Metabolism

– Sum up all the chemical processes that occur within a cell

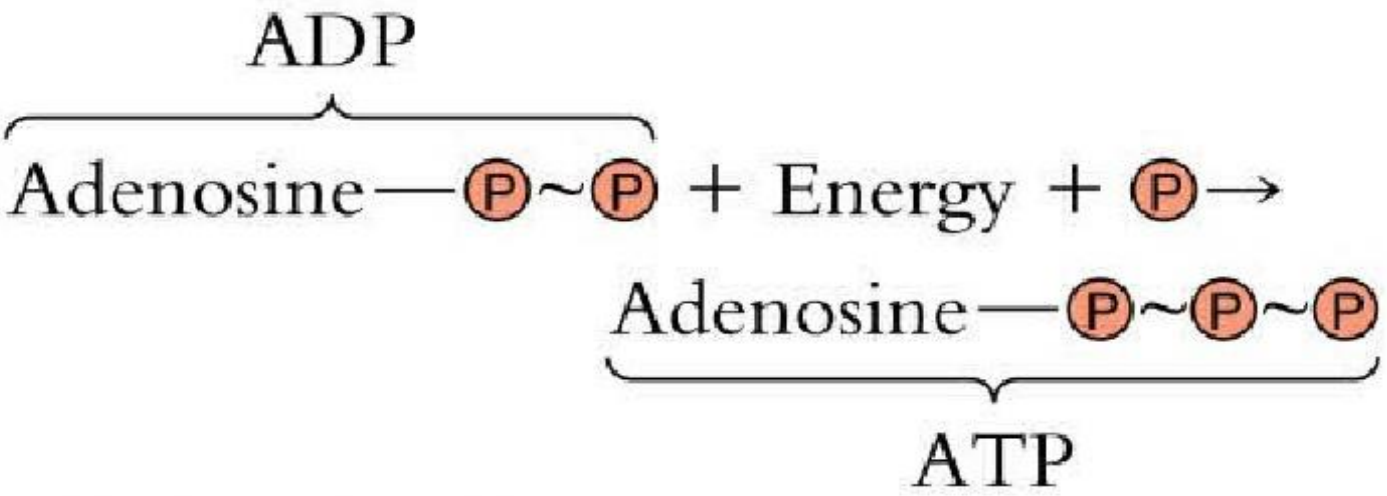
1. Anabolism: Synthesis of more complex compounds and use of energy

2. Catabolism: Break down a substrate and capture energy for growth and maintenance.

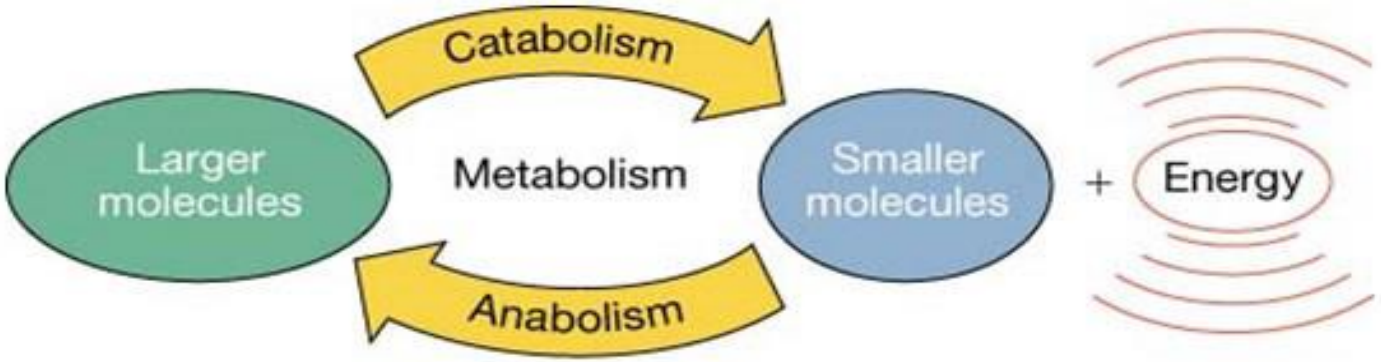
- All cells require the energy supply to survive. The common energy form => ATP (Adenosine Tri-Phosphate)

ATP

is generated by the phosphorylation of ADP



Metabolism Relationships



Microbial metabolism

-Is the means by which a microbe obtains the energy and nutrients, it needs to living and reproduce.

