

↓

HIV specific immune response
(Serum antibody detectable)

↓

1-2 weeks

↓

Clinical latency
(Curtailment of viremia)
(Decline of CD4 T-cell count)

↓

10 years, median

Clinically apparent disease or AIDS-defining illness(Deterioration of immune system)(Increase in plasma viremia)

↓

2 years, average

↓

Death from AIDS

Acute retroviral syndrome:

- This mononucleosis-like syndrome develops in **40-70% of patients at 3-6 weeks** after primary HIV infection.
- The presenting symptoms may include fever, headache, sore throat, erythematous rash, diarrhea, and generalized lymphadenopathy.
- Laboratory tests may show
  - Leukopenia,
  - Anemia,
  - Thrombocytopenia,
  - Atypical lymphocytosis,
  - Elevated liver enzymes, and
  - Hypergammaglobulinemia.

- The peripheral blood CD4+ T-lymphocyte count (reference normal adult count is usually at least 800/cumm) and the CD4/CD8 ratio (reference normal ratio is about 2) both decline.
- The acute illness usually resolves spontaneously within 2-3 weeks.
- HIV viremia, p24 antigenemia, and viral dissemination to, and replication in, the regional and other lymph nodes occur during this early stage of HIV infection.
- An HIV-specific antibody and cellular immune response follows the primary infection. Serum testing for HIV antibody, by a screening test such as ELISA (enzyme-linked immunosorbent assay) and confirmatory Western blot (showing 2 or more bands of reactivity with Gag, Env, or Pol proteins), is positive in most individuals within 1 to 3 months after primary infection and in 95% within 6 months . (Potentially confounding, the serum of an uninfected (or infected) infant born to a seropositive mother may be expected to contain passively acquired maternal antibody).

The HIV-specific immune response is associated with a marked decline in plasma viremia, but HIV replication continues in lymph nodes or other tissue compartments or organs, such as genital tract or brain.

Clinical latency:

- This is an asymptomatic period of HIV infection and usually has duration of several years (median duration of 10 years). The peripheral blood CD4 T-cell count may return to normal, or stabilize at a somewhat lower level, or decline slowly over time.
- The plasma level of HIV viremia tends to reach a steady state (termed '**viral set point**') at the end of the acute phase following primary infection.
- The steady-state level of viremia (plasma viral load), as measured by assays for the number of copies of HIV-1 RNA per ml of plasma, is a **prognostic indicator** for the rate of HIV disease progression, high viral loads correlating with faster, low with slower, rates of disease progression to AIDS and death.
- Latent, as well as productive, cellular infection by HIV is active in the lymphoid (cervical and axillary lymph nodes, tonsils, adenoids, etc.) and other tissue compartments during this variably prolonged period before the person becomes clinically ill.

Clinically apparent disease:

This clinically apparent, symptomatic stage is a consequence (secondary manifestation) of the progressive and profound deterioration of the immune system that occurs over time in most patients with HIV infection. The **CD4 T-cell count continues downward to the range of 200-400/ cubic mm**. Plasma viremia and p24 antigenemia approach high levels such as seen in the primary infection. Some of the constitutional symptoms, opportunistic infections, and other manifestations of advanced symptomatic HIV disease are as follows:

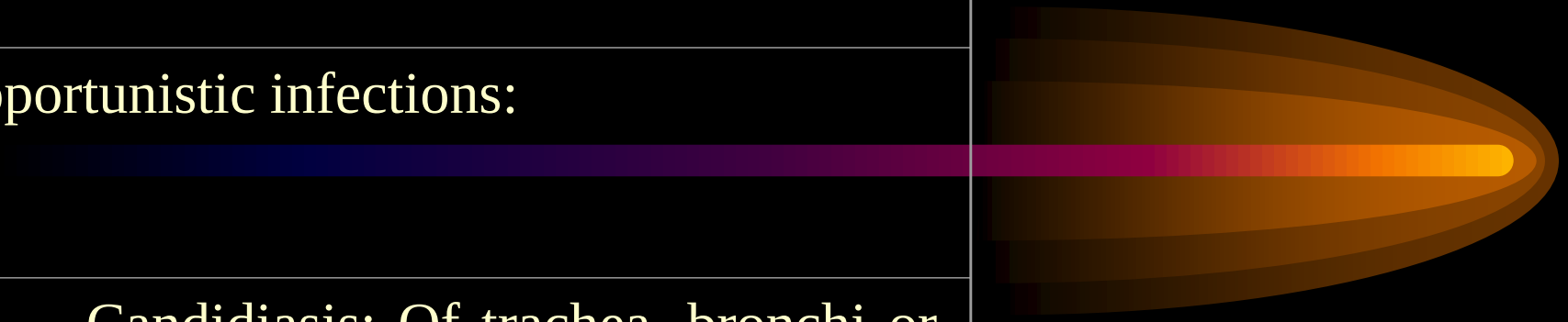
Menifestation of advanced symptomatic diseases (CD4 T cell count 200-400/cu mm)
Constitutional symptoms:
Fever
Weight loss
Fatigue
Nigh sweats
Diarrhea
Persistent generalized lymphadenopathy

Infections:
Oral or vaginal candidiasis
Oral hairy leukoplakia
Herpes simplex
Herpes zoster
Listeriosis
Other:
Idiopathic thrombocytopenic purpura
Neuropathy

- The CD4 T-cell count continues to fall, sometimes precipitously, and reaches levels that define AIDS (**CD4 T-cell count less than 200/cubic mm**) and predispose to AIDS-defining conditions, such as opportunistic infections caused by viruses, bacteria, fungi and protozoa, neoplastic disease, HIV encephalopathy, wasting syndrome, and progressive multifocal leukoencephalopathy that complicate the clinical course and are often the cause of death.

Manifestations when CD4 T-cell count < 200/cu mm

Opportunistic infections:



- Candidiasis: Of trachea, bronchi or lungs or esophagus.
- Coccidiodomycosis,
- Cryptococcosis, extrapulmonary
- Cytomegalovirus diseases along with CMV retinitis(with loss of vision)
- Histoplasmosis,
-

Mycobacterium infection
Pneumonia
Salmonella septicemia
Toxoplasmosis of brain

Neoplastic diseases:

- Cervical carcinoma, invasive
- Kaposi's sarcoma
- Lymphoma (Burkitt's, immunoblastic, or primary in brain)

Hiv encephalopathy(AIDS dementia complex)

Wasting syndrome due to HIV

Progressive multifocal leukoencephalopathy(PML)

1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS among Adolescents and Adults

CD4+ T-Lymphocyte Categories

The lowest accurate CD4+ T-lymphocyte count should be used for classification purposes, even though more recent and possibly different counts may be available.

Clinical Categories

Clinical category A

Conditions:

- Asymptomatic human immunodeficiency virus (HIV) infection
- Persistent generalized lymphadenopathy (PGL)
- Acute HIV infection with accompanying illness or history of acute HIV infection

Conditions listed in category B and category C must not have occurred.

Clinical category B

Symptomatic conditions in HIV-infected adolescents or adults that are not included in clinical category C and meet at least one of the following criteria:

(a) The conditions are attributed to HIV infection or are indicative of a defect in cell-mediated immunity;

(b) The conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection.

Examples of, but not limited to, the following conditions:

- Bacillary angiomatosis
- Candidiasis, oropharyngeal (thrush)
- Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Constitutional symptoms, such as fever (38.5°C) or diarrhea lasting > 1 mo
- Herpes zoster (shingles) involving at least two distinct episodes or more than one dermatome
- Idiopathic thrombocytopenia purpura
- Listeriosis
- Oral hairy leukoplakia
- Pelvic inflammatory disease, particular if complicated by tubo-ovarian abscess
- Peripheral neuropathy

CClinical category C Conditions:

- Candidiasis of bronchi, trachea, or lung
- Candidiasis, esophageal
- Cervical cancer, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (> 1 mo duration)
- *Cytomegalovirus* disease (other than liver, spleen, or nodes)
- *Cytomegalovirus* retinitis (with loss of vision)
- Encephalopathy, HIV related
- Herpes simplex: chronic ulcer(s) (> 1 mo duration); or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary

Isosporiasis, chronic intestinal (> 1 mo duration)

- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- *Mycobacterium avium-intracellulare* complex or *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis,* any site (pulmonary or extrapulmonary)
- *Mycobacterium,* other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis carinii* pneumonia
- Pneumonia, recurrent
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis
- Wasting syndrome due to HIV infection 7

CD4+ T Cells/mm3 or CD4+ Percentage	A: Asymptomatic Acute HIV or PGL	Clinical Categories B:Symptomatic, no A or C Conditions	C:AIDS-Indicator Conditions
≥500 or ≥ 29%	A1	B1	C1*
200–499 or 14–28%	A2	B2	C2
< 200 or < 14%	A3	B3	C3

REVISIED CLASSIFICATION 1993

Group 1: Lesions strongly associated with HIV infection

- Candidiasis
  - Erythematou
  - Pseudomembranous
- Hairy Leukoplakia
- Kaposi's sarcoma
- Non-Hodgkin's lymphoma
- Periodontal disease
  - Lineal gingival erythema
  - Necrotizing ulcerative gingivitis
  - Necrotizing ulcerative periodontitis

Group 2: Lesions less commonly associated with HIV infection

- Bacterial infections
  - Mycobacterium avium-intercellulare
  - Mycobacterium tuberculosis
- Melanotic hyperpigmentation
- Necrotizing ulcerative stomatitis

Group 3: Lesions seen in HIV infectin

- Bacterial infections
  - Actinomyces israelli
  - Escherichia coli
  - Klebsiella pneumoniae
  - Cat-scratch disease

GROUP 3 CONTINUED

Drug reactions (ulcerative, erythema multiforme, Lichenoid reaction, toxic epidermolysis)

Epithelioid (bacillary) angiomatosis

Fungal infections other than candidiasis

- Cryptococcus neoformans
- Geotrictum candidum
- Histoplasma capsulatum
- Miscoraceae (zygomycosis)
- Aspergillus flavus

Neurologic disturbances

- Facial palsy
- Trigeminal neuralgia

Recurrent apthous stomatitis (RAS)

- Viral infections
- CMV
- Molluscum contagiosum

COMMON ORAL AND MAXILLOFACIAL MANIFESTATIONS OF HIV INFECTION:

CANDIDIASIS:

- A number of factors predispose patients to develop candidiasis: infancy, old age, antibiotic therapy, steroid and other immunosuppressive drugs, xerostomia, anemia, endocrine disorders, and primary and acquired immunodeficiency.
- Candidiasis is a common finding in people with HIV infection. Reports describe oral candidiasis during the acute stage of HIV infection, but it occurs most commonly with falling CD4+ T-cell count in middle and late stages of HIV disease. Several reports indicate that most persons with HIV infection carry a single strain of Candida during clinically apparent candidiasis and when candidiasis is quiescent.

