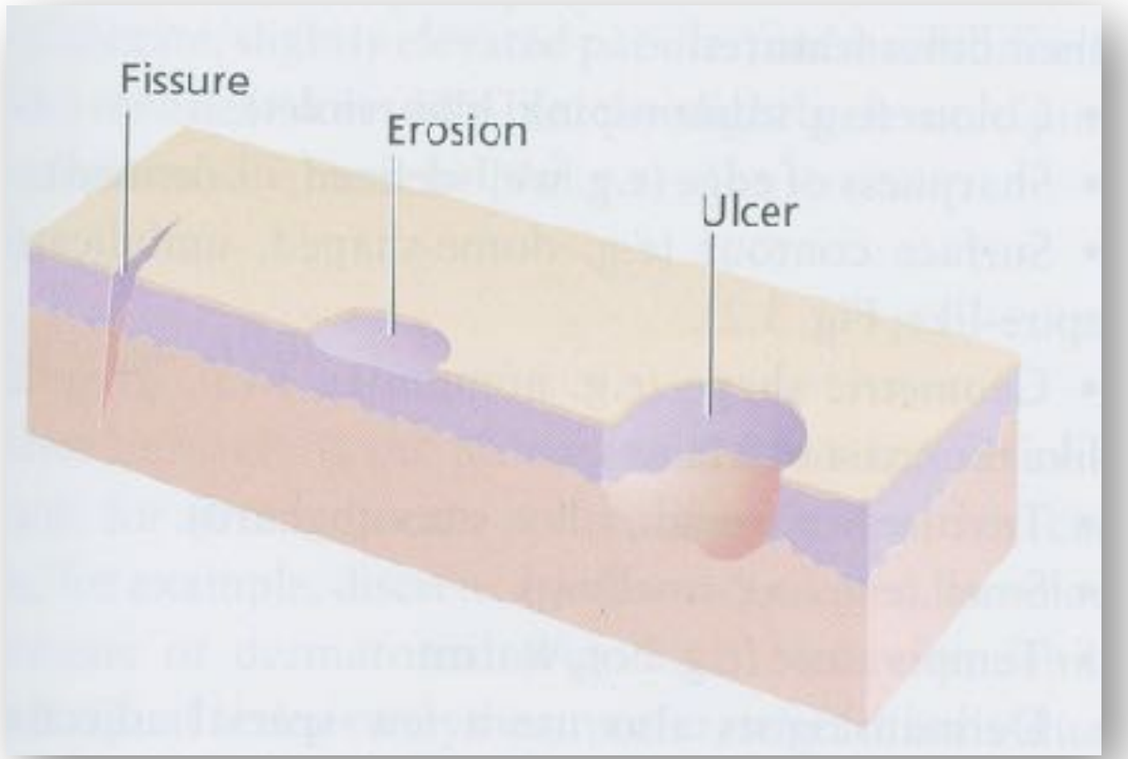
Oral ulcers

Dr. Suhail Al-Amad

10th Oct 2019

- Gross defect of the epithelium
- Can appear following rupture of a blister *(previous lectures)*, or following loss of epithelial lining



Source of illustration: Hunter *el al*. Clinical Dermatology. 3rd ed. 2002

Oral mucosal ulcers

- Reactive
  - Mechanical
  - Factitious
  - Iatrogenic
  - Thermal
  - Therapeutic
- Infectious
  - Bacterial
  - Fungal
- Immune-mediated
  - RAS/BD
  - Erythema Multiforme
  - Drugs
  - Granulomatous disorders
- Neoplastic
  - SCC

Reactive Ulcers

- Common oral presentation
- Trauma should be considered on the top of differential diagnosis list of ulcers
- Mechanical trauma is almost always caused by teeth or dental appliances
  - Affected areas: cheeks, tongue and lips
  - In infants lesions are called *Riga Fede disease*

- Iatrogenic ulcers are related to a recent dental or medical treatment;
  - They are acute
  - History is positive for a recent dental treatment
  - They appear at or near treatment site
  - Examples:
    - removal of a dry cotton role
    - excessive suction
    - RCT chemicals
    - acid itch
    - rotary instruments
    - impression materials
    - improper use of surgical instruments

- Heat induced ulcers are rare.
  - Seen following eating hot food (pizza, potato chips)
  - Or following the application of hot dental material (dental compound)

Ulcer can be chronic…

- Chronic reactive ulcers are caused by injury to mucosa, but with inadequate healing
- Clinically, they present as an indurated deep ulcer with rolled-over edges, sharply demarcated, can be large and non-healing
- Pain is disproportionately small compared to the appearance of the lesion
- Three examples:
    - Factitious ulcers
    - Traumatic Eosinophilic Ulcer
    - Necrotizing Sialometaplasia

- Factitious injuries are difficult to diagnose and treat.

Key features;

- They appear in accessible areas
- They are chronic
- They have abnormal presentation
- In some cases they are linked to psychological disorders

Traumatic Eosinophilic Ulcer

- Histopathology:
  - Granulation tissue formation
  - Deep inflammatory infiltrate extending to muscles
  - Mixed inflammatory cells
  - Significant eosinophilic presence

- Treatment;
  - Remove irritant, keep area clean, observe healing.

Image source: www.pathologyimagesinc.com

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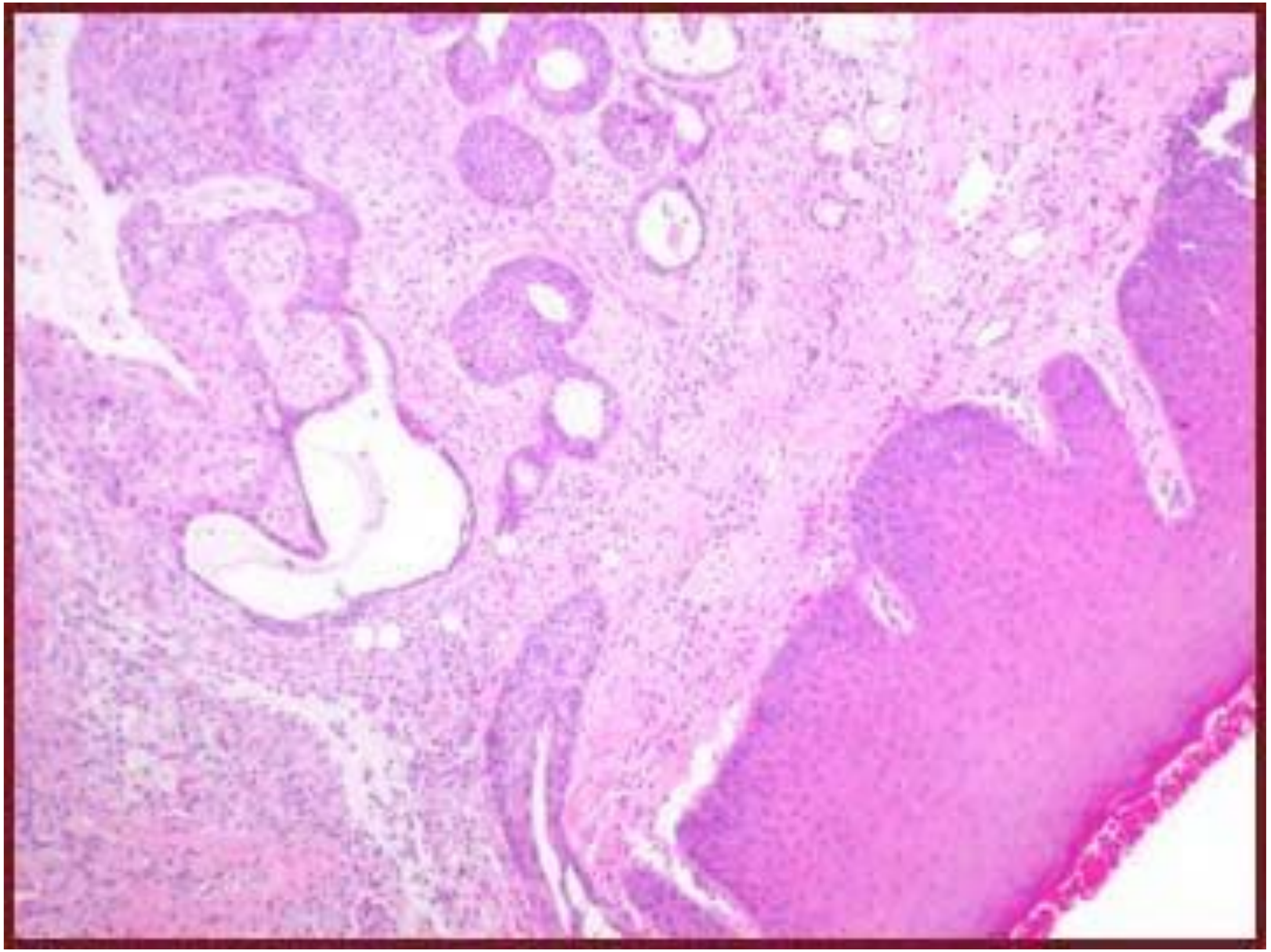

