Viral, fungal infections

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I. ÚP

Viral infections - herpesviruses

- HSV-1, HSV-2: herpetic stomatitis
- Varicella-zoster (VZV, HHV-3): chickenpox, shingles
- EBV (HHV-4): inf. mononucleosis, hairy leukoplakia, ML
- CMV (HHV-5): lesions in immunodeficient p.
- HHV-6: roseola infantum, mononucleosis sy
- HHV-7: roseola infantum?, mononucleosis sy?
- HHV-8: Kaposi sarcoma, effusion lymphoma

Viral infections – other viruses

- Enteroviruses – Coxsackie A: herpangina; hand-foot-and-mouth disease; acute lymphonodular pharyngitis
- Paramyxoviruses – rubeola (measles)
  mumps (parotitis)
- Orthomyxoviruses - influenza
- Togavirus – rubella (German measles)
- HPV – viral warts (papilloma), dysplasia, ca
- HIV - AIDS

Herpetic lesions

Herpes simplex virus

- Mucocutaneous infection, retrograde infection along sensory nerves, latent infection in cranial nerve or dorsal spinal ganglia, mucocutaneous recurrences
- HSV-1
  - Mostly orolabial (cold sores, fever blisters)
  - 20-50% of initial genital herpes
- HSV-2
  - Mostly genital; oral infection with ↑ rate
  - >90% of recurrent genital herpes

HSV – primary infection

- direct contact or droplet spread
- may be asymptomatic
- pharyngotonsillitis possible, mostly in adults
- primary herpetic gingivostomatitis – children 6 months – 5 years
- abrupt onset, fever, chills, nausea, lymphadenopathy
- multiple small vesicles on oral mucosa → ulceration → erythematous mucosa
- satellite vesicles on perioral skin (saliva)

HSV – primary infection

HSV - latency

HSV infects neurons that innervate the epithelial tissue

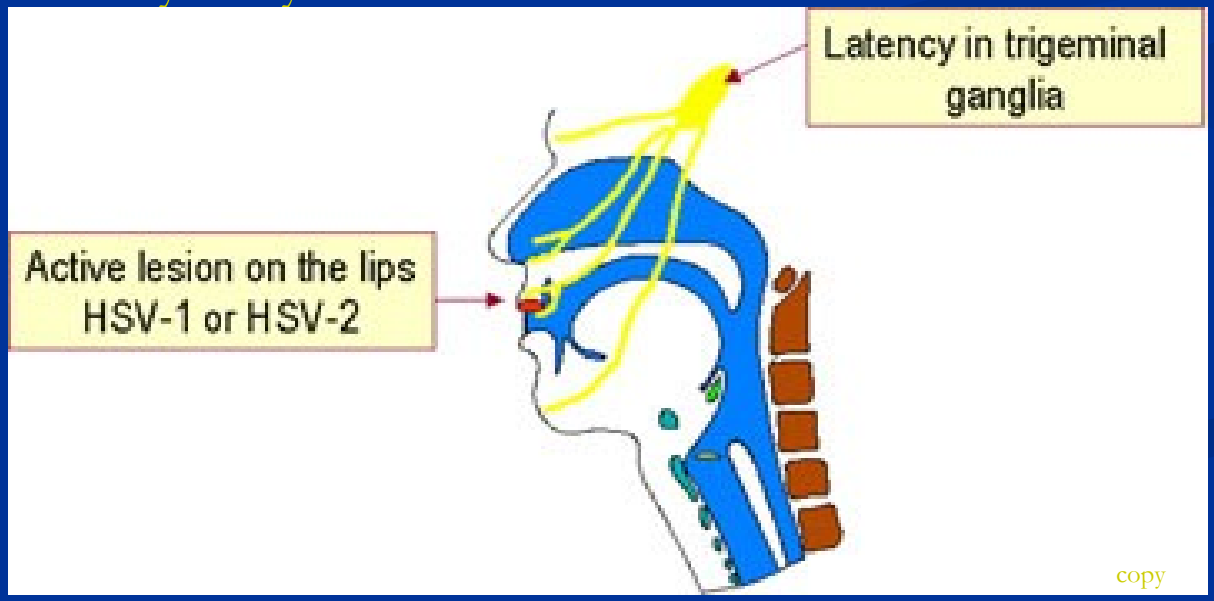
The virus travels along the neuron (retrograde transport on sensory nerves)

oral mucosa ⟶ trigeminal ganglia

genital mucosa → sacral ganglia

Blockage of viral DNA transcription ⟶ latent infection.

↓of host immunity – dysbalance - reactivation



HSV - reactivation

Several agents may trigger recurrence:

stress, fatigue, menstruation, pregnancy

exposure to strong sunlight, local trauma

fever – respiratory or GIT infection

Recurrent infection – at the primary site or near area (same involved ganlion).Vesicles with infectious virus formed on the mucosa → spread.

Recurrent infection usually less pronounced than the primary infection (without systemic signs) and resolves more rapidly

HSV- pathology

The virus replicates in the epithelial tissue → characteristic „fever blister“ or „cold sore“. The blister ulcerates ⟶ crusted lesion → healing without scar formation

Herpes simplex

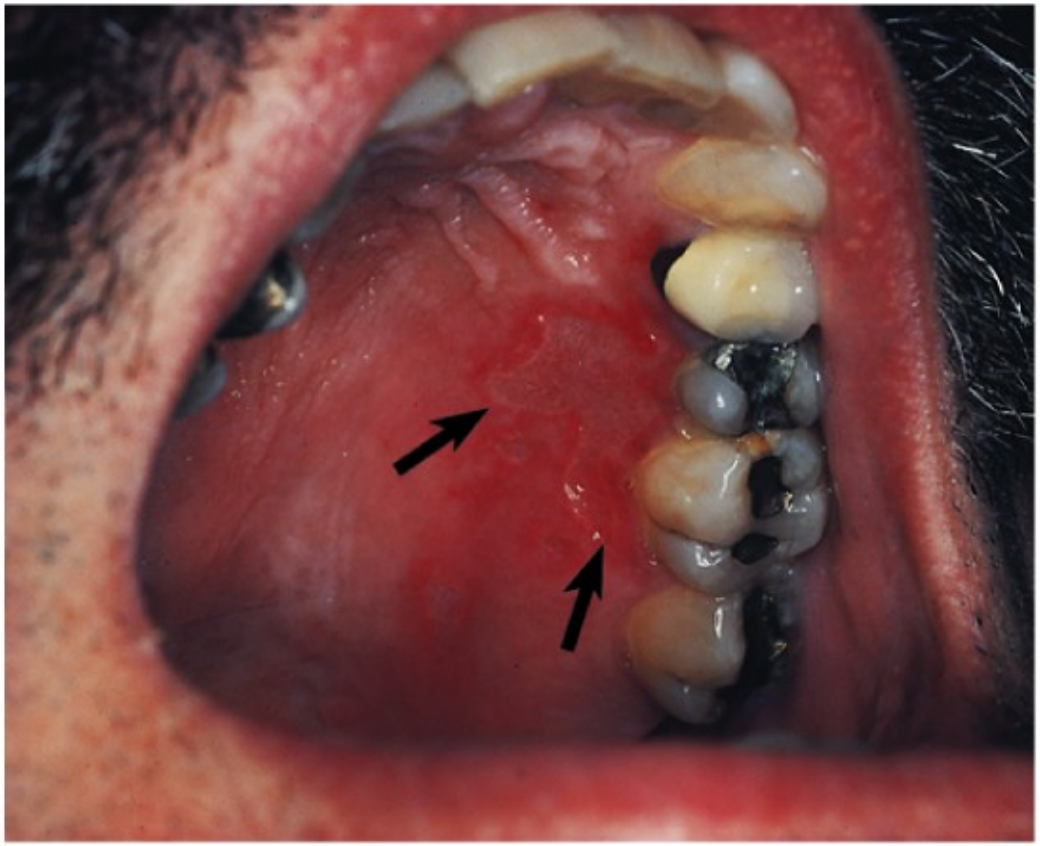
- Immunocompromised patients - lesions may occur throughout the mouth.
- Herpetic ulcer persisting >1 month without known immunosuppression - indicator of possible AIDS.
- Herpetic whitlow: a crusting ulceration on the fingers or hands, extremely painful. ! working on patients with active HSV

Intraoral HSV

Linear vesicles → rupture → ulceration

HSV in immunocompromised

Hard palate HSV in AIDS

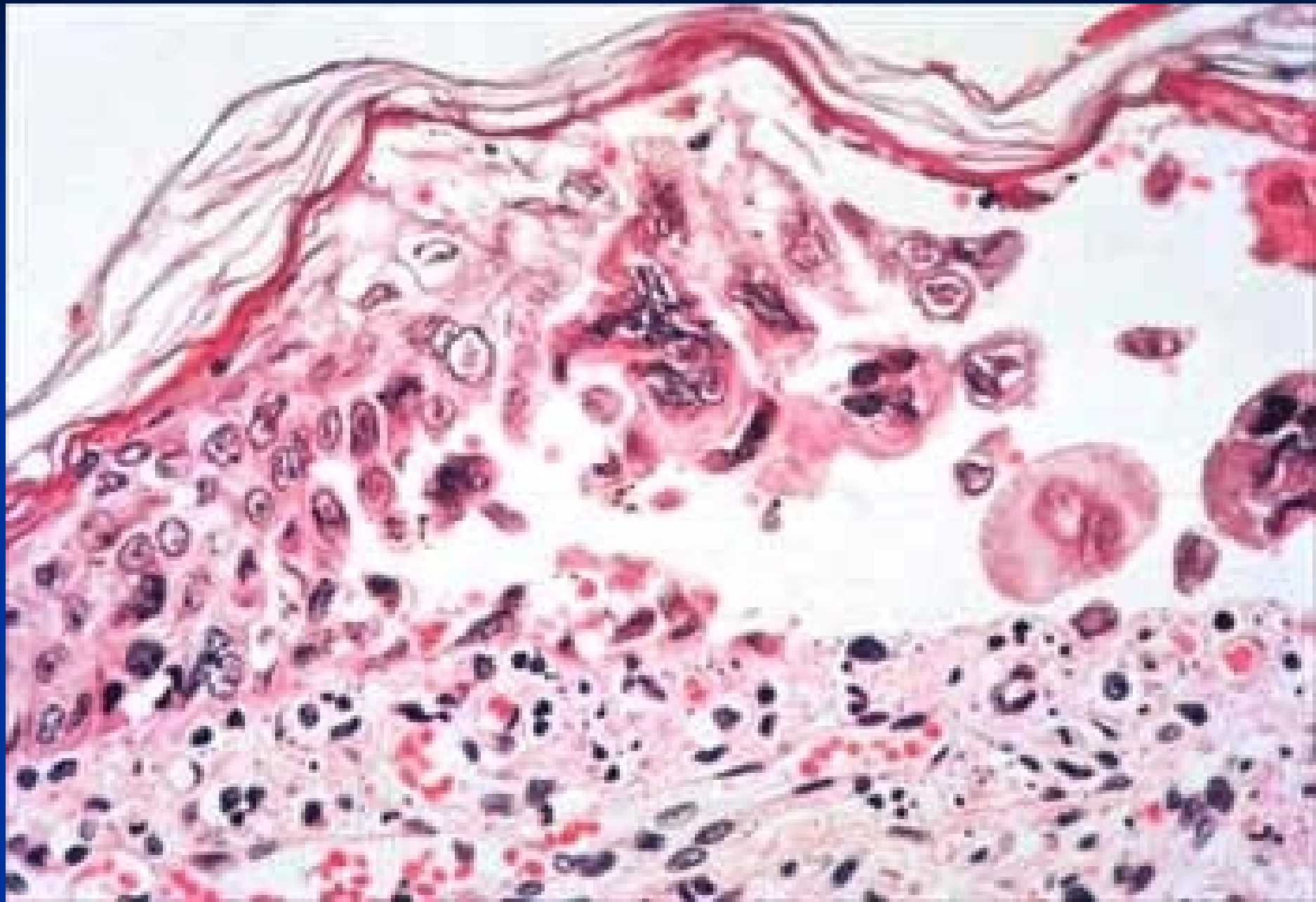


Herpes simplex

other localisations:

- herpetic keratitis → corneal blindness
- herpetic encephalitis
- skin herpetic lesions – in damaged skin (trauma, preexisting disease)

