Immunity

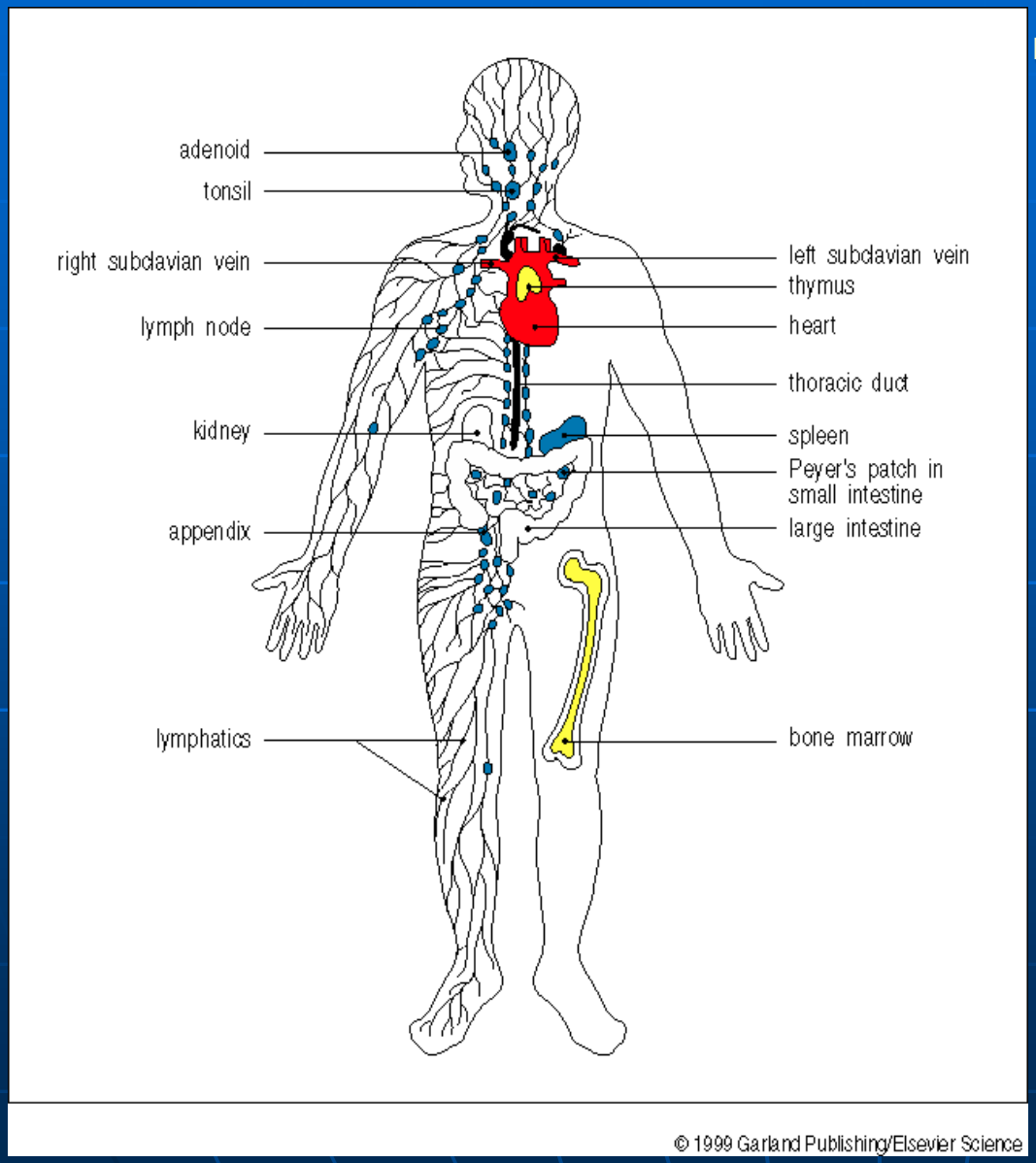
Learning objectives

- Explain what triggers an immune response and where in the body the immune response occurs.
- Understand how the immune system handles exogenous and endogenous antigen differently.
- Define the differences between innate and adaptive immunity and their complementary activities.
- Discuss how antigen specificity is achieved in the immune system.
- Understand the different roles of immune cells and their communication.
- Describe the structure and functions of different antibodies.
- Present an overview of immune system disorders.