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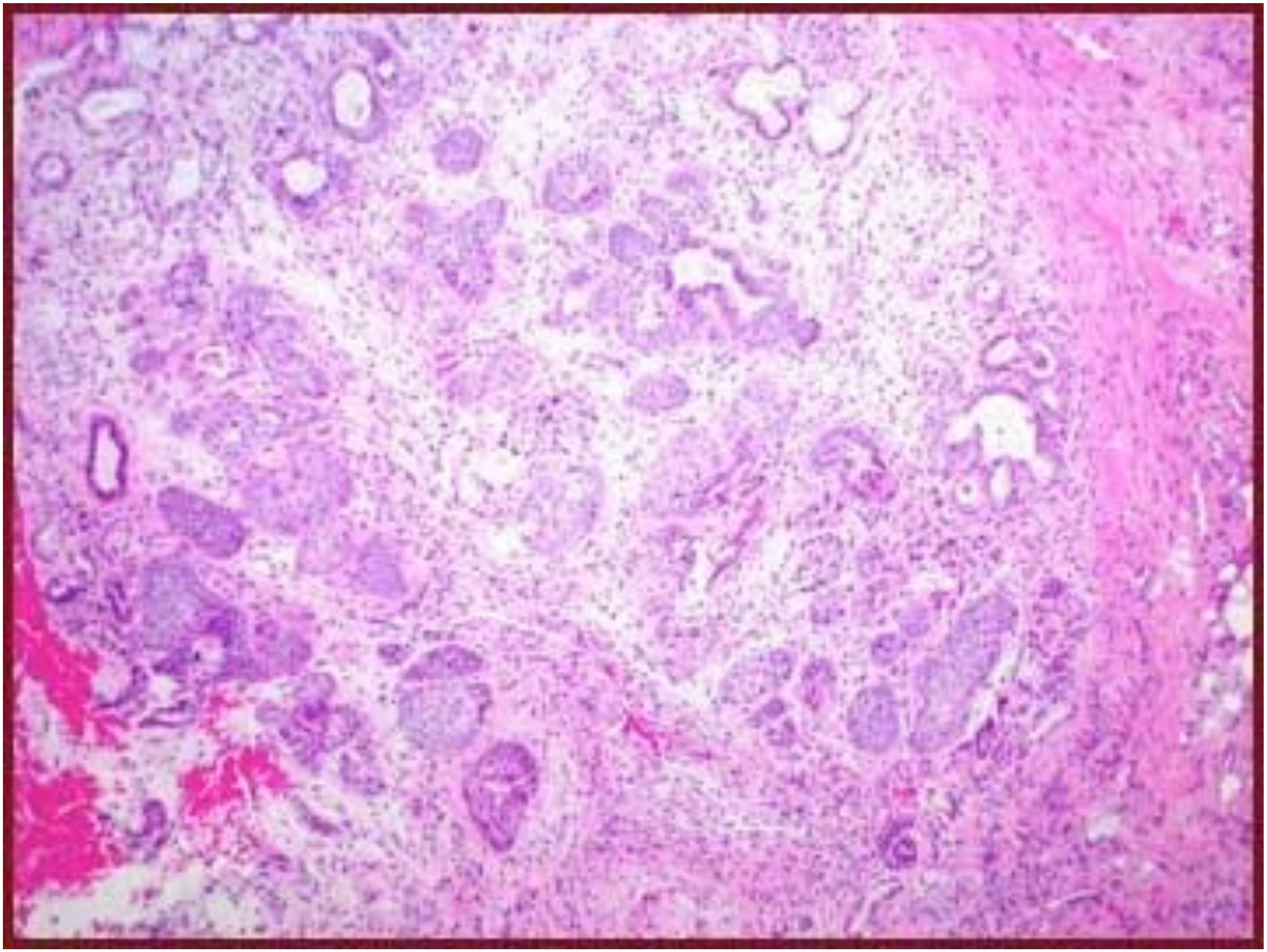

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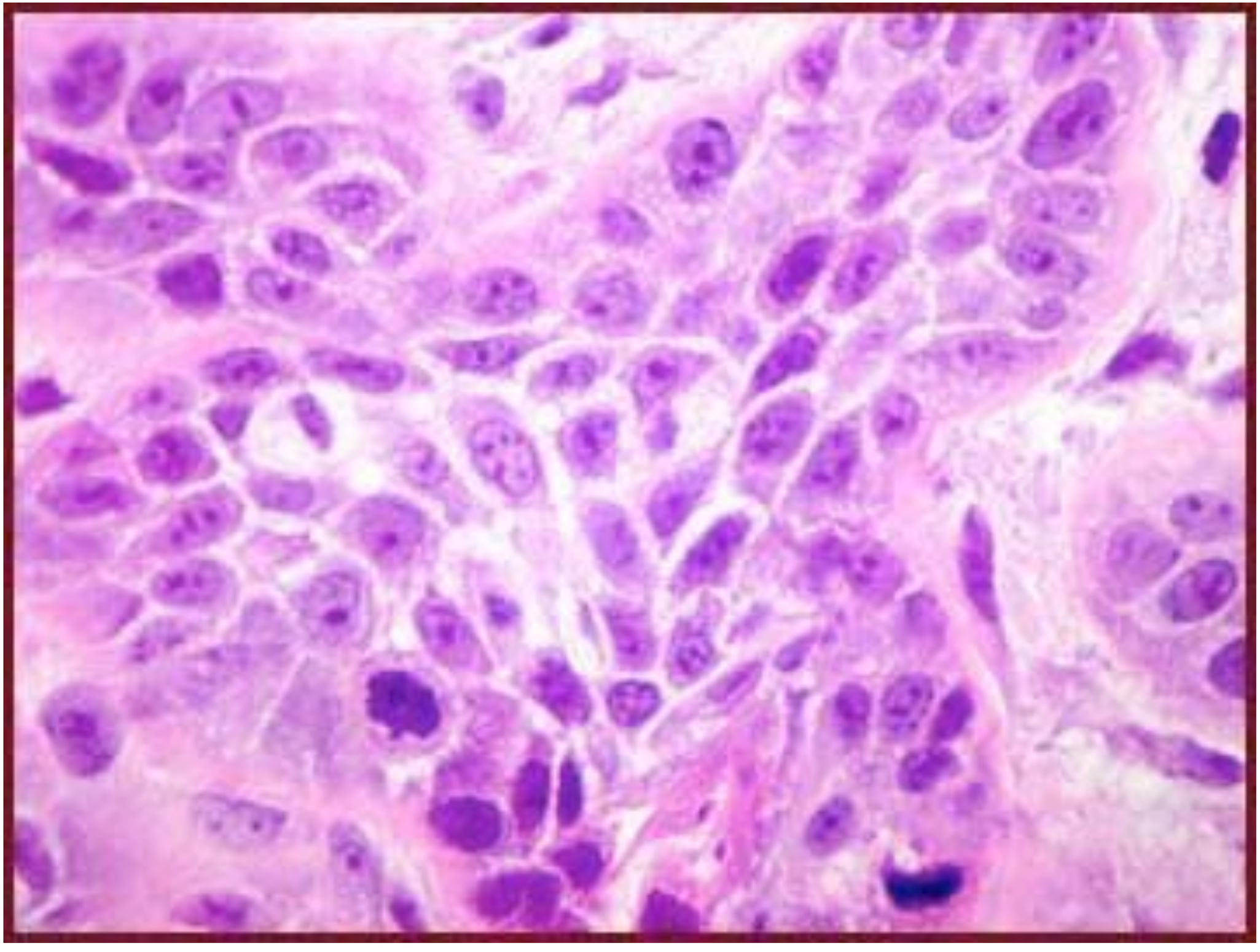

