بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

GOOD MORNING

CHRONIC INFLAMMATION

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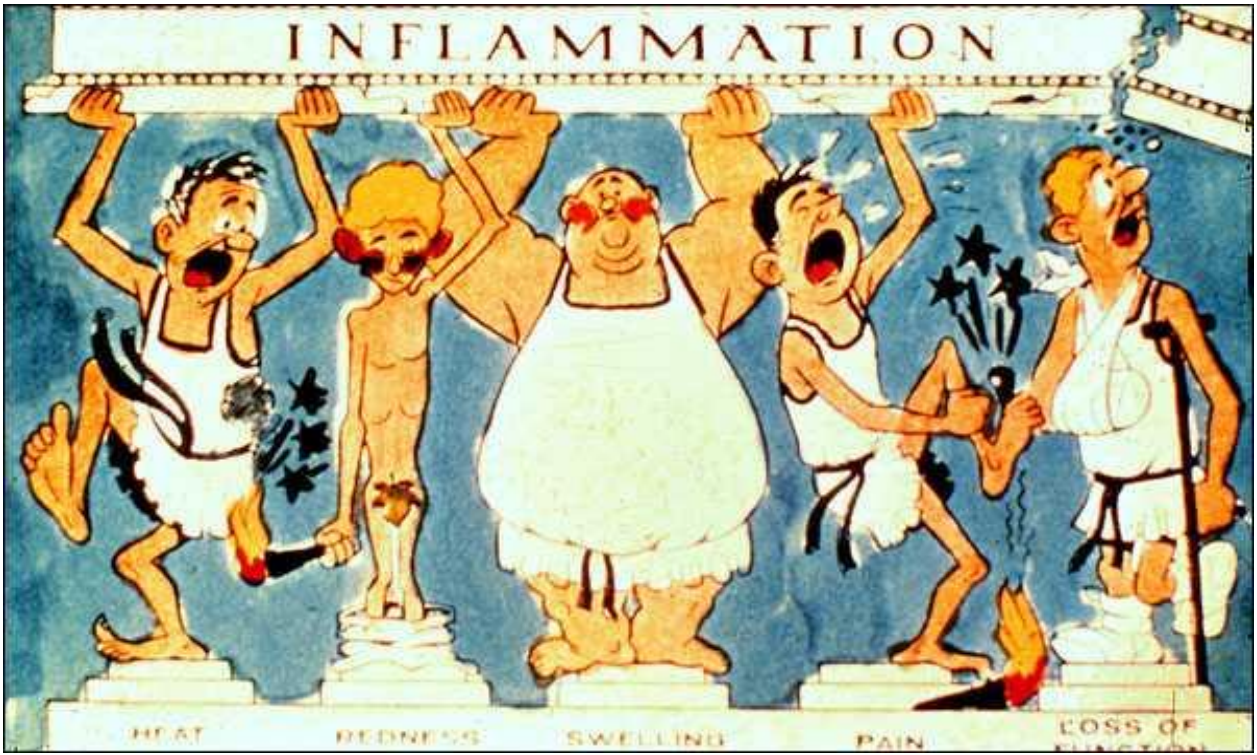
Lecture learning outcomes

By the end of this lecture, students should be able to:

1. Define **chronic inflammation** and list various **causes of chronic inflammation.**
2. Define chronic **granulomatous inflammation and its causes.**
3. Explain the **mechanism involved granulomatous inflammation**.


Discussion
Questions

CARDINAL SIGNS OF ACUTE INFLAMMATION



Heat **Redness** **Swelling** **Pain** **Loss of function**

Celsus (30 BC) Virchow (1902)

TYPES OF INFLAMMATION

ACUTE INFLAMMATION

- **Rapid in onset** (minutes – hours)
- Of **short duration** (hours to weeks)
- Characterized by fluid and plasma protein exudation
- Predominantly **neutrophilic** leukocyte accumulation.

CHRONIC INFLAMMATION

- **More insidious onset**
- Of **longer duration**
- Characterized by influx of **lymphocytes and macrophages** with associated vascular and connective tissue proliferation(fibrosis).