-Microbes use many different types of metabolic strategies, and microbes species can often be differentiated from each other based on metabolic characteristics.

Metabolism of Glucose

- Bacteria can metabolism of glucose, proteins or lipids.

-Bacteria can produce energy from glucose. Glucose breakdown (Glycolysis) can be aerobic (using oxygen) or anaerobic (without oxygen).

-Anaerobic metabolism of glucose is also known as anaerobic glycolysis or fermentation.

-Aerobic metabolism of glucose is known as aerobic glycolysis and respiration.

Catabolism/Aerobic Respiration of Glucose

The breakdown of carbohydrates to release energy

- Glycolysis
- Krebs cycle
- Electron transport chain

Glycolysis

- Glycolytic pathway, the Embden-Meyerhof-Parnas pathway.

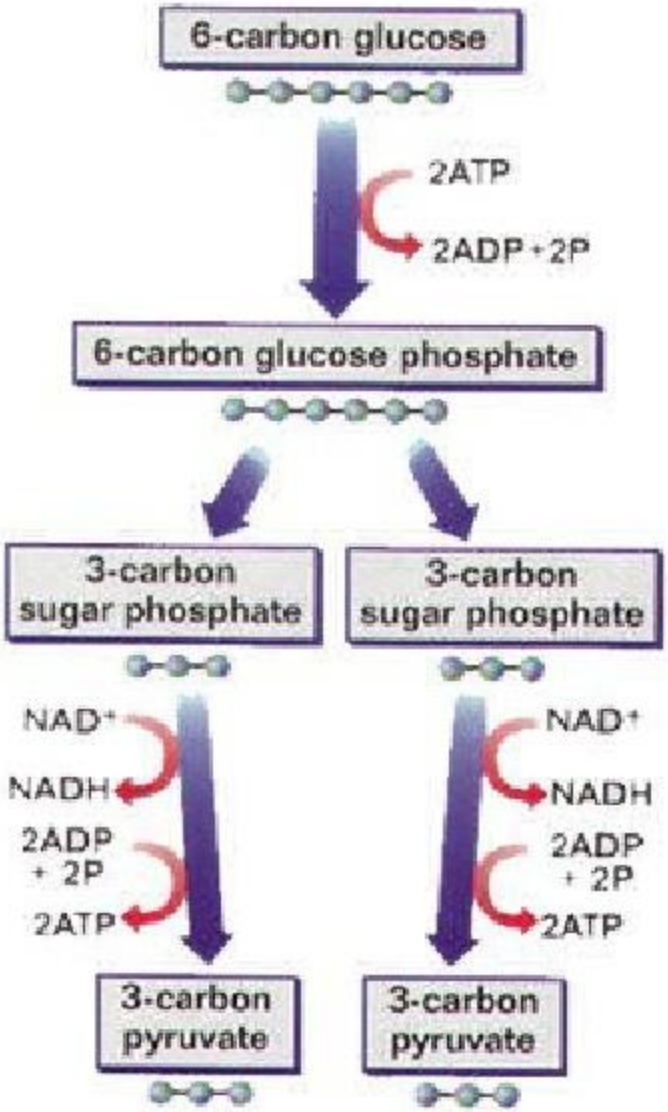
- A nine-step biochemical reactions, each of which requires specific enzymes.

