

Innate vs Acquired Immunity

- Cells of the Innate Immune System
 - Myeloid Cells
- Inflammation
 - 5 Cardinal Signs, and their causes
- Complement
 - Introduction to the complement cascade

Innate Immunity 2

- The Innate Immune system is a **primitive** response, largely conserved throughout evolution, which **non-specifically** defends the body against disease

Cells of the Innate Immune System

- These cells form roughly 50% of the peripheral blood **Leukocytes** (white blood cells).
- They are the monocytes/macrophages, and the **granulocytes** including:
 - Neutrophils (PMNs)
 - Eosinophils
 - Basophils

Inflammation

- Inflammation is the **reaction of vascularized living tissue to local injury**
- While organisms with no vascular system may use **phagocytosis** as a defense mechanism, the *reaction of blood vessels* is central to inflammation

Inflammation - 2

- Inflammation serves to **destroy, dilute, or isolate** the injurious agent, and sets off a series of events which result in healing and **reconstitution** of the damaged tissue

5 Signs of Inflammation

- Rubor - **Redness**
- Tumor - **Swelling**
- Calor - **Heat**
- Dolor - **Pain**
- Functio Laesa - **Loss of function**

These cardinal signs of inflammation are induced by

1. Changes in blood vascular flow and caliber (hemodynamic changes)
2. Changes in vascular permeability (leakiness of blood vessels)
3. Leukocyte influx from the blood.

1. Hemodynamic Changes

- **Vasoconstriction** of vessels carrying blood away from the affected area. Local vessels may also transiently constrict to restrict the release of infectious agent.
- **Vasodilation** of local vessels to permit increased blood flow to the affected area.
- Results in **Heat** and **Redness**

Hemodynamic Changes
cont'd

- **Slowing of the circulation** results in **stasis**. This allows leukocytes (white blood cells) to slow and attach to the wall of the blood vessels.

Changes in Vascular Permeability

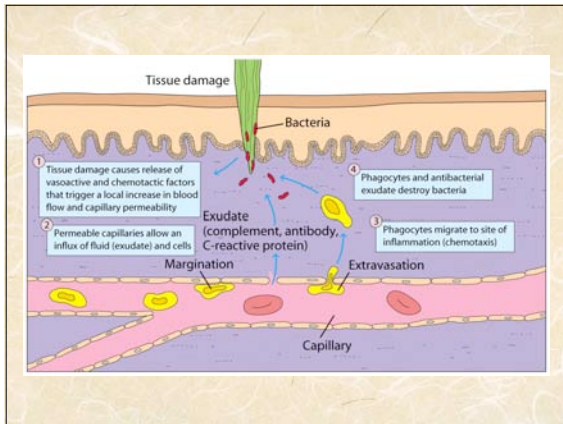
- Soluble factors released at the site of injury result in increased *leakiness* of the blood vessels. The fluid and protein which leaks (called an **exudate**) results in **edema**.
- This edema results in **swelling**

Leukocyte Influx

- **Stasis** allows the leukocytes to attach to the blood vessel walls, and eventually to transmigrate (later lecture).
- **PMNs** are the most effective cells at leaving the blood during this early response. Lymphocytes do not enter until much later.

PMN Extravasation

- In distinct stages:
 - Margination (sticking to the wall of the vessel)
 - Diapedesis/ Extravasation (crawling between adjacent endothelial cells)
 - Chemotaxis (following a scent of soluble mediators to the site of injury)



Soluble Mediators of Inflammation

- Although some of the immediate effects of inflammation are neurological, most are caused by release of chemical mediators
- These mediators may be released **preformed** from cells, **newly formed** in response to the damage, or be present as **plasma proteins**

Preformed Mediators

Histamine: present in **mast cells** and basophils - results in immediate increased vascular permeability, vasodilation.

- **Serotonin:** released from **mast cells** and **platelets** - vasodilation of venules only.

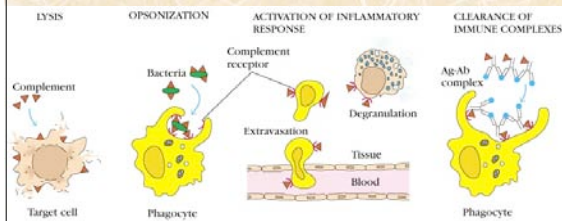
Newly Formed Mediators

- Arachidonic Acid Metabolites (from cell wall components), including the **Prostaglandins** and **Leukotrienes** (PGX_n , LTX_n)
- **Vasodilation** - PGE_1 , PGE_2
- **Vascular Permeability** - LTC_4 , LTD_4 , LTE_4
- **Chemotaxis** - LTB_4
- **Fever** - PGE_2
- **Pain** - PGE_2

Plasma Protein Cascades

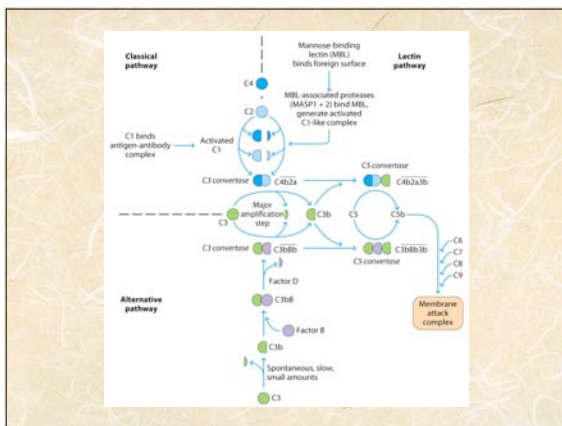
- **Kinins**, including **Bradykinin**
 - Bradykinin causes increased vascular permeability, pain
- **Complement Cascade**
 - Components **C3a** (vascular permeability) and **C5a** (vascular permeability, chemotaxis) derived from plasma proteins

Complement (Chapter 13)



Complement

- Complement is a cascade of serum proteins (like the clotting system) capable of multiple functions following activation
- It can be activated by **the classical pathway** (Ag-Ab), **the alternative pathway** (bacterial cell walls), or **the lectin pathway** (other cell wall components)



Next Lecture

- Complement - Chapter 13
- Acquired Immunity (Introduction)
 - T cells versus B cells
 - Cellular versus Humoral Response
 - Primary and Secondary (memory) responses.
 - Generation of Immune Cells
