General pathology of Leprosy

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Introduction

- ***Definition***:
  - **Leprosy** or **Hansen`s disease** is a chronic specific inflammatory disease caused by **mycobacterium lepra**.
- ***General features***
  - WHO official figures (2010): >213000 people worldwide are infected with leprosy, mainly in Asia and Africa.
  - The disease is endemic in Egypt and had been reported in ancient Egyptian papyrus
  - It develops slowly (from six months to 40 years).
  - Mainly affects skin, peripheral nerves, mucosa of upper respiratory tract.

Introduction

- If not treated, leprosy can cause progressive damage to skin, nerves, limbs and eyes resulting in permanent lesions and deformities that can be very disfiguring.

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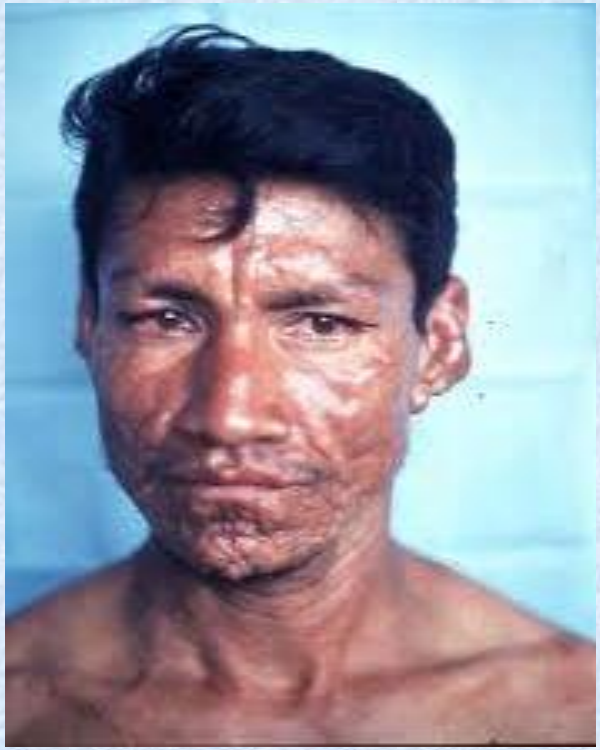
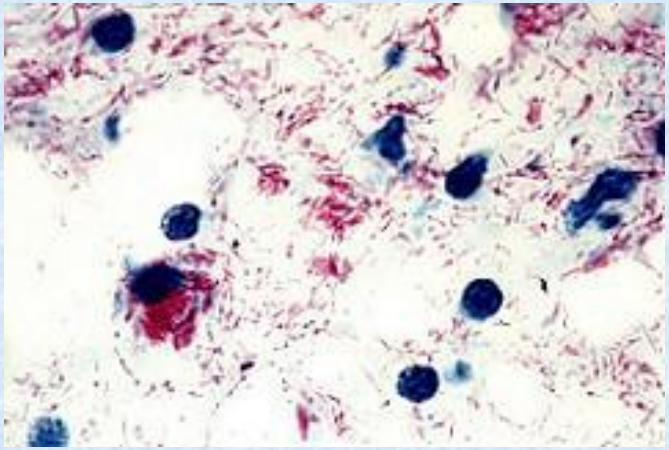


Aetiology

- ***Causative organism:***
  - Mycobacterium lepra, was discovered in 1873 by the Norwegian Dr. Armauer Hansen.
  - It is an obligatory intracellular acid-fast, rod-shaped bacilli.
  - It can be stained by Ziehl-Neelsen stain.



Aetiology

- ***Mode of infection***
  - Leprosy is **NOT** highly infectious.
  - Prolonged exposure to infection is essential for disease transmission.
  - It can be transmitted via droplet infection or close skin contact with untreated cases.
  - The incubation period is very long (up to five years).
  - Symptoms can take as long as 20 years to appear.

Pathology

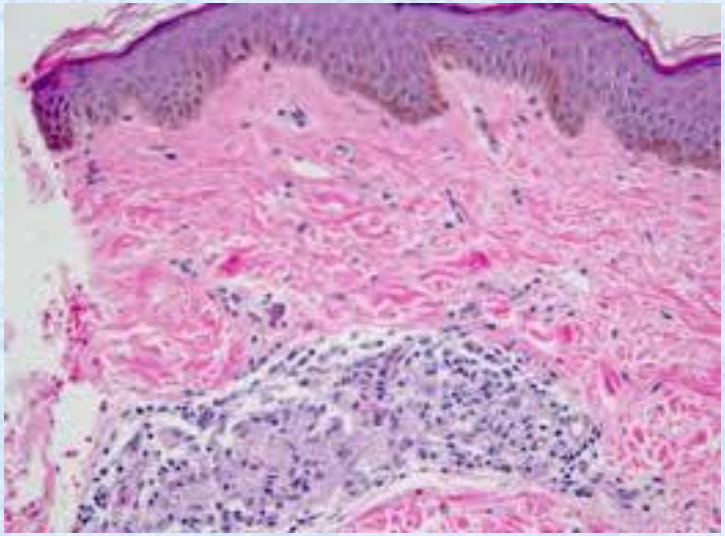
- ***Pathological features***
  - Cell-mediated immune response (Type IV hypersensitivity reaction) is the basis for pathological lesions of leprosy.
  - It results in a **granuloma** formation.
  - Granuloma of leprosy
    - Involves the affected sites, subcutaneous tissue is the predominant site.
    - Usually non-caseating
    - May be localized or diffuse.

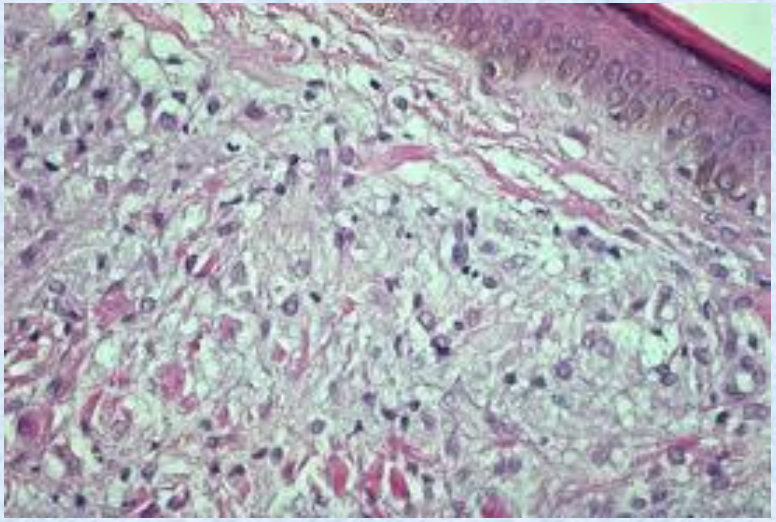
Pathology

- ***Pathological features***
  - The granuloma consists of
    - Large number of epithelioid cells (**Lepra cells**)
      - macrophages that engulfed lepra bacilli.
      - abundant foamy cytoplasm and ill-defined cell borders.
    - Giant cells can be infrequently encountered
    - Lymphocytes and fibroblasts can be present in variable number.

