

Foundation block: pathology

# INFLAMMATION AND REPAIR

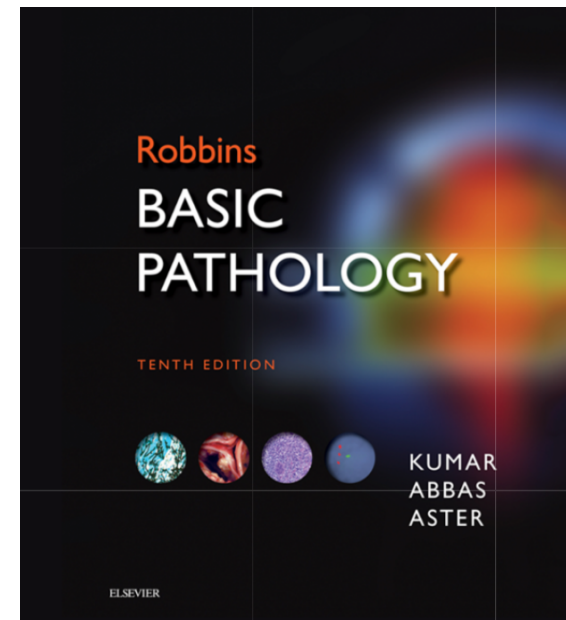
## Lecture 3

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1. Outcomes of acute inflammation
2. Different patterns of inflammation
3. Chronic inflammation

Robbins Basic Pathology 10<sup>th</sup> edition  
Page: 78 to 86

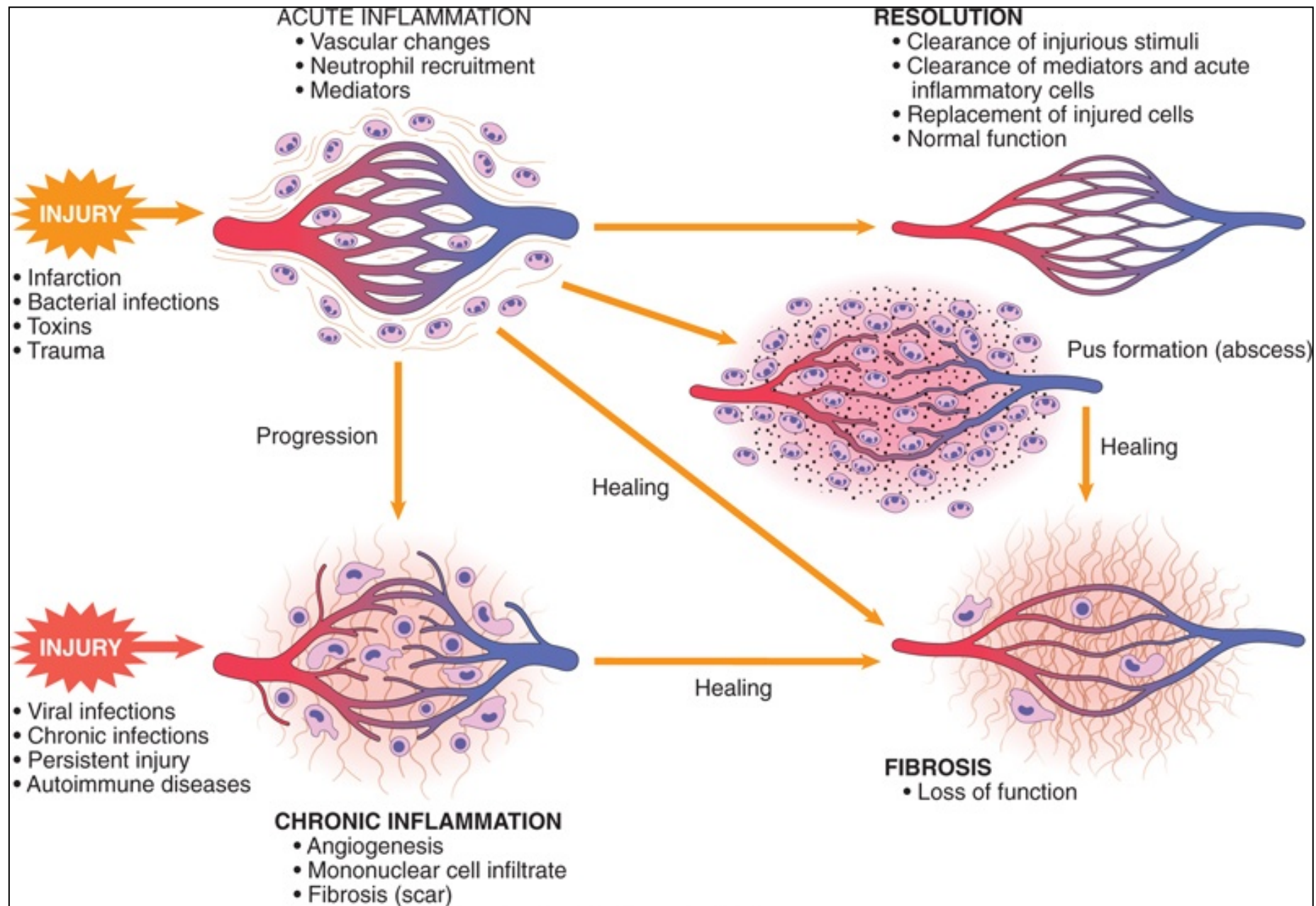




## Objectives

- 1. List and describe the outcome of acute inflammation.**
- 2. Recognize the different patterns of inflammation.**
- 3. Define chronic inflammation with emphasis on causes, nature of the inflammatory response, and tissue changes.**
- 4. Compare and contrast the clinical settings in which different types of inflammatory cells (eosinophils, macrophages, and lymphocytes) accumulate in tissues.**

# 1. List and describe the outcome of acute inflammation.



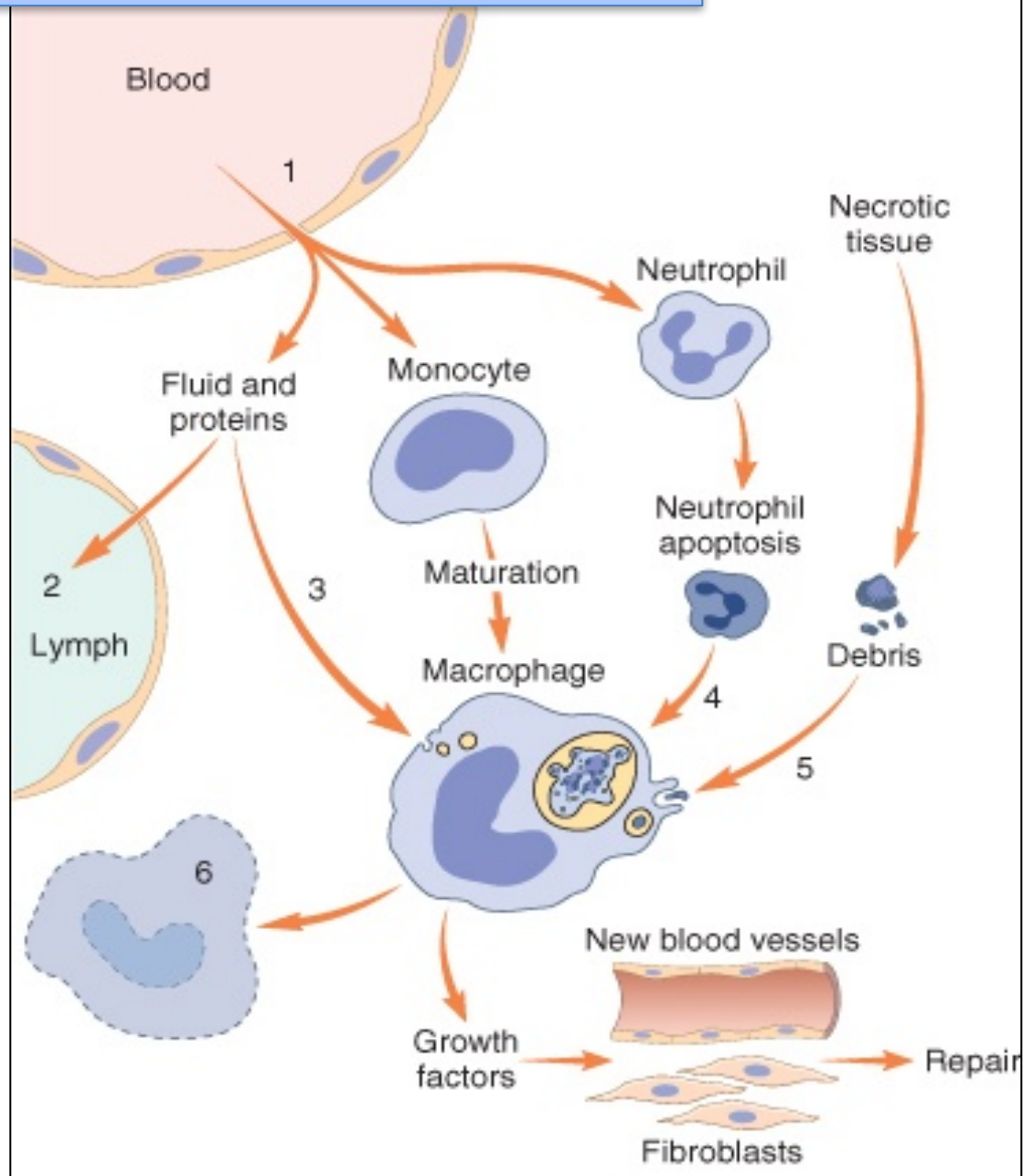
# Outcomes of Acute Inflammation

- Acute inflammation may have one of the four outcomes:
  - *Complete resolution*
  - *Healing by connective tissue replacement (fibrosis)*
  - *Progression of the tissue response to chronic inflammation*
  - *Abscess formation*

# 1. List and describe the outcome of acute inflammation.

Events in **the resolution** of inflammation

- This involves neutralization, decay, or enzymatic degradation of the various chemical mediators; normalization of vascular permeability; and cessation of leukocyte emigration and apoptosis
- The necrotic debris, edema fluid, and inflammatory cells are cleared by phagocytes and lymphatic drainage
- Lymph node become enlarged and inflamed





## Objectives

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## Morphologic Patterns of Acute Inflammation

- Several types of inflammation vary in their morphology and clinical correlates. Why?
  - The severity of the reaction
  - specific cause
  - the particular tissue
  - site involved



