SUMMARY OF MAIN POINTS OF ACUTE INFLAMMATION

- Rapid response of living tissue to any injury.
- Naked eye (Macroscopic): Redness, swelling, heat, pain & loss of function.
- Microscopic: Vascular dilatation, exudate leaks into tissues, neutrophils emigrate.
- Changes controlled by many short-lived chemical mediators. Some can be manipulated by drugs.
- Neutrophils: Fast acting, short-lived phagocytes, engulf & degrade bacteria, dead tissue etc.
- Phagocytosis enhanced by opsonisation of particles, e.g. antibody or complement on surface.
- Bacterial killing largely oxygen dependent.
- Defects in the system lead to severe susceptibility to infection.

Outcomes of acute inflammation

1. **Complete resolution**
2. **Healing by scarring**
3. **Abscess formation**
4. **Progression to chronic inflammation**

CHRONIC INFLAMMATION

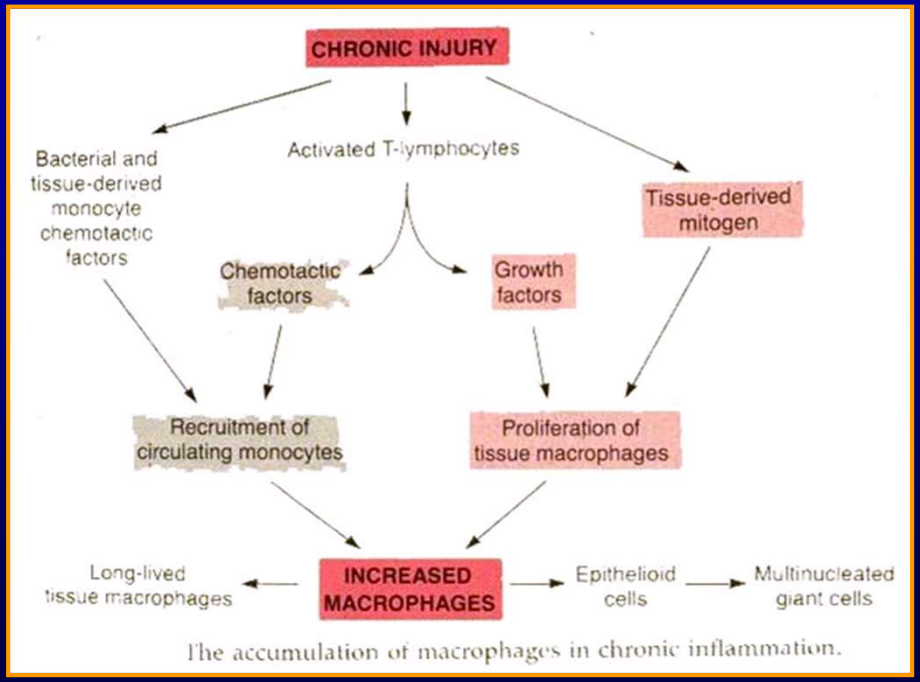
- May 'take over' from acute inflammation
  - if damage is too severe to be resolved within a few days.
- May arise de novo in some circumstances
  - e.g. some autoimmune conditions, some chronic infections
  - i.e. chronic low-level irritation
- May develop alongside acute inflammation
  - in more severe persistent irritation
- **What is chronic inflammation?**
  - Characterised by the microscopic appearances.
  - Most important characteristic is the **type of cell present.**