HSV



Tzanck smear

Varicella - Zoster

- VZV primary infection: chickenpox – fever, malaise, headache, rash: vesicle → pustule → ulcer → crust
- in oral cavity on buccal mucosa + hard palate, resembles aphthous ulcers, 7-10 days

Varicella Zoster – Chicken pox

Photo Courtesy of CDC

Photo Courtesy of CDC - Dr. Heinz F. Eichenwald

Photo Courtesy of CDC

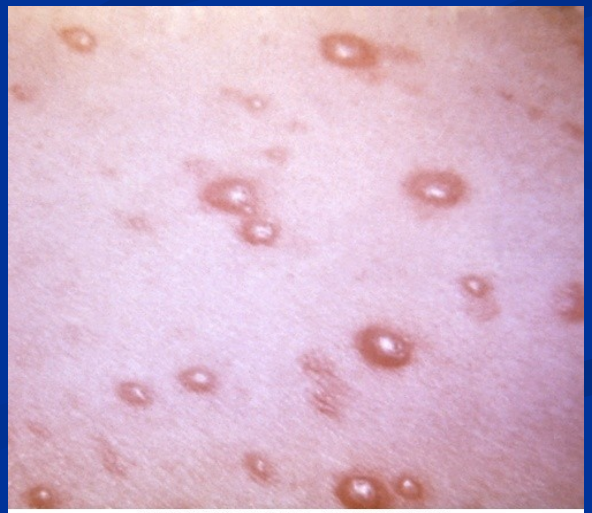


Photo Courtesy of CDC - Dr. K.L. Hermann

Herpes zoster

- Duration of the lesion is dependent on:
  - Age: young ~ 2-3wks, adults~ 5-6wks
  - Severity of lesions
  - Immunosuppression
- Incidence increases with age (esp.>50 yrs) and immunosuppression.
- Vaccination of older people possible.
- Specific antiviral drugs.

Varicella Zoster - Shingles

VZV - unilaterality

Fig. 65.4. Herpes zoster (shingles): painful oral lesions.

Varicella - Zoster

- **Secondary infection (Shingles)**
- Latency within the dorsal root ganglia
  - Rare in the immunocompetent
  - Presentation: Prodrome of burning or pain over dermatome. Over 1-5 days new lesions, typically along a dermatome with some overflow to adjacent dermatomes.
    - Maculopapular rash, development similar to primary form (vesicles → crust). Oral lesions typically after skin involvement

VZV pathology

Trigeminal nerve reactivation

- uveitis, keratitis, conjunctivitis

Cranial nerve reactivation

- **Bells palsy:** weakening or paralysis of facial muscles, involvment of the 7th cranial nerve, not permanent.

- **(Ramsay-Hunt syndrome:** virus spreading to facial nerves. Characterized by intense ear pain, a rash around the ear, mouth, face, neck, and scalp, and paralysis of facial nerves. Symptoms may include hearing loss, vertigo, and tinnitus.)

VZV pathology

Post-herpetic neuralgia: chronic burning or itching pain; hyperesthesia (increased sensitivity to touch)

Epstein Barr virus

Infectious mononucleosis

- **General**: After 3-7 week incubation period, bilateral enlargement of cervical and other LN, fever, malaise, possible splenomegaly. Pharyngitis with hyperplasia of lymphoid tissue, pseudomembranous tonsillitis. Atypical lymphocytes in the blood.

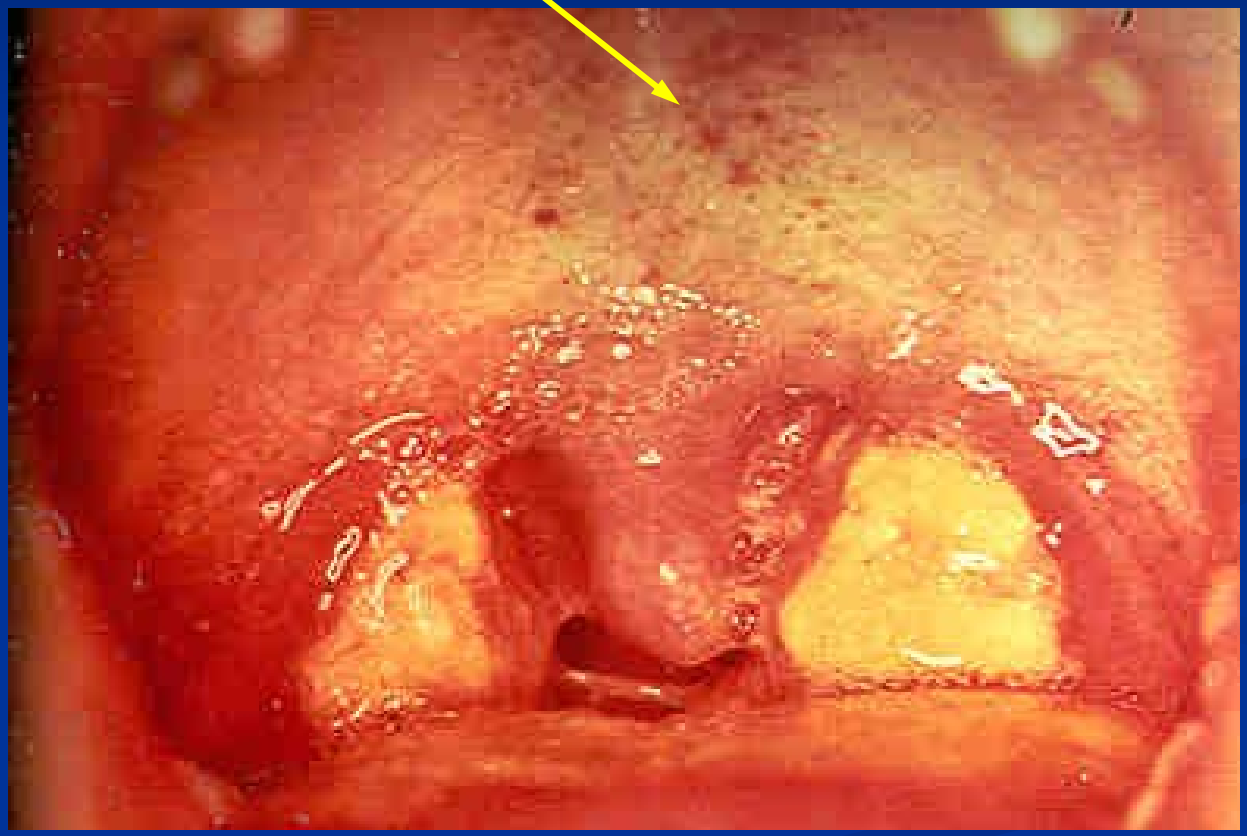
- **Cutaneous presentation**: edema of eyelids, macular or morbilliform rash. Macular eruption on trunk.

- **Mucous membranes** with 5-20 pinhead sized petechiae at junction of soft and hard palate. (Forsheimer spots). Stomatitis with erythema and ulceration.
- Spread by saliva!

Infectious mononucleosis

- Palatal petechial bleeding – Forsheimer spots
- Necrotizing ulcerative gingivitis during mononucleosis possible, ! diff. dg.

Forsheimer spots



Pseudomembranous tonsillitis in inf. mononucleosis

Oral hairy leukoplakia

- Associated with chronic shedding of EBV in the oral cavity in profound immunodeficiency.
- Presentation: Poorly demarcated, irregular, white plaques on lateral aspect of tongue.
- Cannot be removed by scraping (x thrush).
- In immunosuppression (esp. AIDS), HIV workup!
- Diagnosis: microscopy, in situ hybridization
- Management: diagnosis + immunosuppression treatment

Oral hairy leukoplakia

Human herpesvirus 6 and 7

- Roseola infantum (sixth disease)
  - Presentation: Onset of high fever resolving in about 4 days, followed by a morbilliform erythema of rose colored macules on neck, trunk and buttocks, less commonly on the face and extremities.
    - Lesions may be surrounded by halo.
    - Complete resolution in 1-2 days.
- HHV 6 infection is nearly universal.
- HHV 7 similar to 6. May occur later.
- In adults may resemble to mononucleosis.

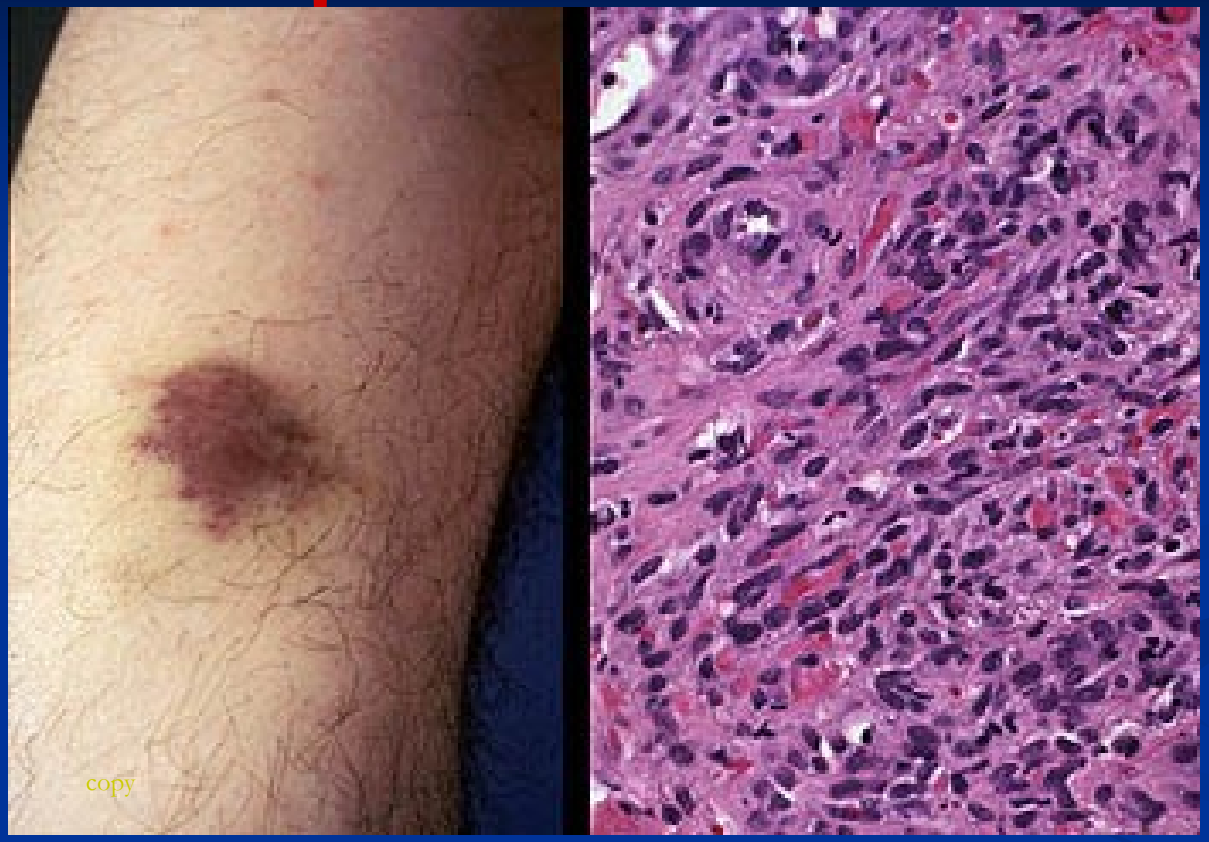
Roseola infantum

Human herpes virus 8

- HHV-8 associated with Kaposi sarcoma in virtually all cases.
  - Includes AIDS, post-transplant, African and Mediterranean cases.
  - HHV-8 is found in KS lesions, saliva, blood and semen of infected individuals.
- Associated with body cavity based B-cell lymphoma.
- Lesions on mucosal membranes possible, usually starts on skin.