Pathology

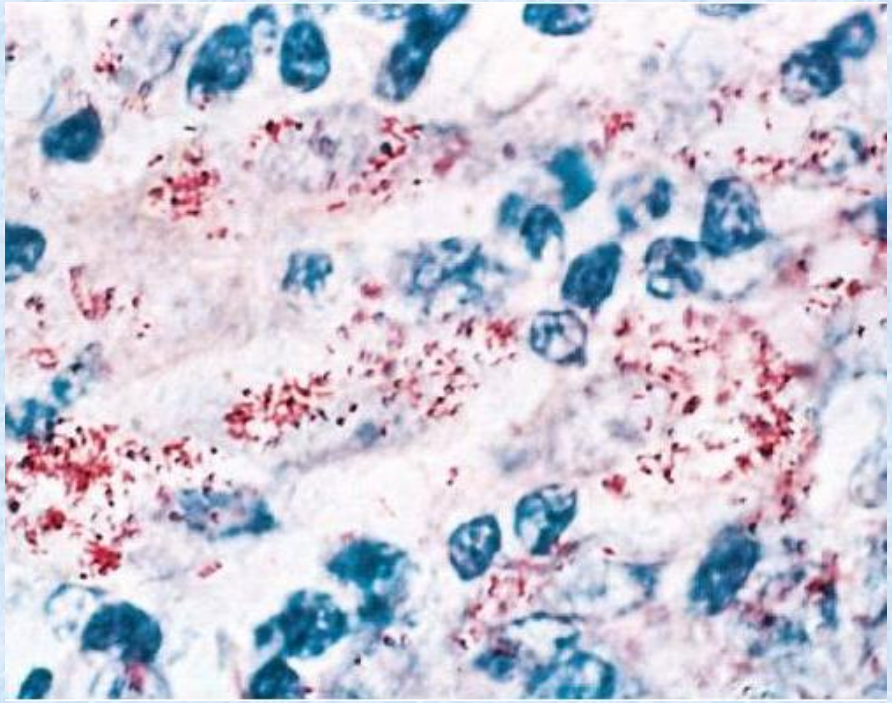
- ***Pathological features***

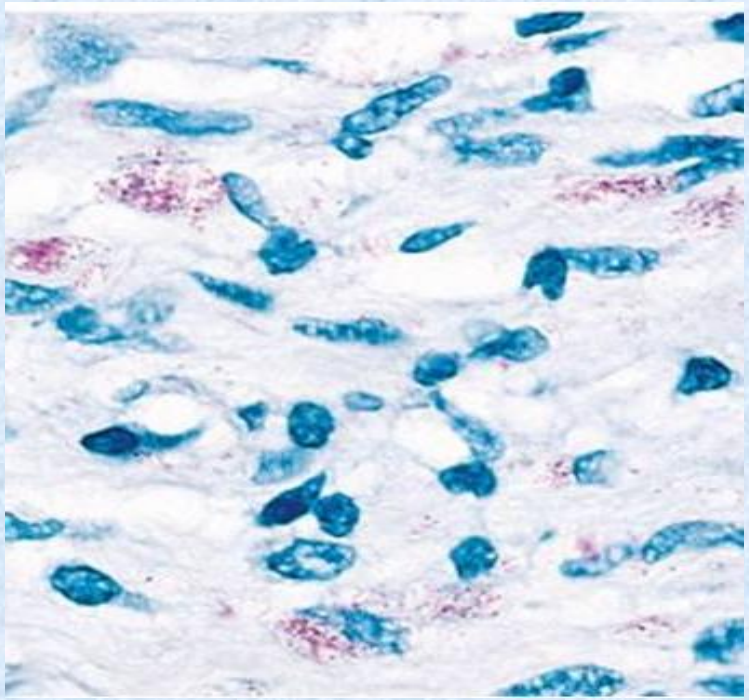




Pathology

- ***Pathological features***





Pathology

- ***Types:***
  - The forms of leprosy are based on the person's immune response to *M. leprae*.

    A. A good immune response leads to **tuberculoid leprosy**, with limited skin and nerve involvement.

    B. A poor immune response leads to l**epromatous leprosy**, characterized by extensive skin and nerve involvement.

    Some patients may have aspects of both forms

Pathology

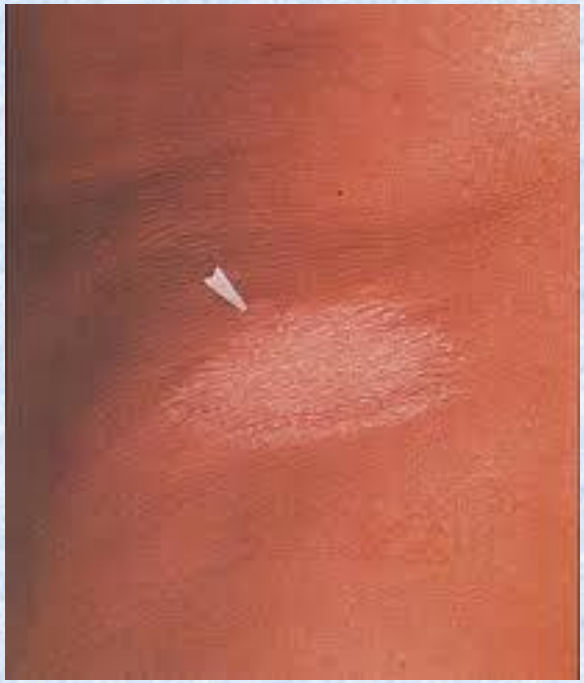
- ***Types:***
  - **WHO** specified five variants of leprosy based on the clinical involvement of the patients:
    - Tuberculoid leprosy
    - Borderline tuberculoid leprosy
    - Borderline form of leprosy
    - Borderline lepromatous leprosy
    - Lepromatous leprosy

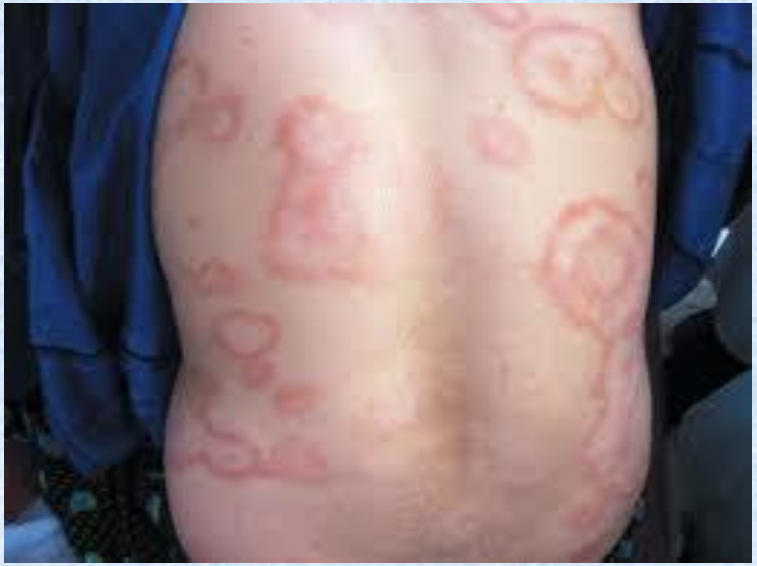
Pathology

- ***Types:***
  - **Tuberculoid leprosy (maculo-anaethetic type)**
    - **Clinically**: mildest form of the disease
      - Skin shows few hypopigmented macules at the face
      - Asymmetric lose of pain sensation due to neural involvement in which nerves become enlarged. This may lead to formation of trophic ulcers.
    - **Microscopically**
      - Well defined granulomatous lesion (describe)
    - **Fate**:
      - spontaneous resolution of may occur in few years
      - The lesions may persists or advances to other forms

Pathology

- ***Types:***
  - **Tuberculoid leprosy (maculo-anaethetic type)**





Pathology

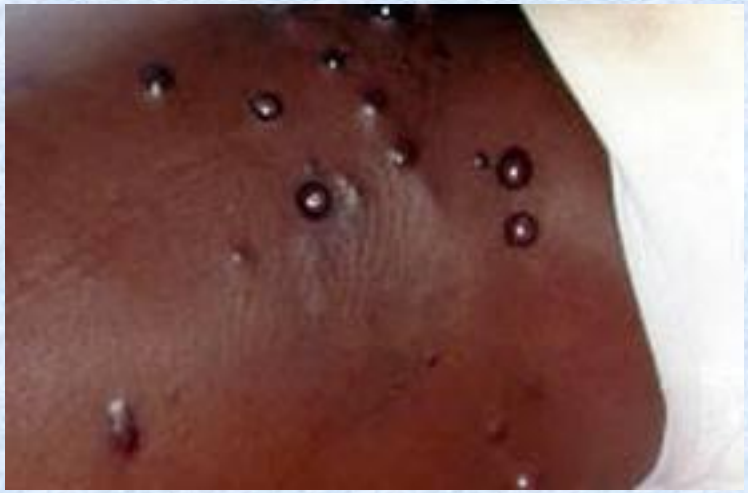
- ***Types:***
  - **Lepromatous leprosy (nodular type)**
    - Clinically: sever form of the disease
      - Skin shows hypo pigmented macules, patch or commonly nodules at the face and extremities
      - Loss of hair of the eye brow and eyelashes
      - Involvement of mucosa of nasal cavity leading to perforation of nasal septum and destruction of nasal bone.
      - Involvement of mucosa of upper respiratory tract.
      - Neural lesions: symmetrical loss of sensation due to neural involvement. The peripheral nerves become thick.
      - Multiple large trophic ulcers at the hands and feet.