Clinical Features:

- The clinical appearances of oral candidiasis vary.
- The most common presentations include pseudomembranous and erythematous candidiasis, which are equally predictive of the development of AIDS, and angular cheilitis. [Dodd CL et al (1991).]
- These lesions may be associated with a variety of symptoms, including a burning mouth, problems eating spicy food, and changes in taste All three of these common forms may appear in one individual.

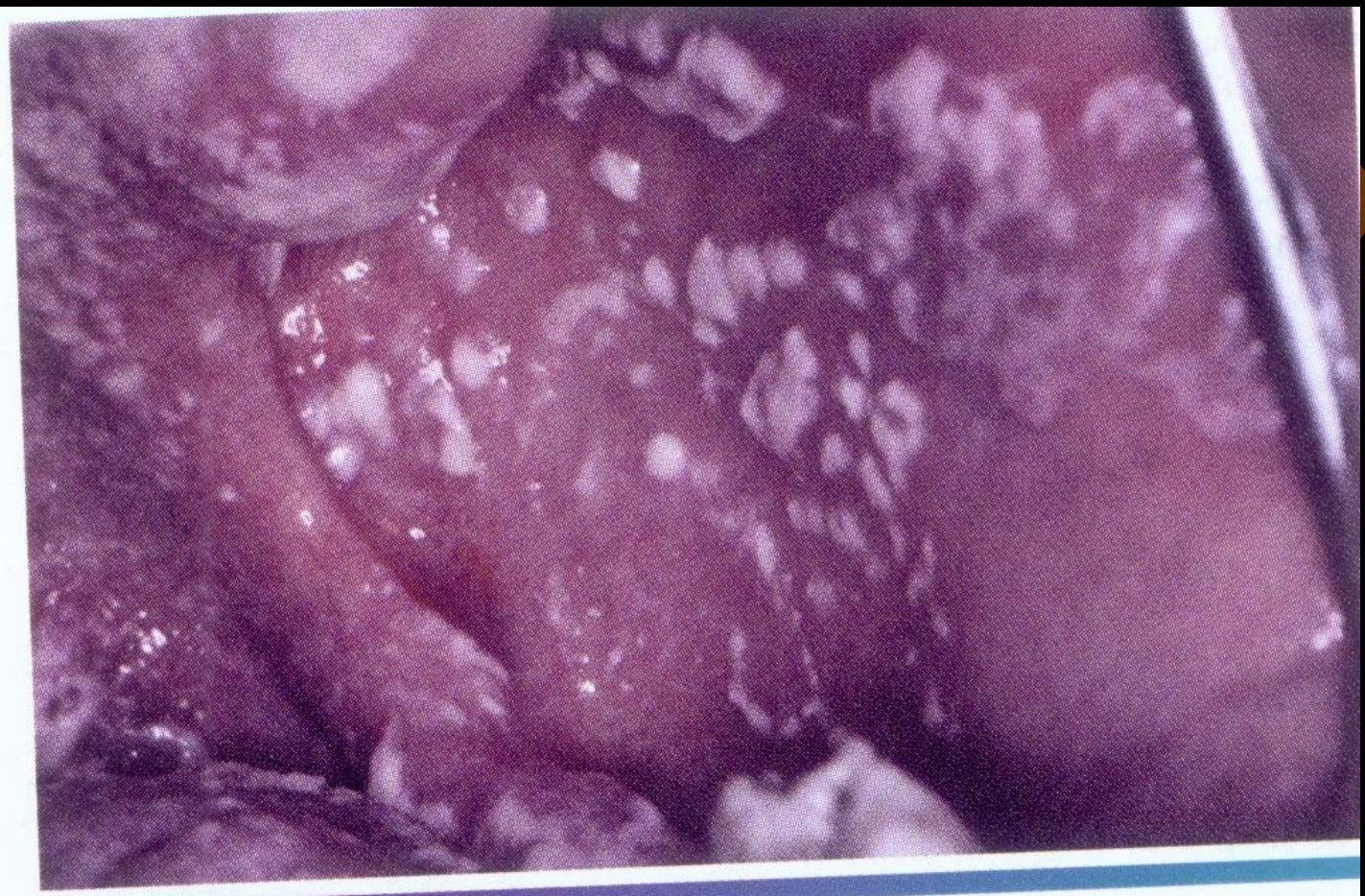


Figure 7-36 • HIV-associated candidiasis. Extensive removable white plaques of the left buccal mucosa.

Pseudomembranous Candidiasis (Thrush):

- Characteristic creamy white, removable plaques on the oral mucosa are caused by overgrowth of fungal hyphae mixed with desquamated epithelium and inflammatory cells. The mucosa may appear red when the plaque is removed. This type of candidiasis may involve any part of the mouth or pharynx.

Erythematous Candidiasis:

- Erythematous candidiasis appears as flat, red patches of varying size. It commonly occurs on the palate and the dorsal surface of the tongue.
- Angular Cheilitis
- Angular cheilitis appears clinically as redness, ulceration, and fissuring, either unilaterally or bilaterally at the corners of the mouth. It can appear alone or in conjunction with another form of candidiasis.

Hyperplastic Candidiasis:

- This type of candidiasis is unusual in persons with HIV infection.
- The lesions appear white and hyperplastic. The white areas are due to hyperkeratosis and, unlike the plaques of pseudomembranous candidiasis, cannot be removed by scraping. These lesions may be confused with hairy leukoplakia.
- Diagnosis of hyperplastic candidiasis is made from the histologic appearance of hyperkeratosis and the presence of hyphae.
- Periodic acid-Schiff (PAS) stain is often used to demonstrate hyphae.

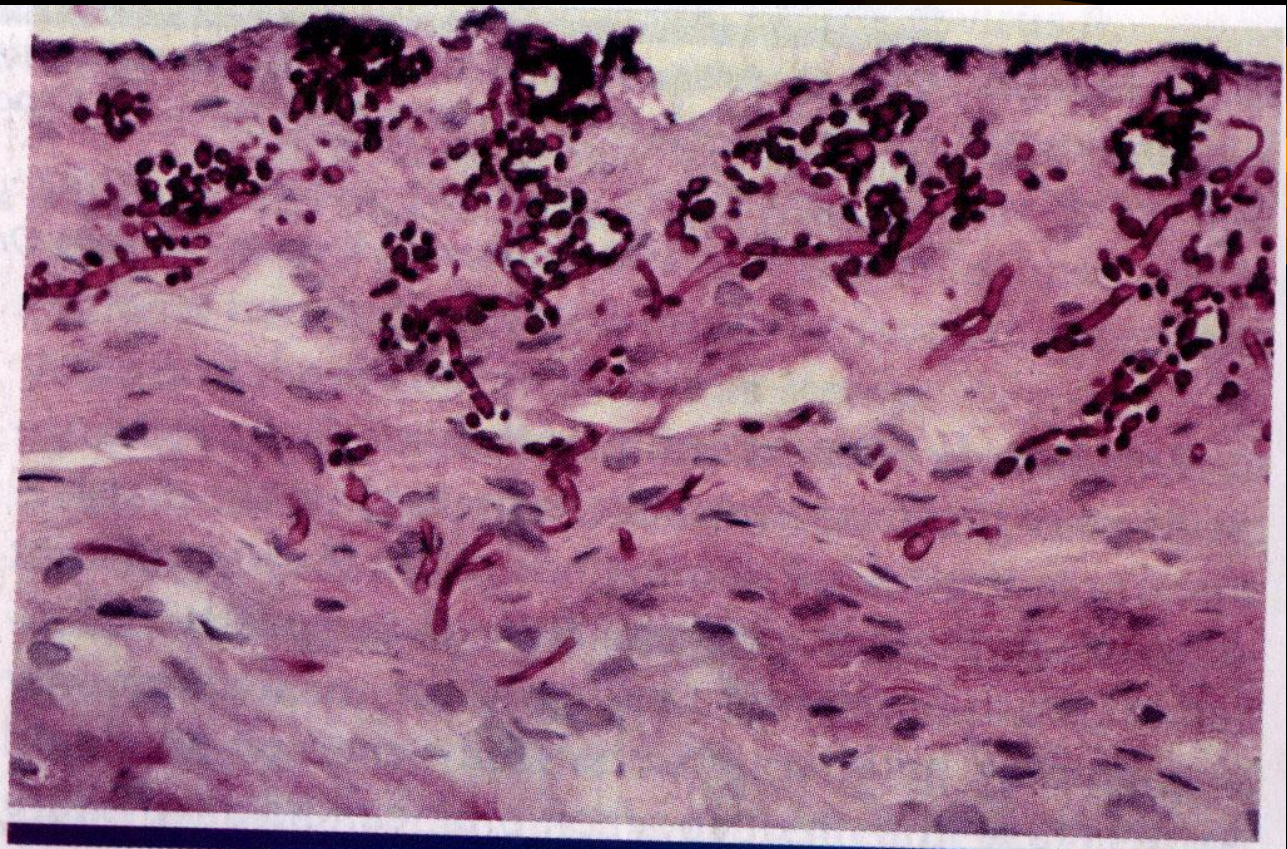


Figure 7-37 ◆ HIV-associated candidiasis. Periodic acid-Schiff (PAS) stain of histopathologic section exhibiting numerous fungal organisms embedded in superficial keratin.