Definition

- The human body has the ability to resist almost all types of organisms or toxins that tend to damage the tissues and organs. This capability is called *immunity*

ANATOMY OF THE IMMUNE SYSTEM



- The immune system is localized in several parts of the body
  - immune cells develop in the **primary organs** - bone marrow and thymus (yellow)
  - immune responses occur in the **secondary organs** (blue)

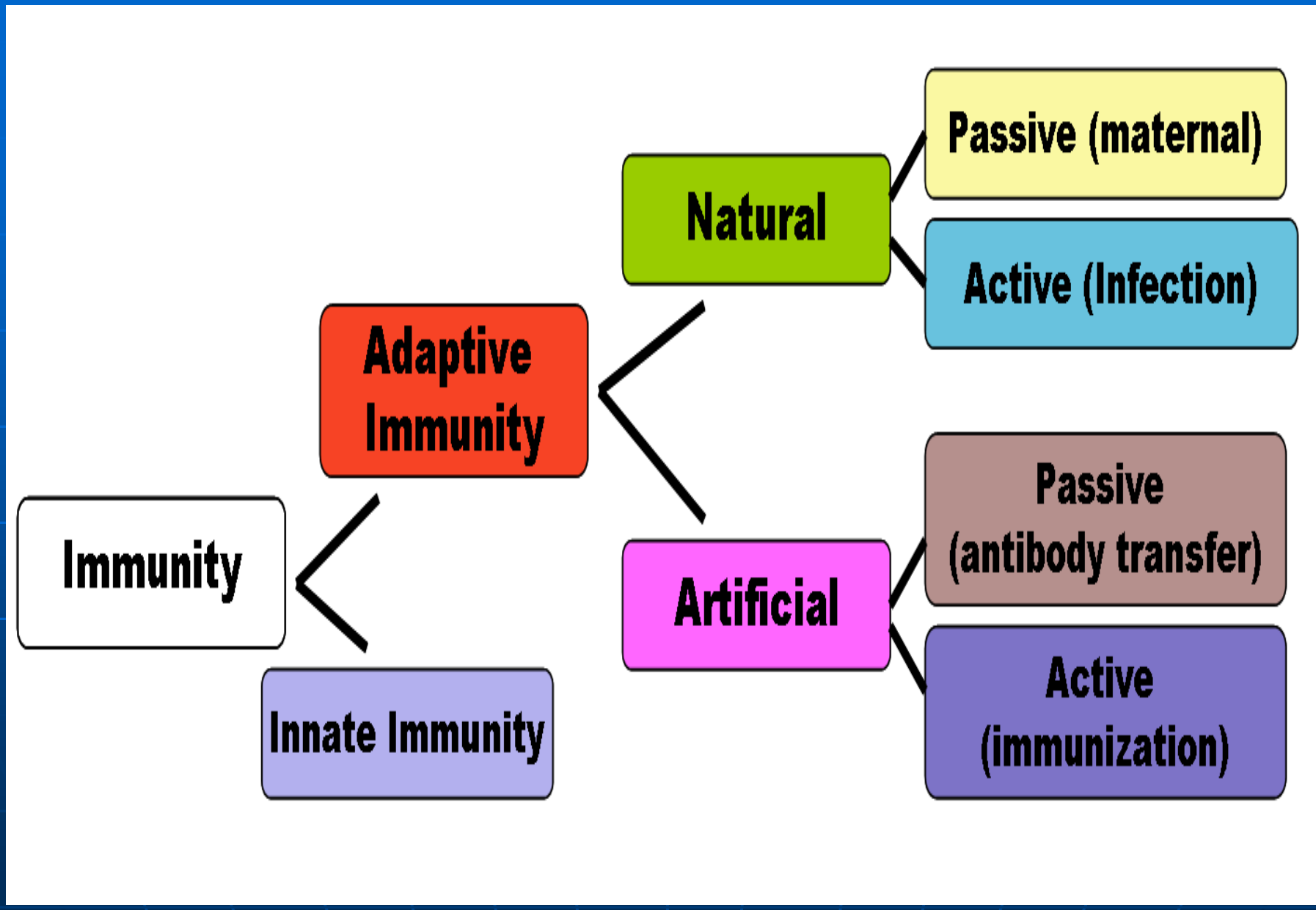
ANATOMY OF THE IMMUNE SYSTEM

- Thymus – glandular organ near the heart – where T cells learn their jobs

- Bone marrow – blood-producing tissue located inside certain bones
  - blood stem cells give rise to all of the different types of blood cells

