Pharmacotherapy of salivary gland disorders, fungal infections and AIDS.

SALIVARY GLAND DISORDERS

SALIVA

- physiological exudation of three pairs of salivary glands:
  - ✓ parotid
  - ✓ submandibular
  - ✓ sublingual
- secreted reflexively
- composed of the mucous and serous components
- normal secretion of saliva:
  - ✓ at rest (non stimulated) – 0,3 – 0,4 ml/min
  - ✓ stimulated (by chewing paraffin cubes) 1 – 2 ml/min

DISORDERS SECRETION OF SALIVA

Reduce the secretion of saliva

(Xerostomia)

Xerostomia spuria

Xerostomia vera

Typ I

(without mucosal atrophy)

Typ II

(with mucosal atrophy)

Increase the secretion of saliva

(Ptyalismus)

Ptyalismus spuria

Ptyalismus vera

Sialoses

SALIVARY DYSFUNCTION CLASSIFICATION

Pseudo xerostomia (xerostomia spuria) is regarded as a product of **vegetative neurosis** - no changes in the salivary glands, accompanied by a strong burning sensation of tongue

SALIVARY DYSFUNCTION CLASSIFICATION

True xerostomia type I (xerostomia vera) can be caused by:

- neurovegetative system disorders (stress, severe mental experiences, medications)
- certain infectious diseases (eg. inflammation of the parotid glands)
- lithiasis of salivary glands
- diabetes, collagenoses, thyroid diseases
- vomiting, diarrhea, loss of blood

SALIVARY DYSFUNCTION CLASSIFICATION

True xerostomia type II is due to degenerative processes affecting salivary glands:

- Sjögren's syndrome
- Mikulicz disease
- irradiation
- congenital salivary gland aplasia

REDUCE THE SECRETION OF SALIVA

Drugs reducing the secretion of saliva:

- antihypertensive drugs
- anticholinergic drugs
- antidepressants
- sedatives
- appetite suppressants
- antihistamines
- bronchodilators
- cytotoxic drugs

TREATMENT

- systemic disorders require treatment targeted towards underlying disease, which can ameliorate symptoms of dry mouth
- in other cases, symptomatic treatment:
  - ✓ smoking cessation
  - ✓ avoiding alcohol, coffee and tea
  - ✓ frequent drink water and neutral liquids
  - ✓ sugar-free chewing gum
  - ✓ vitamins A, B, A + D, A +E - orally, in therapeutical dosages
  - ✓ salivary substitutes
  - ✓ drugs enhancing salivation

TREATMENT

Drugs enhancing salivation:

- 2% solution of potassium iodide – orally 2x5 ml
- pilocarpine – 0.1% solution for mouth rinsing (15-20 drops for a glass of water) - cholinergic agonist
  - ✓ 5 drops orally three times a day and before bedtime; when taken ~30 min before mealtime, patients may benefit from the increased salivation in eating their meal (the total daily dose should not exceed 30 mg)
  - ✓ adverse effects: increased perspiration, greater bowel and bladder motility, feeling hot and flushed
  - ✓ patients with a history of bronchospasm, severe chronic obstructive pulmonary disease, congestive heart disease and angle closure glaucoma should not take pilocarpine

TREATMENT

Drugs enhancing salivation:

- **cevimeline** - cholinergic agonist, has a higher affinity for M1 and M3 muscarinic receptor subtypes so can enhance salivary secretions while minimizing adverse effects on pulmonary and cardiac function
  - ✓ 30 mg (1 capsule) three times a day
  - ✓ adverse effects: sweating, nausea, rhinitis, dificulty breathing, headache, diarrhea, abdominal pain
  - ✓ patients with uncontrolled asthma, significant cardiac disease and angle closure glaucoma **should not take cevimeline**

TREATMENT

Drugs enhancing salivation:

- **neostigmine** - cholinesterase inhibitor, indirectly stimulates both nicotinic and muscarinic receptors
  - ✓ orally 15-20 mg / day, s.c. or i.m. 0,25-0,5 mg / day
  - ✓ adverse effects: dizzines, cardiac arrhythmias, increased bronchial secretion, dyspnea, nausea, muscle cramps and spasms

In the case of irreversible damage to the salivary gland, with atrophy of secretory cells, administration of drugs enhancing saliva becomes pointless.

TREATMENT

Salivary substitutes:

- **artificial saliva and lubricants - contains mucin or carboxymethyl cellulose**
  - ✓ **Sialin-Sigma – solution, introduced into the oral cavity (a few drops) acts approximately 1-3 hours**
  - ✓ **Aquoral Artificial Saliva Spray**
  - ✓ **Biotene Oralbalance – saliva replacement gel**
  - ✓ **Xerostom – saliva substitute gel**

Without adequate salivary output, oral and pharyngeal health declines along with a person's quality of life.

Frequent oral symptoms of dry mouth (often associated with mealtime):

- altered taste
- difficulty in eating, chewing, and swallowing (particularly dry foods)
- impaired eating without drinking accompanying liquids
- insufficient retention of or poorly fitting removable prostheses
- halitosis
- a chronic burning sensation (stomatodynia)
- intolerance to spicy foods (can affect the quality of a person's life)

These problems can lead to:

- changes in food and fluid selection that may compromise nutritional status
- *choking* as well as an increased susceptibility to aspiration pneumonia (with consequent colonization of the lungs with gram-negative anaerobes from the gingival sulcus)

Management of dry mouth-associated problems

Xerostomia-associated problem	*Management strategy*
Dental caries	Daily use of fluoridated dentifrice (0.05% sodium fluoride) Daily use of prescription fluoride gel (1.0% sodium fluoride, 0.4% stannous fluoride) Application of 0.5% sodium fluoride varnish to teeth Dental examinations at least every 6 months and intraoral radiographs for early diagnosis at every 12 months
Dry mouth	Sugarless gums, mints, lozenges Artificial salivary replacements Prescription sialogogues: pilocarpine 5 mg tid and qds; cevimeline 30 mg tid Lubricants on lips q2h
Dysgeusia	Use of fluids during eating
Dysphagia	Careful eating with fluids Copious use of fluids during meals Avoid dry, hard, sticky and difficult to masticate foods
Oral candidiasis	Antifungal rinses: Nystatin oral suspension 100 000 units ml^{-1}, rinse qid Antifungal ointments: Nystatin ointment applied qid Antifungal lozenges dissolved in mouth qid: Nystatin pastilles 200 000 units; Clotrimazole troches 10 mg; Nystatin vaginal suppositories Denture antifungal treatment: daily hygiene, soak prosthesis for 30 min in benzoic acid, 0.12% chlorhexidine, or 1% sodium hypochlorite
Bacterial infections	Systemic antibiotics × 10 days: Amoxicillin with clavulanate 500 mg q8h; Clindamycin 300 mg tid; Cephalexin 500 mg q6h Increase hydration Salivary stimulation with sugarless gums, mints, lozenges
Poorly fitting prostheses	Soft and hard-tissue relines by dentist Denture adhesives

The complaint of a dry mouth (xerostomia) and the objective finding of salivary dysfunction are common occurrences in older individuals, producing transient and permanent oral and systemic problems.

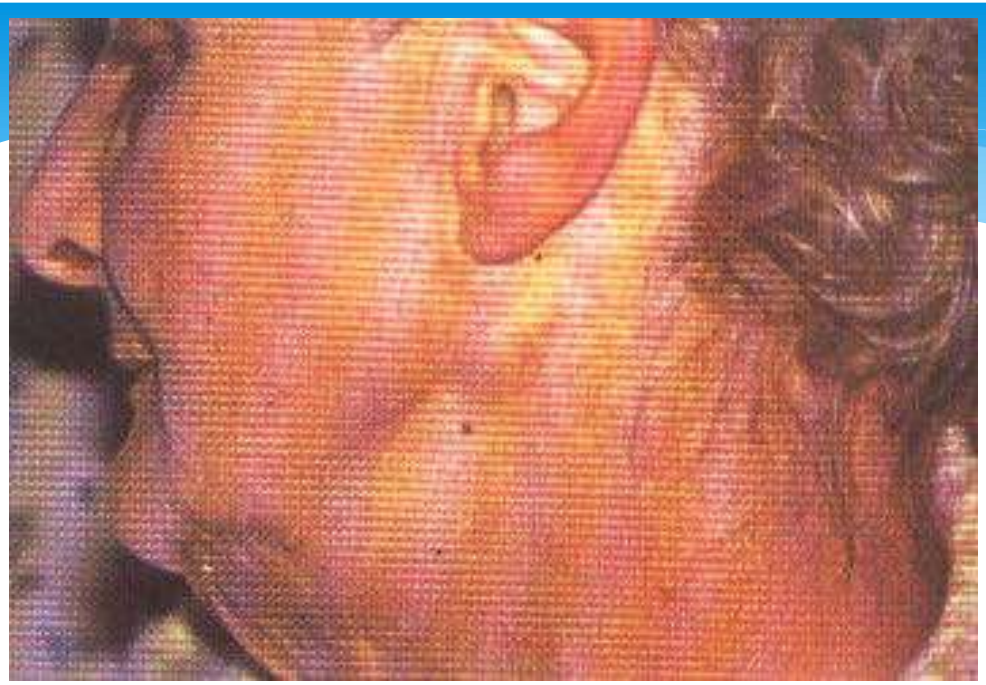
Salivary dysfunction, however, is not a normal consequence of growing older !!!, and is due to systemic diseases, medications, and head and neck radiotherapy.

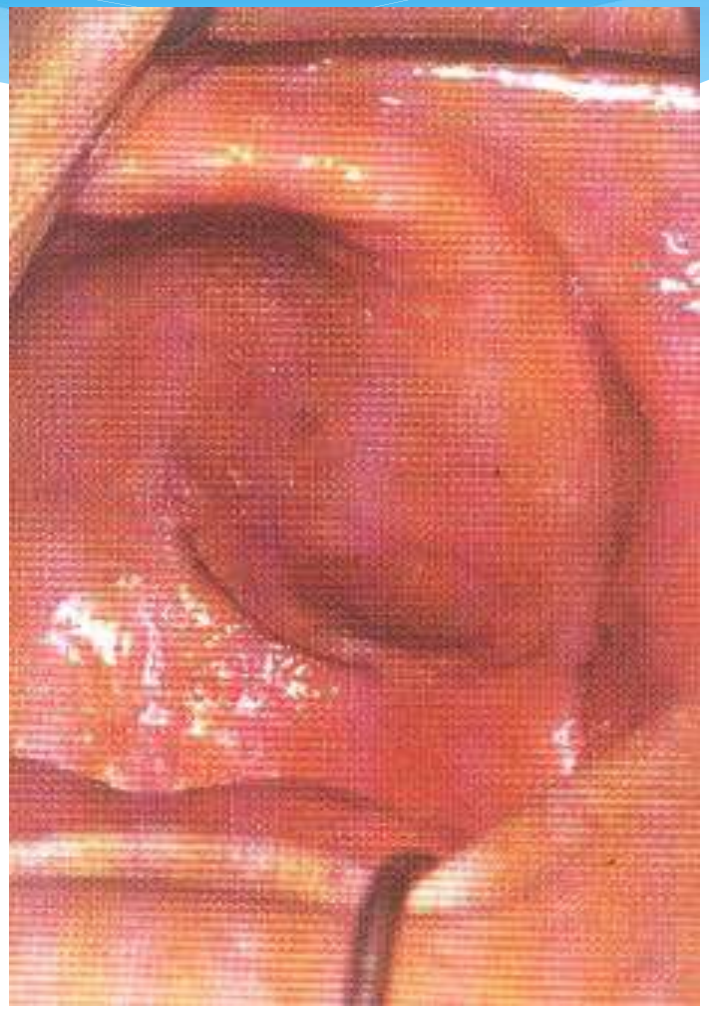
The prevalence of xerostomia and salivary gland disorders is diffcult to ascertain because of methodological differences in study populations and diagnostic criteria.

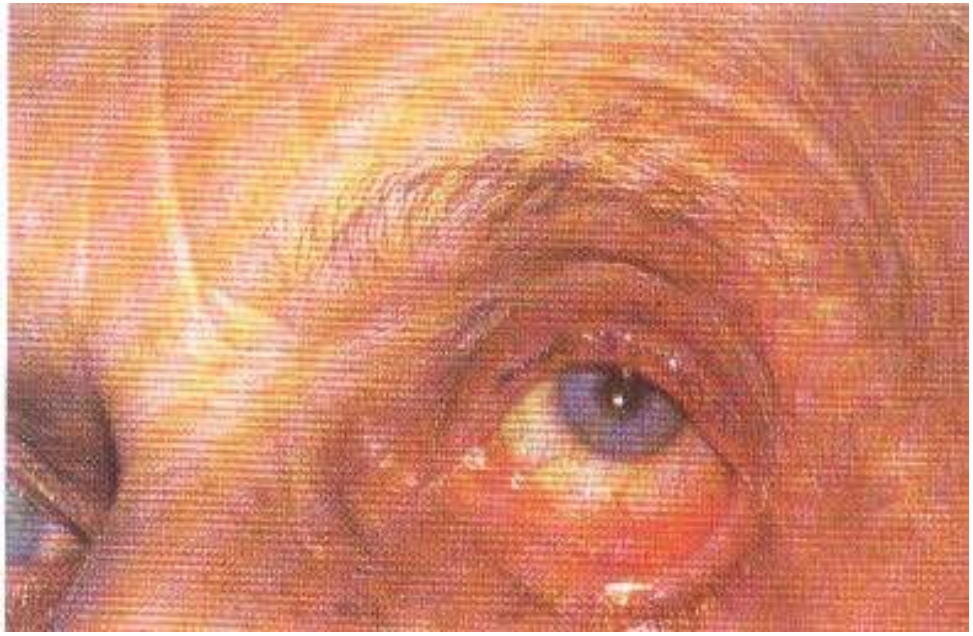
The majority of patients treated for salivary disorders:

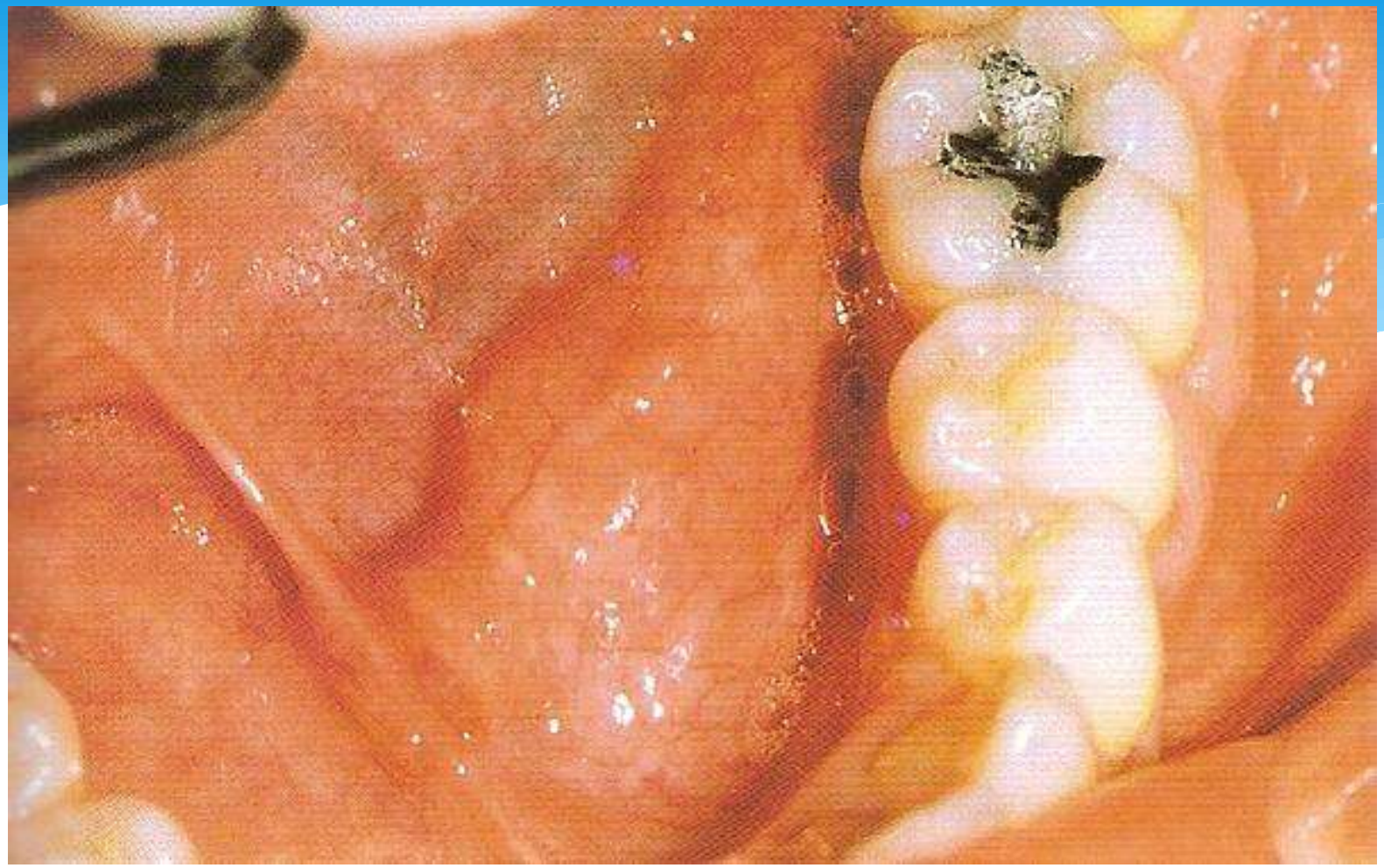
- **with Sjogren's syndrome (SS)**
- **adults treated for head and neck cancer**
- **those taking medications with antisialogogue sequelae**

Combining these populations, the prevalence of xerostomia increases with age, and is probably ~30% of the population aged 65+ years.