Differential Diagnosis:

- Erythematous candidiasis should be differentiated from other red lesions, such as *Kaposi's sarcoma or erythroplakia.*
- Histologically, oral candidiasis contains Candida hyphae in the superficial epithelium when viewed under a PAS stain.
- The inflammatory responses often associated with Candida infection may be absent in immunocompromised patients.
- The creamy white plaques of pseudomembranous candidiasis are removable; the white lesions of hairy leukoplakia are nonremovable.

Diagnosis:

- Candida is a commensal organism in the oral cavity.
- Candidiasis is diagnosed by
§ Characteristic clinical appearance,
§ Detection of organism on smears, or
§ Culturing the organism on specific media i.e. Sabouraud's agar.

Treatment:

- Oral candidiasis may be treated either topically or systemically. Treatment should be maintained for 7 days.

Topical treatment:

- Topical treatments are preferred because they limit systemic absorption, but the effectiveness depends entirely on patient compliance.
- Clotrimazole is an effective topical treatment (one oral troche [10-mg tablet]) when dissolved in the mouth five times daily. Nystatin preparations include a suspension, a vaginal tablet, and an oral pastille. Regimens are nystatin vaginal tablets (one tablet, 100,000 units, dissolved in the mouth three times a day), or nystatin oral pastille (available as a 200,000-unit oral pastille, one or two pastilles dissolved slowly in the mouth five times a day.
- Topical creams and ointments containing nystatin, ketoconazole, or clotrimazole may be useful in treating angular cheilitis.
- Another therapeutic choice is amphotericin B (0.1 mg/ml). Five to 10 ml of oral solution is used as a rinse and then expectorated three to four times daily.

Systemic Treatment:

- Several agents are effective for systemic treatment. Ketoconazole, a 200-mg tablet taken with food once daily. Patient compliance is usually good.
- Fluconazole (Diflucan) is effective as a prophylactic agent, although the most effective prophylaxis dosing regimen is still unclear.
- Itraconazole (100-mg capsules) may be used for the treatment of oral candidiasis (200 mg daily orally for 14 days).

Prognostic Significance:

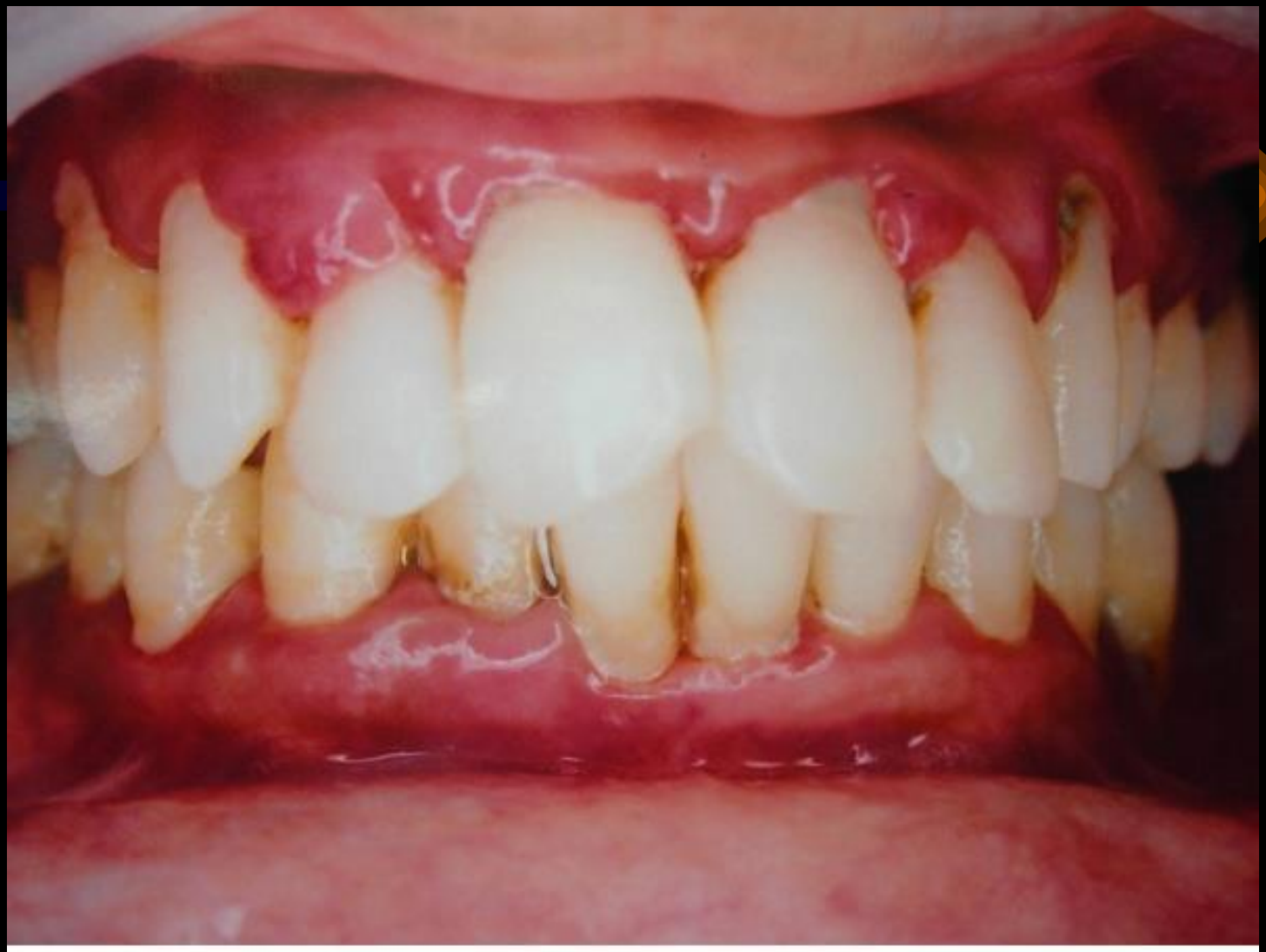
- Both erythematous and pseudomembranous oral candidiasis are associated with increased risk for the subsequent development of opportunistic infections classifying the patient as having AIDS as defined by the Centers for Disease Control (CDC).
- Several studies have shown a statistical correlation between frequency of oral candidiasis in HIV infection and falling CD4+ T-cell counts.

PERIODONTAL DISEASE:

- Periodontal disease is a fairly common problem in both asymptomatic and symptomatic HIV-infected patients.
- Three patterns of periodontal disease are associated strongley with HIV infection.
- Linear gingival erythema
- Necrotizing ulcerative gingivitis
- Necrotizing ulcerative periodontitis

Linear gingival erythema:

- Initially it was termed HIV-associated gingivitis, but ultimately was noted in association with other disease processes
- It appears as a distinctive linear band of erythema that involves the free gingival margin and extends 2 to 3 mm apically.
- In addition, alveolar mucosa and gingival may demonstrate punctate or diffuse erythema in a significant percentage of the cases.
- .



PERIODONTAL LESIONS

Figure 6-12. Linear gingival erythema-P-492

This form of gingivitis typically does not respond to improved plaqaue control and often exhibits a greater degree of erythema than would be expected for the amount of plaque in the area.

- Some investigator believe that LGE occurs from an abnormal host immune response to subgingival bacteria, most believe this pattern of gingivitis represents an unusual pattern of candidiasis

- *Treatment:*
  - It responds to plaque removal, improved oral hygiene and use of chlorhexidine rinses.

Cases resistant to initial therapy typically respond to systemic antifungal medications such as fluconazole or ketoconazole

Necrotizing ulcerative gingivitis (nug):

- It refers to ulceration and necrosis of one or more interdental papillae with no loss of periodontal attachment.
- Patients with NUG have interproximal gingival necrosis, bleeding pain and halitosis.

Necrotizing ulcerative periodontitis (nup):

- It was previously termed HIV-associated periodontitis; however, it has not been deemed to be specific for HIV infection.
- It is characterized by gingival ulceration and necrosis associated with rapidly progressing loss of periodontal attachment.
- Edema, severe pain and spontaneous hemorrhage are common.
- Deep pocketing usually is not seen because extensive gingival necrosis typically coincides with loss fo the adjacent alveolar bone

Loss of more than 6 mm of attachment within a 6-month period is not unusual.

Necrotising stomatitis:

- In patients with gingival necrosis, the process occasionally extends away from the alveolar ridges and creates massive areas of tissue destruction termed necrotizing stomatitis.
- The process clinically resembles noma and may involve predominantly soft tissue or extend into the underlying bone, resulting in extensive sequestration.
- Extreme pain and spontaneous bleeding is there.

