

Inflammation

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Reference

- Robbins and Cotran Pathologic Basis of Disease 8th edition
- Robbins Basic Pathology 8th edition
- Rubin Pathology 5th edition
- General and systemic pathology, 5th edition
- Core pathology, 3rd edition

Tissue Injury , Infection



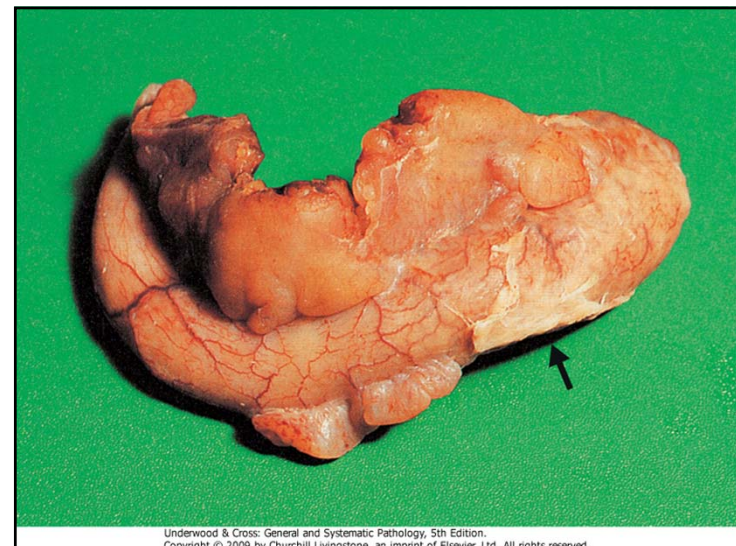
Inflammation



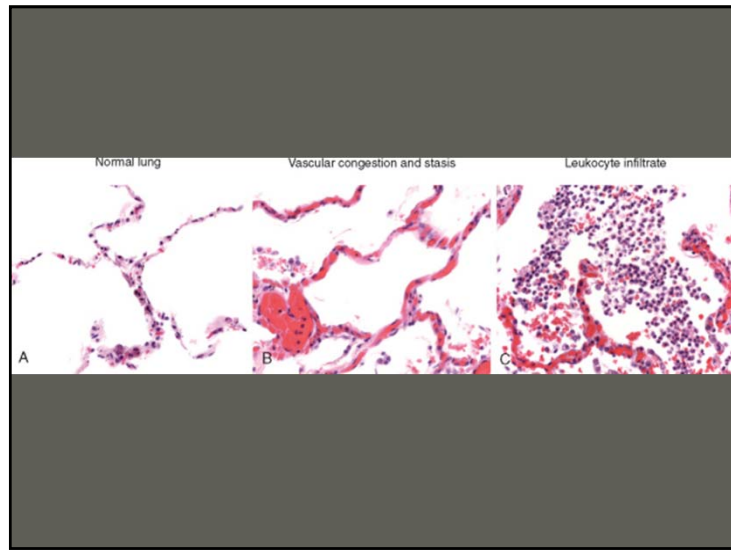
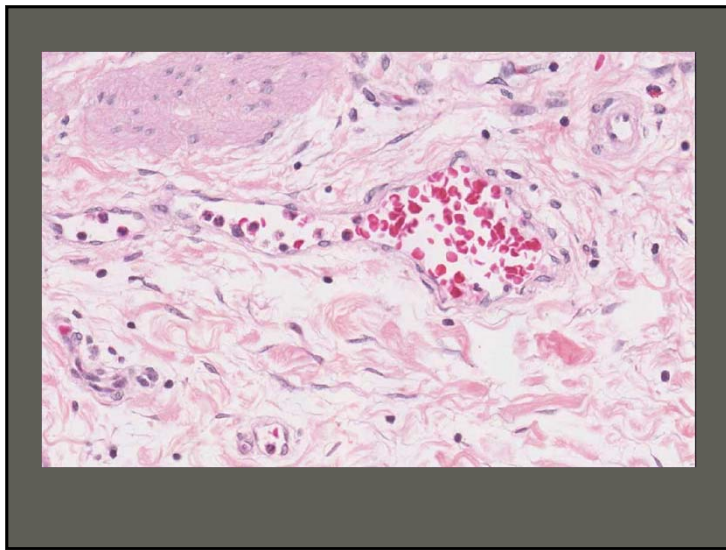
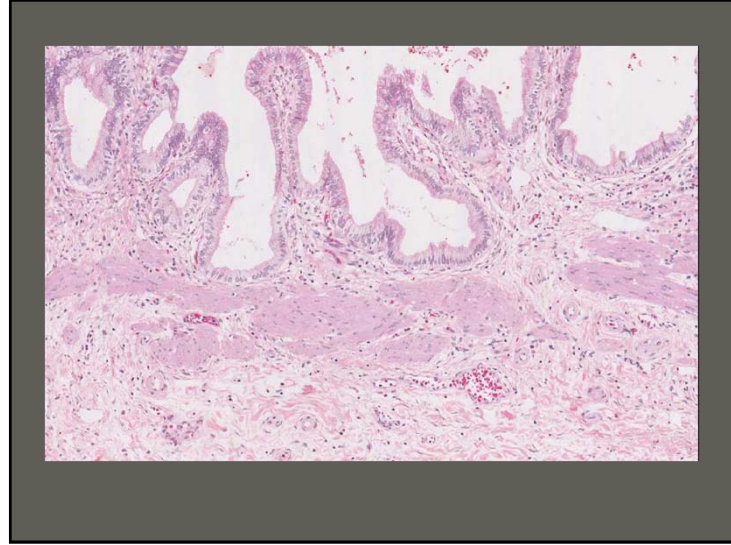
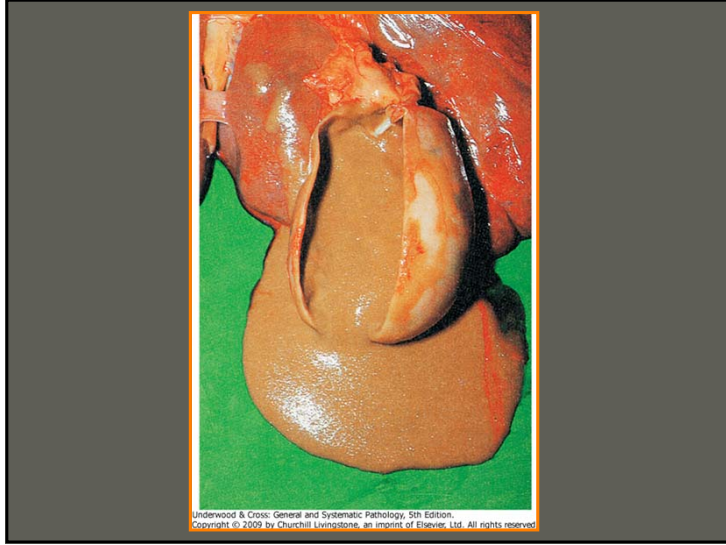
Repair



