Immunity System

- Immunity is the body's resistance against diseases. Immunity is the boy's defense againt diseases.
- Immunology is the study of the ways in which the body defends against disease and infection.

Immune Defenses Perform:

a) Protect against infection caused by microbes
b) Removal of debris and dead cells
c) Destroys cancer cells that arise in the body

Branches of Immunity System

Immune defenses or immunity can be classified into two categories which interact with each other.
The two general types of immunity are:

1. **Non-specific (innate) immunity:**
   - It is a type of defense mechanism that is present at birth.
   - It does not involve specific recognition of a pathogen but fights against all germs in a same way.
   - It is the protection against foreign substances or cells without having to recognize their specific identities.
2. **Specific (adaptive) immunity:**
   - It is a type of defense mechanism which involves specific recognition of pathogen.
   - It involves specific recognition of particular microbe.
   - It is the protection against specific foreign substances

Comparison between Specific and Non-specific Immunity System

Characteristics	Innate Immunity	Adaptive immunity
Presence	Present at birth	Not born with but developed Develops after birth and through vaccination (Develops in response to exposure of a foreign substances called antigens)
Specificity	Non-Specific (general protection against pathogen) (not antigen-specific)	Specific (it is pathogen specific) (antigen-specific) It only acts against one particular microorganisms
Target	Fights any foreign invader (Does not target a particular pathogen)	Fights only specific infection
Speed	Faster response	Slower response
Inheritance	Inherited from parents and passed to offspring.	Cannot be inherited.

Memory	No memory	Has a memory (has memory cell which remember microbes and give strong immune response on re-exposure)

Three Lines of Defense Mechanisms:

Specific and non-specific immunity system can be subdivided into three lines of defense mechanisms, which are:

1. **First line of defense:**
   - It is a non-specific defense mechanism that blocks entry of pathogens into the body and acts all microorganisms in a same way
   - It includes both physical and chemical barriers to prevent germs from entering the body.
   - Does not involve specific recognition of pathogen
   - These include skin, mucus, cilia, tears, sweat and etc
2. **Second line of defense:**
   - Second line of defense starts when the first line of defense fails to protect and enter the body
   - It is a non-specific defense mechanism
   - It does not involve specific recognition of pathogen
   - Contains a group of phagocytes that defend the body if pathogens manage to pass through the first line of defense
3. **Third line of defense:**
   - Any pathogen that passes the first and second lines of nonspecific defenses faces the third line of specific defenses.
   - It involves specific recognition of pathogen.
   - In third line of defense, both chemicals and certain white blood cells (lymphocytes) destroy the microbes
   - It develops memory to each particular destroyed pathogen.

First Line of Defense Mechanisms: Skin and Mucous Membranes

- First line of non-specific defense mechanism includes:

1. Skin:

The skin provides both physical and chemical barriers against invading pathogens

(a) Physical barrier of the skin:

The outermost layer of the skin called **epidermis**, consists of dead **keratinized cells** which provide physical barrier to the entrance of microbes

(b) Chemical barrier of the skin:

The inner layer of the skin called **dermis**, contains **sweat** and **sebaceous glands**

(i) **Sweat**:

Sweat gland secretes **sweat** on the skin surface

Sweat defends the body against invasion of most microorganisms

Sweat contains **lysozyme,** which digests bacterial cell walls

Sweat also lowers the pH of the skin surface to slow the growth of many microorganisms

(ii) **Sebum**

Sebaceous glands secrete an oily substance called **sebum** on the skin surface

Sebum protects the skin from infection of many microorganisms

Sebum inhibits the growth of certain microorganisms on the skin by lowering pH of the skin surface

2. Other External Barriers:

(A) The digestive tract:

The digestive tract plays an important role in the body's non-specific first line of defense mechanisms

(i) Saliva

The salivary glands produce **saliva** into the mouth

Saliva contains **lysozyme** that kills bacteria by rupturing their cell walls

Saliva washes microbes from the teeth and mucous membranes of the mouth

(ii) Hydrochloric acid in gastric juice

Lining of the stomach produces **hydrochloric acid** (low pH) and **digestive enzymes** destroy microorganisms in the swallowed food.

(B) The respiratory tract

The mucous membranes that cover in the respiratory tract secrete **mucus** which traps pathogens and prevent them from entering into the body.