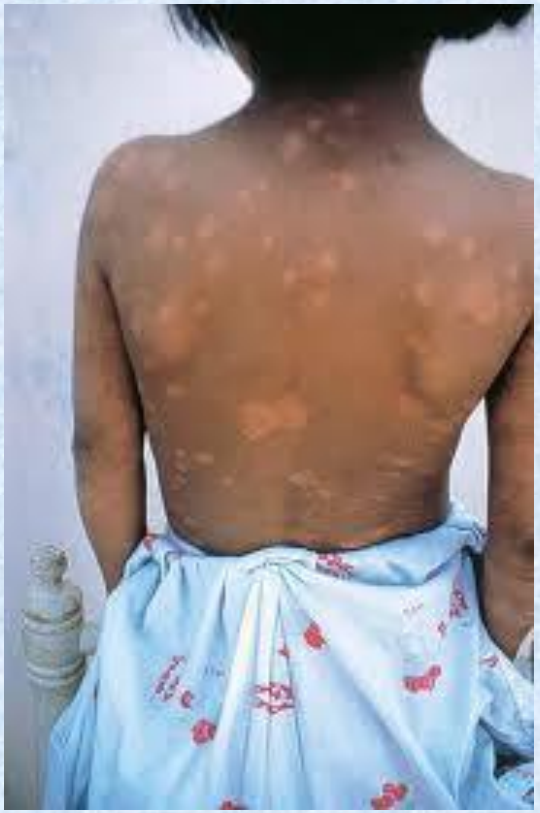
Pathology

- ***Types:***
  - **Lepromatous leprosy (nodular type)**
    - **Microscopically**
      - Ill-defined diffuse granulomatous reaction (describe)
    - **Fate**:
      - Healing of trophic ulcers by fibrosis leads to permanent deformities.
      - Destruction and necrosis of the affected tissues are irreversible.
      - Spread of infection to different organs including liver, lymph nodes and eye.

Pathology

- ***Types:***
  - **Lepromatous leprosy (nodular type)**





Pathology

	Tuberculoid	Lepromatous
Skin	• Few small hypo-pigmented macule • Asymmetrical	• Multiple large Hypo-pigmented macule or nodule • Symmetrical
Nerve	Distinct sensory affection	Less sever sensory affection
H&E	Elongated non caseating granuloma: epithelioid cells, rimmed by lymphocytes + giant cells	Diffuse or multiple collection of epithelioid cells with absent giant cells and few lymphocytes
ZN stain	Few lepra bacilli by	Positive large number of lepra bacilli
Immunity	Good	Low or supressed
Lepromine test	Positive	Negative

Management

- ***Diagnosis***
  - The majority of cases are diagnosed by clinical findings.
  - Skin smears or biopsy that show acid-fast bacilli with Ziehl-Neelsen stain
- ***Treatment:***
  - Early diagnosis and treatment with multi-drug therapy remain the key elements in eliminating the disease.
- ***Prevention***:
  - The best of prevention of leprosy is early diagnosis and treatment.
  - For household contacts: annual examinations are recommended for at least five years after last contact with a person who is infectious.

Other GRANULOMATOUS diseases

Rhinoscleroma

Actinomycosis

Sarcoidosis

Rhinoscleroma

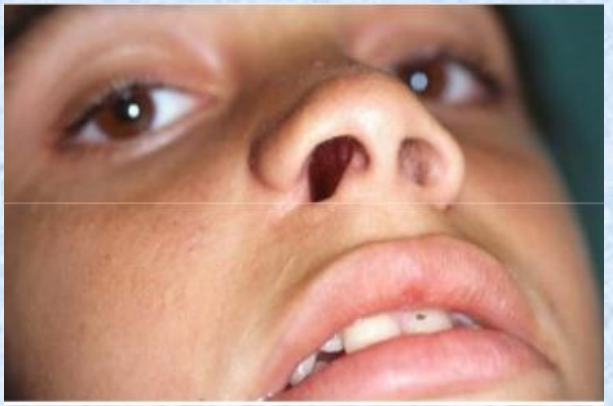
- ***Definition***
  - A slowly progressive chronic infective granuloma of the nose and upper respiratory tract
- ***Etiology:***
  - Caused by klebsiella rhinoscleromatis
  - Transmitted by droplet infection
  - Transmission requires prolonged exposure
- ***Clinically:***
  - Common in young and middle age
  - Early: presents with flu-like symptoms
  - Late: nasal obstruction, discharge, crustations, epistaxis and anosmia on longstanding lesion.

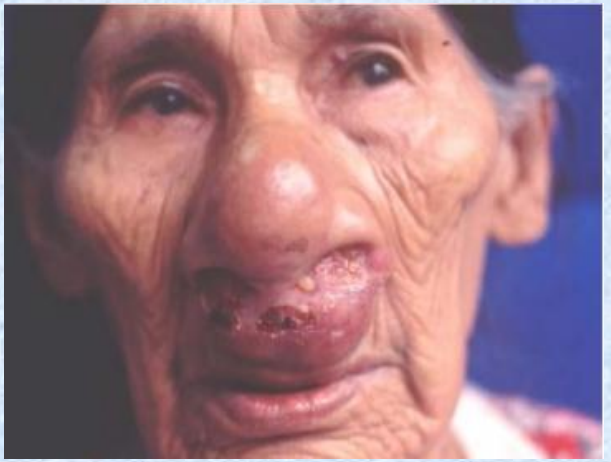
Rhinoscleroma

- ***Pathology***

Grossly:

- Dilated nasal cavity
- Red granular/nodular nasal mucosa
- Diffuse crustation
- In fibrotic stage: deformed nose with bone destruction