CHRONIC INFLAMMATION

Chronic inflammation **is an inflammatory response of prolonged duration (weeks to months to years)**

Provoked by the persistence of causative stimuli

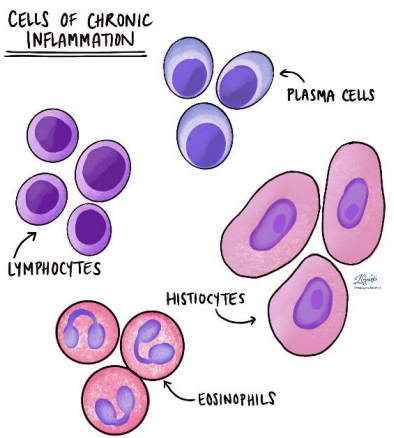
in which *active inflammation, tissue injury, and healing proceeds simultaneously*

Causes of chronic inflammation

1. **Persistent infection by microbes** that are difficult to eradicate(TB, VIRAL)
2. Recurrent attacks or prolong persistence of acute inflammation.
3. **Immune mediated inflammation**

Cells of chronic inflammation

- **MONONUCLEAR CELL INFILTERATION:**
- **Lymphocytes and**
- **Monocytes (macrophages)**
- **Plasma cells**
- **Eosinophils**



MONONUCLEAR CELL INFILTERATION:

Dominant cellular player in chronic inflammation is the **tissue macrophage**

Blood Monocyte

migrate into tissue within 48 hours after injury

and differentiate

Tissue macrophage

names of in different organs:

- Kupffer cell (liver)
- Microglia (CNS)
- Histiocytes (spleen)
- Alveolar (lung)

Characteristics of chronic inflammation:

- ✓ **MONONUCLEAR CELL INFILTERATION: lymphocytes and monocytes (macrophages), sometimes plasma cells.**
- ✓ **TISSUE DESTRUCTION OR NECROSIS:** This is brought about by product of inflammatory cells.
- ✓ **PROLIFERATIVE CHANGES:** Proliferation of small blood vessels (ANGIOGENESIS) and fibroblasts is stimulated resulting in **fibrosis.**

