Innate Immunity

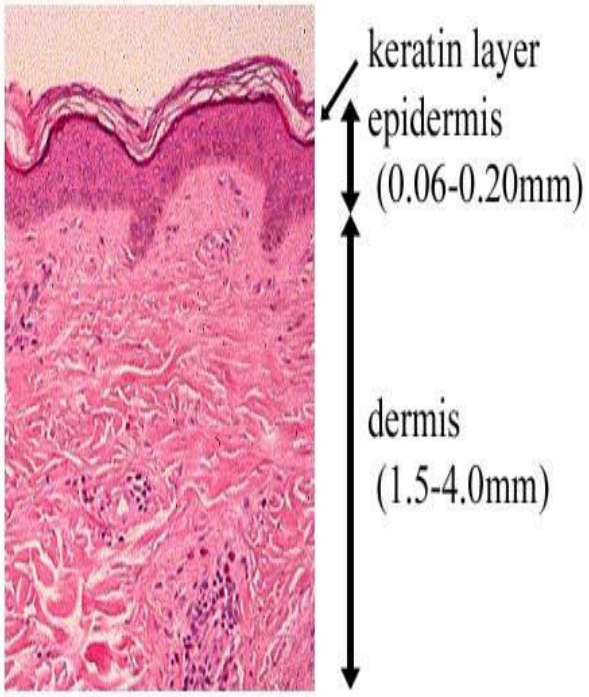
- Body defences are of different types:
  - Some of these are designed to keep out microorganisms altogether,
  - other defences remove the microorganisms if they do get in,
  - & still others combat them if they remain inside.
- Our ability to ward off diseases through our defences is called resistance.
- Vulnerability or lack of resistance is known as susceptibility.
- Body defences are of two general kind:

i) Nonspecific resistance: Defences that protect us from any pathogen , regardless of species.

ii) Specific resistance: Defence against a particular pathogen.

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

Section through human skin



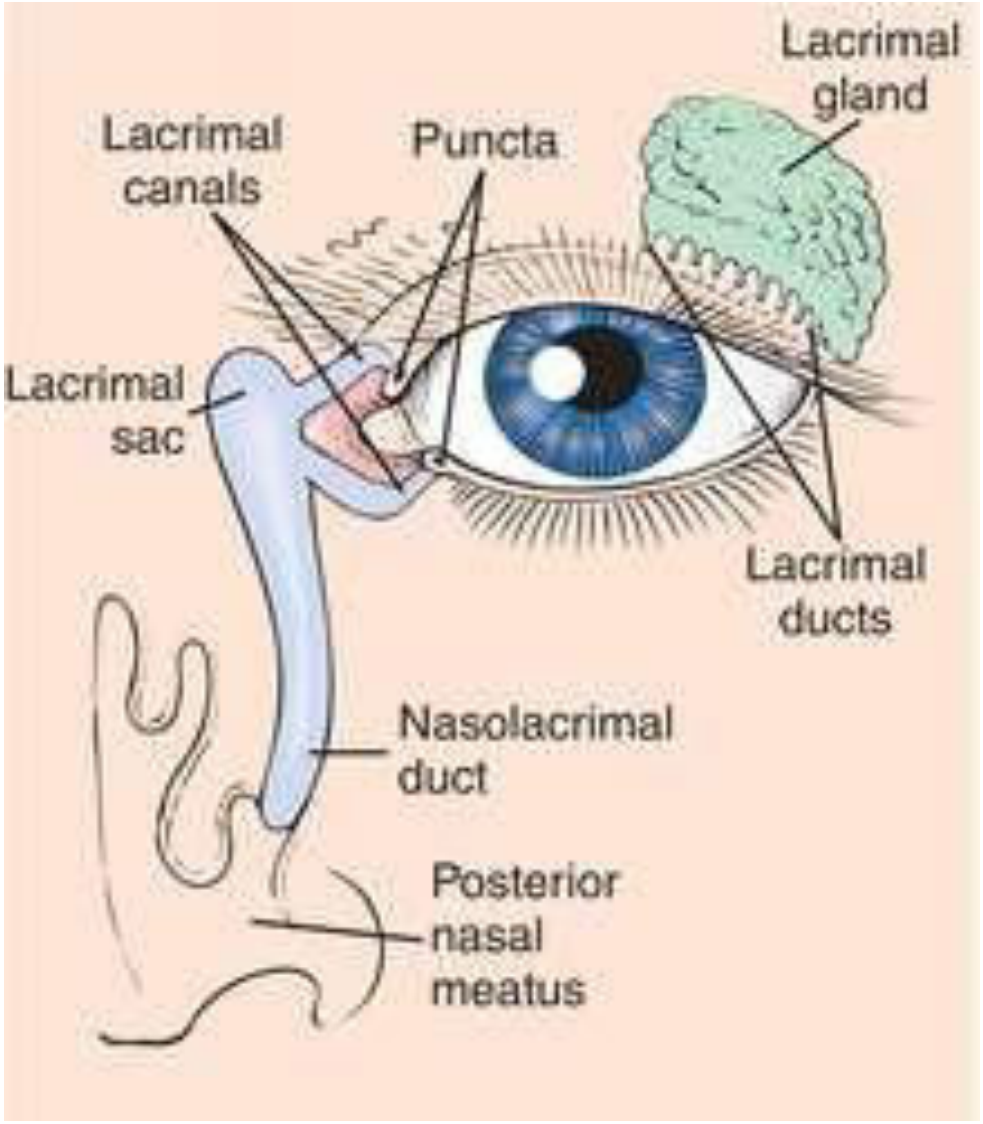
- First line of defence:
- The skin & mucous membranes are the body's first line of defence against pathogens. This function results from both mechanical & chemical factors.

