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.

1

Outcomes of acute inflammation

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

2

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.**

3

Primary chronic inflammation

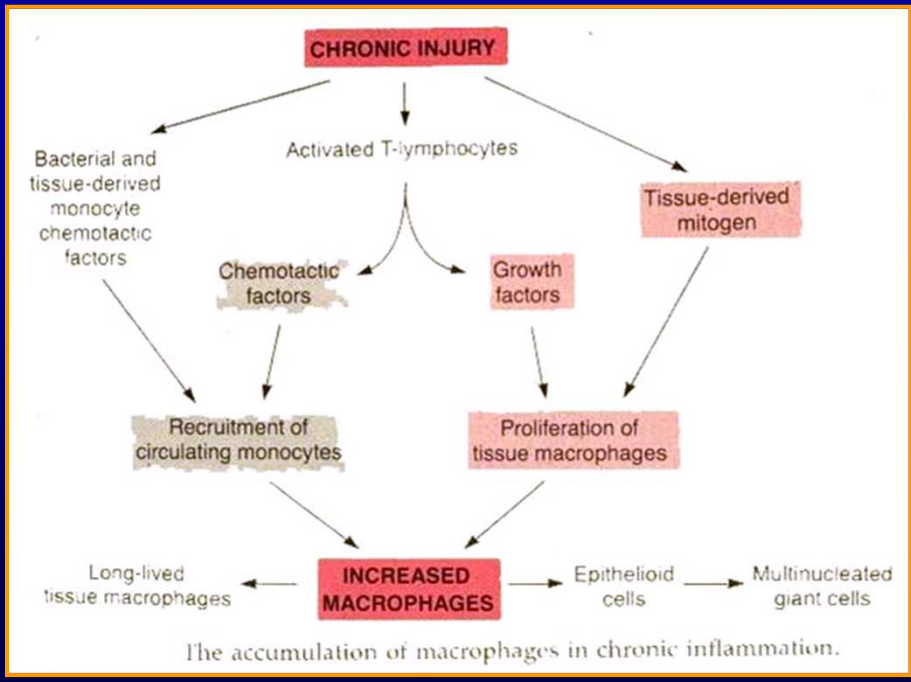
1. Persistent infection
2. Prolonged exposure to nondegradable inanimate material (silica, silicosis)
3. Autoimmune disease

4

Features of chronic inflammation

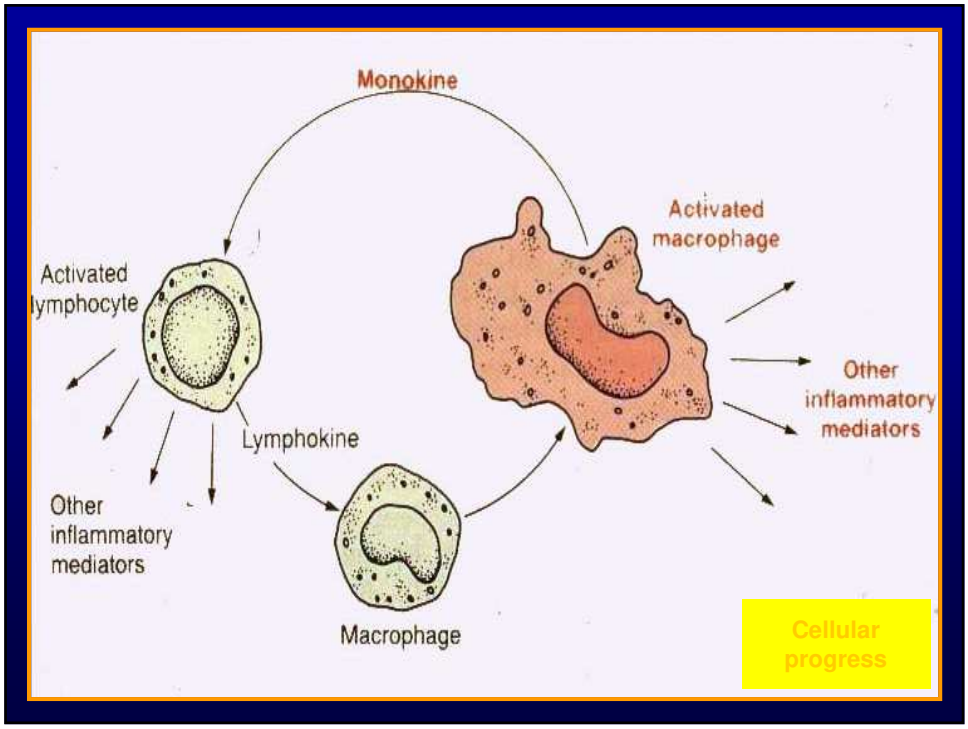
- Small round cell infiltration
- Fibroblasts, proliferation of capillaries
- Necrosis
- Fibrosis – collagenisation
- Signs of regeneration

