Inflammation

Lec. 1

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Objectives of lecture :

1- definition of inflammation in general.

2- main steps of inflammation

3- types of inflammation

4- cardinal signs of inflammation

5- causes of inflammation in general

6- major component of acute inflammation and talk about two of these component

7- response of lymphatic vessels and lymph node to inflammation

Inflammation •

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.

Inflammation suggests a harmful reaction, it is actually a protective response • that is essential for survival. It serves to rid the host of both the initial cause of cell injury (e.g., microbes, toxins) and the consequences of such injury (e.g., necrotic cells and tissues).

The typical inflammatory reaction develops through a series of sequential steps:

1- The offending agent, which is located in extravascular tissues, is recognized by host cells and molecules.
2- Leukocytes and plasma proteins are recruited from the circulation to the site where the offending agent is located.
3- The leukocytes and proteins are activated and work together to destroy and eliminate the offending substance.
4- The reaction is controlled and terminated.
5- The damaged tissue is repaired.

Inflammation may be of two types

acute and **chronic**

acute inflammation: is a rapid response to infections and tissue damage, 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), when acute inflammation achieves its desired goal of eliminating the offenders, the reaction subsides and residual injury is repaired.

Inflammation is induced by chemical mediators that are produced by host cells in response to injurious stimuli, When a microbe enters a tissue or the tissue is injured, the presence of the infection or damage is sensed by resident cells, including macrophages, dendritic cells, mast cells, and other cell types. These cells secrete molecules (cytokines and other mediators) that induce and regulate the subsequent inflammatory response.

The external manifestations of inflammation:

Often called its cardinal signs are

1. heat
2. redness.
3. swelling (tumor).
4. Pain .
5. and loss of function .

CAUSES OF INFLAMMATION

Inflammatory reactions may be triggered by a variety of stimuli:

1. Infections (bacterial, viral, fungal, parasitic) and microbial toxins are among the most common and medically important causes of inflammation. Different infectious pathogens elicit distinct inflammatory responses, from mild acute inflammation that causes little or no lasting damage and successfully eradicates the infection, to severe systemic reactions that can be fatal, to prolonged chronic reactions that cause extensive tissue injury.
2. Tissue necrosis elicits inflammation regardless of the cause of cell death, which may include ischemia (reduced blood flow, the cause of myocardial infarction), trauma, and physical and chemical injury (e.g., thermal injury, as in burns or frostbite; irradiation; exposure to some environmental chemicals). Several molecules released from necrotic cells are known to trigger inflammation .

3- Foreign bodies (splinters, dirt, sutures) may elicit inflammation by themselves or because they cause traumatic tissue injury or carry microbes. Even some endogenous substances stimulate potentially harmful inflammation if large amounts are deposited in tissues; such substances include urate crystals (in the disease gout), and cholesterol crystals (in atherosclerosis).

4- Immune reactions (also called hypersensitivity) are reactions in which the normally protective immune system damages the individual's own tissues. The injurious immune responses may be directed against self-antigens, causing autoimmune diseases, or may be inappropriate reactions against environmental substances, as in allergies, or against microbes. Inflammation is a major cause of tissue injury in these diseases . Because the stimuli for the inflammatory responses in autoimmune and allergic diseases (self and environmental antigens) cannot be eliminated, these reactions tend to be persistent and difficult to cure, are often associated with chronic inflammation, and are important causes of morbidity and mortality.

