Leprosy

- Hansen’s disease
- *M.leprae*
- Affects cooler parts of body - skin, mucous membranes (e.g. nose), peripheral nervous system, eyes and testes.
- Classification
  - Lepromatous
  - Tuberculoid

  The form the disease takes depends on the person's immune response to the infection.

Transmission

- Human to human
- Lepromatous patients shed *M.leprae* from the nasal mucosa
- Minor routes- breast milk, materno-fetal
- M.leprae can survive in environment up to 45 days
- Multiplies very slowly, symptoms can take as long as 20 years to appear

Ridley & Joplings classification

5 groups

- TT (high resistance)
- BT
- BB
- BL
- LL (low resistance)

Classification according to bacilliary index

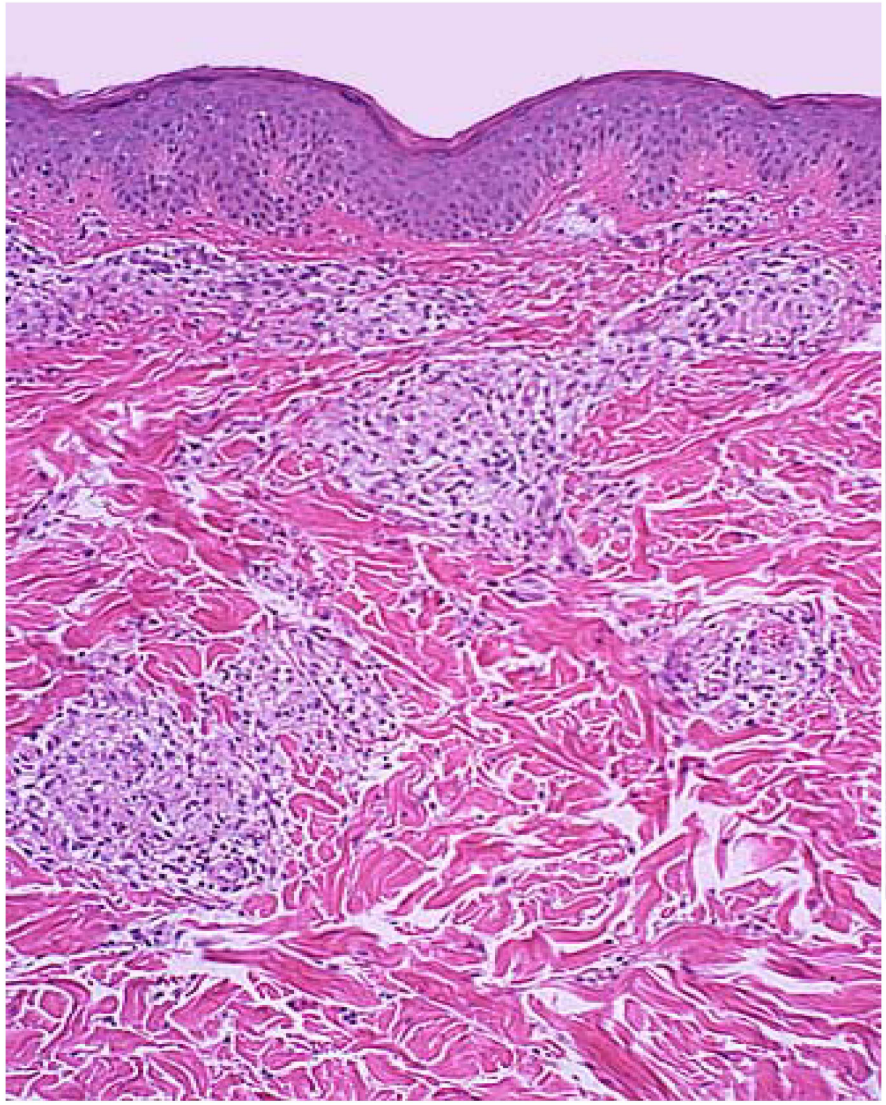
- Pauci-bacillary
- Multi-bacillary

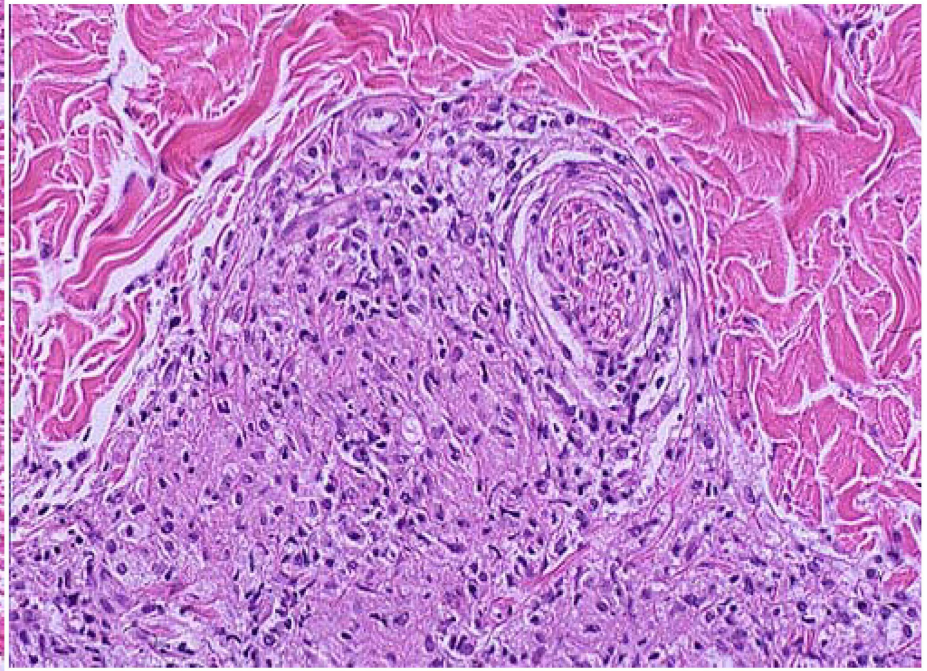
Tuberculoid leprosy

- Can be either one large red patch with well-defined raised borders or a large hypopigmented asymmetrical spot
- Lesions become dry and hairless
- Loss of sensation may occur
- Tender, thickened nerves with subsequent loss of function are common