5



The accumulation of macrophages in chronic inflammation.

6



7

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)

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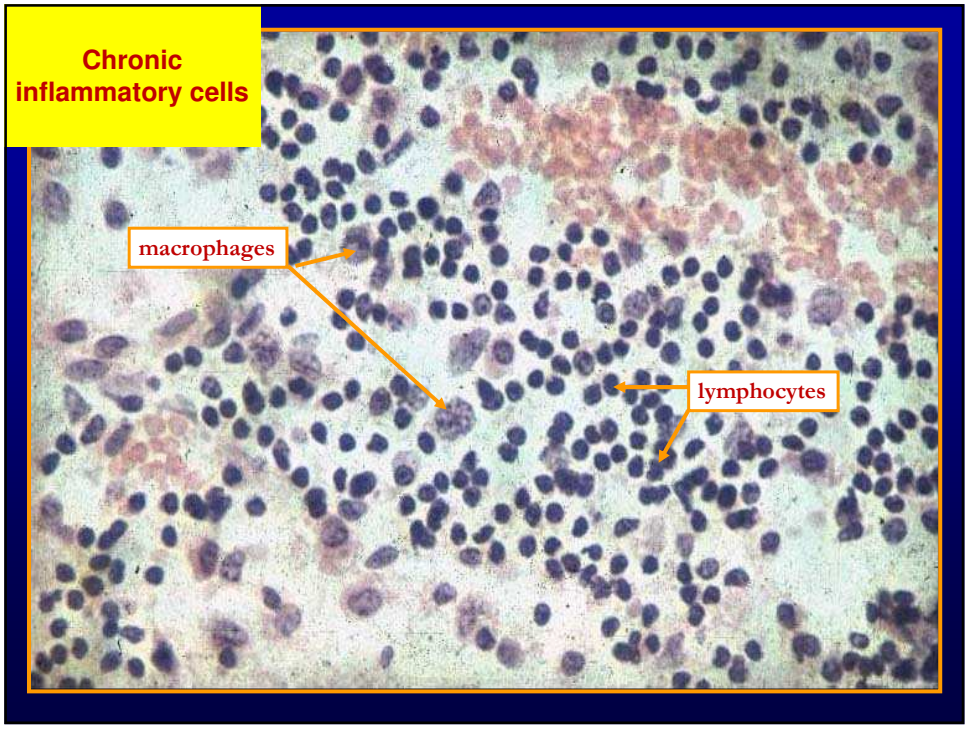
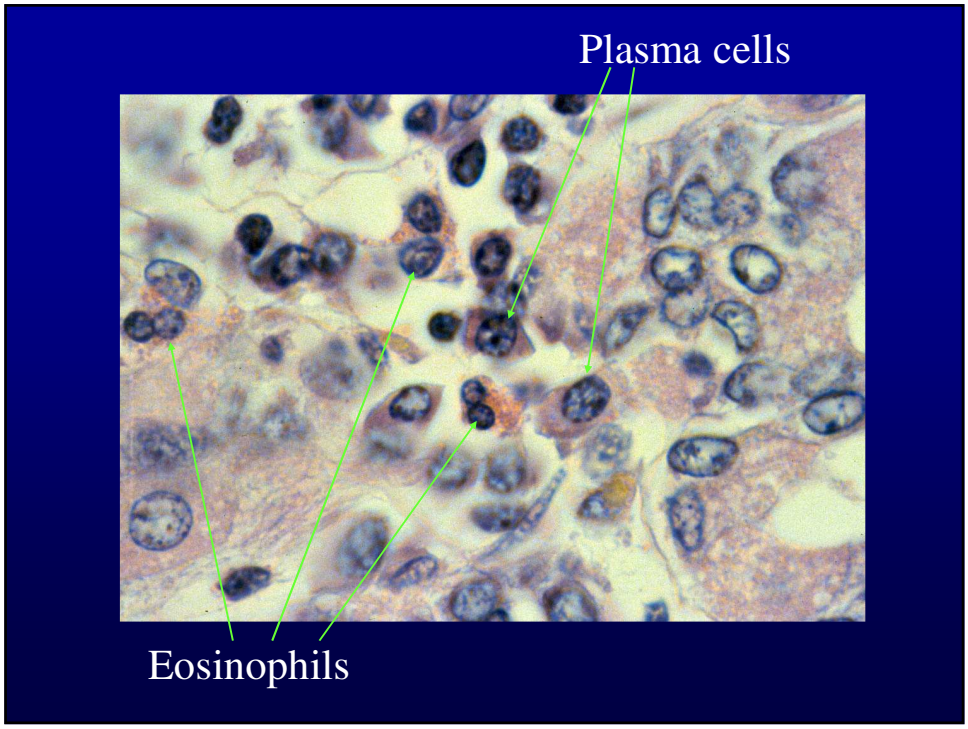