Healing



Underwood & Cross: General and Systematic Pathology, 5th Edition.
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INFLAMMATION

- Complex reactions to injurious agents
- Closely intertwined with the process of repair
- Inflammation is fundamentally a protective response
- Inflammation and repair may be potentially harmful

- Inflammatory reactions are mediated by chemical mediators
- These chemical mediators are derived from plasma proteins or cells and are produced in response to or activated by the stimuli
- Inflammation is divided into
 - Acute inflammation
 - Chronic inflammation

ACUTE INFLAMMATION

Rapid response to injurious agent that serves to deliver mediators of host defense (leukocytes and plasma proteins) to the site of injury

Stimuli for Acute inflammation

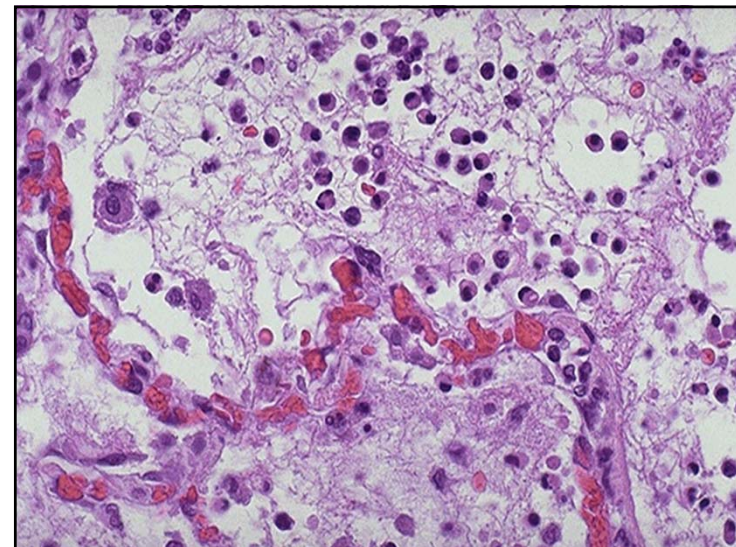
- Infections and microbial toxins
- Trauma
- Physical and chemical agents
- Tissue necrosis
- Foreign bodies
- Immune reactions

- Acute inflammation consists of two components
 - Vascular reaction
 - Cellular reaction

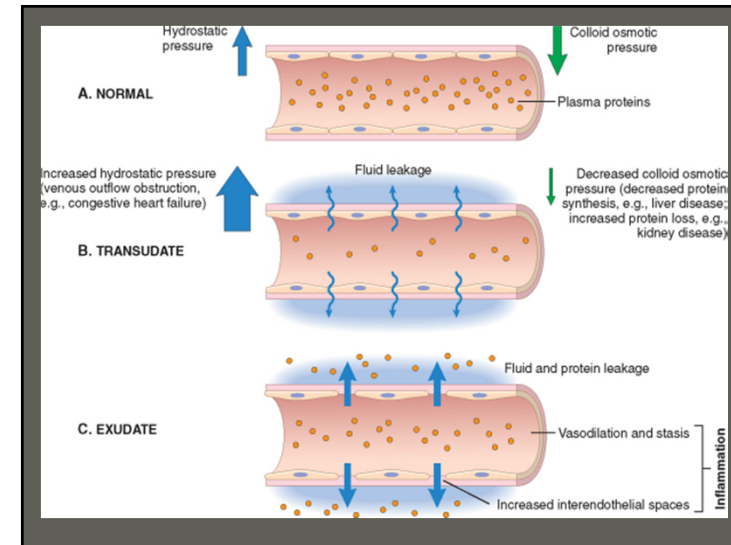
Vascular Changes

- Changes in vascular flow and caliber
 - Vasodilation
 - Earliest manifestation of acute inflammation
 - Stasis → increased blood viscosity
 - Quickly followed by increased vascular permeability

- Increased vascular permeability (vascular leakage)
 - Hallmark of acute inflammation
 - Protein and fluid leakage from the lumen

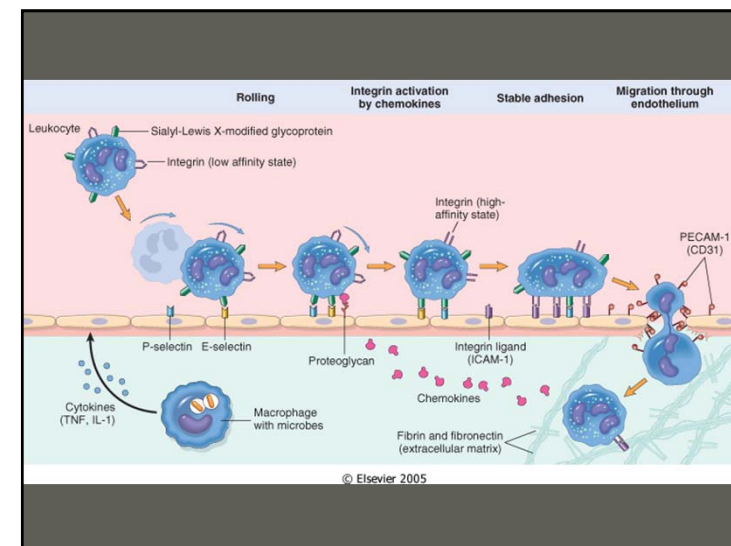


- **Exudate** : extravascular fluid that has high protein concentration
- **Transudate** : extravascular fluid that has low protein concentration
- **Pus or purulent exudate** : leukocytes- rich exudate



