

INFLAMMATION

L 25 - INFLAMMATORY PROCESS

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CHEMOTAXIS

- **Recognition** of the chemotactive factor.
- **Transduction** of the chemotactive stimulus or signal.
- **Orientation** of the cell (arrangement of the microtubules).
- Activation of the **locomotor** apparatus (polarization and assembly of actin and myosin filaments).
- **Ionic fluxes** to maintain membrane and sub-membrane organelle irritability.
- Changes in **membrane charges** and polarity (for maintenance of adherence).
- **Sustained locomotion** with reversible adhesion and renewable gradient detection.

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- Not random but **directional movement** towards a chemical gradient
- At site of inflammatory reaction there is a higher concentration of chemoattractants
- Leukocytes crawl but can swim
- Formation of large surface **lamellipodia** at the leading edge with blunt tail at the rear end which occur within 30 seconds of stimulation.
- They easily change their shape while passing through narrowed spaces.
- Chemotactic mechanism requires
 - adherence,
 - secretion and
 - locomotion

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- **First event**, binding of chemotactic factors with the specific receptors on the leukocytes
 - Chemotactic Factors include
 - Complement components
 - Arachadonic Acid (AA) metabolites
 - Soluble bacterial products (LPS)
 - Chemokines
- When leukocytes realize that they have reached the site of inflammatory process so as to stop the locomotion?
 - When cell reach at the **highest concentration gradient** detected by receptor,
 - It may also be possible that plasma contains some **cell movement inhibitors**

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PHAGOCYTOSIS AND MICROBICIDAL MECHANISM

- **Phagocytosis** (eating), pinocytosis (drinking).
- Phagocytosis (to eat and destroy)
 - Attach
 - Engulf
 - Kill
- Phagocytic cells have enhanced activity against **opsonized** (coated) substances/ microorganisms and the humoral factors those coat (butter) are termed as opsonins.
- **Antibodies, C3b and C4b** are important opsonizing substances, while fibronectin (glycoprotein) can also act as opsonin
- Degranulation and the oxidative burst destroy the engulfed particle

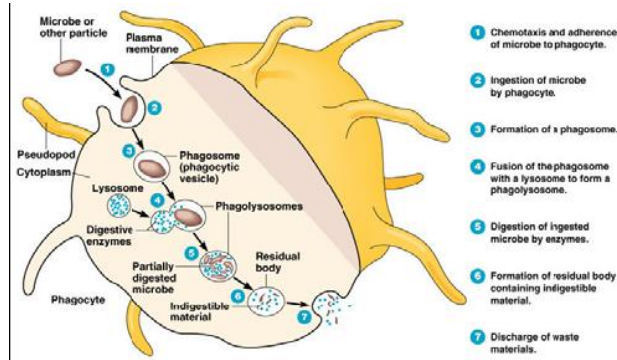
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- Lysosomal enzymes of neutrophils and macrophages participate in the degradation
- Phagocytosis process require recognition of the material to be engulfed, formation of phagocytic vacuole or phagosome and fusion of the phagosome with lysosome -- phagolysosome
- The enzymes and antibacterial products in the lysosome are the central
- The process of phagocytosis is accelerated at higher temperature (fever).

1. OXYGEN DEPENDENT MECHANISM

- In Neutrophil -- **burst of metabolic activity**, increase in O_2^- generation and H_2O_2 formation.
- Hydrogen peroxide combines with myeloperoxidase along with halide (iodide, bromide or chloride) and forms H_2O_2 - **myeloperoxidase-halide system**. Final killer molecule in this system is **hypochlorite** (HOCl)

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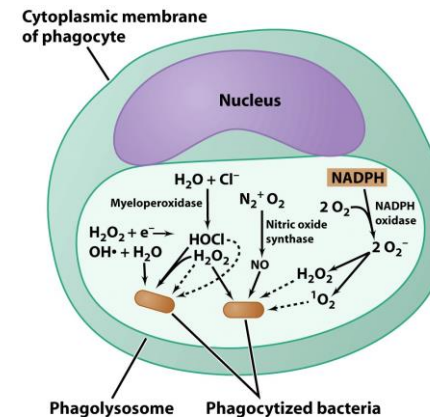


Figure 22-6 Brock Biology of Microorganisms 11/e
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2. OXYGEN INDEPENDENT MECHANISM