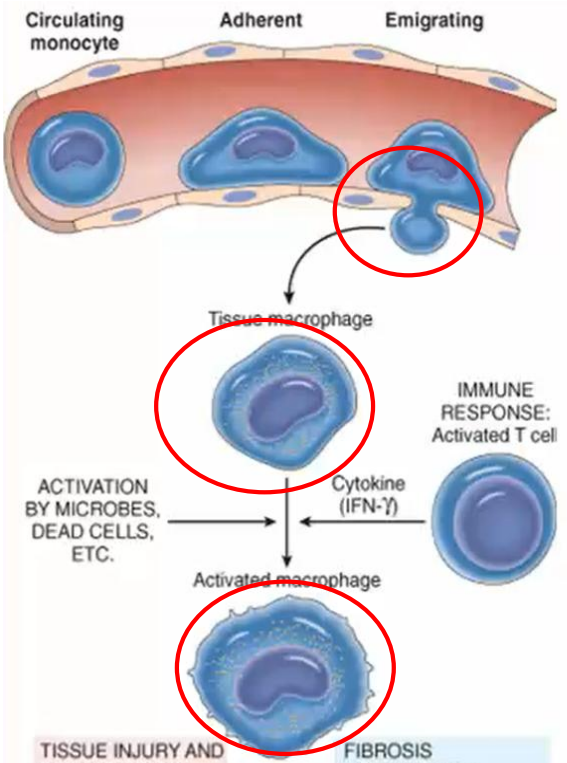
Types of Chronic Inflammation

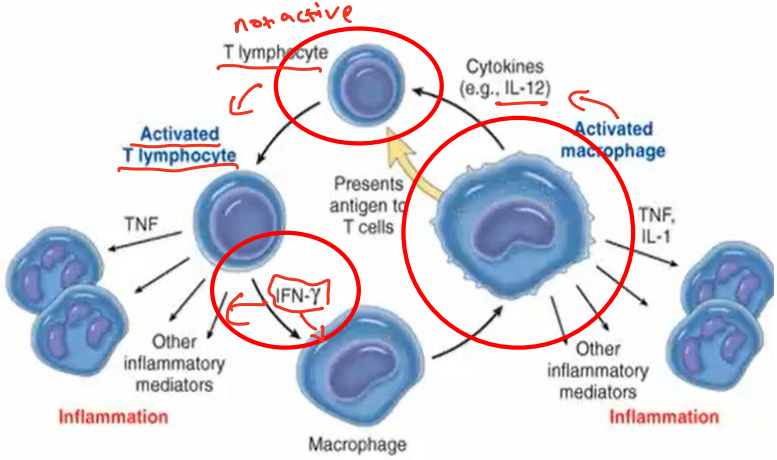
- **Based on etiology –**
- Non Specific – the irritant **(causative) agent is non specific** and results in formation of granulation tissue and fibrosis. Eg: osteomyelitis, chronic ulcer dont know composition

- Specific - the irritant agent causes a **specific histologic response** eg: tuberculosis

- **Based on histologic features**
- Chronic non-specific inflammation
- Chronic granulomatous inflammation specific

Mechanisms in chronic inflammation





Cells Involved in chronic inflammation

Lymphocytes & Macrophages

Mediators involved in chronic inflammation

Interferon – Gamma & IL - 12

Mechanism of chronic inflammation

bacteria

Activated macrophages release IL-12 it will activate T-cell, T-cell (activate) by IFN-γ will do 2 function: 1- Kill Previose bacteria

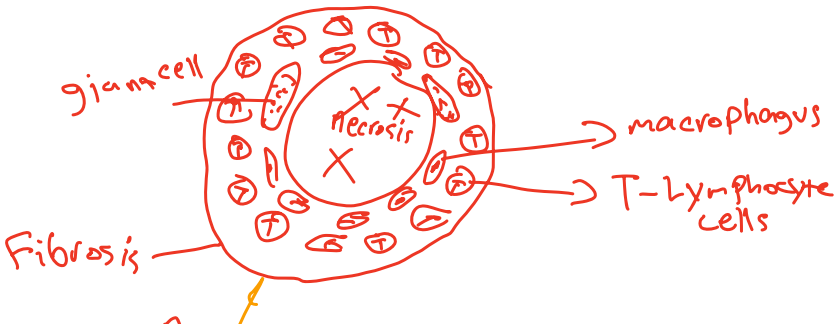
2- will release more monocyte, in the tissue (macrophages) from blood

Granulomatous Inflammation

- Granulomatous Inflammation is a **distinctive pattern of chronic inflammation** characterized by **collection of activated macrophages(also known as epitheloid cells).**
- The formation of granuloma is a **protective defense reaction** by the host but eventually causes tissue destruction because of persistence of the poorly digestible antigen.
- **Tuberculosis is granulomatous diseases** caused by **Mycobacterium tuberculosis** .

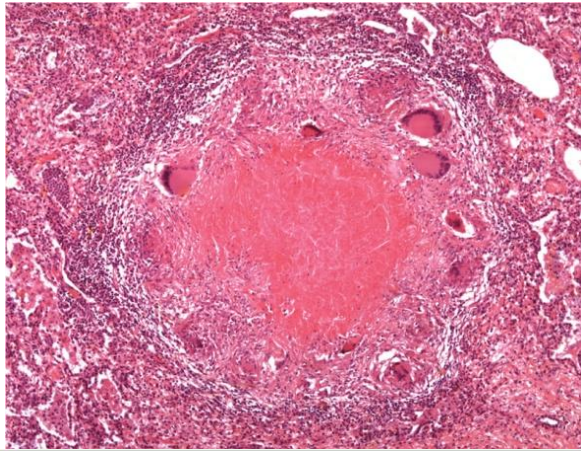
DISEASES WITH GRANULOMATOUS INFLAMMATION