Kaposi‘s sarcoma

Kaposi's sarcoma



Plump spindled cells outlining vascular spaces

Enteroviruses – Coxsackie A

- herpangina
- hand-foot-and-mouth disease; acute lymphonodular pharyngitis
- Transmission: fecal-oral
- 50-80% of infections are asymptomatic
- Possible skin rash, mimics other virus infections
- Common cause of meningitis, myocarditis
  - Children <10
  - Sore throat (herpangina) + vesicles; fever; cutaneous lesions including hand and feet (hand, foot and mouth disease)

Hand, foot and mouth disease herpangina

In mouth similar lesions: red macules→ fragile vesicles → ulcerations. Healing in 7-10 days

Measles

- Rubeola
- Transmission: direct droplet contact; incidence greater in winter-spring months
- Incubation: 2 weeks
- Rash evolves from face to trunk to extremities (including palms and soles)
- Fever and the three Cs: cough, coryza and conjunctivitis
- **Koplik spots**: multiple little white-bluish macules on red background, on the oral (buccal) mucosa opposite to the molar teeth; prior to exanthema; epithelial necrosis
- In malnutrition – necrotizing ulcerative stomatitis, noma, candidiasis
- in early childhood – odontogenesis affected, enamel hypoplasia

Measles

- Complications common (20%), in children and young adults:
- Malnutrition esp. vitamin A deficiency is a major cause of mortality
- Complications include:
  - Otitis media
  - Pneumonia
  - Encephalitis (incl. subacute sclerosing panencephalitis)
- Vaccination

Rubella

- German measles, togavirus
- Transmission: respiratory droplets
- Incubation period: 2-3 weeks
- Infections may be sub-clinical esp. in young children
- Mild to no prodromal phase;
- Rash (nonspecific, difficult to make a clinical diagnosis)
- Adenopathy (swollen lymph nodes)
- **Oral lesions**: small dark red papules on soft palate
- Adults may also get mild arthritis

Rubella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Rubella

- Congenital rubella - the most severe complication
- Most infections and complications occur in the first 16 weeks of pregnancy (90% transmission rate to fetus)
- Infants are born with numerous defects
  - Cardiac abnormalities
  - Cataracts
  - Deafness
  - Brain, liver and organ damage

Human papillomavirus

- Estimated: 10-30% of oral cancers positive for HPV
- Rising tendency in younger patients
- Possible gradual decrease due to vaccination
- +-70 subtypes documented, high risk types 16, 18; low risk 6, 11
- Vaccination

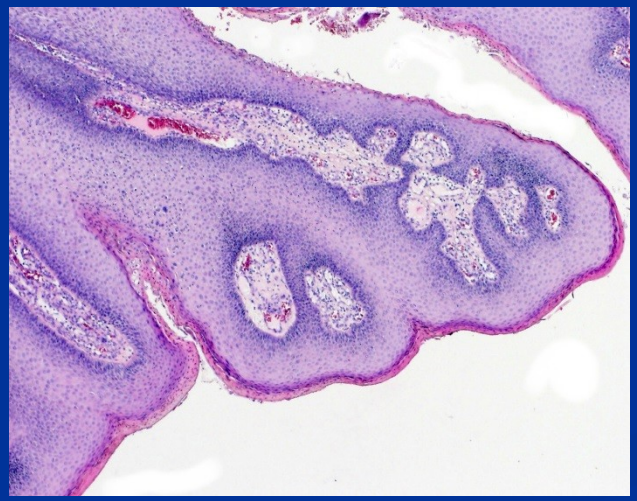
Human papilloma viruses

- HPV lesions commonly self-limited in immunocompetent people.
- Long-standing HPV lesions most commonly in immunocompromised individuals.
- Diagnosis based on history, clinical appearance, and biopsy.
- Common in early HIV infection.
- Spiky warts, raised, cauliflower-like appearance.

Papilloma lesions of the oral cavity

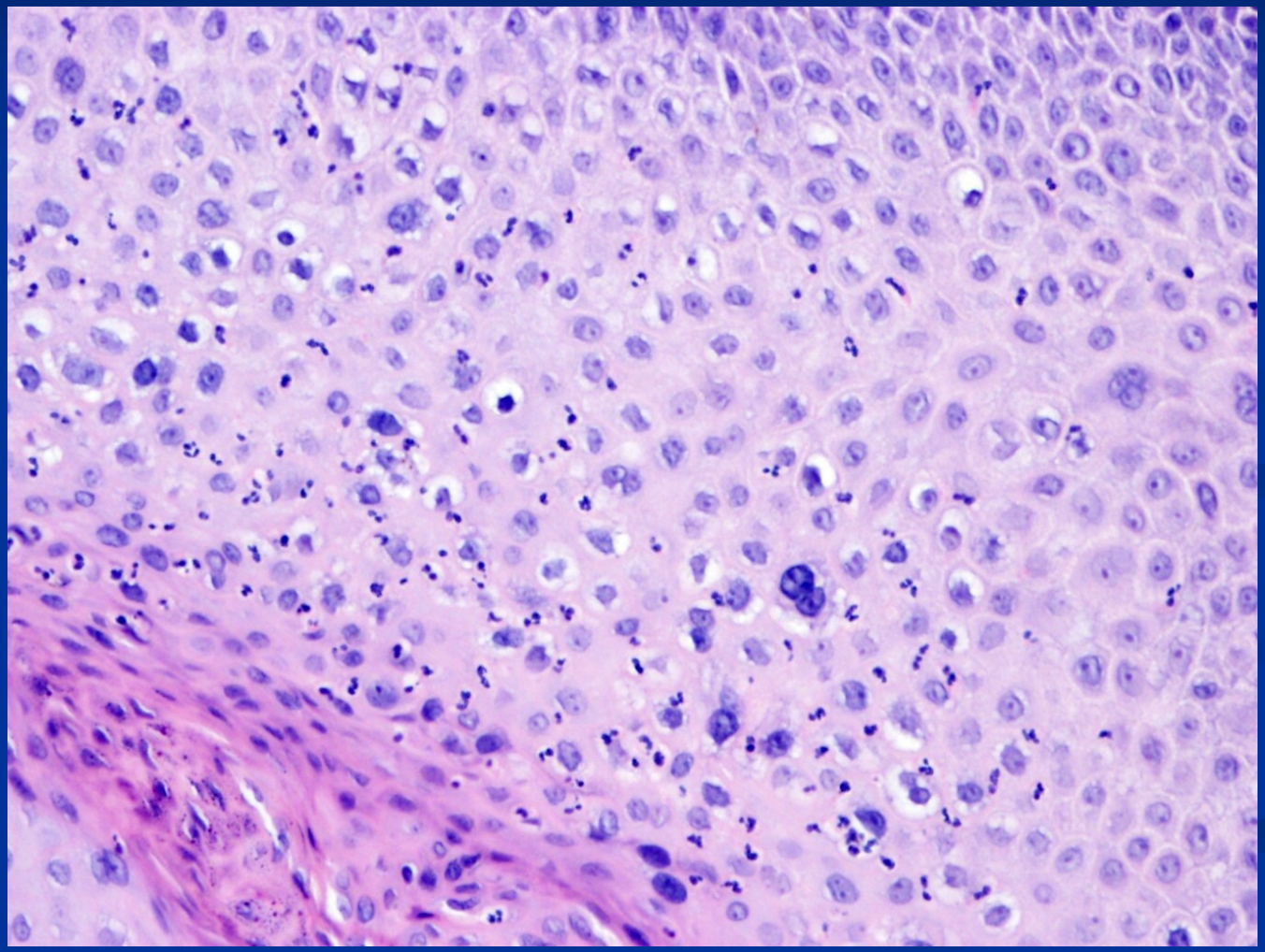
Squamous papilloma:

- Most common in 30 - 50 yr old
- Possible in males and females
- HPV-6, 11 in 50% of the lesions
- Tongue and soft palate common sites



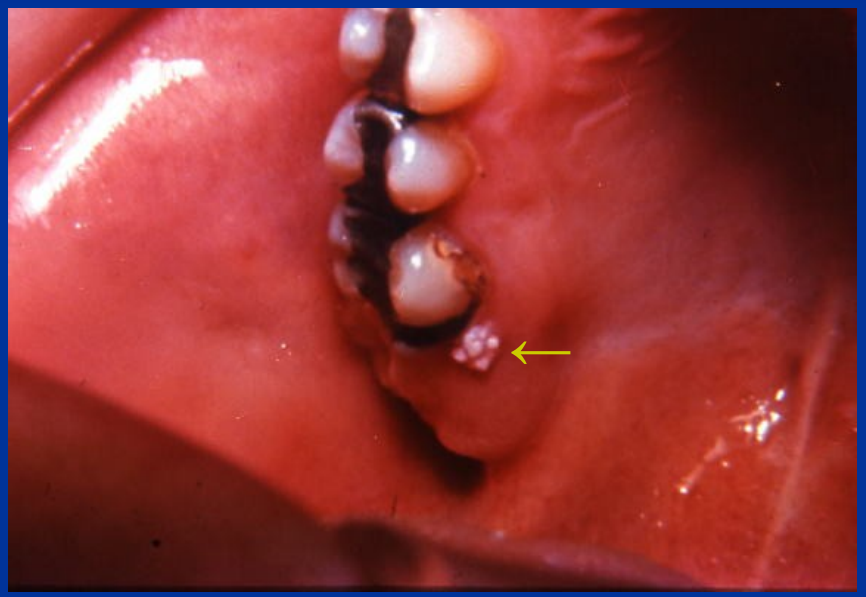
Finger-like projections with fibrovascular core

HPV: koilocytic change of epithelia (perinuclear halo, shrinked nucleus)