- The **lysozyme** attacks bacterial cell walls of especially **gram negative** bacteria (digest **muramic Acid** in membrane)
- **Lactoferrin** is microbicidal at **acid pH**
- **Cathepsin G** (a protease) is antibacterial activity against **gram negative and gram positive** bacteria and some of the fungi.
- **Phagocytin** can also lyse the bacterial cell membranes,
- **Defensins** have broad spectrum activity and kills gram positive, gram negative bacteria, some of the fungi and certain enveloped viruses.
- **Finally digested by acid hydrolases and other enzymes present in the lysosomes.**

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INFLAMMATION

CHEMICAL MEDIATORS

CHEMICAL MEDIATORS OF INFLAMMATION

- **Act on** Blood Vessels and/or Leukocytes and help to initiate infl.
- **Cause**
 - Increase in **Blood Flow**
 - Increase in blood vessel **permeability**
 - **Emigration** of Leukocytes
 - **Chemotaxis**
- **Originate** from plasma or from cells
- **Bind to** specific cellular receptors, have direct enzymatic activity, or mediate oxidative damage
- **One mediator** can stimulate release of additional mediators (amplification or regulation)
- **Effects on multiple cell** types, varying effects on different cells.
- **Short lived**, Quickly decay (AA metabolites), are inactivated enzymatically (kininase), or are scavenged (antioxidants)

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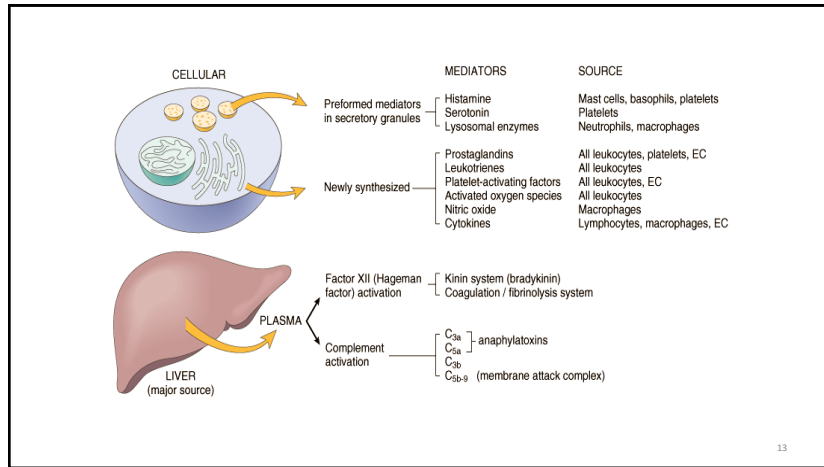
SOURCES

- **Exogenous**
 - Bacterial LPS (Endotoxins)
- **Endogenous**
 - Greater in amount compared with exogenous
 - Plasma, Leukocytes, Tissue Cells

NATURE

- **Amines** Histamine, Serotonin
- **Lipids** LTB4, PAF
- **Glycoproteins** IFN
- **Polypeptide** C5a

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AMINES

➤ Histamine

- Major source is mast cell granules (preformed)
- Formed from **histidine** (amino acid)
- Release stimulated by trauma, IgE mast cell FcR, heat or cold, complement (C3a, C5a), cytokines (IL1, IL8), leukocyte-derived histamine-releasing peptides
- **Acute phase** mediator
- Major action is **arteriolar dilatation** and increased vascular permeability (smooth muscle contraction)
- G-protein coupled receptor

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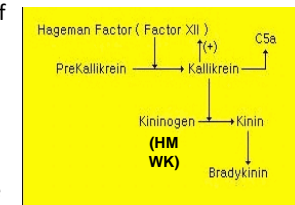
➤ Serotonin (5HT)

- Major source is **platelet** granules (preformed) but other cells include, GIT, Brain, Lung
- Formed from dietary **Tryptophan**
- Platelet aggregation result its release (collagen, thrombin, ADP, PAF from mast cells act as stimulus for platelet activation and aggregation)
- Major action is **arterial dilation** and increased vascular permeability
- Can induce **pain**
- 5-HT receptor

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KININS

- Leads to formation of **bradykinin** from cleavage of precursor (HMWK), Kininogens are formed in liver
 - Vascular permeability
 - Arteriolar dilation
 - Non-vascular smooth muscle contraction (e.g., bronchial smooth muscle)
 - Causes pain
 - Rapidly inactivated (kininases)



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