INCREASED SALIVATION - ptyalism, sialorrhea

True ptyalism (ptyalismus vera) is presented in:

- some infectious diseases (recurrent aphthous stomatitis, rabies)
- mercury and lead poisoning
- pilocarpine and neostigmine overdose
- gastrointestinal diseases
- CNS disorders
- endocrine disorders
- in pregnancy
- after certain drugs (psychotropic)

INCREASED SALIVATION - ptyalism, sialorrhea

Pseudoptyalism (ptyalismus spuria):

- **is a symptom of vegetative neurosis, may accompany hysteria and other mental illness (psychosis)**

INCREASED SALIVATION
- ptyalism, sialorrhea

Symptomatic treatment:

- **atropine – orally or s.c. at a daily dosage not exceeding 2 mg**
- **scopolamine**
- **sedatives**
- **solutions of tannin as mouthwash**

ORAL FUNGAL INFECTIONS

- **fungal infections** are the most frequent pathologies of the oral cavity - they owe its significance in pathology the one form of fungal infection – **oral candidiasis**
- ***Candida*** are common inhabitants of oral cavity, both normal and pathologically changed
- the most frequent oral species of ***Candida*** are: ***C. albicans, C. tropicalis*** and ***C. pseudotropicalis***
- ***candidiasis*** usually affects oral cavity, but can also spread to pharynx, esophagus and trachea
- **sepsis** can develop due to ***C. albicans*** infection, especially in newborns - extremely rare

- yeast-like fungi are opportunistic microorganisms
- in balance condition in the body are not pathogenic
- may cause diseases in the case of defense mechanisms disturbances
- noted increase in the incidence of fungal infections in the 70's and 80's of the twentieth century
- connected with the widespread introduction of the invasive methods in the diagnosis of diseases - endoscopy, biopsy, catheterization

FACTORS PREDISPOSING TO ORAL AND LIPS CANDIDIASIS

General:

- use of certain medications:
  - broad-spectrum antibiotics,
  - immunosuppressants, mainly corticosteroids
  - cytostatics
  - contraceptives
- some of the diseases of the oral mucosa eg. leukoplakia, lichen planus
- diabetes
- diet rich in carbohydrates
- vitamin deficiency (group B vitamins), lack of folic acid, iron
- diseases extending with lowered immunity (eg. AIDS)
- radiotherapy
- debilitating systemic diseases: cancer, uremia, acidosis, tuberculosis
- organs transplantation

FACTORS PREDISPOSING TO ORAL AND LIPS CANDIDIASIS

Local:

- low level of oral hygiene and bad condition of teeth
- reduction of the saliva secretion (eg. Crohn's disease, Sjogren's syndrome)
- wearing prosthetic restorations (poor hygiene, a bad relining, lack of stabilization)
- microinjures
- gingival pockets
- long-term inflammation of the mucous membrane
- occlusal irregularities
- tooth decay
- smoking

CLINICAL CLASSIFICATION OF ORAL AND LIPS CANDIDIASIS

ACUTE

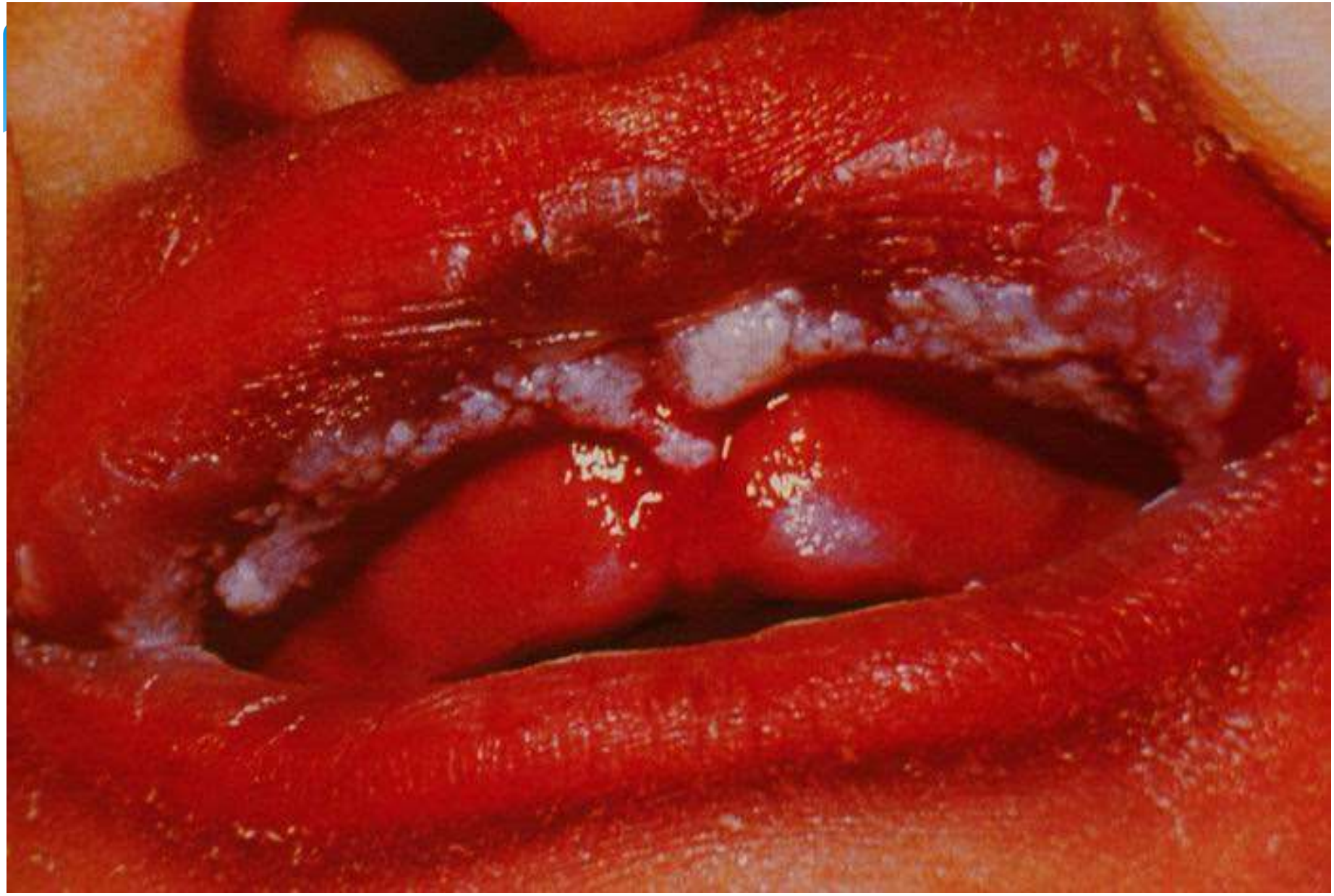
- acute pseudomembranous („thrush")
- acute atrophic („erythematous")

CHRONIC

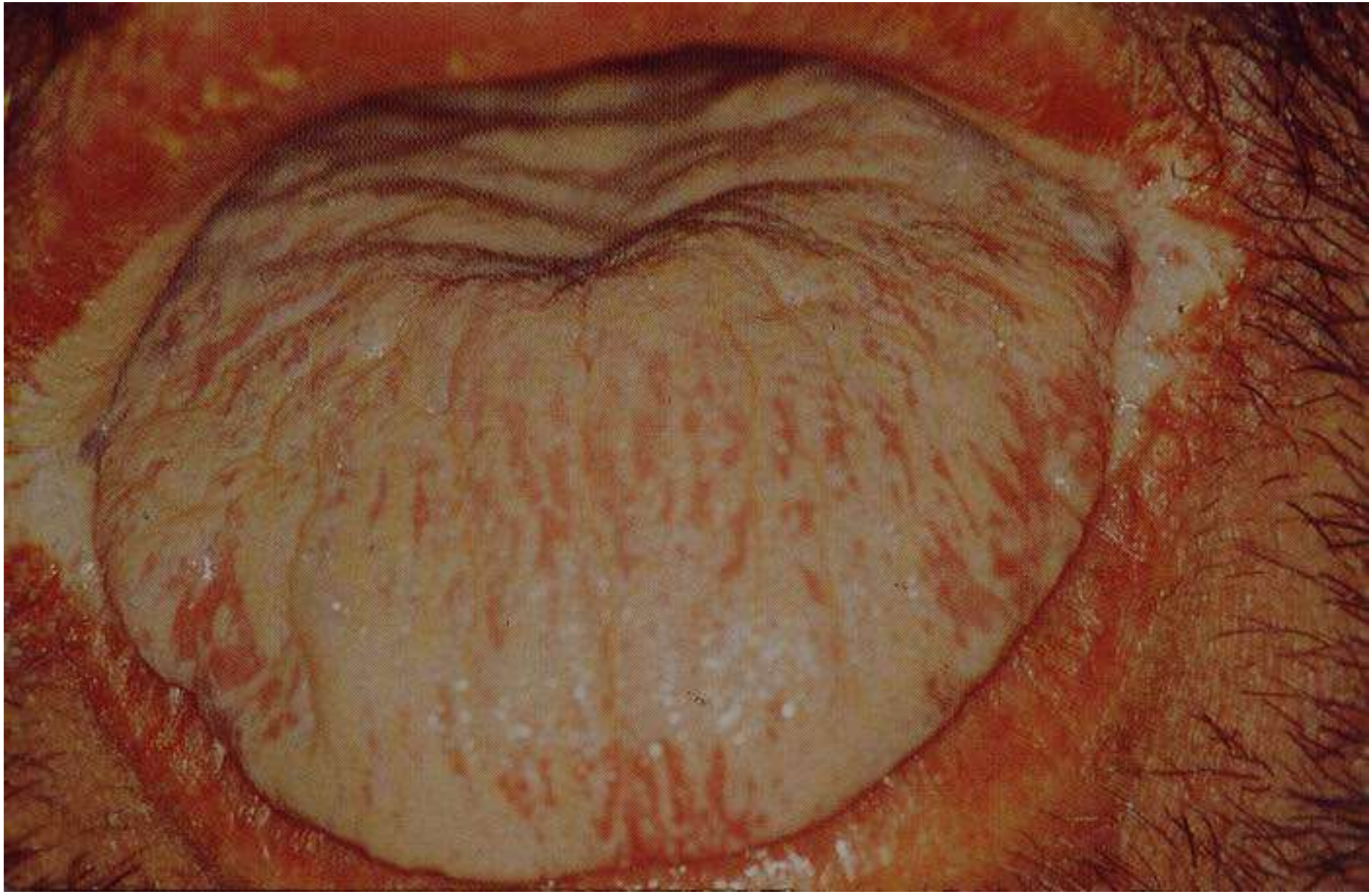
- chronic atrophic (denture-related stomatitis)
- chronic hyperplastic („candidal leukoplakia")
- chronic angular cheilitis („perleche")
- chronic mucocutaneous

Acute Pseudomembraneous Candidiasis (Thrush)

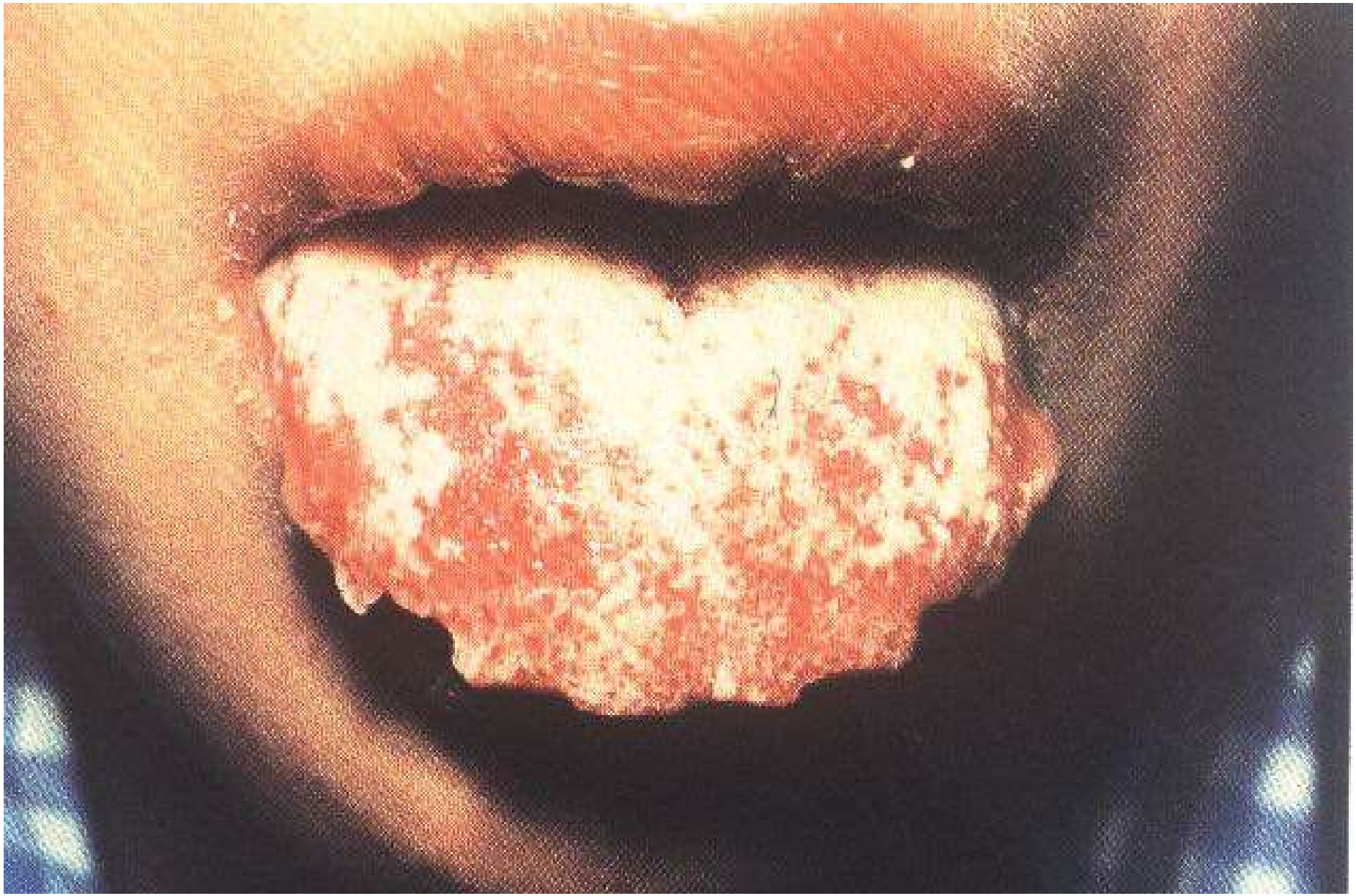
A clinical form of *C. albicans* infection that consists of creamy, loose patches of desquamative epithelium containing numerous matted mycelia over an erythematous mucosa that is easily removed; common in patients with more severe predisposing factors.



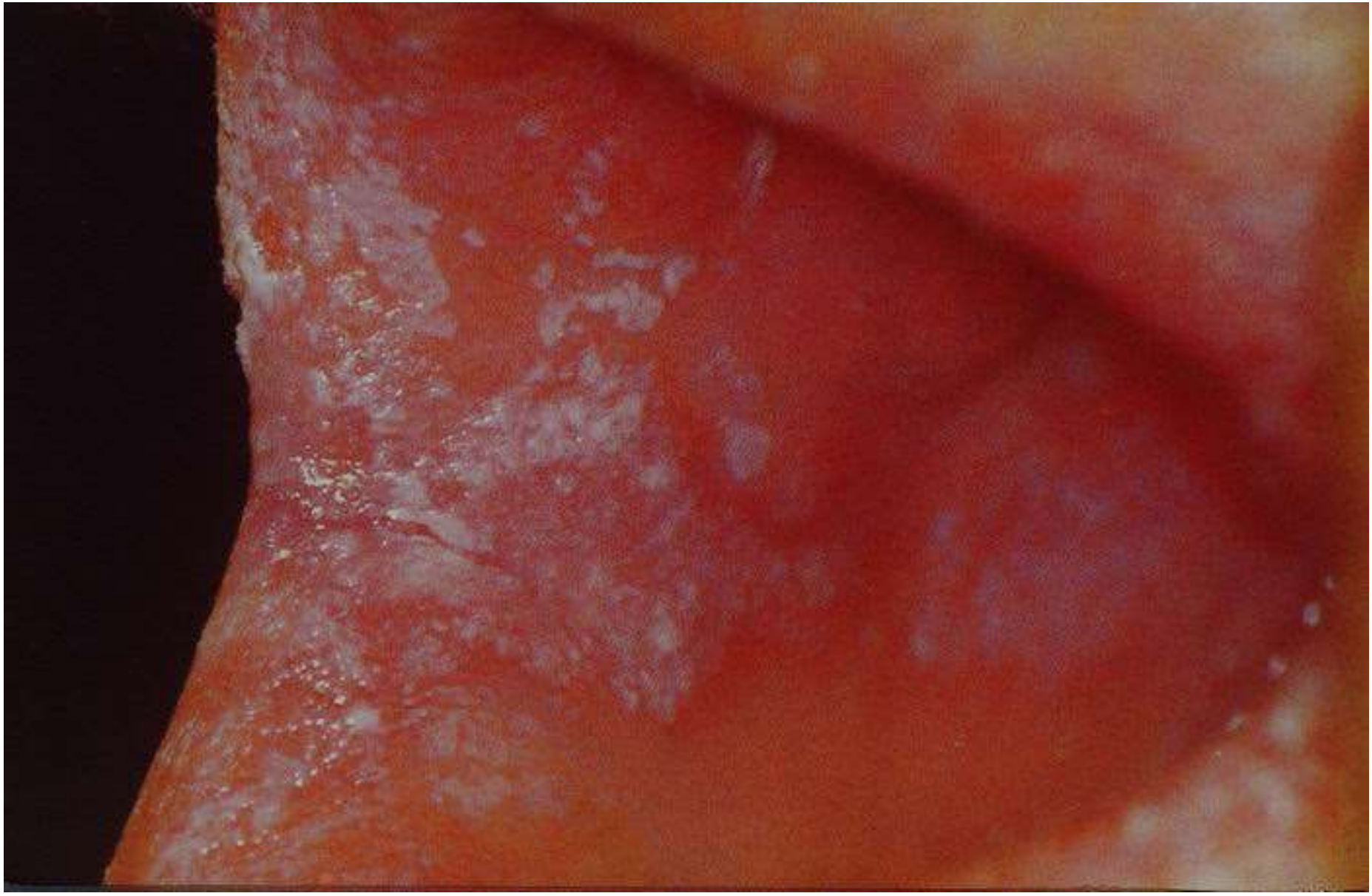
acute pseudomembranous candidiasis (thrush)