9

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.

10



11

EFFECTS OF CHRONIC INFLAMMATION

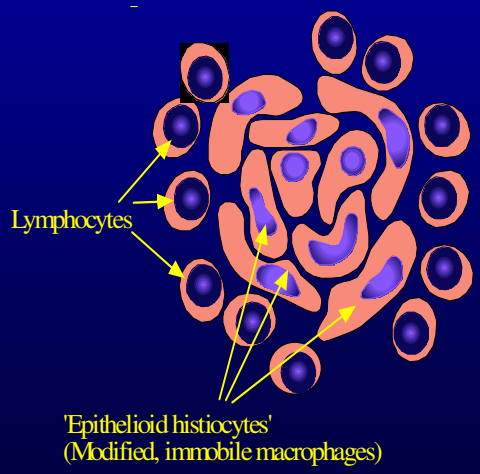
- Fibrosis
  - (see next lecture)
  - e.g. gall bladder (chronic cholecystitis), chronic ulcers..
- Impaired function
  - e.g. chronic inflammatory bowel disease
  - Rarely, increased; e.g. mucus secretion, thyrotoxicosis
- Atrophy
  - e.g. gastric mucosa, adrenal glands
- Stimulation of immune response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

12

GRANULOMATOUS INFLAMMATION

= chronic inflammation with granulomas

What is a granuloma?



