IMMUNOLOGY OF INFLAMMATION.

- Learning objectives.
- Types of inflammation
- Causes of inflammation
- Stimuli for inflammatory processes
- Cellular events- Leukocyte extravasation and phagocytosis.
- Chemical mediators of inflammation.
- Termination of inflammatory response.

Introduction.

- In vascularized tissues, exogenous and endogenous stimuli provoke a host of response called inflammation.
- The unique feature of the inflammatory process is the reaction of blood vessels, leading to the accumulation of fluid and leukocytes in extravascular tissues.
- Inflammatory response is closely intertwined with the process of repair.

Thus:

- Inflammation serves to destroy, dilute, or wall off the injurious agent, and it sets into motion a series of events that try to heal and reconstitute the damaged tissue.

- Inflammation is fundamentally a protective response, the ultimate goal of which is to rid the organism of both the initial causes of cell injury (e.g., microbes, toxins) and the consequences, of such injury (e.g., necrotic cells).

NB: Inflammation and repair may be potentially harmful, however:

Inflammatory reactions, for example, underlie common chronic diseases, such as rheumatoid arthritis, atherosclerosis, and lung fibrosis, as well as life threatening hypersensitivity reactions.

Phases of inflammatory response:

- Inflammatory response consists of two components: a vascular reaction and a cellular reaction.
- The circulating cells include neutrophils, monocytes, eosinophils, lymphocytes, basophils and platelets.

Inflammation is divided into:

- **Acute inflammation** - rapid in onset (seconds or minutes) and is of relatively short duration.
- Its main characteristics are the exudation of fluid and plasma proteins, and the emigration of leukocytes, predominantly **neutrophils**.

- **Chronic inflammation** - is of longer duration and is associated with the presence of **lymphocytes** and macrophages, proliferation of blood vessels, fibrosis, and tissue necrosis.

- The vascular and cellular reactions of both acute and chronic inflammation are mediated by chemical factors that are derived from plasma proteins or cells, and are produced in response to or activated by the inflammatory stimulus.

Acute inflammation.

- Is a rapid response to an injurious agent that serves to deliver mediators of host defense- leukocytes and plasma proteins- to the site of injury.

- Major components:

➢ Alterations in vascular caliber that lead to an increase in blood flow

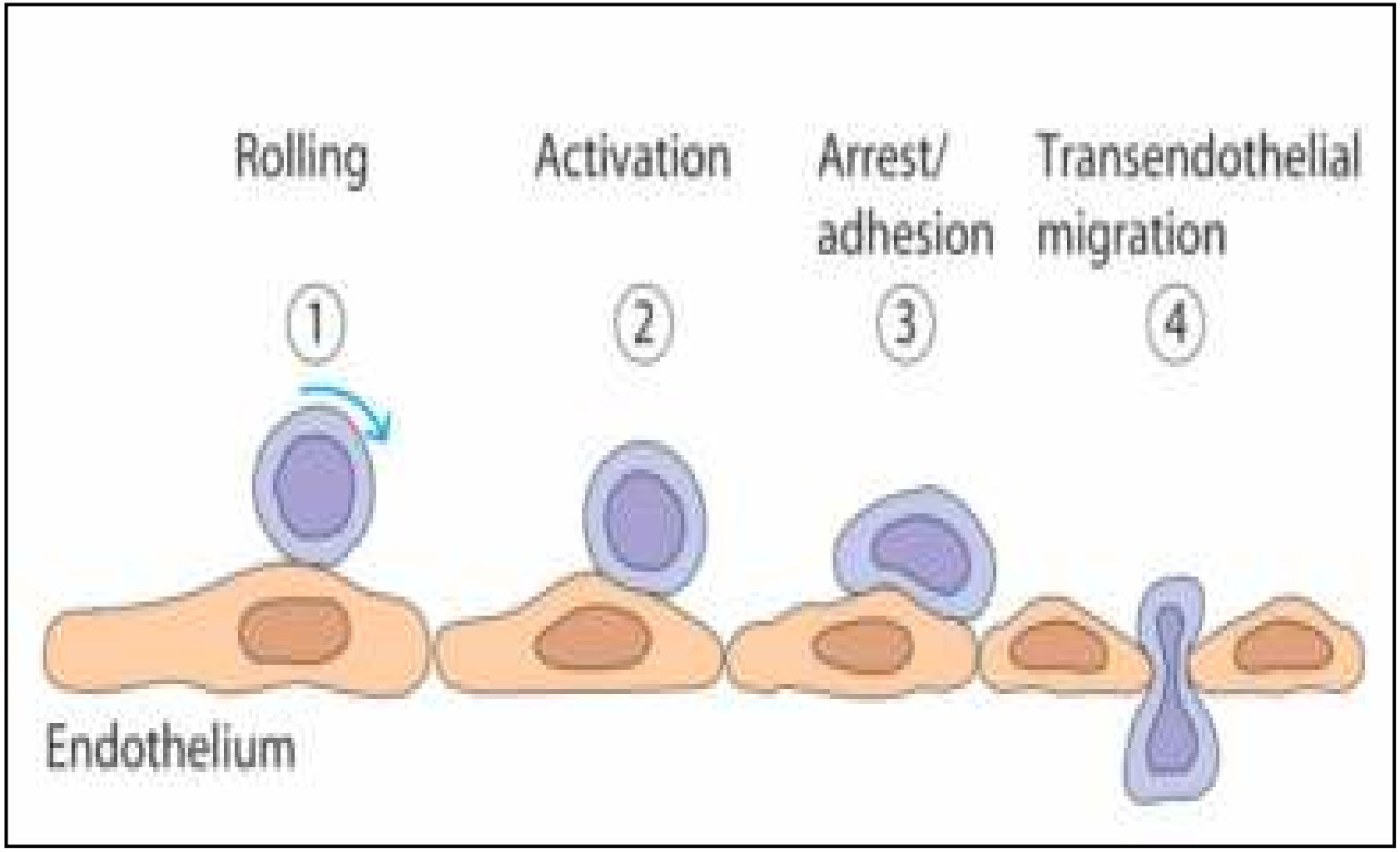
➢ Structural changes in the microvasculature that permit plasma proteins and leukocytes to leave the circulation

➢ Emigration of the leukocytes from the microcirculation, their accumulation in the focus of injury, and their activation to eliminate the offending agent.

Stimuli for acute inflammation.

- Varied and include, among others:
- Infections (bacterial, viral, parasitic) and microbial toxins
- Trauma (blunt and penetrating)
- Physical and chemical agents (thermal injury, e.g. , burns or frostbite; irradiation, e.t.c).
- Immune reactions (also called hypersensitivity)

Homing and movement of cells from peripheral blood into tissue during inflammatory response.



Vascular changes:

- Increased vascular permeability (vascular leakage):

➢ Leading to the escape of a protein-rich fluid (exudate) into the extravascular tissue.

Elicited by :

- histamine,
- bradykinin,
- leukotrienes (naturally produced eicosanoid lipid mediators, which may be responsible for the effects of an inflammatory response)
- Cytokines (IL-1, TNF, IFN-gamma);
- Many other chemical mediators.

Cellular events: leukocyte extravasation and phagocytosis.

- Useful to deliver leukocytes to the site of injury and to activate the leukocytes to perform their normal functions in host defense.
- Leukocytes ingest offending agents, kill bacteria and other microbes, and get rid of necrotic tissue and foreign substances.