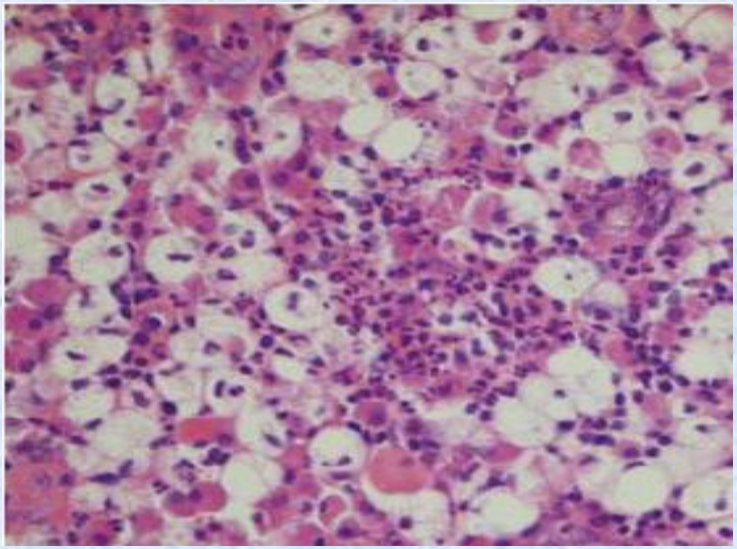


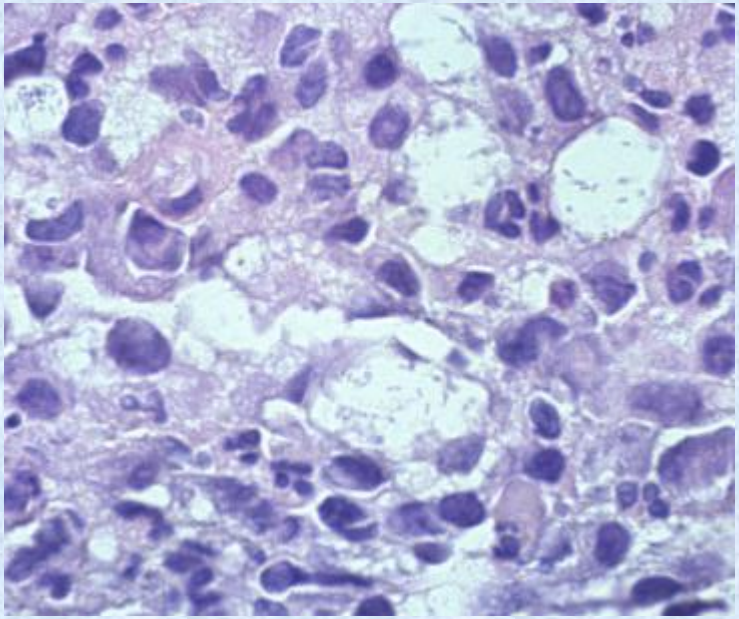
Rhinoscleroma

- ***Pathology***

MP:

- Squamous metaplasia of the respiratory epithelium
- Diffuse mixed inflammatory cells rich in plasma cells
- The pathognomonic cells:
  1. ***Mickulicz cells***: macrophages with abundant foamy (vacuolated) cytoplasm
  2. ***Russell bodies***. Esinophilic bodies (plasma cells with hyalinosis)





Actinomycosis

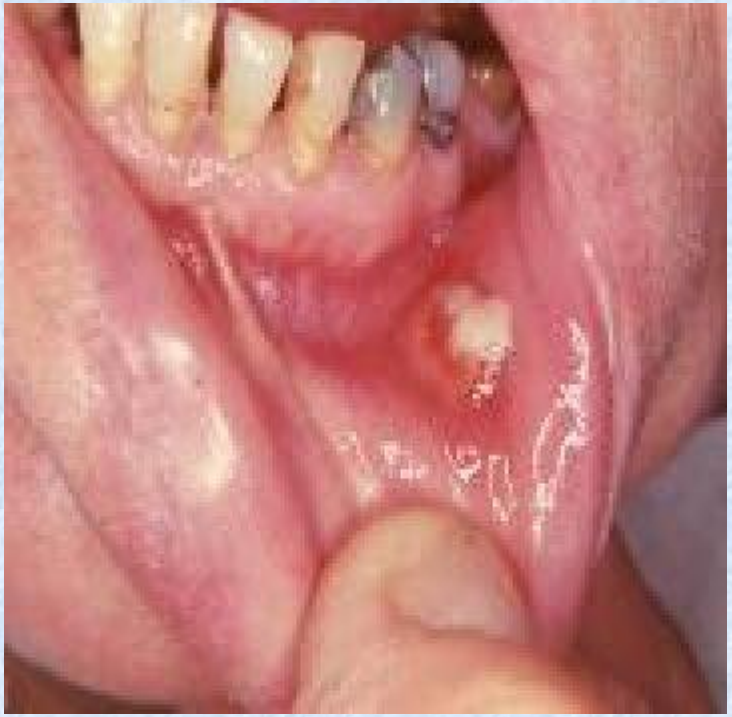
- ***Definition***
  - A chronic suppurative granulomatous inflammation
- ***Etiology:***
  - Caused by Actinomyces Israelii:
    - An anaerobic gram +ve positive
    - One of the commensals at oral cavity and GIT.
  - Endogenous transmission by invasion of the mucosa
- ***Clinical types (sites):***

1. Craniofacial actinomycosis (60% of cases)
2. Intestinal actinomycosis (20% of cases)
3. Pulmonary (thoracic) Common in young and middle age
4. Cutaneous actinomycosis

Actinomycosis

1. Craniofacial actinomycosis

- The commonest
- Infection through oral mucosa after minor operations
- Clinically:
  - Swelling of oral mucosa & jaw
  - Abscess formation
  - Sinus discharging pus containing sulphur granules
- May spread to other sites as lungs



Actinomycosis

2. Intestinal actinomycosis

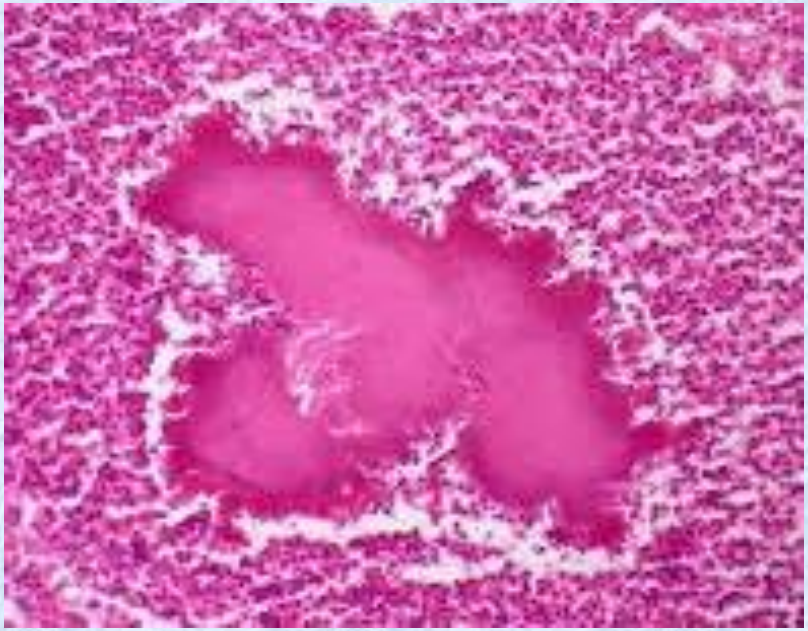
- Involve terminal ileum, ileo-caecum, appendix and liver
- Infection through swallowing of the organism
- Clinically:
  - Produce ileo-caecal abscess
  - May open to reteroperitoneum or to abdominal wall with sinus discharging pus.
  - Intestinal fistula.