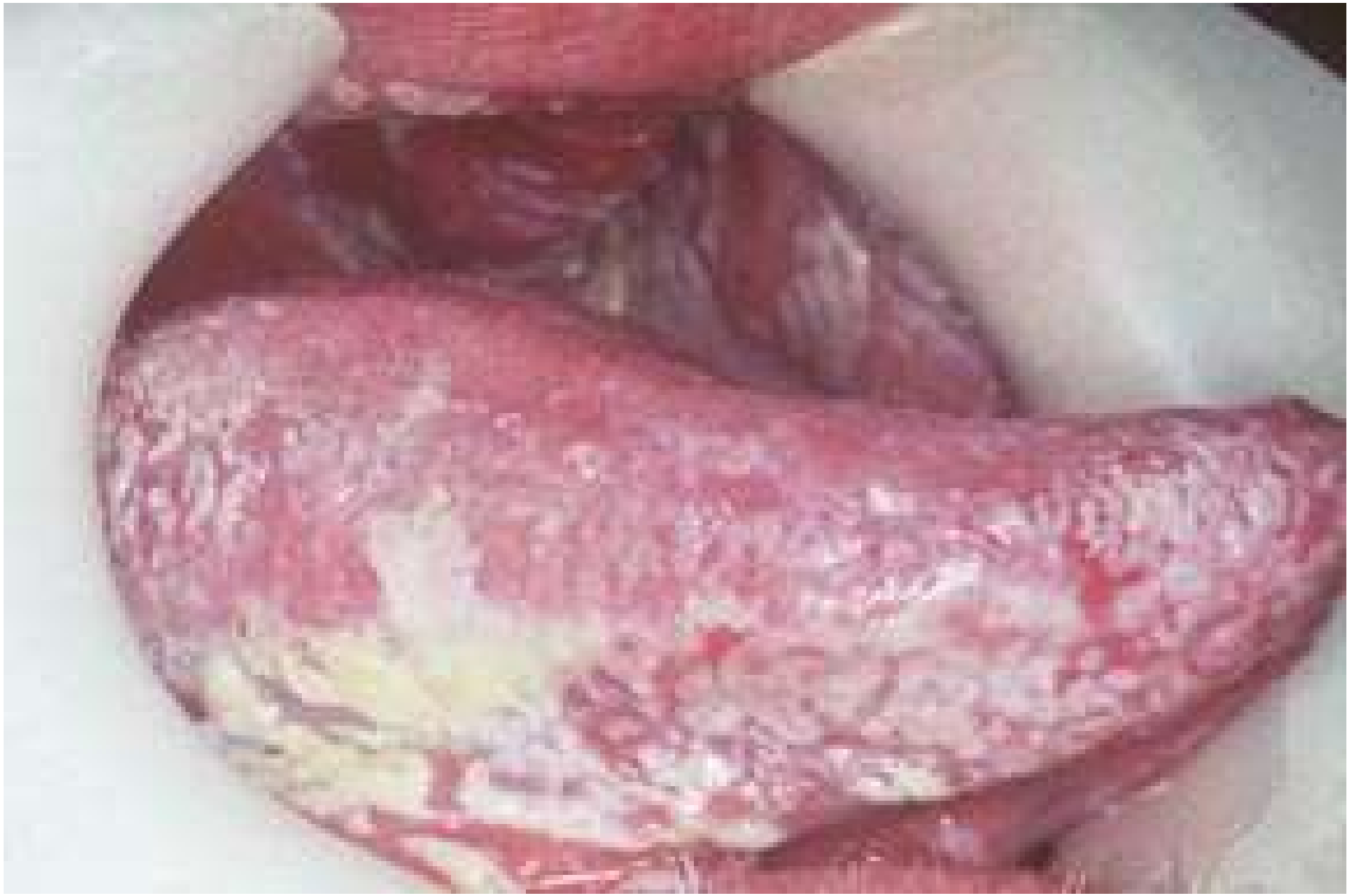
acute pseudomembranous candidiasis (thrush)



acute pseudomembranous candidiasis (thrush)



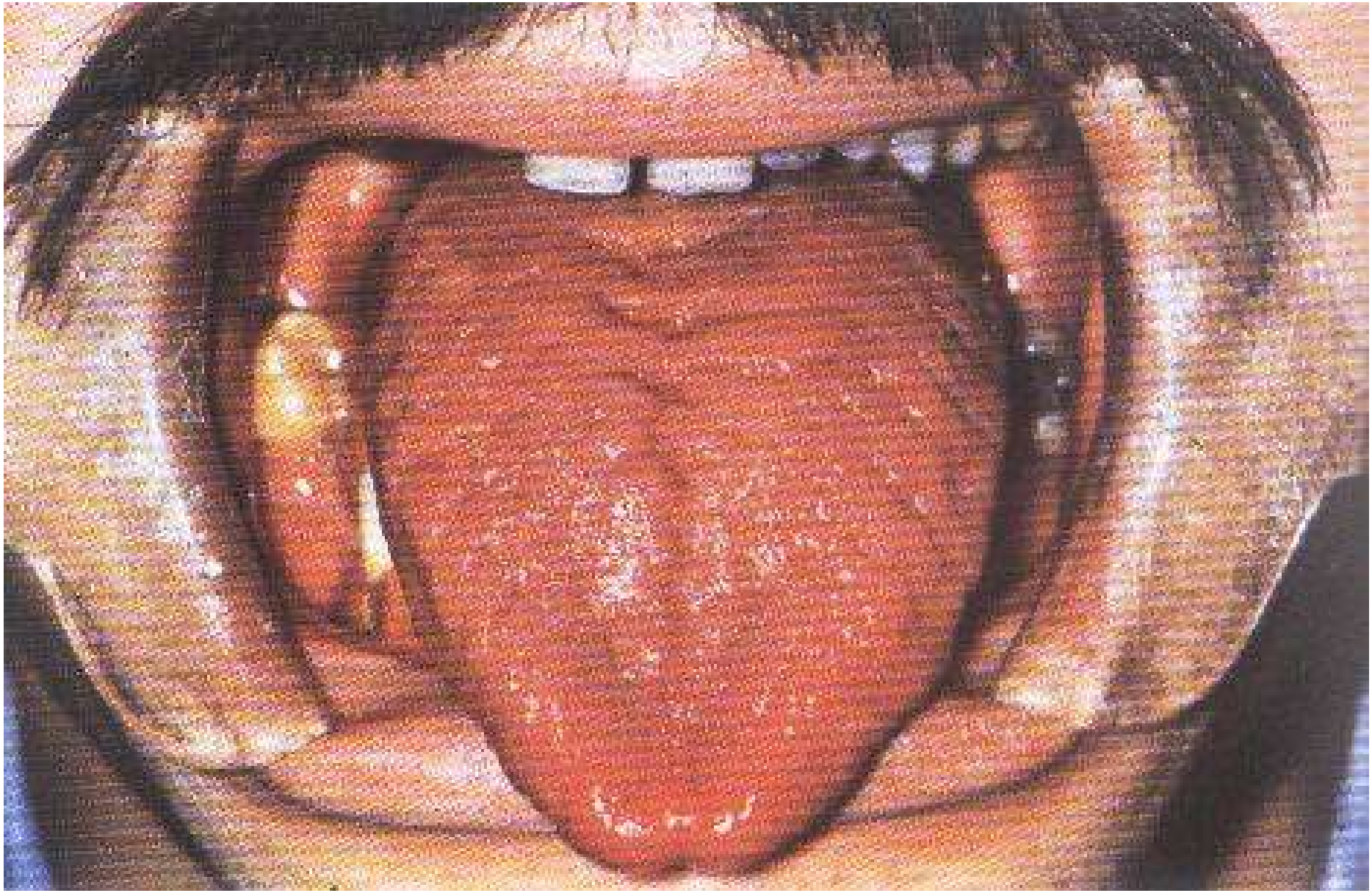
acute pseudomembranous candidiasis (thrush)



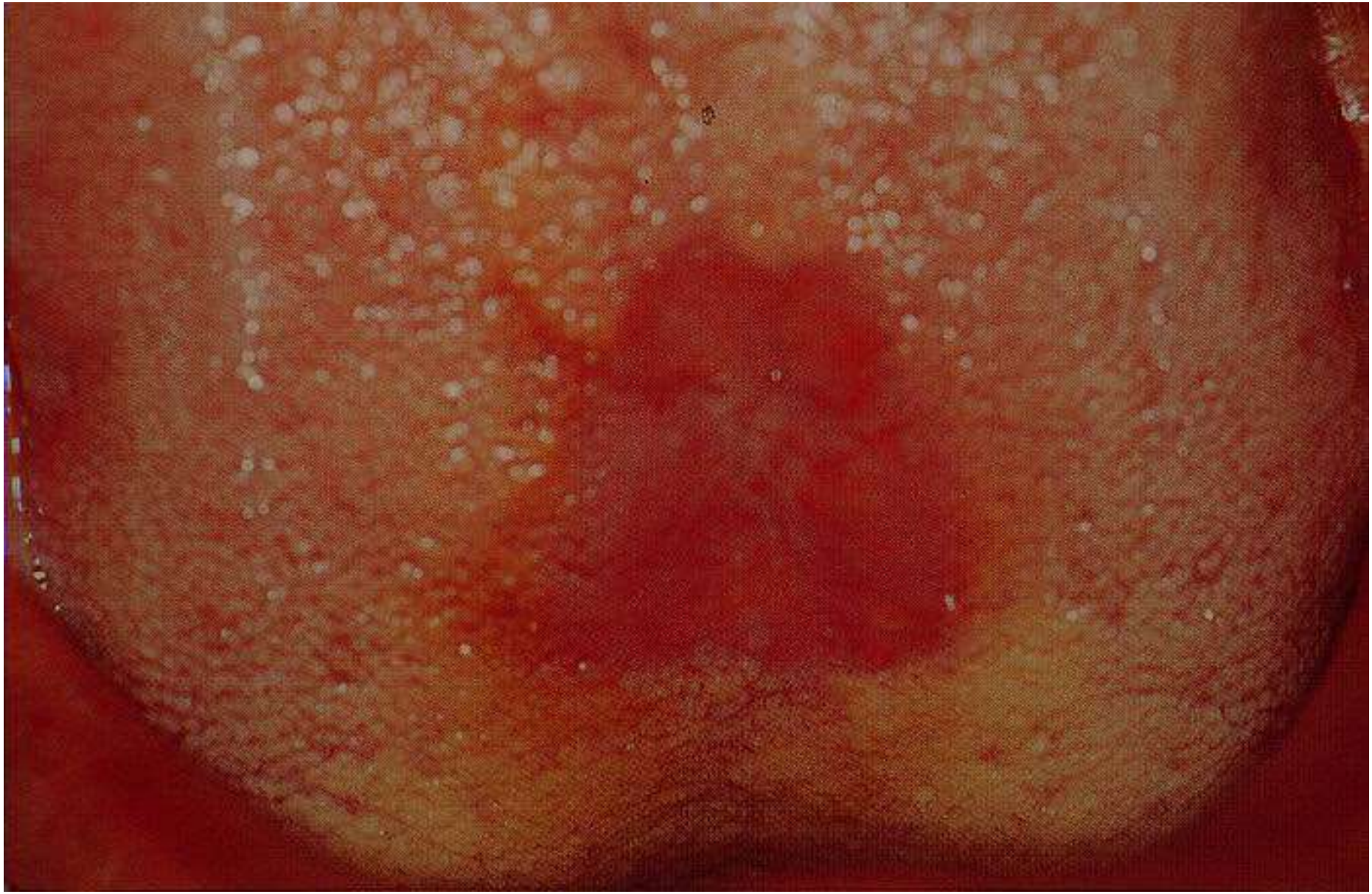
acute pseudomembranous candidiasis (thrush)

Atrophic (Erythematous) Candidiasis

A clinical form of *C. albicans* infection in which the mucosa is thinned, smooth, and bright red with symptoms of burning and increased sensitivity; commonly found on the palate under a denture but also on the tongue and other mucosal surfaces.



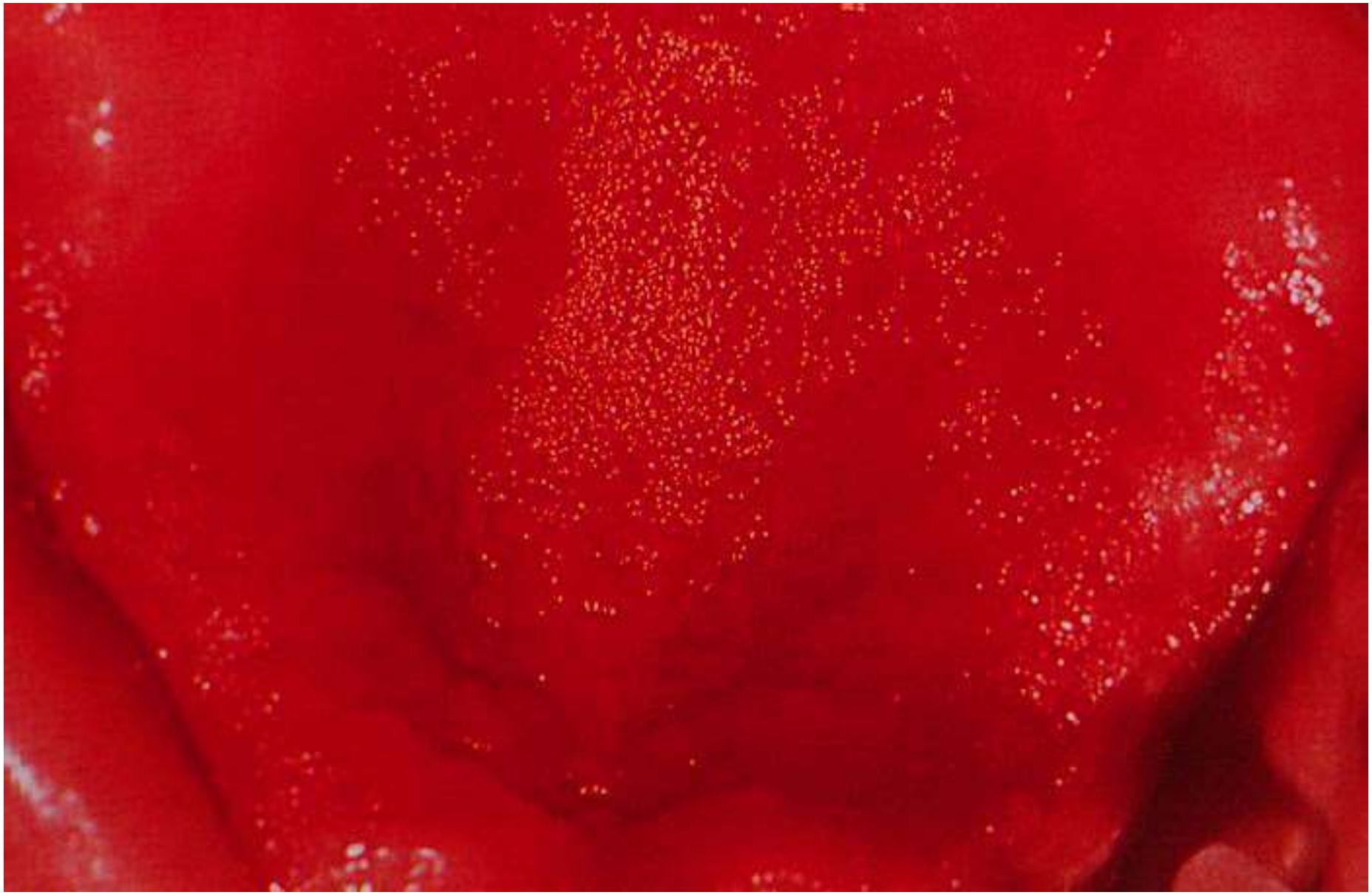
acute atrophic (erythematous) candidiasis