Cellular Events

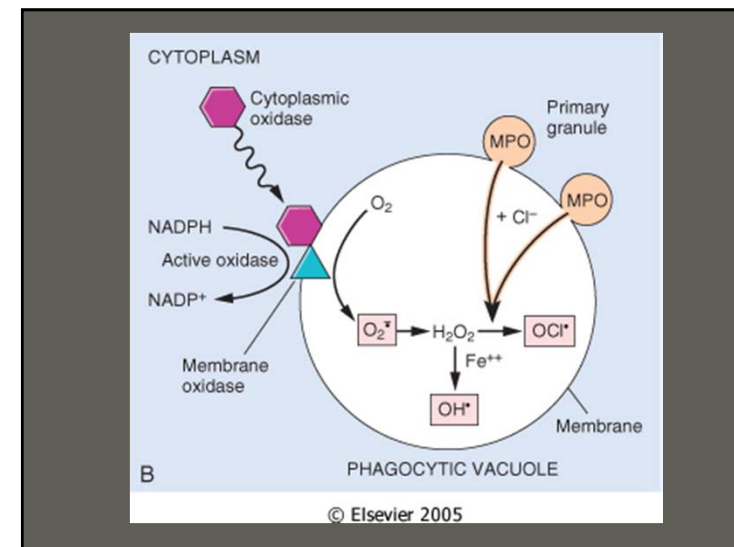
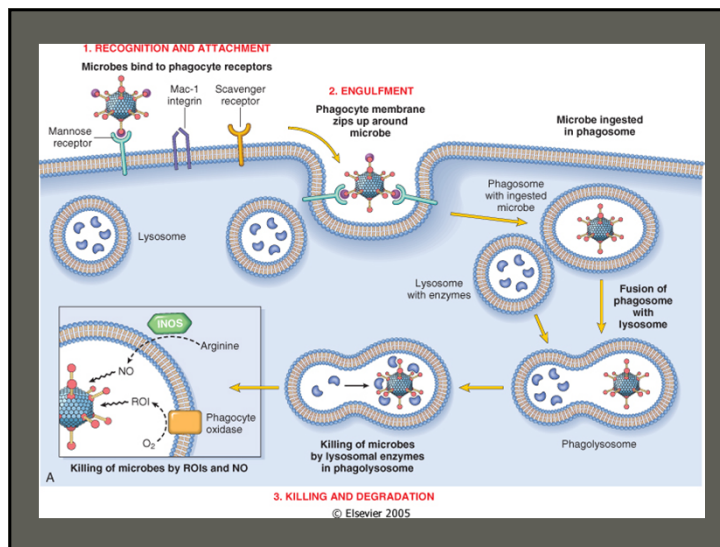
- Margination
- Rolling
- Adhesion
- Transmigration (diapedesis)
- Migration → chemotaxis
- Phagocytosis



- Margination
- Rolling
 - Selectin \leftrightarrow Sialyl-Lewis X-modified GP
- Adhesion
 - ICAM-1, VCAM-1 \leftrightarrow Integrin
- Transmigration (diapedesis)
 - PECAM-1 (CD31)
- Migration \rightarrow chemotaxis
 - Extracellular matrix (heparan sulfate) \leftrightarrow CD44, Integrin

PHAGOCYTOSIS

- Recognition and attachment
- Engulfment
- Killing and degradation
 - Oxygen-dependent mechanisms
 - NO
 - ROI : NADPH oxidase
 - HOCl : MPO (myeloperoxidase)
 - Oxygen-independent mechanisms
 - Bactericidal permeability increasing protein (BPI)
 - Lysozyme, major basic protein, defensin



DEFECT IN LEUKOCYTE FUNCTION

Genetic

- Leukocyte adhesion deficiency 1
- Leukocyte adhesion deficiency 2
- Chronic granulomatous disease
- Chediak-Higashi syndrome
- Integrins
- Sialyl-Lewis X modified GP
- NADPH oxidase
- Phagocytosis

Acquired

- Thermal injury, Diabetes, Malignancy, Sepsis, Immunodeficiency
- Hemodialysis, Diabetes
- Leukemia, Anemia, Sepsis, Diabetes, Neonates, Malnutrition
- Chemotaxis
- Adhesion
- Phagocytosis and bactericidal activity

CHEMICAL MEDIATORS OF INFLAMMATION

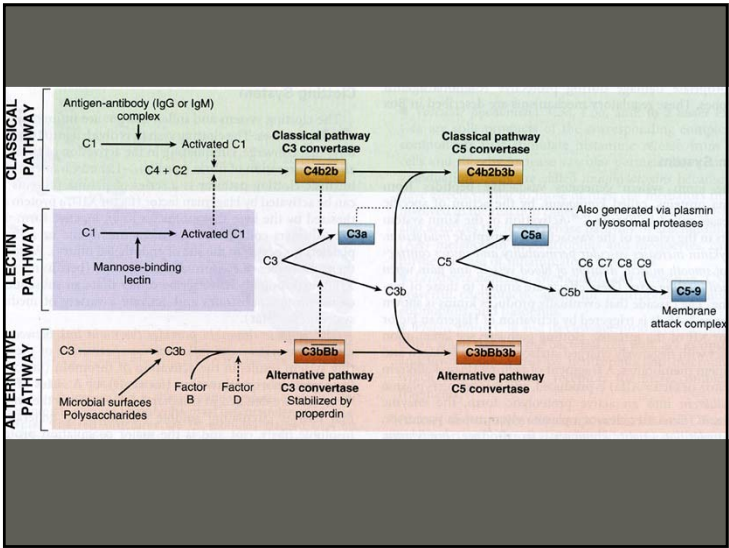
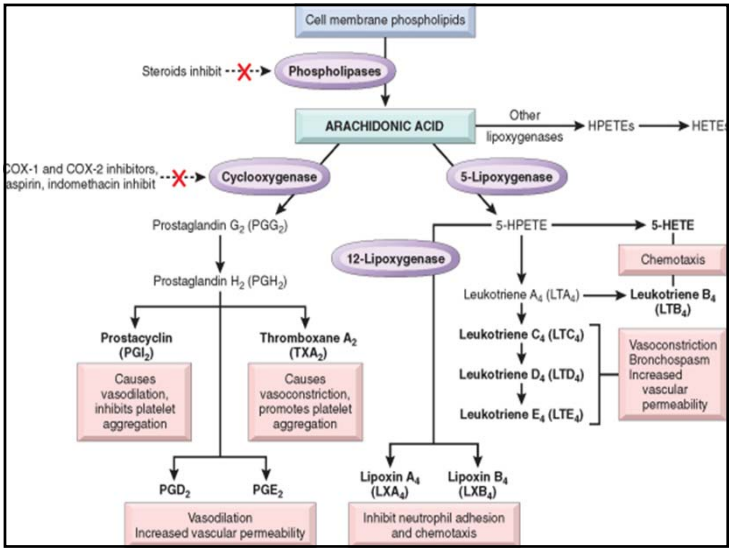
- Mediators originate either from plasma or from cells
- The production is triggered by microbial products or by host proteins, other chemical mediators
- Mediators perform activity by binding their specific receptors
- One mediator can stimulate the release of other mediators
- Mediators have different effects on different cell types
- Most mediators are short-lived