Image source: www.pathologyimagesinc.com

Necrotizing Sialometaplasia

- Histopathology
  - Squamous metaplasia of ductal epithelium
  - Pseudo-epitheliomatous hyperplasia
  - Necrosis of salivary glands
  - Deep inflammatory infiltrate

- Treatment;
  - Reassurance, mouthwash and observation of healing

Image source: screening.iarc.fr

Ulcers secondary to therapy

- Ulcers may appear among mucositis following chemo-therapy or radio-therapy of head and neck tumours
- The ulcers are acute and multiple
- They appear as a result of compromised epithelial regeneration capacity
- Ulcers can persist after therapy due to haematological deficiencies

Oral mucosal ulcers

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  - ~~Mechanical~~
  - ~~Factitious~~
  - ~~Iatrogenic~~
  - ~~Thermal~~
  - ~~Therapeutic~~
- Infectious
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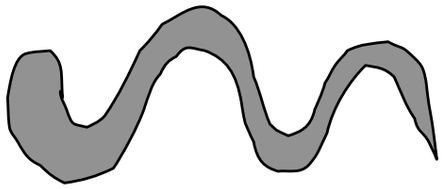
  - Drugs
  - Granulomatous disorders
- Neoplastic
  - SCC

Infections

- Some bacteria and fungi result in oral mucosal ulceration
- Bacterial toxins cause necrosis of the epithelium, which manifests clinically as ulcers
- Infections:
  - Syphilis
  - Gonorrhea
  - Tuberculosis

Syphilis

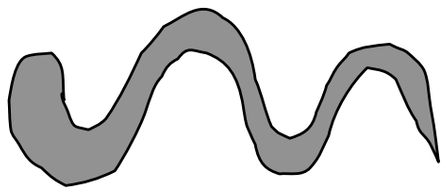
- Caused by *treponema pallidum*
- Transmitted sexually, by blood transfusion or trans-placental
- Three stages; deep ulcers are seen in the primary stage (chancre)



T.Pallidum

Through direct contact

OR



T.Pallidum

Through blood or trans-placental

Primary syphilis

latency

Secondary syphilis

latency

Tertiary syphilis

Chancre; indurated deep well demarcated and painless ulcer

Lymphadenopathy; non-tender and non-suppurative

Spirochetemia; fever, skin rash, ***lymphadenopathy***,

Mucosal lesions; condyloma latum, Mucosal white patches

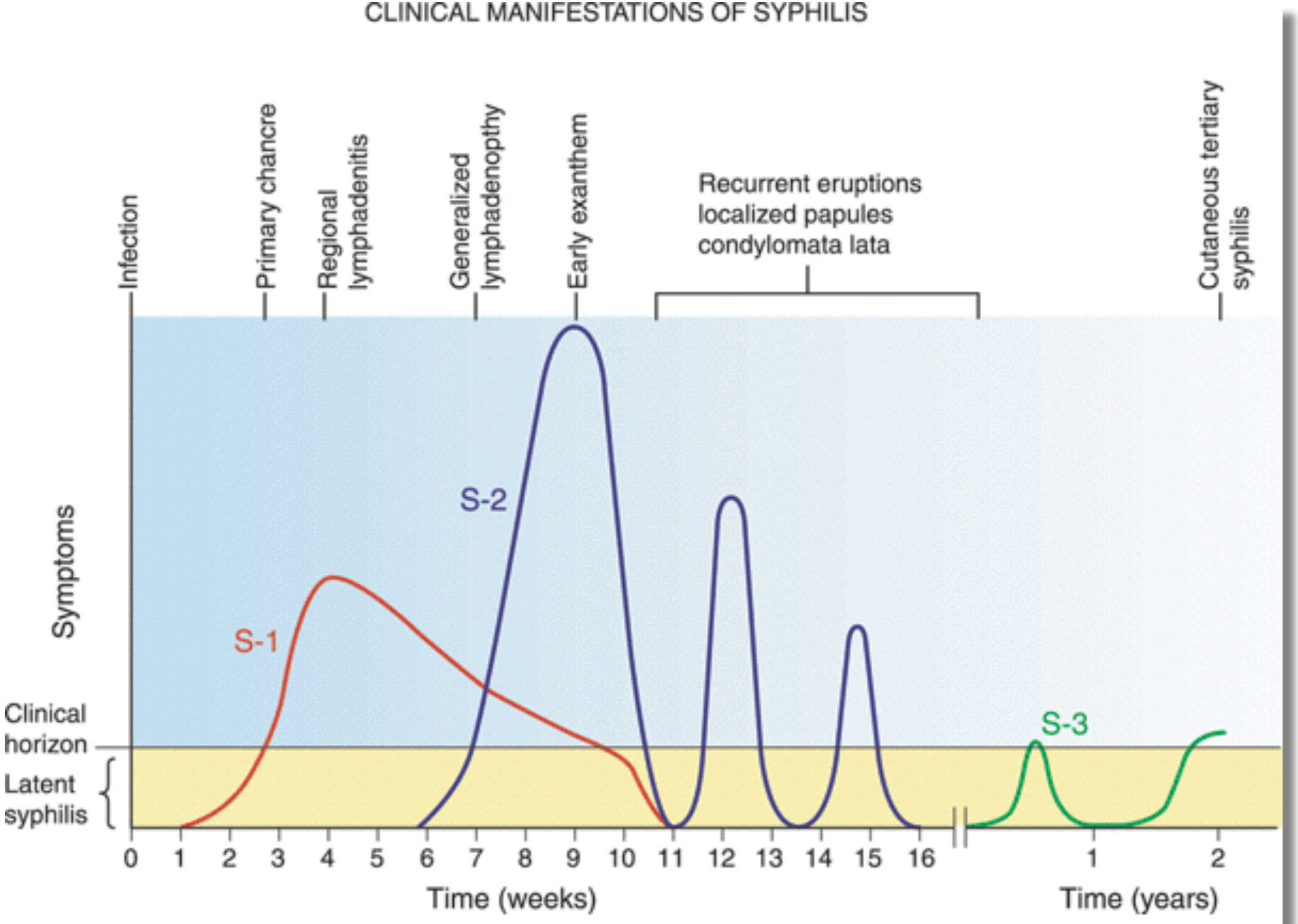
Systematic involvement; CNS and CVS

Gumma; focal necrosis

Glossitis

Risk of SCC ?

CLINICAL MANIFESTATIONS OF SYPHILIS



Source: Wolff K, Johnson RA: *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 6th Edition:* http://www.accessmedicine.com

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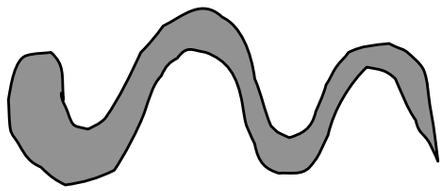
Congenital syphilis

Secondary syphilis in mother



T.Pallidum

Trans-placental route

Spirochetemia in fetus

Systematic involvement; interstitial keratitis, CN VIII deafness, skeletal abnormalities (saddle nose, periostitis of tibia).

Dental involvement; mulberry molars, notched incisors.

- Diagnosis;
  - Darkfield examination of exudate from an active lesion
  - Silver stain
  - Serology

- Treatment;
  - Penicillin

Source: Schorge JO, Schaffer JI, Halvorson LM, Hoffman BL, Bradshaw KD, Cunningham FG: *Williams Gynecology*: http://www.accessmedicine.com

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Gonorrhea

- Caused by Neisseria gonorrhea *(Gram negative diplococci)*
- Infects mucous membranes; genital, rectal, oral…etc
- Route: sexual contact
- Clinically appears as generalized erythema and non-specific mucosal ulcerations, pharyngitis and lymphadenopathy.

Gonorrhea

- Diagnosis;
  - Swabs and gram stain and/or culture.
  - Serology
  - Immuno-histochemistry
- Treatment;
  - penicillin

Tuberculosis

- Common worldwide
- Caused by the acid-fast aerobic bacillus Mycobacterium
- Four forms of Mycobacteria are known;
  - *M. tuberculosis*
  - *M. Bovis*
  - *M. avium*
  - *M. intracellulare*

Incidence per 100,000

0-24	50-99	300 or more
25-49	100-299	No estimate

Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

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- *M. tuberculosis* spreads by airborne route.
- The bacteria are then phagocytosed by macrophages in lungs.
- Bacteria are not degraded by macrophages because of their thick waxy coat.
- Macrophages then aggregate to form multi-nucleated giant cells (Langhans cells) and granulomas result.
- The disease is the result of both the bacterial damage, and the cell-mediated immune response.