Primary chronic inflammation

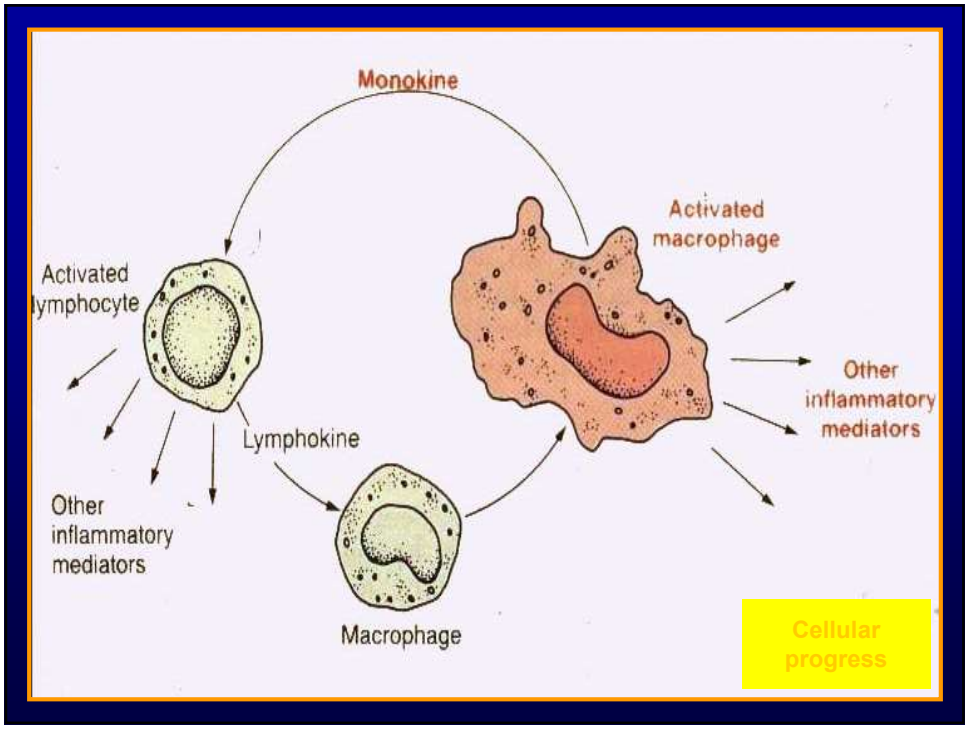
1. Persistent infection
2. Prolonged exposure to nondegradable inanimate material (silica, silicosis)
3. Autoimmune disease

Features of chronic inflammation

- Small round cell infiltration
- Fibroblasts, proliferation of capillaries
- Necrosis
- Fibrosis – collagenisation
- Signs of regeneration

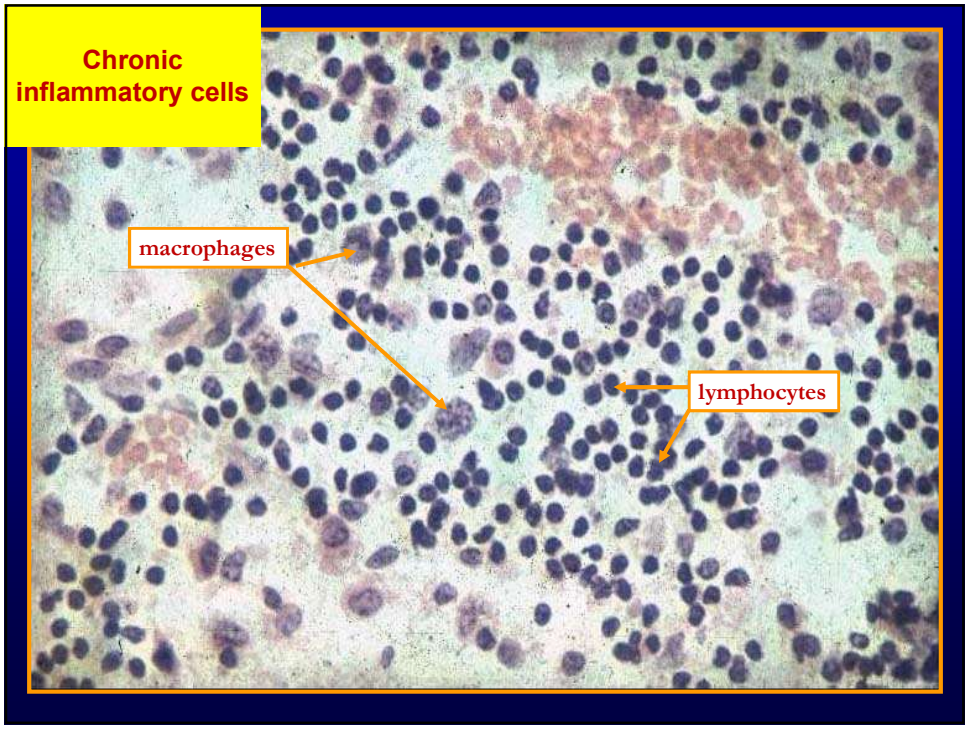


The accumulation of macrophages in chronic inflammation.