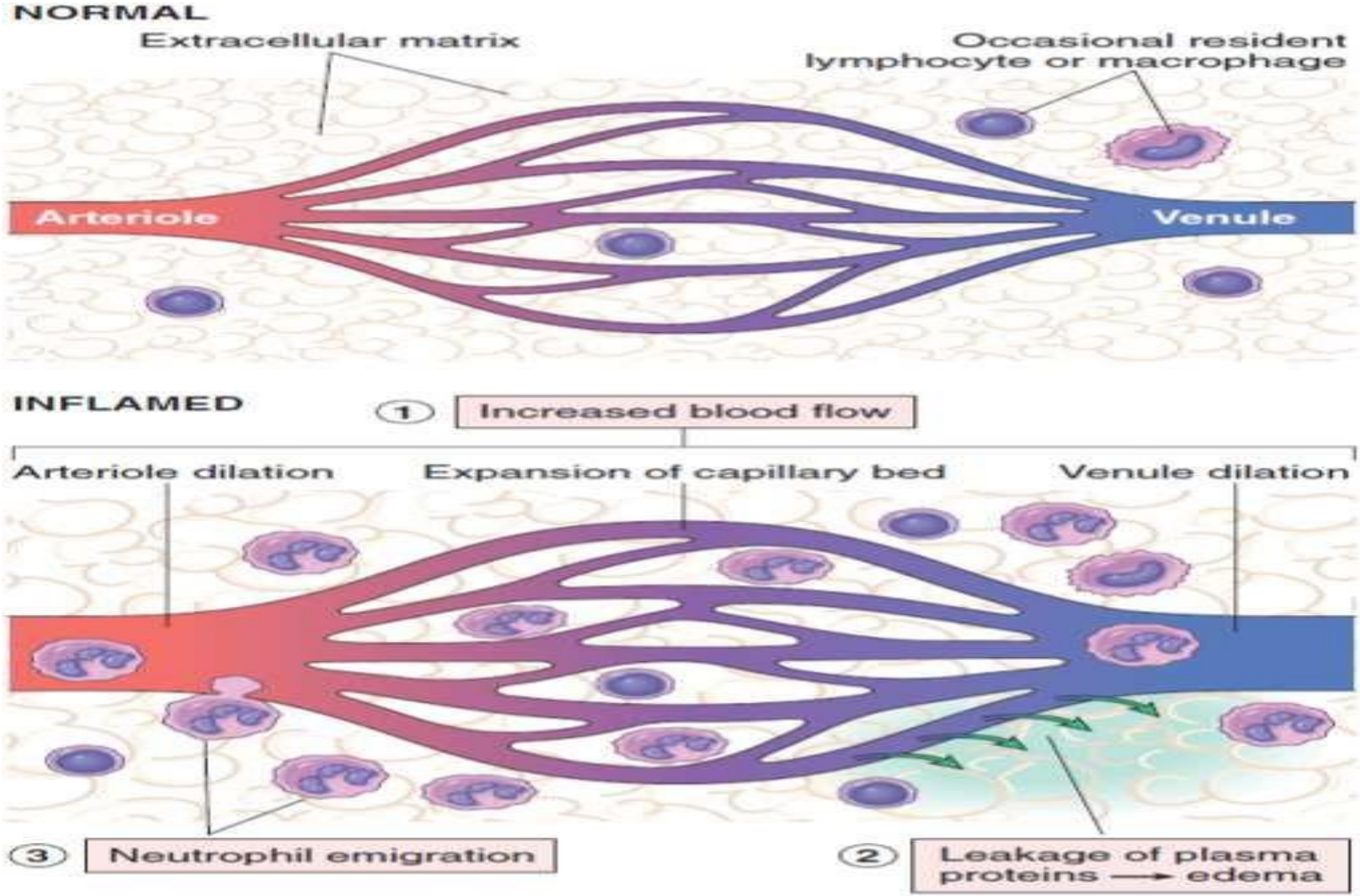
ACUTE INFLAMMATION •

Acute inflammation has three major components: •

(1) dilation of small vessels, leading to an increase in blood flow. •

(2) increased permeability of the microvasculature, enabling plasma proteins •
and leukocytes to leave the circulation.

(3) emigration of the leukocytes from the microcirculation, their accumulation •
in the focus of injury, and their activation to eliminate the offending agent ,when an injurious agent, such as an infectious microbe or dead cells, is encountered, phagocytes that reside in all tissues try to eliminate these agents. At the same time, phagocytes and other sentinel cells in the tissues recognize the presence of the foreign or abnormal substance and react by liberating soluble molecules that mediate inflammation. Some of these mediators act on small blood vessels in the vicinity and promote the efflux of plasma and the recruitment of circulating leukocytes to the site where the offending agent is located.