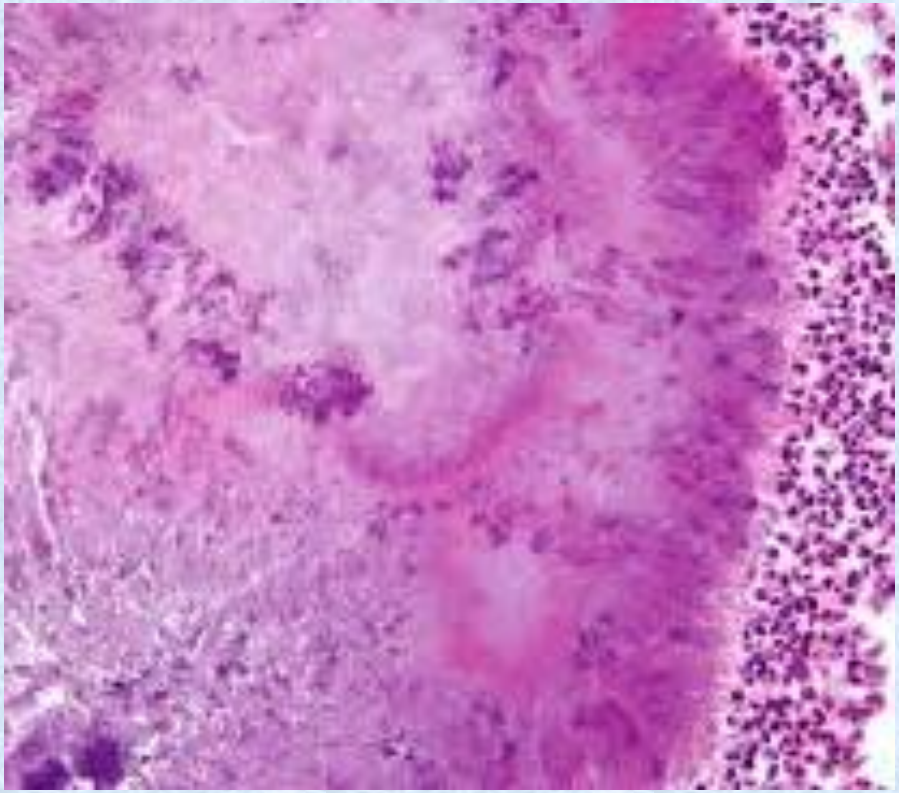
3. Pulmonary actinomycosis

- Occurs by inhalation of the organism or by direct spread from craniofacial infection
- Main pathology is lung abscess formation discharging sulphar granules

Actinomycosis

- ***MP***
  1. Bacterial colonies: large aggregates at the centre of the micro-abscess: peripheral clubs and central filaments
  2. Surrounding inflammatory cells: neutrophils, pus cells, plasma cells, lymphocytes, histeocytes & giant cells





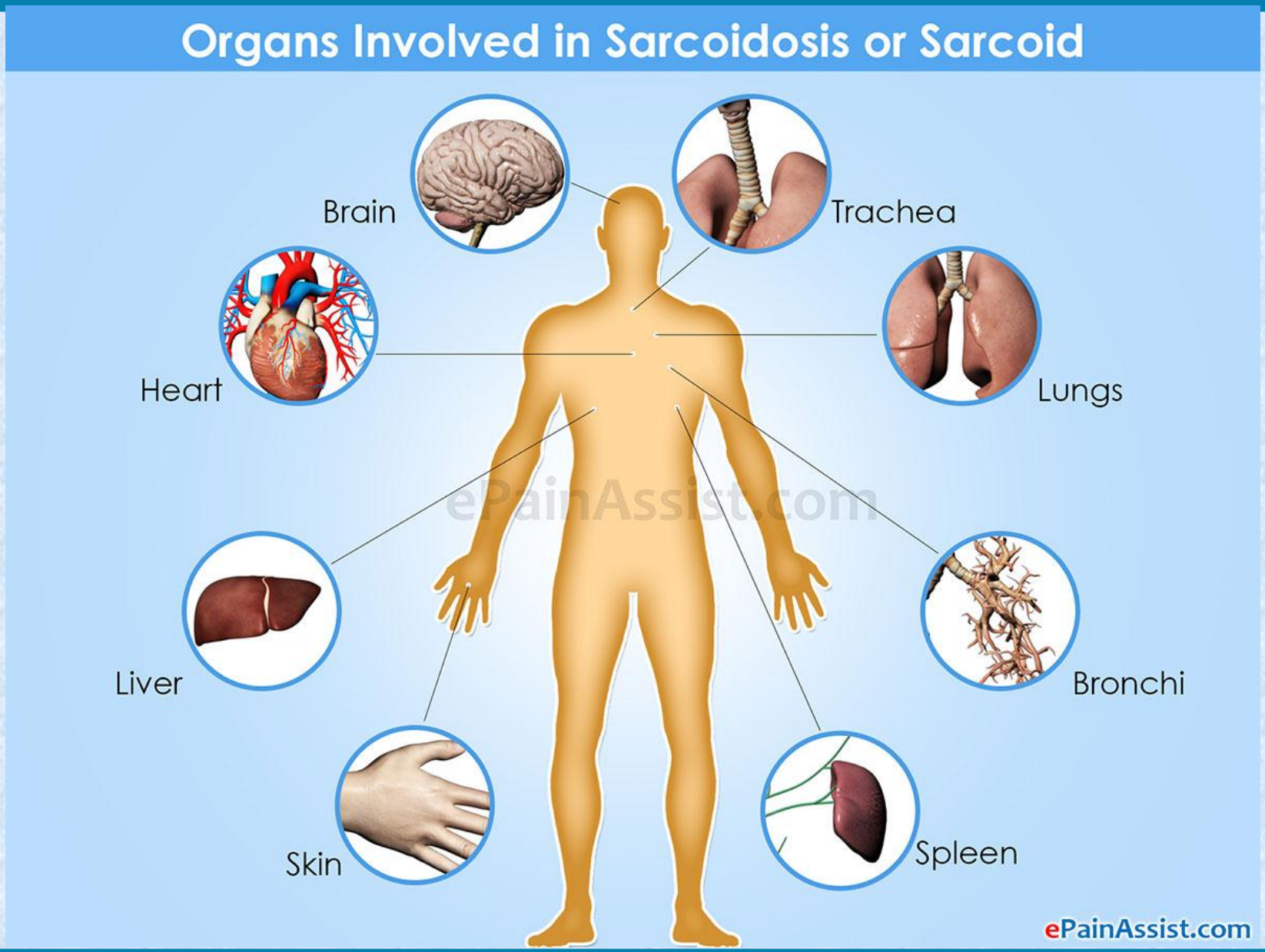
Sarcoidosis

- ***Definition***
  - A multisystem granulomatous disease of unknown etiology
- ***Theories:***
  - Genetically predisposed individuals
  - Cell mediated type IV hypersensitivity reaction
- ***Sites and clinical presentation:***
  - Usually presents in early adult life (2-40 years)
  - Involves several organs
    1. Lungs: involved in ±90% of cases. Patients may develop interstitial pulmonary fibrosis and subsequent pulmonary hypertension
    2. Lymph nodes: involved in ±75 of cases. Significant lymphadenopathy (hilar and mediastinal groups).