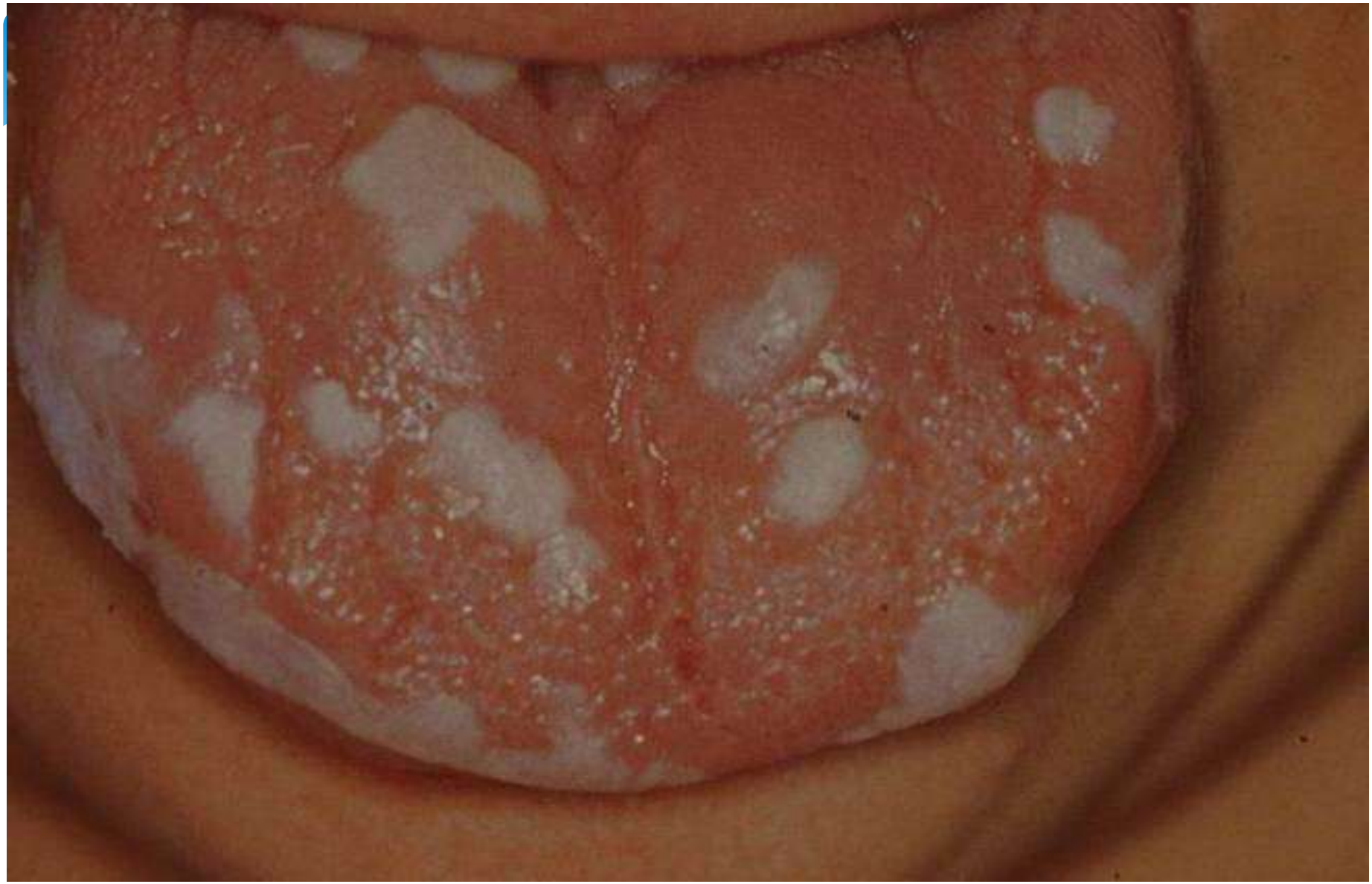
acute atrophic (erythematous) candidiasis

CHRONIC ATROPHIC CANDIDIASIS (DENTURE-RELATED STOMATITIS)

- the characteristic presenting signs of denture-induced stomatitis are chronic erythema and oedema of the mucosa that contacts the fitting surface of the denture
- in about 90% of cases, *Candida* species are involved
- the patient may occasionally experience slight soreness but is usually free of symptoms



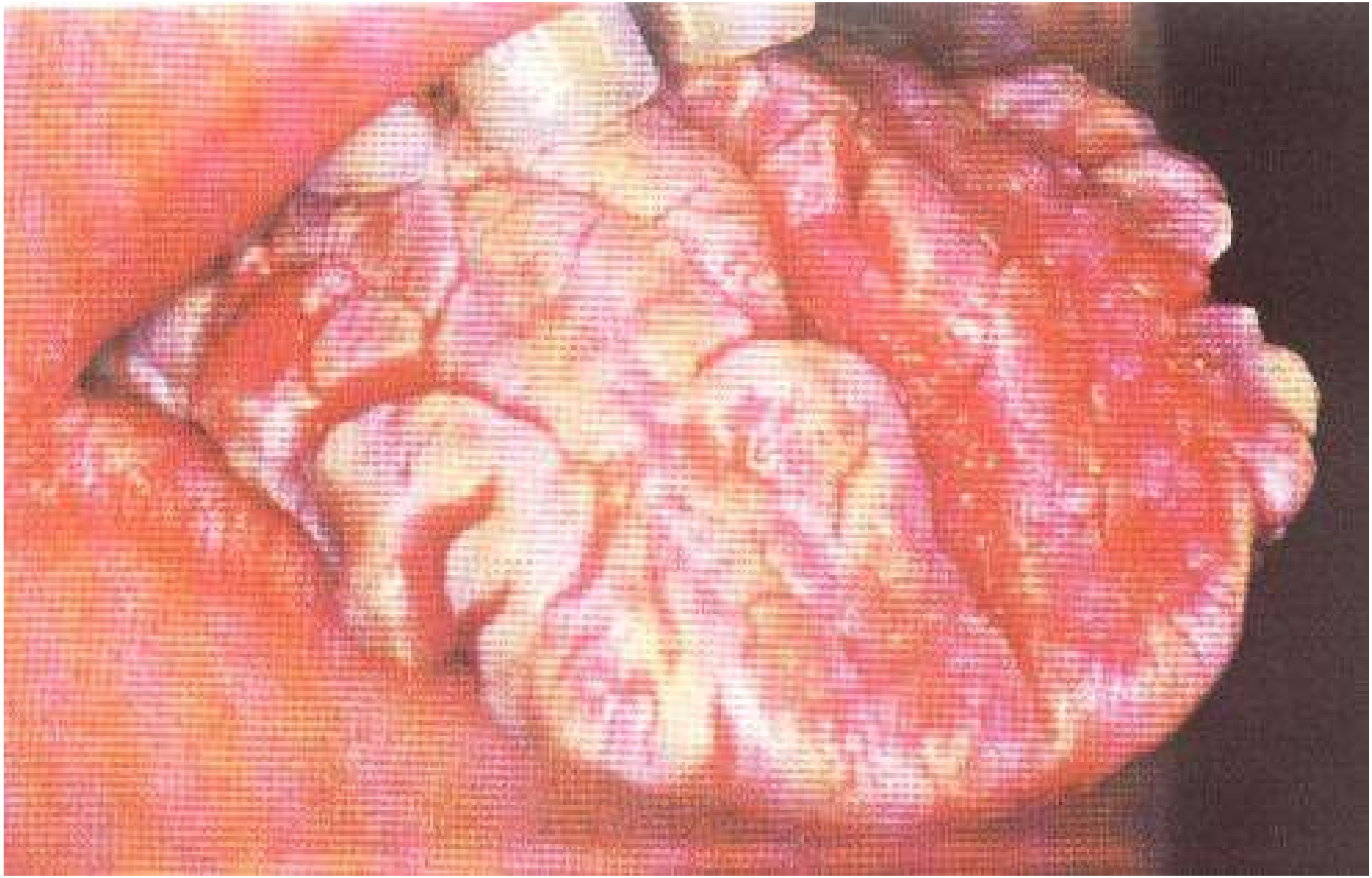
chronic atrophic candidiasis



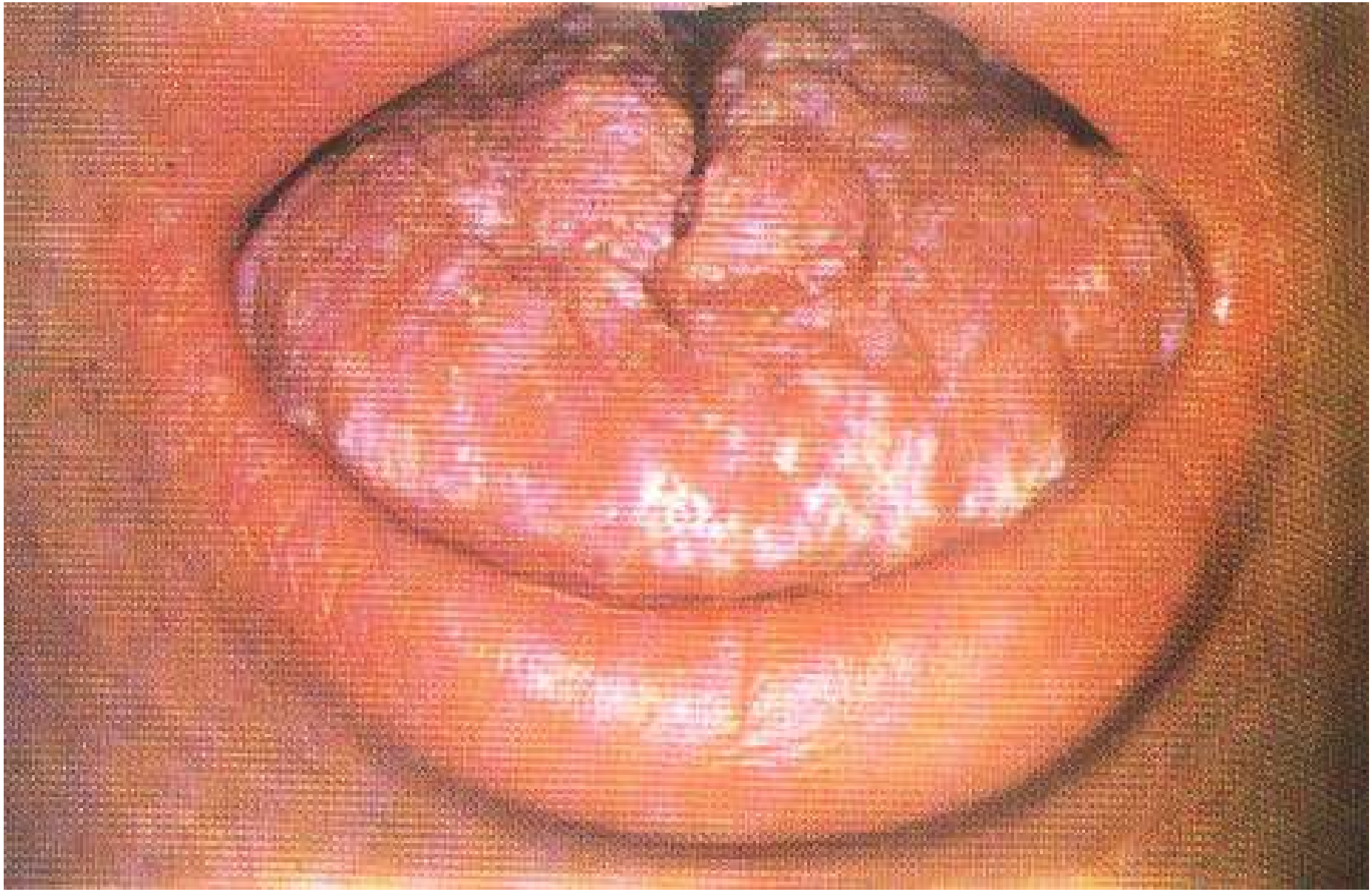
chronic atrophic candidiasis

Chronic Hyperplastic Candidiasis

A clinical form of *C. albicans* infection consisting of white plaques or papules against an erythematous background containing hyphae in the parakeratin layer of the thickened epithelium.



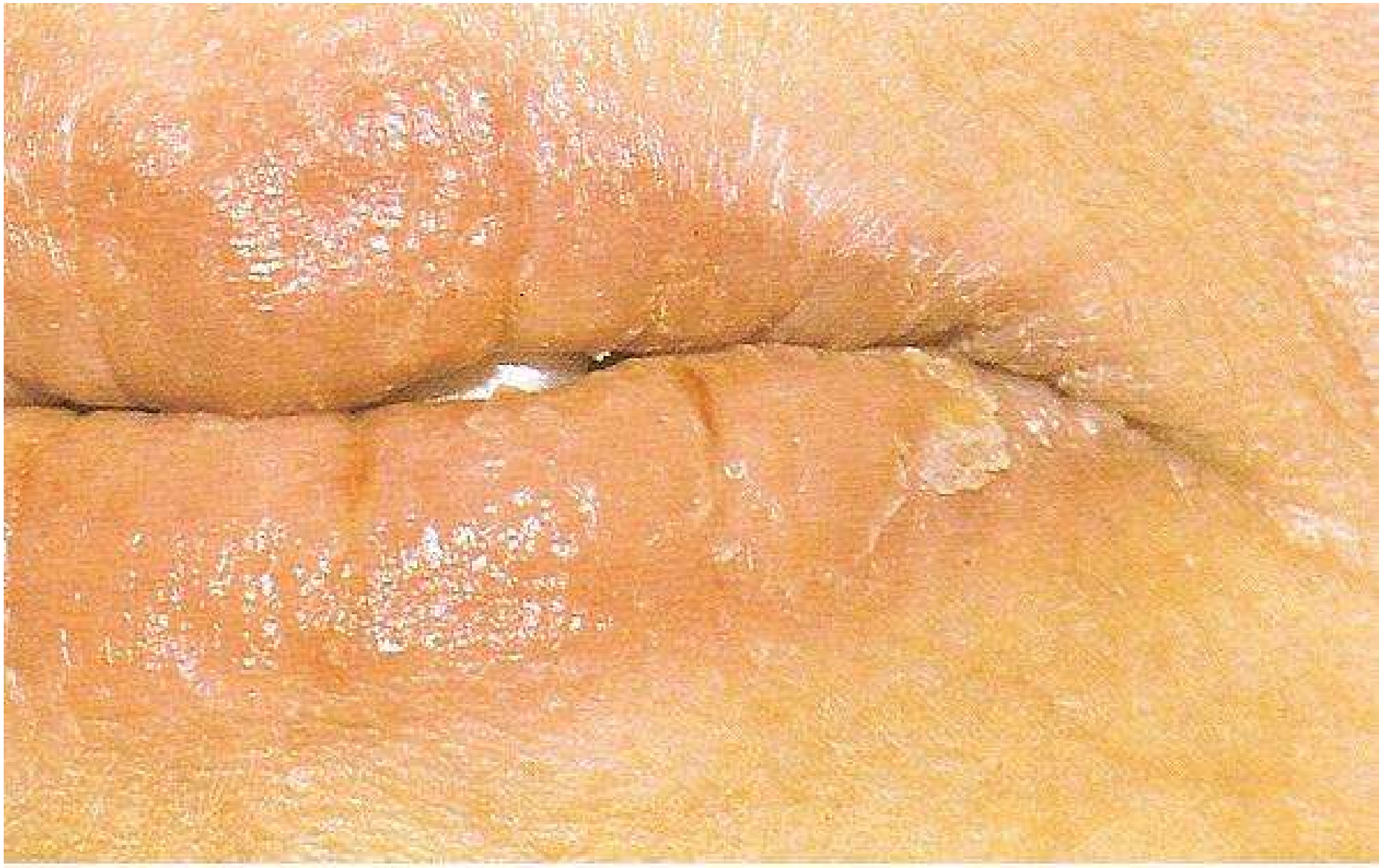
chronic hyperplastic candidiasis



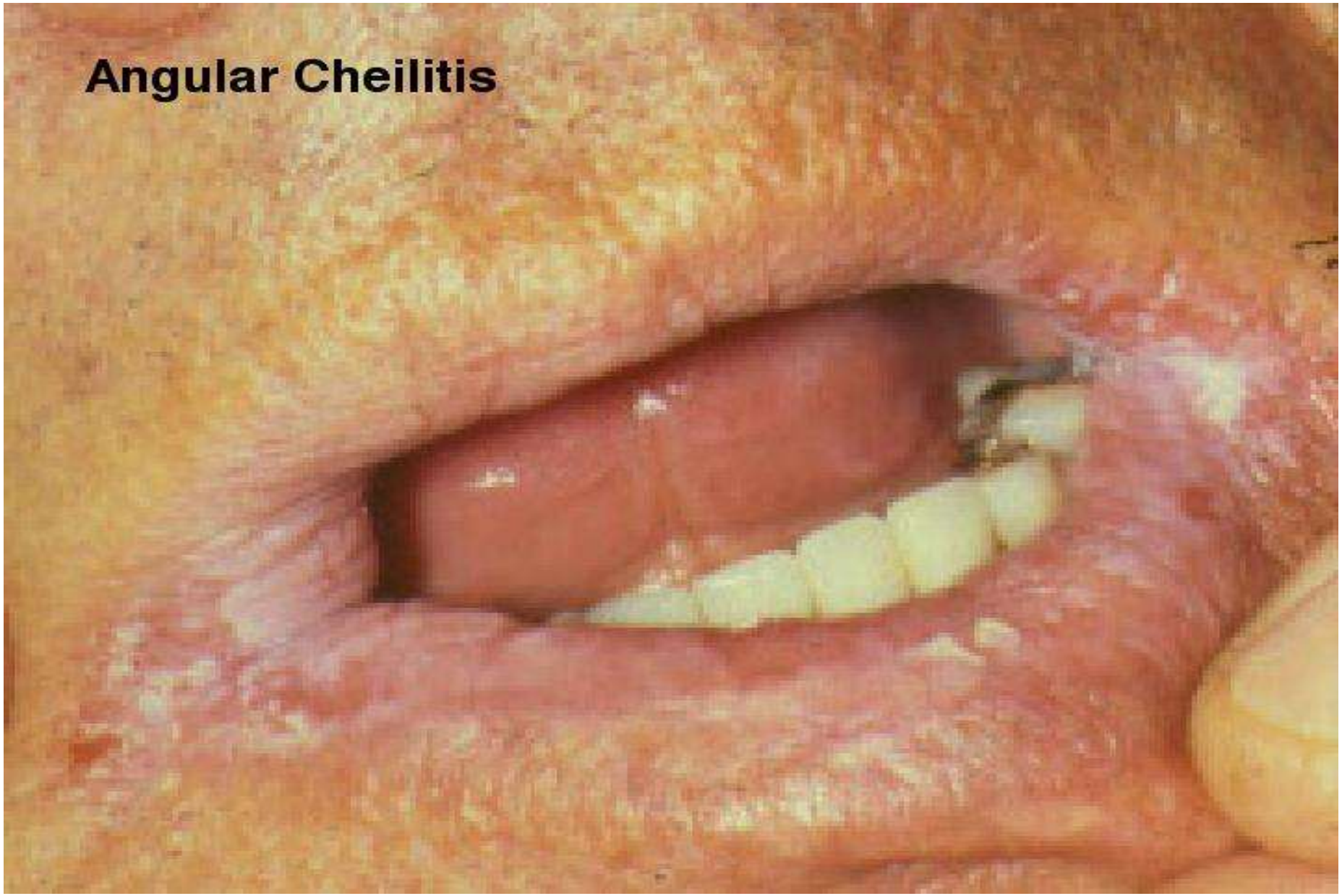
chronic hyperplastic candidiasis

Angular Cheilitis (Perleche)

Symptomatic, bilateral fissures of the corners of the mouth that are common in patients with C. albicans infection in other parts of the mouth. It is often intensified with mouth over closure and requires treatment with antifungal medication.