However:

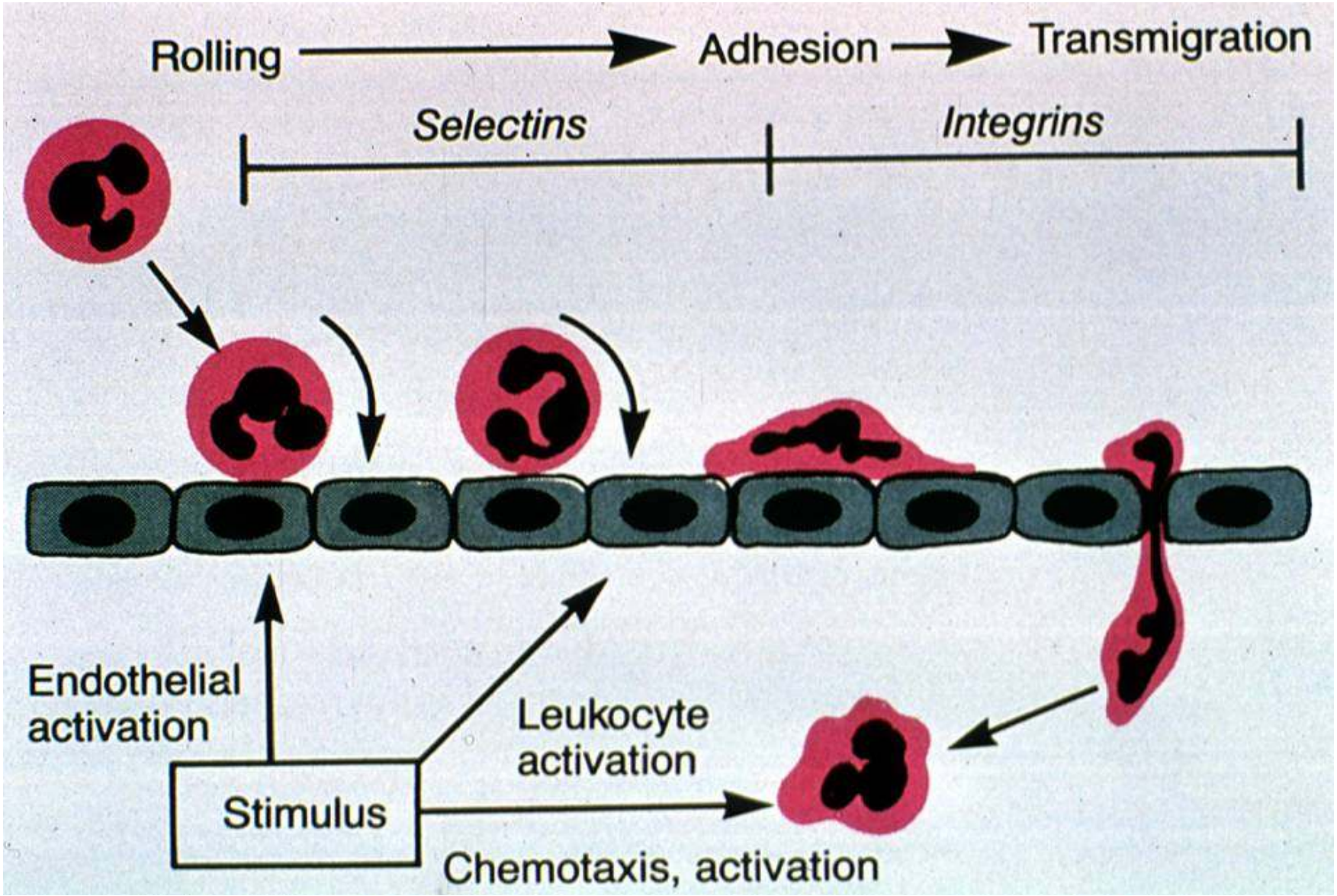
- A price paid for the defensive potency of leukocytes is that they may induce tissue damage and prolong inflammation, since the leukocyte products that destroy microbes and necrotic tissues can also injure normal host tissue.

Leukocyte adhesion and transmigration.

- Are regulated largely by the binding of complementary adhesion molecules on the leukocyte and endothelial surfaces, and
- chemical mediators- chemo attractants and certain cytokines- affect these processes by modulating the surface expression or avidity of such adhesion molecules.