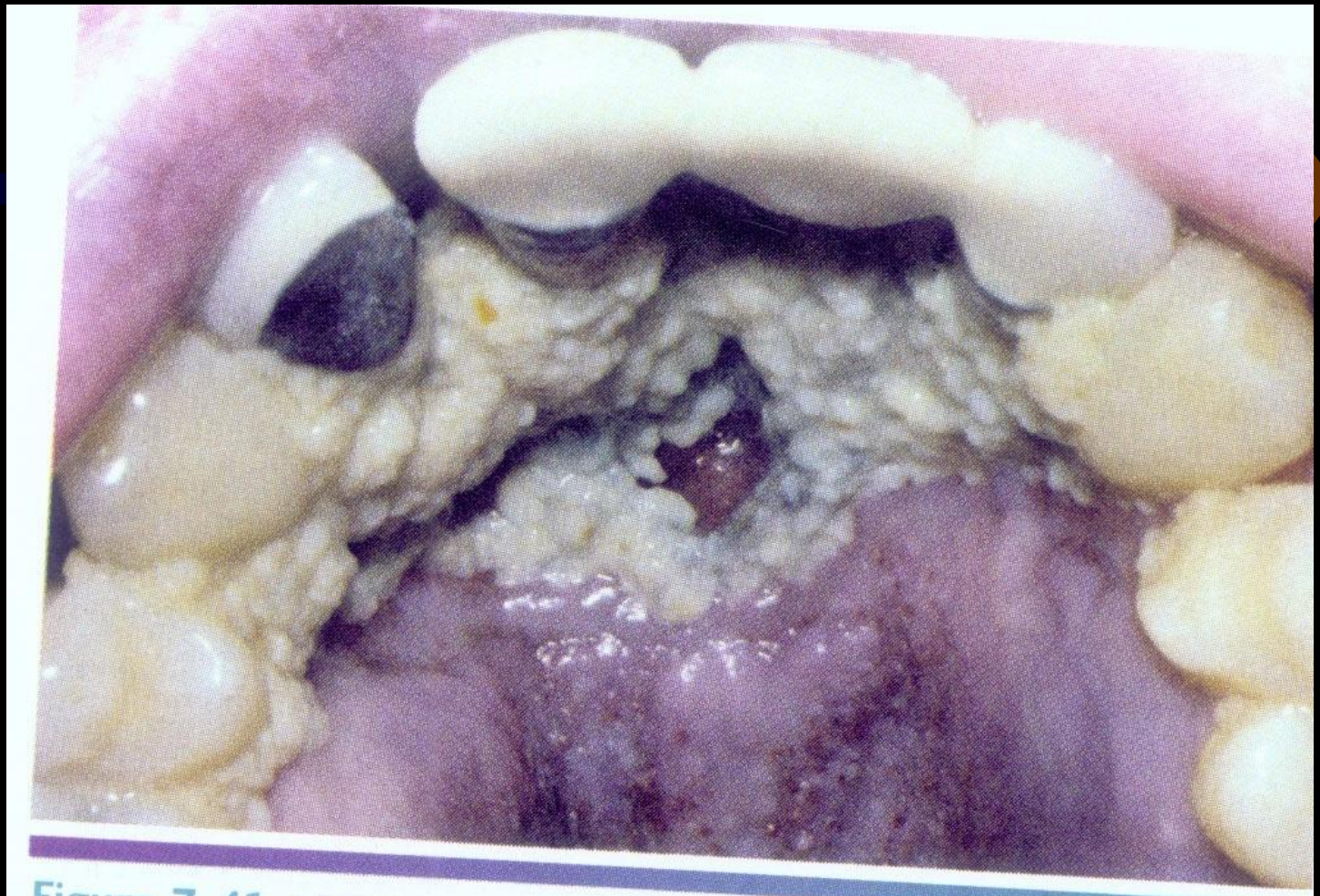


Figure 7-41 • **HIV-associated necrotizing stomatitis.** Massive necrosis of soft tissue and bone of the anterior maxilla.

Diagnosis:

- Acute onset periodontitis, with severe pain, rapid destruction of bone, devoid of deep pockets, in an extremely clean mouth is suggestive of HIV- related periodontal disease.

Treatment:

- The following protocol has achieved reasonable success:
  - Plaque removal,
  - Local debridement,
  - Irrigation with povidone-iodine,
  - Scaling and root planning, and
  - Maintenance with a chlorhexidine mouth rinse once or twice daily.
  - Studies show that the addition of chlorhexidine to this regimen produces significant improvement in periodontal condition.
- In cases of NUP,
  - Metronidazole (one 250-mg tablet four times daily),
  - Amoxicillin/clavulanate (Augmentin)(one 250-mg tablet three times daily), or

Clindamycin (one 300-mg tablet three times daily) should be added to the treatment regimen

VIRAL LESIONS:

HERPES SIMPLEX:

- It occurs in 10 to 15 % of HIV infected patients.
- Herpes simplex causes both primary and secondary or recurrent disease in the oral cavity. Primary herpetic gingivostomatitis commonly occurs in children and young adults and may be followed by frequent recurrences.
- Following the primary episode, the virus becomes latent in the trigeminal ganglion. Recurrent oral herpes occurs at any age extra orally or intra orally.

Clinical features:

- Once CD4 counts fall to less than 50, HSV infection increases.
- Recurrent herpes labialis occurs on the vermilion border of the lips. The patient may report a history of itching or pain, followed by the appearance of small vesicles. These rupture and form crusts.
- Recurrent intraoral herpes appears as clusters of painful small vesicles that rupture and ulcerate and usually heal within 1 week to 10 days. The lesions usually occur on the keratinized mucosa, such as the hard palate and gingiva, although lesions may arise on the dorsal surface of the tongue.
- Persistence of active sites of HSVinfection for more than 1 month in patients infected with HIV is one accepted definition of AIDS.

Diagnosis:

- Clinicians can distinguish between recurrent intraoral herpes simplex lesions, which always occur on keratinized mucosa (such as the hard palate and gingiva), and recurrent aphthous ulcers, which always appear on nonkeratinized mucosa.
- Recurrent intraoral herpes may appear more frequently in HIV-infected patients. The lesions may be painful and slow to heal.

Histopathology:

- Acantholysis, nuclear clearing, nuclear enlargement, which is termed ballooning degeneration.
- Nucleolar fragmentation with chromatin margination.
- Multinucleated, infected epithelial cell formed by fusion of epithelial cells
- Intercellular edema, which forms intraepithelial vesicle.

Laboratory techniques:

- ***Rising antibody titers*** from initial and convalescent sera confirm primary herpetic gingivostomatitis.
- Examining ***smears*** of lesions (treated with Papanicolaou stain) for multinucleated giant cells confirms recurrent herpes.
- It is possible to demonstrate herpes simplex type 1 or type 2 by applying ***monoclonal antibodies*** to smears from the lesions.
- ***Swabs*** taken from fluid-filled vesicles may grow herpes simplex in ***culture*** if vesicles are a few days or less old.

HERPES ZOSTER:

- The reactivation of varicella zoster virus (VZV) causes herpes zoster (shingles). The disease occurs in the elderly and the immunosuppressed.
- In HIV patient, the course is more severe. It generally affects the patients younger than age 40.
- In early stages of HIV, the disease is usually confined to dermatome but persists longer than usual.

Clinical Features:

- Oral herpes zoster generally causes skin lesions.
- Following a prodrome of pain, multiple vesicles appear on the facial skin, lips, and oral mucosa.
- Skin and oral lesions are frequently unilateral and follow the distribution of the maxillary and/or mandibular branches of the trigeminal nerve. The skin lesions form crusts and the oral lesions coalesce to form large ulcers.
- When present intraorally, the involvement often is severe and occasionally leads to bone sequestration and loss of teeth.
- The ulcers frequently affect the gingiva, so tooth pain may be an early complaint.

Differential diagnosis:

- The appearance of the lesions and their distribution are pathognomonic

Treatment:

- Acyclovir limits the duration of the lesions
- For herpes zoster, the standard oral dosage is *800 mg five daily for 7 to 10 days*, which is considerably higher than that recommended for treatment of herpes simplex.

ORAL HAIRY LEUKOPLAKIA:

- Oral hairy leukoplakia (HL), which presents as a nonmovable, corrugated or "hairy" white lesion on the lateral margins of the tongue, occurs in all risk groups for HIV infections, although less commonly in children than in adults.
- HL occurs in about 20% of persons with asymptomatic HIV infection and becomes more common as the CD4+ T-cell count falls
- No report describes HL in mucosal sites other than the mouth.
- HL has occurred in non-HIV-infected people including recipients of bone marrow, cardiac, and renal transplants.
- Diagnosis of HL is an indication of both HIV infection and immunodeficiency; it is an indication for a work-up to evaluate and treat HIV disease.
- HL correlates with a statistical risk for more rapid progression of HIV disease

Clinical Appearance and Manifestations:

- HL lesions vary in size and appearance and may be unilateral or bilateral.
- It is the most common EBV infection
- Lesions occur most commonly on the lateral margins of the tongue and may spread to cover the entire dorsal surface. The surface is irregular and may have prominent folds or projections, sometimes markedly resembling hairs, however some areas may be smooth and flat.
- OHL may occur on buccal mucosa and soft palate on rare occasions.

Histopathology:

- OHL exhibits thickened parakeratin, which demonstrates surface corrugations or thin projections.
- The epithelium is hyperplastic and contains a patchy band of lightly stained "***balloon cells"*** in the upper spinous layer.
- Scattered cells with nuclear clearing and a characteristic pattern of peripheral margination of chromatin. These nuclear alterations are created by extensive EBV replication that displaces the chromatin to the nuclear margin.
- No dysplasia.
- Heavy candidial infection may be seen but associated inflammatory reaction to the fungus usually is absent.

