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
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 $\rightarrow$ 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 <-> Sialyl-Lewis X-modified GP
• Adhesion
  ICAM-1, VCAM-1 <-> Integrin
• Transmigration (diapedesis)
  PECAM-1 (CD31)
• Migration → chemotaxis
  Extracellular matrix (heparan sulfate) <-> 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

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*Image of diagrams explaining the processes of phagocytosis.*
DEFECT IN LEUKOCYTE FUNCTION

**Genetic**
- Leukocyte adhesion deficiency 1
- Leukocyte adhesion deficiency 2
- Chronic granulomatous disease
- Chediak-Higashi syndrome

**Acquired**
- Thermal injury, Diabetes, Malignancy, Sepsis, Immunodeficiency
- Hemodialysis, Diabetes
- Leukemia, Anemia, Sepsis, Diabetes, Neonates, Malnutrition

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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
  - Lysosome
  - 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

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**Cause of chronic inflammation**

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

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**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