- The adhesion receptors involved belong to 4 molecular families:

- The selectins (e.g. E-selectin, mucin-like glycoproteins- GlyCAM-1, CD34)
- The immunoglobulin superfamily (e.g. ICAM, VCAM)
- The integrins
- Mucin-like glycoproteins (e.g. heparan sulfate)


Rolling
Adhesion
Transmigration
Selectins
Integrins
Endothelial activation
Leukocyte activation
Stimulus
Chemotaxis, activation

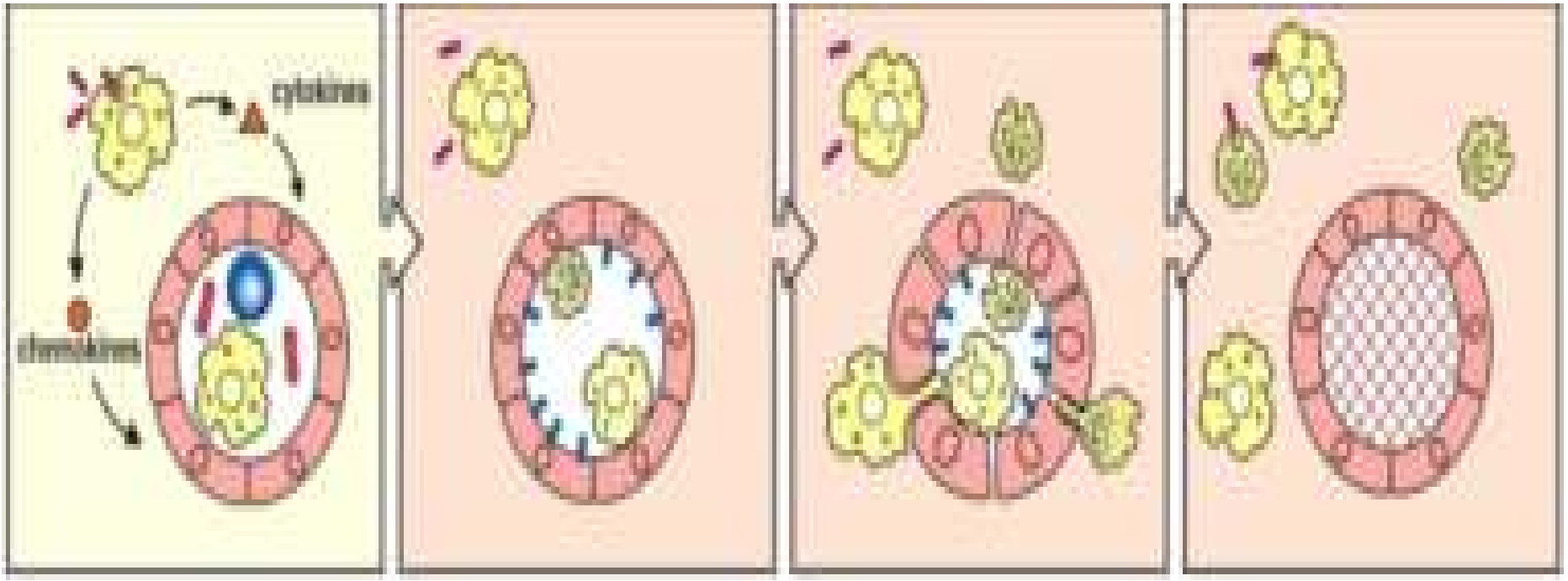
Acute Inflammatory Response.

Cytokines produced by Macrophages cause dilation of small blood vessels

Leukocytes move to periphery of blood vessels as a result of increased expression of adhesion molecules

Leukocyte extra vasate at the site of infection

Blood clotting occurs in the micro vessels.



Symptoms of Inflammatory response

- Wheal Response
- Pain
- Redness
- Heat
- Swelling

Chronic inflammation.

- Macrophages-
  - ➢ Interferon gamma (IFN-gamma)
  - ➢ Tumor necrosis factor alpha (TNF-alpha)

Anti-inflammatory agents.

- Reduce Extravasation

 - Anti-LFA antibodies

- Corticosteroids

 - Immune-suppressive, induce apoptosis.

- Non-steroidal anti-inflammatory drugs (NSAID)-

- Aspirin, ibuprofen, phenylbutazone, acetameniophen.