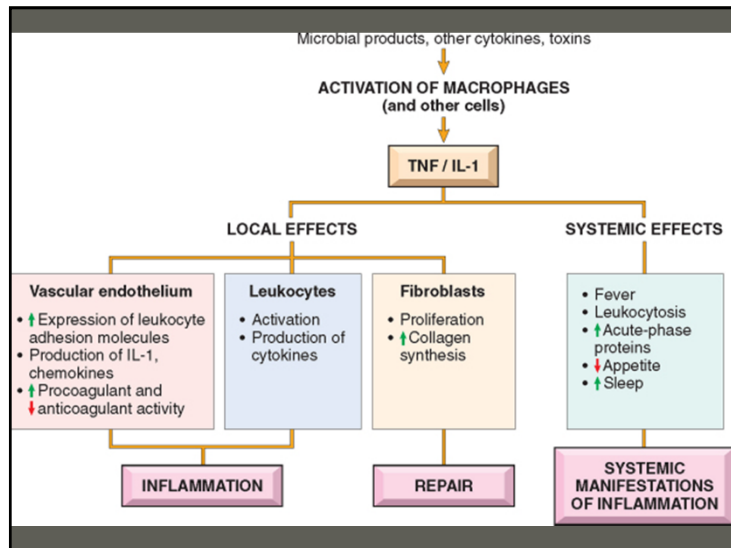
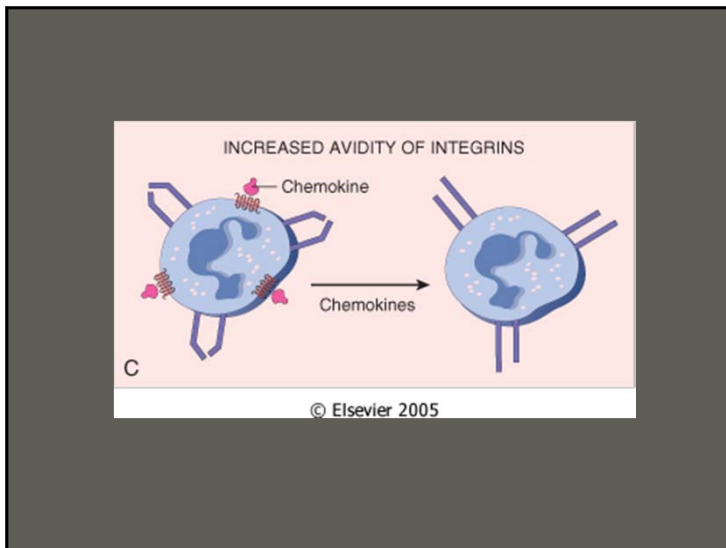
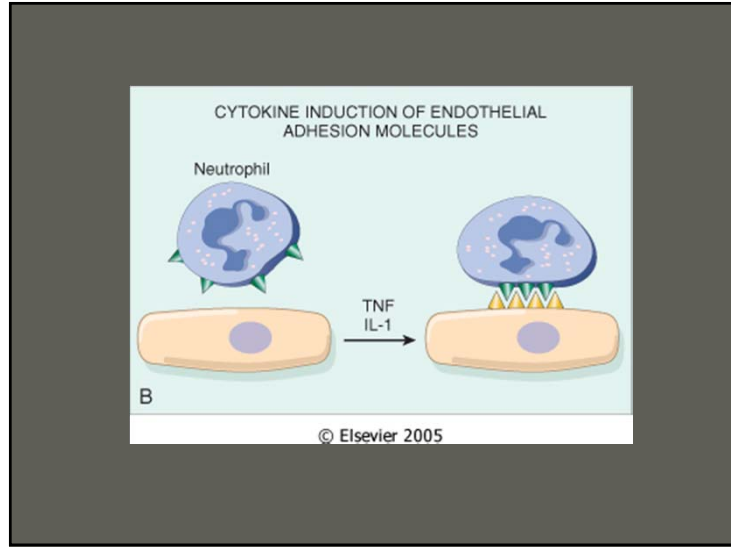
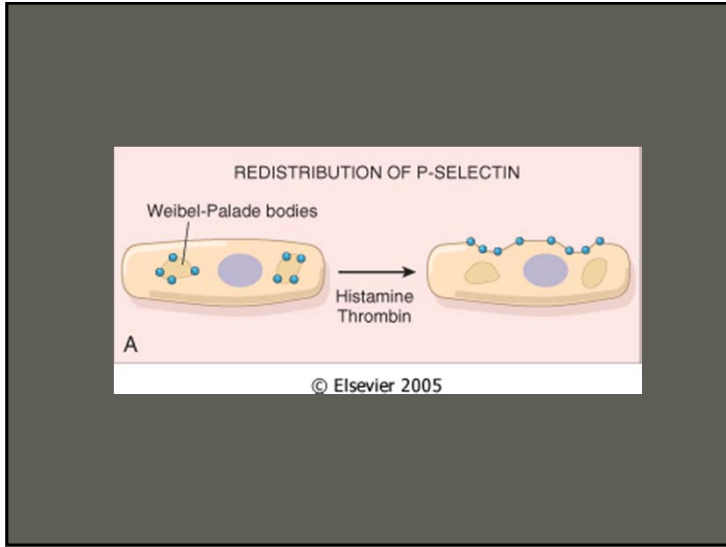
- Chemical mediators
 - Vascular response
 - Cellular response (chemotaxis)
- Different reaction of inflammation
 - Vasodilation
 - Increased vascular permeability
 - Chemotaxis, leukocyte recruitment and activation
 - Fever
 - Pain
 - Tissue damage