- Spleen – serves as a filter for the blood
  - removes old and damaged red blood cells
  - removes infectious agents and uses them to activate cells called lymphocytes

- Lymph nodes – small organs that filter out dead cells, antigens, and other "stuff" to present to lymphocytes
- Lymphatic vessels – collect fluid (lymph) that has "leaked" out from the blood into the tissues and returns it to circulation


Immunity
Innate Immunity
Adaptive Immunity
Natural
Passive (maternal)
Active (Infection)
Artificial
Passive (antibody transfer)
Active (immunization)

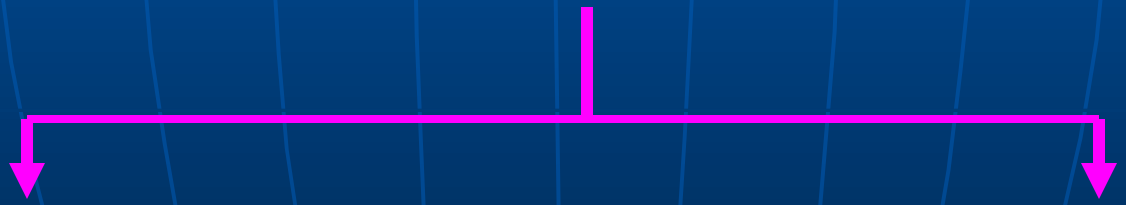
Innate Immunity

Innate Immunity

Defensive mechanisms include :

1) Innate immunity (Natural or Non specific)

2) Acquired immunity (Adaptive or Specific)



Cell-mediated immunity Humoral immunity

Component of Innate Immunity

Innate Immune system

First line

1) Mechanical barriers
2) Chemical & biochemical inhibitors
3) Normal flora

Second line

A- cells
- 1- Natural killer
- 2- Phagocytes

B- Soluble factors

C- Inflammatory barriers

Three Lines of Defense Against Infection

Nonspecific defense mechanisms		Specific defense mechanisms (immune system)
First line of defense	Second line of defense	Third line of defense
• Skin • Mucous membranes • Secretions of skin and mucous membranes	• Phagocytic white blood cells • Antimicrobial proteins • The inflammatory response	• Lymphocytes • Antibodies

First line

1) Mechanical barriers

- Intact skin
- Mucous coat
- Mucous secretion
- Blinking reflex and tears
- The hair at the nares
- Coughing and sneezing reflex

First line

2) Chemical & biochemical inhibitors

- Sweet and sebaceous secretion
- Hydrolytic enzymes in saliva
- HCl of the stomach
- Proteolytic enzyme in small intestine
- Lysozyme in tears
- Acidic pH in the adult vagina