❖ Mechanical Factors:

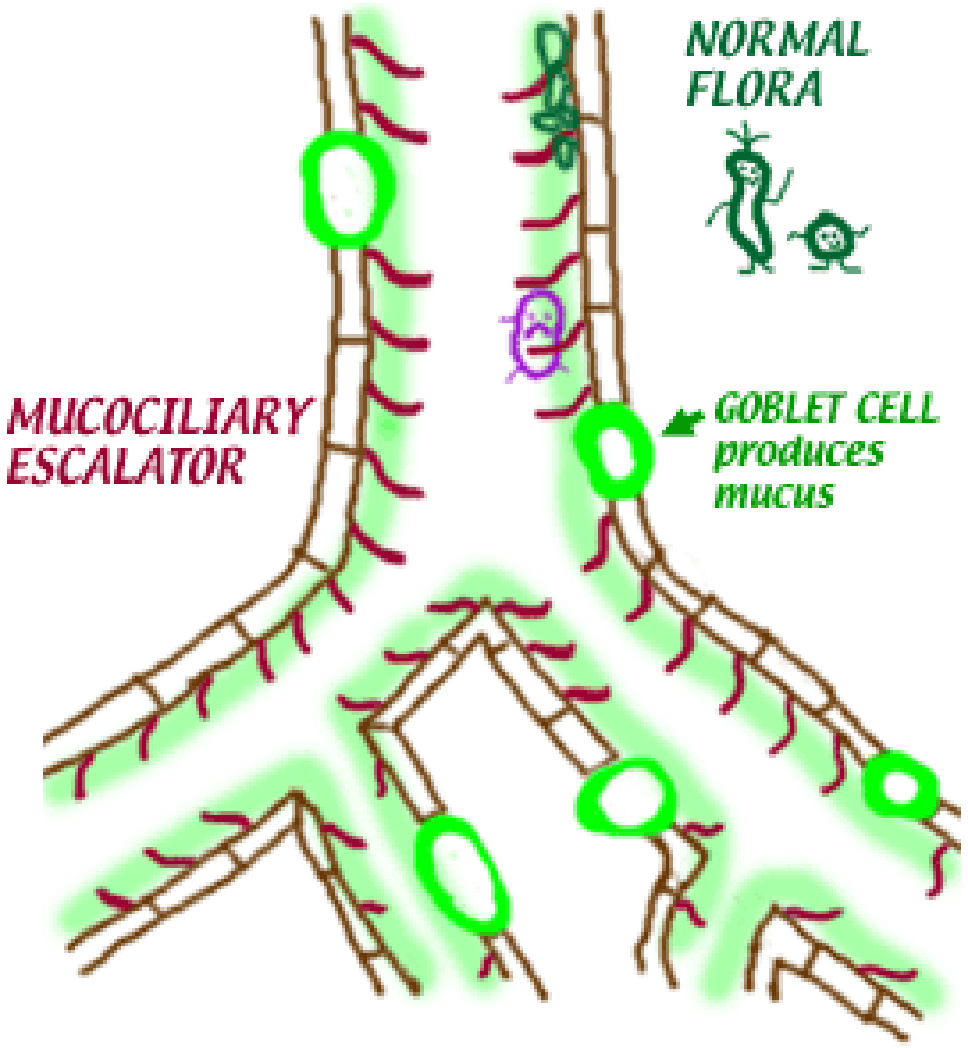
- Skin: Largest organ in terms of surface area. Consist of two distinct regions, the dermis & epidermis.
- Two types of cells in the epidermis, Langerhans & Granstein cells participate in immunity.
- Top layer of epidermal cells is dead & contains a waterproofing protein called keratin.
- Intact skin acts as a barrier to the entry of microorganisms.