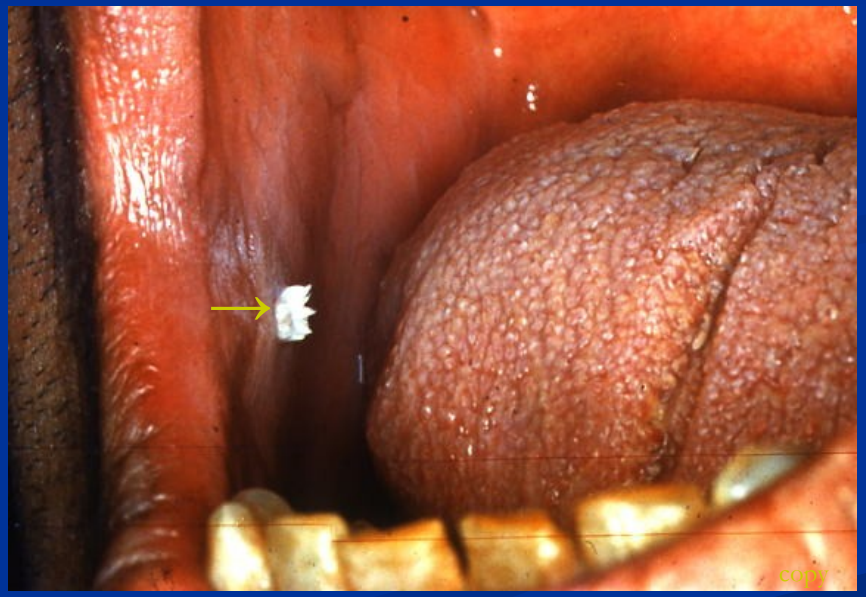


Verruca vulgaris

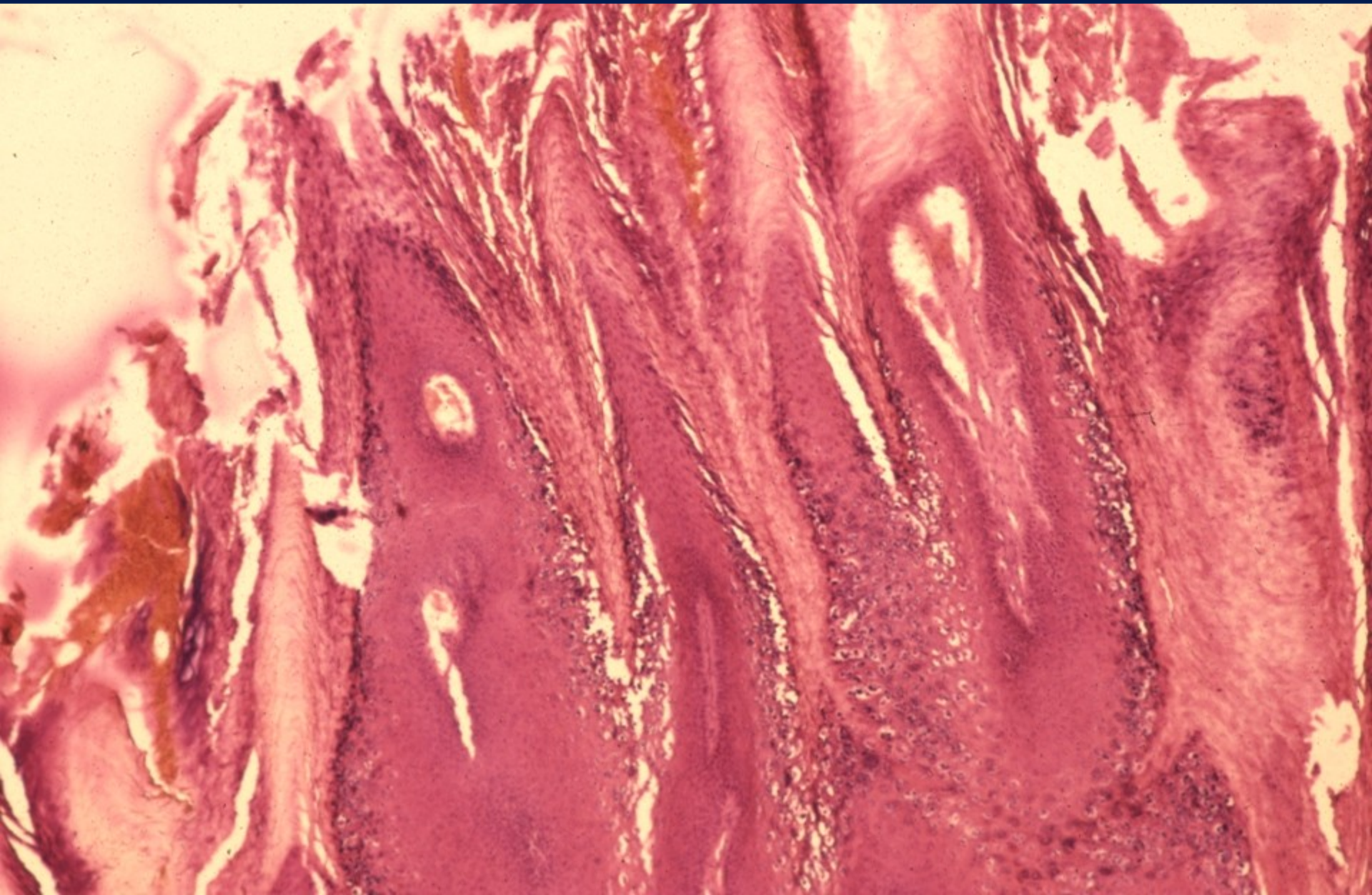
Attached gingiva



Labial/buccal mucosa



Verruca vulgaris



Condyloma accuminatum (venereal vart)

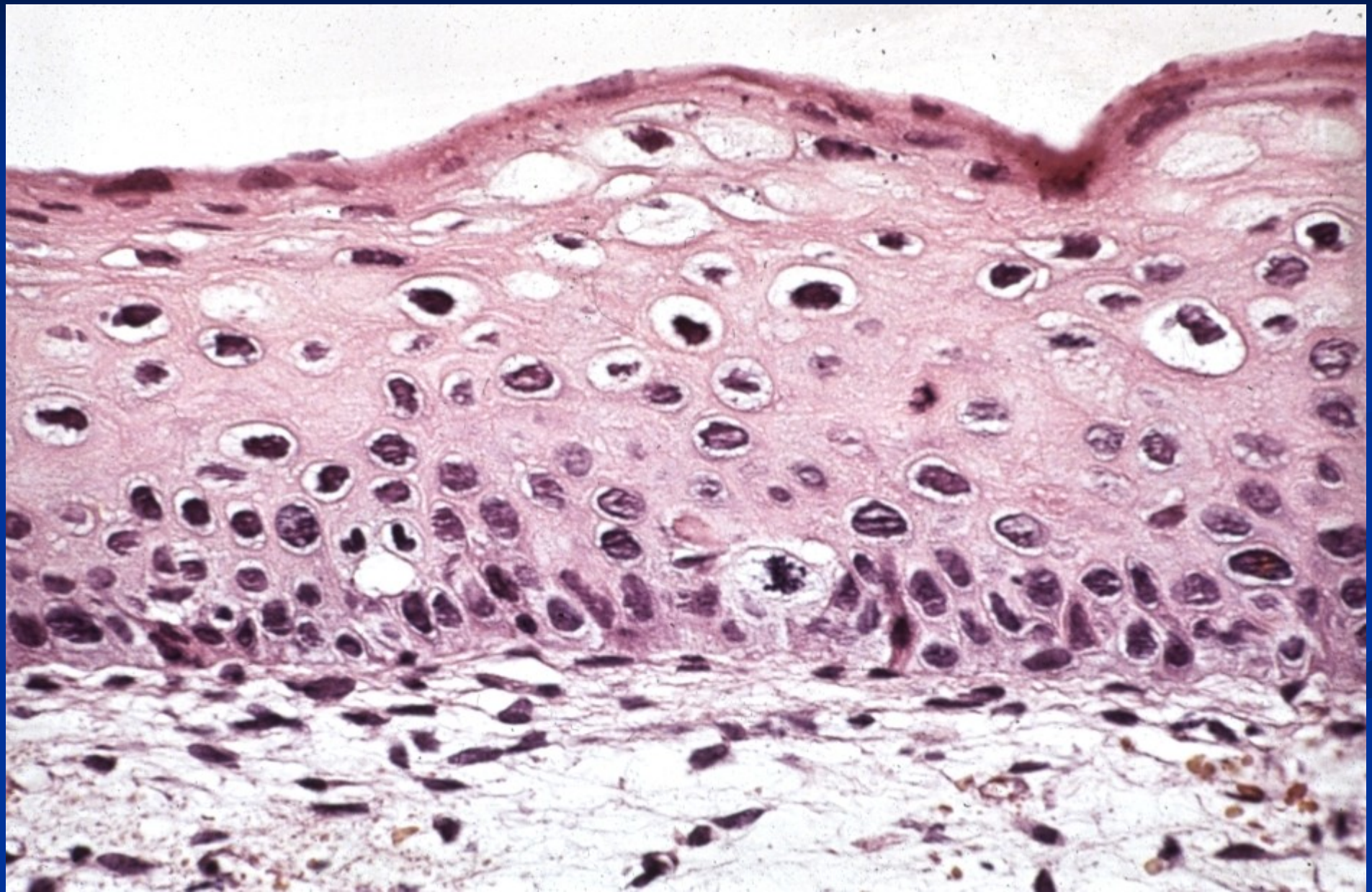
STD associated lesion.

Mouth and genitalia.

HPV- 6, 11, ...

Complete virions produced

HPV mild dysplasia, **koilocytes**



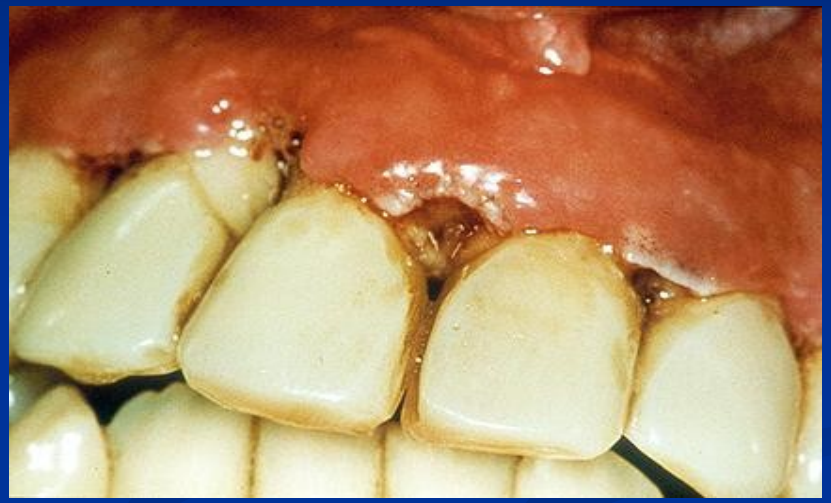
Acquired immunodeficiency syndrome (AIDS)

- Oral lesions - prominent features of AIDS and HIV infection.
- Oral lesions due and according to the rate of loss of T-helper cells.
- Early studies: approximately 90% of HIV+ patients will present with at least one oral lesion in the course of their illness.
- Current studies report the prevalence or oral lesions has significantly declined
(HAART – highly active antiretroviral therapy)

Special importance of oral health in HIV patients

Oral lesions in patients with HIV may be particularly large, painful or aggressive

Aphthous ulcerations



Necrotizing ulcerative periodontitis

HIV/AIDS oral-pharyngeal syndromes

- Interferes with oral hygiene

  → more oral+pharyngeal pathology

- Interferes with nutritional intake

  → wasting syndrome

  HIV treatment compliance may be impacted by oral pain, xerostomia, dysphagia

- Psychosocial dimensions

  Avoidance of social contact due to facial appearance

  Depressive effects of persistent oral pain

Medications

- HIV patients frequently on numerous antiretroviral medications with complex dosing regimens.
- Numerous drug-to-drug interactions documented.
- Complete list of all medications essential to minimize potential adverse drug interaction to medications that may be prescribed by the dental provider.

Lesions strongly assoc. with HIV

- Candidiasis – erythematous, hyperplastic, pseudomembranous
- Hairy leukoplakia (EBV)
- HIV-associated periodontal disease – HIV gingivitis, NUG, HIV periodontitis, necrotizing stomatitis
- Kaposi sarcoma (HHV-8)
- Non-Hodgkin malignant lymphoma (EBV)

Lesions less assoc. with HIV

- Atypical ulceration (oropharyngeal)
- Idiopathic thrombocytopenic purpura
- Salivary gland lesions – xerostomia, major salivary gland enlargement
- Opportunistic viral infections (CMV, HSV, VZV, HPV)
- Opportunistic bacterial infections (Mycobacterium avium-intracellulare)
- Opportunistic fungal infections (aspergillosis, histoplasmosis)

Lesions possibly assoc. with HIV

- Bacterial infections other than gingivitis/periodontitis
- Melanotic hyperpigmentation
- Neurologic disorders (n. facialis palsy, trigeminal neuralgia)
- Squamous cell carcinoma (HPV)

HIV/AIDS oropharyngeal syndromes – most common

- Candidiasis 28%-75%
- Necrotizing gingivitis
- HSV, CMV, HIV, EBV ulcers
- Recurrent aphthous ulcers
- Drug-derived ulcers
- Kaposi sarcoma
- Dental abscesses

Candidiasis

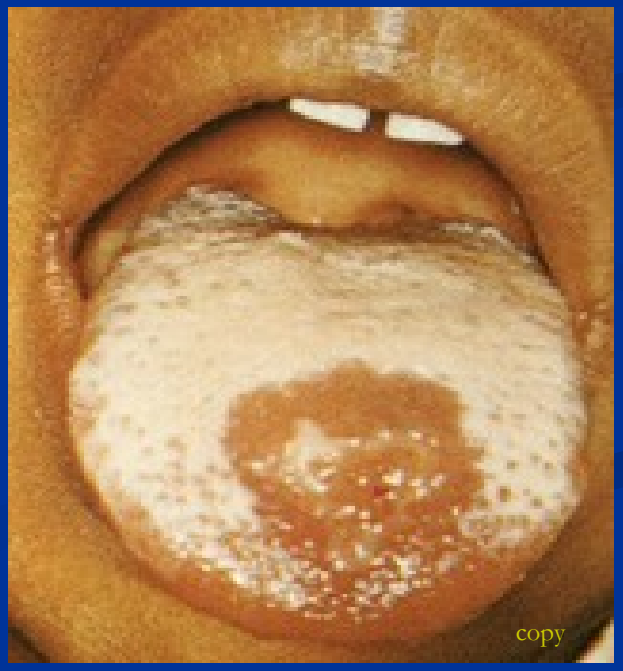
- Candida albicans in immunodeficient patients (HIV, iatrogenic – chemo/radiotherapy, posttransplant, other immunosuppressive therapy)
- Commonly chronic multifocal lesions
- Forms: **pseudomembranous**

  erythematous (palate, tongue ~ median rhomboid glossitis)

  hyperplastic (cheeks)