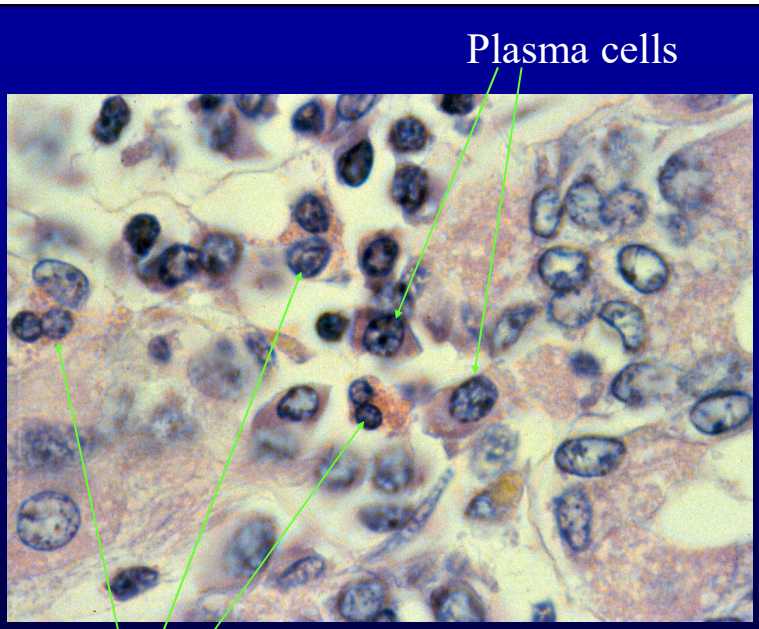
Products released by macrophages

- Enzymes
- Plasma proteins
- Reactive metabolites of oxygen
- Arachidonic acid metabolites
- Cytokines (IL-1, TNF, IL-8)
- Growth factors (PDGF,EGF,FGF)



Other cells involved in chronic inflammation

- Plasma cells:
  - Differentiated antibody-producing B lymphocytes. Implies considerable chronicity.
- Eosinophils:
  - Allergic reactions, metazoal infestations, some tumours.
- Fibroblasts/Myofibroblasts:
  - Recruited by macrophages; make collagen. See next lecture.



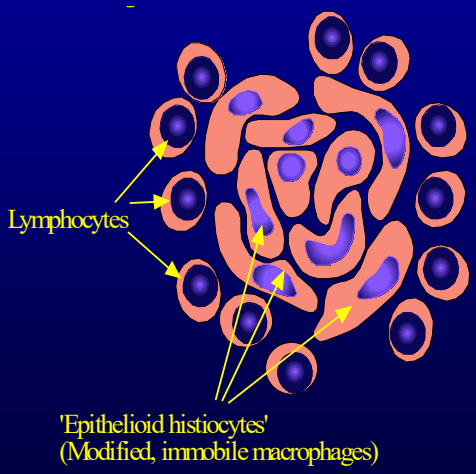
EFFECTS OF CHRONIC INFLAMMATION

- Fibrosis
  - (see next lecture)
  - e.g. gall bladder (chronic cholecystitis), chronic ulcers..
- Impaired function
  - e.g. chronic inflammatory bowel disease
  - Rarely, increased; e.g. mucus secretion, thyrotoxicosis
- Atrophy
  - e.g. gastric mucosa, adrenal glands
- Stimulation of immune response
  - Macrophage - lymphocyte interactions

GRANULOMATOUS INFLAMMATION

= chronic inflammation with granulomas

What is a granuloma?