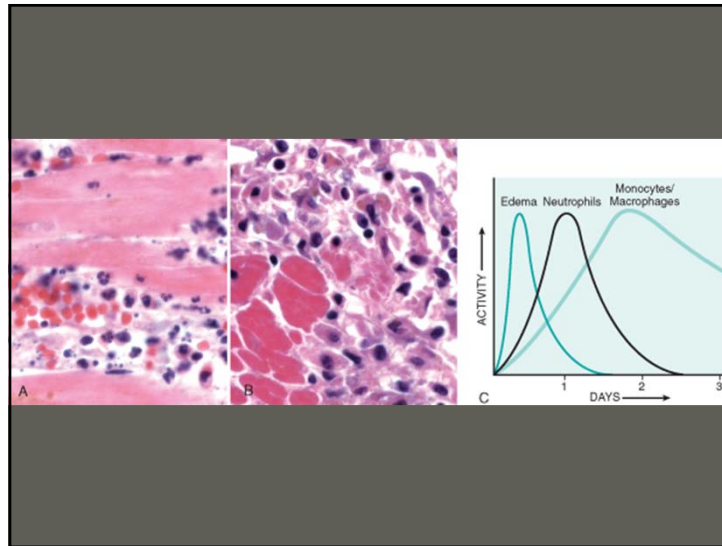
- Vasodilation
 - Prostaglandins
 - Nitric oxide
 - Histamine
- Increased vascular permeability
 - Histamine and serotonin
 - C3a and C5a
 - Bradykinin
 - Leukotriene C4, D4, E4
 - PAF

- Chemotaxis
 - TNF, IL-1
 - Chemokines
 - C3a, C5a
 - Leukotriene B4
 - Bacterial products

- Fever
 - IL-1, TNF
 - Prostaglandins
- Pain
 - Bradykinin
 - Prostaglandins
- Tissue damage
 - Lysosyme
 - ROS, NO

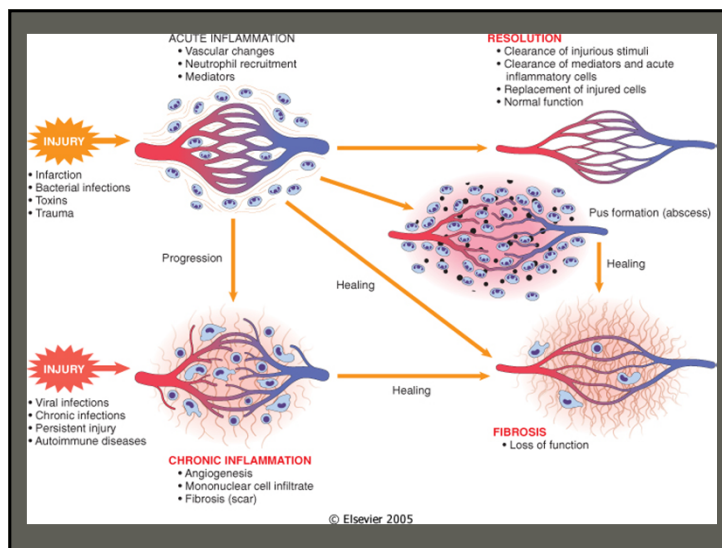






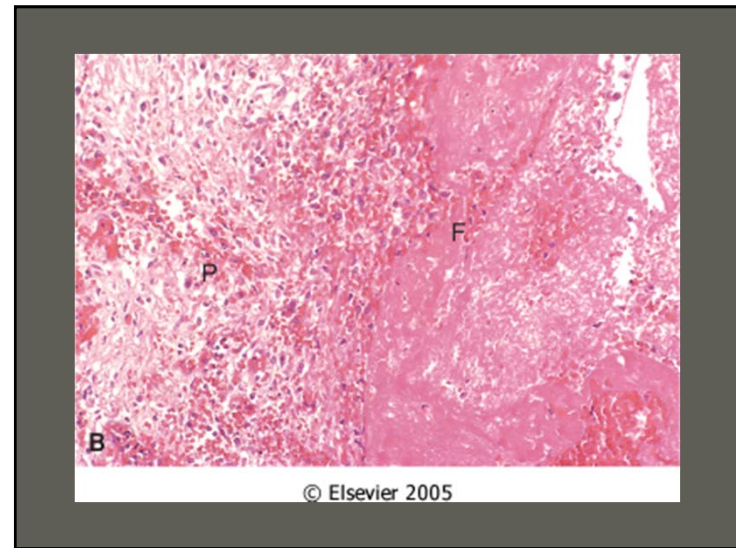
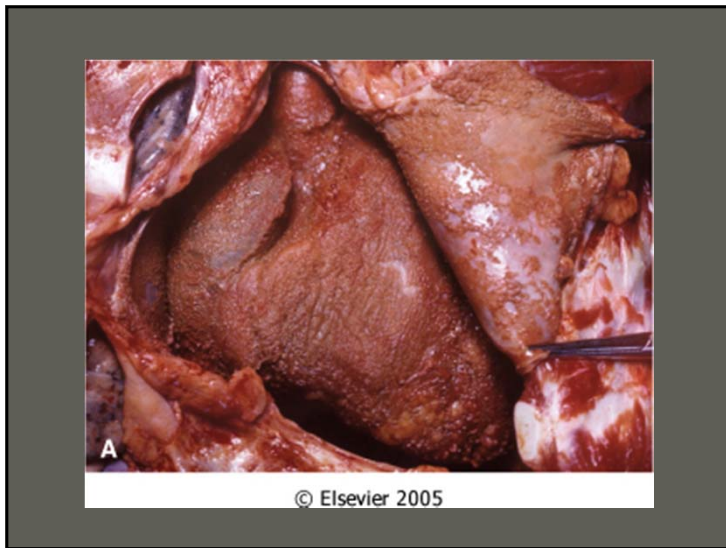
OUTCOME OF ACUTE INFLAMMATION