- Oral mucosal infections of TB are mostly secondary to pulmonary infections through seeding by sputum.
- Palate and tongue are the main sites of involvement.
- Clinically —> a chronic, indurated, non-healing ulcer.
- Haematogenous spread results in lesions anywhere, including jaw bones.

- Histopathology;
  - Granulomatous inflammation with caseous necrosis
  - Langhans multinucleated giant cells

AND

  - Presence of acid-fast bacilli *(detected by Ziehl-Neelsen stain or Fite stain)*

- Treatment;
  - Strong antibiotics and chemotherapeutic agents *(isoniazid, ethambutol, streptomycin…etc)* usually in combination.

Deep Fungal Infections

- Fungi inhaled --> pulmonary disease --> oral ulcers (seeding by infected sputum).
- Pulmonary manifestations include; cough, fever, night sweating, weight loss.
- Oral involvement include; chronic, painful, indurated, non-healing ulcer.

Deep Fungal Infections

- Four types, all are rare outside North America;
  - Histoplasmosis
  - Coccidioidomycosis
  - Blastomycosis
  - Cryptococcosis

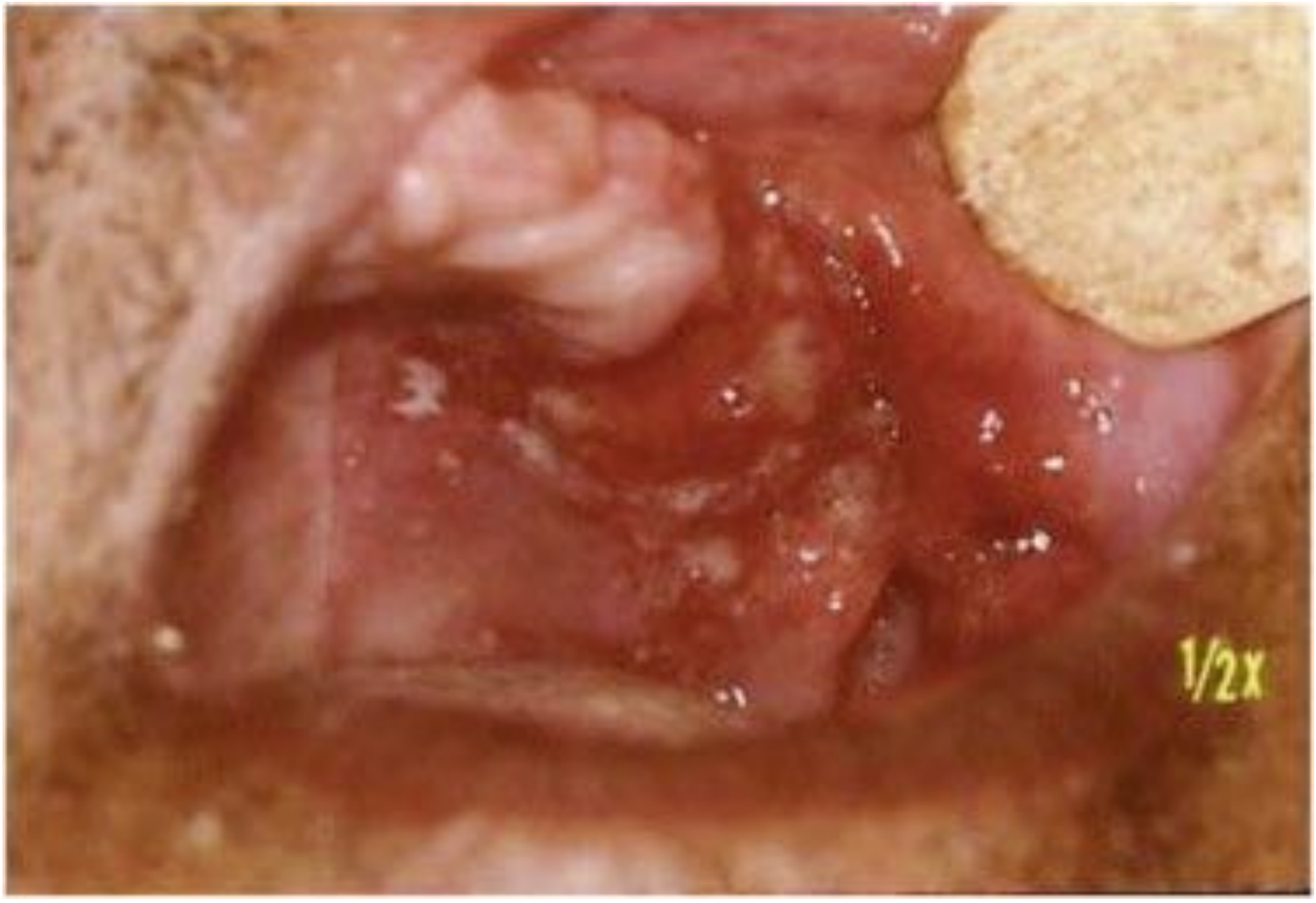
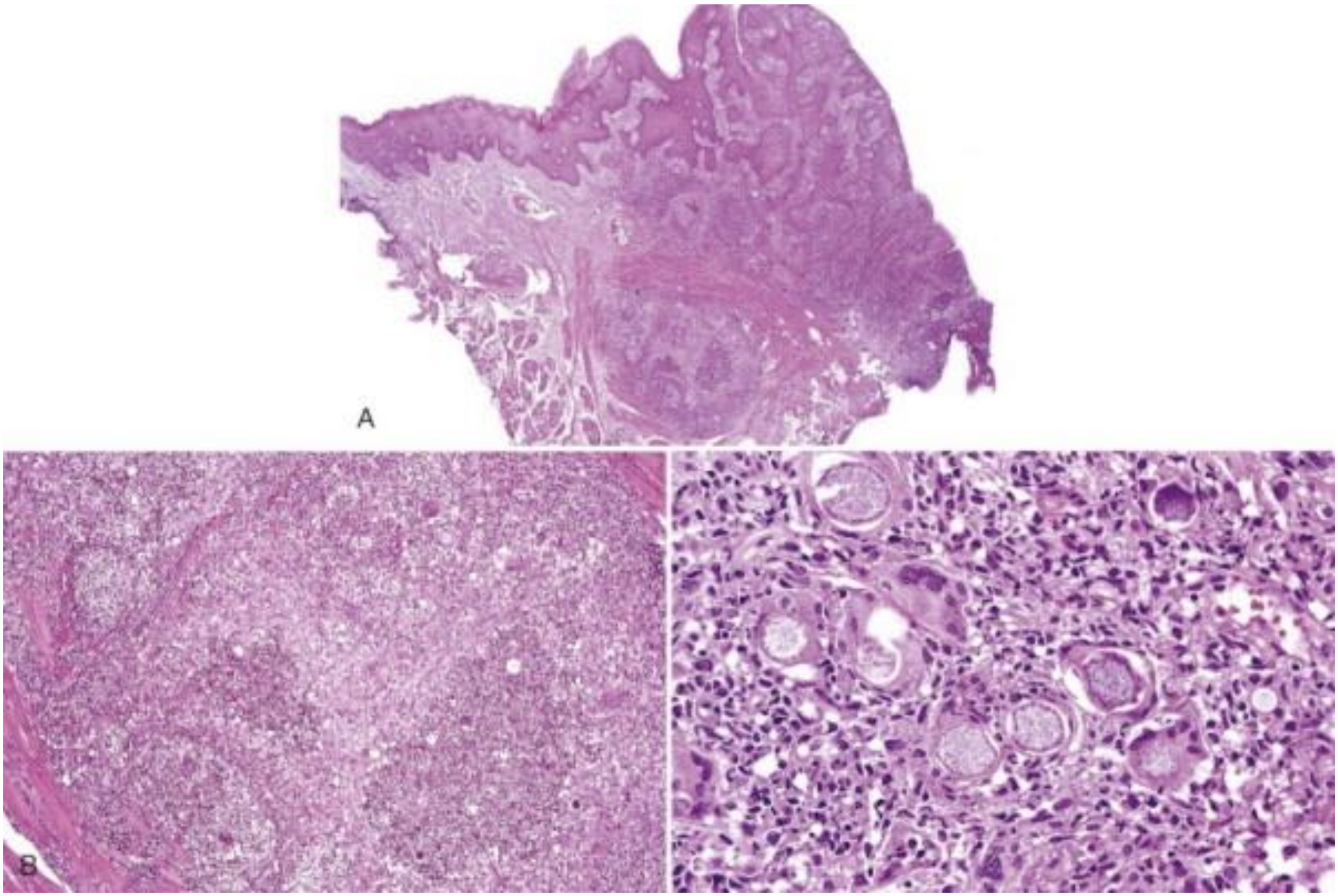