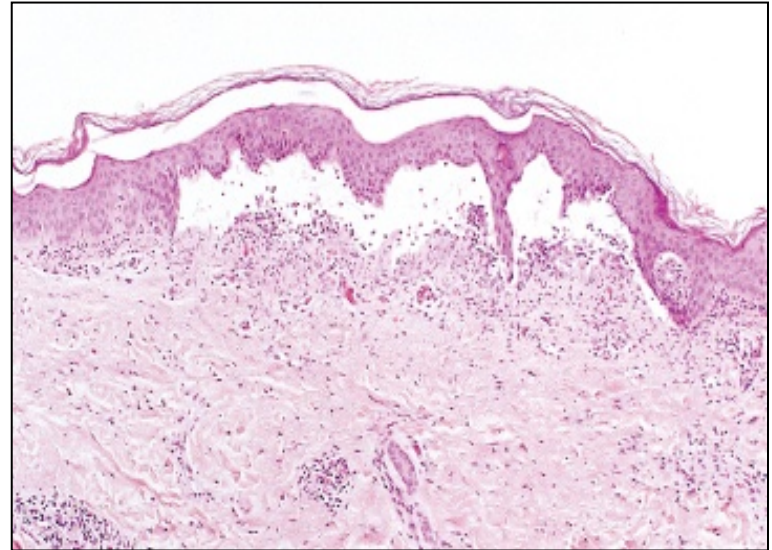
## Morphologic Patterns of Acute Inflammation

- **SEROUS INFLAMMATION**
- **FIBRINOUS INFLAMMATION**
- **SUPPURATIVE OR PURULENT INFLAMMATION**
- **ULCERS**

## 2. Recognize the different patterns of inflammation.

# SEROUS INFLAMMATION:

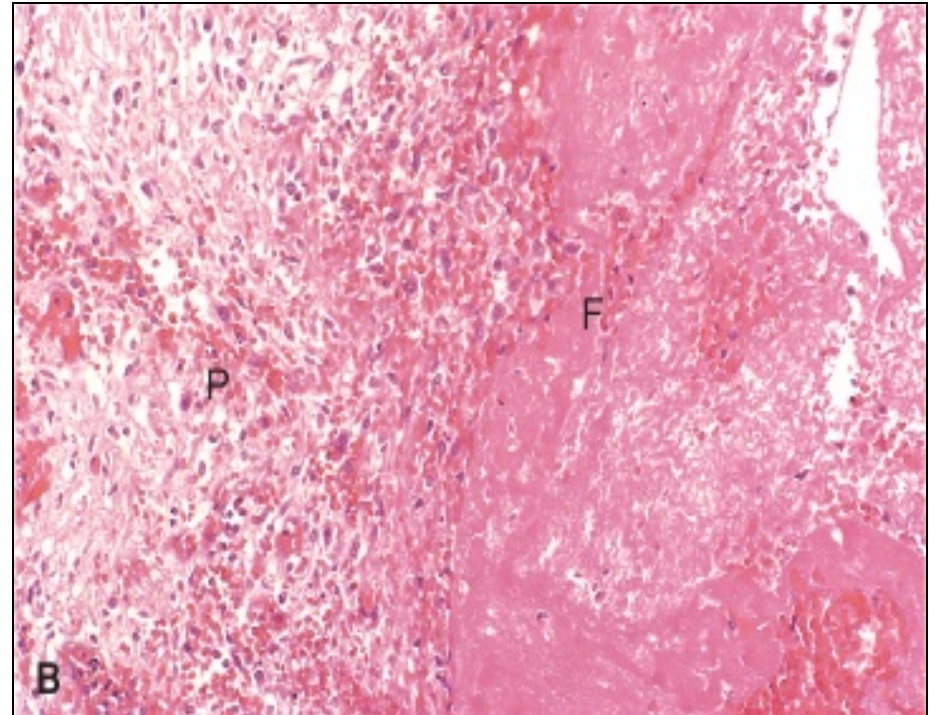
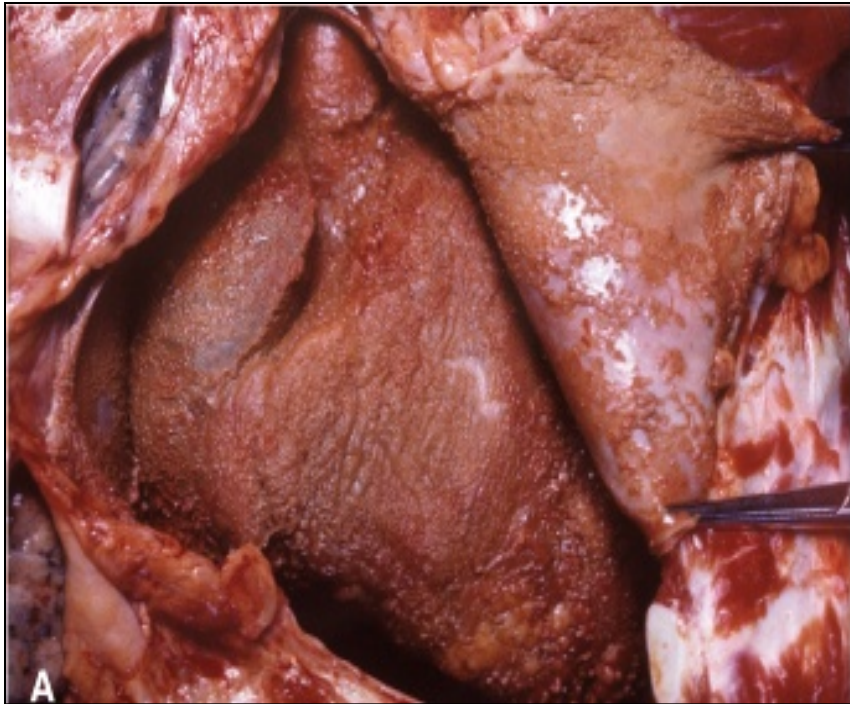
marked by the outpouring of a thin fluid



## 2. Recognize the different patterns of inflammation.

# FIBRINOUS INFLAMMATION

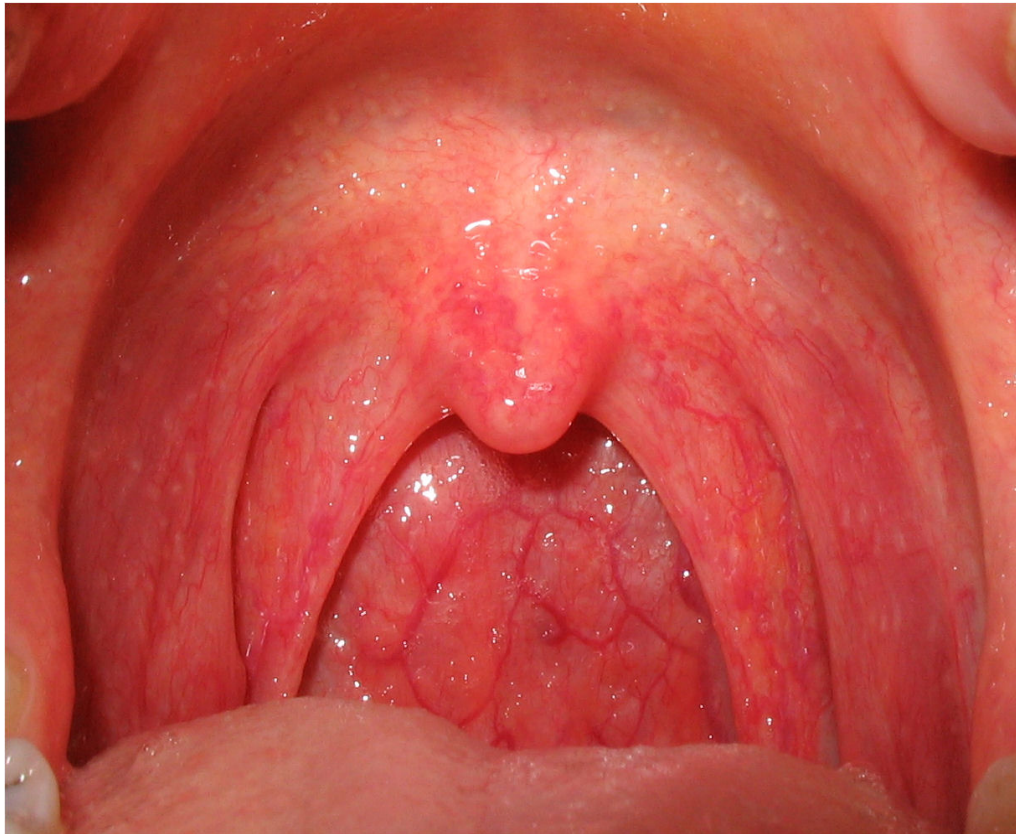
- A fibrinous exudate is characteristic of inflammation in the lining of body cavities, such as the meninges, pericardium and pleura (larger molecules such as fibrinogen pass the vascular barrier)
- Fibrinous exudates may be removed by fibrinolysis,
- **if not:** it may stimulate the ingrowth of granulation tissue (*organization*)



2. Recognize the different patterns of inflammation.

## Catarrhal inflammation

- Inflammation affects mucosa-lined surfaces with the outpouring of **watery mucus**



## SUPPURATIVE OR PURULENT INFLAMMATION

**characterized by the production of large amounts of pus or purulent exudate consisting of neutrophils, necrotic cells, and edema fluid caused by pyogenic (pus-producing) bacteria**

## 2. Recognize the different patterns of inflammation.

# Suppurative abscess

- An abscess is a cavity lined by granulation tissue and containing neutrophils, necrotic cells, bacteria and fibrinous material

An enclosed collection of pus consists of a mixture of neutrophils and necrotic debris