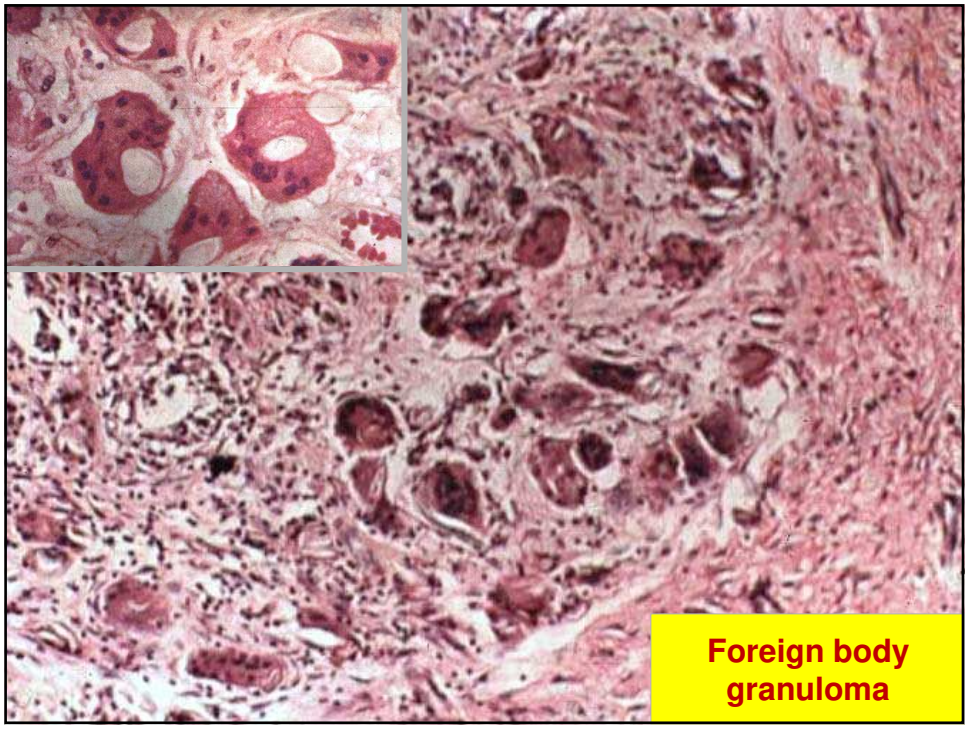
Granuloma:

collection of epitheloid cells
collar of lymphocytes
+ giant cells

Different types:

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

13



14

Granulomas arise with:

- Persistent, low-grade antigenic stimulation
- Hypersensitivity

15

Main causes of granulomatous inflammation:

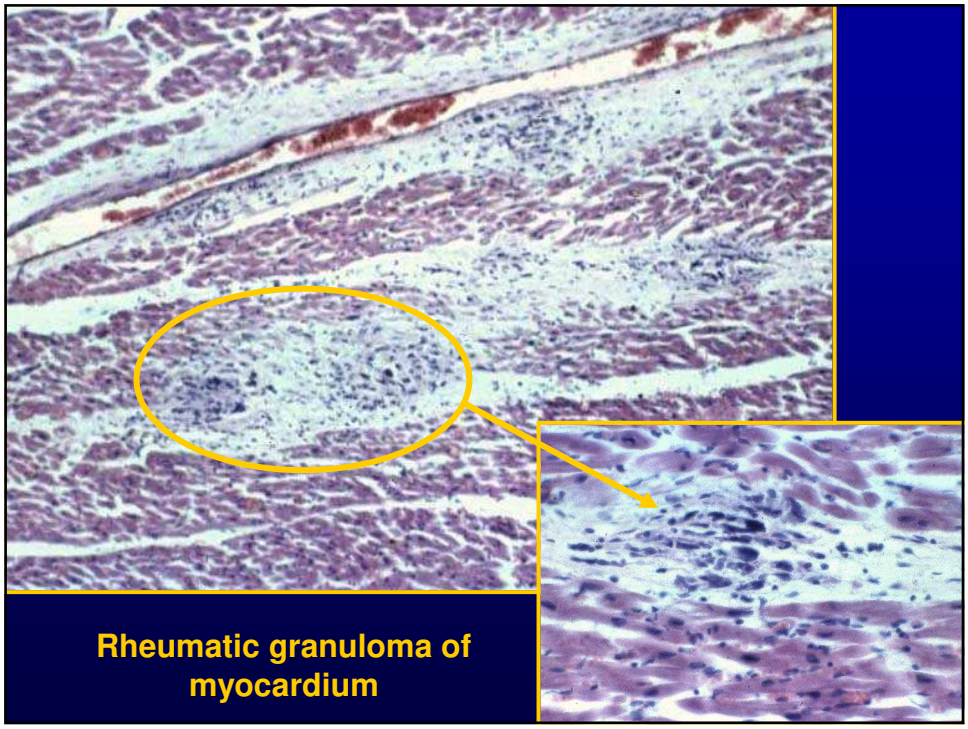
- Mildly irritant 'foreign' material
- Mycobacteria: Tuberculosis, leprosy
- Syphilis
- Other rare infections e.g. some fungi
- Unknown causes: Sarcoid
  Wegener's granulomatosis
  Crohn's disease