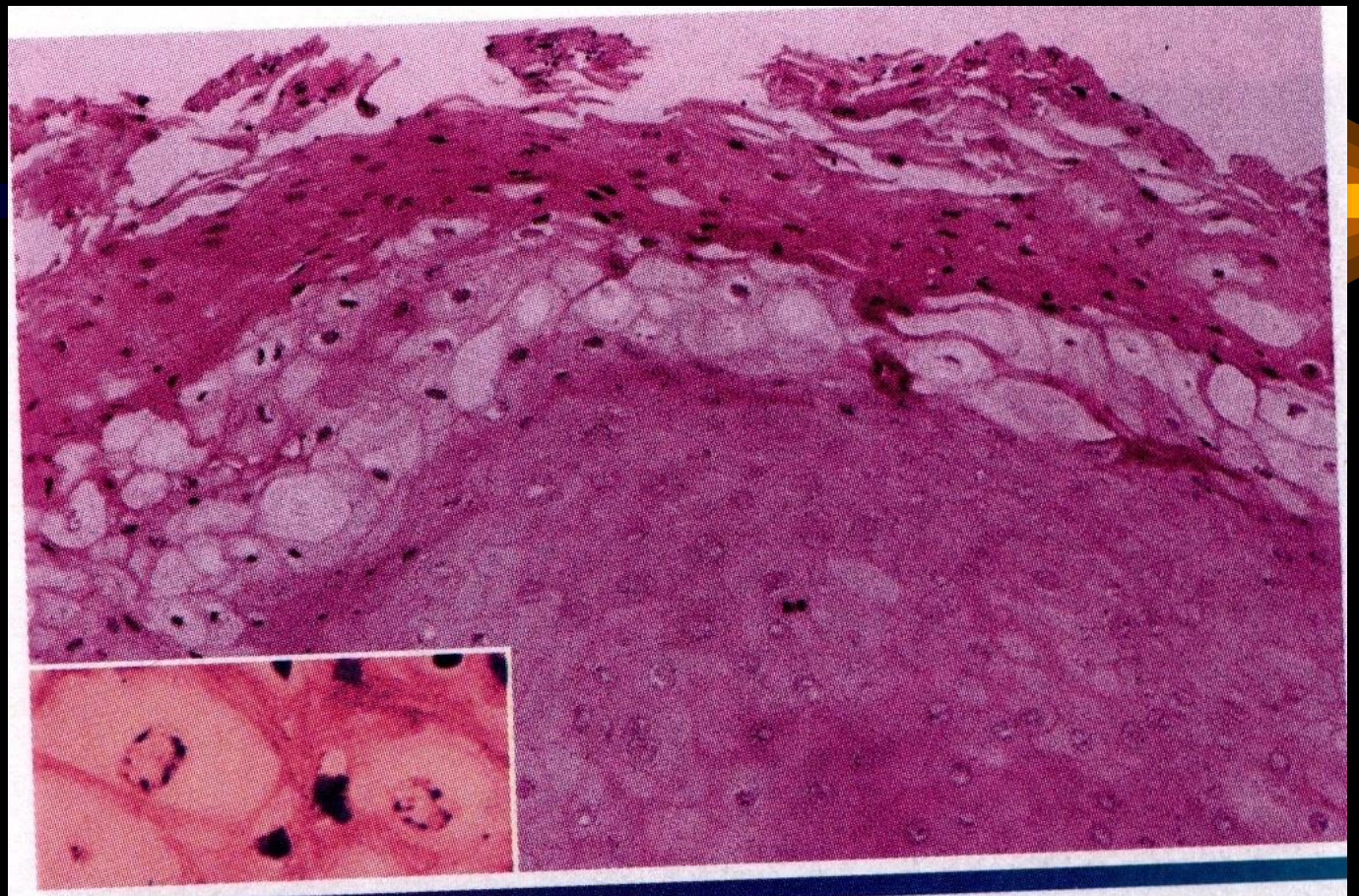


Figure 7-45 • HIV-associated oral hairy leukoplakia (OHL). Oral epithelium exhibiting hyperparakeratosis and layer of "balloon cells" in the upper spinous layer. Inset reveals high-power magnification of epithelial cells that demonstrate nuclear beading.

Differential Diagnosis:

- **Candida albicans** may be found in association with many HL lesions, and hyphae can be seen in specimens taken from lesions.
- Clinicians must distinguish them from other white lesions, such as *lichen planus, idiopathic leukoplakia, white sponge nevus, dysplasia, and squamous cell carcinoma*.

Diagnosis:

- Biopsy is mandetary for diagnosis.
- Definitive diagnosis of HL requires demonstration of EBV.
- EBV may be readily demonstrated in biopsy specimens by a variety of techniques. (I/H/C, EM, southern blotting etc).
- Cells taken from the HL lesion by scraping can be used for a noninvasive diagnosis using in situ hybridization.

Treatment:

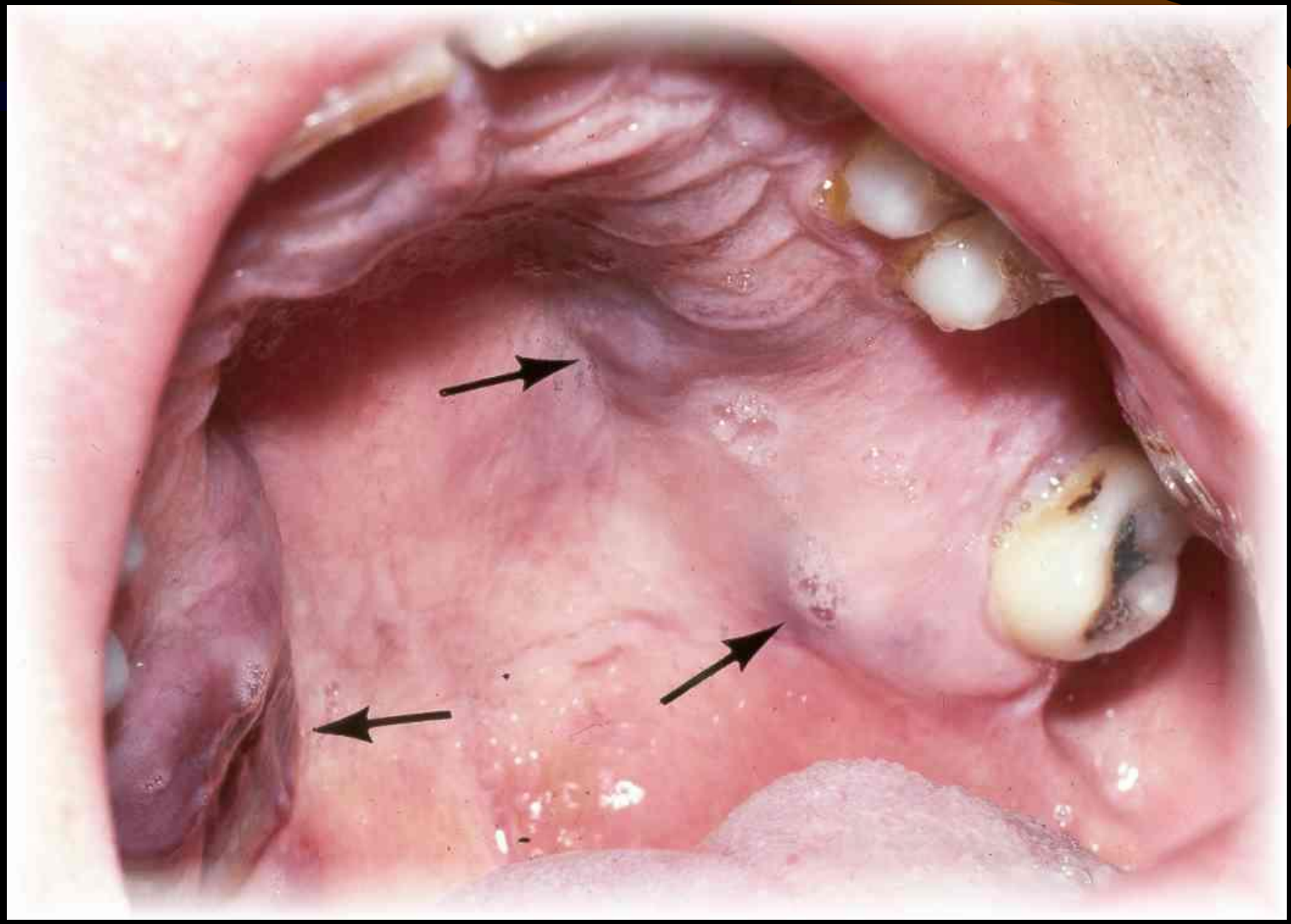
- Hairy leukoplakia usually is asymptomatic and does not require treatment.
- HL is almost always a manifestation of HIV infection, and clinicians should arrange evaluation of HIV disease and appropriate treatment for patients with HL.
- Acyclovir given in high doses, 2.5 to 3 mg per day for 2 to 3 weeks usually eliminate HL, but the lesion usually recurs with cessation of treatment.
- Elimination or almost complete clinical resolution of the lesion has occurred in patients treated with agents such as desciclovir, an analog of acyclovir, phosphonoformate, Retin A, and podophyllin resin, although lesions tend to recur within a few months.
- Case reports describe HL disappearing during treatment with ganciclovir, zidovudine, and aerosolized pentamidine.
- Antifungal medications for candida infection.

KAPOSI'S SARCOMA:

- KS is a mulifocal neoplasm of vascular endothelial cell origin.
- Before AIDS, KS was rare in North America and was found classically in patients over the age of 60 years.
- HHV-8 is noted within the tumor and thought to be involved in the neoplasm’s development.
- KS occurs most commonly in men but also has been observed in women.

Clinical Features:

- KS can appear as a red, blue, or purplish lesion. It may be flat or raised, solitary or multiple.
- Oral lesion may develop in approximately 50% of affected patients.
- The most common oral site is the hard palate, but lesions may occur on any part of the oral mucosa, including the gingiva, soft palate, and buccal mucosa and in the oropharynx.
- Three clinical stages can be distinguished: patch, plaque, nodular.
- Occasionally, yellowish mucosa surrounds the KS lesion.
- Oral KS lesions may enlarge, ulcerate, and become infected. Good oral hygiene is essential to minimize these complications.



Differential Diagnosis:

- KS must be distinguished from vascular lesions such as hematomas, hemangiomas, other vascular tumors, pyogenic granulomas, bacillary angiomatosis, and pigmented lesions such as oral melanotic macules.
- Diagnosis is made from histologic examination:
  - Patch stage: proliferation of minature blood vessels which results in irregular jagged vascular network that surrounds preexisting vessels. Endothelial cell has bland appearance.
  - Plaque stage: further proliferation of blood vessels along with significant spindle cell component.
  - Nodular stage: spindle cell increase to form nodular tumour mass resembling fibrosarcoma.
- There are usually no bleeding problems associated with a biopsy of oral KS. However, aspiration of a lesion prior to biopsy may be useful to rule out a hemangioma.

Providers should ensure that a patient with KS receives evaluation and follow-up care for the underlying HIV disease.