- Most common bacteria which cause infection in broken skin surface are Staphylococci that normally inhabit the epidermis, hair follicles, sweat glands & oil glands.

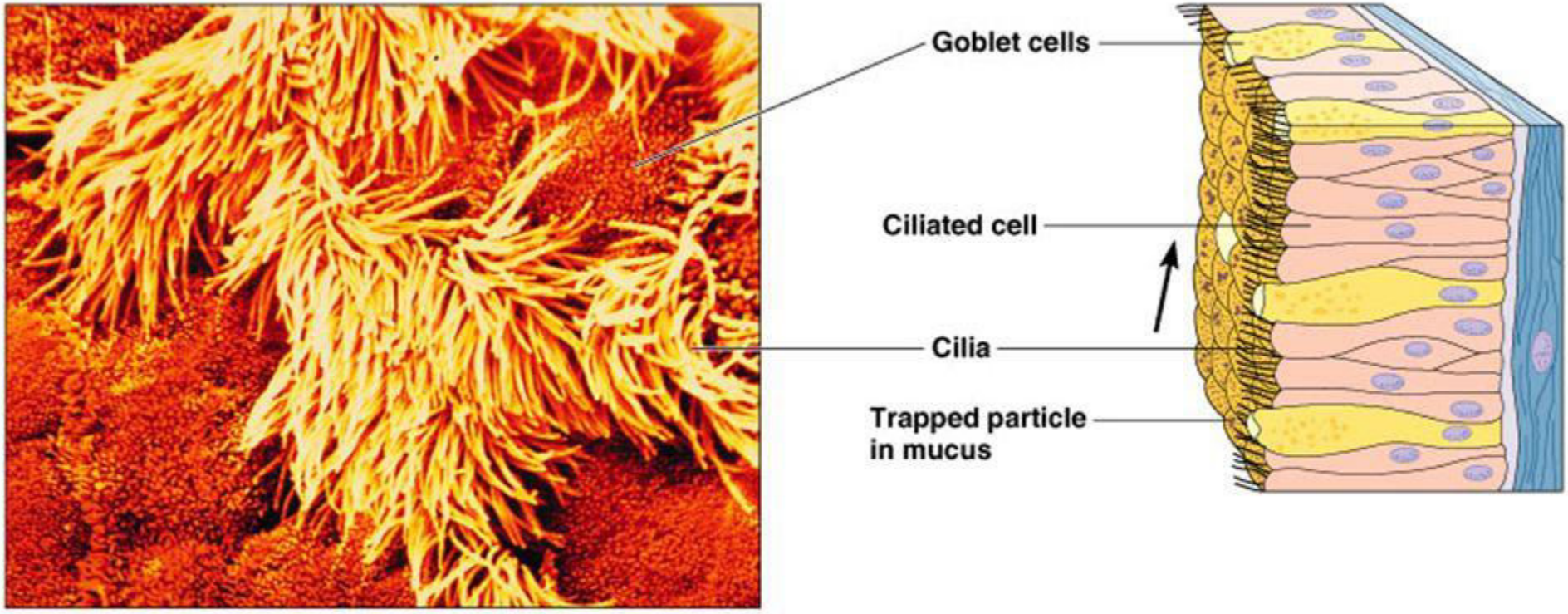
- Mucous membranes: Also consists of an epithelial layer & underlying connective tissue layer.
- Line the entire gastrointestinal, respiratory urinary & reproductive tracts.
- Although mucous membranes prevent the entry of many microorganisms, they offer less protection than the skin.
- Lacrimal apparatus: A group of structures that produces & drain away tears. Continual washing action of tears helps to keep the microorganisms from settling on the surface of the eye.


Lacrimal gland
Lacrimal canals
Puncta
Lacrimal sac
Lacrimal ducts
Nasolacrimal duct
Posterior nasal meatus

- Salivary glands: Prevents colonization of microbes.
- The ciliary escalator: Synchronous movement of the cilia propel inhaled dust & microorganisms trapped in mucus upward towards the throat.