16

Granulomatous diseases

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

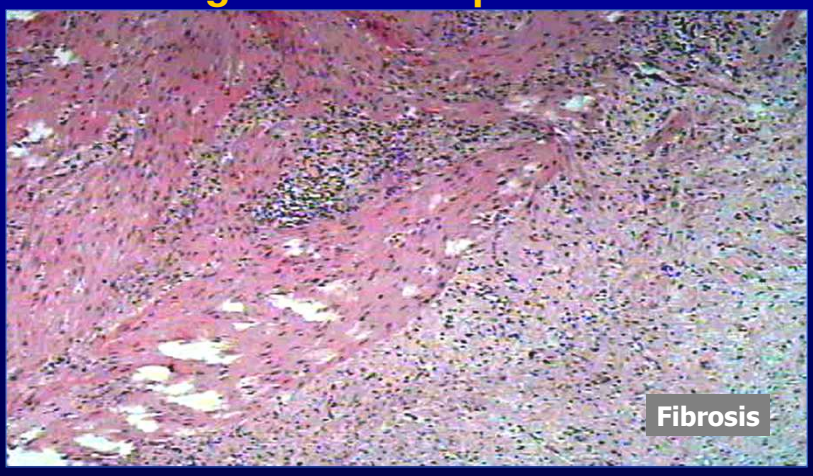
17



Rheumatic granuloma of myocardium

18

Light microscope - H&E



Dg.: Cholecystitis chronica calculosa

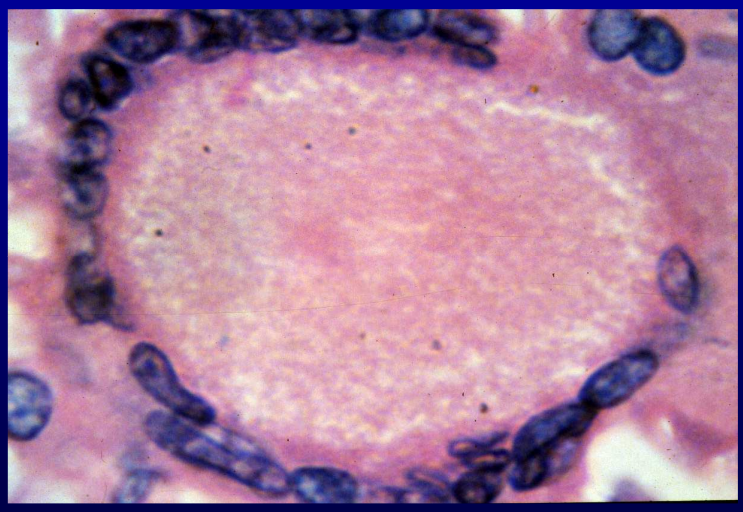
19

'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.