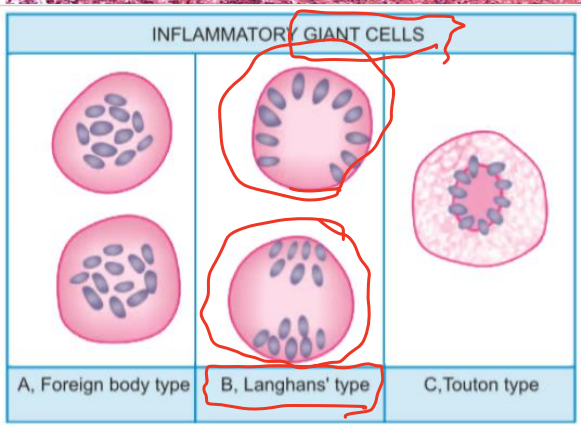
Disease	Cause	effects
Tuberculosis	Mycobacterium tuberculosis	Caseating granuloma
Laprosy	Mycobacterium laprae	Non caseating granuloma



End result is

GRANULOMA:

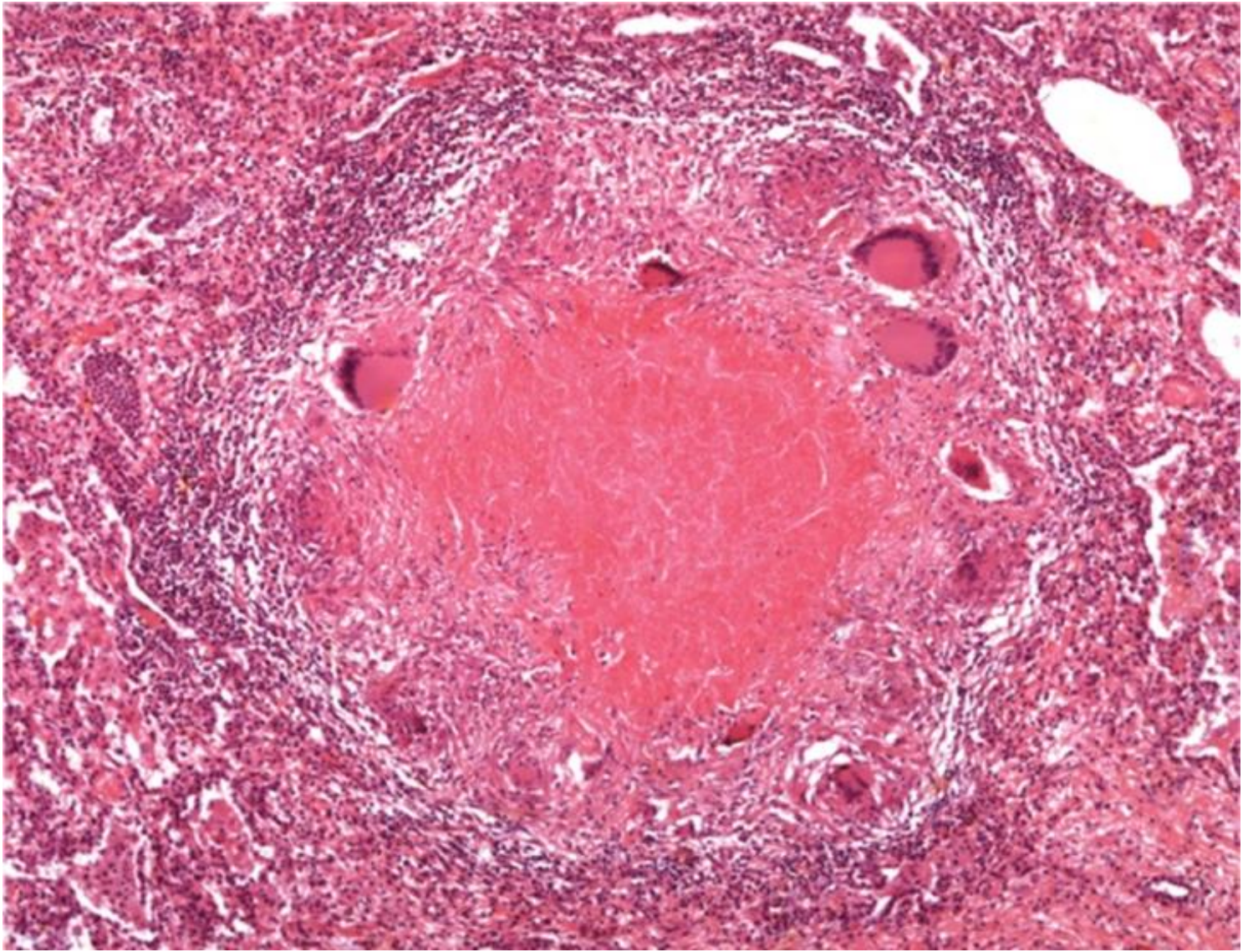




- Granuloma is a circumscribed, tiny lesion, composed predominantly of collection of modified macrophages called epitheloid cells, and rimmed at the periphery by lymphoid cells.