The **nasal hairs** and secreted **mucus** in the nose trap any pathogen and dust particles from the inhaled air, where sneezing helps their removal from the body

Ciliated mucus membranes lining the air passages (such as trachea and bronchi) keep harmful substances from entering the lungs\

Mucus traps microorganisms and dust particles in the inhaled air while **cilia** remove them upwards to the throat where it is swallowed into the stomach.

(C) Tears

The lacrimal glands of the eyes produce **tear**

Tears contain **lysozyme** that kills certain pathogens by rupturing their cell walls

Tears make unfavorable condition for bacterial growth

Tears wash away irritating substances and microbes

(D) Urine and vaginal secretions

Low pH in the urine slows down microbial growth in the urinary system

Urine washes microbes from urethra

Low pH in the vagina slows down bacterial growth and also vaginal secretions also move microbes out of the body in females

Defecation and vomiting also expel microbes

(E) Blood clotting

Blood clothing helps to seal wounds rapidly, until a permanent repair is produced by mitosis of the cells surrounding the wound

Blood clothing stops pathogens entering into the wound.

Second Line of Defense Mechanisms: Cellular counterattack

When pathogens pass both physical and chemical barriers of the skin and mucous membranes, they encounter a second line of defense.

The inflammatory Response:

Damaged tissues by a physical injury or entry of microbes lead inflammatory response.

The inflammatory response is the way in which the body reacts when pathogens damage tissue cells

Inflammatory response is a localized nonspecific response to infection or injury

The inflammatory response is characterized by four signs, which are **redness, heat (warm), swelling** and **pain**

When tissue damage occurs, **mast cells** in the body tissues release a number of chemicals including, **histamine, cytokines** and **prostaglandins** which initiate the inflammatory response.

Mechanisms of inflammatory responses are including;

1. Dilation of local blood vessels (**vasodilatation**)
2. Increasing the blood flow to the site of infection or injury and causes the area to become **red** and **warm**
3. Increase the permeability of capillaries in the area, causing **edema** (tissue swelling).
4. The more permeable capillaries allow **phagocytes** (neutrophils and macrophages) to migrate from the blood to the infected area, where they can attack any pathogens

5. **Neutrophils** arrive first at the site of infection to engulf and digest bacteria by using lysozymes and the whitish liquid or **pus,** associated with some infections contains dead cells, neutrophils and dead pathogens
6. **Macrophages** arrive to and engulf pathogens and the dead cells
7. Stimulation of pain receptors

Inflammatory response continues until the foreign material is eliminated and the wound is repaired

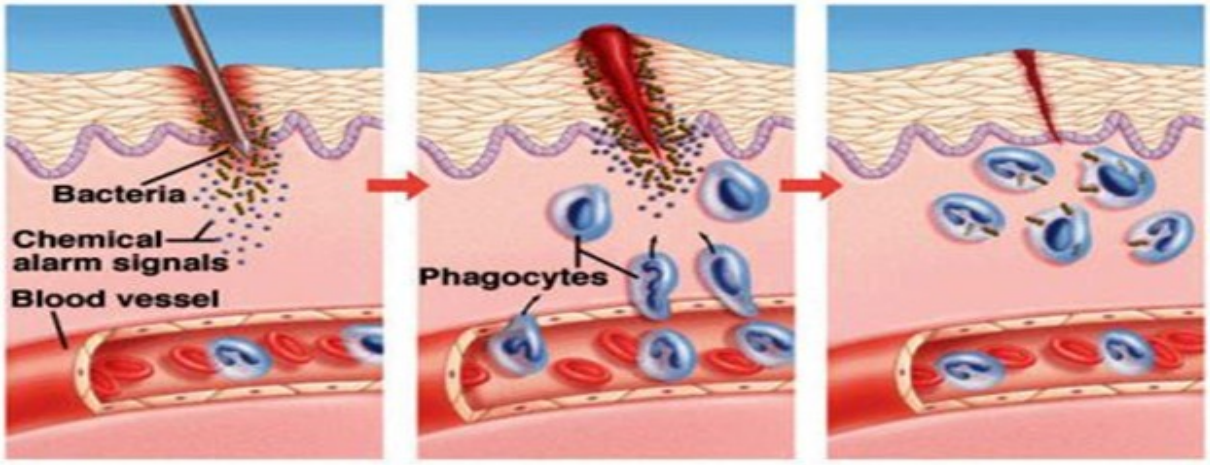


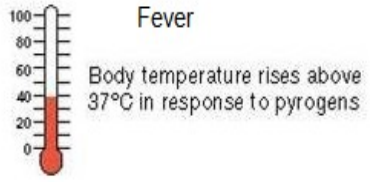
Figure: Events in the process of local inflammation