NORMAL
FLORA
MUCOCILIARY
ESCALATOR
GOBLET CELL
produces
mucus

Ciliary escalator

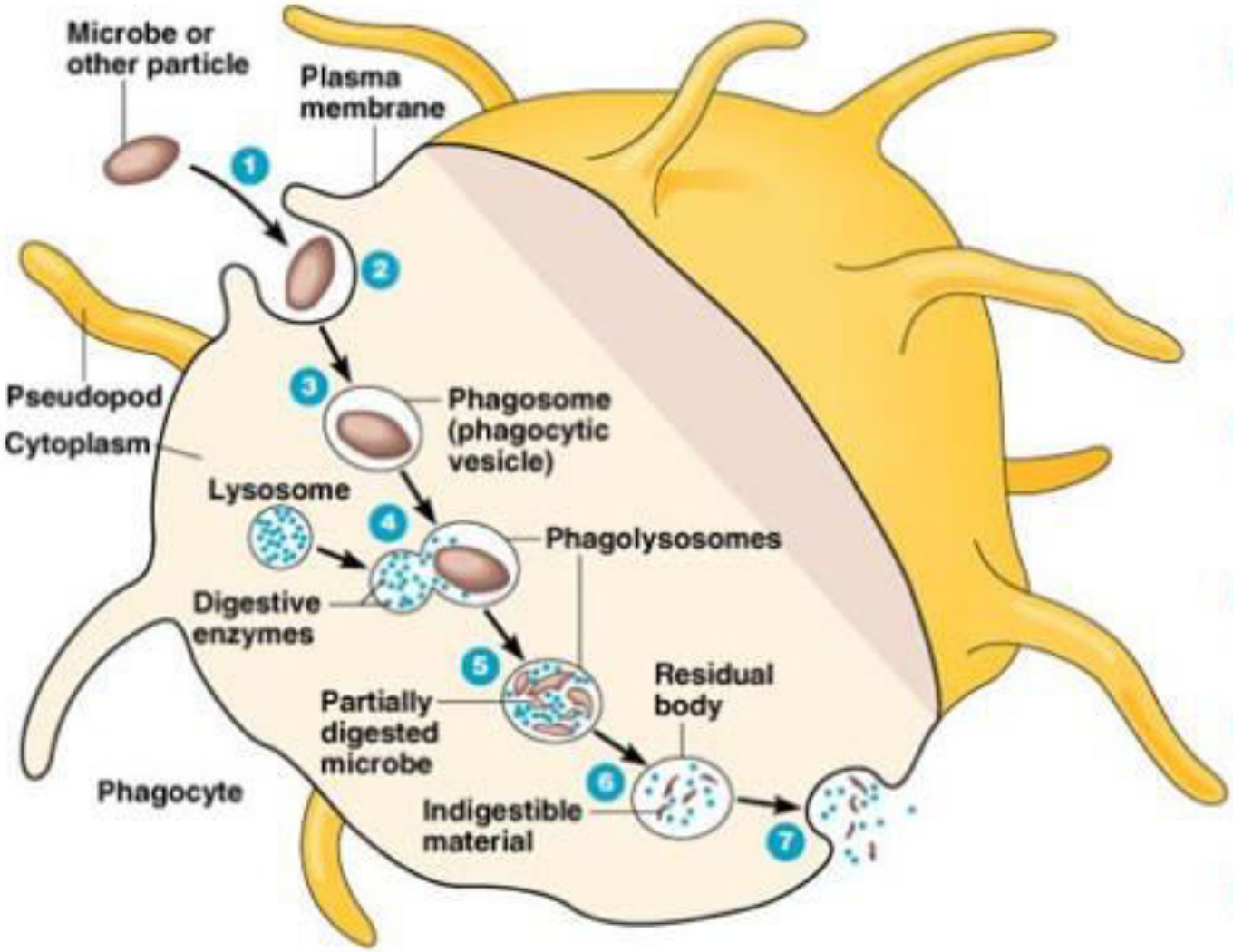


- Microbes trapped in mucus produced by goblet cells, then propelled upward by cilia

- Chemical factors:
- Sebaceous glands: Sebum, an oily substance produced by these glands forms a protective film over the surface of the skin.One of the component of sebum, unsaturated fatty acids, inhibit the growth of certain pathogenic bacteria & fungi.
- Sweat glands: Produces perspiration, which helps to maintain body temperature, eliminate certain wastes & flush microorganisms from the surface of the skin.
- Also contains lysozyme, an enzyme capable of breaking down of cell walls of bacteria.
- Gastric juice: Produced by the glands of the stomach. It is a mixture of hydrochloric acid, enzymes & mucus. The very high acidity (pH 1.2 to 3) preserves the usual sterility of the stomach.