- Besides the presence of epitheloid cells, granulomas have presence of fibrosis, necrosis and giant cells.

Formed by fusion of epitheliod cells.
May have 20 or more nuclei.
Types: foreing body; langhans; toutons.



- Certain factors favor the formation of a granuloma:

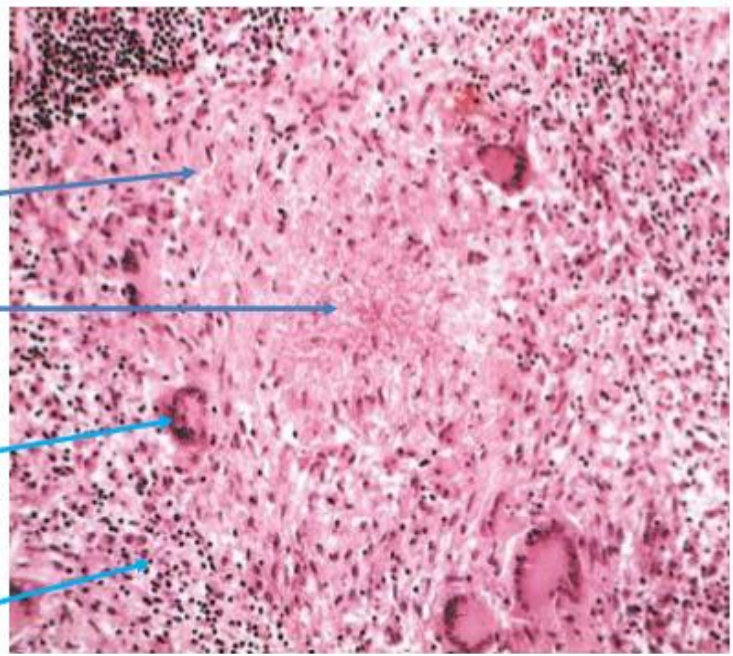
i. Presence of poorly digestible irritant

ii. Presence of cell mediated immunity to the irritant.