- Complete resolution
- Healing by connective tissue replacement
- Chronic inflammation

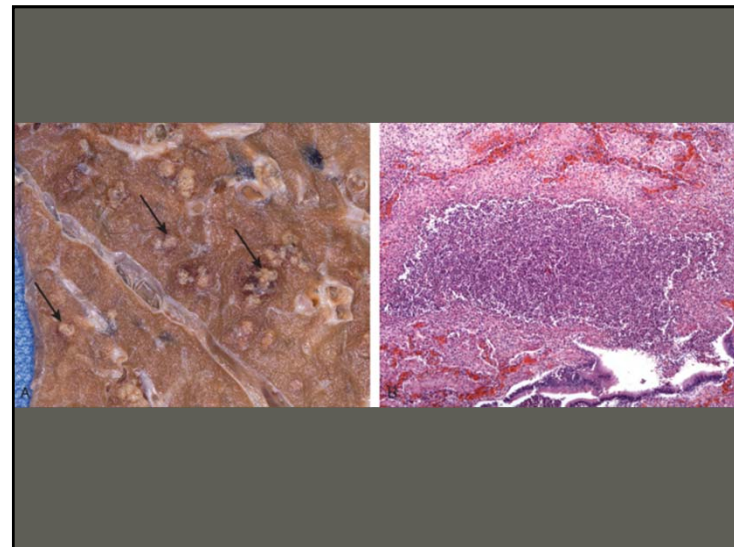
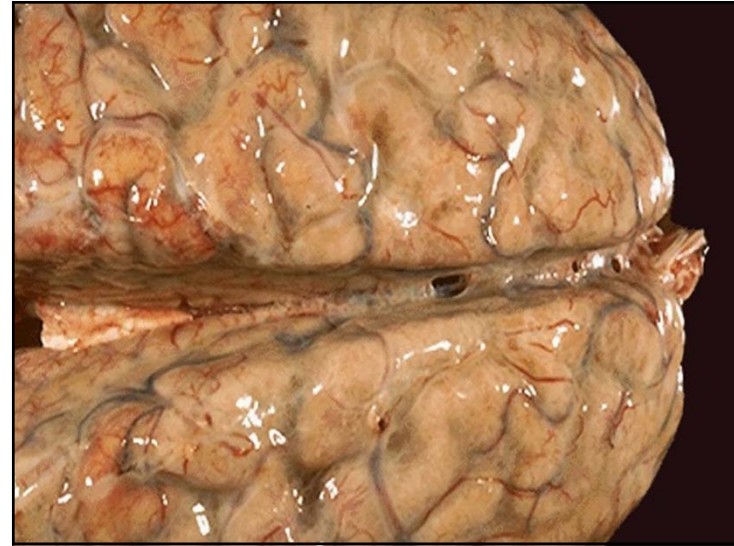


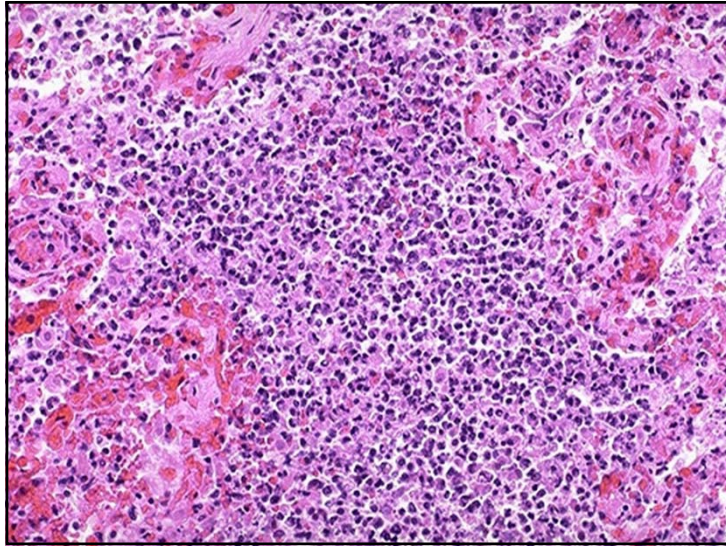
MORPHOLOGIC PATTERN OF ACUTE INFLAMMATION

- Serous inflammation
 - Burn
 - Inflammation in the body cavity
- Fibrinous inflammation
 - Severe injury, results in greater vascular permeability
 - Leakage of fibrinogen

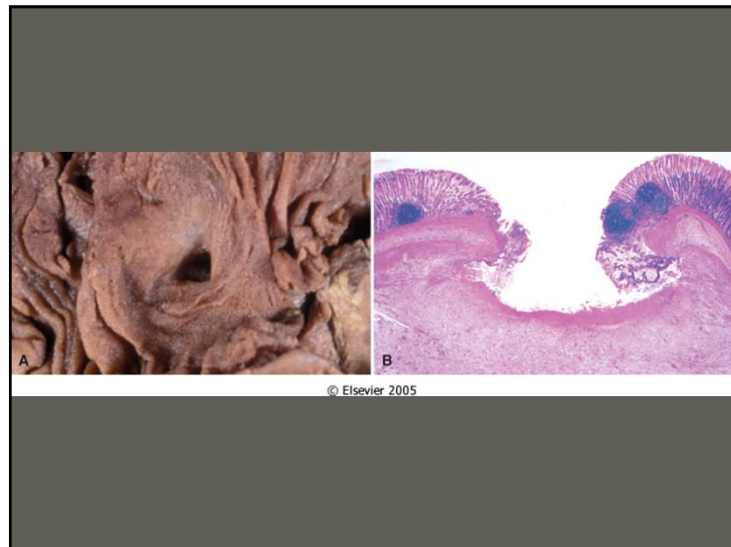


- Suppurative or purulent inflammation
 - Inflammation with pus or purulent exudate formation
 - Acute appendicitis
 - Acute meningitis
 - Abscess : localized collections of purulent inflammatory tissue
 - Fibrinopurulent inflammation