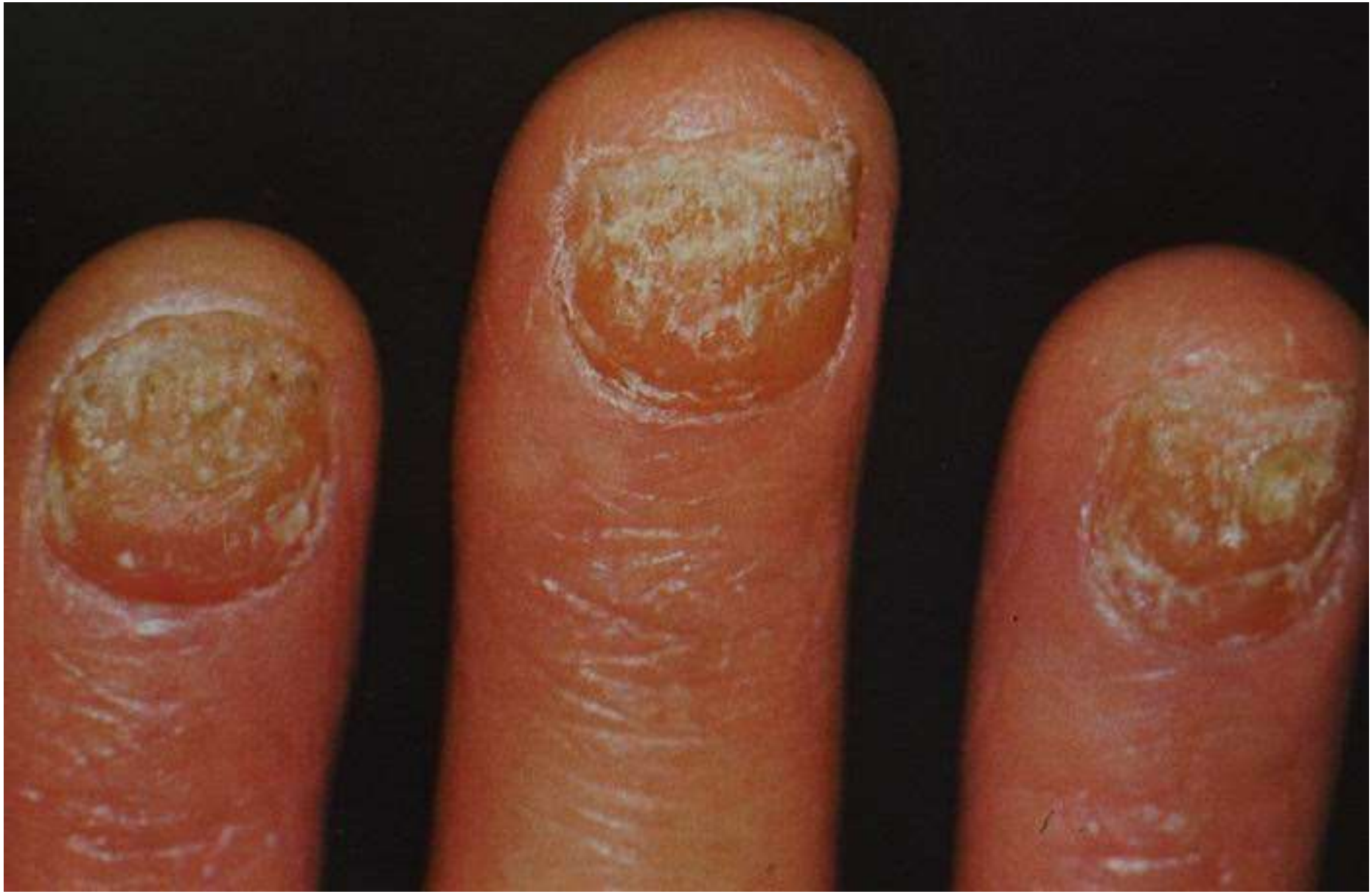
chronic angular cheilitis candidiasis



chronic angular cheilitis candidasis

Chronic Mucocutaneous Candidiasis

A condition in which persistent and refractory candidiasis occurs on the mucous membranes, skin, and nails of the affected patient. Most patients exhibit defects in their endocrine or immune systems.



chronic mucocutaneous candidiasis

TREATMENT

- necessary is conducting of appropriately antifungal treatment
- the condition for effective treatment is a thorough analysis of each clinical case and determine the primary or secondary cause of the infection

TREATMENT

- limitation of carbohydrates in the diet
- administration of vitamins (in particular B2 and PP)
- administration of antifungal antibiotics (according to antifungal susceptibility testing)
- in the alternative can be given analgesic, antipruritic, antiseptic and a local anesthetic

ANTIFUNGIAL ANTIBIOTIC - POLYENE ANTIBIOTICS

Nystatin

- NYSTATYNA - tabl. 500 000 j.m.
- MORONAL - drag. 500 000 j.m.
- CANDIO HERMAL – susp. (1 mL = 100 000 j.m.)
- MYCUNDEX – susp. (1 mL = 100 000 j.m.)

Natamycin

- PIMAFUCORT- lotio (*natamycin* + *hydrocortisone* + *neomycin*)
- PIMAFUCIN - 2,5% gtt., tabl.

Amphotericin B

- AMPHO-MORONAL – tabl.; susp.
- AMBISOME – amp. (amphotericin B liposomal)
- AMPHOCIL – amp.

AMPHOTERICIN B

- acts by binding to the sterol component, ergosterol, of the cell membrane - forms transmembrane channels leading to alterations in cell permeability through which monovalent ions (Na+, K+, H+, and Cl-) leak out of the cell resulting in cell death
- reserved for the treatment serious, life threatening fungal infections
- characterized by nephrotoxicity - newer agents (AmBisome and Amphocil) are significantly less toxic than conventional form
- despite the high toxicity remains a crucial antifungal antibiotic

IMIDAZOLE DERIVATIVES

Miconazole

- ORAVIG - buccal tablets 50 mg
- FUNGIDAL BT – buccal tablets 100 mg
- DAKTARIN - 2% dental gel

Clotrimazole

- CLOTRIMAZOLUM - 1% gel

Ketoconazole

- KETOCONAZOLE, KETOZOL, NIZORAL - cream, shampoo

IMIDAZOLE DERIVATIVES

- blocks the synthesis of ergosterol, a key component of the fungal cell membrane
- used in the treatment and prevention of oral and throat candidiasis – only topically
- oral form cause hepatotoxicity – actually are not used

TRIAZOLE DERIVATIVES

Fluconazole

- DIFLUCAN - caps. 50, 100, 150, 200 mg, vial (iv) 100, 200, 400 mg
- TRIFLUCAN – caps., vial (iv)
- FLUCONASOLE - caps., vial (iv)

Itraconazole

- ORUNGAL – caps. 100 mg, vial (iv) 250 mg
- SPORANOX – caps., vial (iv), oral solution
- ITRACONAZOLE – caps.

Voriconazole

- VFEND – tabl., susp., vial (iv)

Pozaconazole

- Noxafil – susp., vial

TRIAZOLE DERIVATIVES

- blocks the synthesis of ergosterol, a key component of the fungal cell membrane
- used to prevent and treat a variety of fungal and yeast infections – eg. oropharyngeal, oesophageal candidiasis
- characterized by a relatively low toxicity and are used as first-line drugs for fungal infections
- the newest drug are voriconazole and pozaconazole
  - broad-spectrum antifungal drugs, particularly recommended for treatment severe, life-threatening infections and patients with impaired immunity

OTHER DRUGS

- **Flucytosine, caspofungin and anidulafungin are used in severe systemic mycosis and candidiasis when treatment with other drugs is ineffective**
- **Flucytosine**
  - ✓ **ANCOBIN – tabl. 500 mg**
- **Caspofungine**
  - ✓ **CANCIDAS – vial 50, 70 mg**
- **Anidulafungin**
  - ✓ **ECALTA – vial 100 mg**

OTHER DRUGS

Dequalinium chloride

- DEQUADIN
- oral rinse solution, gel, lozenges

Sodium tetraborate

- APHTIN, NATRIUM BIBORICUM
- oral rinse solution

Chlorhexidine digluconate

- PERIDEX, PERIOGARD
- oral rinse solution

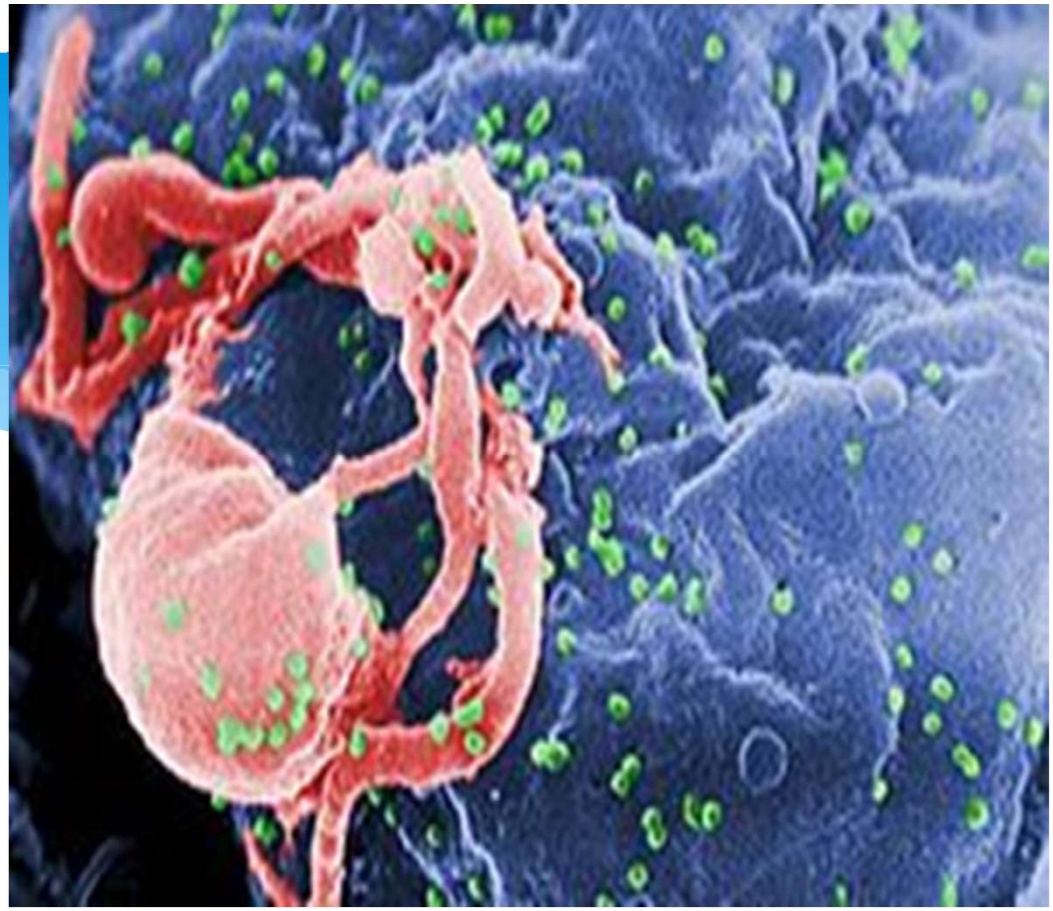
Gentian violet

- topical solution, spray

Undecylenic acid

- GORDOCHOM – luquid for skin

HIV/AIDS



H **Human**

I **Immunodeficiency**

V **Virus**

AIDS - ACQUIRED IMMUNODEFICIENCY SYNDROME

- chronic, potentially life-threatening condition caused by the human immunodeficiency virus (HIV)
- HIV infection weakens the immune system that results in high susceptibility to numerous infections and certain types of cancers

HIV TRANSMISSION

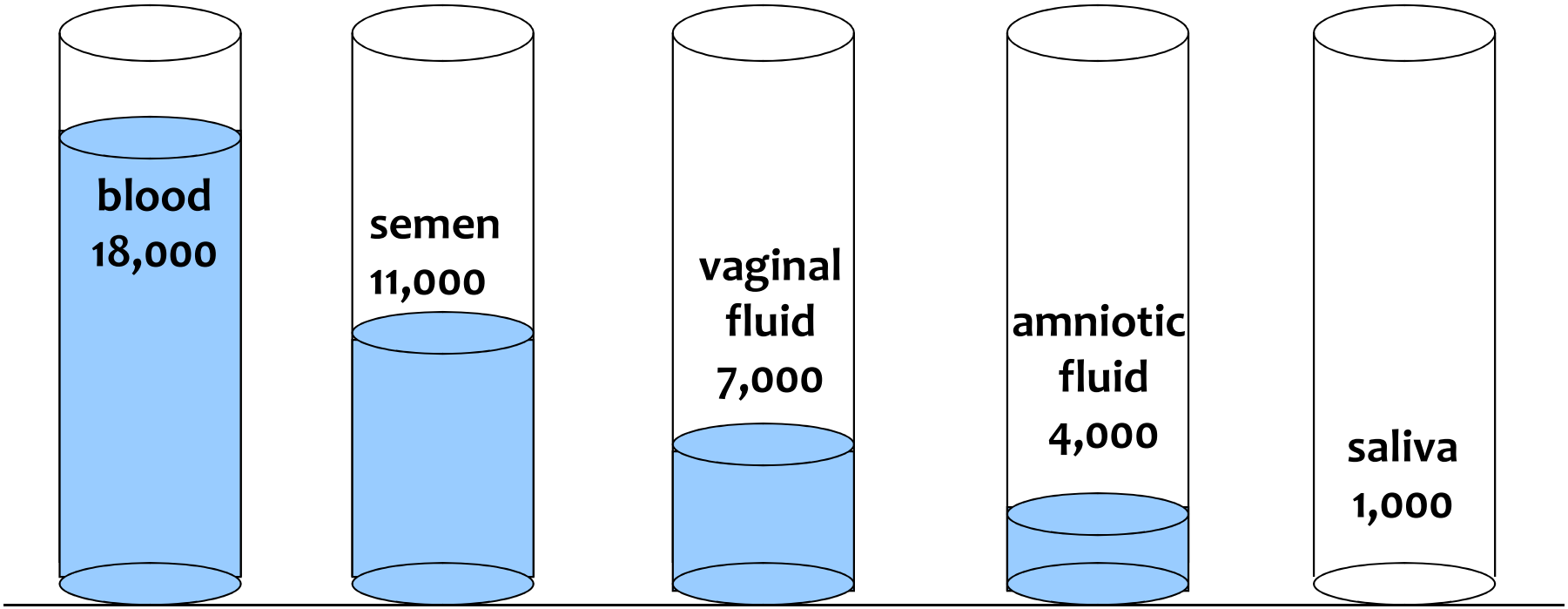
- **HIV enters the bloodstream through:**
  - ✓ **open wounds**
  - ✓ **skin injury**
  - ✓ **mucous membranes**
  - ✓ **direct injection**

HIV TRANSMISSION

Body fluids that can transmit virus:

- **blood**
- **semen**
- **pre-seminal fluid**
- **vaginal fluids**
- **rectal fluids**
- **breast milk**

HIV IN BODY FLUIDS



Average number of HIV particles in 1 ml of these body fluids

WINDOW PERIOD FOR HIV INFECTION

- the length of time after infection that it takes for the virus to become detectable by HIV diagnostic tests
- the length of the window period varies depending on the type of diagnostic test used and the method it employs to detect the virus
  - ✓ first-generation and second-generation HIV antibody tests detect one type of HIV antibody - can detect antibodies 42-60 days after infection
  - ✓ third-generation tests detect all types of antibodies, which makes them more sensitive - can detect antibodies about 21-24 days after infection
  - ✓ fourth-generation tests can simultaneously detect both HIV antibodies and antigens - tests that look for the p24 antigen can detect it within 14-15 days; tests can detect plasma HIV RNA (ribonucleic acid) within about 10 days of infection