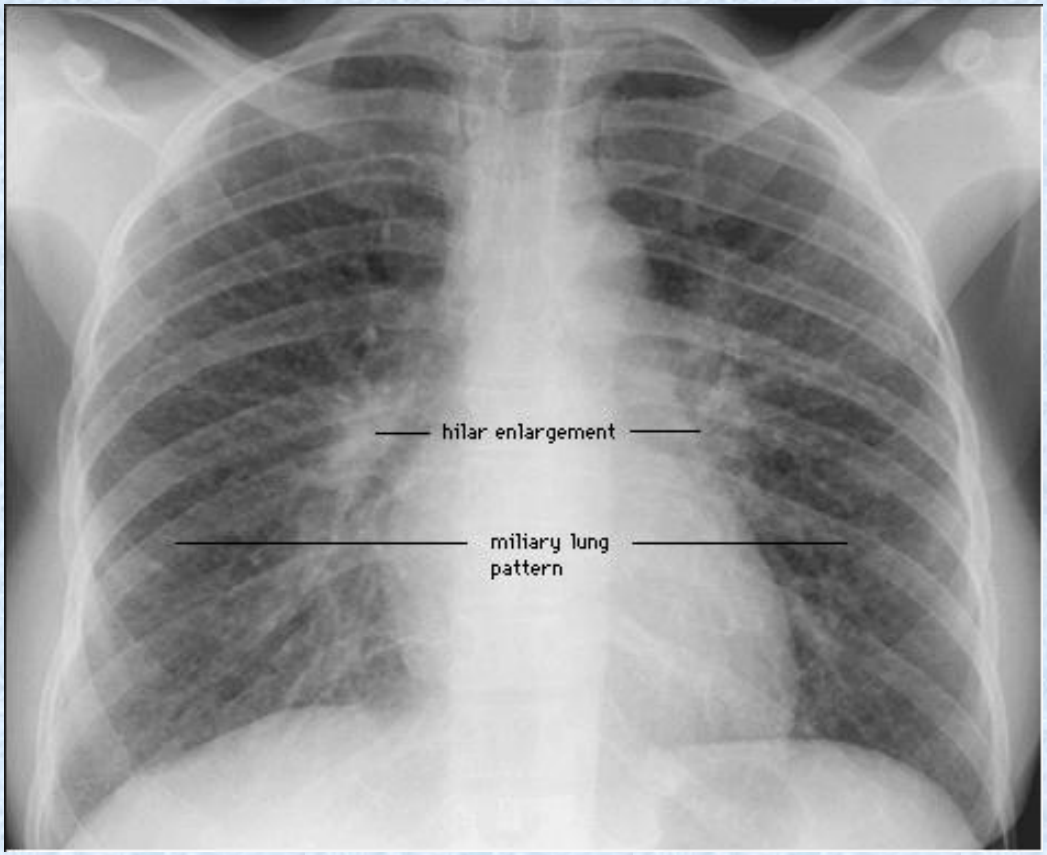
Sarcoidosis

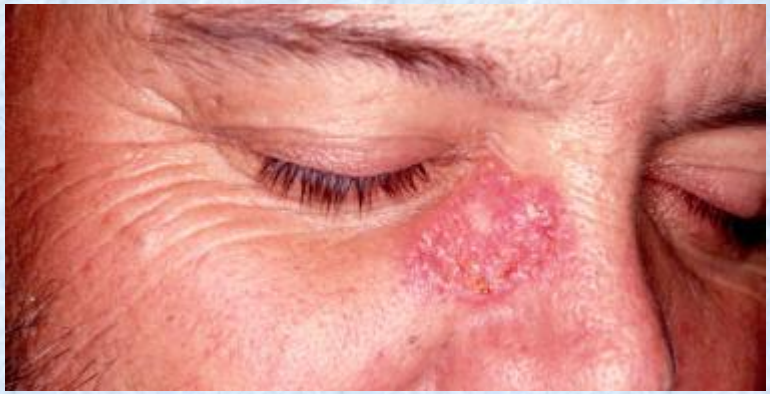
- ***Sites and clinical presentation:***
  3. Eye: involves in ±50 of cases. Leads to uveitis and dry eye.
  4. Skin: lesds to erythema plaques of discolouration of cheek and face
  5. Liver: in 10% of cases; leads to hepatic focal lesions
  6. Less common sites: bone marrow, parotid, kidneys
- ***Diagnosis***
  - ❑ Clinical and radiological features
  - ❑ Laboratory findings
    - ▪ Hypercalcemia (excess absorption of vitamin D)
    - ▪ Increased ACE level (produced by macrophages
- ***Prognosis:*** Unpredictable

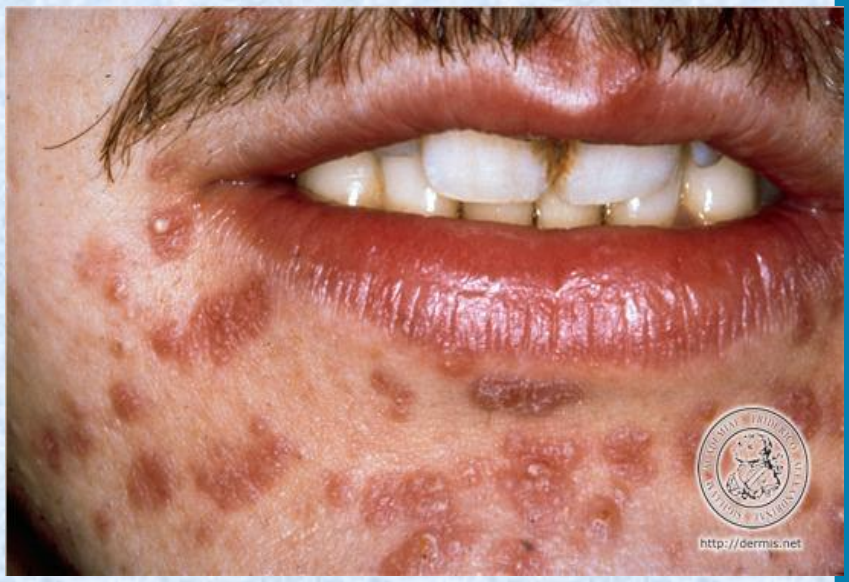
Sarcoidosis



Sarcoidosis

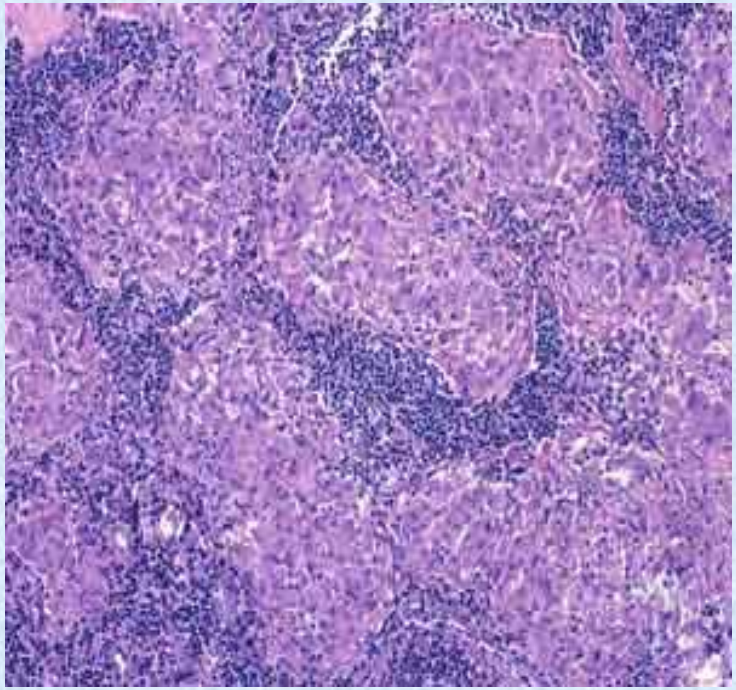


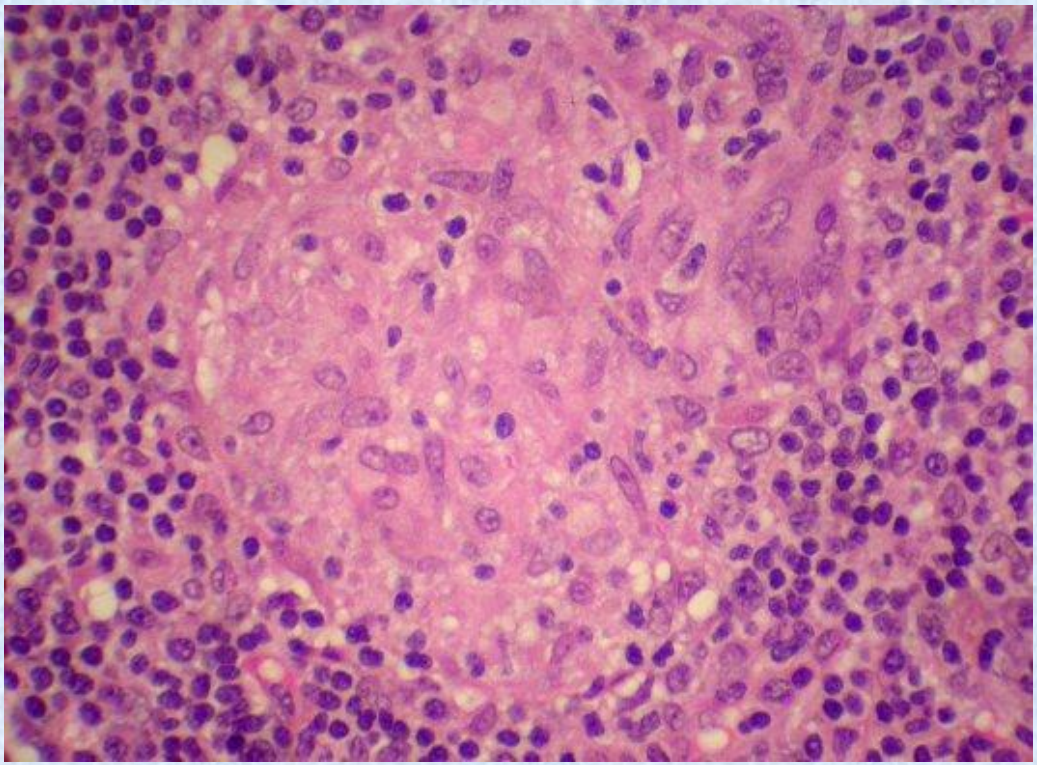




Sarcoidosis

- ***MP:***
  - Large number of small non caseating epithelioid cells granulomas
  - Significance: DD of granulomatous lesions especially TB