- Spontaneous resolution may occur in a few years
- or it may progress to borderline or rarely lepromatous types

Skin biopsy

- collections of epithelioid cells surrounded by many groups of lymphocytes
- occasionally “Giant Cells”
- such cell collections are present mainly around the appendages of the skin such as the nerves and the hair follicles.
- inflammatory cell collection may spread even up to the epidermis.
- hair-follicles, sweat glands destroyed
- Lepra bacilli

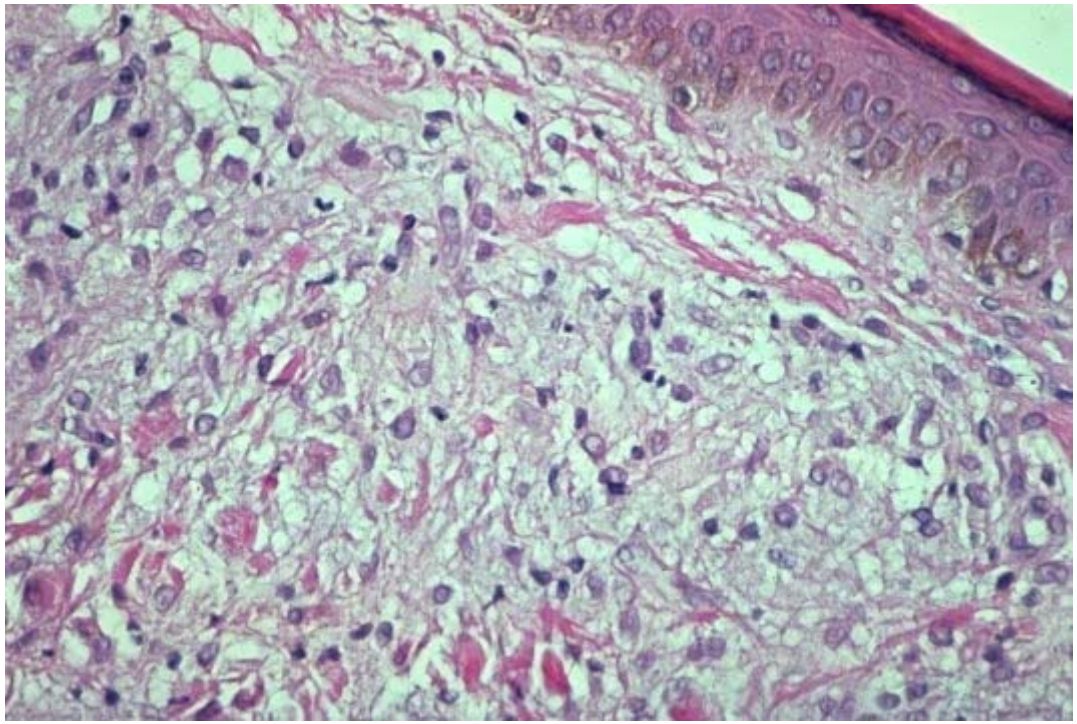




Lepromatous leprosy

- Numerous lesions - plaques, macules, papules and nodules
- Early symptoms include nasal stuffiness, discharge and bleeding, and swelling of the legs and ankles
  - Skin thickens over forehead (leonine facies),
  - eyebrows and eyelashes are lost,
  - nose becomes misshapen or collapses, ear lobes thicken,
  - Eye involvement : photophobia , glaucoma and blindness
  - Testicles shrivel causing sterility
  - Slow scarring of peripheral nerves resulting in nerve thickening and sensory loss. Fingers and toes become deformed due to painless repeated trauma.