First line

3) Normal bacterial flora

- Competition for essential nutrients

- Production of inhibitory substances

Second line

A) cells

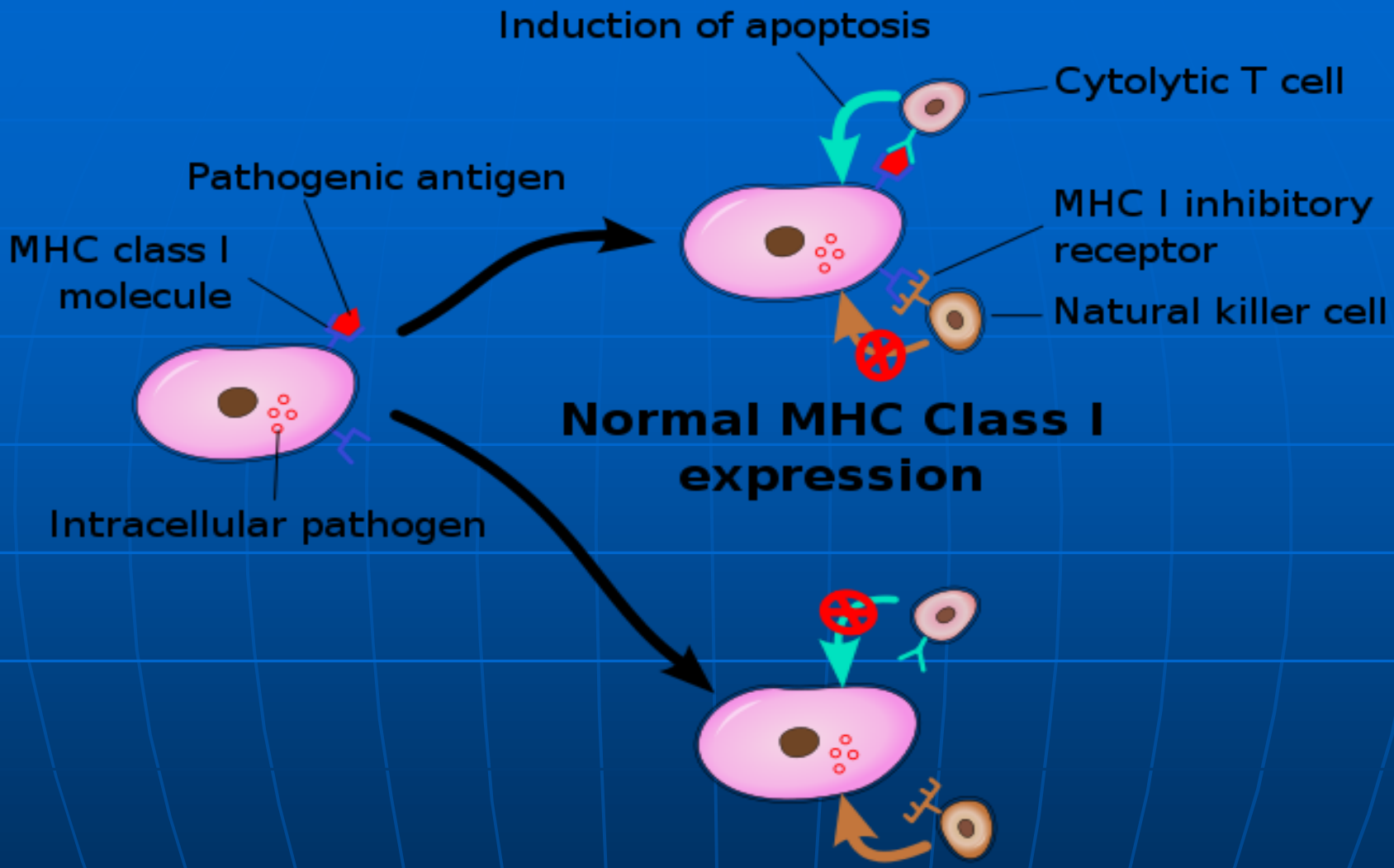
1- Natural killer (NK)

Definition: Large granular lymphocytes
Innate cytotoxic lymphocytes

Source : Bone marrow precursors

Location : 10% or 15% of lymphocytes in peripheral blood
1% or 2% of lymphocytes in spleen

Function : Cytotoxic for → Tumor cells
Viral infected cells
Responsible for → Bacterial, fungal, parasitic infection
antibody–dependent cell mediated cytotoxicity (ADCC)


Induction of apoptosis
Cytolytic T cell
Pathogenic antigen
MHC I inhibitory receptor
MHC class I molecule
Natural killer cell
Normal MHC Class I expression
Intracellular pathogen
MHC Class I downregulation by pathogen: "Missing Self"

Natural killer cells (NK cells)

- Instead of attacking the invaders, they attack the body's own cells that have become infected by viruses
- They bind to cells using an antibody "bridge", then kill it by secreting a chemical (perforin) that makes holes in the cell membrane of the target cell. With enough holes, the cell will die, because water rushing inside the cell will induce osmotic swelling, and an influx of calcium may trigger apoptosis.