  angular cheilitis

Oral-pharyngeal candidiasis



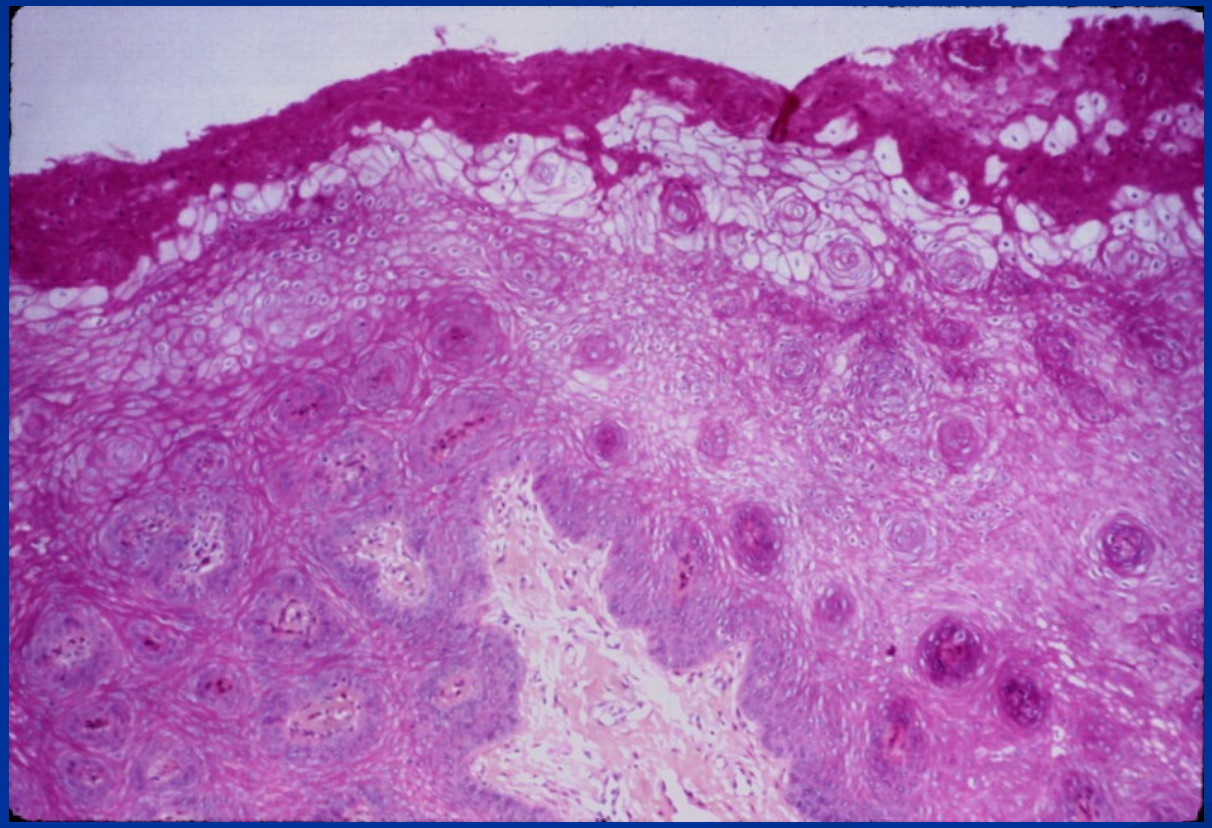
Hairy leukoplakia

- Possible *early* manifestation of AIDS status.
- Filamentous white plaque (hyperkeratotic, non-removable) uni-/bilaterally on lateral borders, anterior portion of the tongue.
- Borders irregular or jagged in contour, sharply delineated.
- Possible on entire dorsal surface of the tongue. On buccal mucosa flat appearance.
- Micro: acanthosis, parakeratosis

Hairy leukoplakia

The surface texture is grainy, rough or „shaggy“ in appearance.

Oral hairy leukoplakia



Differential diagnosis

- Physiologic hyperkeratosis.
- Idiopathic leukoplakia.
- Lichen planus.
- Hyperplastic candidiasis.

HIV-associated periodontal disease

- HIV-associated periodontis resembles acute necrotizing ulcerative periodontitis superimposed on rapidly progressive (necrotizing ulcerative) gingivitis, possible progression into necrotizing stomatitis.
- Other symptoms include:
  - Interproximal necrosis and cratering
  - Marked swelling
  - Intense erythema over the free and attached gingiva
  - Intense pain
  - Spontaneous bleeding and bad breath

Atypical periodontal disease in a patient with HIV infection.

HIV-associated gingivitis

- Linear gingival erythema: a bright red line along the border of the free gingival margin (atypical gingivitis).
- Possible progression over the attached gingival and alveolar mucosa.
- Not specific for HIV, possibly due to hyperemia, candidiasis?

HIV gingivitis

Opportunistic infections

- Important for diagnosis and prognosis (type according to the CD4+ T-cell count)
- Common antibiotic/antiviral/antifungal prophylaxis for opportunistic infections
- Inflammation
- Malignancies

Kaposi sarcoma (KS – HHV-8)

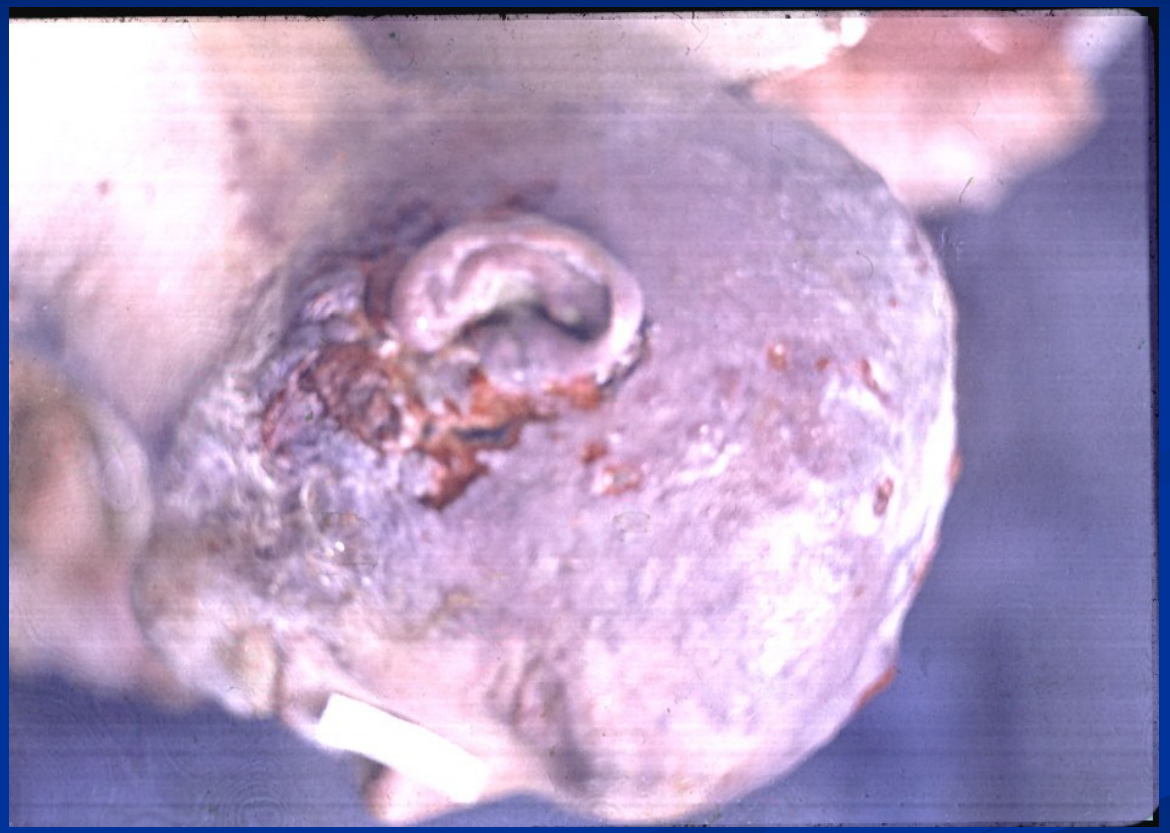
Non-Hodgkin lymphoma (NHL - EBV)

Squamous cell carcinoma (SCC – HPV)

Kaposi sarcoma

- Kaposi sarcoma: HHV-8 opportunistic infection in immunodeficiency
- Vascular – endothelial sarcoma
- Solitary or multiple bluish, blackish, or reddish macules – elevated lesions - ulcerations.
- Kaposi sarcoma is one of the intraoral AIDS–defining lesions.

Kaposi sarcoma



HIV cervical lymphadenopathy

- Enlargement of the cervical (neck) nodes.
- Lymphadenopathy frequently seen in association with HIV – PGL – persistent generalized lymphadenopathy
- Diff. dg. x ML, metastasis

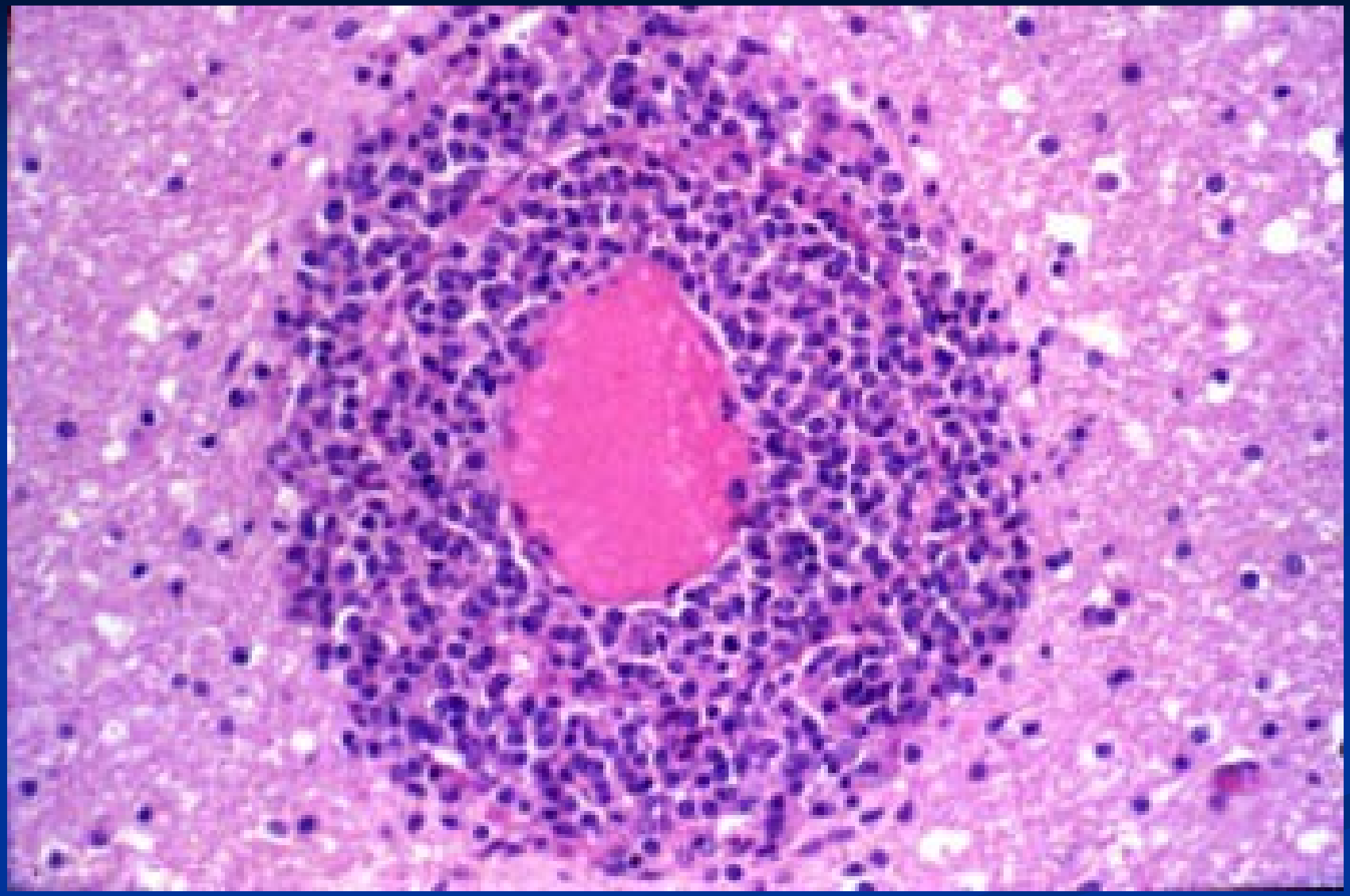
HIV cervical lymphadenopathy

HIV lymphoma

- Solitary lump or nodule, swelling, or nonhealing ulcer anywhere in the oral cavity.
- The swelling possibly ulcerated or covered with intact, normal-appearing mucosa.
- Usually painful, the lesion grows rapidly in size, may be the first evidence of lymphoma.
- Common association with EBV
- Several histopathologic types, atypical localization

HIV lymphoma

Primary malignant lymphoma (brain)



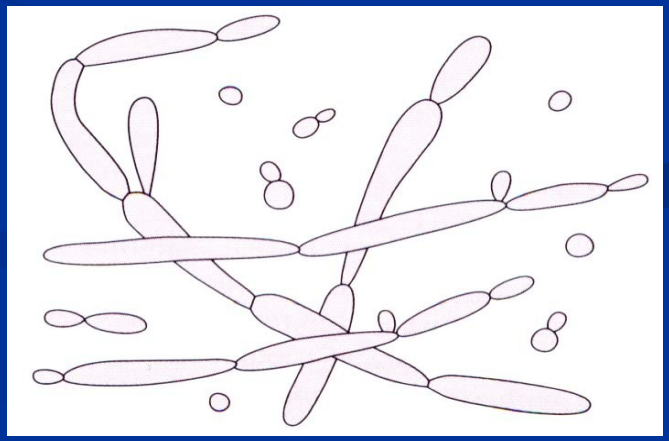
HPV lesion on the lip of a patient with AIDS.