- M/E



- Diagnosis
  - split skin smear
  - biopsy & histopathology

Lepromin Test

- Used for classifying leprosy on the basis of immune response
- CMI suppressed in LL but TT pt. have good immune response
- I/D inj of lepromin reveals delayed hypersensitivity reaction in tuberculoid leprosy
- Early Fernandez reaction---indurated area in 24-48 hrs
- Late Mitsuda reaction—delayed granulomatous lesion appearing after 3-4 weeks

Reactions in leprosy

Type I: Borderline reactions- two types

- Upgrading reaction-

  Occurs in BL pt. on treatment who upgrade towards tuberculoid type.

- Downgrading reaction-

  Occurs in BT pt. who downgrade towards lepromatous type

Type II : Erythema nodosum leprosum (ENL)---

Occurs in lepromatous pt after treatment

Tender cutaneous nodules, fever, iridocyclitis

Features	Tuberculoid Leprosy	Lepromatous Leprosy
Skin lesions	Few erythematous or hypopigmented plaques with flat centers and raised, demarcated borders; peripheral nerve damage with complete sensory loss; visible enlargement of nerves	Many erythematous macules, papules, or nodules; extensive tissue destruction (e.g., nasal cartilage, bones, ears); diffuse nerve involvement with patchy sensory loss; lack of nerve enlargement
Histopathology	Infiltration of lymphocytes around center of epithelial cells; presence of Langhans' cells; few or no acid-fast bacilli observed	Predominantly "foamy" macrophages with few lymphocytes; lack of Langhans' cells; numerous acid-fast bacilli in skin lesions and internal organs
Infectivity	Low	High
Immune response		
Delayed hypersensitivity	Reactivity to lepromin	Nonreactivity to lepromin
Immunoglobulin levels	Normal	Hypergammaglobulinemia
Erythema nodosum leprosum	Absent	Usually present

SYPHILIS

- *T.pallidum*
- Coiled spiral filament 10um long
- Cannot be cultured
- Demonstrated by
  - Dark ground illumination
  - Fluorescent antibody technique
  - Silver impregnation technique