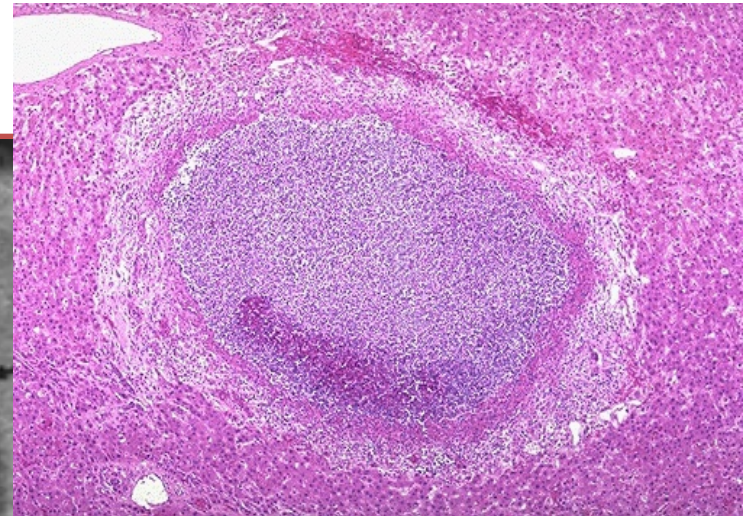
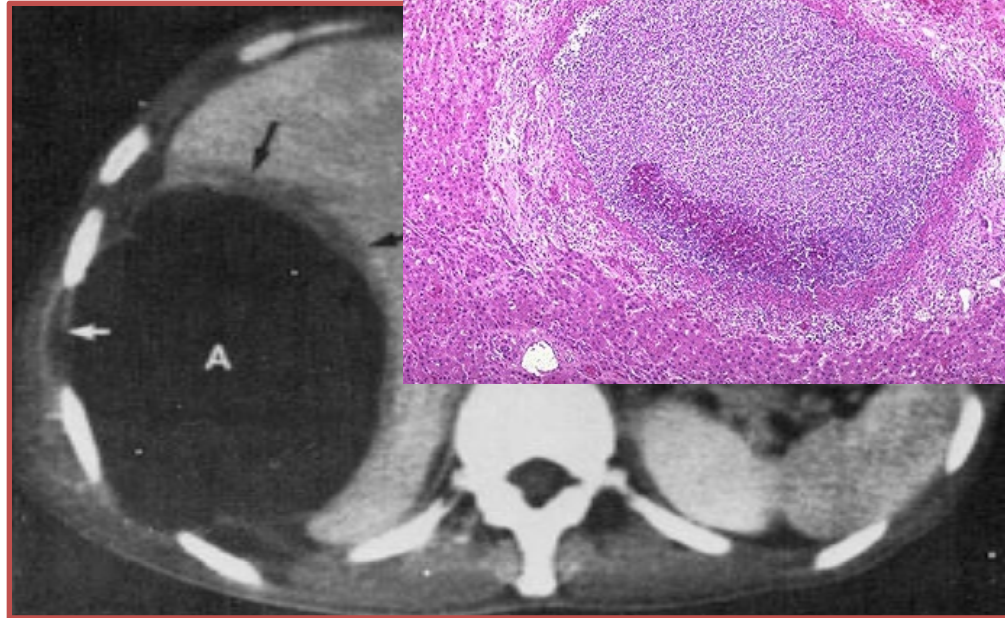


## 2. Recognize the different patterns of inflammation.

# Morphologic Patterns of Acute Inflammation

## SUPPURATIVE OR PURULENT INFLAMMATION

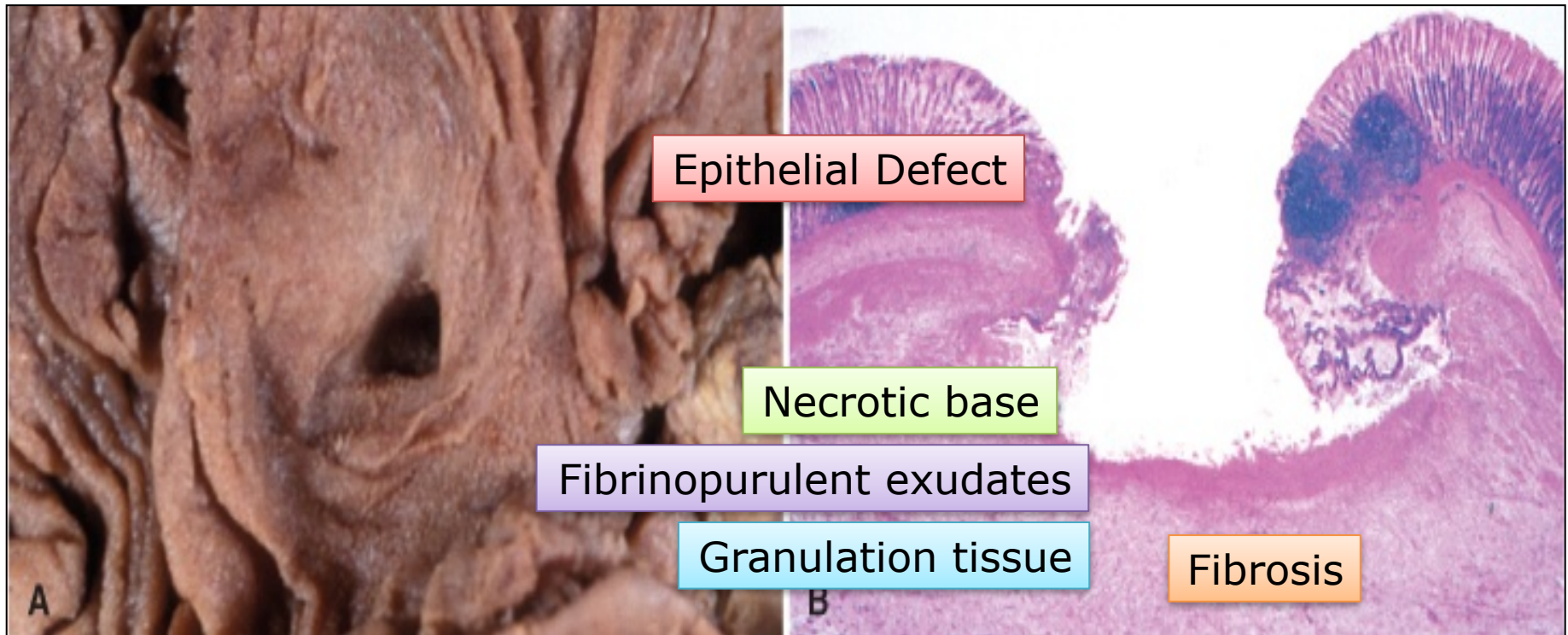
- **Abscesses : A localized collections of purulent inflammatory tissue caused by suppuration buried in a tissue, an organ, or a confined space**



## 2. Recognize the different patterns of inflammation.

### ULCERS

An ulcer is a local defect of the surface of an organ or tissue that is produced by the sloughing (shedding) of inflammatory necrotic tissue





2. Recognize the different patterns of inflammation.

## Sinus

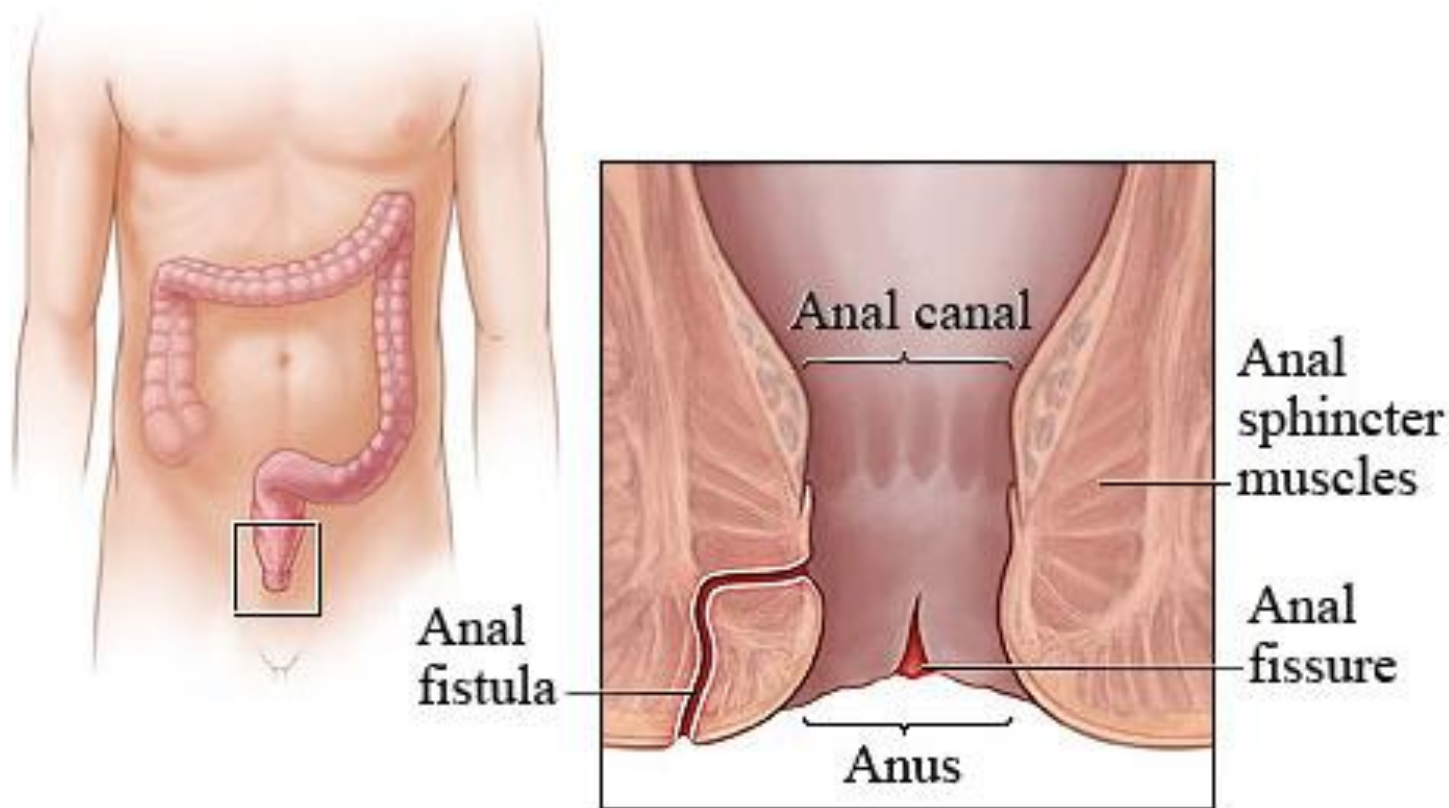
- A tract between the abscess and a surface.



## 2. Recognize the different patterns of inflammation.

# Fistula

- A tract between two surfaces.



## 2. Recognize the different patterns of inflammation.

# Cellulitis

- denotes a spreading of acute inflammation through interstitial tissues.





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## CHRONIC INFLAMMATION

- **It is slow evolving (weeks to months) resulting into fibrosis**
- The essential changes are:
  1. Absence of polymorphs (natural life span of 1–3 days); replaced by macrophages, lymphocytes and often plasma cells
  2. Continuous tissue injury and necrosis
  3. Proliferation of vascular endothelium by ‘budding’ – formation of new capillaries (angiogenesis)
  4. Proliferation of fibroblasts with collagen production leading to Fibrosis.