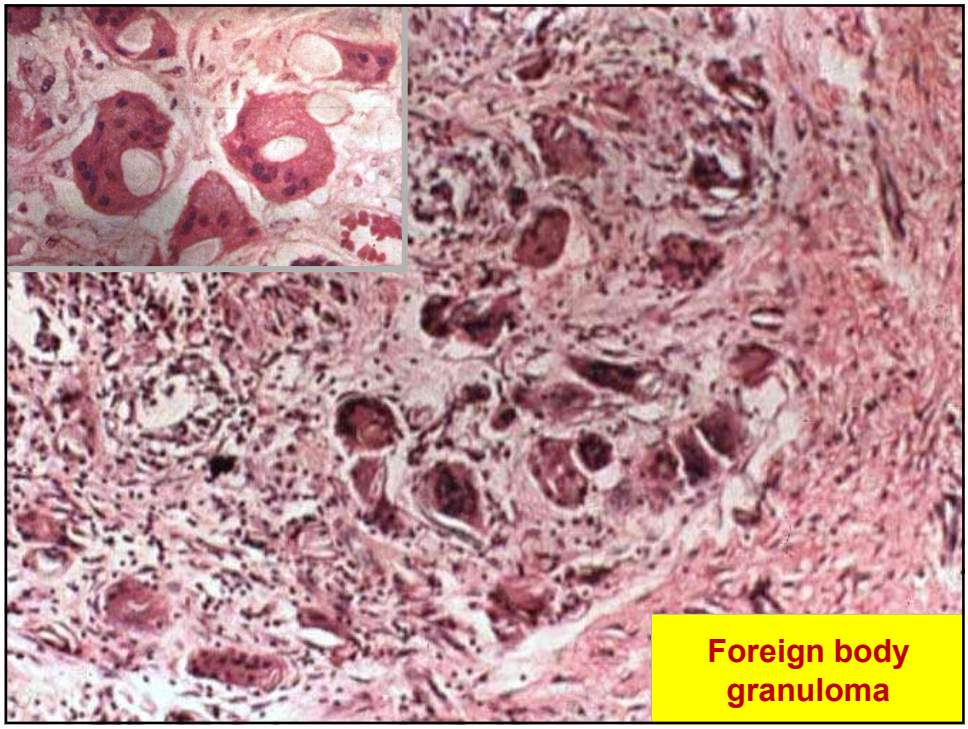


Granuloma:

collection of epitheloid cells
collar of lymphocytes
+ giant cells

Different types:

- Immune granulomas
  - caseating
  - non-caseating granulomas
- Foreign body granulomas



Granulomas arise with:

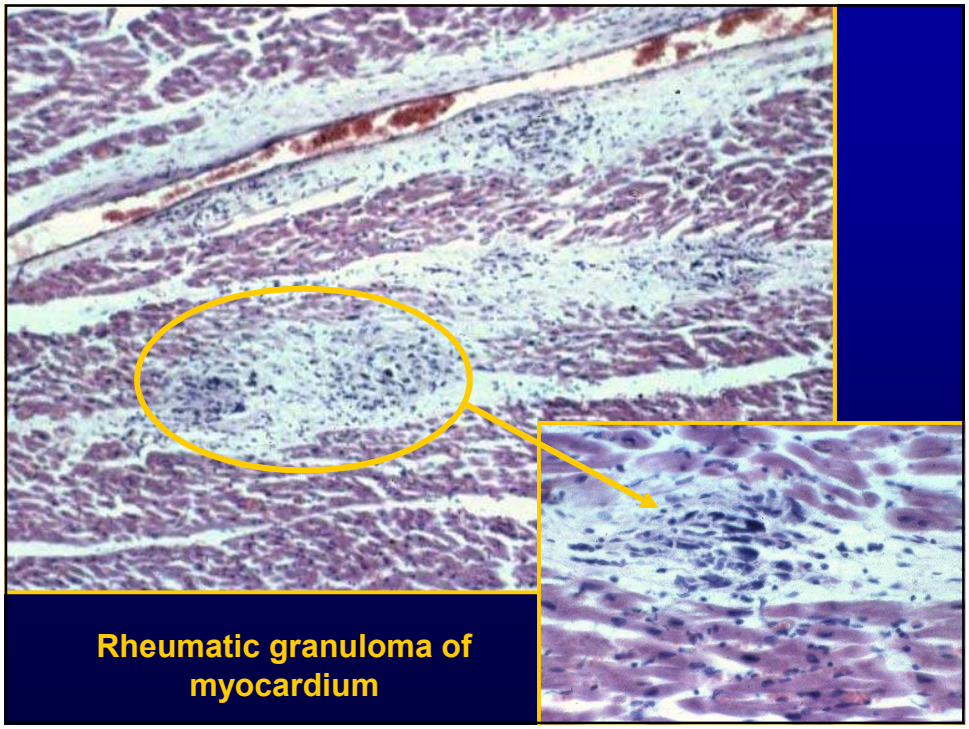
- Persistent, low-grade antigenic stimulation
- Hypersensitivity

Main causes of granulomatous inflammation:

- Mildly irritant 'foreign' material
- Mycobacteria: Tuberculosis, leprosy
- Syphilis
- Other rare infections e.g. some fungi
- Unknown causes: Sarcoid
  Wegener's granulomatosis
  Crohn's disease

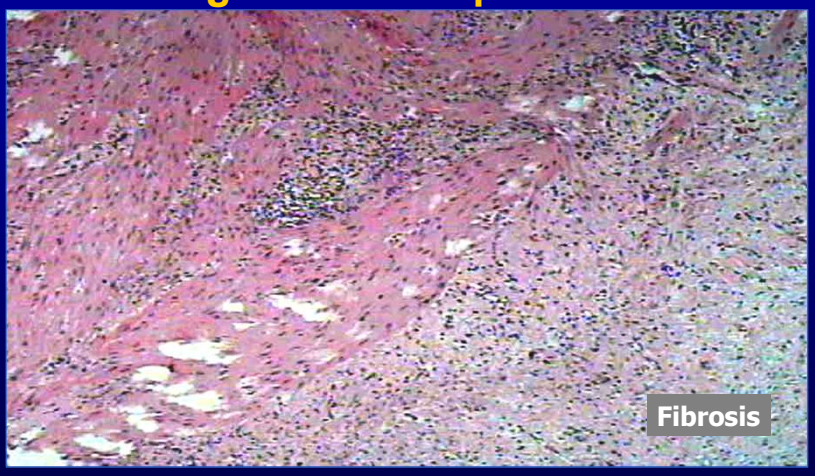
Granulomatous diseases

Tuberculosis
Leprosy
Syphilis
Cat-scratch disease
Lymphogranuloma venereum
Tularaemia
Sarcoidosis
Schistosomiasis (parasitic)
Fungal infections