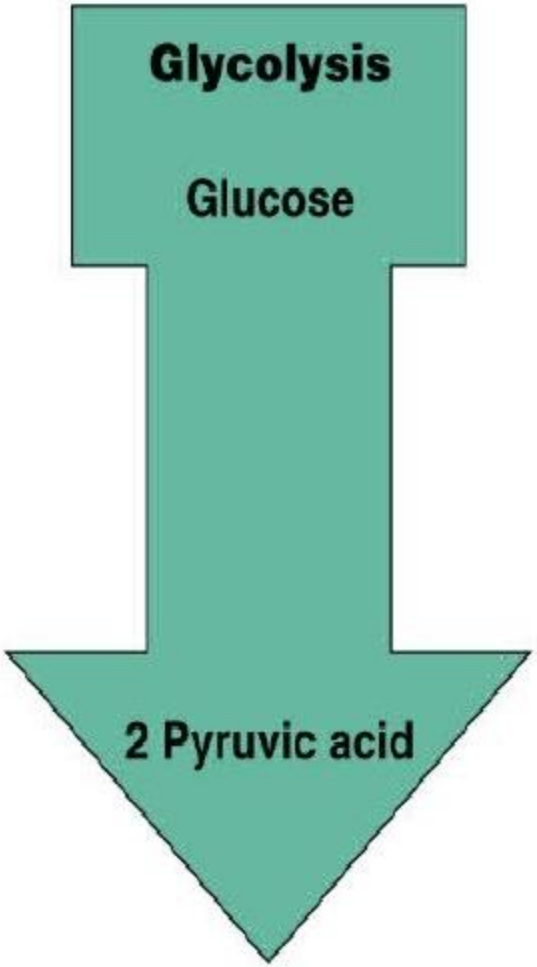
Six-carbon molecule of glucose is broken down into three-carbon molecules of pyruvic acid

- Can take place with or without oxygen

- Produces very little energy–only 2 ATP

- Takes place in the Cytoplasm of both prokaryptic and eukaryotic cells.


6-carbon glucose
2ATP
2ADP + 2P
6-carbon glucose phosphate
3-carbon sugar phosphate
3-carbon sugar phosphate
NAD+
NADH
2ADP + 2P
2ATP
NAD+
NADH
2ADP + 2P
2ATP
3-carbon pyruvate
3-carbon pyruvate


Glycolysis
Glucose
2 Pyruvic acid

Metabolism of Glucose

$C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O + 38$ ATP

-i) the splitting of glucose to 2 pyruvate (pyruvic acid)

-(i) 2 ATP are used

-(ii) 4 ATP are produced (a net gain of 2)

-(iii) 2 NADH (nicotinamide adenine dinucleotide phosphate hydrogen) are produced

Krebs Cycle

- The pyruvic acid produced during glycolysis are converted into acetyl-CoA.