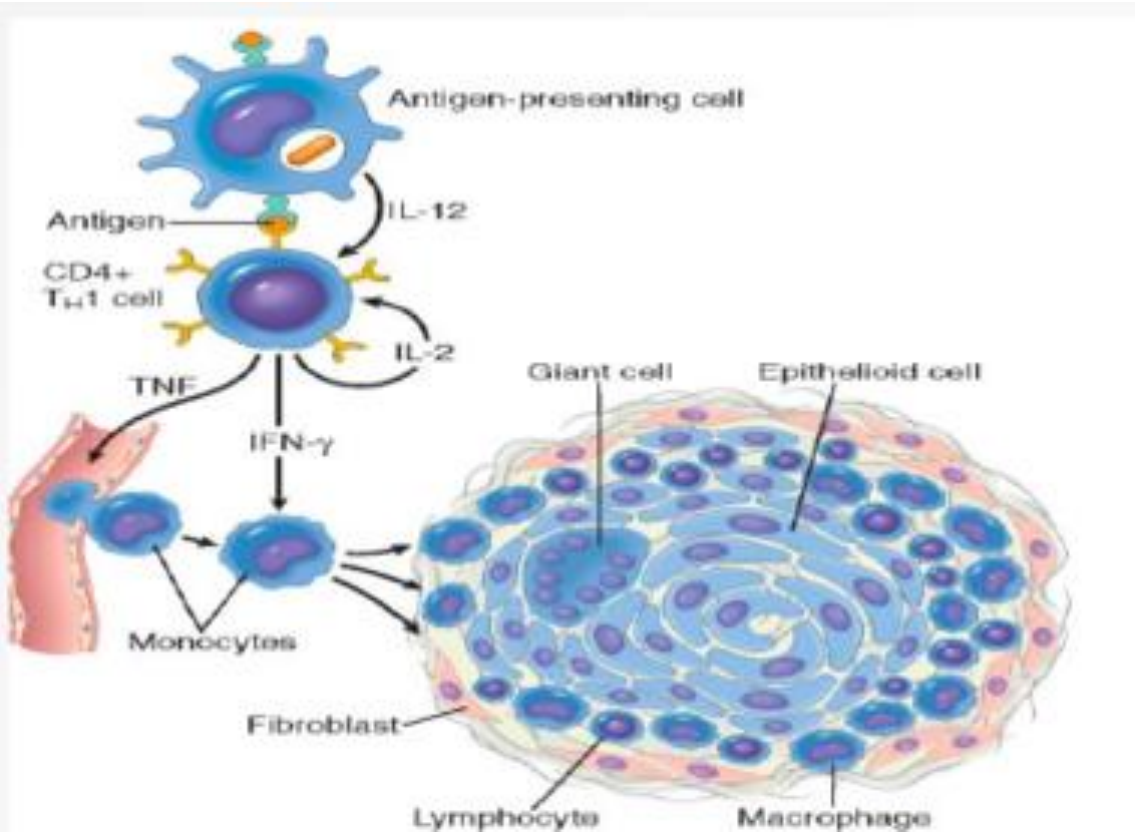
COMPOSITION OF A GRANULOMA

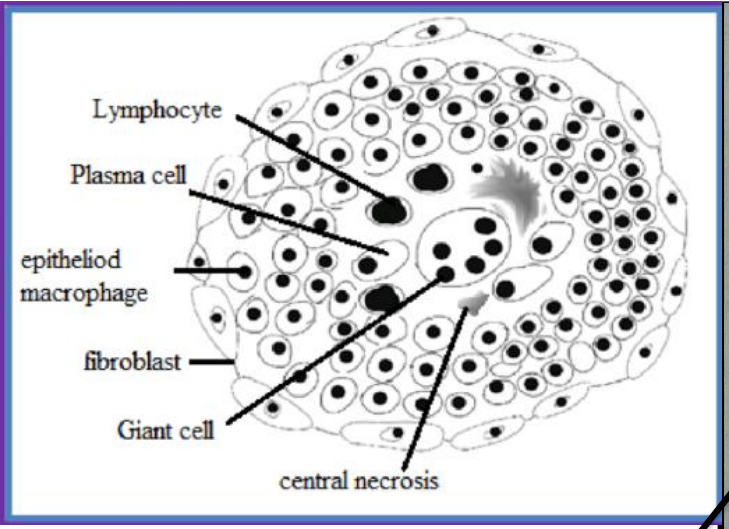
Thus, a granuloma so formed have

1. Activated macrophages, which develop **abundant pink granular cytoplasm** with **indistinct cell boundaries** and become **epithelioid cells** (like epithelial cells)
2. Sometimes associated with **central necrosis** (caseating), as in tuberculosis
3. Some activated macrophages fuse to form **multinucleated giant cells (Langhans** type in TB) – It contains a large cytoplasm with many nuclei
4. Surrounded peripherally by T cells
5. Depending upon the age of granuloma, it may have a rim of **fibroblasts** and collagen