Second line
2- Phagocytes

Specialized cells for capture, Ingestion and destruction of invading microorganisms

* Polymorphonuclear leucocytes, mainly neutrophils:
granulocytes circulate in blood

* Mononuclear cells (macrophages)

- Monocytes in blood

- Histocytes in connective tissues

- Fixed reticuloendothelial cells in liver spleen, lymph nodes, bone marrow

Mononuclear Phagocyte System

- examples:
  - Kupffer cell in the liver
  - Alveolar macrophages in the lung
  - Professional antigen presenting cells like the dendritic cell in the lymph node
  - Peritoneal macrophages in the abdomen
  - Osteoclasts on the bone
  - Microglia in the nervous system
  - Histiocytes in the connective tissues
  - Giant cells at the site of a granulomatous infection
  - Macrophages in a maturing scar

Second line

B- Soluble factors

1- Acute phase protein (Plasma protein, CRP=C reactive protein, Fibrin.)

2- Complement (proteins in serum, body fluids)

2- Interferons (Proteins against viral infections)

3- Properdin (Complement activation)

4- Beta lysine (Antibacterial protein from Platelets)

5- Lactoferrrin,Transferrin (Iron binding protein)

6- Lactoperoxidase (Saliva & Milk)

7- Lysozyme (Hydrolyze cell wall)

Interferons

Proteins usually produced by virally infected cells

* Types of interferons:

1- Alpha interferon — Secreted by Macrophages; Induced by Viruses or Polynucleotide

2- Beta interferon — Secreted by Fibroblasts, Viruses

3- Gamma interferon — T- lymphocytes, Specific antigens

Interferons

Protective action of interferons:

1) Activate T-cells

2) Activate macrophages

3) Activate NK

Complement

- complement is not a cell but a group of proteins

- these proteins circulate in the blood
- complement plays a role in inflammatory responses of both the innate and adaptive immune responses

Two mechanisms of complement activation:

1. Classical Pathway: Initiated by an immune reaction of antibodies.

2. Alternative Pathway: Initiated by direct interaction of complement proteins with microbial polysaccharides.

Both pathways cleave a complement protein called C3, which triggers a series of events.

Consequences of Complement Activation:

1. **Cytolysis: Due to the formation of a membrane attack complex (MAC) which produces lesions in microbial membranes.**
2. **Inflammation: Complement components (C3a) trigger the release of histamine, which increases vascular permeability.**
3. **Opsonization: Complement components (C3b) bind to microbial surface and promote phagocytosis.**
4. **Inactivation of Complement: Regulatory proteins limit damage to host cells that may be caused by complement.**

Phagocytosis

The engulfment, digestion, and subsequent processing of microorganisms by macrophages and neutrophils

1) Chemotaxis & attachment:

a- Attraction by chemotactic substances (microbes, damaged tissues)

b- Attachment by receptors on surfaces of phagocytes

Phagocytosis

2) Ingestion:

* Phagocyte pseudopodia surround organism forming phagosome.

* Opsinins and co-factors enhance phagocytosis

* Fusion with phagocyte granules and release digestive, toxic contents

Phagocytosis

3- Killing (two microbicidal routes)

a- Oxygen depended system (powerful microbicidal agents)

Oxygen converted to superoxide, anion, hydrogen peroxide, activated oxygen and hydroxyl radicals.

b- Oxygen-independent system (anaerobic conditions)

Digestion and killing by lysozyme. Lactoferrin, low pH, cationic proteins and hydrolytic and proteolytic enzymes