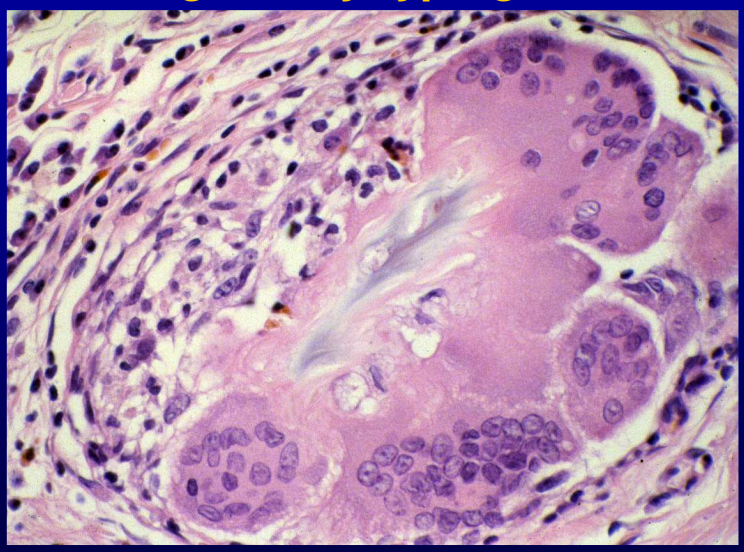
20

Langhans type giant cell - Tuberculosis



21

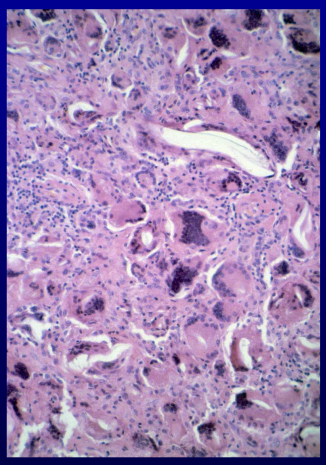
Foreign body type giant cells

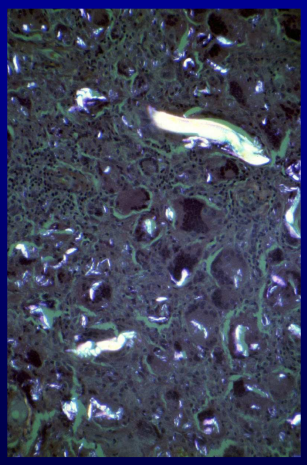


22

Foreign material from breakdown of artificial joint

Examined through 'crossed polaroids':