Rheumatic granuloma of myocardium

Light microscope - H&E

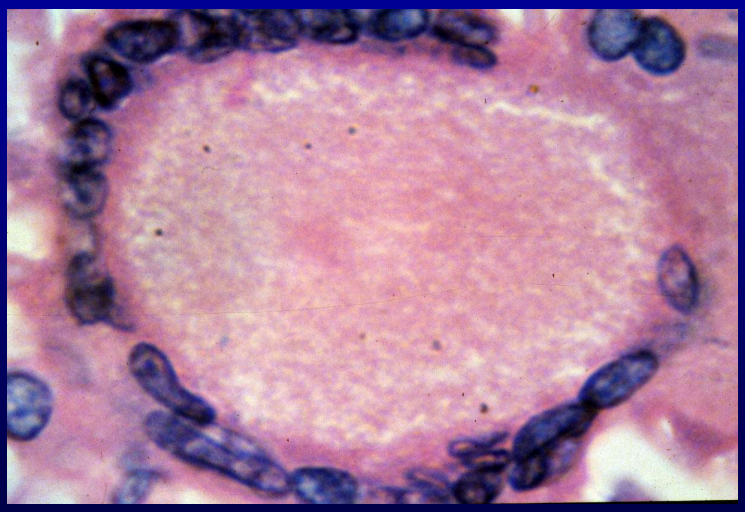


Dg.: Cholecystitis chronica calculosa

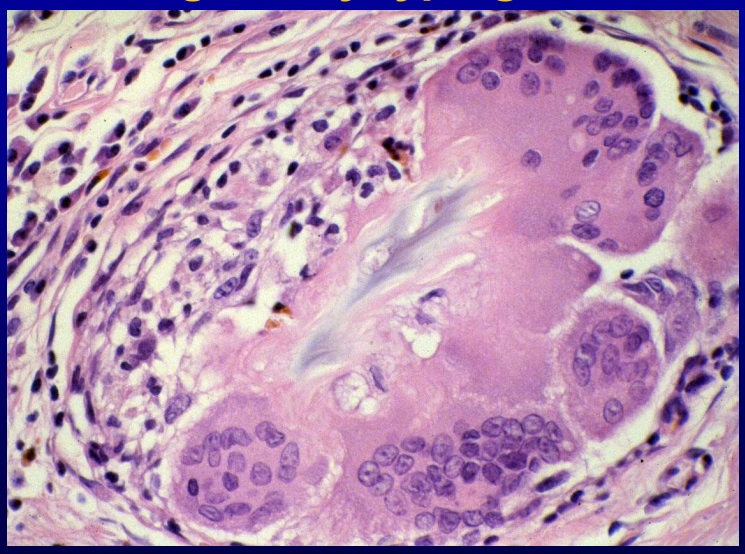
'Giant' Cells

- Multinucleate cells made by fusion of macrophages.
- Morphology of most chronic inflammatory reactions is non-specific, BUT proportions of each cell type may vary in different conditions.
- For example:
  - Rheumatoid arthritis: Mainly plasma cells.
  - Chronic gastritis: Mainly lymphocytes.
  - Leishmaniasis (a protozoal infection): Mainly macrophages.
  - Giant cell type may be a help to diagnosis.

Langhans type giant cell - Tuberculosis

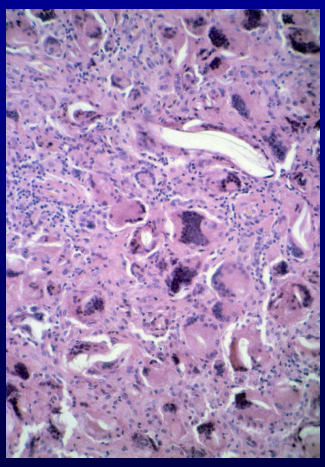


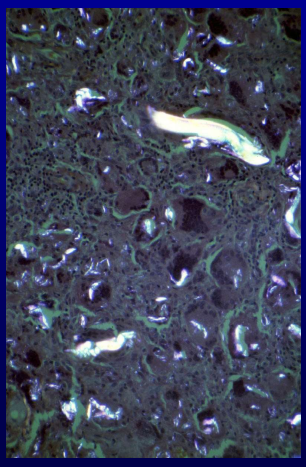
Foreign body type giant cells



Foreign material from breakdown of artificial joint

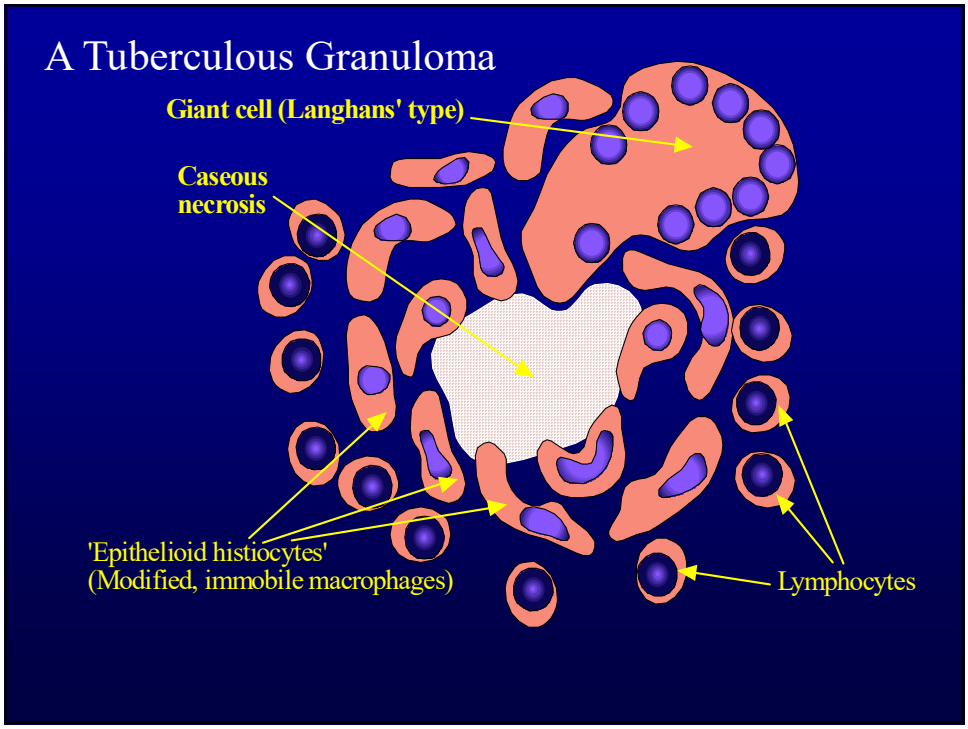
Examined through 'crossed polaroids':