NORMAL
Extracellular matrix
Occasional resident lymphocyte or macrophage
Arteriole
Venule
INFLAMED
1
Increased blood flow
Arteriole dilation
Expansion of capillary bed
Venule dilation
3
Neutrophil emigration
2
Leakage of plasma proteins → edema

Reactions of Blood Vessels in Acute Inflammation •

- The vascular reactions of acute inflammation consist of changes in the flow of blood and the permeability of vessels, both designed to maximize the movement of plasma proteins and leukocytes out of the circulation and into the site of infection or injury. The escape of fluid, proteins, and blood cells from the vascular system into interstitial tissues or body cavities is known as exudation. An exudate is an extravascular fluid that has a high protein concentration and contains cellular debris. Its presence implies that there is an increase in the permeability of small blood vessels, typically during an inflammatory reaction. In contrast, a transudate is a fluid with low protein content, little or no cellular material, and low specific gravity, the inflammatory exudate rich in leukocytes (mostly neutrophils), the debris of dead cells, and, in many cases, microbes.

Changes in Vascular Flow and Caliber

Changes in vascular flow and caliber begin early after injury and consist of the following:

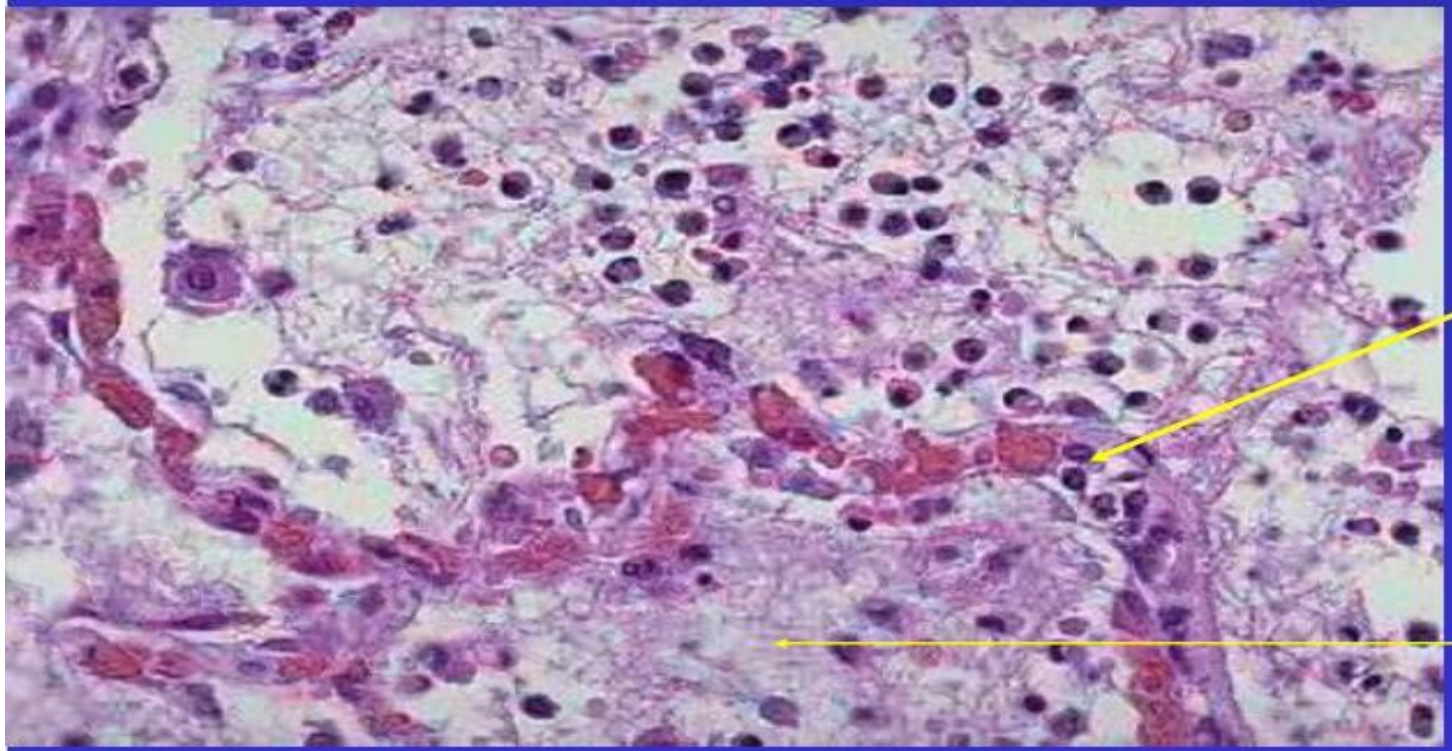
1- Vasodilation is induced by the action of several mediators, notably histamine, on vascular smooth muscle. It is one of the earliest manifestations of acute inflammation, and may be preceded by transient vasoconstriction. Vasodilation first involves the arterioles and then leads to the opening of new capillary beds in the area. The result is increased blood flow, which is the cause of heat and redness (erythema) at the site of inflammation.