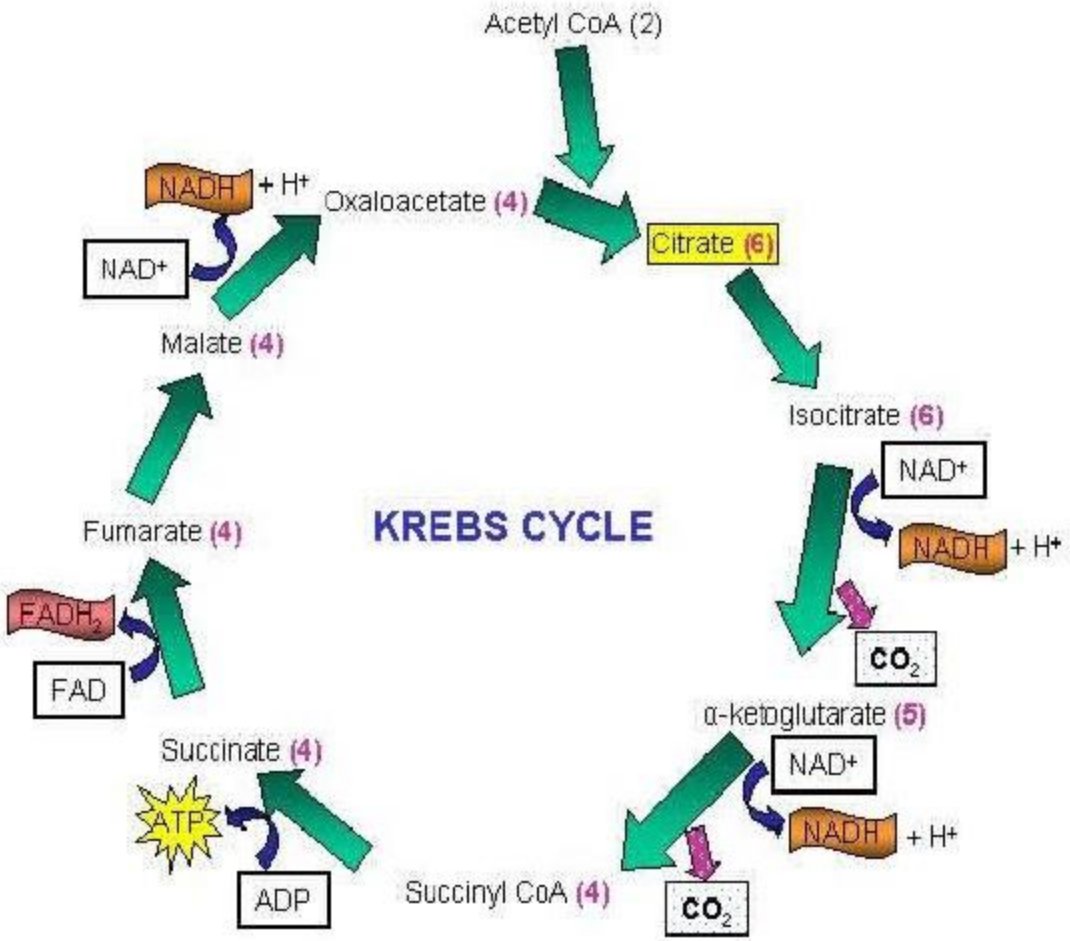
-The Krebs Cycle is consists of eight reactions.

-Acetyl-CoA combine with oxalate to produce citric acid (tricarboxylic acid).

-Only 2 ATP produced, but a number of products like

NADH, FADH 2 and H ions

Mitochondria (eukaryotes); cell membrane (prokaryotes).


Acetyl CoA (2)
Oxaloacetate (4)
Citrate (6)
Isocitrate (6)
α-ketoglutarate (5)
Succinyl CoA (4)
Succinate (4)
Fumarate (4)
Malate (4)
KREBS CYCLE
NAD+
NADH + H+
CO2
ATP
ADP
FADH2
FAD

Electron Transport Chain

- Certain of the products produced during the Krebs cycle enter the **electron transport chain**

