ACUTE INFLAMMATION: CELLULAR EVENTS
OUTLINE

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INTRODUCTION

• Inflammation is a response of living, vascularized tissues to infections or injury
• A protective response
• Normally controlled but may be harmful
• May be acute or chronic
CARDINAL SIGNS OF INFLAMMATION

- Rubor (redness)
- Calor (heat)
- Tumor (swelling)
- Dolor (pain)
- functio laesa (Loss of function)
CAUSES OF INFLAMMATION

• Infection
• Tissue necrosis
• Foreign bodies
• Immune reaction
ACUTE INFLAMMATION

• The initial, rapid response to infections and tissue damage is called acute inflammation.
• It typically develops within minutes or hours and is of short duration, lasting for several hours or a few days;
• its main characteristics are the exudation of fluid and plasma proteins (edema) and the emigration of leukocytes, predominantly neutrophils (also called polymorphonuclear leukocytes).
### Differences between Acute and Chronic Inflammation

<table>
<thead>
<tr>
<th>Feature</th>
<th>Acute</th>
<th>Chronic</th>
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<tbody>
<tr>
<td>Onset</td>
<td>Fast: minutes or hours</td>
<td>Slow: days</td>
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<tr>
<td>Cellular infiltrate</td>
<td>Mainly neutrophils</td>
<td>Monocytes/macrophages and lymphocytes</td>
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<tr>
<td>Tissue injury, fibrosis</td>
<td>Usually mild and self-limited</td>
<td>Often severe and progressive</td>
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<tr>
<td>Local and systemic signs</td>
<td>Prominent</td>
<td>Less</td>
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Steps in inflammatory response (5 R's)

• Recognition of injurious agent
• Recruitment of leukocytes
• Removal of the agent
• Regulation of response
• Resolution
Recognition of microbes and damaged cells

- Cell receptors for microbes (toll-like receptors)
- Sensors of cell damage (inflammosome)
- Dendritic cell, macrophages and other leukocytes
Recruitment of leukocytes to the site of inflammation

- change in blood flow and vascular permeability lead to influx of leukocyte
- journey from vessel to lumen is mediated and controlled by adhesion molecules and cytokines called chemokines
- process of leukocyte recruitment can be divided into sequential phases:
  1. in the lumen
  2. migration across the endothelium
  3. migration in the tissue toward a chemotactic stimulus
The multistep process of leukocyte migration through blood vessels, shown here for neutrophils.
leukocyte Adhesion to Endothelium

• Margination
• Rolling mediated by selectins(L,E,P)
• Adhesion mediated by integrins (LFA-1, MAC-1, VLA-4)
Leukocyte Migration through Endothelium

• also called transmigration or diapedesis
• Migration through interendothelial space mediated by PECAM-1(CD 31)
• Piercing of basement membrane by secreting collagenase
Chemotaxis of leukocyte

• leukocytes move in tissue towards site of injury by a process called chemotaxis
• endogenous and exogenous substances act as chemoattractants
• endogenous agents are cytokines, component of complement system, arachidonic acid; exogenous agents are bacteria product-peptides that possess an N-formylmethionine terminal amino acids and some lipids
• chemotactic agents bind to specific G-protein-coupled receptors on the surface of leukocytes. Signals initiated from these receptors result in activation of second messengers that increase cytosolic calcium and activate small guanosine triphosphatases.
• These signals induce polymerization of actin, resulting in increased amounts of polymerized actin at the leading edge of the cell and localization of myosin filaments at the back. The leukocyte moves by extending filopodia that pull the back of the cell in the direction of extension.
Scanning electron micrograph of a moving leukocyte in culture showing a filopodium (upper left) and a trailing tail.
Phagocytosis and Removal of Offending agent/leukocyte activation

• Phagocytosis involves three sequential steps:

(1) recognition and attachment of the particle to be ingested by the leukocyte; (by phagocytic receptors)
(2) engulfment, with subsequent formation of a phagocytic vacuole; and
(3) killing or degradation of the ingested material (ROS)
Neutrophil Extracellular Traps

• NETs are extracellular fibrillar networks
• NETs provide a high concentration of antimicrobial substances at sites of infection
• NETs prevent the spread of the microbes by trapping them in the fibrils.
• They are produced by neutrophils in response to infectious pathogens (mainly bacteria and fungi) and inflammatory mediators (e.g., chemokines, cytokines [mainly interferons], complement proteins, and ROS)
• In the process of NET formation, the nuclei of the neutrophils are lost, leading to death of the cells.
Regulation of acute inflammatory response

• Inflammation declines after the offending agents are removed simply because the mediators of inflammation are produced in rapid bursts, only as long as the stimulus persists, have short half-lives, and are degraded after their release.

• In addition, as inflammation develops, the process itself triggers a variety of stop signals that actively terminate the reaction.

• These active termination mechanisms include a switch in the type of arachidonic acid metabolite produced, from proinflammatory leukotrienes to antiinflammatory lipoxins, and the liberation of antiinflammatory cytokines, including transforming growth factor-β (TGF-β) and IL-10, from macrophages and other cells.
Outcomes of acute inflammation

• complete resolution
• healing by connective tissue replacement
• chronic inflammation
Conclusion

Acute inflammation is the rapid response of living vascularised tissue to infection or injury. It is normally controlled but may be harmful and leukocytes play a major role in acute inflammation.