Image source: Oral Pathology a comprehensive atlas and text. By Sook-Bin Woo



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Deep Fungal Infections

- Histopathology;
  - Pseudo-epitheliomatous hyperplasia
  - Granulomatous inflammation
  - Sometimes with abscess (blastomycosis)

AND

  - Demonstration of the micro-organisms

- Treatment;
  - Azole group
  - Amphotericin B

Opportunistic Fungal Infections

- Two forms; phycomycosis (mucormycosis) and Aspergillosis
- Route of infection is either through the GIT (contaminated food) or pulmonary (contaminated air)
- Affects medically-compromised patients

Opportunistic Fungal Infections

- Cause necrosis and ulceration of the tissues (nasal, sinuses or oro-pharynx)
- Aggressive lesions --> perforate palate, nasal cavity and orbit, and extends to the brain.
- Death is a common.

Opportunistic Fungal Infections

- Histopathology;
  - Necrosis
  - Chronic and acute inflammatory reaction
  - Presence of the microorganisms

- Treatment;
  - Amphotericin B and surgical debridement

Oral mucosal ulcers

- Reactive
  - ~~Mechanical~~
  - ~~Factitious~~
  - ~~Iatrogenic~~
  - ~~Thermal~~
  - ~~Therapeutic~~
- Infectious
  - ~~Bacterial~~
  - ~~Fungal~~
- Immune-mediated
  - RAS/BD
  - Erythema Multiforme
  - Drugs
  - Granulomatous disorders
- Neoplastic
  - SCC

Recurrent Aphthus Stomatitis
RAS

- Also called canker sores
- Common mucosal lesion; prevalence from 10-25%
- Mainly seen in higher socio-economic class, and globally seen more in developed countries.
- Affects any age, starts in childhood.
- Slight female predilection.

Aetiology

- **Genetic;**
  - 1/3 positive family history
  - Frequency of HLA-A2, A11, B12, DR2
- **Haematological deficiency;**
  - Iron (Fe-deficiency anaemia)
  - B_{12} (pernicious anaemia)
  - Folic acid (folic acid anaemia)
- **Cyclic neutropenia**
- **GIT disorders;**
  - Coeliac disease
  - Crohn's disease
  - Ulcerative colitis
  - H. pylori

Aetiology

- **Hormonal changes;**
  - Relation to drop in progesterone during luteal phase
- **Allergies;**
  - To certain types of foods
- **Stress**

Other disorders with similar RAS presentation

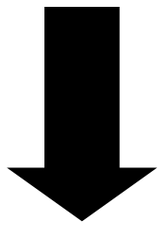
- **Behçet disease (syndrome)** (oral, genital ulcers, eye lesions and skin papulo-pustular lesions)
- **HIV-related ulcers**
- **PFAPA** (*P*eriodic *F*ever, *A*phthus, *P*haryngitis, *A*denitis)
- **Sweet syndrome** (oral ulcers, conjunctivitis and inflamed skin nodules)

Recurrent Aphthus Stomatitis
RAS

- Clinically;
  - RAS is diagnosed when other diseases with oral ulcers are excluded.
  - Three clinical presentations:
    - Minor aphthae (80% of RAS)
    - Major aphthae (15-20% of RAS)
    - Herpetiform aphthae (>1% of RAS)

Pathogenesis

- Unclear, most likely RAS is a manifestation of an immune-dysfunction.
  - Per-ulcerative lesions have CD4+ cells (helper)
  - Ulcerative lesions have CD8+ cells (cytotoxic)



Epithelial necrosis and delayed healing

- Trigger for the immune response:
- Micro-organisms (*Strep. Snagius*, CMV, HSV, HIV)
- Trauma

Minor RAS

- Small round to oval ulcers
- Surrounded by an erythematous halo
- Floor is white (CT) --> yellow (Fibrin) --> grey (granulation tissue)
- Seen mainly on non-keratinized mucosae
- 1-6 lesions at a time
- Heals in about 1 week
- Recurs in 1-4 months
- Does not leave a scar
- Painful

Major RAS

- Large round to oval ulcers (around 1cm in diameter)
- Surrounded by an erythematous halo
- Floor is white (CT) --> yellow (Fibrin) --> grey (granulation tissue)
- Seen on any mucosal surface
- 1-6 lesions at a time
- Heals in about 10-40 days
- Recurs frequently
- Might leave a scar
- Can be painful

Herpetiform RAS

- Multiple minute pinhead ulcers which coalesce into large ragged ulcers
- Surrounded by an erythematous halo
- Seen on any mucosal surface
- Heals in at least 10 days
- Recurs very frequently, almost continuous oral ulceration
- Often extremely painful

- **Histopathology**;
  - Non-specific ulcer
  - Inflammatory cells in the submucosa, starting with CD4+ cells, then CD8+ cells
  - Granulation tissue on the ulcerated surface

- **Treatment**;
  - First, R/O other systemic causes, treat and/or refer if necessary.
  - Encourage high standards of oral hygiene
  - Topical corticosteroids
  - Tetracycline/nystatin mouthwash
  - Intra-lesion injection of corticosteroids
  - Systemic corticosteroids
  - Systemic immune suppressants

Behçet disease

- Also called Behçet's syndrome.
- A group of systemic symptoms affecting mainly the mouth, eyes, genitalia and skin. CNS and CVS may also be involved.
- Affects males (2:1), young adults (20-30 years), and is seen in countries around the Silk Road (Middle East to Japan).
- Rare in the west.

Aetiology

- There is evidence of vasculitis related to immune-complexes affecting the involved tissues.
- Cross reactivity between the epithelial proteins and bacterial (*Strep. Sangus*) proteins have been found.
- Other correlations were seen with HSV, pesticides, certain foods and heavy metals.
- Immune dysregulation in lesions; abnormal ratio of CD4/CD8, abnormal NK cell activity, increase in cytokines activities.
- Strong link between BD and HLA-B51

- **Clinically**;
  - It is a multi-system disease.
  - Commonly, symptoms are preceded by generalized weakness, pharyngitis, generalized pain and headaches, weight loss…etc.
  - In most patients, oral ulcers precede other components of BD.
  - Similar to minor RAS, but are frequently larger in size, located in posterior mouth, and show more ragged edges.

- **Clinically**;
  - **International Study Group on BD established diagnostic criteria:**

I. RAS,

plus two of the following:

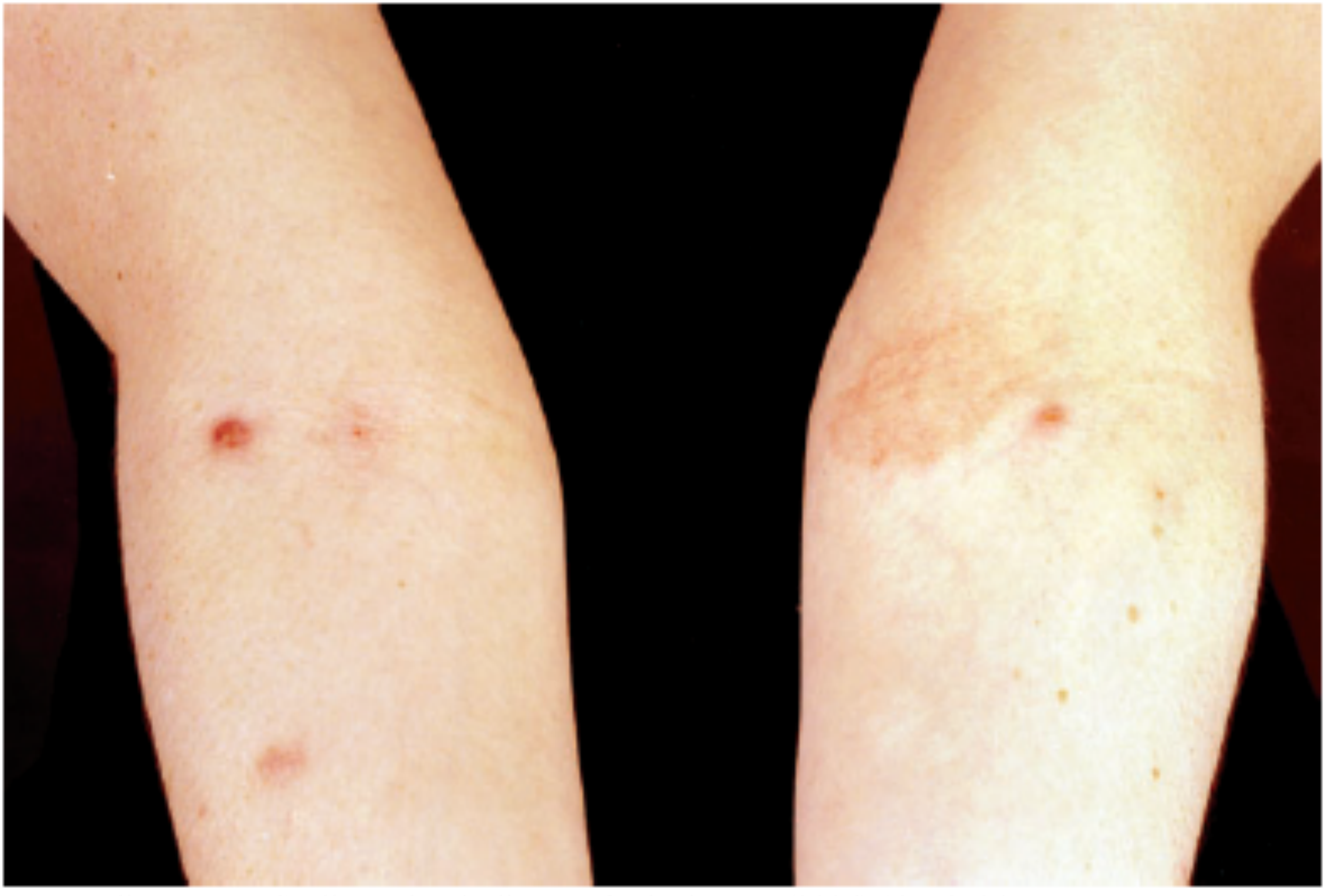
II. Recurrent genital ulceration

III. Eye lesions (posterior uveitis)

IV. Skin lesions (erythema nodosum, acneiform nodules)

V. Positive pathergy test

Escudier, Bagan, Scully; Behçet's disease. Oral Diseases (2006) 12, 78–84



Escudier, Bagan, Scully; Behçet's disease. Oral Diseases (2006) 12, 78–84

- **Histopathology**;
  - Ulcers are non-specific.
  - Presence of vasculitis in the connective tissue

- **Treatment;**
  - Topical cortico-steroids and/or tetracycilne mouthwash.
  - Systemic cortico-steroids.
  - Systemic immune suppressants

- **BD is a leading cause of blindness in young males, and might result in death from CNS or CVS complications.**

Oral mucosal ulcers

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Source: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ: *Fitzpatrick's Dermatology in General Medicine*, 7th Edition: http://www.accessmedicine.com

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Erythema Multiforme EM

- Uncommon, self-limiting mucocutaneous disorder.
- Mainly affects young adults (20-40y).
- > in males.
- Ranges in severity.
- Ranges in clinical symptoms --> multiforme.
- Oral lesions are seen in 70% of cases.
- Three types: Minor EM, Major EM (SJS) and Toxic Epidermal Necrolysis (TEN).

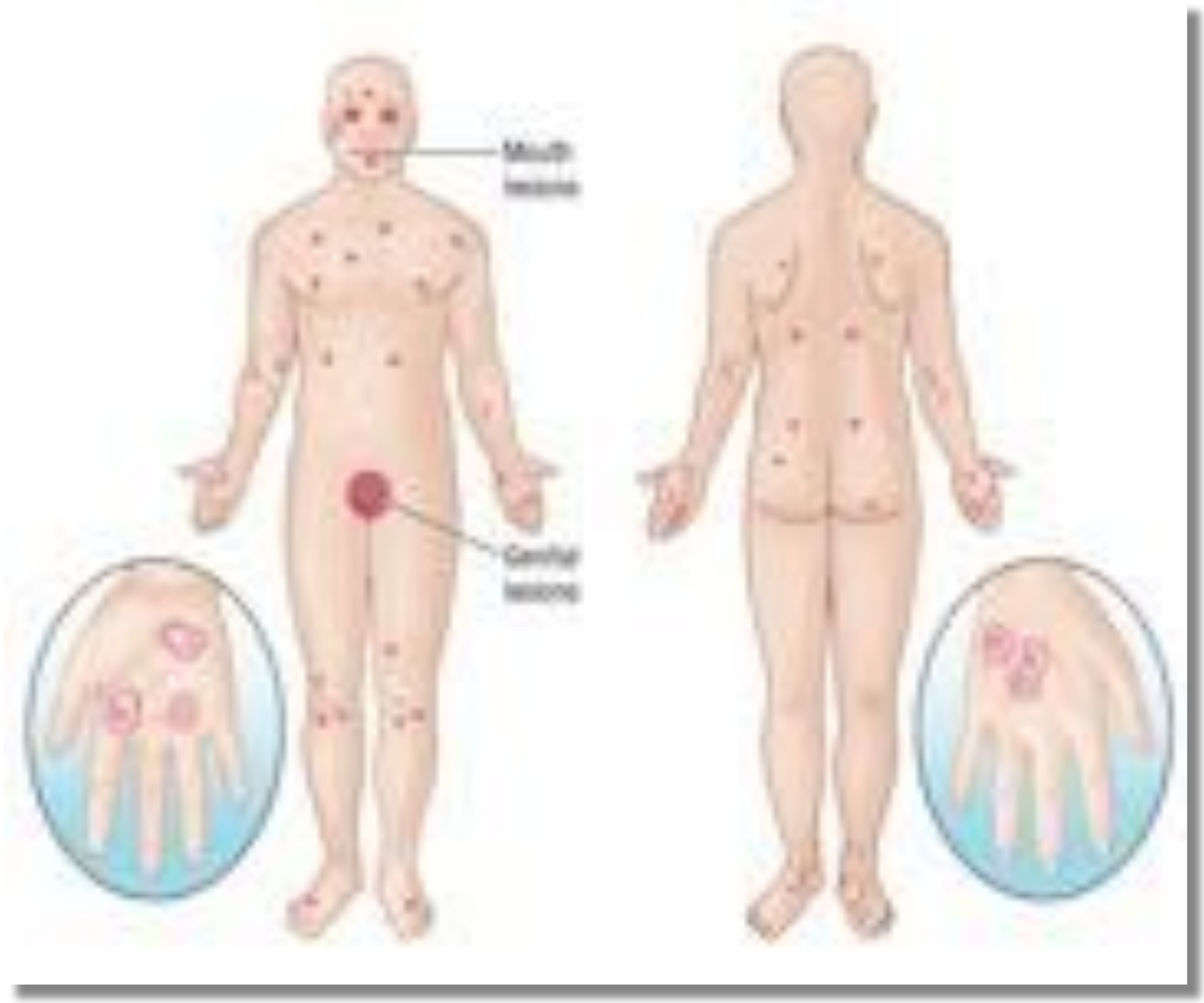
Clinically;

- Mainly affects the anterior mouth.
- Mainly non-keratinized mucosa.
- Lips --> cracked, crusted and edematous.
- Macules --> blisters --> ulcers.
- All stages can be seen together.
- Recurrent episodes, lasting 10-20 days.
- Skin; erythematous macules that are well-demarcated, called target or iris lesions.
- Might evolve into papules and/or ulcers.
- Other organs; eyes and genitals.

Source of image: McGraw-Hill Access Medicine

Clinically;

- Minor form --> affects one site, and is less severe (self-limited).
- Major form --> almost always involves the oral mucosa (severe pain, lip crusting), plus;
  - Preceded by a prodromal flu-like symptoms
  - Involvement of pharynx, oesophagus
  - Involvement of eyes (scarring might lead to blindness) and genitals (ulcers).
  - Symmetrical involvement of skin
- EM symptoms have an acute, or even explosive onset.