Chronic inflammation may arise in the following settings:

1. *Persistent infections* by microbes that are difficult to eradicate.

e.g.

- *Mycobacterium tuberculosis*
  - *Treponema pallidum* (the causative organism of syphilis)
  - certain viruses and fungi
- Persistent infections elicit a T lymphocyte-mediated immune response called *delayed-type hypersensitivity*.

2. *Immune-mediated inflammatory diseases*  
(*hypersensitivity diseases- Autoimmune diseases*)

e.g.

- Rheumatoid arthritis
- Inflammatory bowel disease
- Psoriasis

or

- Immune responses against common environmental substances that cause *allergic diseases*, such as bronchial asthma.

### 3. Define chronic inflammation, its causes, effects and patterns

#### *3. Prolonged exposure to potentially toxic agents.*

- Examples are nondegradable exogenous materials such as inhaled particulate silica, which can induce a chronic inflammatory response in the lungs (silicosis)
- Endogenous agents such as cholesterol crystals, which may contribute to atherosclerosis
- Other examples:
  - neurodegenerative disorders such as Alzheimer disease
  - metabolic syndrome and the associated type 2 diabetes,
  - some forms of cancer in which inflammatory reactions promote tumor development

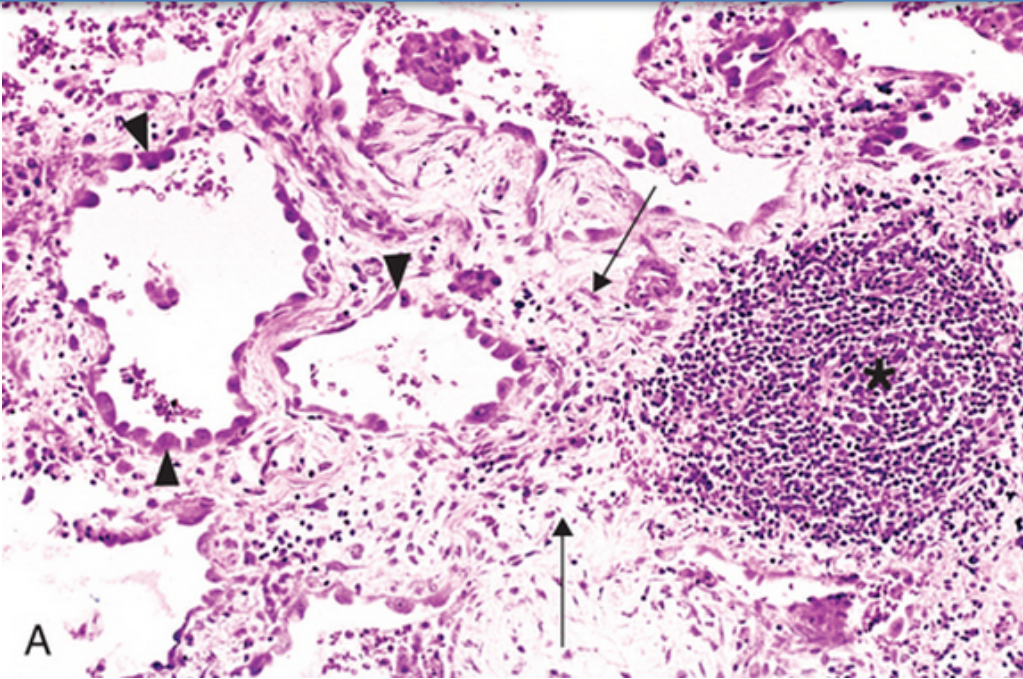


### 3. Define chronic inflammation, its causes, effects and patterns

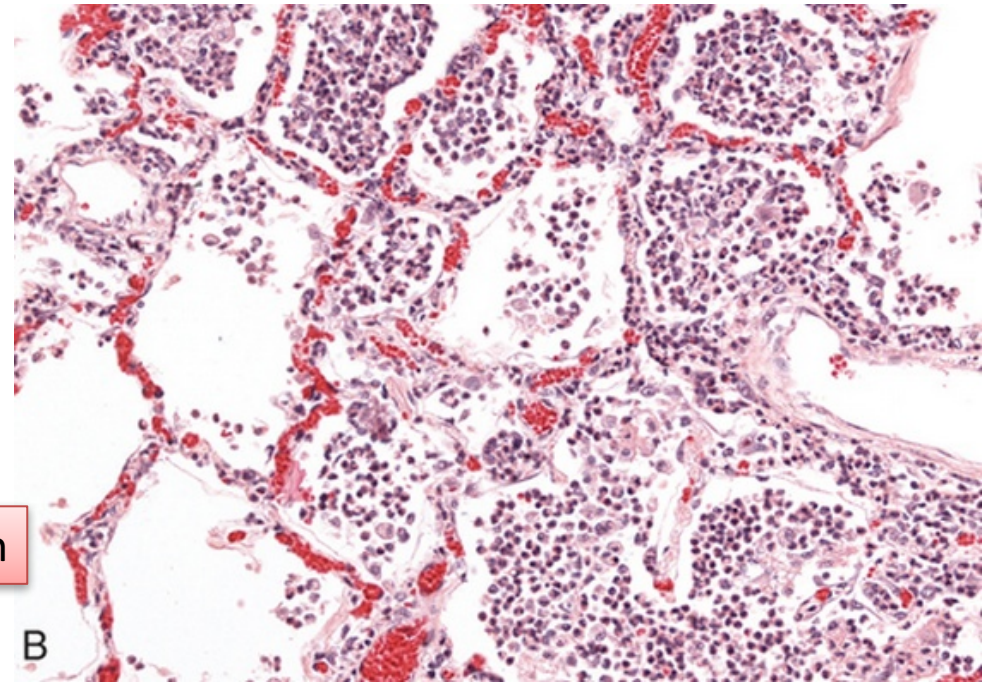
- Chronic inflammation is characterized by a 3 different set of reactions:
  1. *Infiltration with mononuclear cells*, including:
    - i. Macrophages
    - ii. Lymphocytes
    - iii. Plasma cells
  2. *Tissue destruction*, largely induced by the products of the inflammatory cells
  3. *Repair*, involving new vessel proliferation (angiogenesis) and fibrosis

Acute inflammation is distinguished by vascular changes, edema, and a predominantly neutrophilic infiltrate

### 3. Define chronic inflammation, its causes, effects and patterns



Lung chronic inflammation

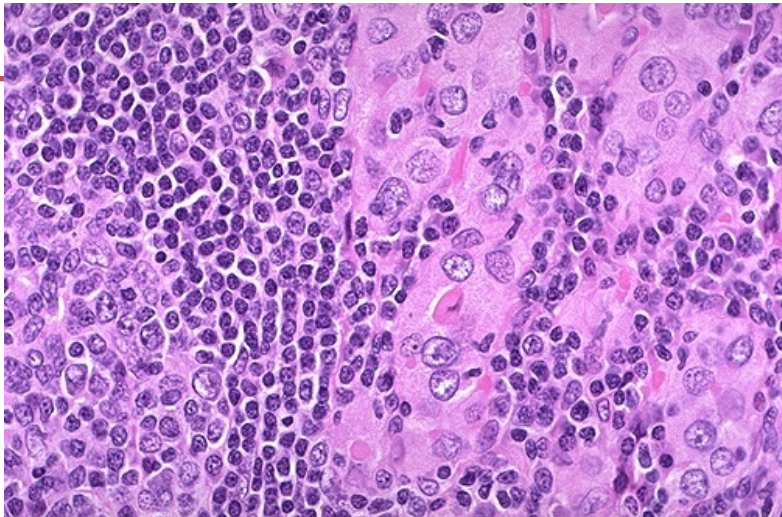


Lung acute inflammation

# Chronic inflammation patterns

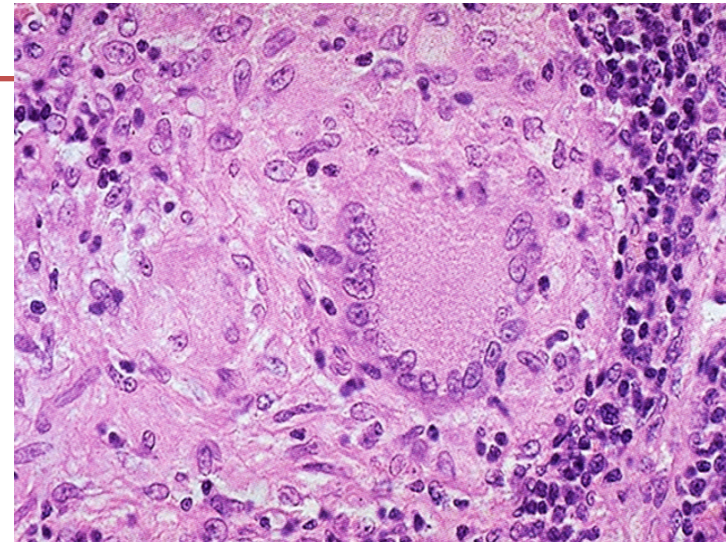
## Chronic non specific inflammation

- Features of chronic inflammation e.g.:
  - Foreign material, e.g. silicates, including asbestos.
  - Auto-immune diseases, e.g. auto-immune thyroiditis



## Chronic granulomatous inflammation

- Chronic inflammation in which modified macrophages (epithelioid cells) accumulate in small clusters surrounded by lymphocytes. The small clusters are called: **(GRANULOMAS)**
- Example: TUBERCULOSIS





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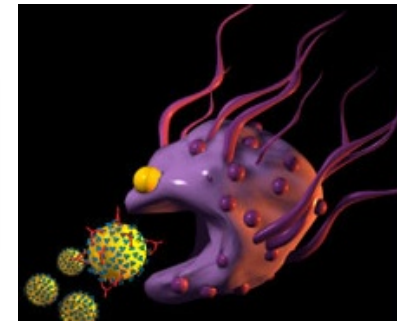
## Cells in Chronic inflammation

- Complex interactions between several cell populations and their secreted mediators.
- Mediated by the interaction of monocyte/macrophages with T and B lymphocyte, plasma cells and others