Treatment:

- The choice of therapy depends on the effect of treatment on the adjacent mucosa, pain associated with treatment, interference with eating and speaking, and the patient's preference.
- It is important to perform thorough dental prophylaxis before initiating therapy for KS lesions involving the gingiva.
- Local treatment is appropriate for large oral KS lesions that interfere with eating and talking.
- Oral KS can be treated surgically or with localized intralesional chemotherapy.
- Surgical removal is suitable for small, well-circumscribed lesions such as gingival or tongue lesions.
- Intralesional vinblastine is useful for treating small lesions, particularly on the palate or gingival.
- Radiation therapy may be indicated for large, multiple lesions.

APTHOUS ULCERATION:

- Oral ulcers resembling recurrent aphthous ulcers (RAUs) in HIV-infected persons are reported with increasing frequency.
- The cause of these ulcers is unknown. Proposed causes include stress and unidentified infectious agents.
- In HIV-infected patients, the ulcers are well circumscribed with erythematous margins. All the three forms are seen. Surprisingly however, almost 2/3rd of the patients have usually uncommon herpetiform & major variants.
- As immunosuppression become more profound major apthous ulcers demonstrate increased prevalence.
- It should be differentiated from the lesions of coxsackievirus infection, malignancy, such as lymphoma, or opportunistic infection, such as histoplasmosis.
- Treatment includes topical steroids, mouth rinses, and systemic steroids, if indicated.

ORAL SQUAMOUS CELL CARCINOMA:

- It appears that HIV infection may accelerate the development of oral SqCC, may be because of impaired immune surveillance and an increased chance of human papilloma virus infection are a few suggested cases.

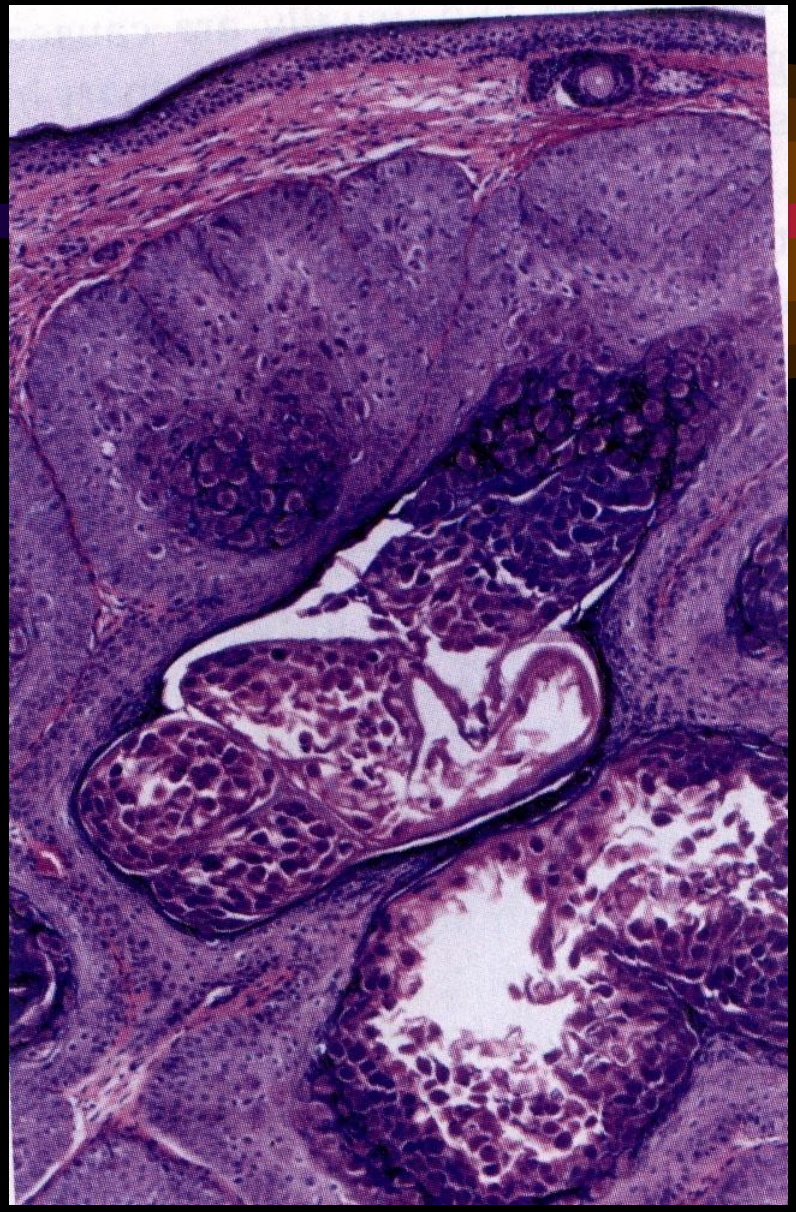
MULLOSCUM CONTAGIOSUM:

- It is an infection of skin caused by poxvirus.
- Clinically, lesions are pink, smooth surface, sessile, nonhemorrhagic papules, 2 to 4 cm in diameter, which may show small central indentation or keratin like plug from which a curd like substance can be expressed.
- In immunocompetent patient, these lesions are self-limiting and typically involve genital region or trunk. But in immunocompromised patient there is a little tendency to undergo spontaneous resolution and facial skin is commonly involved.
- Approximately 5-10% of HIV patients are having mulloscum contagiosum.

- Diagnosis:

- Histopathology is must.
- Surface epithelium from numerous hyperplastic down growth with the cells exhibiting large intracytoplasmic inclusions known as mulloscum boies.
- In center of lesion, keratin layer of disintegrate and releases mulloscum bodies.

Treatment: No treatment, if there is esthetic problem, cryosurgery is adviced.



THROMBOCYTOPENIC PURPURA:

- Reports have described idiopathic thrombocytopenic purpura (ITP) in HIV-infected patients. Oral lesions may be the first manifestation of this condition.
- Clinical Features:
  - Petechiae, ecchymoses, and hematoma can occur anywhere on the oral mucosa.
  - Spontaneous bleeding from the gingiva can occur, and patients may report finding blood in their mouths on waking.
- Differential Diagnosis:
  - The clinician must distinguish ITP from other vascular lesions and KS.

Because of potential bleeding risk, the clinician should obtain blood and platelet counts before performing other diagnostic procedures.

SALIVARY GLAND DISEASE

- Noted in 5% of patients
- Salivary gland disease associated with HIV infection (HIV-SGD) can present as xerostomia with or without salivary gland enlargement. Reports describe salivary gland enlargement in children and adults with HIV infection usually involving the parotid gland. The enlarged salivary glands are soft but not fluctuant. In some cases, enlarged salivary glands may be due to lymphoepithelial cysts.
- In HIV-SGD, however, the lymphocytic infiltrate is predominantly CD8 cells, unlike that in Sjogren's syndrome, which is predominantly CD4 cells.
- *Xerostomia* is sometimes seen in individuals with HIV-SGD. HIV-infected patients may also experience dry mouth in association with taking certain medications that can hinder salivary secretion, such as antidepressants, antihistamines, and antianxiety drugs.

- Management:

○ Removal of the enlarged parotid glands is rarely recommended.
○ For individuals with xerostomia, the use of salivary stimulants such as sugarless gum or sugarless candies may provide relief.
○ Candies that are acidic should be avoided as frequent use may lead to loss of tooth enamel.
○ An increase in caries can occur, so fluoride rinses (that can be bought over the counter) should be used daily, and visits to the dentist should occur two to three times per year.

PERSISTENT GENERALIZED LYMPHADENOAPTHY (PGL):

- Prevalence – 70% of HIV patients are having PGL.
- It consists of lymphadenopathy that has been present for longer than 3 months & involves 2 or more extra inguinal sites.
- Most frequently involved sites are
  - Posterior & anterior cervical lymph nodes
  - Submandibular lymph nodes
  - Axillary lymph nodes
  - Occipital lymph nodes.
- Size: greater than 1 cm, varies from 0.5 to 5 cm.
- Histopathology:
  - Florid follicular hyperplasia.
  - Biopsy indicated to differentiate from lymphoma, which is also common in HIV patients.
- Prognostic significance:
  - PGL warn progression of AIDS & patient with PGL have AIDS symptom in 5 years.

LESS COMMON LESIONS ASSOCIATED WITH HIV INFECTION:

FUNGAL INFECTION:

ASPERGILLOSIS:

- Aspergillosis is a fungal disease that is characterized by noninvasive and invasive forms.
  - Noninvasive form usually affects a normal host, appearing either as an allergic reaction or a cluster of fungal hyphae
  - Localized invasive infection of damaged tissue may be seen in a normal host, but a more extensive invasive infection is often evident in the immunocompromised patient.
- With the advent of AIDS epidemic, prevalence of invasive aspergillosis has increased dramatically in the past 20 years.

It presents as painful gingival ulcerations and diffuse, gray or violaceous swelling of the mucosa and soft tissue.

Diagnosis:

- *Biopsy*:
  - It shows aspergillus lesions with varying numbers of branching, septate, hyphae, 3 to 4 um in diameter. These hyphae show a tendency to branch at an acute angle and to invade adjacent small blood vessels.
  - Occlusion of the vessels often results in the characteristic pattern of necrosis associated with this disease.
  - In immunocomprised patient, inflammatory response is weak or absent, leading to extensive tissue destruction.
- Demonstration of hyphae within the tissue
- Culture of the organism from the lesion.

Treatment and prognosis:

- Surgical debridement is usually undertaken.
- Prognosis in immunocompromised patient is very poor, particularly if the infection is disseminated.

HISTOPLASMOSIS:

- It is produced by histoplasma capsulatum.
- In healthy patients, the infection is typically subclinical and self-limiting but immunocompromised patients, clinically evident infection may occur from reactivation of previous sub clinical infection.
- Clinical features associated with disseminated disease are nonspecific and includes fever, weight loss, splenomegaly, pulmonary infiltration.
- Oral lesions are uncommon.
- Mostly, chronic indurated mucosal ulceration with raised border.

Histopathology:

- Small fungal organisms are visible in cytoplasm of histiocytes and multinucleated giant cells, which are present in sheets or organized granulomas.

