# Pathology

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# Chronic Inflammation

## Seventh Lecture

### Granulomatous Inflammation ( Granulomas )

It is a distinctive ( specific ) form of chronic inflammation characterized by localized nodular collection of Epithelioid Cells ( Modified Macrophages ) and are surrounded by a cuff or a collar of lymphocytes, plasma cells and fibroblasts, may have multinucleated giant cells and central necrosis may be present as in tuberculosis, caseous necrosis ( whitish cheesy material ).

## Causes of Granulomas :

Granulomas can be divided into 3 groups according to the causes :

1. **Immune granulomas** : are formed by immune T cell-mediated response ( Type - IV Hypersensitivity ) to persistent non- degradable agents :

   - Infectious granulomas : are seen in certain diseases due to infections such as Tuberculosis ( common cause ) Leprosy, Syphilis, Fungal Infection, Parasitic Diseases, Cat - Scratch Disease, Toxoplasmosis, and others.
   - Non-Infectious granulomas : Sarcoidosis, Crohn disease, Hypersensitivity Pneumonitis ( Allergic Alveolitis ) and lymph node draining area of Malignancy ( Lymphomas ).

2. **Foreign-Body granulomas** : Foreign-material such as Suture Material, Urate Crystal in Gout and Talc.

3. **Toxic granuloma :** Silica → Silicosis and Berylliosis of the Lungs.

# Pathogenesis of Granuloma :

- Engulfment by macrophages: when the macrophages fail or unable to kill the MO like TB-bacilli ➔ Presenting it to the T- lymphocytes.
- T-Lymphocyte activation and releasing of Cytokines ( Interferon-ɣ, ILs, TNF ) and macrophage chemotactic factors.
- Macrophage accumulation and activation by interferon-ɣ ➔ undergo morphologic change to Epithelioid Cells and secrete Cytokines ( IL -1 and TNF ), lysosomal enzymes, reactive oxygen metabolites, NO ( Tissue damage ) and fibroblast proliferation factor ( Fibrosis ).

# Diagnosis of the cause of Granuloma :

- Histological appearance ( presence or absence of caseous necrosis ).
- Certain technique E.g. :
  - Special stain as AFB ( Acid Fast Bacilli ).
  - Serological tests as in Syphilis, Toxoplasmosis and others .
  - PCR : Polymerase Chain Reaction.

# Epithelioid cells :

- ✓ They are essential for histological diagnosis of granuloma ( Epithelial-like cells ).
- ✓ Epithelioid cell is a Large Modified Macrophage with abundant pinkish cytoplasm and vesicular nuclei.

# Giant cells :

- Large multinucleated cells result from fusion of many activated macrophages ( Epithelioid Cells ) to engulf difficult particles.

- **Langhans giant cells** : The nuclei arrange at the periphery of the cytoplasm in horse - shoe pattern ( Tuberculosis and Sarcoidosis ).
- **Foreign body giant cells** : The nuclei arrange irregularly in the center of the cells ( Suture Material and Urate Crystals ).

# Outcomes of Granuloma :

☒ Granulomas persist for long time, may slowly resolve and disappear without tissue destruction ( very rare ).

☒ Healing by fibrosis and scarring.

☒ Tissue destruction by formation of large cavities filled by caseous material as in pulmonary tuberculosis ( TB ) ( usually ).

# Systemic Effects of Inflammation

❖ Fever: due to pyrogens ➔➔ Exogenous ( bacteria products ) or Endogenous pyrogens such as ( TNF and IL-1 ).

❖ Systemic Acute- phase Proteins: C-Reactive Protein ( CRP ), Fibrinogen and serum Amyloid- A protein by liver ( IL-6 and TNF ).

❖ Leukocytosis: Increase WBC count above 12000/µL ( TNF and IL-1 ).

- Neutrophilia ( Bacterial Infection )
- Eosinophilia ( Allergy and Parasitic Infestations ).
- Lymphocytosis ( Viral Infection ).
- Leukopenia ( Typhoid Fever ).

❖ Increased Blood Pressure, Pulse Rate ( Tachycardia ), and Repiratory Rate ( Tachpnea ) and increased ESR.

❖ Chills, Rigors ( Shivering ), Weakness, Tiredness, Malaise, loss of Appetite, Drowsiness, Sleepiness, , Lipolysis and decreased Sweating, which are due to effects of Cytokines on the CNS

❖ Severe Bacterial Infection → Sepsis ( Septic Shock ), Hypotension and Disseminated Intravascular Coagulation (DIC) ( TNF and IL-1 ).

❖ Chronic Inflammation → Wasting Syndrome ( Cachexia ).

| Characters | Acute | Chronic |
|---|---|---|
| Duration | Short ( Days ) | Long ( Weeks to Months ) |
| Onset | Acute ( Fast ) | Insidious ( Slow ) |
| Specificity | Nonspecific | Specific ( where immune response is activated ) |
| Inflammatory Cells | Neutrophils | Lymphocytes, Macrophages, Plasma cells Eosinophils ,Mast cells, Fibroblasts |
| Vascular Changes | Active Vasodilation, Increased Permeability | New Vessel Formation ( Angiogenesis ) |
| Fluid Exudation and Edema | + | – |
| Cardinal Clinical Signs ( Redness, Heat, Swelling, Pain & Loss of Function ) | + | – |
| Tissue Necrosis | – ( Usually )<br>+ ( Suppurative and Necrotizing Inflammation ) | + ( Ongoing ) |
| Fibrosis ( Collagen Deposition ) | – | + |
| Operative Host Responses | Plasma Factors : Complement, Immunoglobulins, etc; Neutrophils, Phagocytosis | Immune Response, Phagocytosis, Repair |
| Systemic Manifestations | Fever, often High | Low-grade Fever, Weight Loss, Anemia |
| Changes in Peripheral Blood | Neutrophil Leukocytosis; Lymphocytosis ( in Viral Infections ) | Frequently none; variable Leukocyte changes, Increased Plasma Immunoglobulins |