## Macrophages

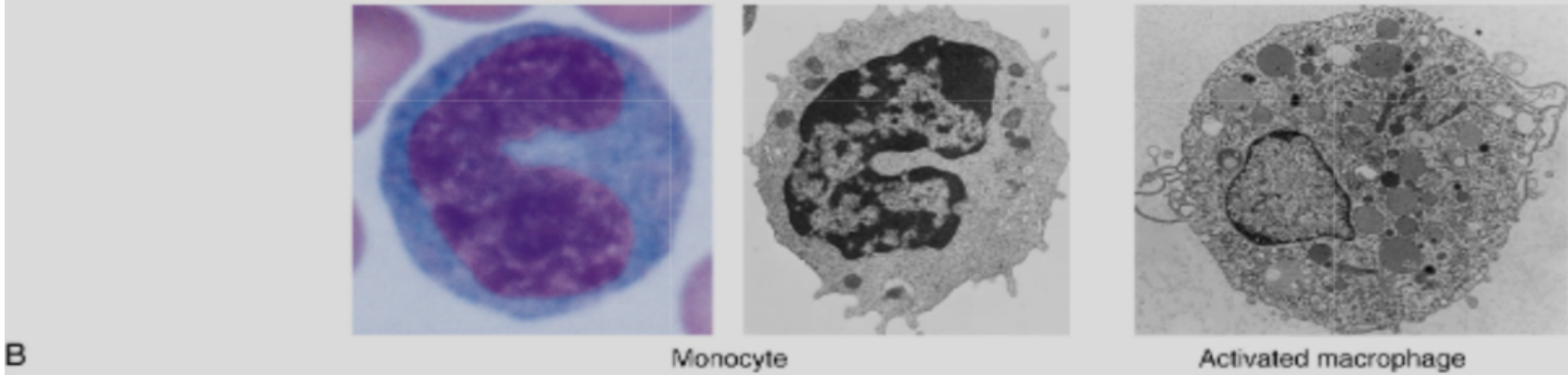
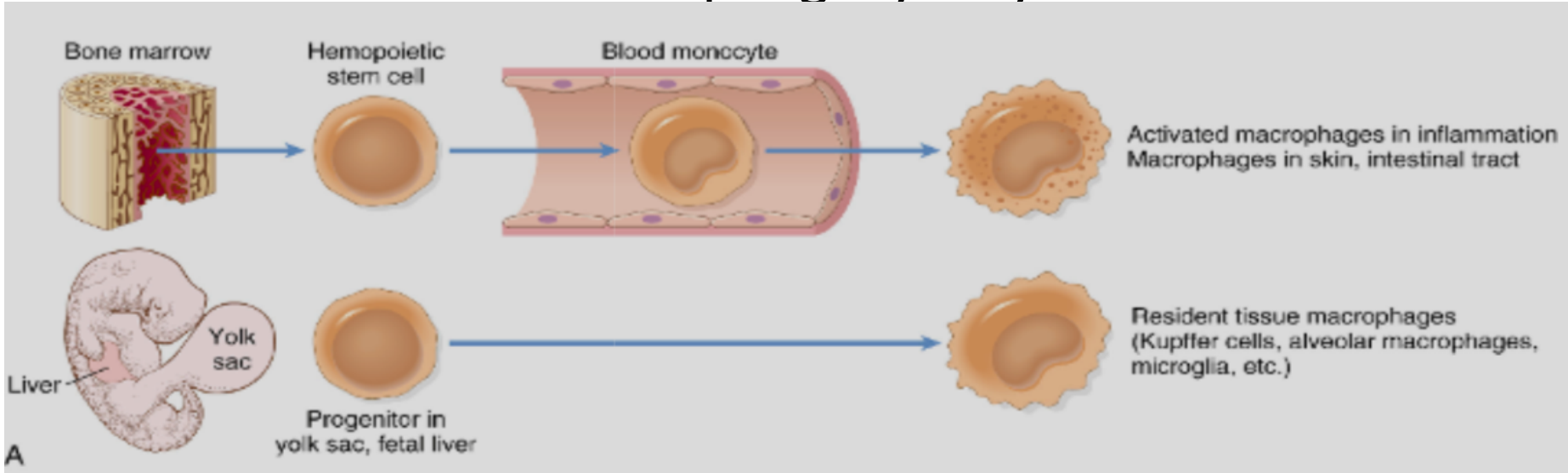
- In tissue:
  - the liver (Kupffer cells)
  - spleen and lymph nodes (sinus histiocytes)
  - central nervous system (microglial cells)
  - and lungs (alveolar macrophages)
- In blood: monocytes
  - Under the influence of adhesion molecules and chemokines, they migrate to a site of injury within 24 to 48 hours after the onset of acute inflammation (macrophages)

*Monocytes are likely to be seen in an inflammatory response to salmonella typhi infection*

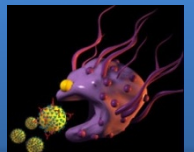


# 4. Different types of inflammatory cells accumulate in tissues

## mononuclear phagocyte system



monocytes begin to emigrate into extravascular tissues quite – early in acute inflammation and within 48 hours they may constitute the predominant cell type

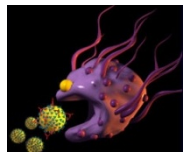
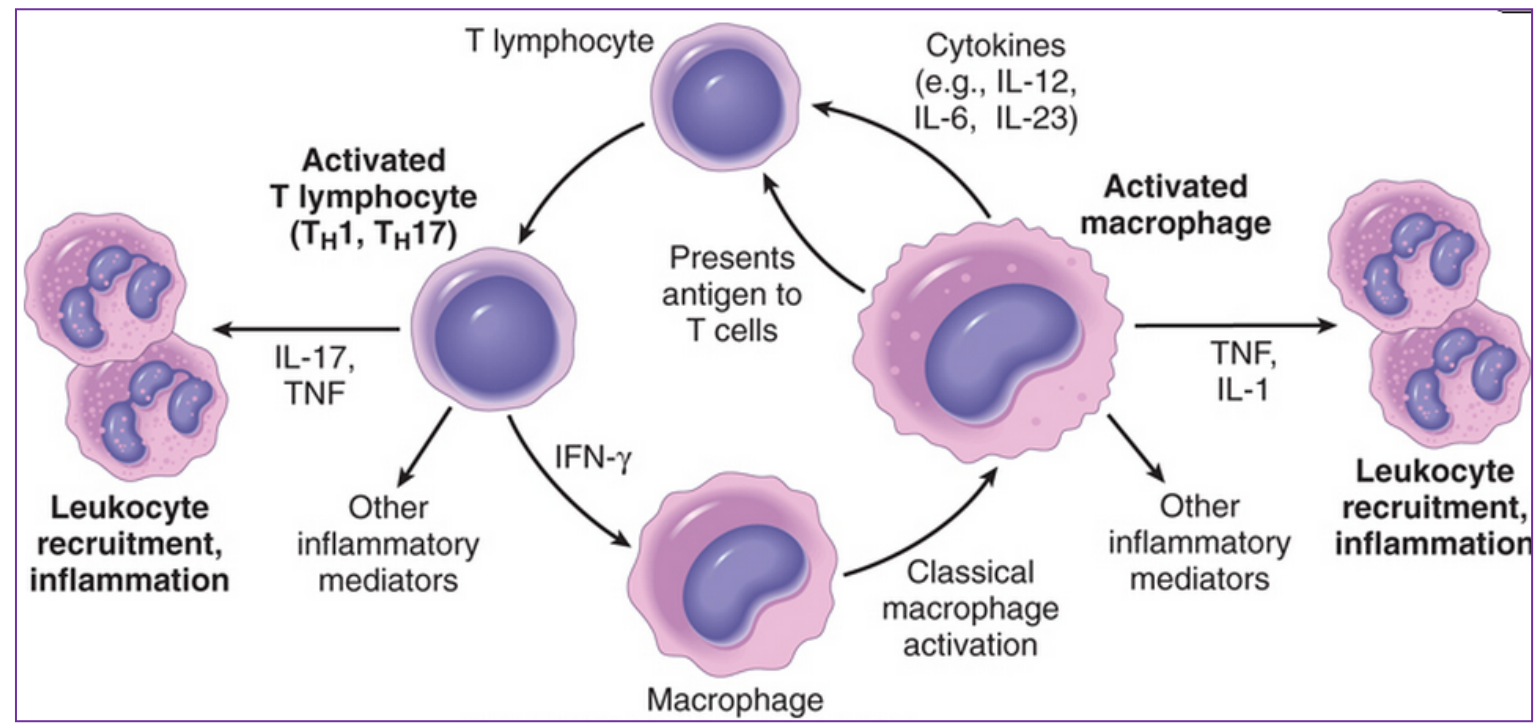


# 4. Different types of inflammatory cells accumulate in tissues

## MONONUCLEAR CELL INFILTRATION

### Macrophages

- Macrophages may be *activated* by a variety of stimuli, including:
  - cytokines (e.g., IFN- $\gamma$ ) secreted by sensitized T lymphocytes and by NK cells
  - bacterial endotoxins