- This acidity also bacteria & most bacterial toxins.
- Blood: Also contains antimicrobial chemicals. For example, protein transferrins which inhibit bacterial growth.
- Second line of defence:
- Phagocytosis: Phagocytosis is ingestion of a microorganism particulate matter by the cell.
- Agranulocytes: Monocytes leave circulating blood, enter body tissues & mature into macrophages. Known as wandering macrophages.
- Fixed macrophages (histiocytes) are located in certain tissues & organs of the body. They are-
- In liver- Kupffer's cells.
- In lungs- Alveolar macrophages.
- In nervous system- microglial cells.

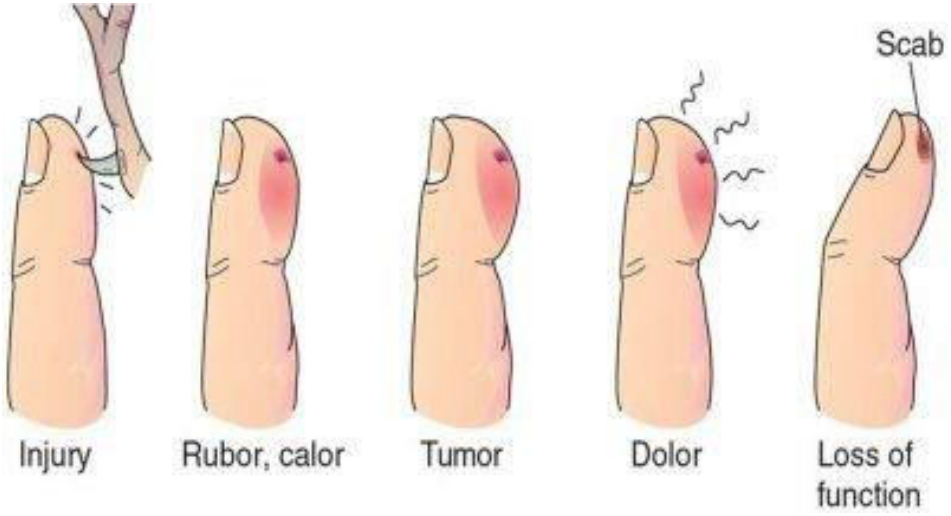
- Also present in bronchial tubes, spleen, lymph nodes, bone marrow & the peritoneal cavity surrounding abdominal organs.
- Various macrophages of the body constitute the mononuclear phagocytic system (reticuloendothelial system).
- Granulocytes: Neutrophils & eosinophils are phagocytic primarily against microbes during the initial phase of infection.
- Mechanism of phagocytosis: Four main phases- Chemotaxis, adherens, ingestion & digestion.