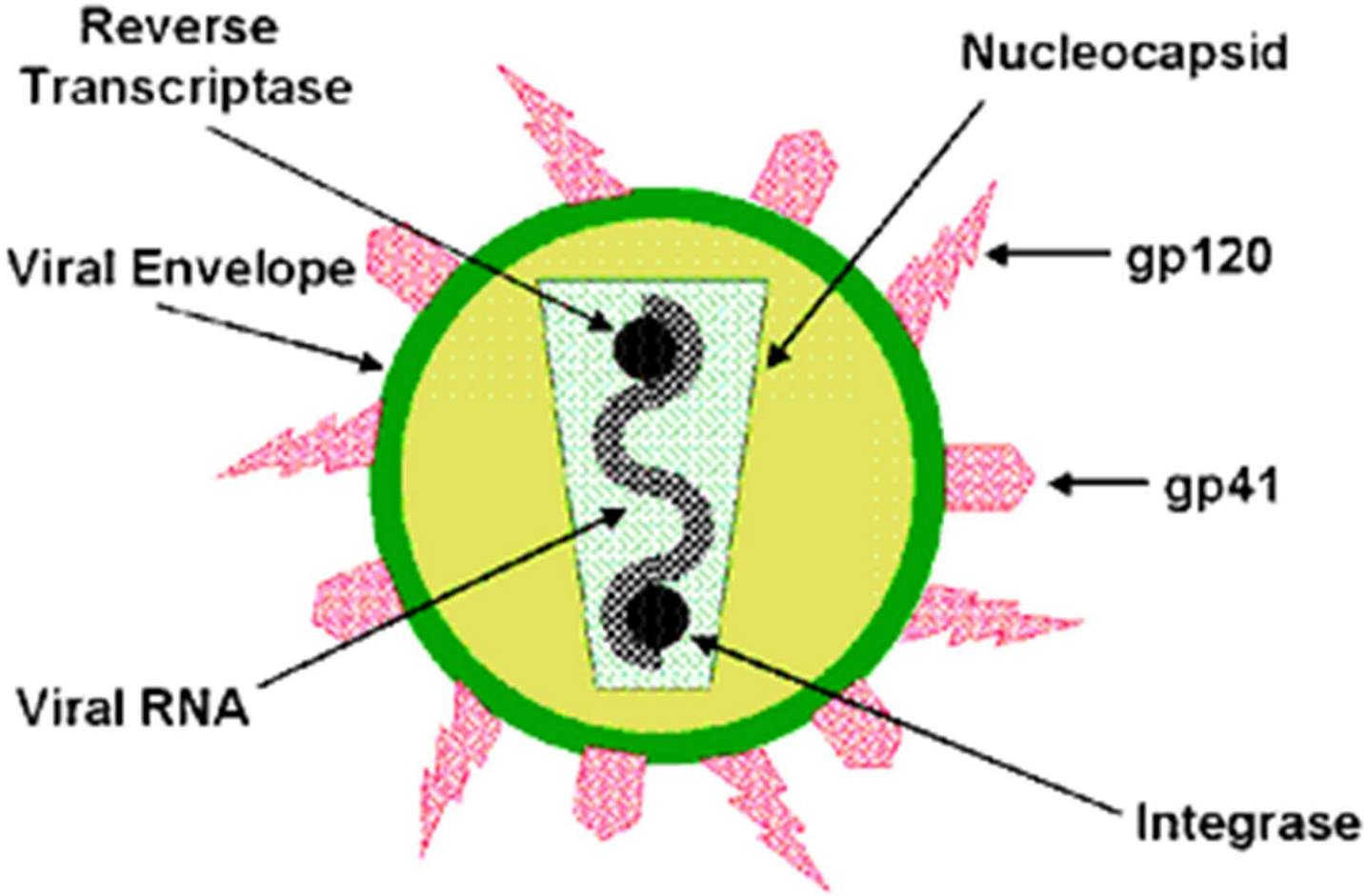


Figure 1. **Human Immunodeficiency Virus**

VIRAL ATTACHMENT

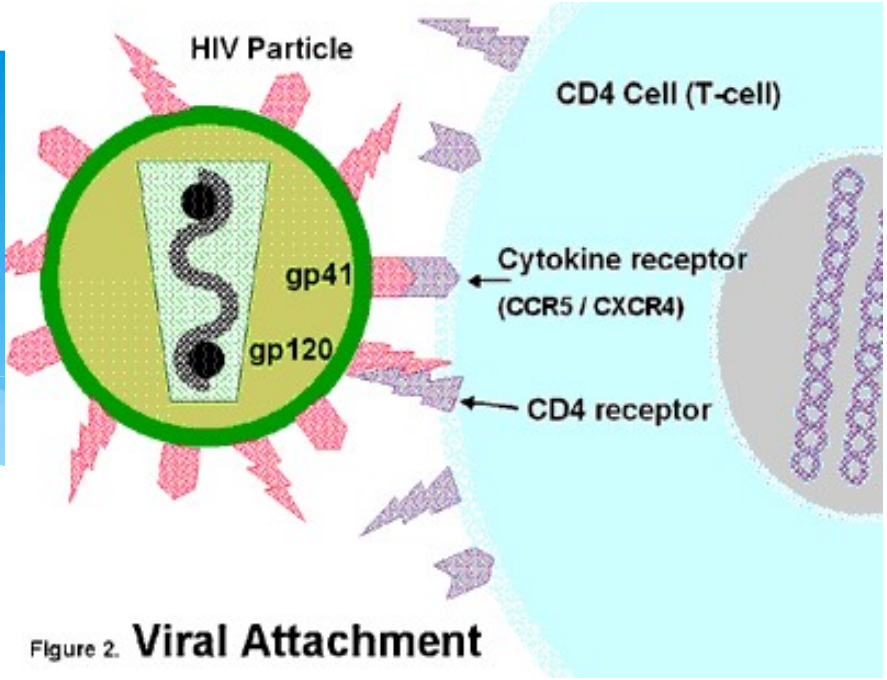


Figure 2. Viral Attachment

- ✓ 2 receptors: CD4 and a co-receptor (CCR5 or CXCR4) are used by HIV to bind to the cell via proteins gp120 and gp41
- ✓ maraviroc - human receptor antagonist for CCR5 chemokines, entry inhibitor

VIRAL PENETRATION/FUSION

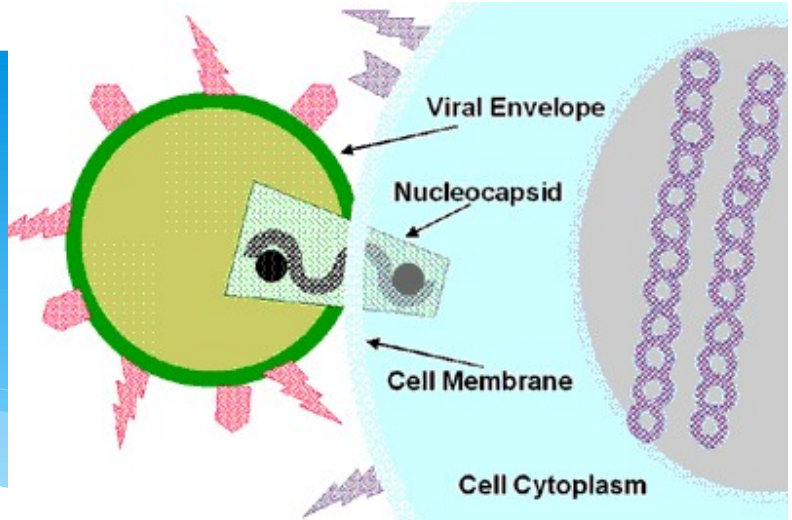


Figure 3. Viral Penetration / Fusion

- ✓ after attachment is completed, viral penetration occurs
- ✓ penetration allows the nucleocapsid - the genetic core of the virus, to be injected directly into the cell's cytoplasm
- ✓ the viral envelope and the cell membrane are brought into direct contact and essentially melt into each other
- ✓ drugs called fusion inhibitors prevent the binding of gp41 and the chemokine

VIRAL UNCOATING

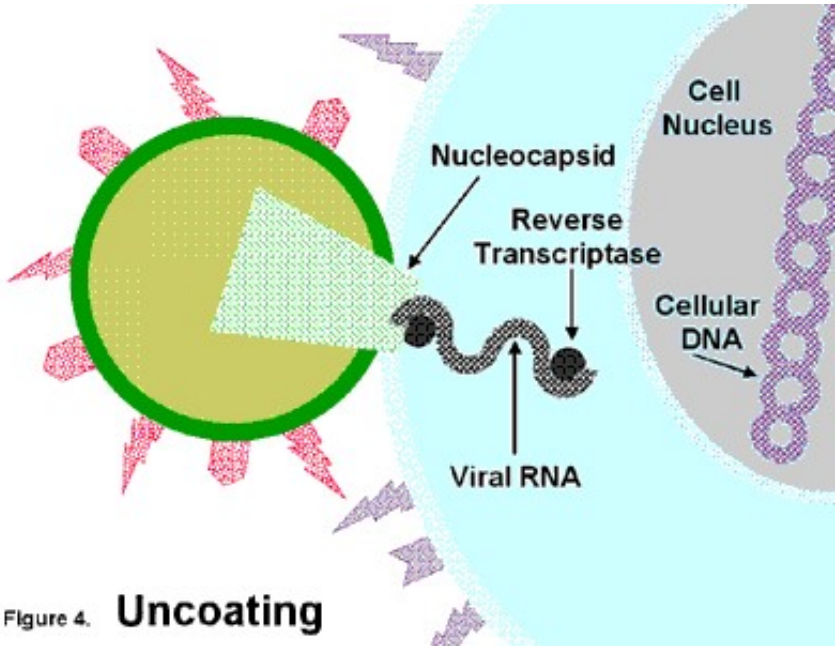


Figure 4. **Uncoating**

- ✓ once HIV has penetrated the cell membrane, it is ready to release its genetic information (RNA) into the cell
- ✓ the viral RNA is protected in the nucleocapsid that needs to be partially dissolved so that the virus's RNA can be converted into DNA

REVERSE TRANSCRIPTION

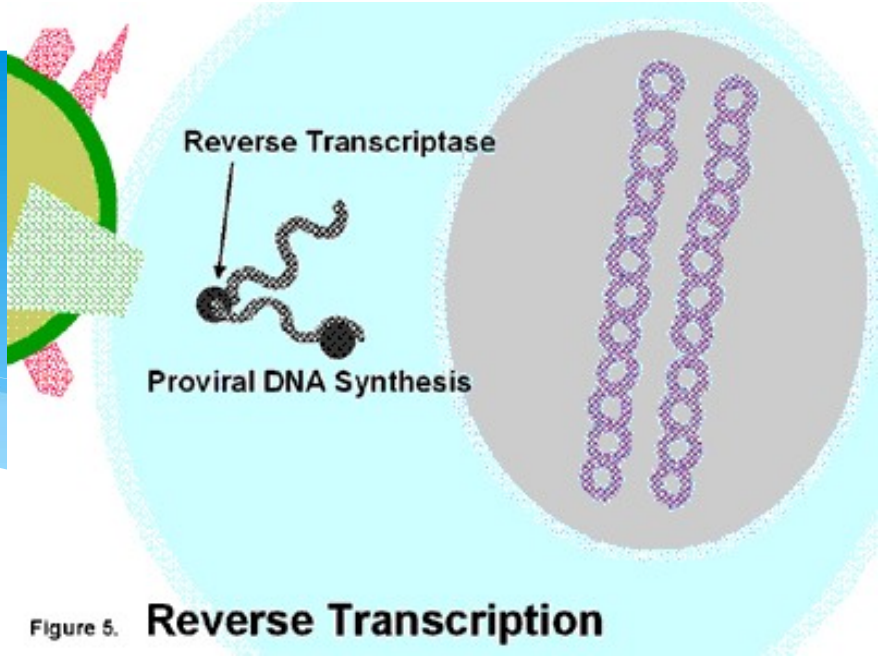


Figure 5. Reverse Transcription

- ✓ the process by which HIV's RNA is converted to DNA by using an enzyme **reverse transcriptase**
- ✓ reverse transcriptase uses nucleotides - building blocks of DNA - from the cell cytoplasm

REVERSE TRANSCRIPTION

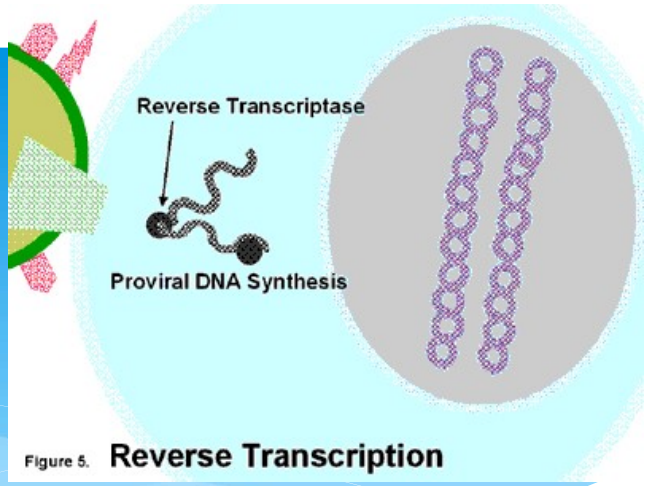


Figure 5. Reverse Transcription

- drugs called reverse transcriptase inhibitors block HIV's reverse transcriptase from using these nucleotides
- nucleoside and nucleotide analog reverse transcriptase inhibitors (NRTIs) contain faulty imitations of the nucleotides found in a T-cell's cytoplasm
  - ✓ instead of incorporating a nucleotide into the growing chain of DNA, the imitation building blocks in NRTIs are inserted, which prevents the double strand of DNA from becoming fully formed
- non-nucleoside reverse transcriptase inhibitors (NNRTIs) block reverse transcription by attaching to the enzyme in a way that prevents it from functioning

INTEGRATION/RNA TRANSCRIPTION

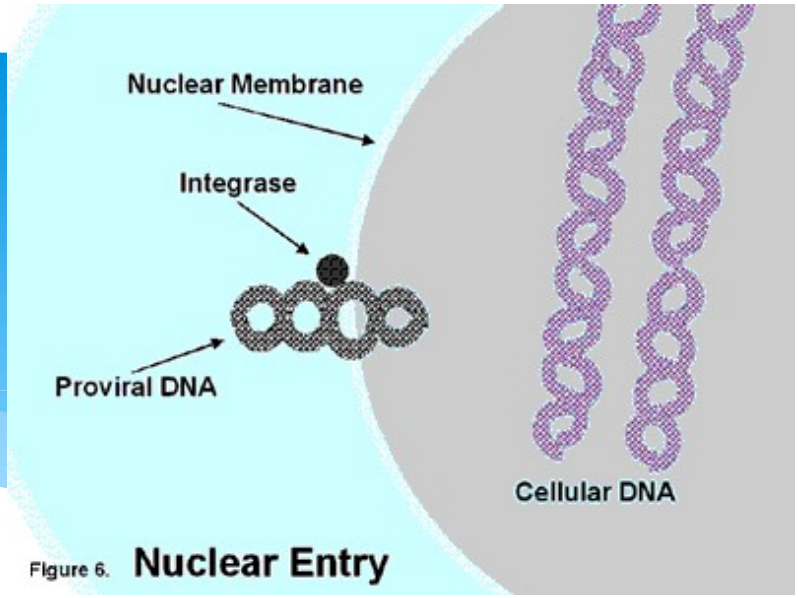


Figure 6. Nuclear Entry

- ✓ if HIV succeeds in translating its instructions from RNA to DNA, HIV must then insert its DNA (also called the preintegration complex) into the cell's DNA
- ✓ in order for integration to occur, the newly translated DNA must be transported across the nuclear membrane into the nucleus

INTEGRATION/RNA TRANSCRIPTION

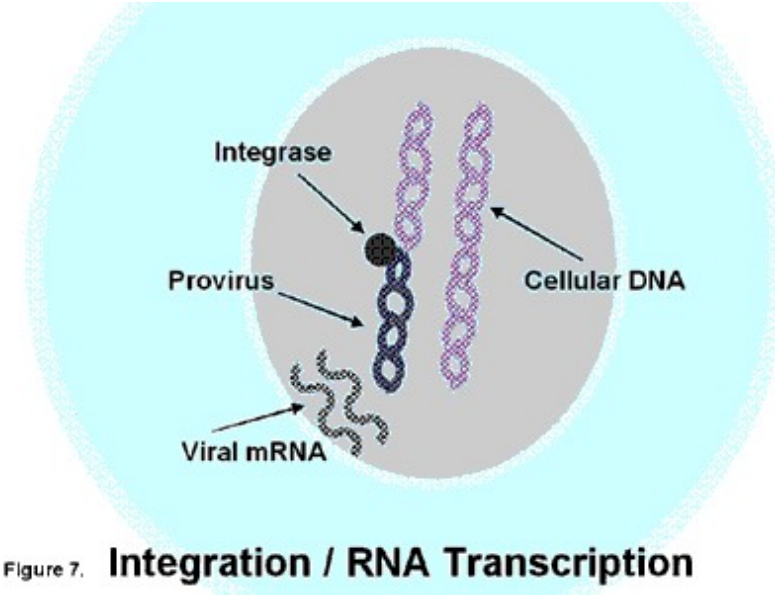


Figure 7. Integration / RNA Transcription

- ✓ once the viral RNA has successfully bridged the nuclear membrane and been escorted to the nucleus, HIV uses an enzyme called integrase to insert HIV's double-stranded DNA into the cell's existing DNA.
- ✓ drugs that inhibit the HIV preintegration complex from traveling to the nucleus called integrase inhibitors – (raltegravir)

VIRAL LATENCY AND PROTEIN SYNTHESIS

- after successful integration of the viral DNA, the host cell is now latently infected with HIV - this viral DNA is referred to as provirus
- when the immune cell becomes activated, this latent provirus awakens and instructs the cellular machinery to produce the necessary components of HIV

CLEAVAGE AND VIRAL ASSEMBLY

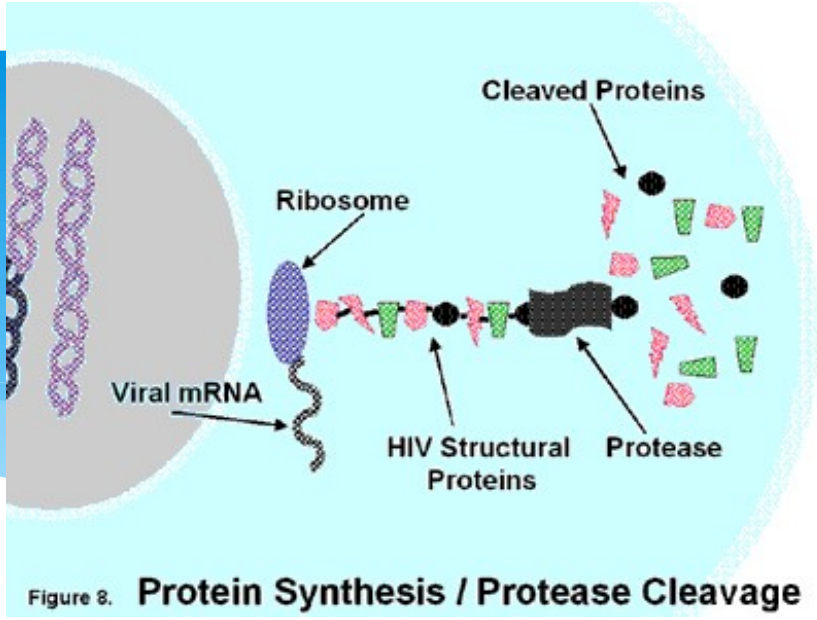


Figure 8. Protein Synthesis / Protease Cleavage

- ✓ once the various viral subunits have been produced and processed, they must be separated for the final assembly into new virus
- ✓ this separation, or cleavage, is accomplished by the viral protease enzyme
- ✓ drugs called protease inhibitors - bind to the protease enzyme and prevent it from separating, or cleaving, the subunits