Treatment: IV amphotericin B, itraconazole/ketokonazole

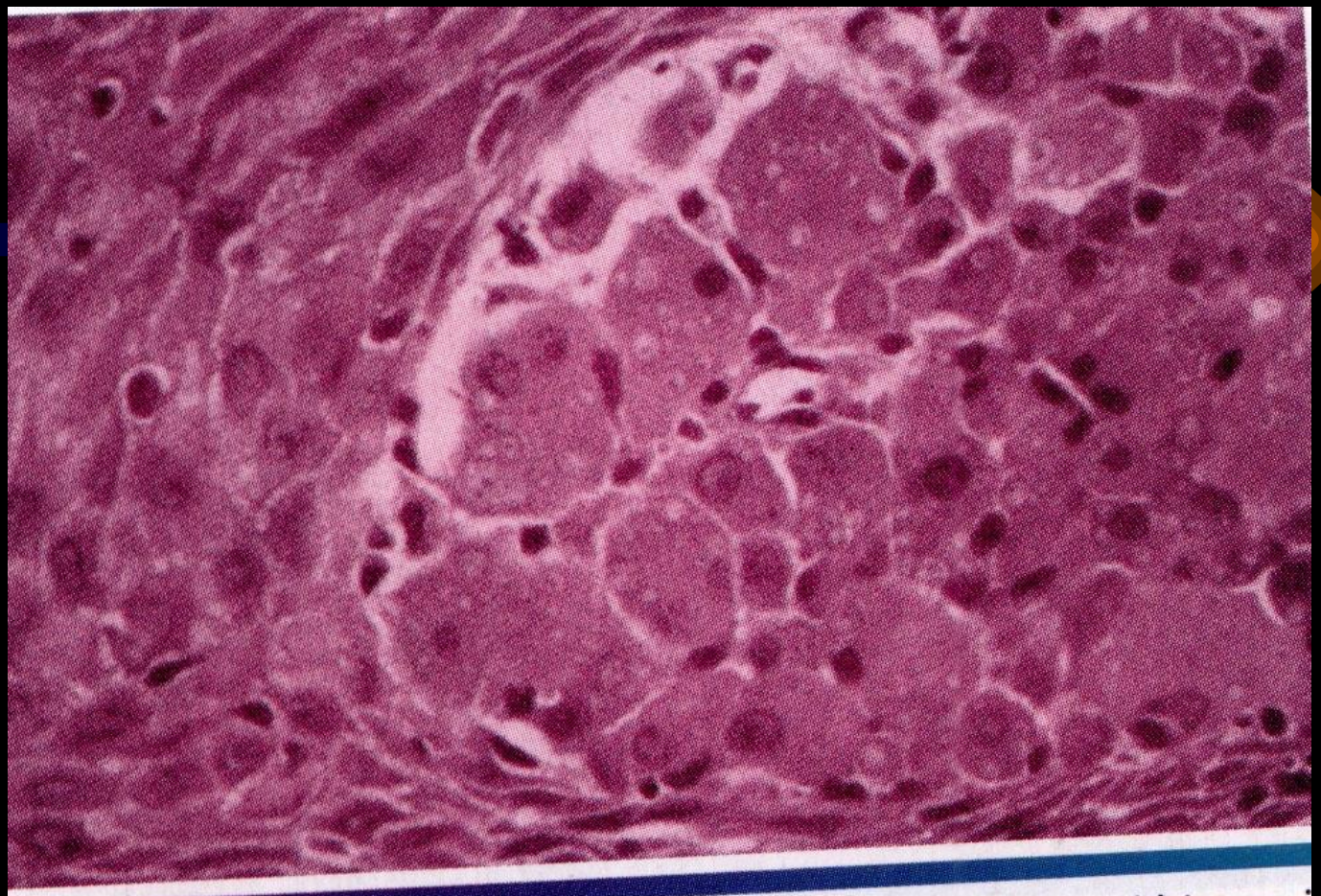


Figure 7-59 • HIV-associated histoplasmosis. Mucosal biopsy i
which the connective tissue is filled with numerous enlarged histi
ocytes. Numerous small, clear-appearing fungal organisms are
located within the cytoplasm of the histiocytes.

COCCIDIOMYCOSIS:

- Patients with end stage of AIDS may develop coccidiomycosis (very rare).

Clinical features:

- Along with fatigue, cough, chest pain, myalgia, and headache, patient may development a hypersensitivity reaction that cause the development of erythema multiforme or erythema nodosum,
- Erythema nodosum is characterized by the appearance of multiple painful erythematous inflammatory nodules in the subcutaneous connective tissue.

Diagnosis: culture or identification of the organism in biopsy material.

VIRAL LESIONS:
HUMAN PAPILLOMA VIRUS:

- Oral warts, papillomas, skin warts, and genital warts are associated with the human papillomavirus (HPV).
- Lesions caused by HPV are common on the skin and mucous membranes of persons with HIV disease. Anal warts have frequently been reported among homosexual men

Clinical Features:

- HPV lesions in the oral cavity may appear as solitary or multiple nodules. They may be sessile or pedunculated and appear as multiple, smooth-surfaced raised masses resembling focal epithelial hyperplasia or as multiple, small papilliferous or cauliflower-like projections.

Differential Diagnosis:

- A biopsy is necessary for histologic diagnosis.

Prognosis:

- There is *no known association* between oral HPV lesions and more rapid progression of HIV disease, but oral warts are seen more commonly in HIV-infected persons than in the general population.

Treatment:

- Oral HPV lesions can be removed surgically using local anesthetic.

- Carbon dioxide laser surgery can remove multiple flat warts, but relapses occur and several repeat procedures may be necessary.

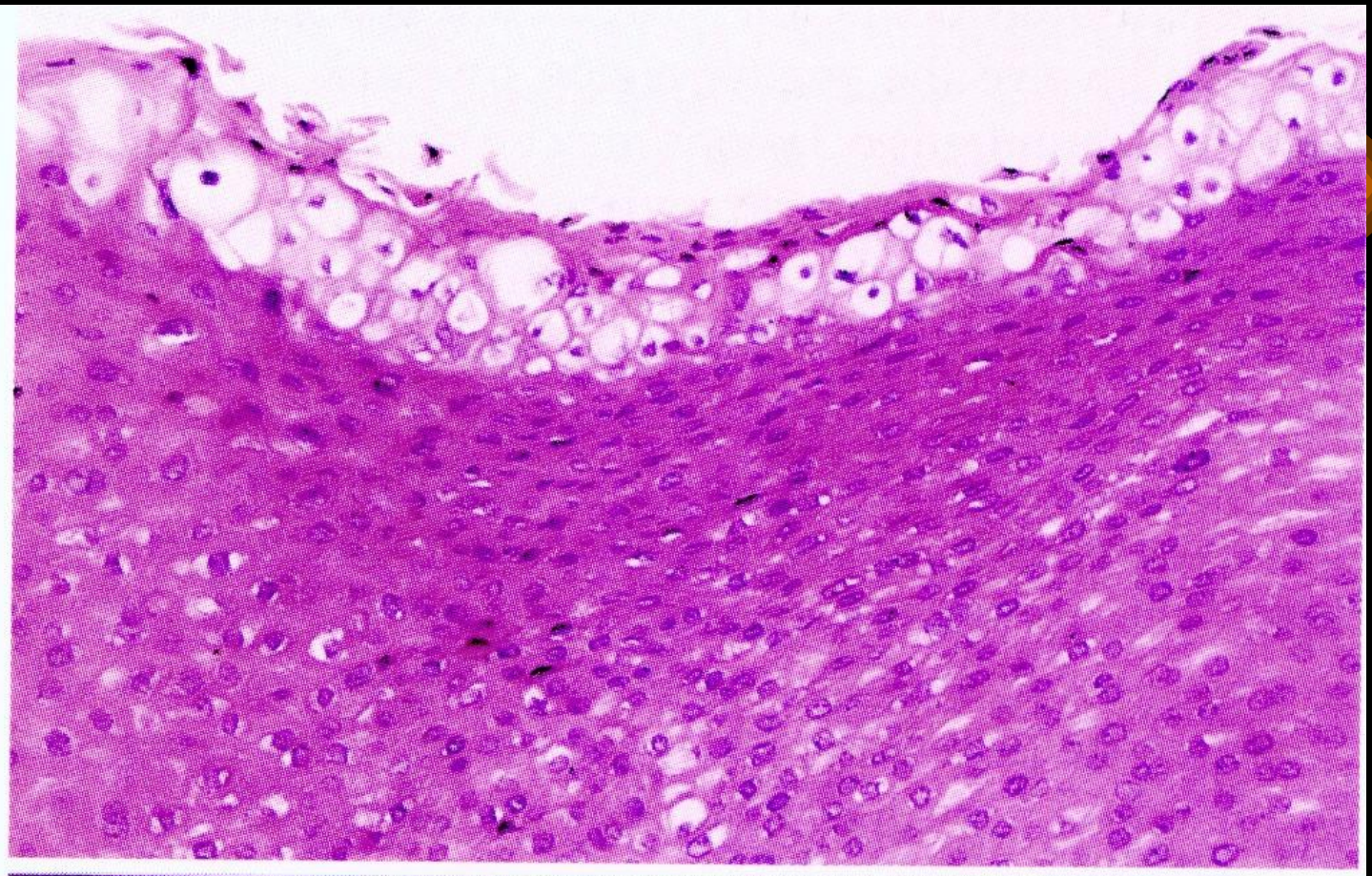


Figure 7-56 • HIV-associated human papillomavirus (HPV) infection. Oral mucosa exhibiting extensive koilocytosis in the superficial spinous cell layer.

CYTOMEGALOVIRUS:

- Oral ulcers caused by cytomegalovirus (CMV) have been reported.
- These ulcers can appear on any mucosal surface and may be confused with aphthous ulcers, narcotizing ulcerative periodontitis (NUP), and lymphoma.
- Unlike aphthous ulcers, however, which usually have an erythematous margin; CMV ulcers appear necrotic with a white halo.
- Diagnosis of CMV ulcers is made from a biopsy. Immunohistochemistry may be helpful.
- CMV ulcers in the oral cavity usually occur in individuals with disseminated CMV disease. Therefore, diagnosis of CMV-infected oral ulcers should be followed by examination for the systemic disease. CMV ulcers resolve when Ganciclovir is used to treat CMV disease.