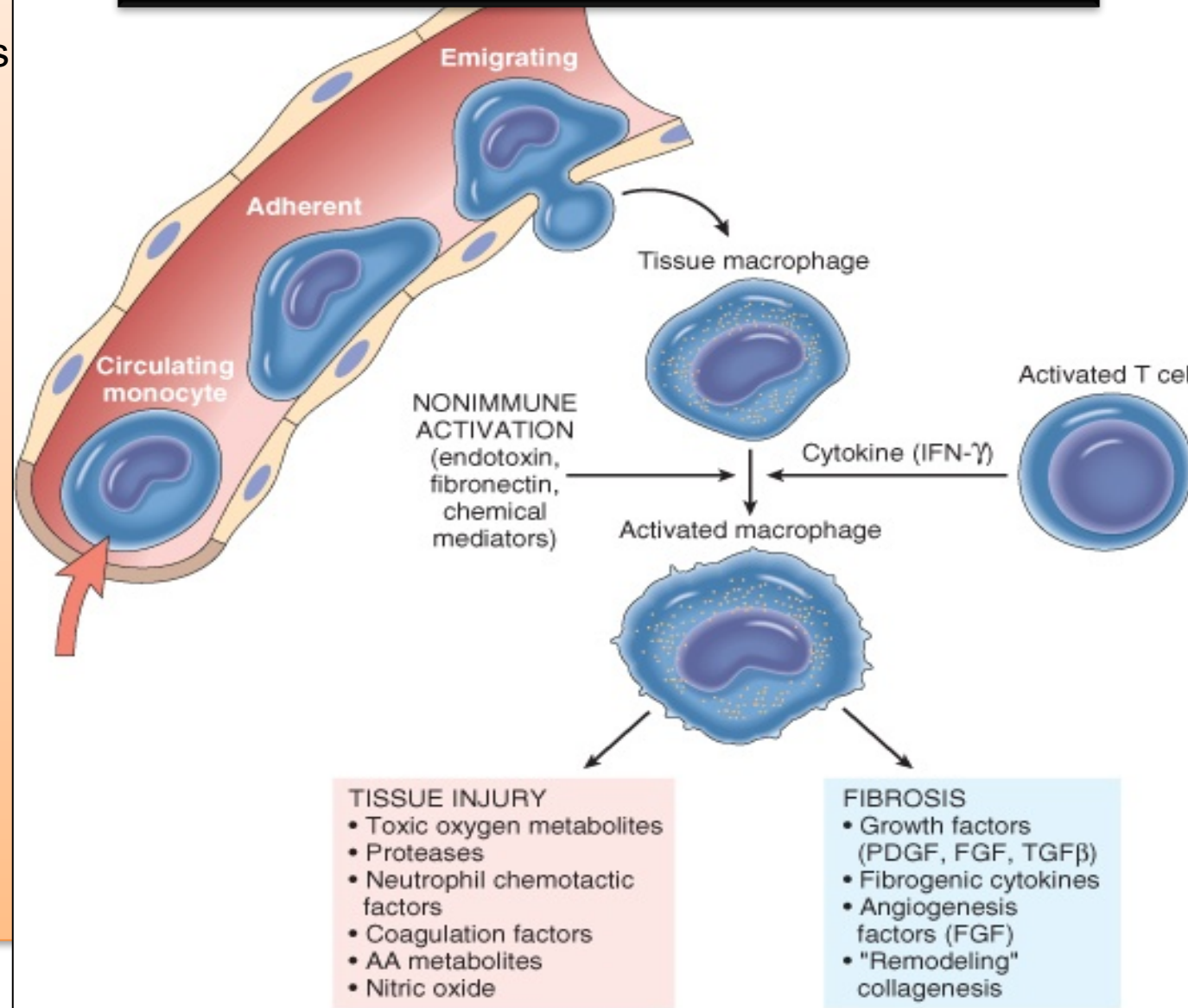




## 4. Different types of inflammatory cells accumulate in tissues

- to eliminate injurious agents such as microbes
- to initiate the process of repair
- secrete mediators of inflammation, such as cytokines (TNF, IL-1, chemokines, and eicosanoids).
- display antigens to T lymphocytes and respond to signals from T cells, thus setting up a feedback loop
- It is responsible for much of the tissue injury in chronic inflammation

### The roles of activated macrophages in chronic inflammation



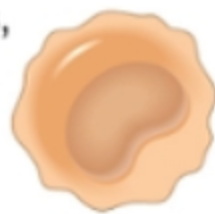
**CLASSICALLY  
ACTIVATED  
MACROPHAGE (M1)**



ROS, NO,  
lysosomal  
enzymes

Microbicidal  
actions  
Phagocytosis  
and killing  
of bacteria  
and fungi

Microbial  
TLR-ligands,  
IFN- $\gamma$



Monocyte

IL-1, TNF, IL-12,  
IL-6,  
chemokines



Inflammation

**ALTERNATIVELY  
ACTIVATED  
MACROPHAGE (M2)**



IL-10,  
TGF- $\beta$

Anti-inflammatory  
effects, wound  
repair, fibrosis

IL-13  
IL-4

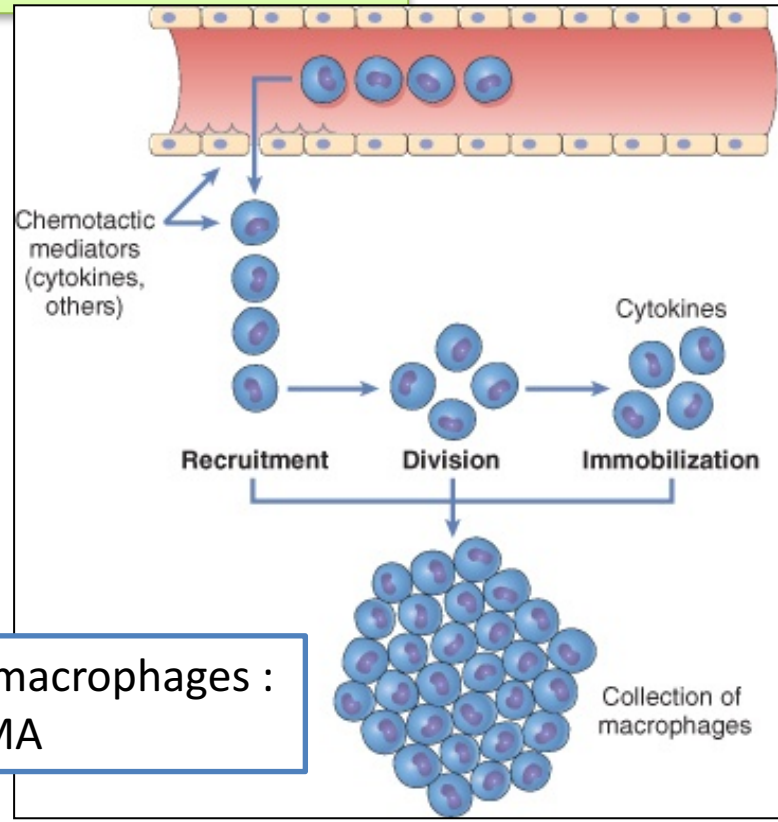


#### 4. Different types of inflammatory cells accumulate in tissues

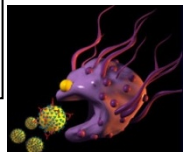
### Macrophages/Monocytes

- In chronic inflammation, macrophage accumulation persists, this is mediated by different mechanisms:

- Recruitment of monocytes from the circulation*
- Local proliferation of macrophages*
- Immobilization of macrophages*



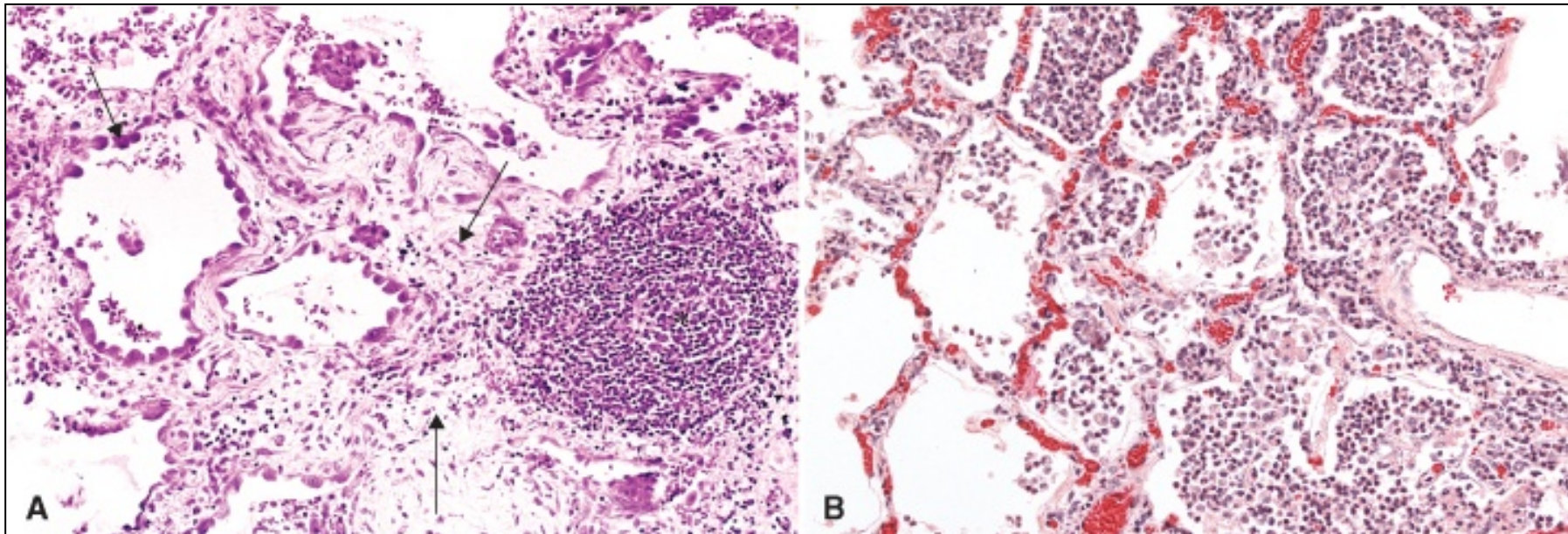
Collection of activated macrophages :  
GRANULOMA



## ***CELLS IN CHRONIC INFLAMMATION***

### **Lymphocytes**

- Both T & B Lymphocytes migrates into inflammation site
- most commonly seen in tissue affected by chronic inflammation
- Role: mediators of adaptive immunity, which provides defense against infectious pathogens