Temperature Response:

During the invasion of the body by microbes, certain bacteria secrete **endotoxins** which stimulate macrophages to release a regulatory molecule called **interleukin-1** and also **endogenous pyrogens** (pyrogens, *Greekwords*, *pyro*, '*fire'* and *gen*, '*generator'*) which stimulate the **hypothalamus** to raise the body temperature several degrees above the normal value of **37°C.** The elevated temperature results a **fever.**

Fever is the elevation of several degrees above normal body temperature.

Fever is an abnormally elevated body temperature.



Fever assists the body's defense by

1. Stimulating the process of **phagocytosis** in the infected area (increase activity of phagocytes)
2. Causing the liver and spleen to store iron, reducing blood levels of iron; which many bacteria require in large amounts to grow and reproduce
3. Inhibiting bacterial growth as many disease-causing bacteria do not grow at high temperature.
4. Increasing in the metabolic rate, which speeds up tissue repair

Fever is a common symptom of illness that shows the body is responding to an infection.

However, very high fever is dangerous because excessive heat can

inactivate enzymes in the body.
Temperatures greater than 39°C are considered dangerous, and those greater than 41 °C (105°F) can often be fatal.

Nonspecific Cellular Defenses

The cellular defenses in second line of innate immunity are **phagocytes** (white blood cells) that attack and destroy invaders which pass the first line of defense.
White blood cells originate and are produced continually by **stem cells (**hematopoietic stem cells) in the **red bone marrow** as shown below;

Phagocytes

- **Phagocytes** are types of **white blood cells** (leukocytes) that are made in the bone marrow
- **Phagocytes** are produced throughout life by the **stem cells** in the bone marrow
- **Phagocytes** are stored in the bone marrow before distributed around the body in the blood
- **Phagocytes** engulf and digest microbes through **phagocytosis**
- **Phagocytosis** is the process by which the invading microorganisms are engulfed and destroyed by **phagocytes** (phagocytes)
- The four types of phagocytes are
  1. Neutrophils
  2. Monocytes which mature into macrophages
  3. Eosinophils and
  4. Basophils
- **Neutrophils** and **macrophages** are the most common phagocytes
- Phagocytes can be grouped into:

Granulocytes or **polymorphonuclear leukocytes**	**Agranulocytes** or **mononuclear leukocytes**
Have granular cytoplasm	Have smooth cytoplasm
Have lobed nucleus	Have no lobed nucleus
e.g. Neutrophils, Eosinophils and basophils	e.g. Monocytes which mature into macrophages