CLEAVAGE AND VIRAL ASSEMBLY

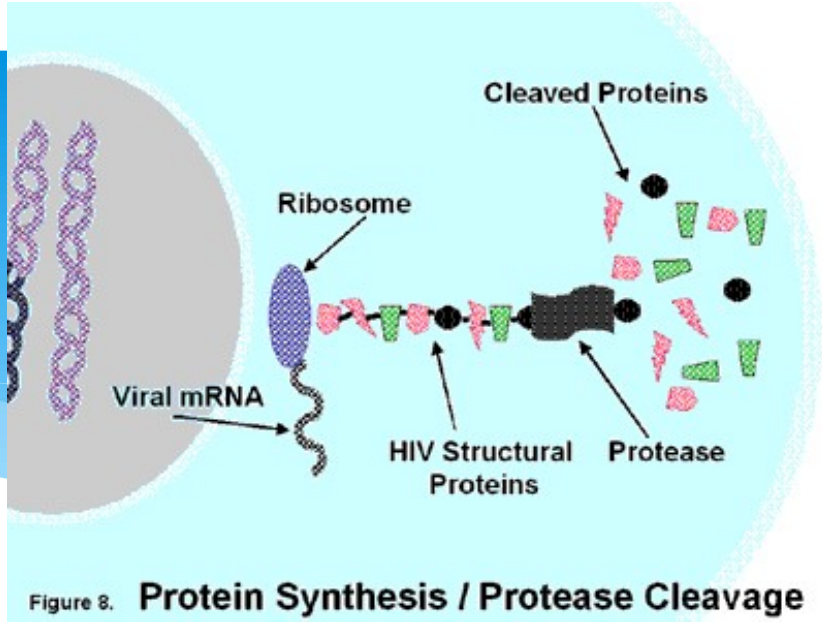


Figure 8. Protein Synthesis / Protease Cleavage

- ✓ if cleavage is successfully completed, the HIV subunits combine to make up the content of the new virons
- ✓ in the next step of the viral life cycle, the structural subunits of HIV mesh with the cell's membrane and begin to deform a section of the membrane
- ✓ this allows the nucleocapsid to take shape and viral RNA is wound tightly to fit inside the nucleocapsid
- ✓ researchers are looking at drugs called zinc finger inhibitors, which interfere with the packaging of the viral RNA into the nucleocapsid

BUDDING

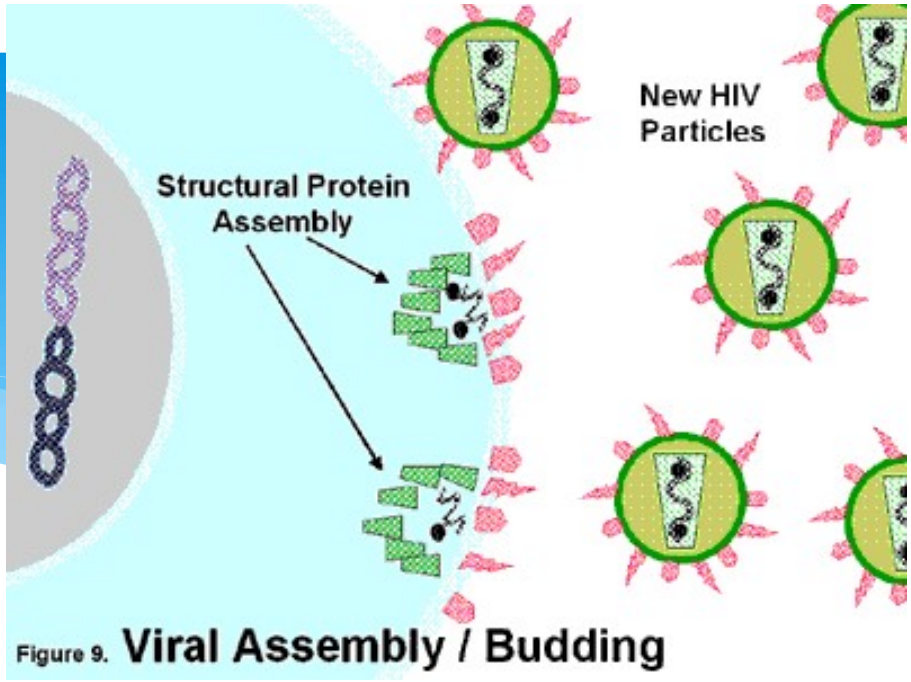


Figure 9. Viral Assembly / Budding

- ✓ the final step of the viral life cycle
- ✓ the genetic material enclosed in the nucleocapsid merges with the deformed cell membrane to form the new viral envelope
- ✓ with its genetic material tucked away in its nucleocapsid and a new outer coat made from the host cell's membrane, the newly formed HIV pinches off and enters into circulation, ready to start the whole process again

Nucleoside Reverse Transcriptase Inhibitors (NRTI)

Brand name	Generic name	Other name	Manufacturer name
Combivir	zidovudine + lamivudine	AZT +3TC	GlaxoSmithKline
Emtriva	emtricitabine	FTC	Gilead Sciences
Epivir	lamivudine	3TC	GlaxoSmithKline
Epzicom	abacavir + lamivudine	ABC + 3TC	GlaxoSmithKline
Hivid	zalcitabine	ddC	Roche
Retrovir	zidovudine	AZT or ZDV	GlaxoSmithKline
Trizivir	abacavir + zidovudine + lamivudine	ABC + AZT + 3TC	GlaxoSmithKline
Truvada	tenofovir + emtricitabine	TDF + FTC	Gilead Sciences
VIDEX	didanosine, dideoxyinosine, ddI	ddI	Bristol-Myers Squibb
VIDEX EC	enteric coated didanosine, ddI EC	ddI	Bristol-Myers Squibb
Viread	tenofovir DF	TDF	Gilead Sciences
Zerit	stavudine	d4T	Bristol-Myers Squibb
Ziagen	abacavir	ABC	GlaxoSmithKline

Non Nucleoside Reverse Transcriptase Inhibitors (NNRTI)

Brand name	Generic name	Other name	Manufacturer name
Edurant	rilpivirine		Tibotec Therapeutics
Intelence	etravirine		Tibotec Therapeutics
Rescriptor	delavirdine	DLV	Pfizer
Sustiva	efavirenz	EFV	Bristol Myers-Squibb
Viramune (Immediate Release)	nevirapine	NVP	Boehringer Ingelheim
Viramune XR (Extended Release)	nevirapine	NVP	Boehringer Ingelheim

Protease Inhibitors - PI

Brand name	Generic name	Other name	Manufacturer name
Agenerase	amprenavir	APV	GlaxoSmithKline
Aptivus	tipranavir	TPV	Boehringer Ingelheim
Crixivan	indinavir	IDV	Merck
Invirase	saquinavir mesylate	SQV (HGC)	Roche
Kaletra	lopinavir and ritonavir	LPV/RTV	Abbott Laboratories
Lexiva	fosamprenavir calcium	FOS-APV	GlaxoSmithKline
Norvir	ritonavir	RTV	Abbott Laboratories
Prezista	darunavir		Tibotec Inc.
Reyataz	atazanavir sulfate	ATV	Bristol-Myers Squibb
Viracept	nelfinavir mesylate	NFV	Agouron Pharmaceuticals

Fusion Inhibitors (FI)

Brand name	Generic name	Other name	Manufacturer name
Fuzeon	enfuvirtide	ENF, T-20	Hoffmann-La Roche & Trimeris

Entry Inhibitors - CCR5 co-receptor antagonist

Brand name	Generic name	Other name	Manufacturer name
Selzentry	maraviroc		Pfizer

HIV Integrase Strand Transfer Inhibitors (INSTI)

Brand name	Generic name	Other name	Manufacturer name
Isentress	raltegravir		Merck

Multi-class Combination Products

Brand name	Generic name	Manufacturer name
Atripla	efavirenz, emtricitabine and tenofovir disoproxil fumarate	Bristol-Myers Squibb and Gilead Sciences
Complera	emtricitabine, rilpivirine, and tenofovir disoproxil fumarate	Gilead Sciences

HAART – HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

- HAART is the name given to aggressive treatment regimens used to suppress HIV viral replication and the progression of HIV disease
- the usual HAART regimen combines three or more different drugs such as two nucleoside reverse transcriptase inhibitors (NRTIS) and a non-nucleoside reverse transcriptase inhibitor (NNRTI), two NRTIS and protease inhibitor (PI), two NRTIS and a integrase inhibitor (INSTI) or other such combinations
- proven to reduce the amount of active virus (< 500 copies RNA /ml plasma during 6-52 weeks) and in some cases until it is undetectable by current blood testing techniques
- it allows to partial reconstruction of immune system
- can cause serious, life-threatening side effects

(*Paterson et al., 2000; Goodman and Gilman, 2005*)

ORAL COMPLICATIONS OF HIV INFECTION

Fungal Candidiasis Histoplasmosis Geotrichosis Cryptococcosis Aspergillosis	**Neoplastic** Kaposi's sarcoma Non-Hodgkin's lymphoma Squamous cell carcinoma
Bacterial HIV-associated gingivitis HIV-associated periodontitis Necrotizing stomatitis Mycobacterium avium complex Klebsiella stomatitis Bacillary angiomatosis	**Other** Recurrent aphthous ulcers Immune thrombocytopenic purpura Salivary gland disease
Viral Herpes simplex Herpes zoster Cytomegalovirus ulcers Hairy leukoplakia Warts	

ORAL COMPLICATIONS OF HIV INFECTION

I. Candidiasis

- oral candidiasis often precedes the development of AIDS in HIV - seropositive individuals
  - ✓ the most common form of oral candidiasis is pseudomembranous candidiasis, appearing as white plaques on any oral mucosal surface, which may be as small as 1 to 2 mm or may be widespread
  - ✓ lesions can be wiped off, leaving an erythematous or bleeding mucosal surface
  - ✓ the erythematous form of candidiasis appears as smooth red patches on the hard or soft palate, buccal mucosa, or dorsal tongue
  - ✓ angular cheilitis due to Candida infection produces erythema, cracks, and fissures at the corner of the mouth

ORAL COMPLICATIONS OF HIV INFECTION

I. Candidiasis

- diagnosis of oral candidiasis is by potassium hydroxide preparation of a smear from the lesion
- oral candidiasis in patients with HIV infection usually responds to topical antifungal agents, including nystatin oral pastilles
- fluconazole (Diflucan) is an extremely effective treatment for oral candidiasis, although resistance has been reported
- ketoconazole (Nizoral), 200 mg orally once daily, is a systemic antifungal agent that can also be used
- angular cheilitis usually responds to topical nystatin-triamcinolone (Mycolog II), clotrimazole (Mycelex), or ketoconazole (Nizoral) cream

ORAL COMPLICATIONS OF HIV INFECTION

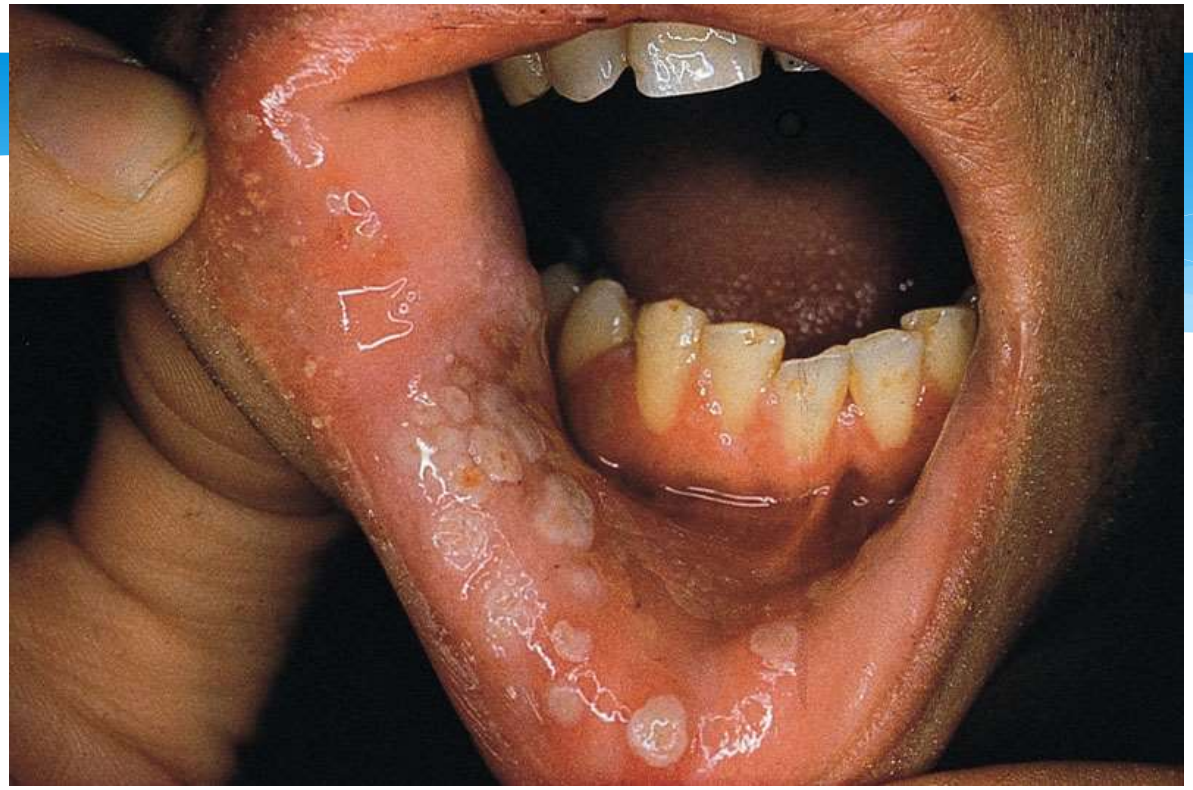
II. Gingivitis and periodontitis

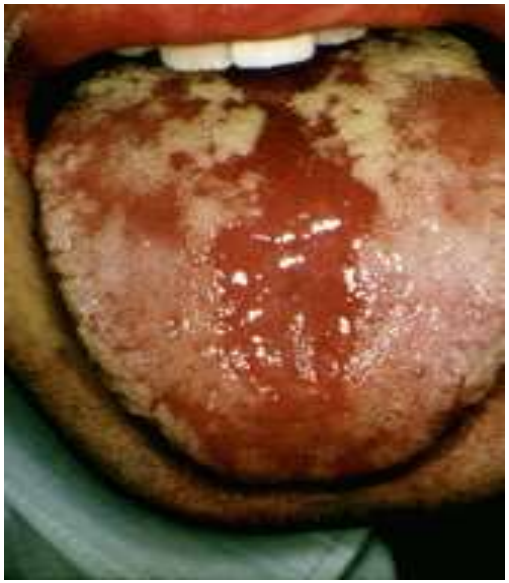
- gingivitis and periodontal disease is often seen in HIV infection, appearing as gingival erythema
- necrotizing ulcerative periodontitis occurs in 30% to 50% of AIDS patients
- treatment involves débridement and curettage, followed by application of a topical antiseptic (povidone-iodine [Betadine]) irrigation, followed with chlorhexidine (Peridex) mouthwashes and a 4- to 5-day course of metronidazole or amoxicilline/clavulanique acid

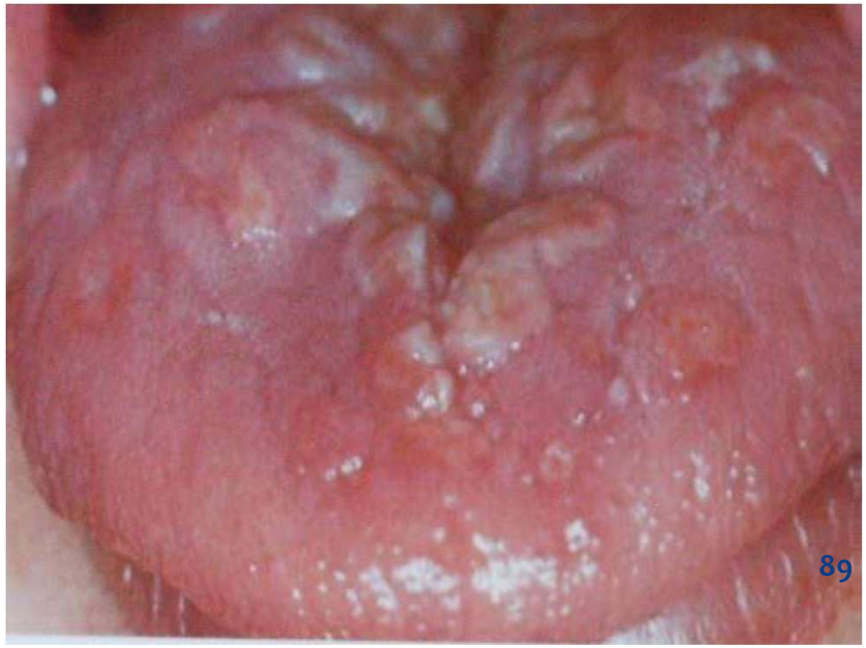
ORAL COMPLICATIONS OF HIV INFECTION

III. Herpes simplex

- oral herpes lesions are a common feature of HIV infection, occurring as recurrent intraoral lesions with crops of small, painful vesicles that ulcerate
- lesions commonly appear on the palate or gingiva
- HSV can be identified using monoclonal antibodies and immunofluorescence
- treatment consists of oral acyclovir
- foscarnet is used for lesions that are resistant to acyclovir