Fungal infections

- Candidiasis:
- Histoplasmosis
- Blastomycosis
- Cryptococcosis
- Aspergillosis
- ...

Candida albicans and other *Candida* species

- Harmless inhabitants of the skin and mucous membranes of all humans
- Normal immune system keeps candida on body surfaces - **skin and mucous membranes integrity**
- **Presence of normal bacterial flora**
- Opportunistic infection



The most important risk factors

- Neutropenia, anaemia (acquired in leukemia, radio/chemotherapy, …)
- Diabetes mellitus
- AIDS
- SCID + other inborn immunodeficiencies (myeloperoxidase defects)
- Broad-spectrum antibiotics, steroids
- Local factors – trauma incl. chronic (denture), hygiene, smoking, carbohydrate diet, xerostomia

The most important risk factors

- Indwelling catethers
- Major surgery
- Organ transplantation
- Age dependent – neonates, very old
- Severity of any illness
- Intravenous drug addicts
- Poor nutritional status

Candidiasis

- Confirmation with KOH smear, tissue PAS or silver stains
- Treatment - topical or systemic
- Primary problem treatment

Candidiasis

- Symptoms: burning, dysgeusia, sensitivity, generalized discomfort
- Angular cheilitis, coinfection with staph. may be present
- Acute - atrophic red patches or white plaque-like surface colonies.
- Chronic - denture related form confined to area of appliance

Candidiasis

- Acute (and chronic in immunocompromised)
  - Pseudomembraneous („Thrush“) - white
    - *DOES* scrape off
  - Atrophic („Erythematous“) - red
    - (Does *NOT* scrape off)
- Chronic
  - Hyperplastic („Candidal leukoplakia“) - white
    - (Does *NOT* scrape off)

Candidiasis

- Candida-associated primary oral lesions

  Denture stomatitis

  Angular cheilitis

  Median rhomboid glossitis

- Secondary oral lesions in generalized candidiasis

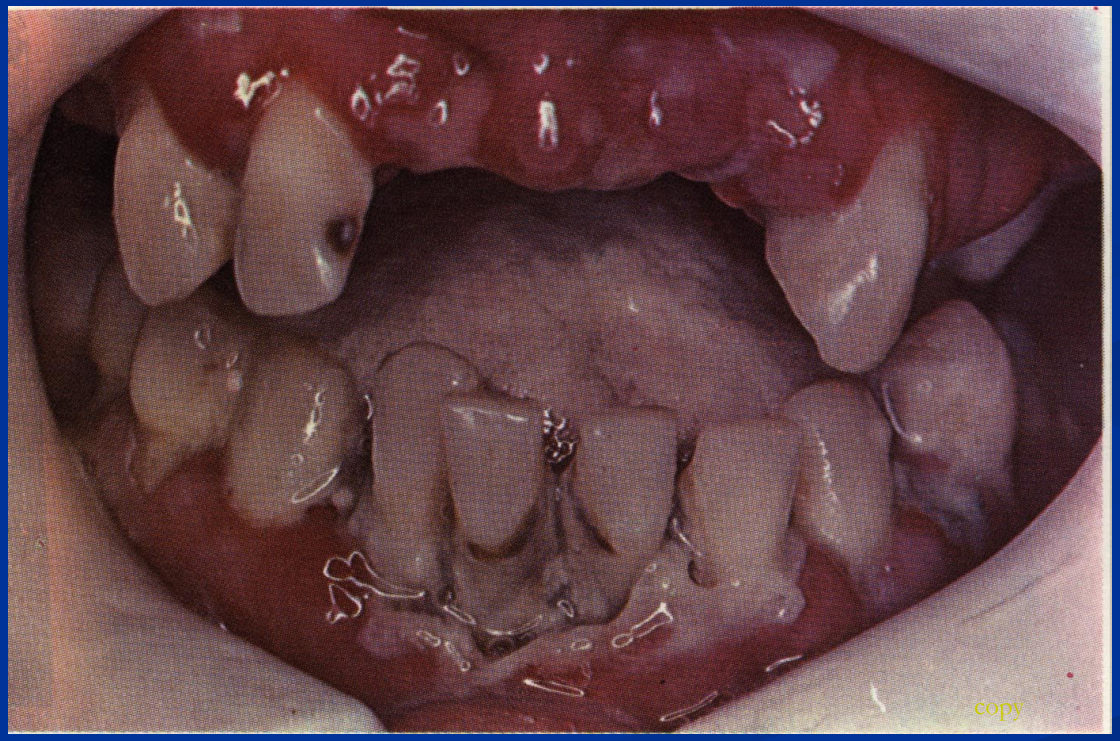
  Systemic mucocutaneous c.

Candidiasis: Acute pseudomembraneous

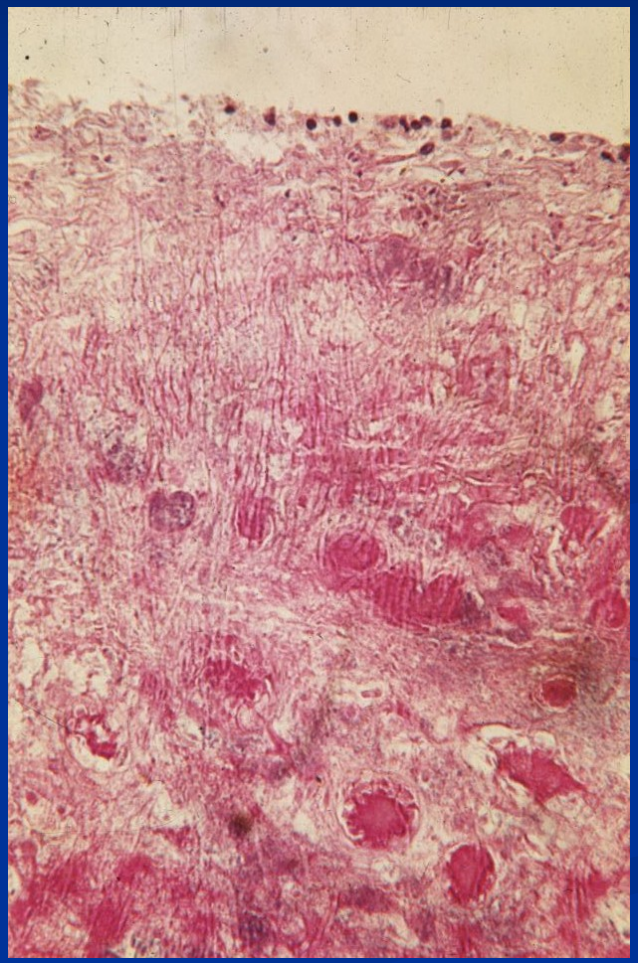
- White thick lesion - trush
- Underlying tissue: erythematous, haemorrhagic, pruritic
- Superficial necrosis + hyphae + yeast forms, infl. infiltrate – mostly neutrophils
- Newborns, old debilitated p., p. with risk factors

Thrush/ Candidiasis

Candidiasis



Pseudomembrane with yeasts



Erythematous candidiasis.

Mainly on tongue + palate,
in ATB/corticosteroid therapy
(ATB sore tongue) –
microorganism dysbalance
red, painful

Candidiasis: Chronic hyperplastic - candidal leukoplakia

- Keratotic plaques or papules, white, rough surface (no scraping off), erythematous background, vague borders
- Hyperkeratosis with acanthosis, oedema, neutrophils + microabscesses, plasma cells + lymphocytes in stroma
- Sites: labial commissure, labial, buccal vestibule
- Risk factors: smoking, poor oral hygiene (dentures), xerostomia
- Cancer risk: Biopsy mandatory of all speckled erythroplakia or erythroleukoplakia,↑ SCC risk reactive atypia x dysplasia

Candidiasis: Red chronic oral lesions

- Angular cheilitis – Perleche (poor oral closure, saliva accumulation)
- Median rhomboid glossitis
- Denture stomatitis – atrophic c. on palate

Angular cheilitis (Perleche)

- Labial commisures, moist fissures
- Elderly – facial and dental architecture
- Youth – thumbsucking, lollipops
- Thrush in DM II or HIV
- Multifactorial: candida associated, Str., Staph., deficiency of iron, riboflavin, vitamin A, E, etc.
- Erythema, fissuring, pain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Candidiasis

Angular chelitis

Median rhomboid glossitis

- Shiny oval or diamond shaped elevation, midline, directly in front of the circumvallate papillae. Asymptomatic.
- *Candida* species may be present + trauma
- Micro: Chronic inflammation with fibrosis with possible hyphae in areas of parakeratosis, loss of papillae


copy

Denture stomatitis

- Tissue trauma – dentures + poor hygiene → secondary c.
- Palate: erythema, oedema, symptomless
- Localized – spotty erythema
- Generalized – diffuse erythema
- Chronic inflammatory papillary hyperplasia – erythema + rough granular surface
- Micro: superficial overgrowth, no epithelial invasion by c.

Hairy tongue

- Diffuse elongation of the filiform papillae of the dorsum surface of the tongue
- Candida usually present (exfoliative cytology)
- Superficial candidiasis stimulates epithelial hyperplasia to produce the thickened layer
- Coffee, tea, tobacco - secondary staining - black hairy tongue

Hairy tongue

Chronic mucocutaneous candidiasis

- Persistent superficial infection – oral + other mucosae, skin + adnexa
- Immunodeficiency, endocrine dysfunction