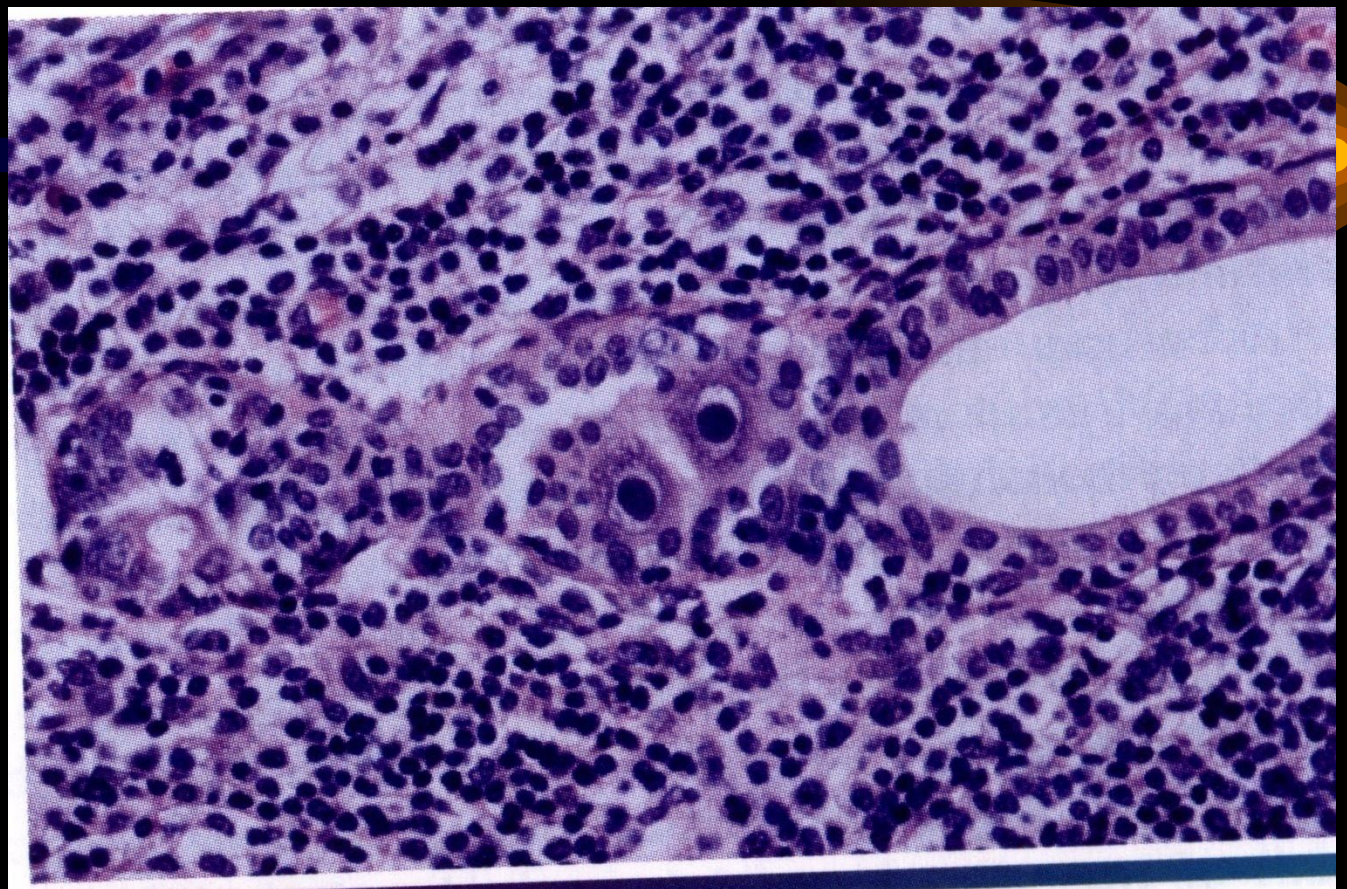


Figure 7-22 ◆ Cytomegalovirus (CMV) infection. Salivary ductal epithelium exhibiting distinctive "owl eye" alterations.

BACTERIAL INFECTIONS:

- Odontogenic infection (periapical pathology) may fail to resolve or may spread to produce ***submandibular cellulitis.***
- Extraction socket may infected or heal slowly and actinomycosis has been recorded.
- Rare opportuinistic infection with ***Klebsiella pneumonie, enterobacter cloacae, escherichia coli*** may be seen in HIV patients.

Tuberculosis:

- It can occur in HIV disease especially in drug abusers in Africa, there have been few reports of oral lesion.
- Tuberculous cervical lymphadenopathy and oral ulcers are sometimes associated with ***mycobacterium auium intercellulare*** has been described.

MALIGNANT LESIONS:

NON-HODGKIN'S LYMPHOMA:

- Clinical Features:
  - Diffuse, undifferentiated non-Hodgkin's lymphoma (NHL) is the second most common HIV-associated malignancy.
  - Most are of B cell origin, and Epstein-Barr virus occurs in cells from several cases. Lymphoma can occur anywhere in the oral cavity, and there may be soft tissue involvement with or without involvement of underlying bone.
  - The lesion may present as firm, painless swelling that may be ulcerated. Some oral lesions may appear as shallow ulcerations.
  - Oral NHL may appear as solitary lesions with no evidence of disseminated disease.

Differential Diagnosis:

- Oral NHL may be confused with major aphthous ulcers and rarely as a pericoronitis associated with an erupting third molar. Diagnosis of NHL must be made by histologic examination of biopsy specimens.

- Treatment:

- After diagnosis of the oral lesions, the patient must be referred for further evaluation for disseminated disease and its subsequent treatment.

HIV RELATED EMBRYOPATHY:

- A group of perioral anomalies including hypertelorism, prominent box like forehead, flattened nasal bridge, triangular philtrum, prominent upper vermilion border.
- However, specificity of these features to HIV infection is disputed..

GRANULOMA ANNULARE:

- It is a common skin lesion of uncertain etiology that usually resolves spontaneously.
- In oral cavity, it presents as popular lesion on buccal mucosa of AIDS patients.
- Exfoliative cheilitis can be seen 1-9 % of HIV patients.

HYPERPIGMENTATION:

- Hyperpigmentation of skin, nails and mucosa have been reported in HIV infected patients.
- Causes:
  - Medication taken by AIDS patients i.e., ketoconazole, clofazimine, pyrimethamine, zidovudine etc.
  - Adreno cortical destruction resulting in addisonian pattern of pigmentation.
  - It may be result of HIV infection.
- Diagnosis made by…
  - *History*: recent onset, brown to brownish black, usually bilateral distribution, pigmentation ranging from 5 mm to 2 cm.
  - *Histopathology*: similar to focal melanosis with increase melanin pigments in basal cell layer of epithelium.

NEUROPATHY:

- Facial nerve palsy, resembling bell's palsy have been reported in HIV infection.
- Neuropathy may involve many of cranial nerve, particularly viii and v and may cause facial sensory loss.
- Such neuropathies may have central or peripheral causes related especially to AIDS encephalitis, tumors, infection etc.

LABORATORY DIAGNOSIS OF HIV:

- Confirmation of HIV infection can be made by viral culture or by detection of HIV antibodies or antigens.

DIAGNOSIS BY ANTIBODIES TO HIV:

- The standard screening tool is the *ENZYME IMMUNOASSAY (EIA)* for antibodies to HIV. It should followed by the more accurate *WESTERN BLOT ANTIBODY ASSAY.*
- Other alternative include
  - Radioimmunoprecipitation,
  - Rapid latex agglutination assay,
  - Dot-blot immunobinding assay

DIAGNOSIS BY VIRAL ANTIGEN DETECTION:

- There are few assays that detect viral antigens. These tests are not used widely and include the p24 antigen capture assay and polymerase chain reaction (PCR) for detection for HIV DNA that may be integrated into host DNA. This method can be used to identify someone who was infected recently or HIV carriers who otherwise have negative antigen or antibody findings.
- The diagnosis of AIDS is indicated when patient has laboratory evidence of HIV infection combined with documentation of less than 200 CD4+ T lymphocytes per micro liter or a CD4+ T lymphocytes percentage of total lymphocytes of less than 14.

TREATMENT:

- The introduction of highly active antiretroviral therapy (HAART) has altered the course of the epidemic.
- Three types of medications are available. Initial regimens consist of two nucleoside reverse transcriptase inhibitors and one or two protease inhibitors. Alternatively two nucleoside reverse transcriptase inhibitors and nonnucleoside reverse transcriptase inhibitor can be used.

- ***ANTIRETROVIRAL THERAPY***:
- Nucleoside reverse-transcriptase inhibitors
  - Abacavir, didanosine, lamivudine, stavudine, zalcitabine or zidovudine.
- Non nucleoside reverse transcriptase inhitors
  - Delavirdine, efavirenz, or nevirapine
- Protease inhibitors
  - Amprenavir, indinavir, nelfinavir, ritonavir, or saquinavir

- Although antiretroviral therapy is effective for many patients, it is expensive. In addition, this treatment often is associated with significant adverse reactions, may not be effective in all patients, or may fall after a period of initial success.
- The current therapeutic approaches have driven HIV to undetectable levels in many patients, with a resultant clinically significant reconstitution of the immune system. With the current antiretroviral medications, total HIV eradication would take at least a decade and presently is not a realistic goal.
- Although no cure exists, survival time is increasing as a result of earlier diagnosis and improved therapy.
- Work is proceeding toward the development of a safe and effective vaccine against HIV infection, but complex issues slow the progress.
- Advances in therapy and prevention of HIV infection occur daily, however, the best defense against the disease is prevention of the initial infection.