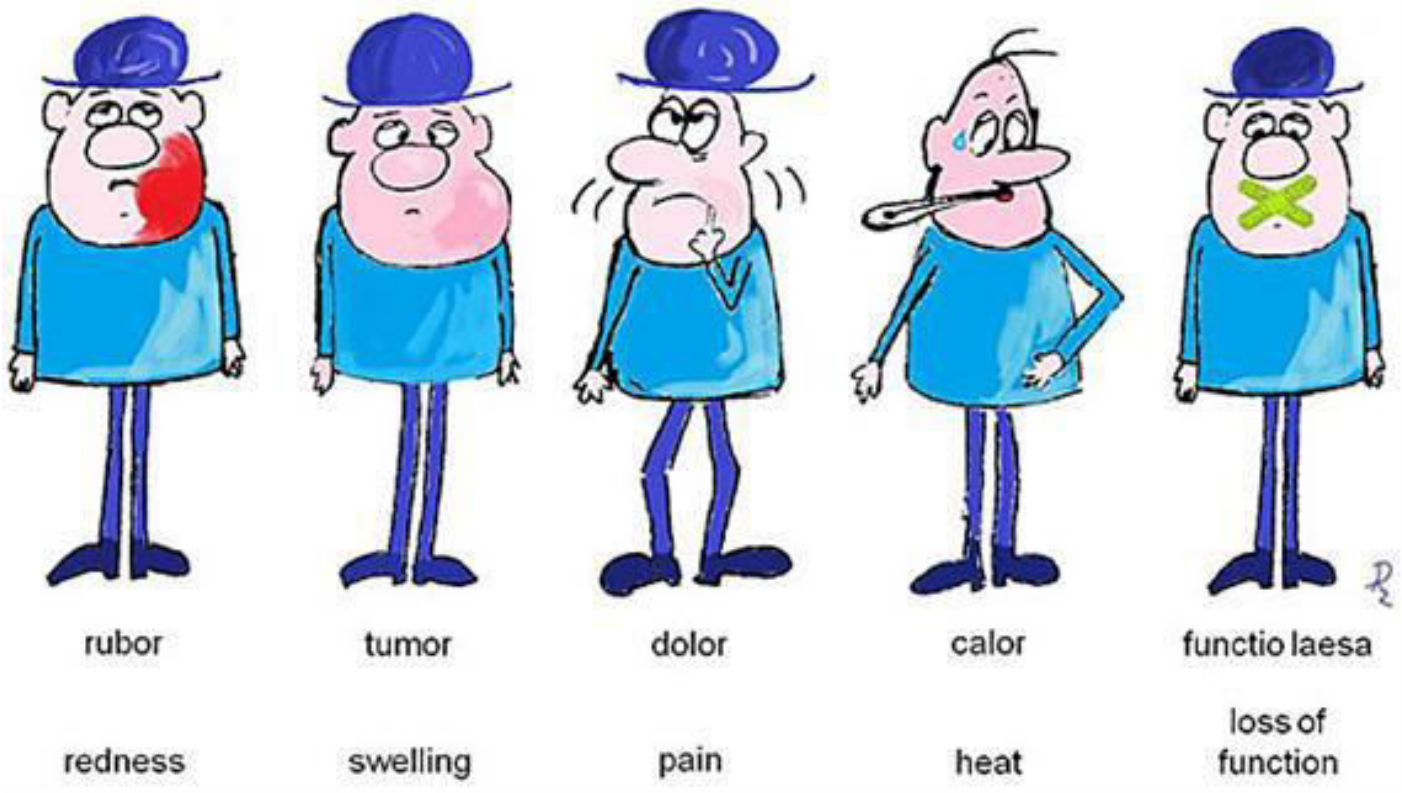


1. Chemotaxis and adherence of microbe to phagocyte.
2. Ingestion of microbe by phagocyte.
3. Formation of a phagosome.
4. Fusion of the phagosome with a lysosome to form a phagolysosome.
5. Digestion of ingested microbe by enzymes.
6. Formation of residual body containing indigestible material.
7. Discharge of waste materials.

(a) Phases of phagocytosis

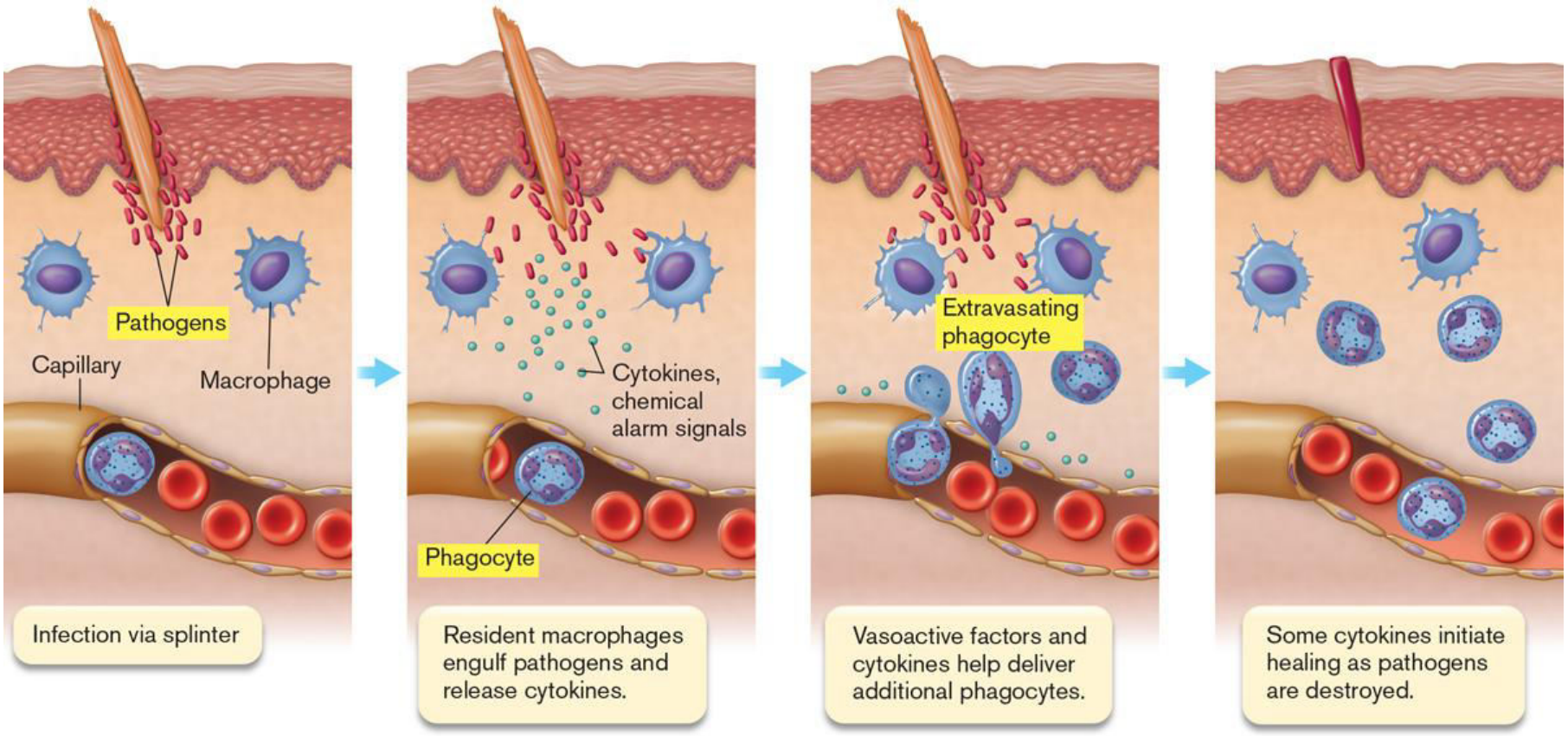
- Inflammation: The inflammatory response is a reaction to any traumatic event in the tissues like microbial infection, physical agents (such as heat, radiant energy, electricity, sharp objects), or chemical agents (such as acids, bases & gases).
- The classic signs & symptoms of inflammation have been known for centuries as : i)*ruber, ii)calor, iii)tumor, iv)dolor & v)functio laesa.*
- i) Rubor (redness) is caused by increased circulation & vasodilatation in the injured tissues. Chemicals such as histamine, prostaglandins, leukotrienes (released by damaged cells), kinins (present in blood plasma) causes vasodilatation & increase in permeability of blood vessels.
- Ii) Calor (warmth) is the heat given off by the increased flow of blood.


