Chronic inflammation

- Inflammation of prolonged duration in which active inflammation, tissue destruction and repair proceed simultaneously
- May follow ac infl or begins insidiously
- Causes:
  - persistent infections, organisms of low toxicity & evoke delayed HS
  - prolonged exposure to toxic agents –exogenous (silica) or endogenous (lipid)- Atherosclerosis
  - autoimmunity- autoAg evoke immune reaction to cause tissue damage eg RA, SLE
**Acute**

- Pathogens, injured tissues
- Neutrophils, monocytes, macrophages
- Vasoactive amines, eicosanoids
- Immediate (Few days)
- Resolution, abscess formation, chronic inflammation

**Chronic**

- Persistent acute inflammation - non-degradable pathogens, foreign bodies, or autoimmune
- Monocytes, macrophages, lymphocytes, plasma cells,
- IFN-γ and other cytokines, GFs, hydrolytic enzymes
- Delayed (months or years)
- Tissue destruction, fibrosis
Systemic effects of inflammation

- Fever
- Anemia
- Leucocytosis
- ESR
- Amyloidosis
Morphologic features of chronic inflammation

- Infiltration with mononuclear cells
  - by chemotactic factors & adhesion molecules, continuous infiltration
  - local proliferation
  - longer survival
- Tissue destruction
  macrophages release proteases, elastase, collagenase, NO, reactive oxygen radicals, cytokines (IL1,8, TNF)
- Healing by fibrosis & angiogenesis
Types of chronic inflammation

• Chronic non-specific
  ch. osteomyelitis, lung abscess
• Chronic granulomatous inflammation
  tuberculosis, syphilis, actinomycosis
Granulomatous Inflammation

- Distinctive pattern of chronic inflammation, in which the predominant cells are activated macrophages, which are enlarged, oval or elongated with indistinct cell boundary and called epithelioid cells.
- Granuloma – (granule + oma)- circumscribed, tiny lesion (1mm) composed predominantly of collection of epithelioid cells & rimmed at the periphery by lymphoid cells
- Diagnosis of granuloma rests on the identification of epithelioid cells.
- Epithelioid cells may coalesce to form multinucleated giant cells
Injury (e.g. M.tb, talc)

Failure to digest agent

Weak acute inf. response

Persistence of infectious agent

T cell mediated immune response

Poorly digestible agent

Activation of CD4+T cells
Release of IL-1,2, growth factors-IFN, MCF

Accumulation of tissue macrophages

Macrophages activated by IFN-Y

Transformed epithelioid cells, giant cells

GRANULOMA
Pathogenesis of granuloma formation

Expert Reviews in Molecular Medicine 2005 Published by Cambridge University Press
Granulomatous conditions

- Bacterial
  - Tuberculosis
  - Leprosy
  - Syphilis
  - Granuloma inguinale
  - Cat scratch disease

- Fungal
  - Actinomycosis
  - Blastomycosis
  - Cryptococcosis
  - Histoplasma
  - Coccidoides immitis

- Parasitic
  - Schistosomiasis
Granulomatous conditions

- Inorganic metals and dusts
  - Silicosis
  - Berylliosis
  - Pneumoconiosis
  - Asbestosis
- Misc
  - Sarcoidosis
  - Crohns disease
  - Foreign body granuloma
Symptoms

TB can be related to cough, fever, and weight loss. If untreated, fatal in over 50% of cases.
Giant cells

- Foreign body giant cells
- Langhans’ giant cells
- Touton giant cells
- Aschoff giant cells
- Tumor giant cells
- Reed-Sternberg cells
Foreign body giant cell
Langhans giant cell
Tuoton giant cell
Aschoff giant cell
Tumor giant cell
RS cell  Osteoclastic giant cell
Two types of granuloma

(i) Foreign body granulomas: Incited by inert foreign bodies. Example: suture materials, splinter, breast prosthesis, silica, asbestos etc.

(ii) Immune granulomas: It is Type IV hypersensitivity and mediated by T-cells, typically seen in tuberculosis.
Mononuclear phagocyte system

- Blood monocytes
- Tissue macrophages
  - macrophages in inflammation
  - kupffer cells
  - alveolar macrophages
  - sinus histiocytes
  - osteoclasts
  - microglial cells
  - langerhans’ cells
  - Hoffbauer cells
  - mesangial cells