Modes of transmission

- Sexual
- Person to person contact
- Transfusion
- Materno-foetal transmission

Stages

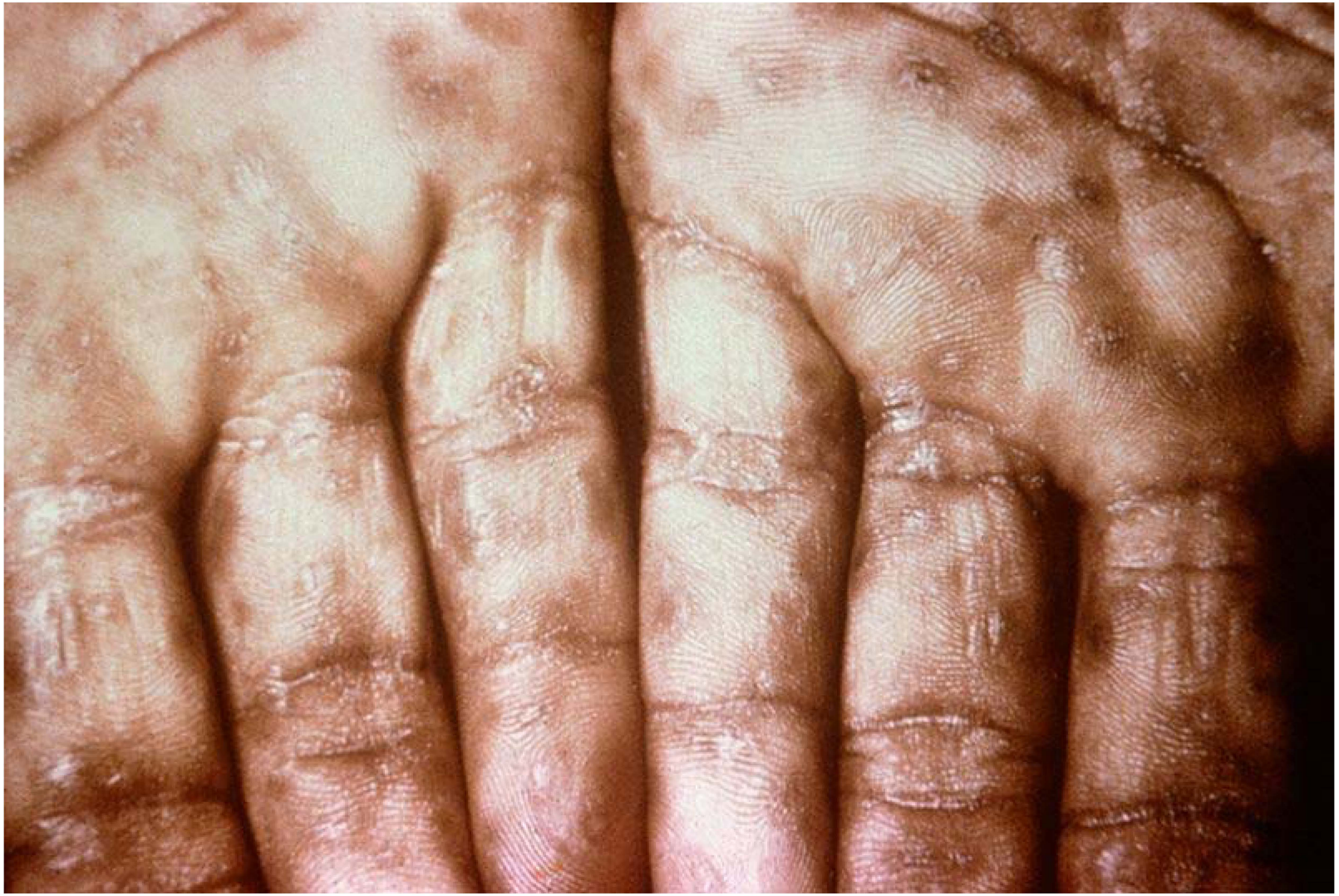
- Primary
- Secondary
- Tertiary

Primary Syphilis

- Chancre on penis, scrotum, vulva or cervix. Firm red papule, erodes to create an ulcer, indurated- Hard Chancre
- 2-4 wk after acquiring infection
- Heals without scarring even in absence of treatment
- Ab test positive in 1-3 wk after appearance of chancre
- Histologically– dense infiltrate of lympho, plasma cells & macrophages
  - Perivascular aggregates of plasma cells
  - endarteritis obliterans

Secondary Syphilis

- Mucocutaneous lesions & painless lymphadenopathy in 2-3 months after exposure
- Mucous patches on mouth, pharynx, palms, soles. Condyloma lata in anogenital region- red brown papular lesions
- Highly infective stage
- Spirochetes easily demonstrated in mucocutaneous lesions
- Ab tests always positive
- M/E



Tertiary Syphilis

- 2-3 years following first exposure
- Less infective
- 2 types of lesions

Syphilitic gumma—solitary, localized, rubbery lesion with central necrosis in testis, bone, brain, liver (hepar lobatum)

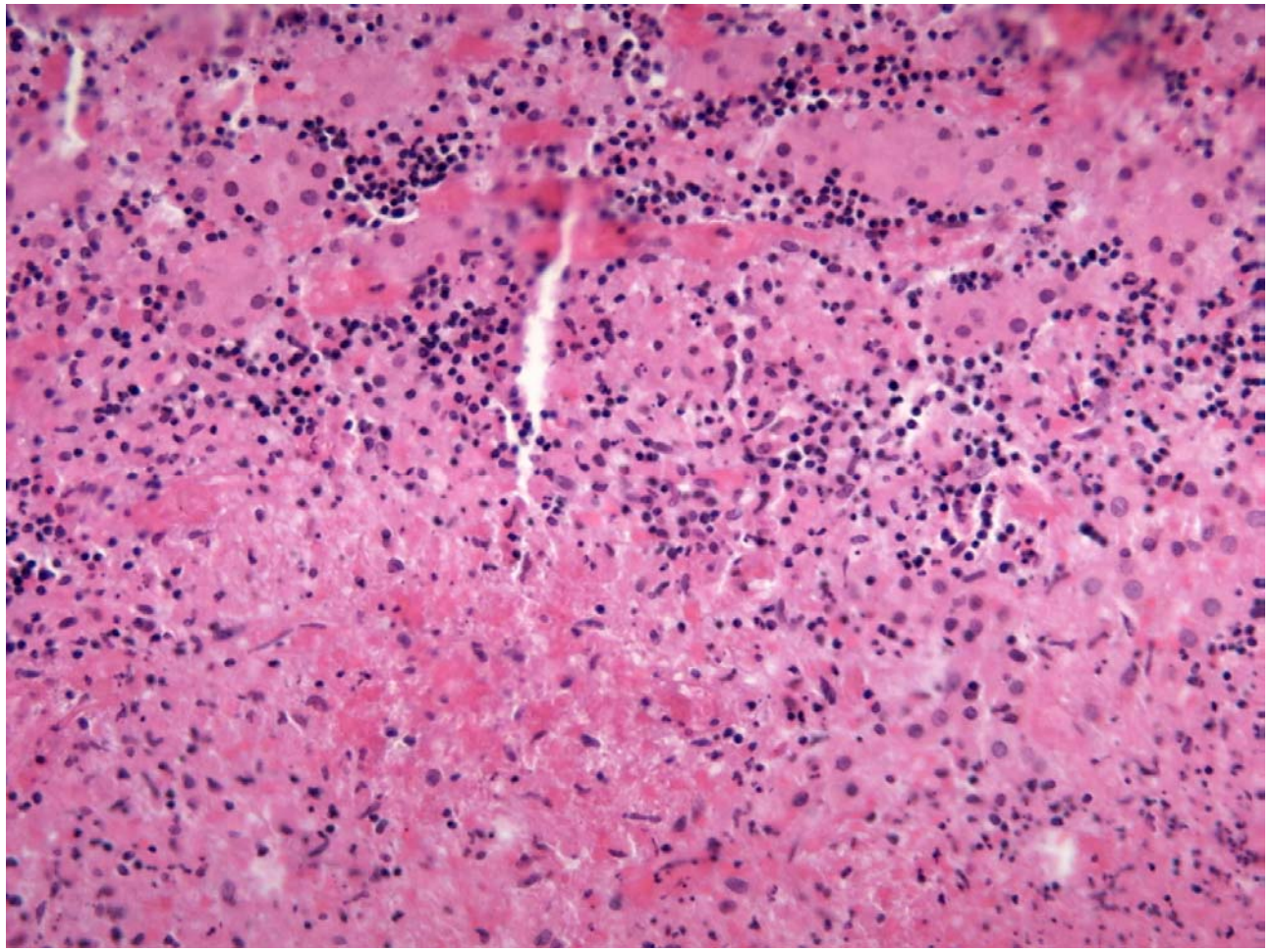
M/E- granuloma containing central necrotic material, palisaded macrophages, mononuclear cells