2- Vasodilation is quickly followed by increased permeability of the microvasculature, with the outpouring of protein-rich fluid (an exudate) into the extravascular tissues.

3- The loss of fluid and increased vessel diameter lead to slower blood flow, concentration of red cells in small vessels, and increased viscosity of the blood. These changes result in stasis of blood flow, engorgement of small vessels jammed with slowly moving red cells, seen histologically as vascular congestion and externally as localized redness (erythema) of the involved tissue.

4- As stasis develops, blood leukocytes, principally neutrophils, accumulate along the vascular endothelium. At the same time endothelial cells are activated by mediators produced at sites of infection and tissue damage, and express increased levels of adhesion molecules. Leukocytes then adhere to the endothelium, and soon afterward they migrate through the vascular wall into the interstitial tissue .

Acute Inflammation



Vascular congestion:

dilated capillary

Fluid exudate:

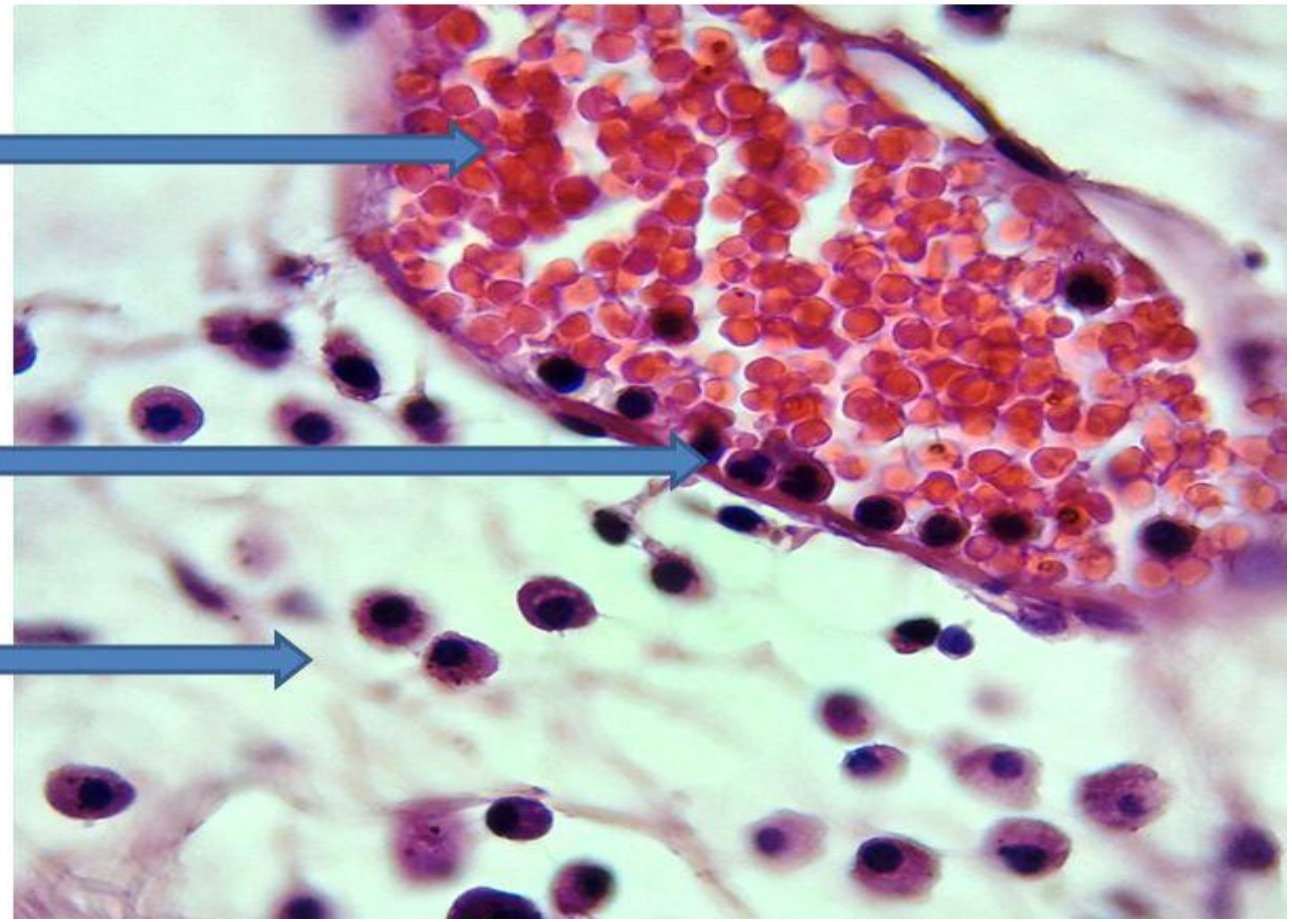
Protein rich fluid moved from vessels to extravascular space