Scab
Injury
Rubor, calor
Tumor
Dolor
Loss of function


rubor
redness
tumor
swelling
dolor
pain
calor
heat
functio laesa
loss of function

- iii) Tumor (swelling) is caused by increased fluid escaping into the tissues.
- iv) Dolor (pain) is caused by the stimulation of nerve endings.
- V) Functio laesa (loss of function).
- The first four signs are described by Celsus (30 BC-38 AD) & fifth by Galen (129 AD-200-216 AD).

- The flow of major events in inflammation can be represented as follows:
- Injury → Reflex narrowing of the blood vessels (vasoconstriction) lasting for a short time → Increased diameter of blood vessels (vasodilatation) → Incrased blood flow → Increased vascular permeaebility → Leakage of fluid (plasma) from blood vessels into tissues (exudate formation) → Edema → Infiltration of site by neutrophils → Infiltration by macrophages & lymphocytes → Repair either by complete resolution & return of tissue



Leukocyte extravasation

- Fever: Inflammation is local response of body to injury. One of the most important systemic or overall response is fever.
- Most frequent cause of fever is infection from bacteria (& their toxins) or viruses.
- Hypothalamus- body's thermostst.
- Infection changes (thermosts setting) i.e. hypothalamus response.
- Up to a certain extent, there are several benefits of fever:
- i) Fever inhibits multiplication of temperature sensitive microorganisms such as polio virus,

Cold virus, herpes zoster virus, fungal pathogens, Mycobacterium species etc.

- ii) Fever impedes the nutrition of bacteria by reducing the availability of iron.
- iii) Fever increases metabolism & stimulates immune reaction & naturally protective physiological processes. It speeds up hematpoiesis, phagocytosis & specific immune reactions.