Diffuse lesions

CVS- aortic aneurysm

Neurosyphilis- meningovascular
tabes dorsalis
general paresis

Gumma



- **Neurosyphilis**
- General paresis- results in personality changes, emotional changes, hyperactive reflexes
- Tabes dorsalis- a disorder of the spinal cord, often results in a characteristic shuffling gait
- Imaging of the brain usually shows atrophy.
- **Syphilitic aortitis**- syphilis affects the ascending aorta causing aortic dilation and regurgitation, massive hypertrophy of the left ventricle (over 1,000 grams)
- Heart is termed cor bovinum (cow's heart).
- Tunica intima: tree bark appearance

Congenital Syphilis

- Develop in fetus >16 wk gestation who is exposed to maternal spirochaetemia
- 3 types of lesions

1. Child born dead
2. Infantile type

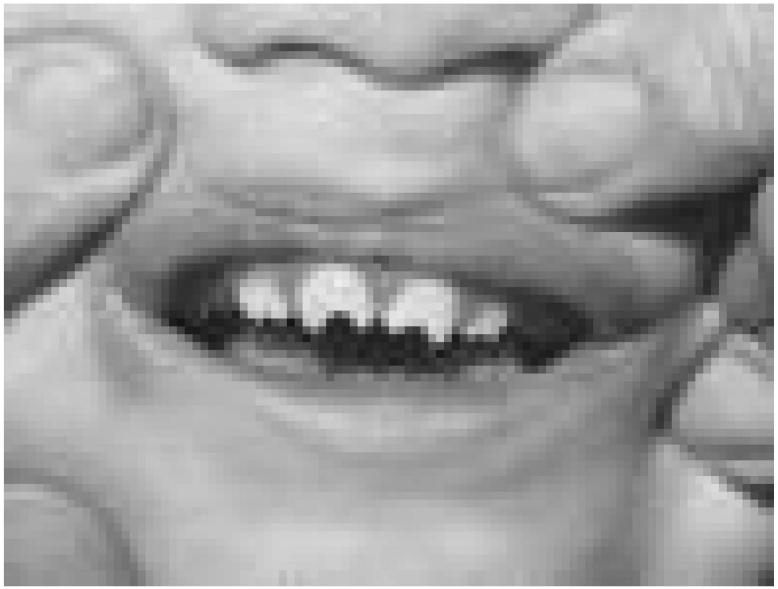
   - muco-cutaneous lesions- diffuse sloughing of epithelium, teem with spirochaetes

   - bony lesions- osteochondritis, perichondritis, saddle nose deformity, saber shin