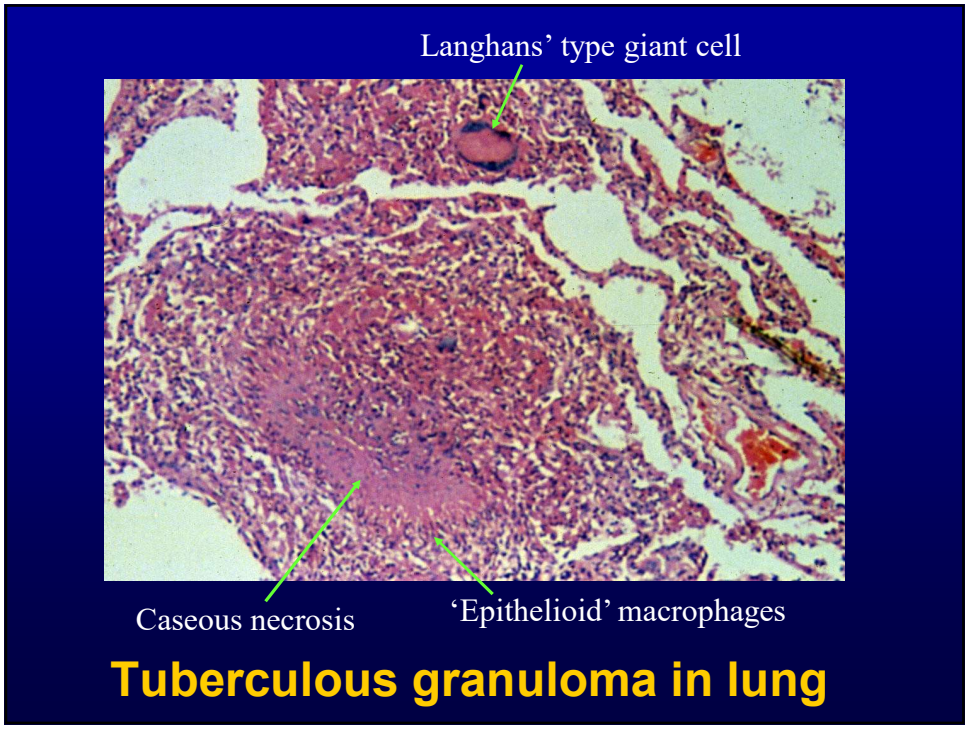




TUBERCULOSIS

- Caused by Mycobacteria
  - especially M. tuberculosis. Difficult & slow to culture.
- Nature of organism: see microbiologists
  - n.b. wall lipids (Mycosides).
- Produces no toxins or lytic enzymes
- Causes disease by persistence and induction of cell-mediated immunity.


A Tuberculous Granuloma
Giant cell (Langhans' type)
Caseous necrosis
'Epithelioid histiocytes'
(Modified, immobile macrophages)
Lymphocytes


Langhans' type giant cell
Caseous necrosis
'Epithelioid' macrophages
Tuberculous granuloma in lung

Patterns of disease:

- Primary: Non-sensitized individual
  - Usually heals with some scarring & persistent bacteria in lung
  - OR Progressive primary tuberculosis.
    1) Massive hilar lymph nodes
    2) Tuberculous bronchopneumonia
    3) 'Miliary' tuberculosis
- Secondary: Previously exposed individual
  - Re-activation or re-infection?
  - PATTERN OF DISEASE IMMENSELY VARIABLE

Outcomes:

1) Arrest, fibrosis, scaring.
2) Erosion into bronchus
   - bronchopneumonia
   - T.B. in Gastro Intestinal Tract
3) Erosion into pleura & tuberculous empyema
4) Erosion into blood stream

Many bugs: MILIARY TUBERCULOSIS

Few bugs: SINGLE ORGAN TUBERCULOSIS

- Organs: Cervical lymph nodes, Meninges & brain, Kidney, Adrenals, Bone, Fallopian tube, Epididymis, etc.

GRANULOMATOUS DISEASES OF UNKNOWN CAUSE

- Sarcoidosis
  - Variable clinical manifestations
    Young adult women
    Non-caseating granulomas, giant cells
    Involves lymph nodes, lungs, spleen, marrow, skin, liver...
- Crohn's Disease
  - 'Regional enteritis': patchy full-thickness inflammation throughout bowel
- Wegener's granulomatosis
- and many others

Sarcoid granulomas in a lymph node