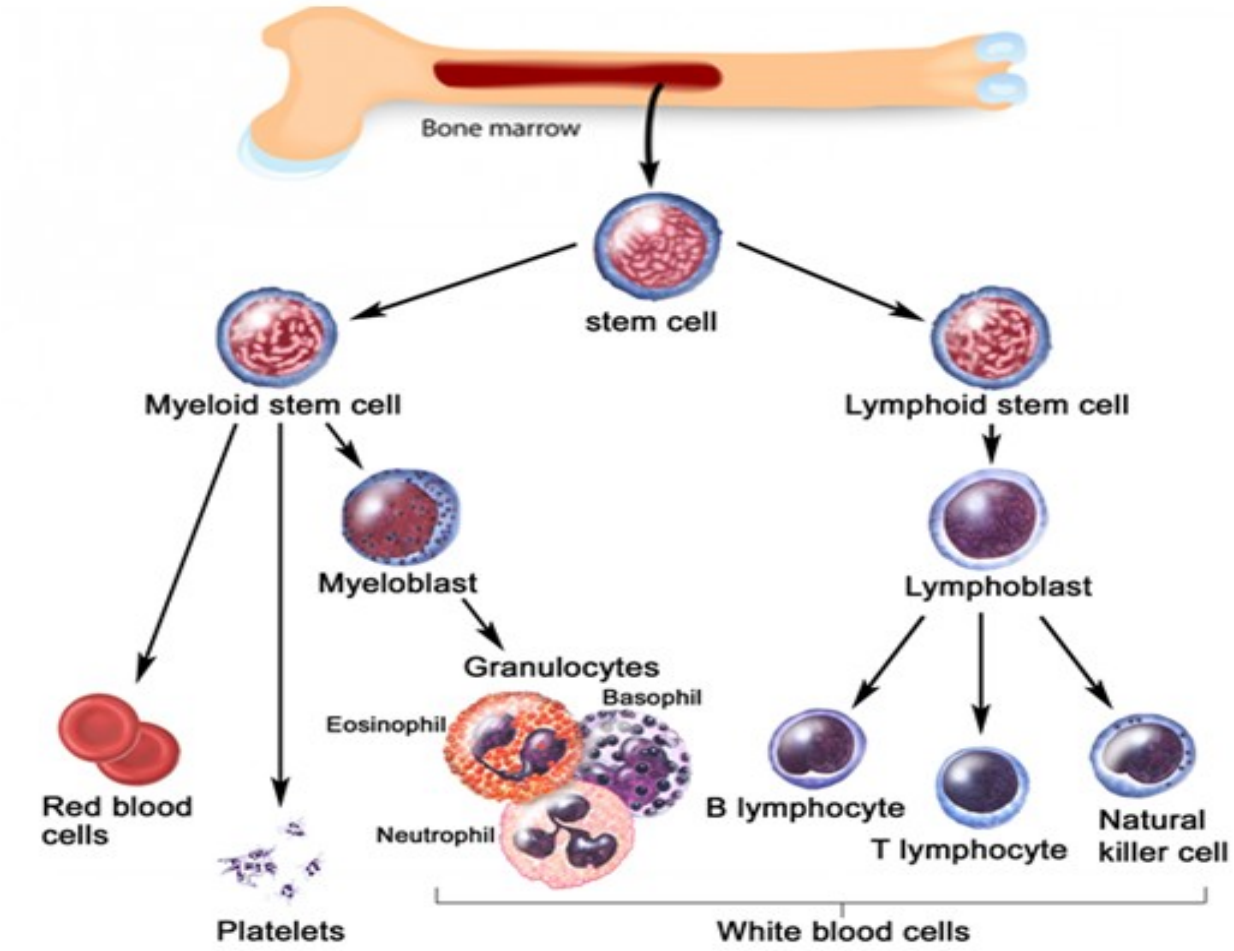


Fig. Origin and development of white blood cells

Neutrophils:

- Neutrophils are kind of **phagocytes**
- They form about 60% of the white blood cells in the blood
- Neutrophils mature in the bone marrow and released into blood circulation. They travel throughout the body
- **Neutrophils** can squeeze through the walls of blood capillaries to patrol the tissues
- During infection, **neutrophils** are released in large numbers
- **Neutrophils** ingest and kill pathogens by **phagocytosis**
- They are short-lived cells around few hours or days

Monocytes and Macrophages:

- Monocytes are **phagocytes** that are made in the bone marrow by **stem cells**
- Monocytes leave the bone marrow and mature in the bloodstream
- Monocytes form about 4% of the white blood cells in the blood
- Monocytes leave the bloodstream and migrate into the tissues, where they develop into **macrophages**. Macrophages are also known as '**big eaters**'.
- Some **macrophages** settle in the lungs, liver, spleen, kidneys, lymph nodes and thymus.
- Macrophages are larger than neutrophils
- Macrophages are long-lived cells
- A macrophage is also referred to as an **antigen-presenting cell** as they play an important role in initiating **adaptive immune response** since they do not destroy pathogens completely, but cut them to display **antigens** that can be recognized by **lymphocytes**
- Macrophages release a **cytokine** called **interleukin-1** that increases the body's temperature which decrease the chance of invading microbes to reproduce