Diapédèse leucocytaire

Congestion

Margination + Adhésion Leucocytaire

Œdème inflammatoire

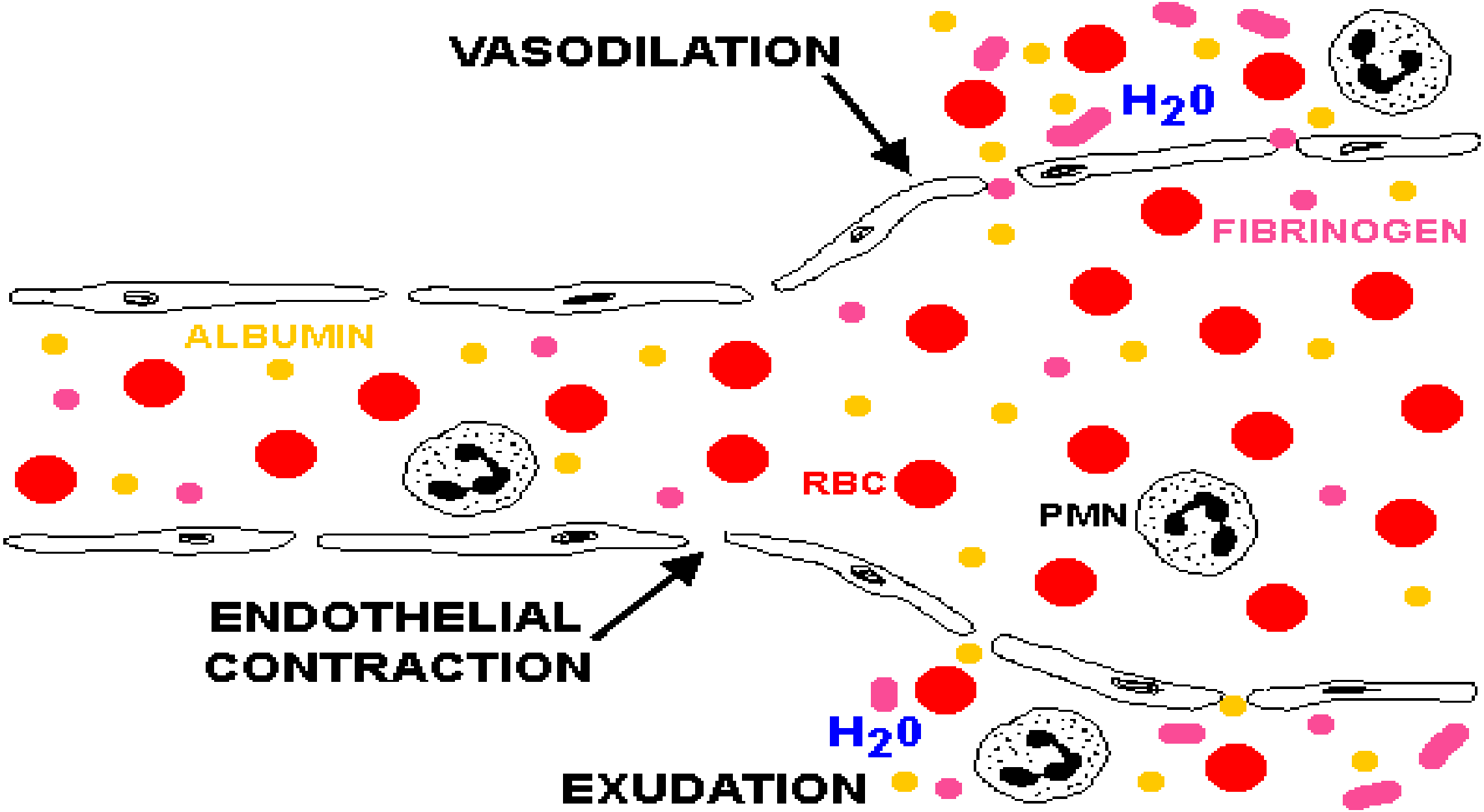


Increased Vascular Permeability (Vascular Leakage)

- Several mechanisms are responsible for increased vascular permeability in acute inflammation which include:

1- Retraction of endothelial cells resulting in opening of inter-endothelial spaces is the most common mechanism of vascular leakage, it is elicited by histamine, bradykinin, leukotrienes, and other chemical mediators. It occurs rapidly after exposure to the mediator (within 15 to 30 minutes) and is usually short-lived; hence, it is referred to as the immediate transient response, to distinguish it from the delayed prolonged response that follows endothelial injury, the main sites for this rapid increase in vascular permeability are post capillary venules.

2- Endothelial injury, resulting in endothelial cell necrosis and detachment. Direct damage to the endothelium is encountered in severe injuries, for example, in burns, or is induced by the actions of microbes and microbial toxins that target endothelial cells. Neutrophils that adhere to the endothelium during inflammation may also injure the endothelial cells and thus amplify the reaction. In most instances leakage starts immediately after injury and is sustained for several hours until the damaged vessels are thrombosed or repaired.


VASODILATION
H_2O
FIBRINOGEN
ALBUMIN
RBC
PMN
ENDOTHELIAL
CONTRACTION
H_2O
EXUDATION

Responses of Lymphatic Vessels and Lymph Nodes•

- In addition to blood vessels, lymphatic vessels also participate in acute inflammation. The system of lymphatics and lymph nodes filters and polices the extravascular fluids. Lymphatics drain the small amount of extravascular fluid that seeps out of capillaries under normal circumstances. In inflammation, lymph flow is increased to help drain edema fluid that accumulates because of increased vascular permeability. In addition to fluid, leukocytes and cell debris, as well as microbes, may find their way into lymph. Lymphatic vessels, like blood vessels, proliferate during inflammatory reactions to handle the increased load. The lymphatics may become secondarily inflamed (lymphangitis), as may the draining lymph nodes (lymphadenitis). Inflamed lymph nodes are often enlarged because of increased cellularity. This constellation of pathologic changes is termed reactive, or inflammatory, lymphadenitis. For clinicians the presence of red streaks near a skin wound is a telltale sign of an infection in the wound. This streaking follows the course of the lymphatic channels and indicates the presence of lymphangitis; it may be accompanied by painful enlargement of the draining lymph nodes, indicating lymphadenitis.