3. Late type--- Hutchinson's teeth

   - Interstitial keratitis

   - Deafness



Infectious Granulomatous Diseases

Examples of Diseases with Granulomatous Inflammations

Disease	Cause	Tissue Reaction
Tuberculosis	*Mycobacterium tuberculosis*	Noncaseating tubercle (granuloma prototype): a focus of epithelioid cells, rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cell; caseating tubercle: central amorphous granular debris, loss of all cellular detail; acid-fast bacilli
Leprosy	*Mycobacterium leprae*	Acid-fast bacilli in macrophages; non-caseating granulomas
Syphilis	*Treponema pallidum*	Gumma: microscopic to grossly visible lesion, enclosing wall of histiocytes; plasma cell infiltrate; central cells are necrotic without loss of cellular outline
Cat-scratch disease	Gram-negative bacillus *Bartonella henselae*	Rounded or stellate granuloma containing central granular debris and recognizable neutrophils; giant cells uncommon

ACTINOMYCOSIS

- *Actinomycetes israelli*
- Gram positive, non acid fast
- Commensal in oral cavity, alimentary tract & vagina
- Endogenous in origin, never person to person
- Four types

Cervicofacial actinomycosis

- Commonest & have best prognosis
- Infection enters from tonsils, carious tooth
- Abscesses & sinuses
- Discharging pus contains typical tiny yellow sulphar granules.

ACTINOMYCOSIS

Thoracic actinomycosis

- Aspiration of organism from oral cavity
- Initially resembles pneumonia & subsequently spreads to whole of lung, pleura, ribs & vertebrae

Abdominal actinomycosis

- Common in appendix, caecum & liver
- Results from swallowing of organism from oral cavity or extension from thoracic cavity

ACTINOMYCOSIS

Pelvic actinomycosis

- Complication of IUCD

Microscopy

- Granuloma with central suppuration
- Centre of abscess contains bacterial colony (sulphar granule) characterized by radiating filaments with hyaline, eosinophilic club ends

Sarcoidosis

- Systemic disease of unknown etiology characterized by noncaseating granulomas
- More common in women, 20-40 years

Etiology

- Disease of disordered immune regulation in genetically predisposed individuals exposed to certain environmental agents

- Immunologic factors
  - cell mediated response
  - accumulation of CD+4 T cells,
  CD4:CD8 ratio—5:1-15:1
  - ↑T cell derived cytokines- IL-2, IFN
- accumulation of monocytes, macrophages and activated T-lymphocytes,
- increased production of mediators: TNF-alpha, IFN-gamma, IL-2 and IL-12, characteristic of a Th1 response
- Genetic factors
  - familial, racial clustering
- Environmental factors
  - Mycobacteria, Rickettesia