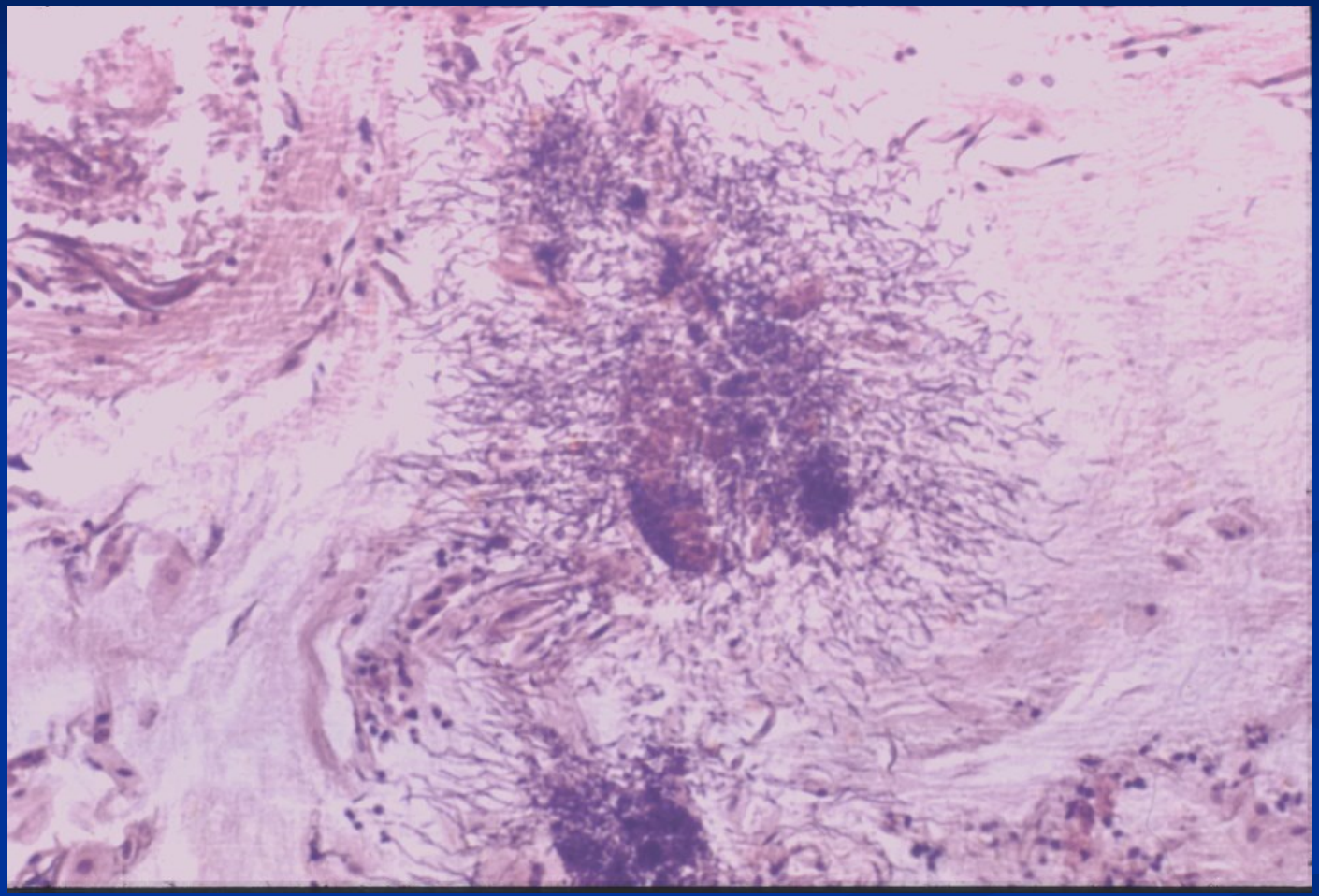
Invasive fungal infections

- Fungi that commonly cause invasive infection can be divided into two groups:
  - Opportunistic fungi, (that occur widely)
    - e.g. *Aspergillus* spp., *Candida* spp., *Cryptococcus*, *Zygomycetes*
  - Geographically defined, „dimorphic fungi“
    - e.g. *Histoplasma capsulatum*
    - *Coccidioimycosis*

Invasive fungal infections

- Diagnosis
  - Microscopic
    - Secretions, KOH
    - Histology
- Culture
  - ! may occur as a contaminant
- Laboratory (antigenes, PCR)

Fungal colony



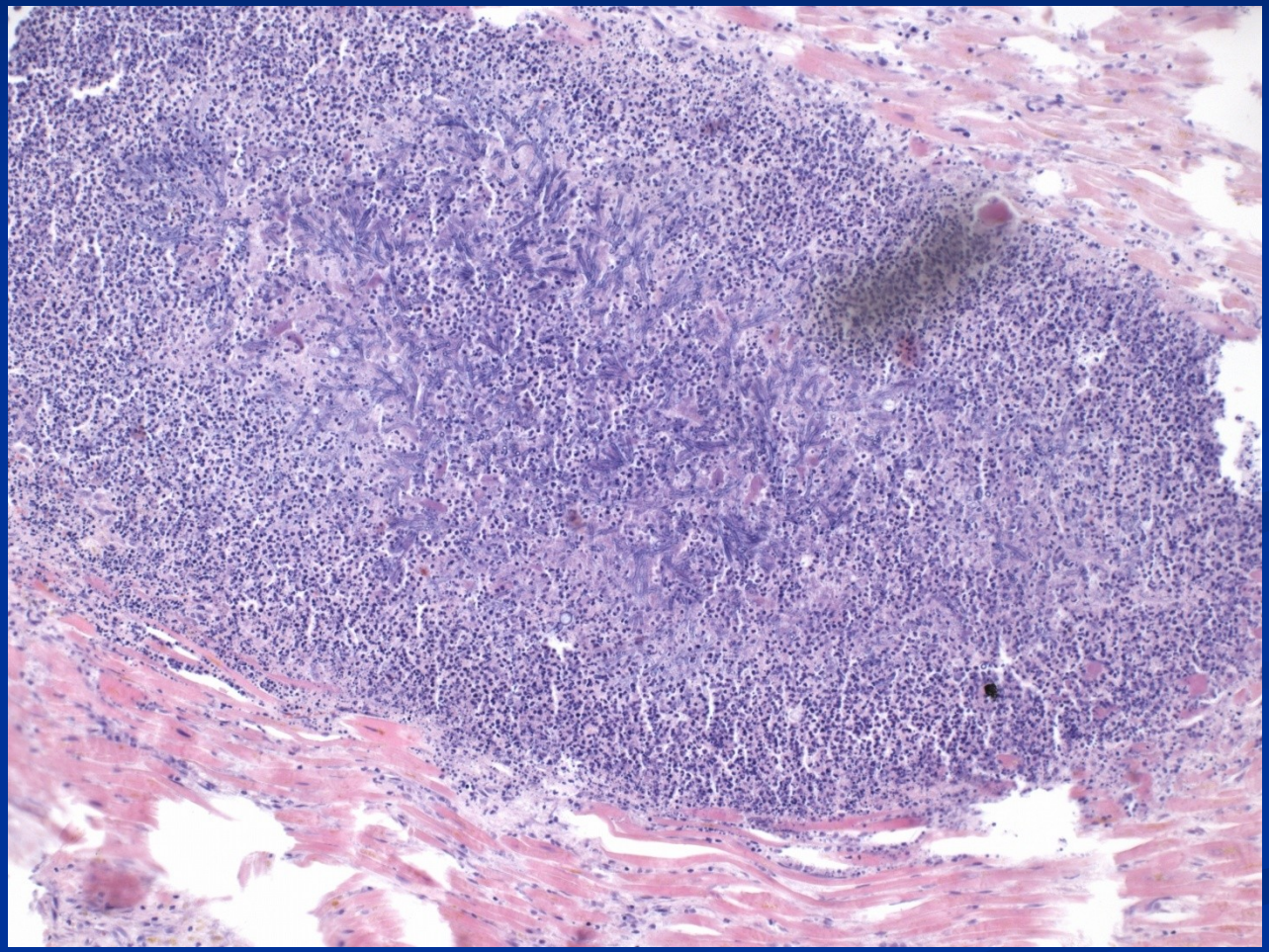
Invasive candidiasis

- Usually begins with candidemia (but in only about 50% of cases candidemia can be proven)
- If phagocytic system normal, invasive infection stops in this stage
- Progression – secondary deep visceral candidiasis

Invasive fungal infections

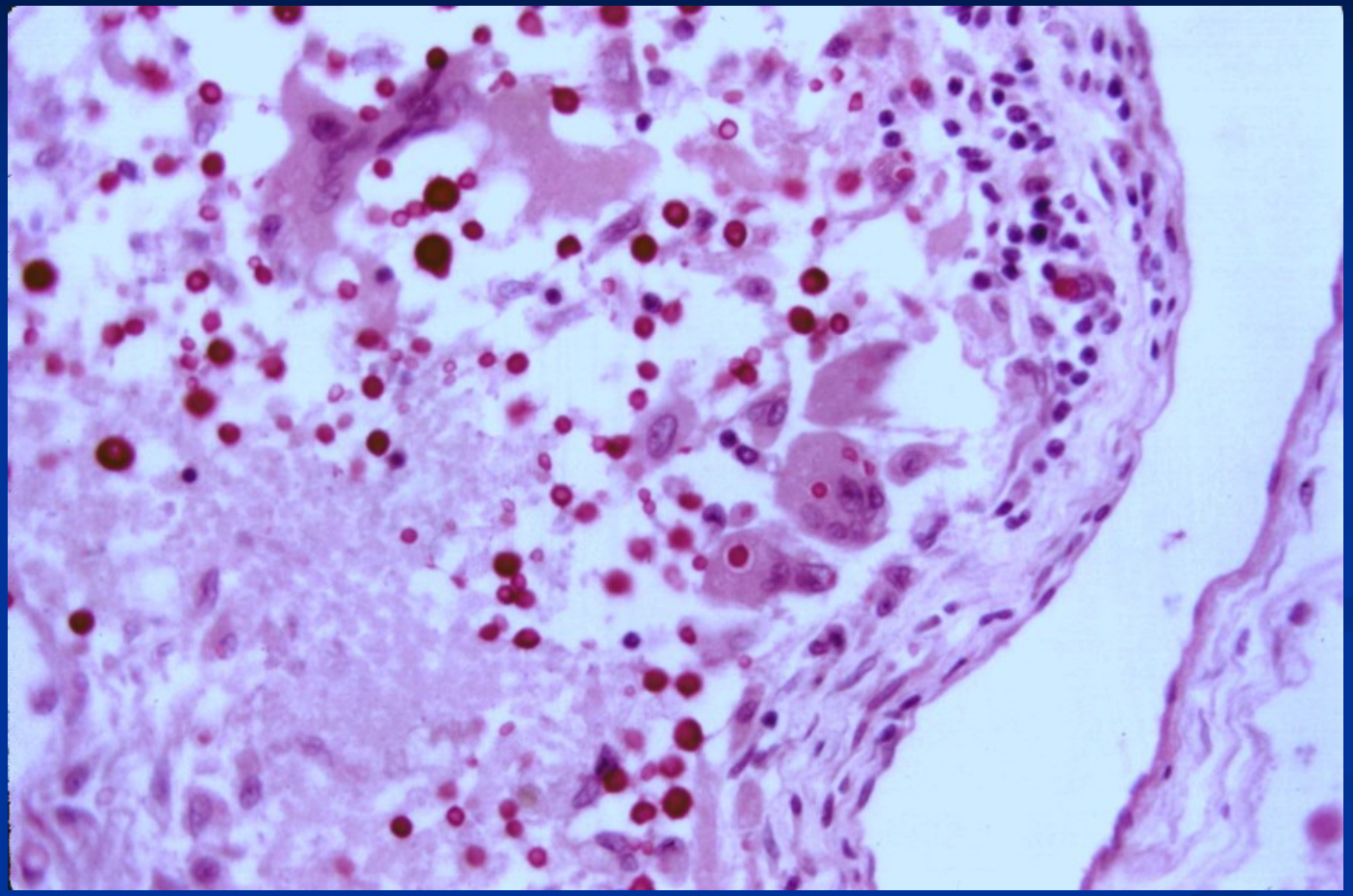
- *Aspergillus* spp (esp. *A. fumigatus*)
  - Epidemiology
    - Widespread, grows on rotting vegetation. Spores commonly present in air. Important predisposing factor: immunosuppression
  - Clinical presentations
    - Allergic bronchopulmonary aspergillosis - Asthma-like symptoms. - Fungus grows in bronchial secretions.
    - Aspergilloma (fungal ball) - develops in cavities (- lungs, sinuses).
    - Invasive disease - tissue destruction, pneumonia.