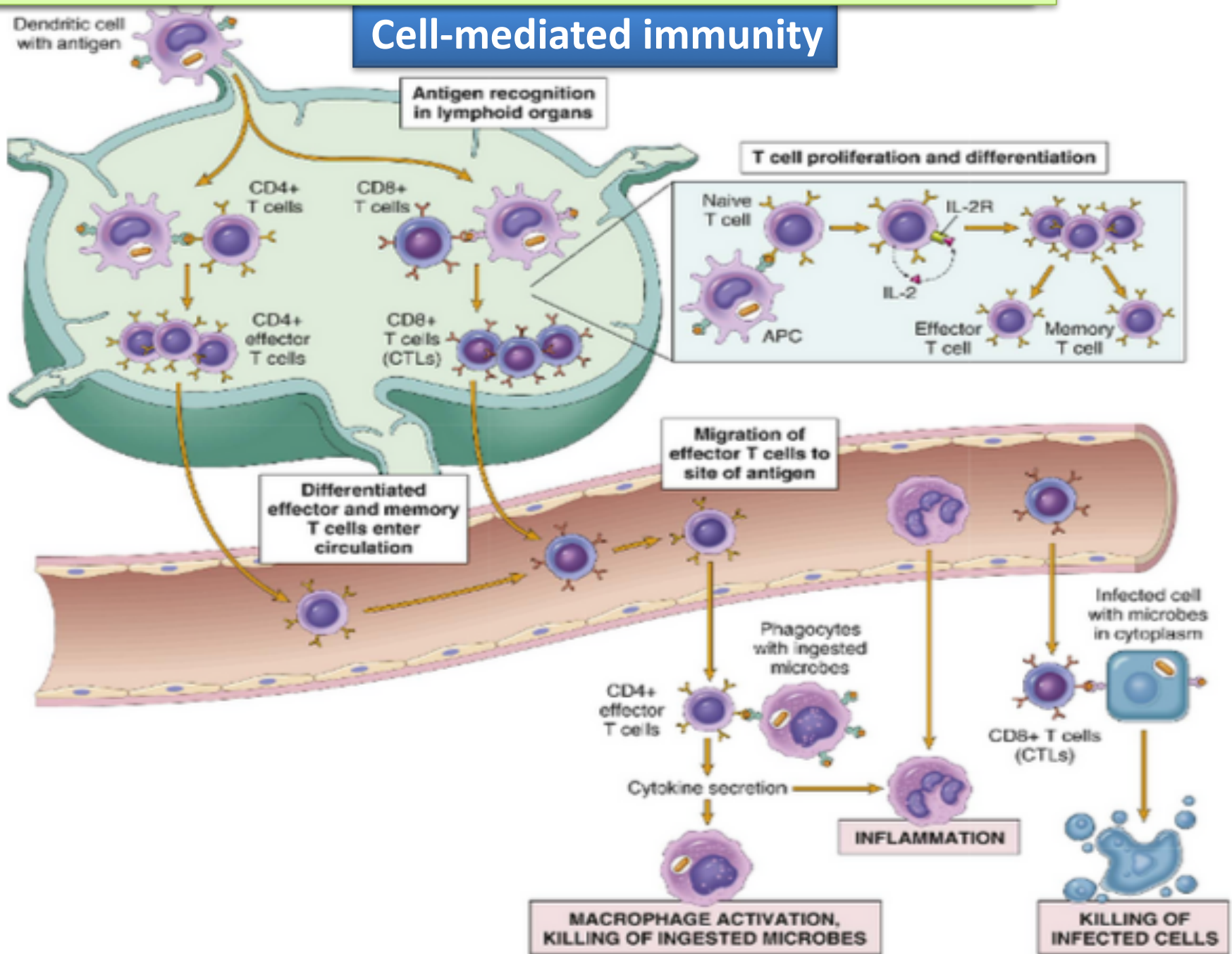


# Lymphocytes

- T lymphocytes are activated to secrete cytokines:
  - *CD4+ T lymphocytes promote inflammation and influence the nature of the inflammatory reaction*

# 4. Different types of inflammatory cells accumulate in tissues

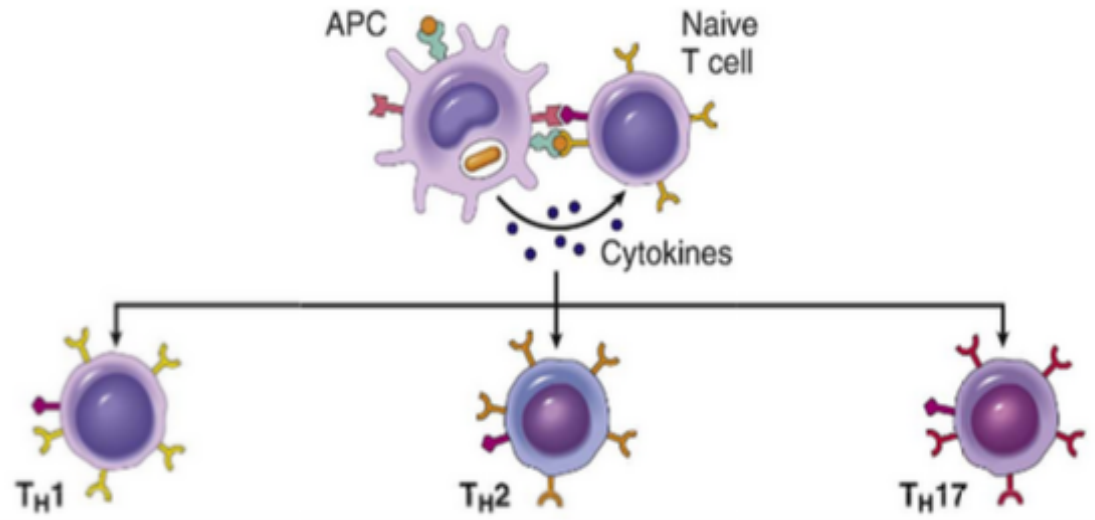
## Cell-mediated immunity



# 4. Different types of inflammatory cells accumulate in tissues

## Subsets of helper T (TH) cells

In response to stimuli (mainly cytokines) present at the time of antigen recognition, naive CD4+ T cells may differentiate into populations of effector cells that produce distinct sets of cytokines and perform different functions.



<b>Major cytokines produced</b>	IFN- $\gamma$	IL-4, IL-5, IL-13	IL-17, IL-22
<b>Cytokines that induce this subset</b>	IFN- $\gamma$ , IL-12	IL-4	TGF- $\beta$ , IL-6, IL-1, IL-23
<b>Immunological reactions triggered</b>	Macrophage activation, stimulation of IgG antibody production	Stimulation of IgE production, activation of mast cells and eosinophils	Recruitment of neutrophils, monocytes
<b>Host defense against</b>	Intracellular microbes	Helminthic parasites	Extracellular bacteria, fungi
<b>Role in disease</b>	Autoimmune and other chronic inflammatory diseases (such as IBD, psoriasis, granulomatous inflammation)	Allergies	Autoimmune and other chronic inflammatory diseases (such as IBD, psoriasis, MS)

IBD, inflammatory bowel disease

MS, multiple sclerosis

## CD4+ helper T cells

There are three subsets of CD4+ helper T cells :

- **T<sub>H</sub>1 cells** produce the cytokine IFN- $\gamma$ ,

Function: activates macrophages in the classical pathway.

- **T<sub>H</sub>2 cells** secrete IL-4, IL-5, and IL-13

Function: recruit and activate eosinophils and are responsible for macrophage activation.

- **T<sub>H</sub>17 cells** secrete IL-17 and other cytokines

Function: induce the secretion of chemokines responsible for recruiting neutrophils and monocytes into the reaction.



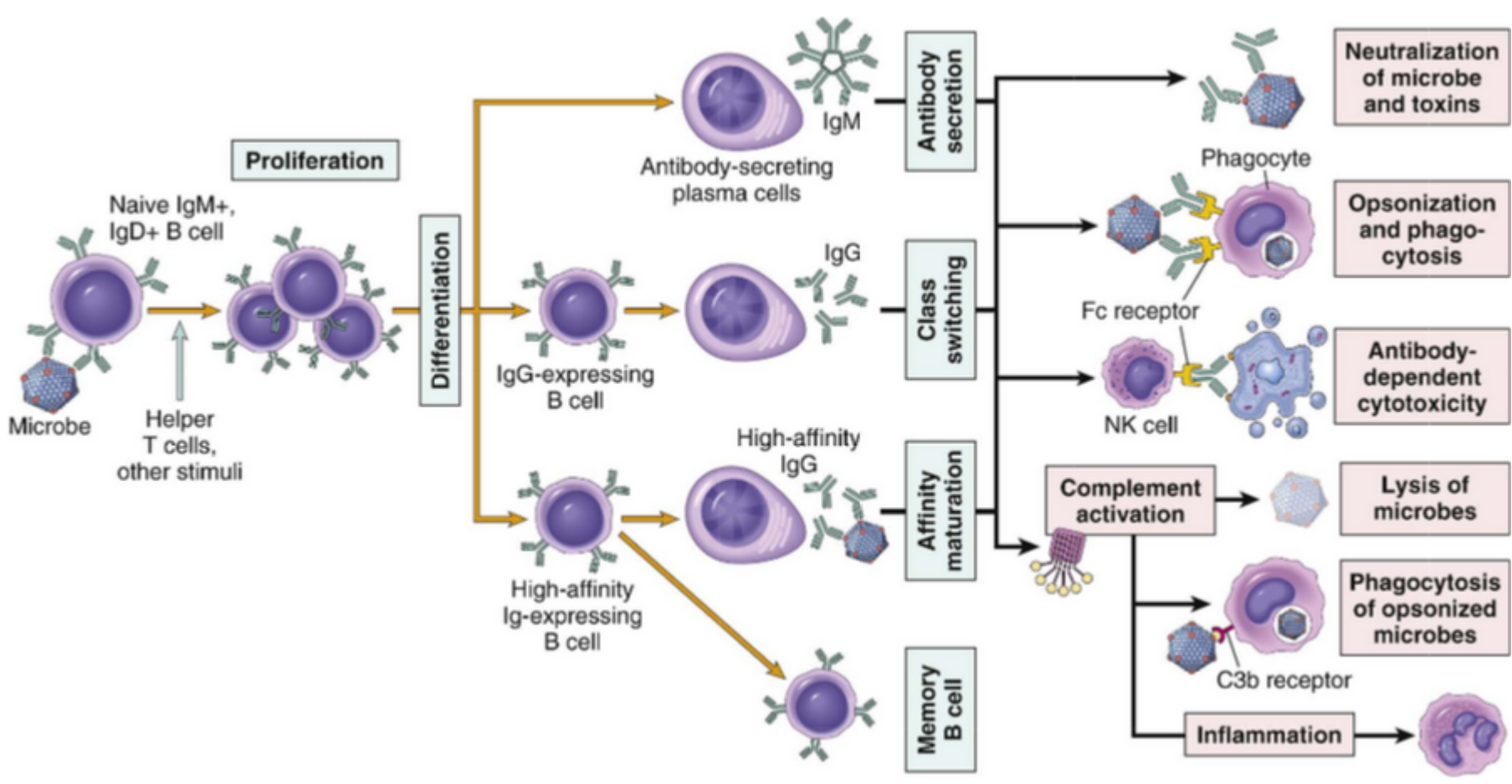
#### 4. Different types of inflammatory cells accumulate in tissues

### B lymphocytes

- B lymphocytes may develop into *plasma cells*, which secrete antibodies (Humoral immunity)
- Naive B lymphocytes recognize antigens, and under the influence of TH cells and other stimuli, the B cells are activated to proliferate and to differentiate into antibody-secreting plasma cells.