- Ulcers
 - Local defect or excavation of the surface of an organ or tissue
 - Most common encounter in
 - Oral mucosa
 - Subcutaneous tissue

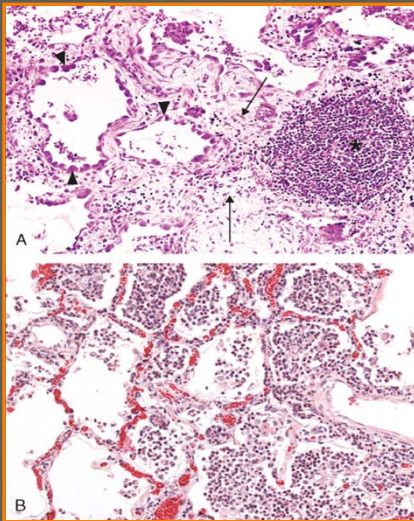


CHRONIC INFLAMMATION

Inflammation of prolonged duration (weeks or months) in which active inflammation, tissue destruction and attempts at repair proceeding simultaneously

Cause of chronic inflammation

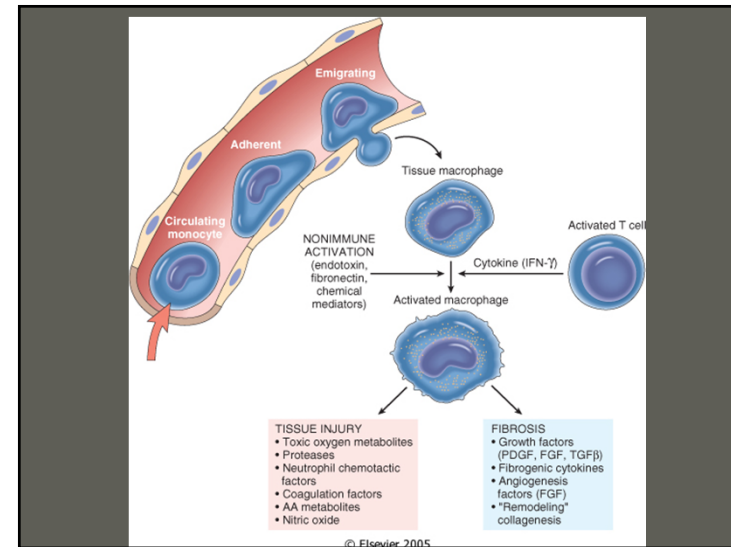
- Persistent infection
- Prolonged exposure to potentially toxic agents, either exogenous or endogenous
- Autoimmunity



Morphologic features

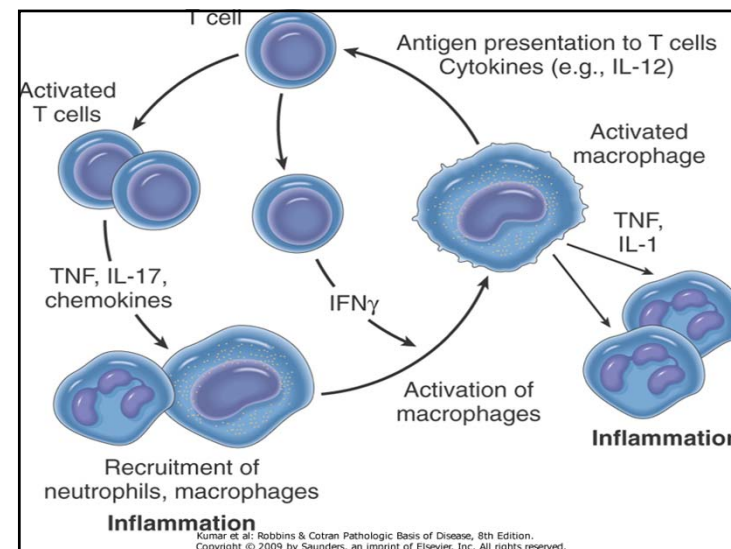
- Infiltration with mononuclear cells, including macrophages, lymphocytes and plasma cells
- Tissue destruction
- Healing by connective tissue replacement of damaged tissue

- Persistent macrophage accumulation in chronic inflammation is mediated by
 - Recruitment of monocytes from the circulation : C5a, PDGF, TGF- α
 - Local proliferation of macrophages
 - Immobilization of macrophages
- The products of activated macrophages are responsible for much of tissue injury

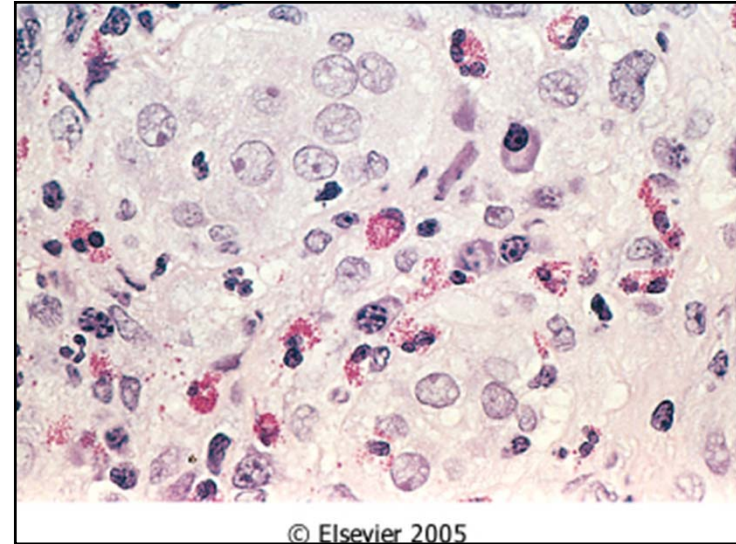


OTHER CELLS IN CHRONIC INFLAMMATION

- Lymphocytes
 - Lymphocytes and macrophages interact in a bidirectional way and these reactions play an important role in chronic inflammation