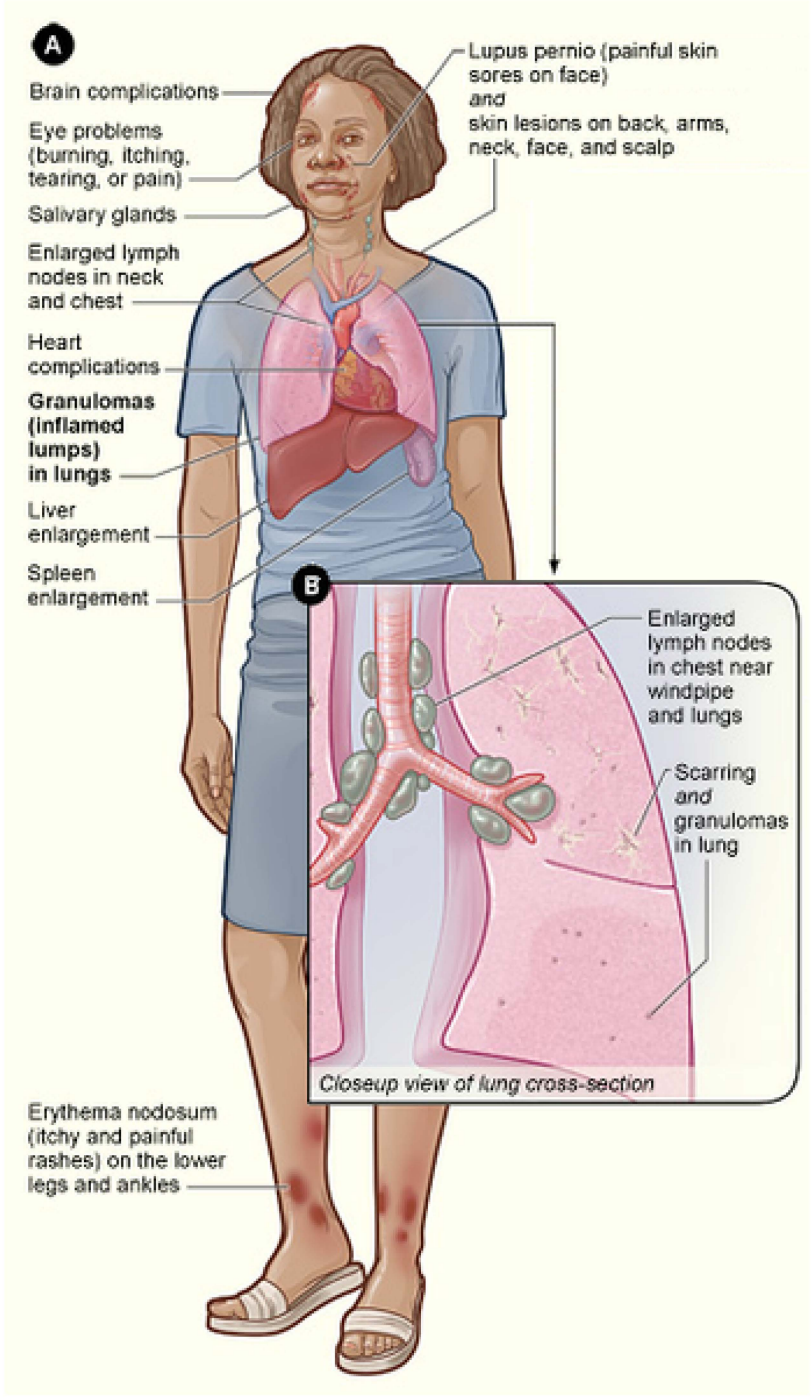
Morphology

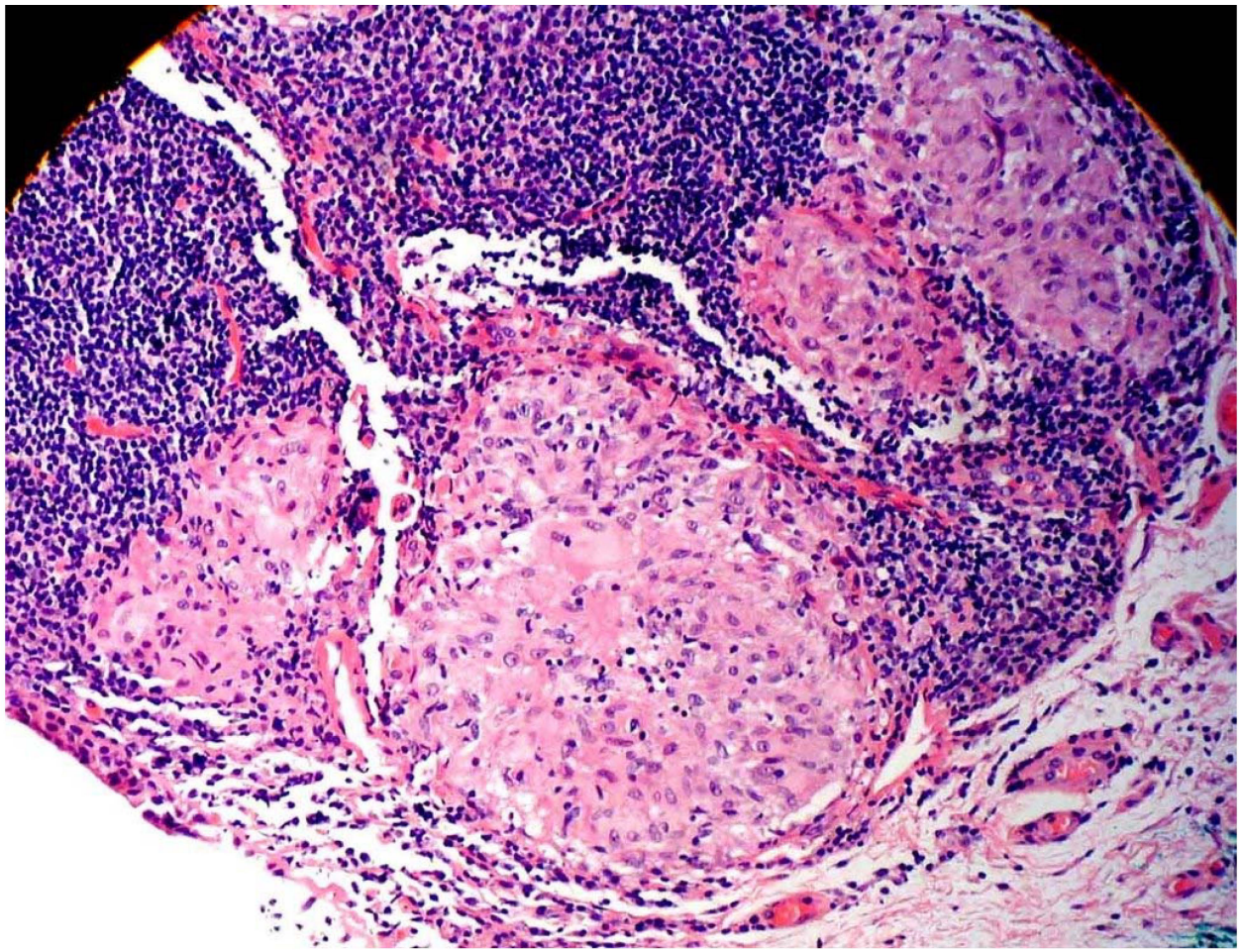
Organs involved

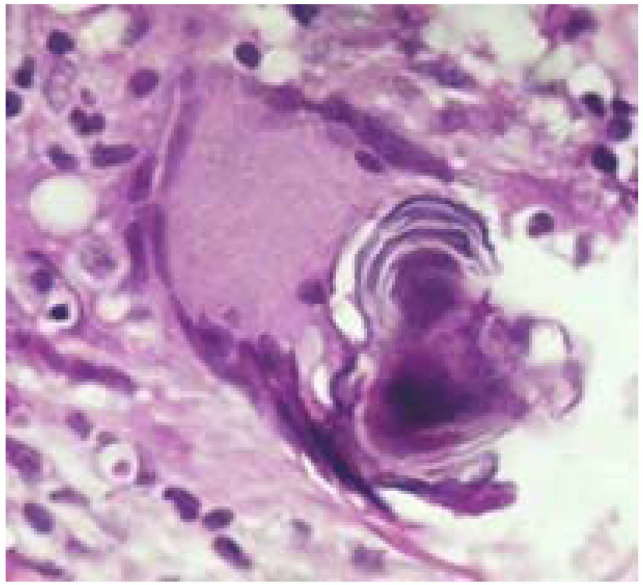
- Lungs
- Hilar & mediastinal lymphadenopathy
- Spleen/Hepatomegaly
- Bone
- Skin
- Eye
- Salivary glands
- Muscles

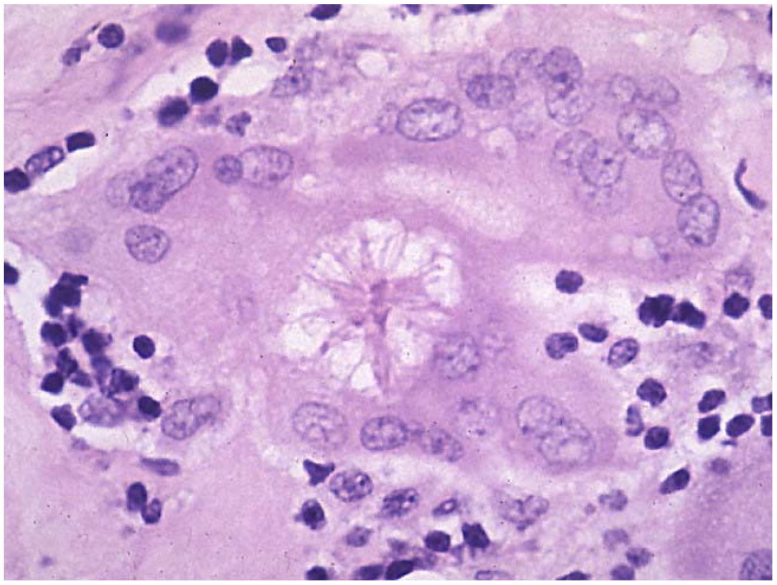
M/E- non caseating granuloma

- Schaumann bodies-laminated concretions
- Asteroid bodies- stellate inclusions


A
Brain complications
Eye problems (burning, itching, tearing, or pain)
Salivary glands
Enlarged lymph nodes in neck and chest
Heart complications
Granulomas (inflamed lumps) in lungs
Liver enlargement
Spleen enlargement
Lupus pernio (painful skin sores on face)
and
skin lesions on back, arms, neck, face, and scalp
Erythema nodosum (itchy and painful rashes) on the lower legs and ankles
B
Enlarged lymph nodes in chest near windpipe and lungs
Scarring
and
granulomas in lung
Closeup view of lung cross-section







Clinical features

- Symptoms are vague: shortness of breath, cough, chest pain, haemoptysis, fever, fatigue, weight loss, anorexia
- presents as a restrictive disease of the lungs, decrease in lung volume and decreased compliance, vital capacity
- Arthritis
- Dry eyes, blurry vision
- Skin lesions; range from rashes and nodules to erythema nodosum.

Diagnosis

- X-ray chest, CT scan
- CT-guided biopsy, mediastinoscopy,
- Bronchoscopy with biopsy
- Special stains to rule out microorganisms, matter of exclusion.
- ACE- blood levels are used in diagnosis and monitoring of sarcoidosis.
- Serum calcium and 24-hour urine calcium

Prognosis

- Progressive chronicity or periods of activity with remissions
- 65-70% recover with minimal or no residual manifestations
- 20% permanent loss of lung function
- 10-15% die of cardiac/CNS manifestations