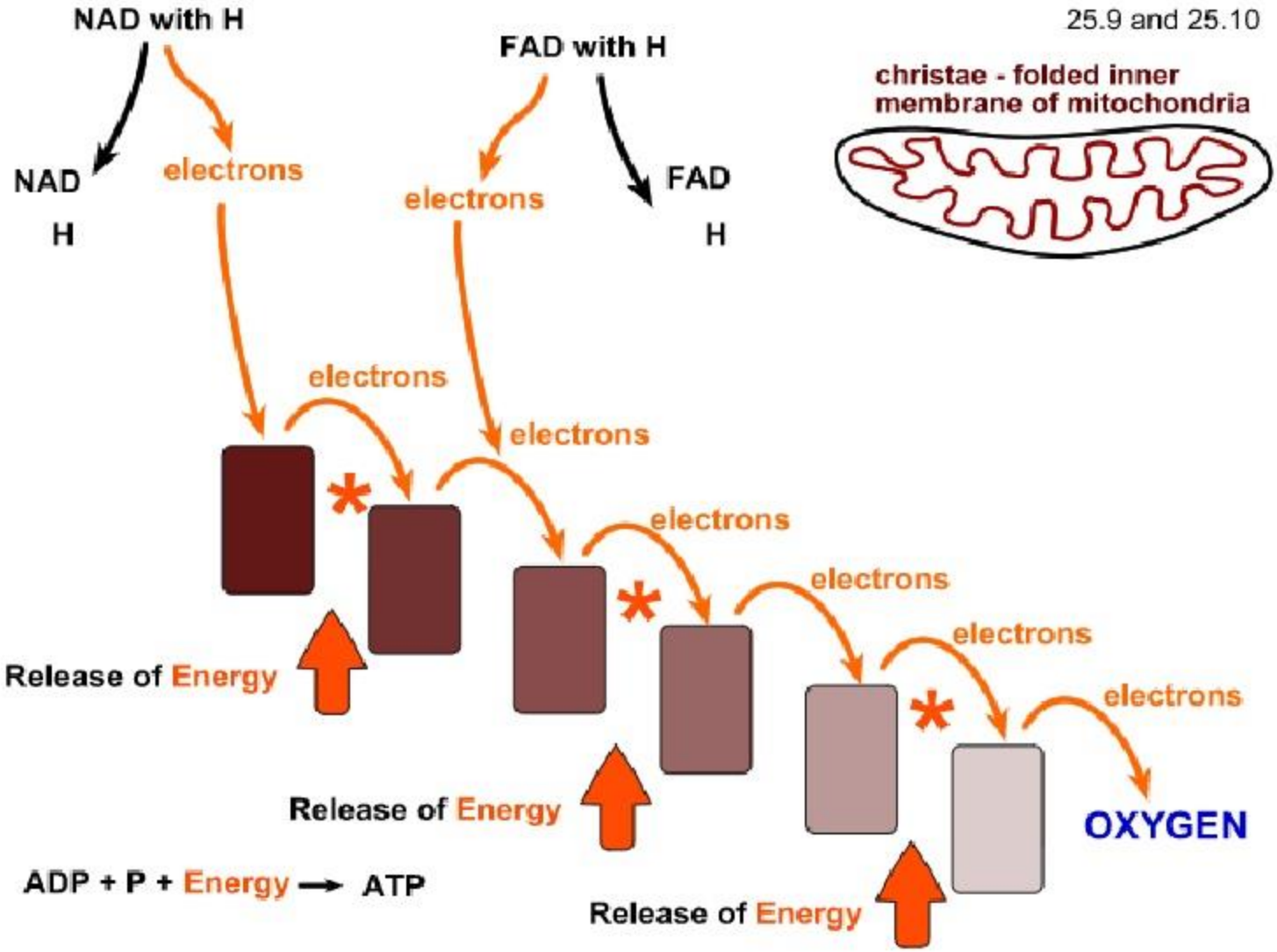
- Consist of a series of **oxidation-reduction reactions**, whereby energy is released as electrons are transferred from one compound to another.

- **Oxygen** is the end of the chain; referred to as then final or terminal electron acceptor.

- **Cytochrome oxidase** enzyme responsible for transferring electrons to oxygen.

- Produces **32 ATP** in prokaryotic cells, and **34ATP**

in eukaryotic cells.


NAD with H
NAD
H
electrons
FAD with H
electrons
FAD
H
25.9 and 25.10
christae - folded inner membrane of mitochondria
electrons
electrons
electrons
electrons
electrons
electrons
Release of Energy
Release of Energy
Release of Energy
OXYGEN
ADP + P + Energy → ATP

Number of ATP Produced From One Molecule of Glucose by Aerobic Respiration

Biochemical pathways	Prokaryotic	Eukaryotic
Glycolysis	2	2
Kreps cycle	2	2
ETC	32	34
Total ATP	36	38

Immunology

Introduction

By

Prof. Dr. Batool Hassan Al-Ghurabi

Immunology

- **Immunology** is a branch of biomedical science that covers the study of immune systems in all organisms. It deal with the response of an organism to antigenic challenge.
- **Immunity (resistance)**
- The word immunity was derived from the Lain word “immunis” meaning exempt.
- It is the sum of all naturally occurring defense mechanisms that protect humans from infectious disease.