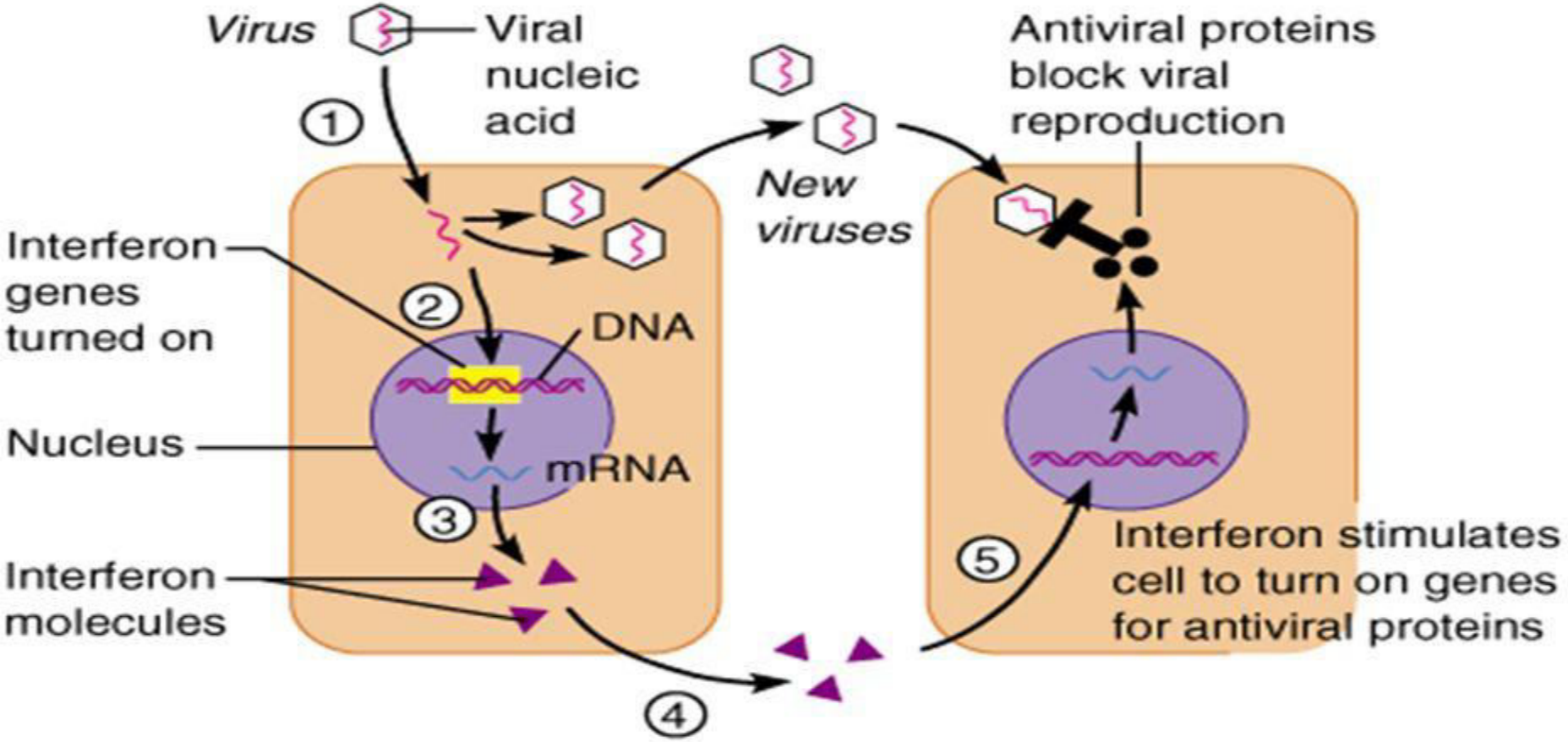
- Antimicrobial substances:
- The body produces certain antimicrobial substances in addition to the chemical factors. Most important are complement system & interferons.
- i) The complement system: Complement is a defensive system consisting of 20 serum protein that participate in lysis of foreign cells, inflammation & phagocytosis.
- The system can be activated by an immune reaction by three pathways: classical pathway, alternative pathway & lectin pathway.

- Complement is nonspecific, the same proteins can be activated in response to any foreign cell. However, in the classical pathway, complement assists specific immunity.
- The sources of complement factors are liver hepatocytes, lymphocytes & monocytes.

- Interferons (IFNs): Interferons are a class of small antivirus proteins produced by certain white blood cells feature of interferons is that they are host& tissue cells after viral stimulation.
- One principal function of interferons is to interfere with viral multiplication.
- One very interesting -cell specific but not virus specific.
- Not only do different animal species produce different interferons, but also different types of cells in an animal produce different interferons.
- Human interferons are of three principal types; i) alpha interferon (α-IFN), beta interferon (β-IFN) & gamma interferon (γ-IFN).

- There are also various subtypes.
- In the human body, interferons are produced by fibroblasts in connective tissue, lymphocytes & also by other leukocytes.
- All interferons are small proteins with molecular wt 15,000 to 30,000.
- They are quite stable at low pH & are fairly resistant to heat.

Interferon



Host Cell 1

Infected by virus; makes interferon; is killed by virus

Host Cell 2

Entered by interferon from cell 1; interferon induces changes that protect it

- Certain limitations of interferons: i) Effective for only short periods.
- Ii) Typically plays a major role in infections that are acute & short term, such as cold & influenza.
- Iii) It has no effect on viral multiplication in cells already infected.