Source of image: McGraw-Hill Access Medicine

Aetiology;

Immune complexex are deposited in the superficial microvasculature of skin and mucosa

↓

Cell-mediated immunity in the area

↓

Necrosis in the affected areas

Aetiology;

- Abnormal hypersensitivity reaction to:

Most cases

Micro-organisms;
HSV, TB, Histoplasmosis

Drugs;
Antimicrobials, NSAID, Sulfonamide
Barbiturates, anticonvulsants

Minor EM

Major EM

Stevens-Johnson syndrome

- EM can also appear in immune conditions; auto-immune diseases, inflammatory diseases; malignancies, RT, and vaccination.
- Genetic predisposition; HLA-B15, HLA-DQ3, HLA-DQB1

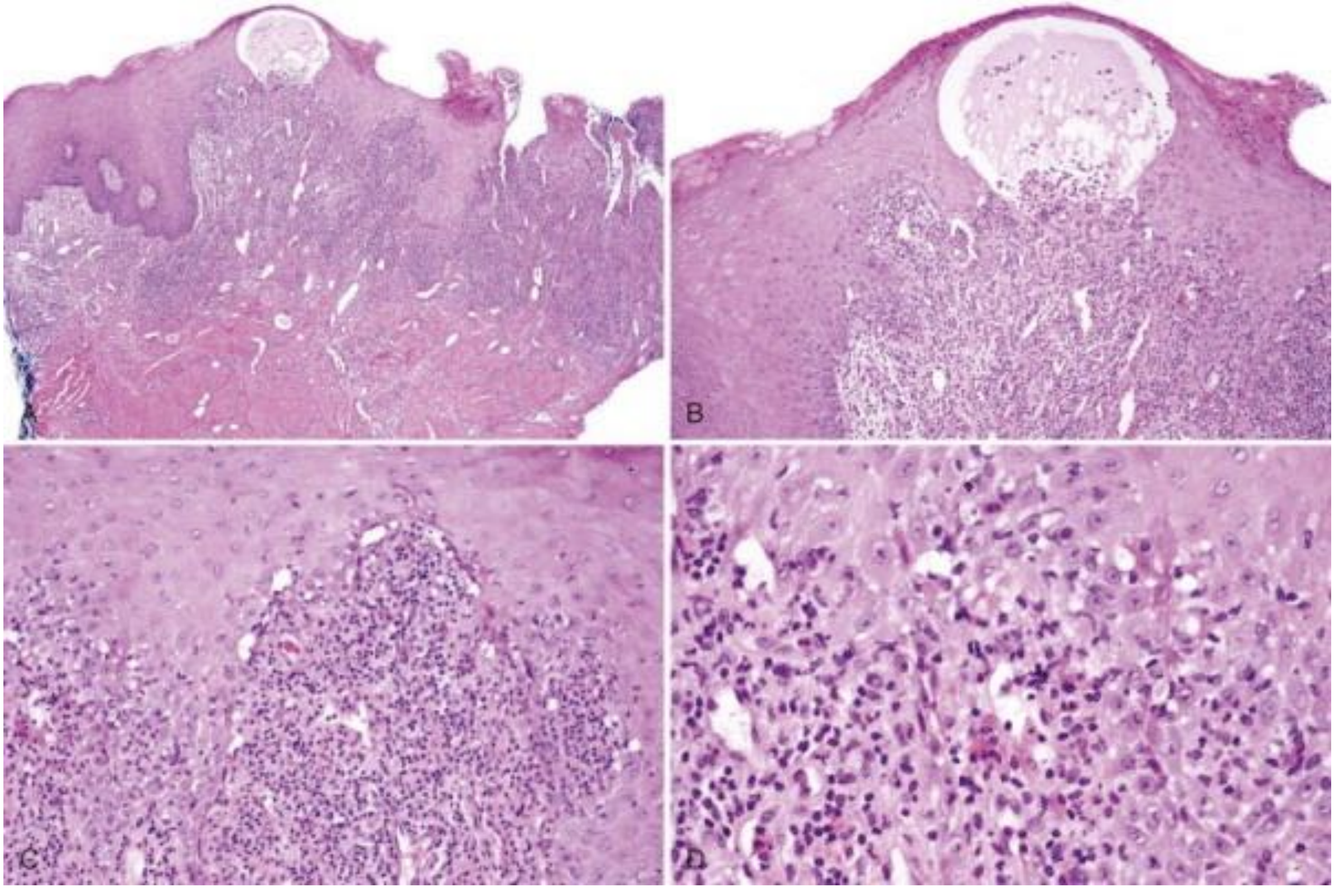


Image source: Oral Pathology a comprehensive atlas and text. By Sook-Bin Woo

Histopathology;

- Hyperplasia and intra-epithelial edema (sometimes vesicles).
- Apoptosis of basal cells.
- Blistersing
- Intense perivascular lymphocytic infiltrate
- Evidence of vasculitis

Treatment;

- Supportive therapy and oral hygiene.
- Precipitating factors should be searched for.
- If viral induced --> acylovir.
- Corticosteroid use is contraversial.
- Plasmapheresis might be indicated in severe EM.
- Referral to ophthalmology and dermatology.

Contact allergy

- Mainly affects the skin, rarely oral mucosa.
- Ulcers can be a symptom of an immunological response to drugs that are antigenic to the body.
- Or the immune response can be a result of the action of the drug on mast cells.
- Possible allergens;
  - Cinnamon and peppermint (flavoring agents)
  - Oral hygiene products
  - Dental materials (mercury, monomer, gold…etc).

Clinically;

- Burning
- Erythema
- Vesicles and ulcers
- Lichenoid reaction

Histopathology;

- CMI in the affected area
- Plasma cell infiltrate

Ulcers related to granulomatous diseases

- **Oro-facial granulomatosis;**
  - Not uncommon.
  - > in females, adulthood.
  - Mainly seen involving the upper lip, then lower lip, then cheeks.
- Should R/O:
  - Crohn's disease
  - Sarcoidosis
  - Foreign body reaction

Ulcers related to granulomatous diseases

- **Sarcoidosis;**
  - Chronic, granulomatous disease.
  - > in females (20-40 y).
  - Black > white
  - Multi-system

mainly:
- lymphoid tissues (almost always)
- skin (25%)
- eyes (25%)
- salivary glands

and/or any other organ

Ulcers related to granulomatous diseases

- **Wegener granulomatosis;**
  - Rare. A form of necrotizing vasculitis.
  - Early manifestation of disease in mouth in 6-13% of cases.
  - Affects mainly the URT, lungs and Kidneys.
  - Initially, sinusitis, epistaxis --> granulomatous inflammation and necrosis --> perforation.
    - Kidneys --> focal necrotizing glumerulonephritis --> renal failure.
    - Lungs --> granulomaous replacement of parenchyma --> respiratory failure.
  - Orally; red and granular masses affecting the gingiva (strawberry appearance).

Image source: Oral Pathology a comprehensive atlas and text. By Sook-Bin Woo

Ulcers related to granulomatous diseases

- **Midline granuloma;**
  - Most likely it is peripheral T-cell lymphoma.
  - Affects the midline of the oro-nasal structures.
  - Clinically, lesions are large necrotic ulcers associated with tissue destruction.