# 4. Different types of inflammatory cells accumulate in tissues

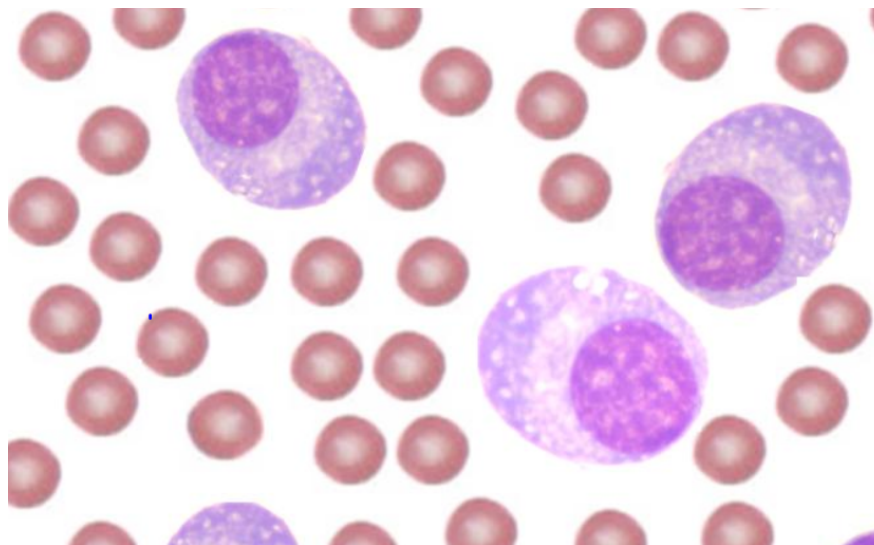
## Humoral immunity



## ***OTHER CELLS IN CHRONIC INFLAMMATION***

### **Plasma cells**

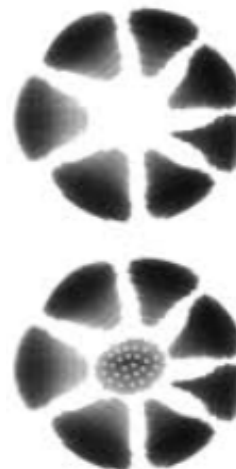
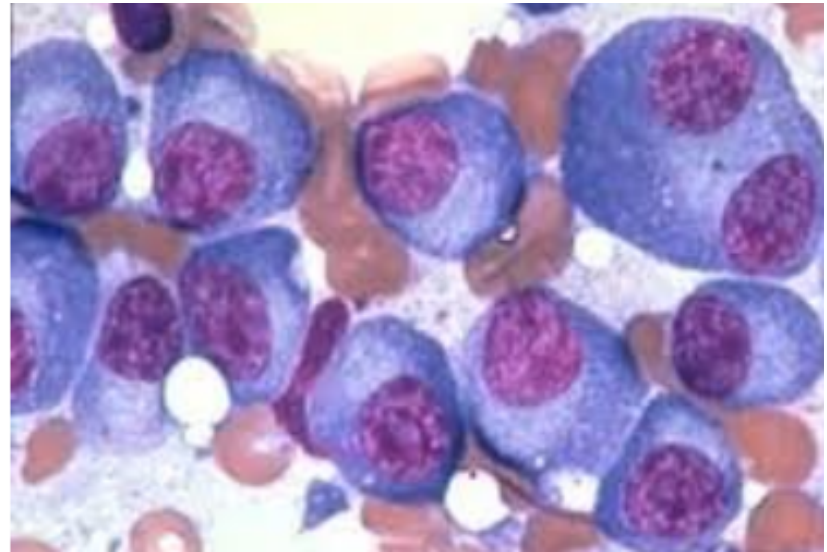
- **Lymphoid cell (Mature B cells)**
- **Common cell in chronic inflammation**
- **Primary source of antibodies**
- **Antibodies are important in inflammation e.g. neutralize antigen and clearance of foreign antigen**



# Plasma cells

## Morphology of plasma cells:

Cells has an eccentric nucleus shows a cartwheel or clock face pattern of nuclear chromatin with a perinuclear halo

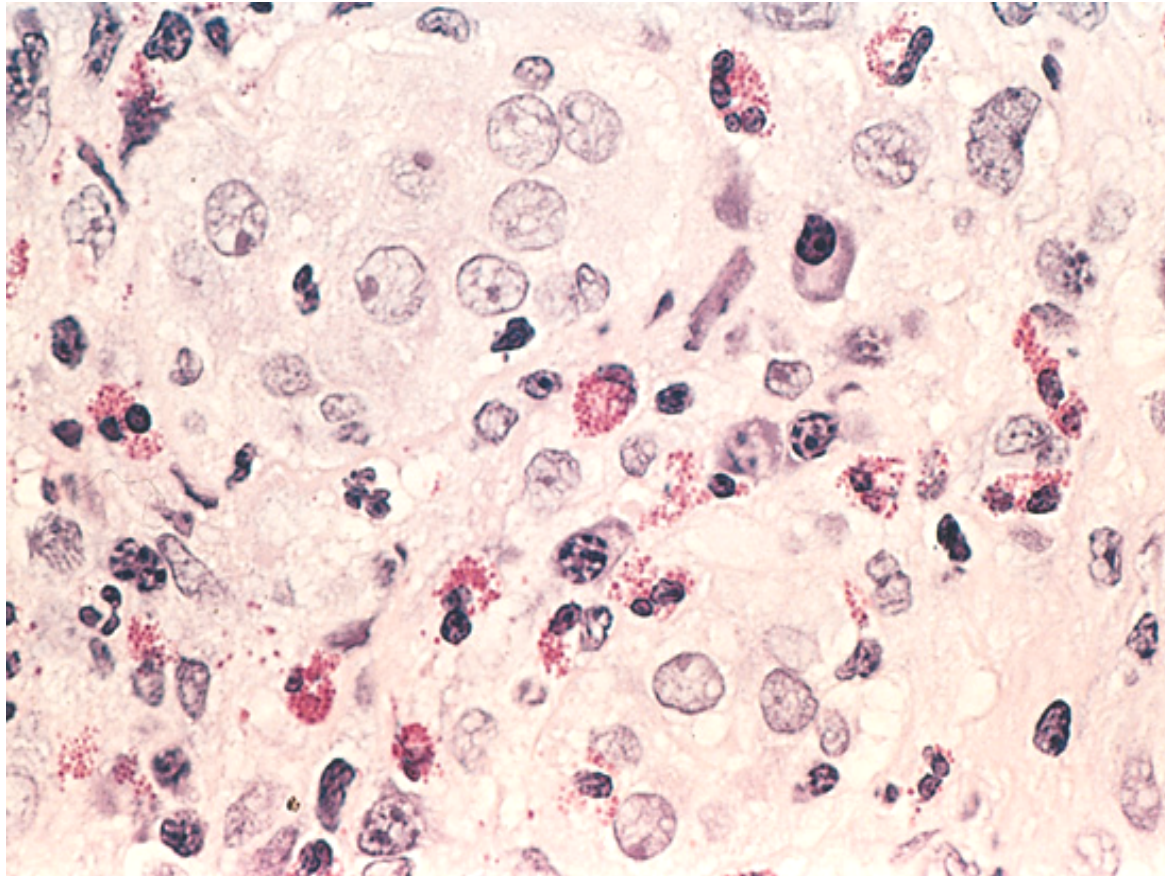


## 4. Different types of inflammatory cells accumulate in tissues

### Eosinophils

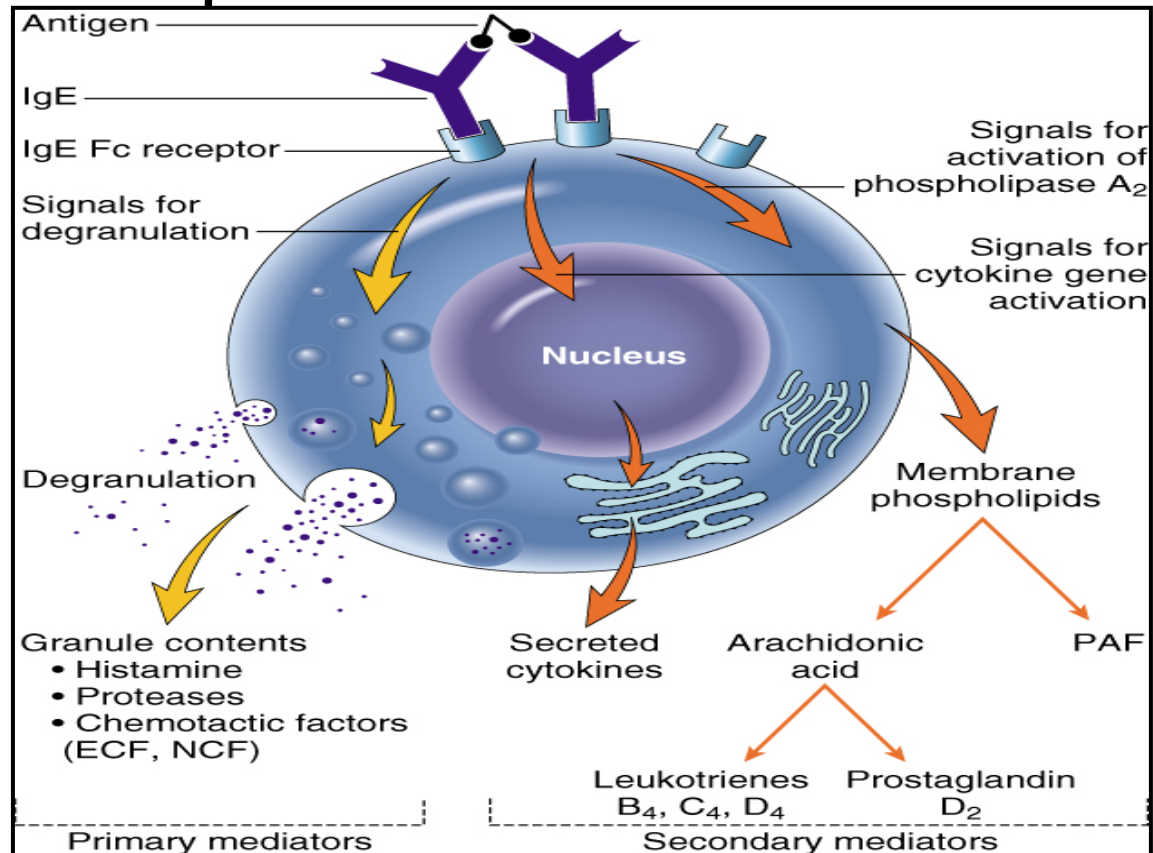
are abundant in immune reactions mediated by IgE in allergic reaction and in parasitic infections


- respond to chemotactic agents derived largely from mast cells
- Granules contain major basic protein: toxic to parasites and lead to lysis of mammalian epithelial cells



## Mast cells

- are widely distributed in connective tissues
- express on their surface the receptor that binds the Fc portion of IgE antibody
  - the cells degranulate and release mediators, such as histamine and products of AA oxidation



- 
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