C) Inflammatory Barriers

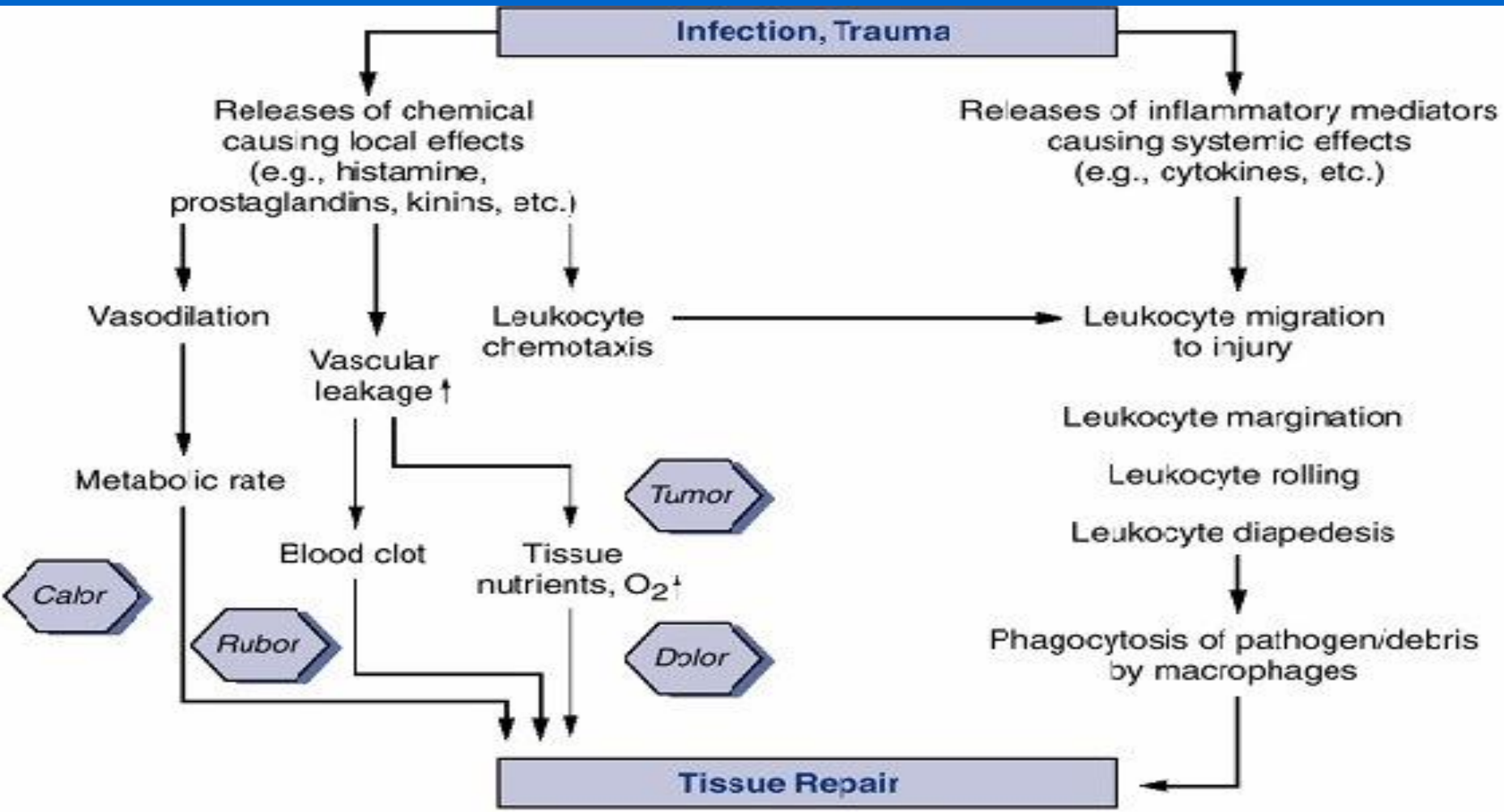
* Tissue damage by a wound or by invading pathogen

* Inflammatory response:

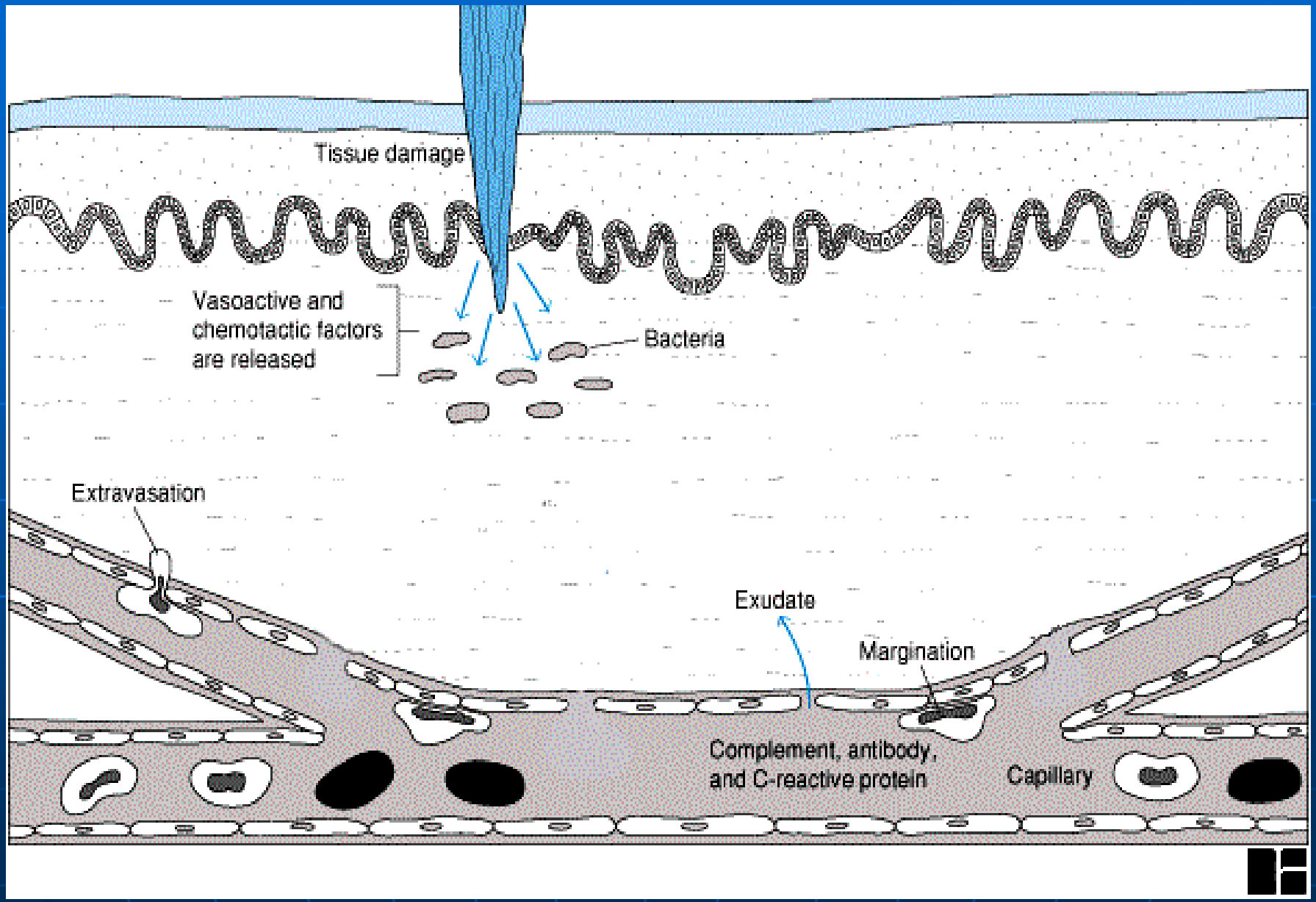
Release of chemical mediators from
- Tissue damage
- Leukocytes
- Invading microbe

(Histamine, fibrin, kinins, cytokines)

Vasodilatation of capillaries
- Redness of tissue
- Tissue temperature
- Capillary permeability
- Influx of fluids
- Influx of phagocytes into tissues



Acute inflammation: Inflammation is a stereotypic but highly complex process controlled by many soluble mediators.


Tissue damage
Vasoactive and
chemotactic factors
are released
Bacteria
Extravasation
Exudate
Margination
Complement, antibody,
and C-reactive protein
Capillary

Fevers have both positive and negative effects on infection and bodily functions

POSITIVE

- indicate a reaction to infection
- stimulate phagocytosis
- slow bacterial growth
  - increases body temperature beyond the tolerance of some bacteria
  - decreases blood iron levels

NEGATIVE

- extreme heat ➔ enzyme denaturation and interruption of normal biochemical reactions
  - > 39° C (103°F) is dangerous
  - > 41°C (105°F) could be fatal and requires medical attention

Further reading:

- Review of Medical Physiology. By W.F. Ganong, Lange Medical Book. Prentice-Hall International.
- Textbook of Medical Physiology, Indu Khurana, Elsevier