Invasive aspergillosis



Cryptococcus

- Mostly in immunosuppressed
- Primary infection in the lungs
- Secondary dissemination (meninges, skin, bone)
- Oral lesions possible – nonhealing ulcers
- Dg. – biopsy – thick mucoid capsule

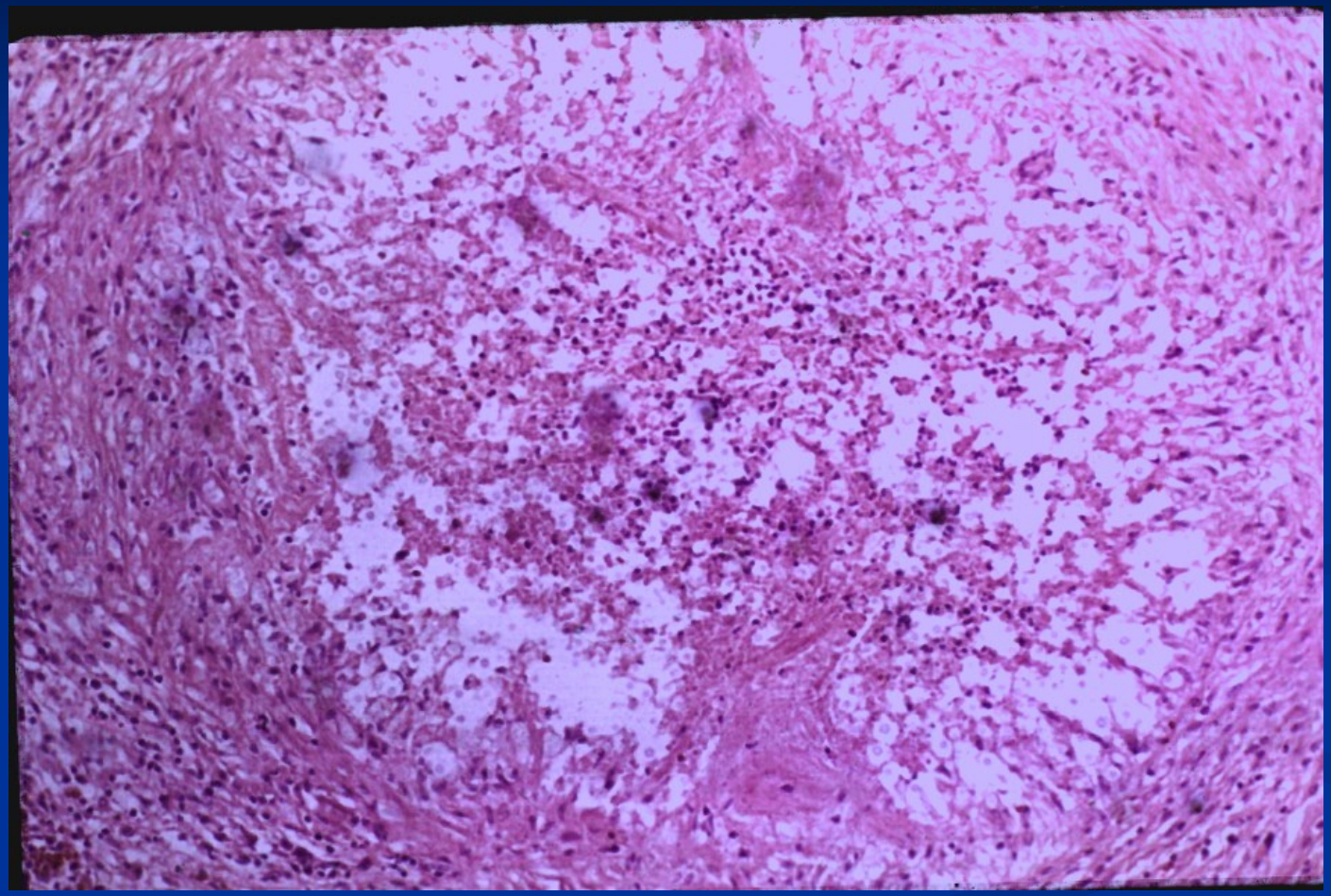


Cryptococcal meningitis

Histoplasmosis

- In US the most common systemic fungal infection
- In non-immunocompromised: mild, self limited acute lung disease
- In immunosuppressed: chronic; disseminated – incl. oral lesions – ulcers (x ca!, biopsy)
- Micro – macrophagic reaction +/- granulomas

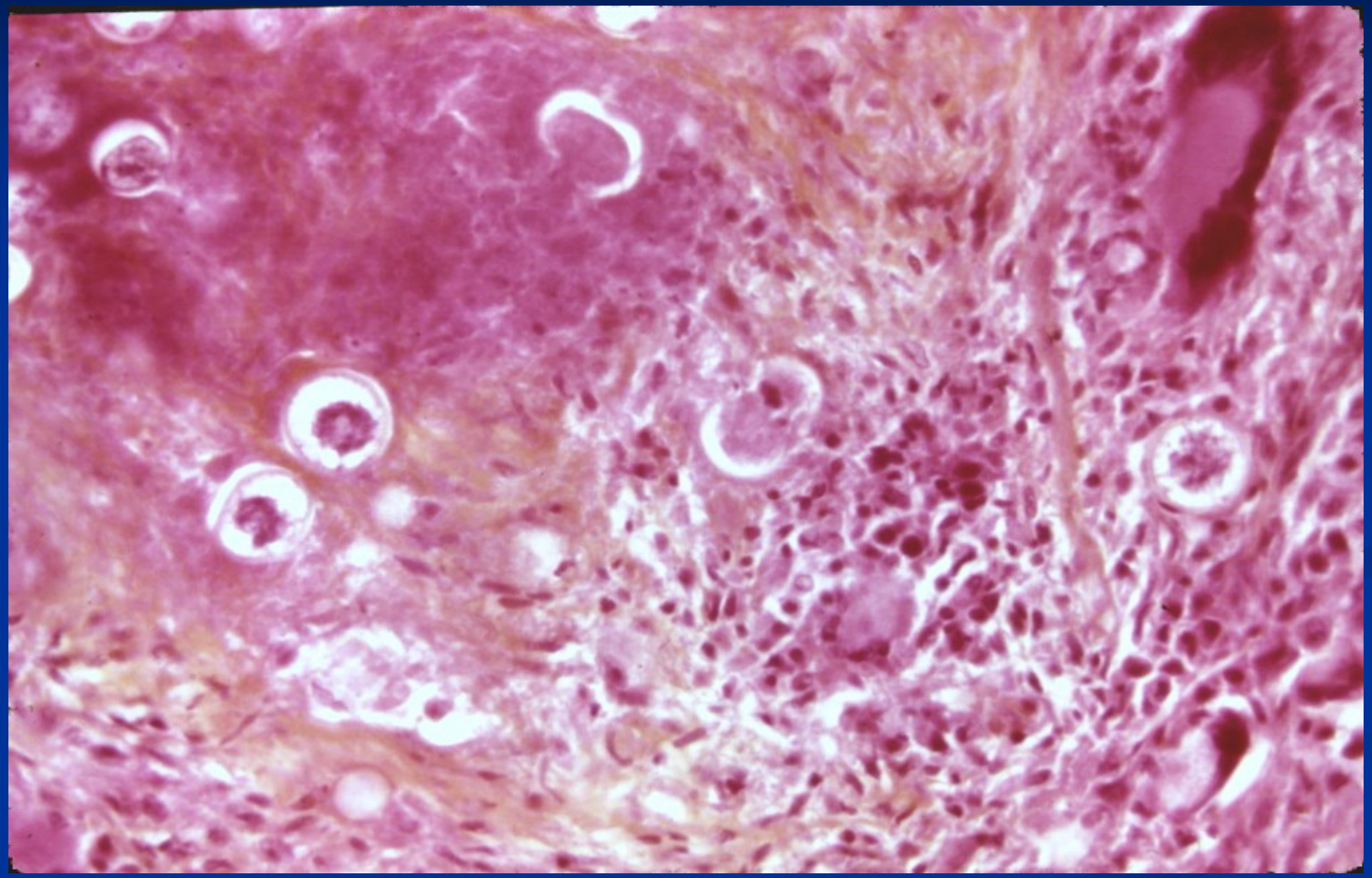
Histoplasmosis



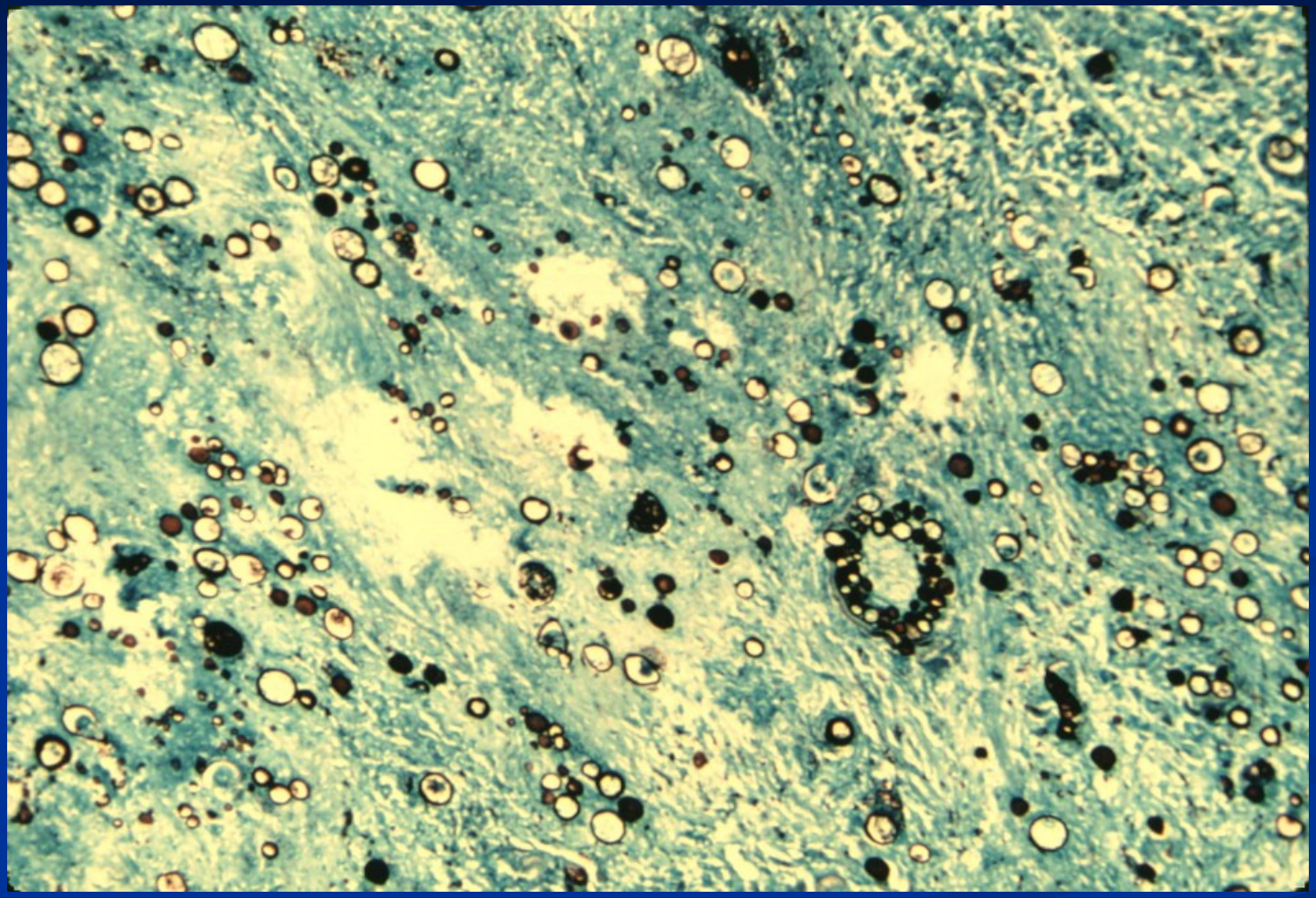
Coccidiomycosis

- Endemic in Americas
- Types similar to histoplasmosis (acute lung dis. – „valley fever“; chronic pulmonary; disseminated)
- Perioral skin lesions possible – papules, abscesses, nodules
- Dg.: biopsy, culture

Coccidiomycosis



Coccidiomycosis



Zygomycosis

Invasive fungal infection (mucormycosis)

Opportunistic in the debilitated, immunocompromised, or acidotic patient.

Aetiology:

Fungal spores in enviroment

Clinical types

1) Rhino-orbito-cerebral
2) Pulmonary
3) Gastrointestinal
4) Cutaneous
5) Disseminated

Zygomycosis

Pathogenesis:

Spore inhalation → germination (hyphae) → local invasion→ nasal mucosa, paranasal sinus, palate, lung

Spread:

- direct extension
- blood vessel invasion → to the orbit and intracranial → ischemia, necrosis, gangrene and brain abscess

Clinical presentation

Fever, facial pain or headache, nasal discharge, epistaxis, visual disturbances, and lethargy

Zygomycosis

Diagnosis: requires a high index of suspicion→ risk factors + evidence of tissue invasion

Biopsy: using fungal stain → broad nonseptate hyphae with right-angle branches

Imaging: X-ray, CT-MRI.