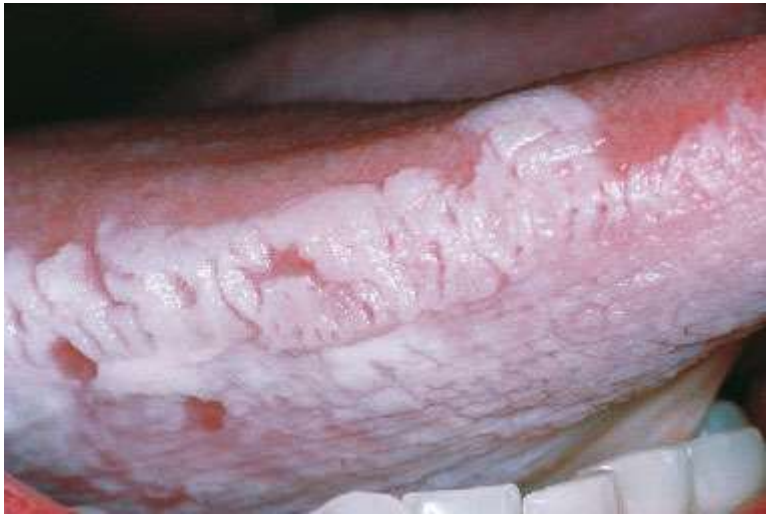


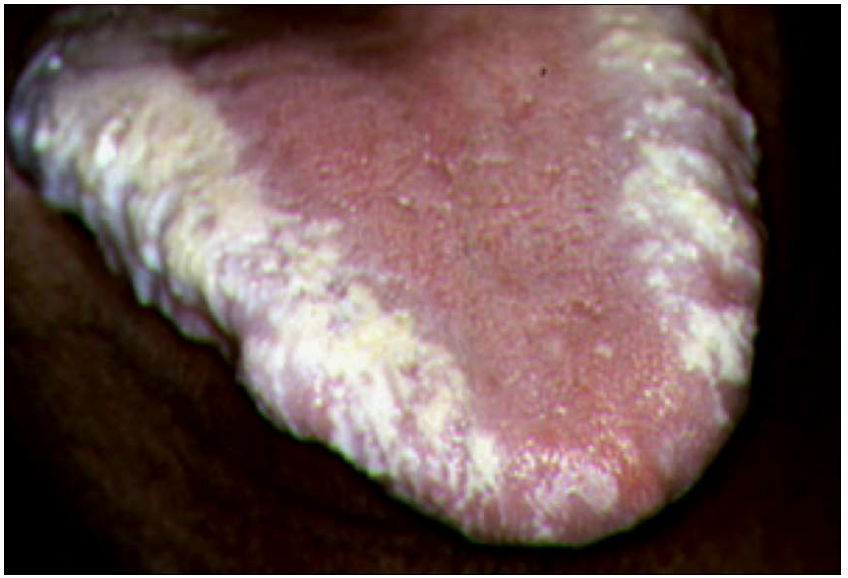


ORAL COMPLICATIONS OF HIV INFECTION

IV. Hairy leukoplakia

- probably caused by a reactivation of Epstein-Barr virus
- may affect the buccal mucosa, soft palate, and floor of mouth
- it appears in all risk groups for AIDS, appearing as a white thickening of the oral mucosa, often with vertical folds or corrugations
- the lesions range in size from a few millimeters to involvement of the entire dorsal surface of the tongue
- the lesions will respond to high doses to acyclovir
- highly effective are valacyclovir and famciclovir
- for milder cases, topical applications of retin-A or podophyllin may be helpful

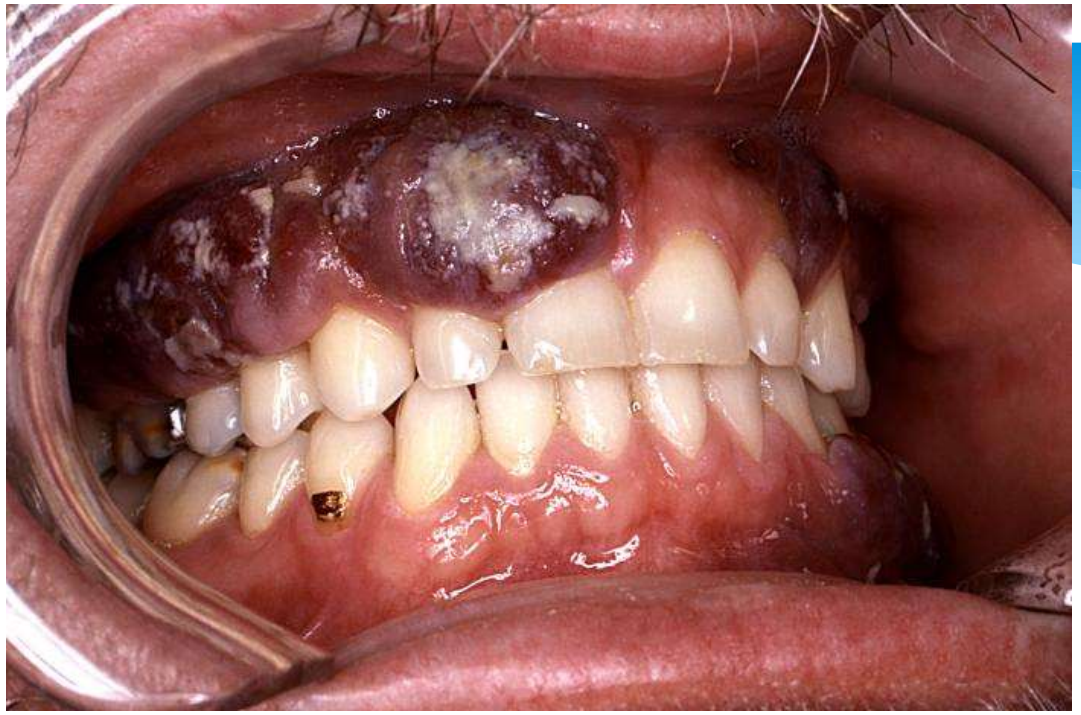


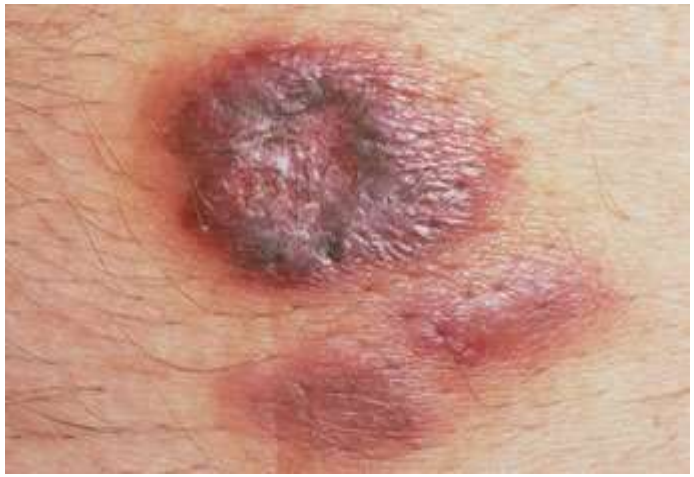


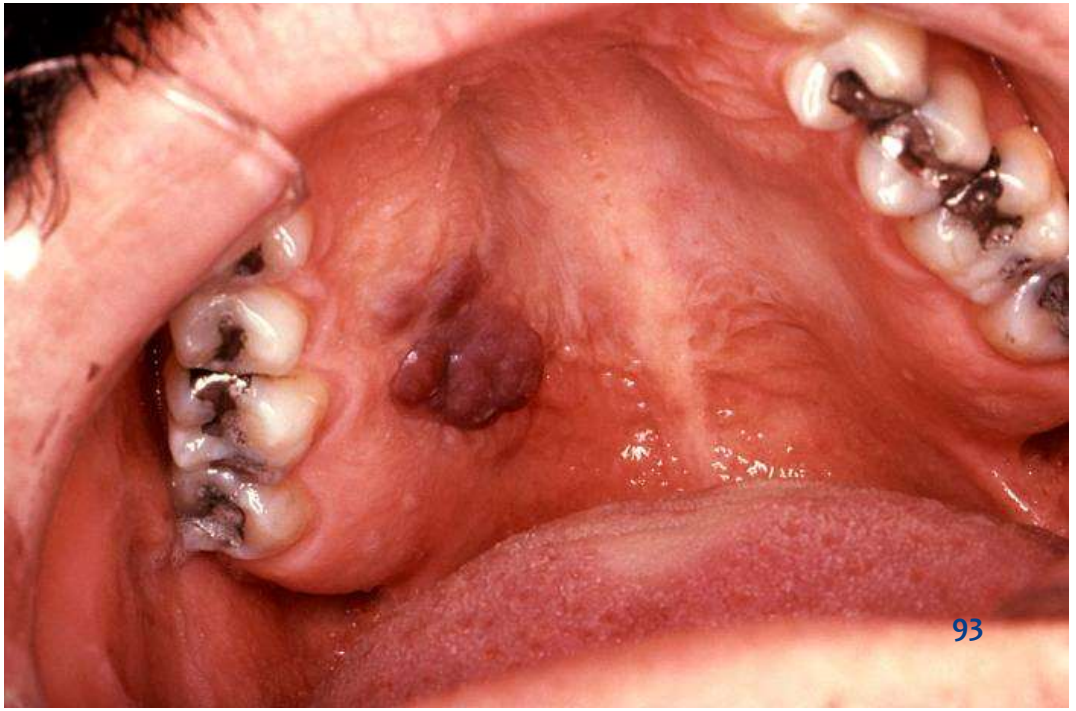
ORAL COMPLICATIONS OF HIV INFECTION

V. Kaposi's sarcoma

- may cause oral lesions in patients with AIDS, appearing as red or purple macules, papules, or nodules
- frequently they are asymptomatic; however, pain may result from traumatic ulceration, inflammation, or infection
- bulky lesions may interfere with speech and mastication
- diagnosis involves biopsy
- treatment consists of surgical excision, local radiation, chemotherapy, or local injection of vinblastine



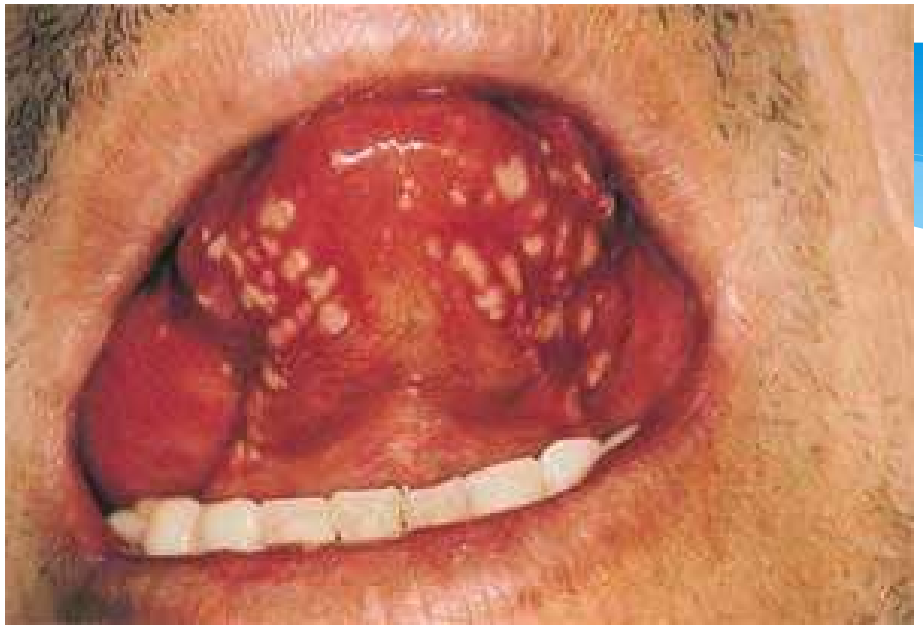


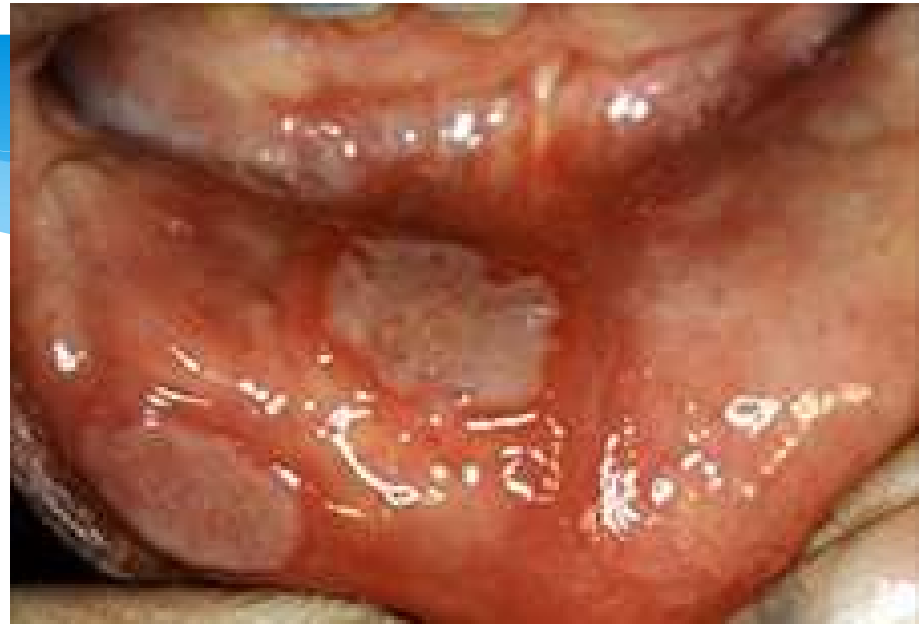


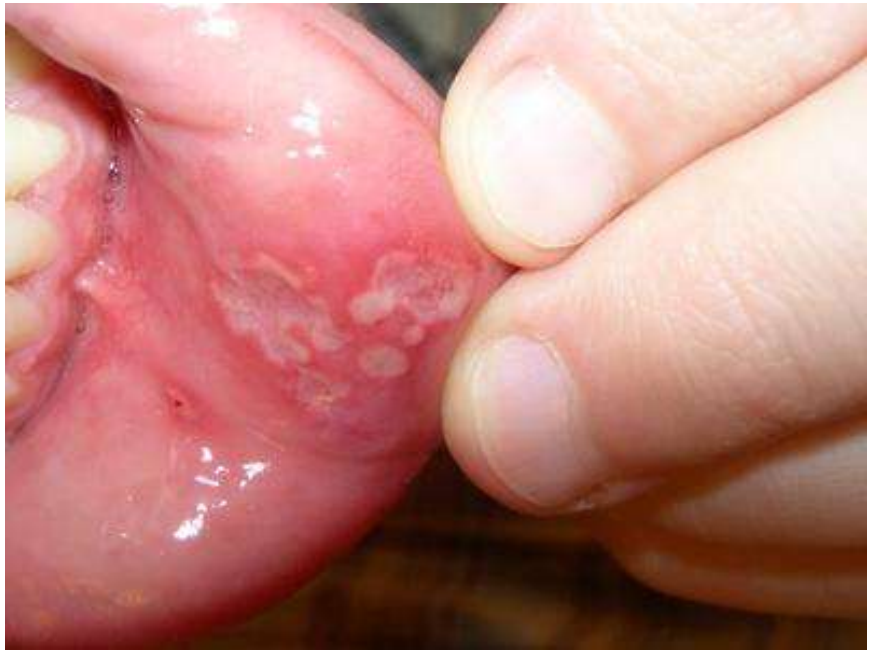
ORAL COMPLICATIONS OF HIV INFECTION

VI. Recurrent aphthous ulcers

- more common among HIV-positive individuals, appearing as recurrent crops of small (1-2 mm) to large (1 cm) ulcers on the oral and oropharyngeal mucosa
- treatment consists of fluocinonide 0.05% ointment, mixed with equal parts of Orabase applied to the lesion up to six times daily, or clobetasol 0.05%, mixed with equal parts of Orabase applied three times daily
- also helpful is dexamethasone elixir 0.5 mg/mL used as a rinse and expectorate
- thalidomide has been found to be useful in the management of steroid - resistant ulcers







HIV OCCUPATIONAL EXPOSURE

- the guidelines emphasize primary prevention strategies and prompt reporting and management of occupational exposures
- if possible, the HIV status of the exposure source patient should be determined to guide the need for HIV PEP
- initiating PEP should be the first priority and should not be delayed pending expert consultation, which is also recommended
- PEP should be started to 4 hours (ideally!), no later than 48 hours
- follow-up appointments should begin within 72 hours of HIV exposure and should include follow-up HIV testing, monitoring for drug toxicity, and counselling
- HIV testing should generally continue for 6 months after exposure
- HIV testing may be concluded at 4 months, provided a newer fourth-generation HIV antigen/antibody combination test is used for follow-up testing

POSTEXPOSURE PROPHYLAXIS (PEP)

- the severity of exposure should not be used to determine the number of drugs to be offered in an HIV PEP regimen
- PEP regimens should contain 3 (or more) antiretroviral drugs for 4 weeks routinely for all occupational exposures to HIV
- examples of recommended PEP regimens include those consisting of a dual NRTI backbone plus an INSTI, a PI (boosted with ritonavir), or a NNRTI
  - ✓ emtricitabine (FTC) plus tenofovir (TDF) (these 2 agents may be dispensed as Truvada, a fixed-dose combination tablet) plus raltegravir (RAL)
  - ✓ zidovudine (AZT) plus lamivudine (3TC) (these 2 agents may be dispensed as Combivir) plus rilpivirine (RPV)
- other antiretroviral drug combinations may be indicated for specific cases (eg, exposure to a source patient harboring drug-resistant HIV)

THANK YOU