PATHOGENESIS OF GRANULOMA FORMATION



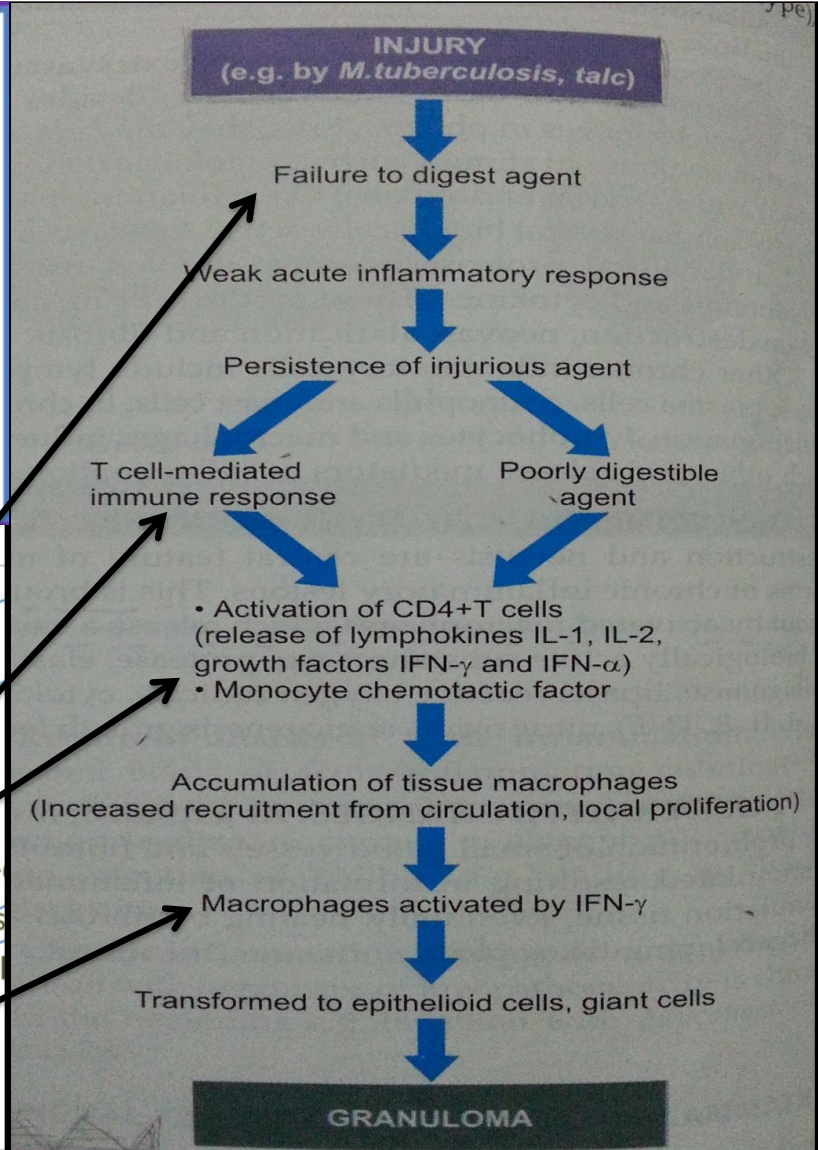


Pathogenesis - Steps

- Macrophages engulf the antigen and try to destroy it. But, they fail to degrade the antigen.
- Macrophages, being antigen-presenting cells (APC), having failed to degrade the antigen, present it to TH cells (CD4+) T cells.
- TH cells gets activated & secrete IL-1, IL-2, IFN-γ, TNF-

Various cytokines formed by activated TH & macrophages

- **IL-1 & IL-2** (auto) stimulate proliferation of more **T cell**
- **IFN-γ** activates **macrophages**
- Macrophages produce **TGF-β, PDGF** (growth factors, which stimulate **fibroblast growth** >> collagen laying



Systemic effects of inflammation:

- **FEVER** – mediated by release of prostaglandins. IL-1; 6 and TNF
  - Bacterial pyrogens (products that induce fever) stimulate leukocytes to release **IL-1, TNF** which ↑ **cyclooxygenases** (convert AA to prostaglandins)
  - Prostaglandins (especially **PGE2**) produced by the **hypothalamus** stimulate the **production of neurotransmitters** which reset the temperature set point to a higher level
  - Note: NSAIDs, aspirin, inhibit prostaglandin synthesis

- **LEUCOCYTOSIS** – neutrophilia, lymphocytosis, eosinophilia

- **INCRESED ESR AND C-REACTIVE PROTEIN**

Inflammation **is the protective response of the body.**

Without inflammation, infections would go uncheck and wound would never heal and progressive destruction of the tissue would compromise the survival of the organism.

Essential reading:

- Harsh Mohan: Essential Pathology for Dental Students (with Practical Pathology). 5th ed; 2017; Jaypee Brothers Medical Publishers
- Harsh Mohan: Textbook of Pathology. 7th ed; 2014; Jaypee Brothers Medical Publishers
- Kumar: Robbins Basic Pathology. 10th ed; 2017; Elsevier
- Shafer's oral pathology – 2015 Elsevier (6^{th} edition)


THANK
YOU!