Source of image: McGraw-Hill Access Medicine

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  - ~~Erythema Multiforme~~
  - ~~Drugs~~
  - ~~Granulomatous disorders~~
- Neoplastic
  - SCC

Regezi, Sciubba and Jordan, **Oral Pathology Clinical Pathologic Correlations** 4th ed. Chapter 2 (p23-p38)

ORAL ULCERS

- Reactive Ulcers (*Riga Fede* in infants)
  Acute: Traumatic (Mechanical), Thermal, Iatrogenic, Therapeutic
  Chronic: Factitious, Traumatic Eosinophilic Ulcer, Necrotizing Sialometaplasia

- Infectious Ulcers
  Bacterial: Syphilis, Gonorrhea, Tuberculosis
  Fungal: Deep fungal infections, opportunistic fungal infections

- Immune-Mediated Ulcers
  RAS/Behcet Disease (DD)
  Erythema Multiforme
  Drugs: Contact Allergy
  Granulamatous Disorders: Oro-facial Granulomatosis, Sarcoidosis, Midline Granuloma, Wegner Granulomatosis

- Neoplastic
  Squamous Cell Carcinoma

LOCATION	
Gonorrhea	Mucous Membranes (genital, rectal, oral)
Tuberculosis	Oral Mucosa (secondary to pulmonary infection by sputum)
Opportunistic Fungal Infections	Nasal, Sinuses or Oro-pharynx
Deep Fungal Infections	Oral Mucosa (secondary to pulmonary infection by sputum)
Minor RAS	Non-Keratinized Mucosa
Major RAS	Mucosal Surfaces
Herpetiform RAS	Mucosal Surfaces
Behcet Disease	Mouth, Eyes, Genitalia, Skin, CNS, CVS (Oral ulcers precede others)
Erythema Multiforme	Mucocutaneous (Oral lesions 70% of cases)
Contact Allergy	Skin (rarely oral mucosa)
Oro-facial granulomatosis	Upper lip, lower lip then cheeks
Sarcoidosis	Lymphoid tissue, skin, eyes, salivary glands
Wegner Granulomatosis	URT, lungs, Kidneys

SYMPTOMS	
Deep fungal infections	Cough, fever, night sweating, weight loss
Behcet	Weakness, pharyngitis, generalized pain, headache, weight loss
Contact Allergy	Burning and Erythema

CAUSE	
Syphilis	Caused by treponema pallidum
Congenital Syphilis	Due to Spirochetemia that resulted from Secondary syphilis in mother
Gonorrhea	Caused by Nesisseria gonorrhea (g-ve)
Tuberculosis	Caused by acid-fast aerobic bacillus mycobacterium (M.Tuberculosis, M.Bovis, M.Avium, M.Intracellulare)
Deep Fungal Infections	Caused by four types (Histoplasmosis, coccidioidomycosis, blastomycosis, cryptococcosis)
Opportunistic Fungal Infections	Phycomycosis (mucormycosis) Aspergillosis
Recurrent Aphthus Stomatitis (RAS/Canker)	**Genetic** (HLA-A2 A11 B12 DR2) **Haematologic** (Iron, pernicious(b12), folic) **Cyclic Neutropenia** **GIT Disorders** (Coeliac, Crohn, Colitis, H. Pylori) **Hormonal** (Progesterone) **Allergy** (Food) **Stress**
Behcet Syndrome	Cross reactivity between epithelial proteins and bacterial proteins (Strep. Sangus) Relation with HSV, pesticide, foods and heavy metals **Genetic** (HLA-B51)
Erythema Multiforme	**Genetic** (HLA-B15 HLA-DQ3 HLA-DQB1) Immune Conditions Immune complex deposition in superficial microvasculature of skin and mucosa which in turn causes cell-mediated immunity in the area. Immune complexes are formed due to hypersensitivity to:
Contact Allergy	Drugs that are antigenic to body Or mast cell immune response to drugs Other allergens such as dental materials, oral hygiene products.
Midline Granuloma	Peripheral T-cell lymphona

Minor EM	**Major EM**
Micro-organisms (HSV, TB, Histoplasmosis)	Drugs (Antimicrobial, NSAID, Sulfonamide, Barbiturate, Anticonvulstants)
	Stevens-Johnson Syndrome

PATH	
Syphilis	Sexually Blood Transfusion Trans-placental
Gonorrhea	Sexually
Tuberculosis	Airborne
Deep Fungal Infections	Airborne
Opportunistic Fungal Infections	GIT (food) Airborne

DIAGNOSIS	
Syphilis	Darkfield examination of exudate from active lesion Silver Stain Serology
Gonorrhea	Swabs and gram stain and/or culture Serology Immuno-histochemistry
Tuberculosis	Ziehl Neelsen Stain or Fite Stain
Behcet	= RAS + two of the following: 1) Recurrent Genital Ulceration 2) Eye lesions (posterior uveitis) 3) Skin Lesions (erythema nodosum, acneiform nodules) 4) Positive pathergy test

TREATMENT	
Traumatic Eosinophilic Ulcer	Remove Irritant | Keep area clean
Necrotizing Sialometaplasia	Mouthwash
Syphilis	Penicillin
Gonorrhea	Penicillin
Tuberculosis	Antibiotics and Chemo agents (Isoniazid, ethambutol, streptomycin)
Deep Fungal Infections	Azole Group Amphotericin B
Opportunistic Fungal Infections	Amphotericin B Surgical Debridement
Minor RAS (recur)	Heals alone in 1 week without scarring
Major RAS (recur)	Heals alone in 10-40 days with chance of scarring
Herpetiform RAS (recur)	Heals alone in 10 days with scarring
RAS Treatments (So it does not recur)	Remove systemic causes Topical / Systemic/ Intralesion Corticosteroids Tetracycline/Nystatin Mouthways Immunosuppressants
Erythema Multiforme	If viral induced → Acyclovir Plasmapheresis might be indicated in severe EM Refer to ophthalmology and dermatology

CHARACTERISTIC FEATURES	
Traumatic Eosinophilic Ulcer	Eosinophilic Presence
Factitious Ulcer	Linked to psychological disorder
Necrotizing Sialometaplasia	Necrosis of salivary glands
Congenital Syphilis	Deafness, mulberry molars and notched incisors
Tuberculosis	Caseous Necrosis Langhan Cells Multi-nucleated Giant Cells
Deep Fungal Infections	Might cause abscess (blastomycosis)
Opportunistic Fungal Infections	Can perforate palate, nasal cavity and orbit
Recurrent Aphthus Stomatitis (RAS/Canker)	Pre-ulcerative presence of CD4+ cells Ulcerative presence of CD8+ cells Surrounded by erythematous halo Floor is white(CT) → yellow (fibrin) → grey (granulation tissue)
Herpetiform RAS	All stated above + Multiple minute pinhead ulcers which coalesce into large ragged ulcers
Behcet Syndrome	Vasculitis (Immune-complex related) Abnormal CD4/CD8 ratio Increased Cytokine Activity Posterior in mouth Ragged Edges
Erythema Multiforme	Apoptosis of basal cells Blistering Vasculitis
Contact Allergy	Lichenoid Reaction Plasma Cell Infiltrate
Wegener Granulomatosis	Vasculitis Orally has a strawberry appearance (Red and granular masses affecting gingiva) Might cause respiratory or kidney failure (due to replacement of lung parenchyma or necrosis of kidney cells)
Midline granuloma	Affect midline of oro-nasal structures Manifestation of T-cell lymphoma

anterior of mouth

- Ulcers that show <u>vasculitis</u>
  1) Behcet Disease
  2) Erythema Multiforme
  3) Wegner Granulomatosis

- Ulcers that has <u>pseudo-epitheliomatous hyperplasia</u>:
  1) Necrotizing Sialometaplasia
  2) Deep Fungal Infections
  3) Erythema Multiforme

- Ulcers that present as indurated, deep with rolled over edges, sharply demarcated, large and non-healing:
    1) Factitious Ulcers (Linked to psychological disorders)
    2) Traumatic Eosinophilic Ulcer
    3) Necrotizing Sialometaplasia
    4) Tuberculosis
    5) Deep fungal infections

- Ulcers that cause granulation tissue formation:
    1) Traumatic Eosinophilic Ulcer
    2) Tuberculosis
    3) Deep Fungal Infections
    4) All types of Recurrent Aphthus Stomatitis (Minor/Major/Herpetiform Aphthae)
    5) Oro-facial Granulomatosis
    6) Sarcoidosis
    7) Midline Granuloma
    8) Wegener Granulomatosis

- Ulcers that cause necrosis:
    1) Necrotizing Sialometaplasia – Salivary Glands Necrosis
    2) Syphilis – Epithelial necrosis by bacterial toxins
    3) Tuberculosis – Caseous Necrosis
    4) Opportunistic Fungal Infections – (Nasal, sinuses or oropharynx)
    5) Recurrent Aphthus Stomatitis (RAS/Canker)
    6) Erythema Multiforme
    7) Wegener Granulamatosis
    8) Midline Granuloma

- Ulcers that have female predilection
    1) Recurrent Aphthus Stomatitis (RAS/Canker)
    2) Oro-facial Granulomatosis
    3) Sarcoidosis
- Ulcers that have male predilection
    1) Behcet Syndrome
    2) Erythema Multiforme
- Ulcers that affect young adults
    1) Behcet Syndrome
    2) Erythema Multiforme
    3) Oro-facial Ganulomatosis
    4) Sarcoidosis