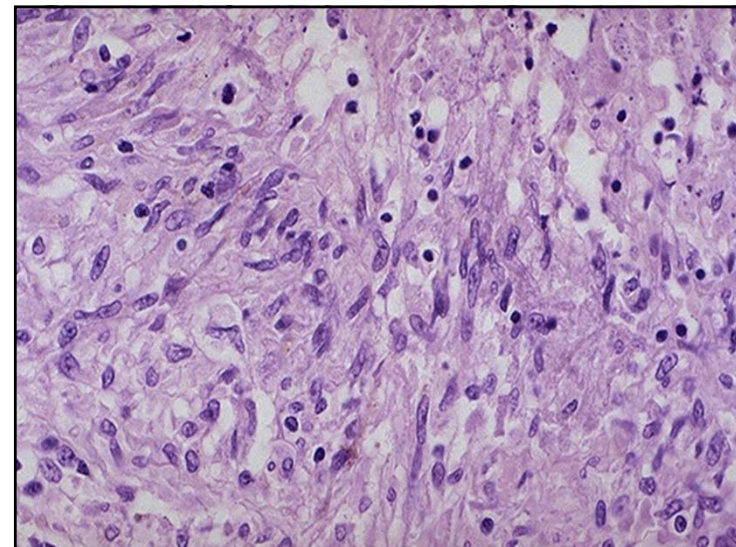


- Eosinophils
 - Immune reaction mediated by IgE
 - Parasitic infestation
 - Contain major basic protein, that is toxic to parasites



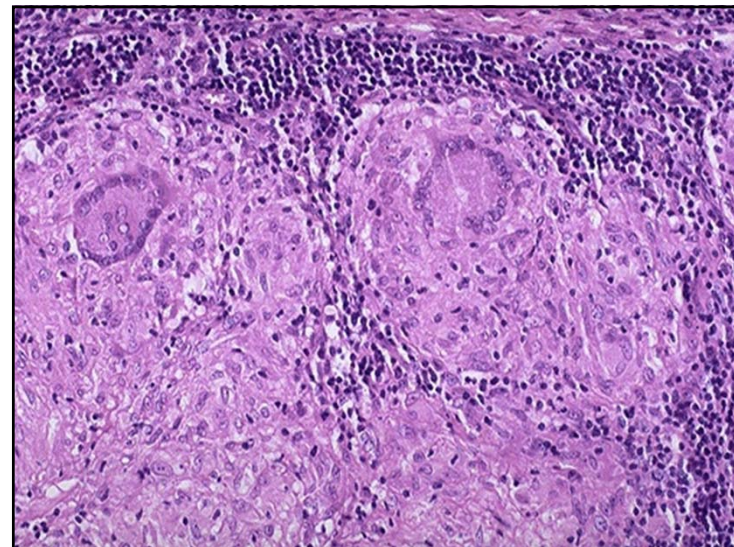
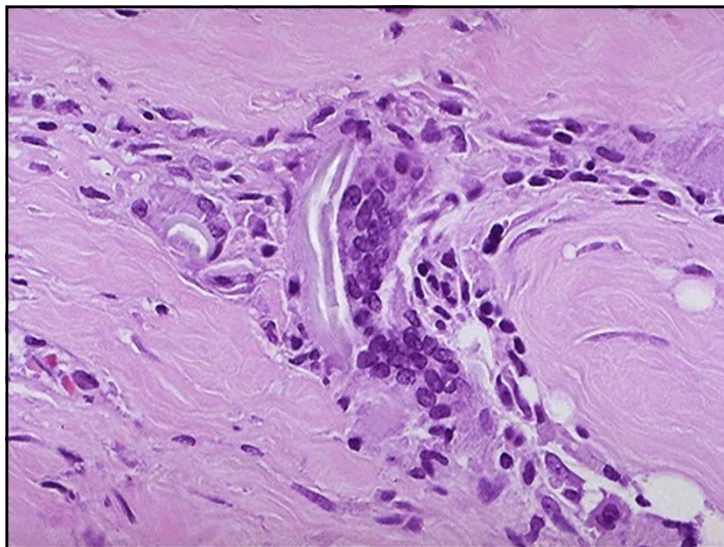
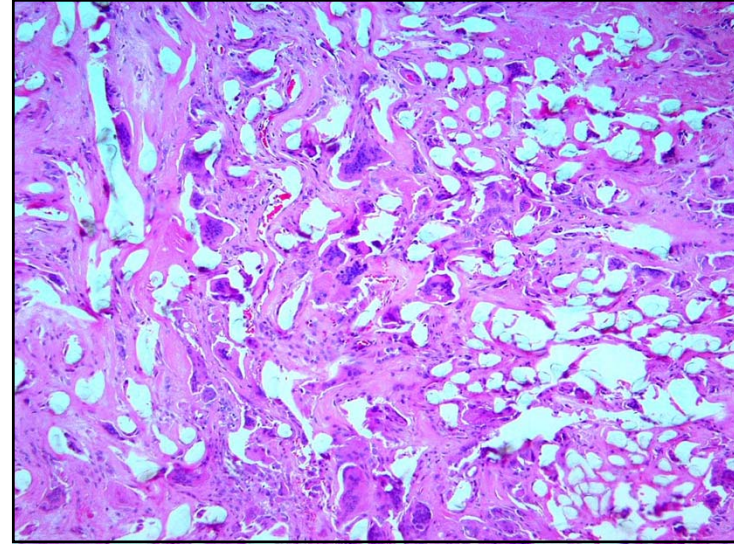
Granulomatous inflammation

- Chronic inflammation, characterized by focal accumulation of activated macrophages which often develop an epithelial-like (epithelioid) appearance
- Granuloma : focal aggregation of epithelioid macrophages and surround by a collar of mononuclear leukocytes



Granuloma

- Foreign body granuloma
 - Foreign body type giant cell
- Immune granuloma
 - Langhans type giant cell
 - Central caseous necrosis



**Thank You
for Your Attention**