Viral infections

Viral infection

- **Introduction**:
  - Viruses are small obligatory intracellular microorganisms of ±30 nm
  - They are composed of nucleic acid and a protein coat (capsid)
  - They are classified into DNA of RNA viruses based on type of nucleic acid
- **Mode of infection:**
  1. Inhalation: as influenza virus
  2. Ingestion as hepatitis A virus
  3. Through blood: as hepatitis B and C viruses
  4. Sexual transmission as AIDS virus
  5. Inucleation as trachoma virus

Viral infection

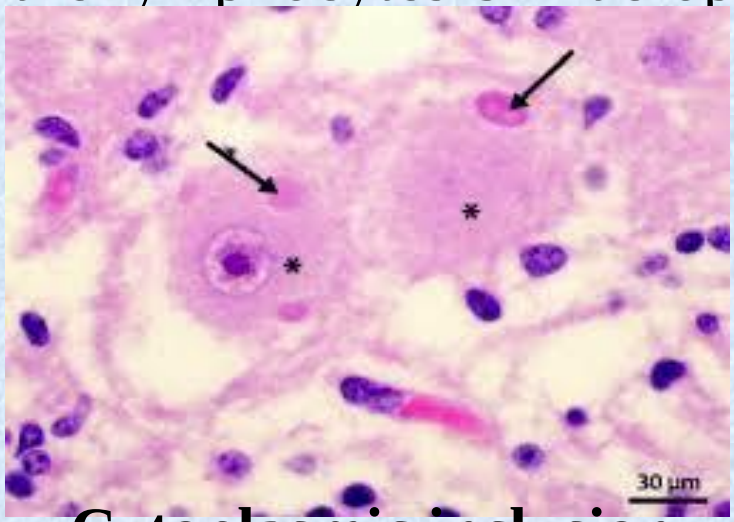
- **Clinical presentation**:
  - No effect (asymptomatic); may lead to a carrier state
  - Acute form: as influenza, mumps, acute hepatitis
  - Chronic form: as HCV, HBV and AIDS
  - They are classified into DNA of RNA viruses based on type of nucleic acid
  - Some viruses have multisystem affection as CMV

- **Mode of cell injury:**
  1. Disruption of DNA and RNA synthesis
  2. Cell membrane injury
  3. Direct cell injury and lysis
  4. Tissue damage through host hypersensitivity reaction

Viral infection

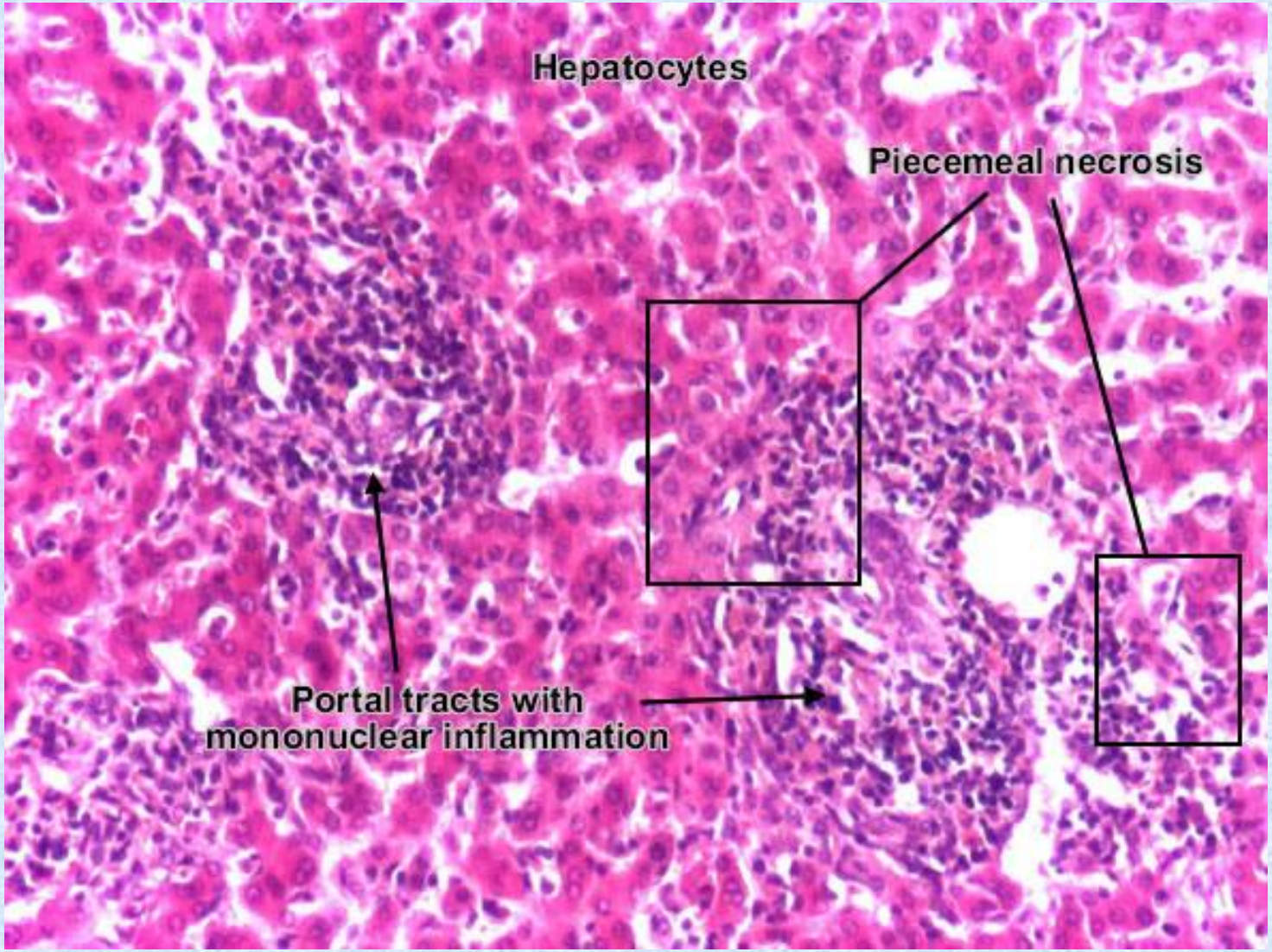
- **Tissue reaction in viral infections:**
  - Cellular changes
    - Intracellular inclusion bodies
    - Degenerative changes as cloudy swelling and fatty changes
    - Cell apoptosis
    - Cell necrosis in sever cases
  - Inflammatory response:
    - The main inflammatory cells are lymphocytes & macrophages