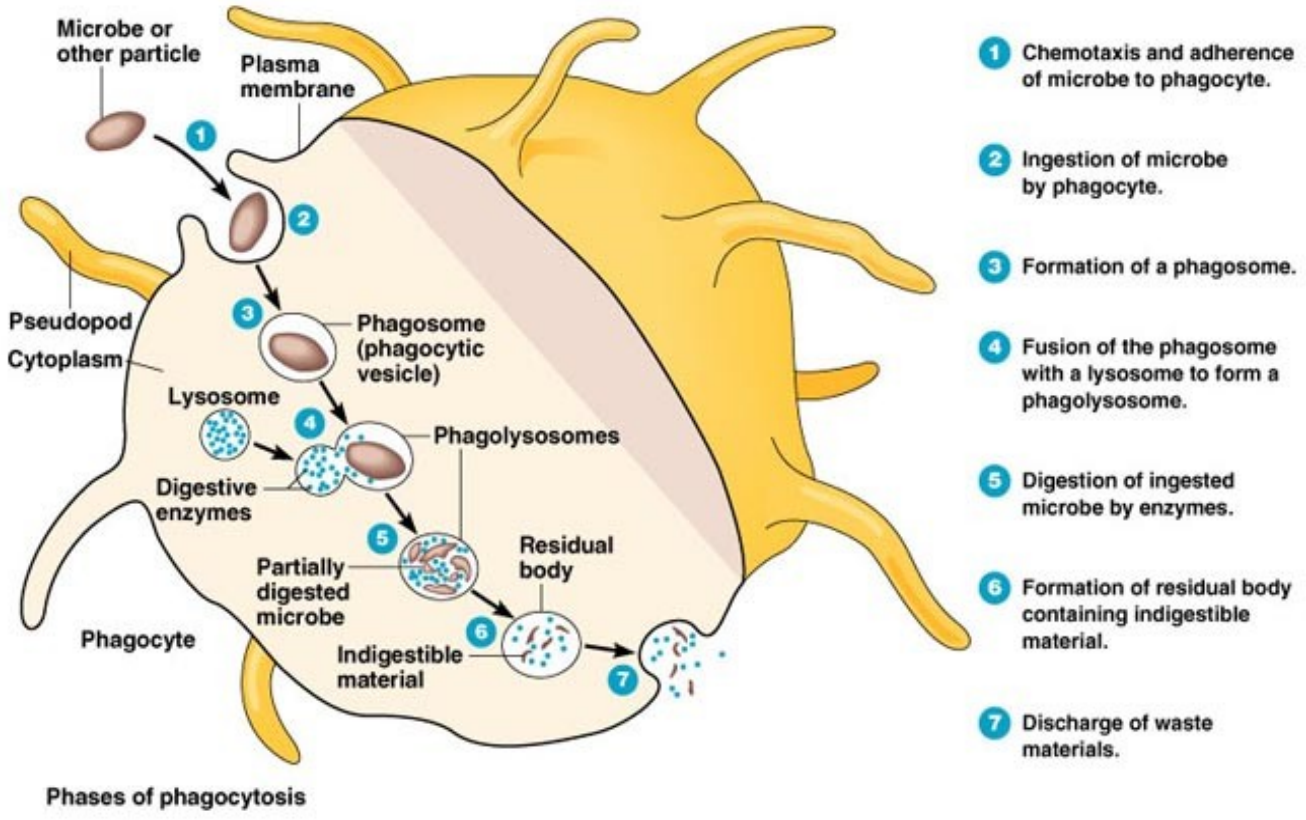
The mechanism of phagocytosis (killing by engulfing)

If a pathogen invades the body and cause an infection, some of the cells under attack respond by releasing chemicals such as **histamine.** **Histamine** and other chemicals secreted by the pathogens attract passing neutrophils to the site

The mechanism or stages of phagocytosis is described below

1. **Chemotaxis:**
   - Chemotaxis is the process of chemically attracting phagocytes to the site of infection
   - Chemicals that attract phagocytes to the site of infection may be secreted by the damaged tissue cells or invading microbes.
   - Inflammatory chemicals attract neutrophils to the injury site
2. **Adherence (attachment):**
   - Phagocyte attaches to the surface of the pathogen or foreign material
3. **Ingestion (Endocytosis):**
   - This is engulfment of pathogen by a phagocyte.
   - The plasma membrane of the phagocyte extends projections that form **pseudopodia** (false feet)around the pathogen and engulf it through a process called **ingestion.**
4. **Vacuole formation (Formation of phagosome and fusion of lysosome):**
   - Inside the phagocyte, the pathogen is enclosed in a vacuole called **phagosome** or **phagocytic vesicle.**