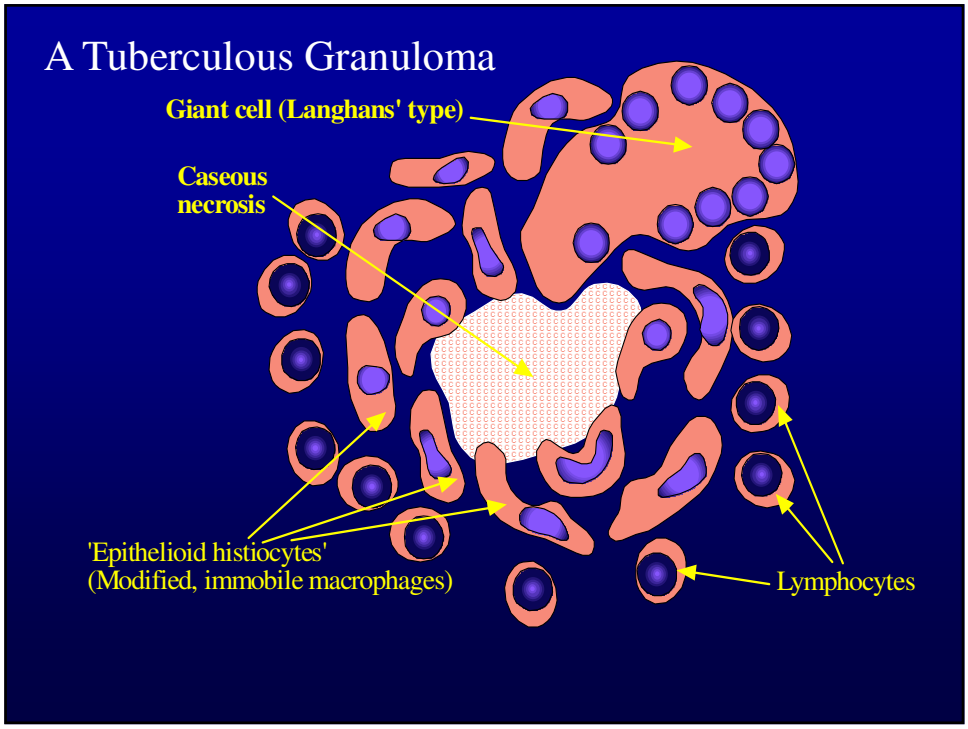


23

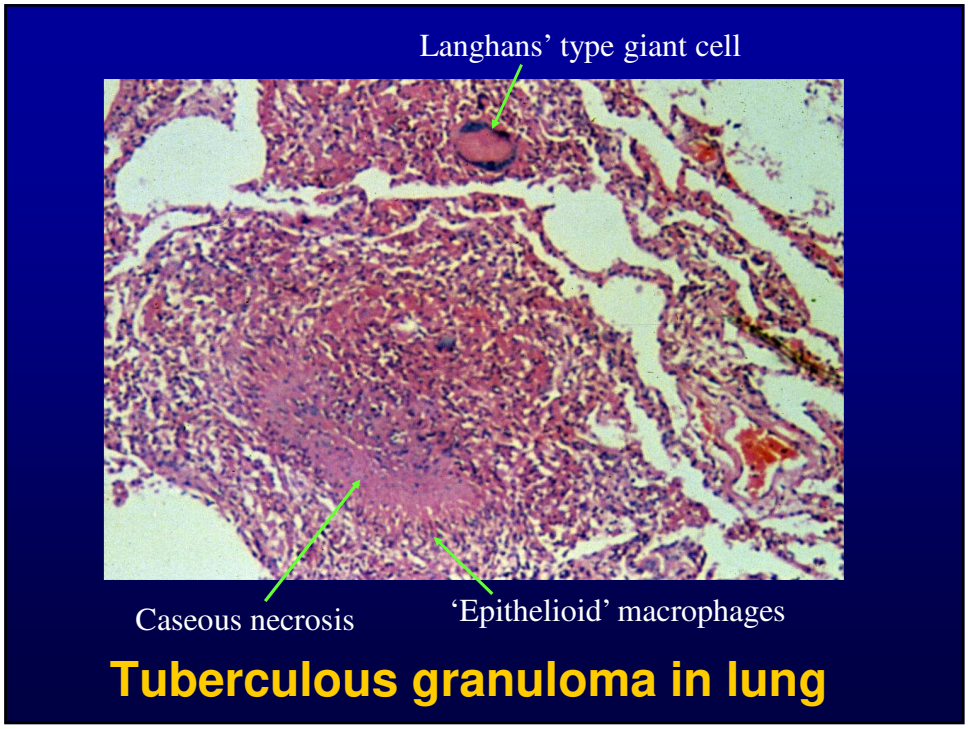
TUBERCULOSIS

- 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.

24


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

25


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

26

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

27

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.

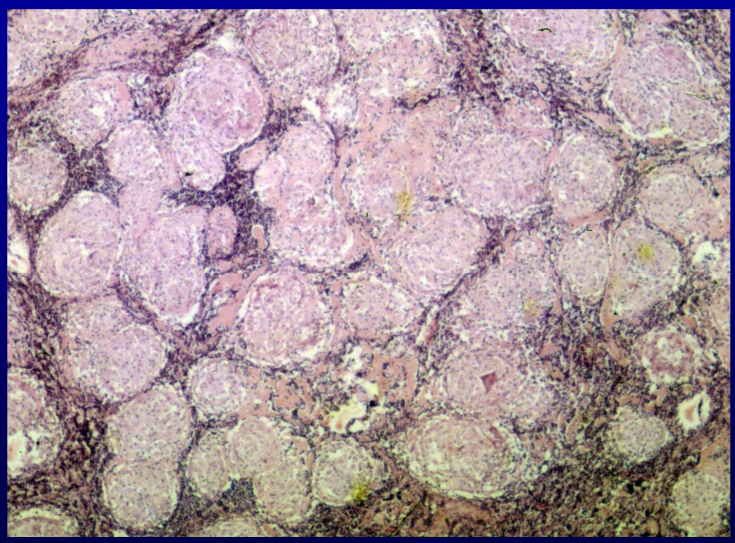
28

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

29

Sarcoid granulomas in a lymph node



30