Nuclear inclusion



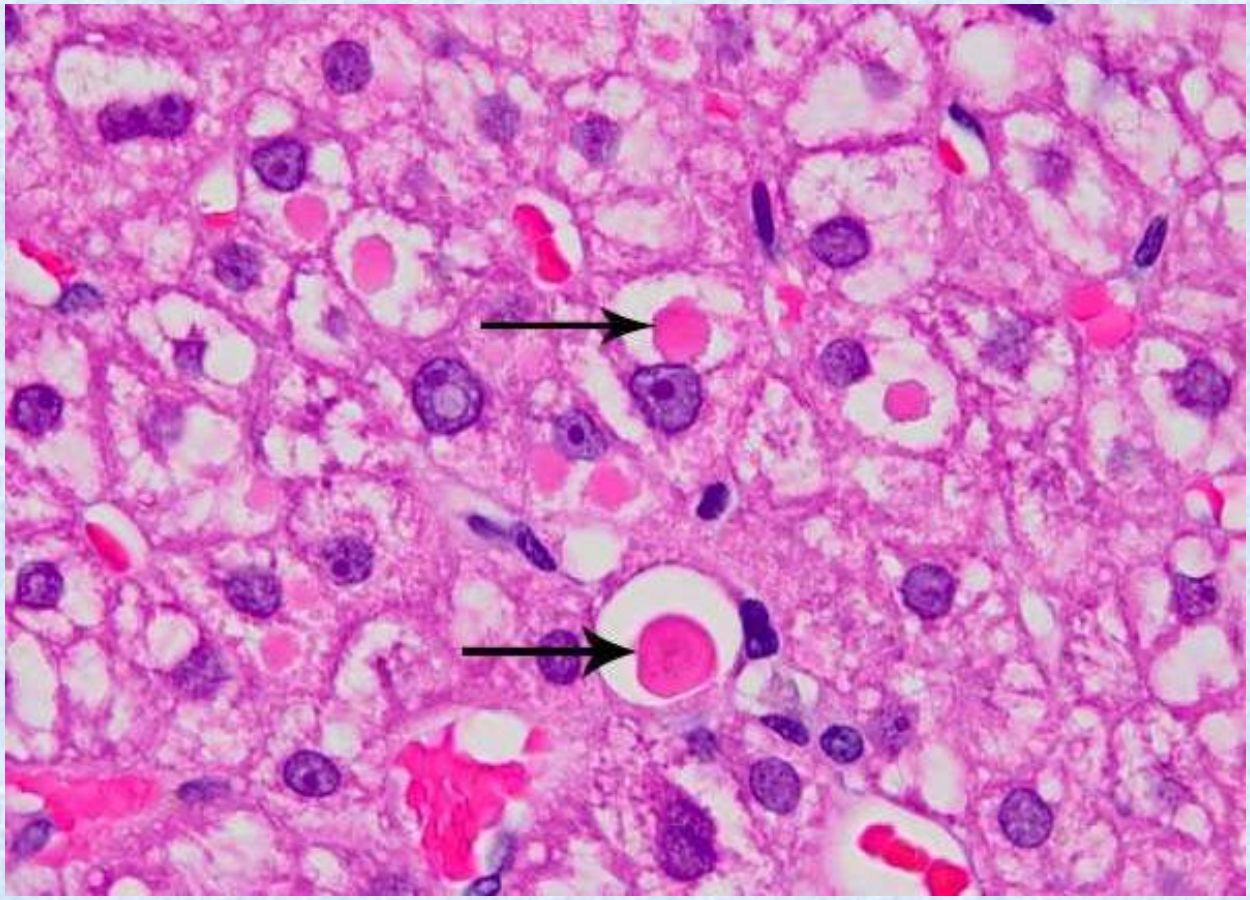
Cytoplasmic inclusion

Viral infection



Chronic viral hepatitis

Viral infection

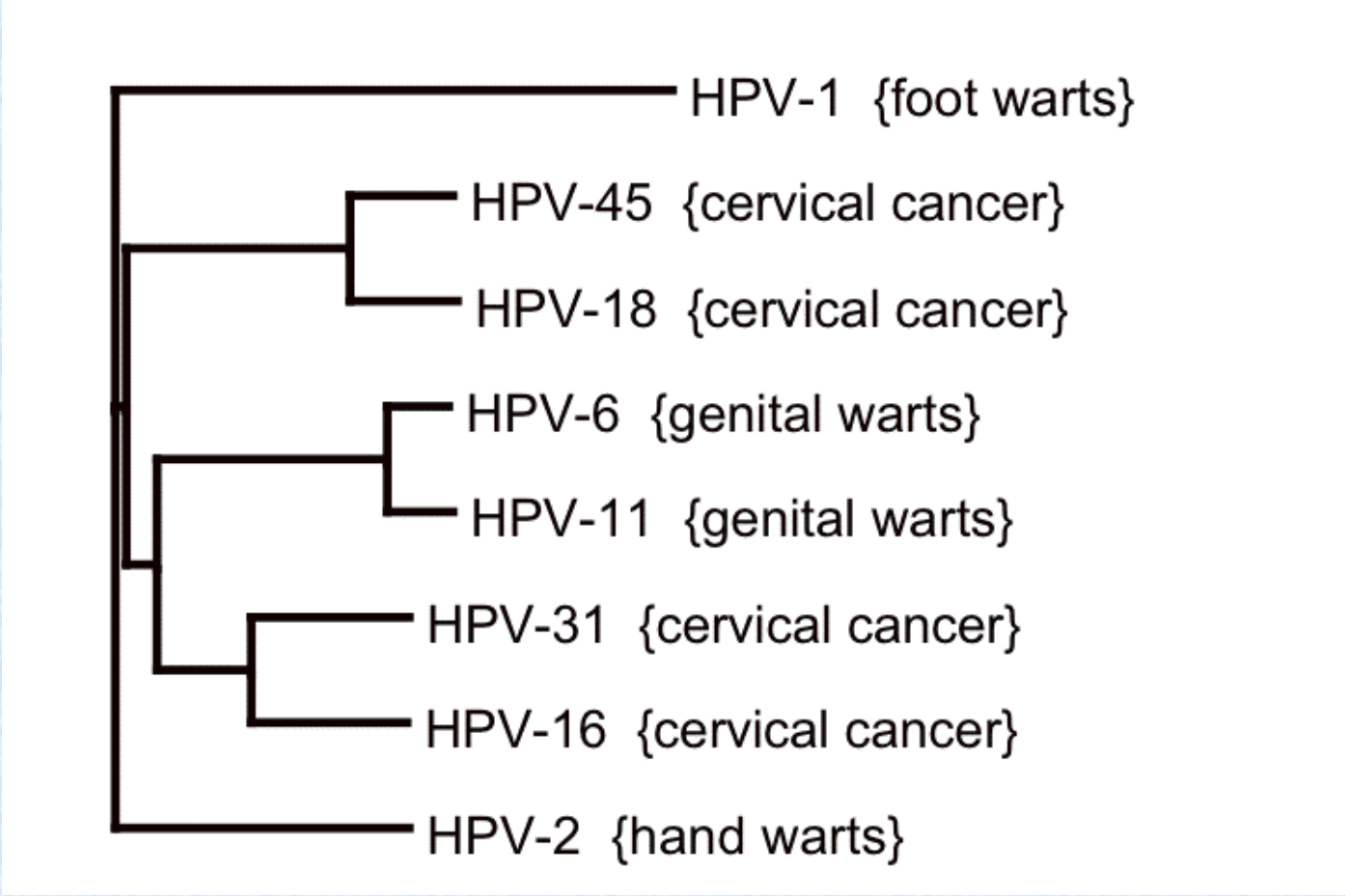


Chronic viral hepatitis

Viral inclusion bodies

Viral infection

- **Common oncogenic viruses:**
  - **A. Human papilloma virus:**



Viral infection

- **Common oncogenic viruses:**

B. EB virus

1. Infectious mononucleosis
2. Hodgkin`s lymphoma
3. Burkett's lymphoma
4. Nasal T/NK lymphoma
5. Nasopharyngeal carcinoma

2. HBV and HCV: Hepatocellular carcinoma

3. AIDS virus:

1. B cell non hodgkin`s lymphoma
2. Kaposi sarcoma

Thank you