- **Lysosome** fuses with the **phagosome** forming a **phagolysosome** and initiate the digestion of target pathogen



Phases of phagocytosis

5. Killing and digestion:

- The lysosome releases digestive enzymes called **lysozyme** into the vacuole and the ingested microbe is digested and killed

6. Exocytosis:

Formation of **residual body** containing **ingestible material** (microbial debris) which is discharged or removed from the cell by the process of **exocytosis**

Natural Killer Cells:

Natural killer cells (also known as **NK cells,** or **Killer cells**) are a type of lymphocytes (a white blood cell) and part of the innate immunity system.

Natural killer cells do not attack invading microbes directly, but destroy **virus-infected body**

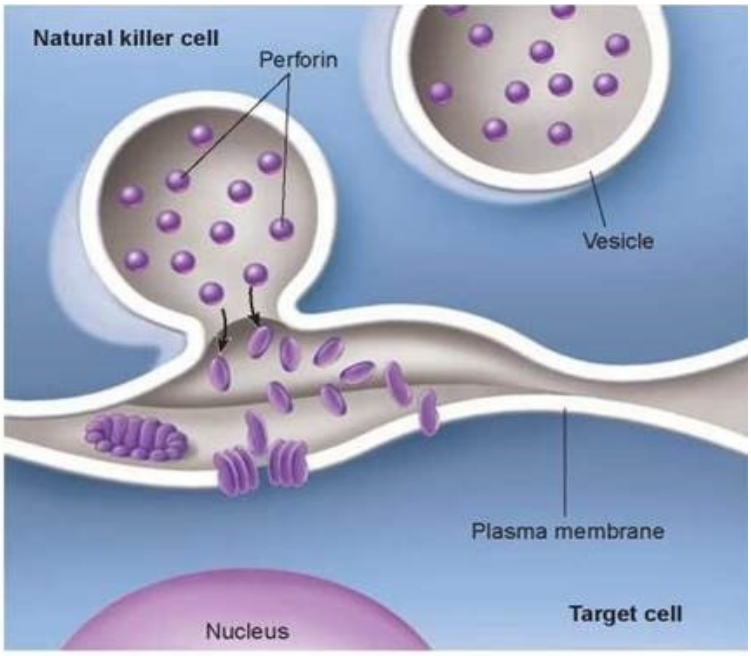
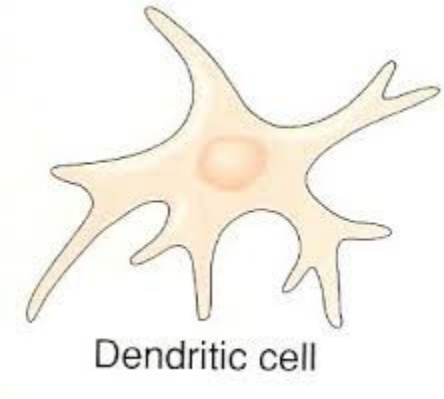


Figure: How natural killer cells kill target cells

cells.
Natural killer cells do not phagocytize virus-infected cells
Natural killer cells attach and make a hole in the plasma membrane of the target cell.
Natural killer cells release a protein called **perforin** and inserted into the membrane of the target cell, forming a pore.
This pore allows water to rush into the target cell, which then swells and bursts that cause the infected cell to rupture (to **lyse)** or bring about **apoptosis** (programmed cell death)
Natural killer cells also lyse and kill cancer cells

Dendritic Cells:

Dendritic cells link between the innate and the adaptive immune system.
Dendritic cells are **antigen presenting cells** (APC) as they present the antigen of phagocytized microbes to the lymphocytes (**T cells**) for activation and initiation of adaptive immune response.


Dendritic cell

Proteins that Kill Invading Microbes (Antimicrobial proteins):

- Antimicrobial proteins enhance the innate defenses by attacking microorganisms directly or by hindering their ability to reproduce
- The most important proteins that kill invading microbes are:

1. Interferons and
2. Complement system

To be contunued .... Get next part