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INFLAMMATION 1

Inflammation is a response of vascularized tissues to infections and tissue damage that brings cells and molecules of host defense from the circulation to the sites where they are needed, to eliminate the offending agents.

THE TYPICAL INFLAMMATORY REACTION DEVELOPS THROUGH A SERIES OF SEQUENTIAL STEPS:

Recognition → Recruitment → Activation → Termination → Repair

CARDINAL SIGNS

The external manifestations of inflammation are:
heat (calor in Latin). redness (rubor) swelling (tumor), pain (dolor),
loss of function (functio laesa).

Recognition

CELLULAR RECEPTORS FOR MICROBES

The best defined of these receptors belong to the family of Toll-like receptors (TLRs)

Recognition of microbes by these receptors stimulates the production proteins.

These proteins include:

cytokines that induce inflammation.

anti-viral cytokines (interferons).

cytokines and membrane proteins.

SENSORS OF CELL DAMAGE

uric acid (a product of DNA breakdown),
ATP (released from damaged mitochondria),
reduced intracellular K+ concentrations (reflecting loss of ions because of plasma membrane injury),
DNA (when it is released into the cytoplasm).

The receptors activate inflammasome, which induces the production of the cytokine interleukin-1 (IL-1), that recruits
leukocytes and thus induces inflammation

THE INFLAMMASOME ALSO HAS BEEN IMPLICATED IN INFLAMMATORY REACTIONS TO
urate crystals (the cause of gout, pseudogout)
cholesterol crystals (in atherosclerosis)
lipids (in metabolic syndrome and obesity-associated diabetes)
amyloid deposits in the brain (in Alzheimer disease).

CIRCULATING PROTEINS

The complement system reacts against microbes and produces mediators of inflammation

Important

Table 3.2 Disorders Caused by Inflammatory Reactions

Disorders	Cells and Molecules Involved in Injury
Acute	
Acute respiratory distress syndrome	Neutrophils
Asthma	Eosinophils; IgE antibodies
Glomerulonephritis	Antibodies and complement; neutrophils, monocytes
Septic shock	Cytokines
Chronic	
Arthritis	Lymphocytes, macrophages; antibodies?
Asthma	Eosinophils; IgE antibodies
Atherosclerosis	Macrophages; lymphocytes
Pulmonary fibrosis	Macrophages; fibroblasts

Table 3.1 Features of Acute and Chronic Inflammation

Feature	Acute	Chronic
Onset	Fast: minutes or hours	Slow: days
Cellular infiltrate	Mainly neutrophils	Monocytes/macrophag and lymphocytes
Tissue injury, fibrosis	Usually mild and self-limited	May be severe and progressive
Local and systemic signs	Prominent	Less

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Reactions of Blood Vessels in Acute Inflammation:

1.Vasodilation:

-induced by histamine, acting on vascular smooth muscle
-The result is increased blood flow, which is the cause of heat and redness (erythema) at the site of inflammation.

2. increased permeability :

HOW DOSE THE VASCULAR PERMEABILITY INCREASED?

1. Retraction of endothelial cells (immediate transient response):
It is elicited by histamine, bradykinin, leukotrienes.
2. Endothelial injury:
3. transcytosis:
Increased transport of fluids and proteins

3.emigration of the leukocytes :

In inflammation, lymph flow is increased to help drain edema fluid that accumulates because of increased vascular permeability.

The lymphatics may become secondarily inflamed (lymphangitis), as may the draining lymph nodes (lymphadenitis).

RESPONSES OF LYMPHATIC VESSELS AND LYMPH NODES

3. vascular congestion:
stasis of blood flow, engorgement of small vessels due to slow blood flow.
4. blood leukocytes, principally neutrophils, accumulate along the vascular endothelium, endothelial cells are activated and leukocytes then migrate through the vascular wall into the interstitial tissue

Clinically:

*Edema denotes an excess of fluid in the interstitial tissue or serous cavities; it can be either an exudate or a transudate.
*Pus: a purulent exudate, is an inflammatory exudate rich in leukocytes (mostly neutrophils), the debris of dead cells, and, in many cases, microbes.

	Neutrophils	Macrophages
Origin	HSCs in bone marrow	• HSCs in bone marrow (in inflammatory reactions) • Many tissue-resident macrophages: stem cells in yolk sac or fetal liver (early in development)
Life span in tissues	1–2 days	Inflammatory macrophages: days or weeks Tissue-resident macrophages: years
Responses to activating stimuli	Rapid, short-lived, mostly degranulation and enzymatic activity	More prolonged, slower, often dependent on new gene transcription
• Reactive oxygen species	Rapidly induced by assembly of phagocyte oxidase (respiratory burst)	Less prominent
• Nitric oxide	Low levels or none	Induced following transcriptional activation of iNOS
• Degranulation	Major response; induced by cytoskeletal rearrangement	Not prominent
• Cytokine production	Low levels or none	Major functional activity, requires transcriptional activation of cytokine genes
• NET formation	Rapidly induced, by extrusion of nuclear contents	No
• Secretion of lysosomal enzymes	Prominent	Less

HSC, Hematopoietic stem cells; *iNOS*, inducible nitric oxide synthase; *NET*, neutrophil extracellular traps.
This table lists the major differences between neutrophils and macrophages. The reactions summarized above are described in the text. Note that the two cell types share many features, such as phagocytosis, ability to migrate through blood vessels into tissues, and chemotaxis.