Immune system

The immune system refers to a collection of organs, cells and proteins that function to protect all the body (skin, respiratory and intestinal tract and other areas) from foreign antigens, such as microbes (bacteria, fungi, viruses and parasites).

Two important types

I. Innate (natural) or non-specific immunity

II. Adaptive (acquired) or specific immunity

- **Protection Against Invading Pathogens**

1. **First Line of Defense: Non-specific natural barriers which restrict entry of pathogen.**

   Examples: Skin and mucous membranes.

2. **Second Line of Defense: Innate non-specific immune defenses provide rapid local response to pathogen after it has entered host.**

   Examples: Fever, phagocytes (macrophages and neutrophils), inflammation, and interferon.

3. **Third line of defense: Antigen-specific immune responses, specifically target and attack invaders that get past first two lines of defense.**

   Examples: Antibodies and lymphocytes.

Natural or innate or non-specific immunity

-It is present at birth.

- Has the ability to resist infection by means of normally present body functions.

- Many of these mechanisms are subject to influence by factors as nutrition, age, fatigue, stress, and genetic determinants.

Innate defenses can be classified into three main groups:

1. Barriers to infection
2. Humoral factor (Soluble proteins).
3. Cells

1. Barriers to infection

- **Physical and mechanical barriers**

Skin and mucosal membranes act as physical barriers to the entry of pathogens. Tight junctions between cells prevent the majority of pathogens from entering the body.

- The flushing actions of tears, saliva and urine protect epithelial surfaces from colonization.

- High oxygen tension in the lungs, and body temperature, can also inhibit microbial growth.
- In the respiratory tract, mucus is secreted to trap microorganisms. They are then mechanically expelled by:
- Beating cilia
- Coughing
- Sneezing.

Chemical barriers

-The growth of microorganisms is inhibited at acidic pH (e.g. in the stomach and vagina).

-Lactic acid and fatty acids in sebum (produced by sebaceous glands) maintain the skin pH between 3 and 5.

-Enzymes such as lysozyme (found in saliva, sweat and tears) and pepsin (present in the gut) destroy microorganisms.

- Biological barriers (normal flora)

Normal flora is formed when non-pathogenic bacteria colonize epithelial surfaces. Normal flora protects the host by:

- Competing with pathogenic bacteria for nutrients and attachment sites
- Production of antibacterial substances.

2. Humoral factor (Soluble proteins).

When infectious agents have penetrated tissues another innate defense mechanism play role in protection. Humoral factors play an important role in inflammations, and these factors found in serum or they are formed at the site of infection.

- 1. Complement system: is a group of serum proteins which inactive functionally, but when activated they damage the membranes of the pathogenic organisms, either destroying the pathogens or facilitating their clearance.
- 2. Beta-lysin: is a protein produce by platelets during coagulation can lyses many bacteria by chemotactic agents for phagocytic cells.
- 3. Interferons (INF): which are group of proteins produced by virus infected cells. Among the many functions of INF is the ability to bind to nearby cells and induce a generalized antiviral state. There are three types of them (IFN α, γ, β).

- 4. Lactoferrin and transferrin: are iron-binding proteins that compete with microorganisms for iron, an essential metabolite.

5. Lysozyme: bactericidal enzyme in mucus, saliva, tears, sweat and breast milk, it cleaves peptidoglycan in the cell wall of microorganisms.

6. Cytokines: Tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1) and IL-12.

3. Cells of innate immunity

The cells of the innate immune system consist of:

1. Phagocytes (Macrophage and Neutrophils)
2. Natural killer cells.

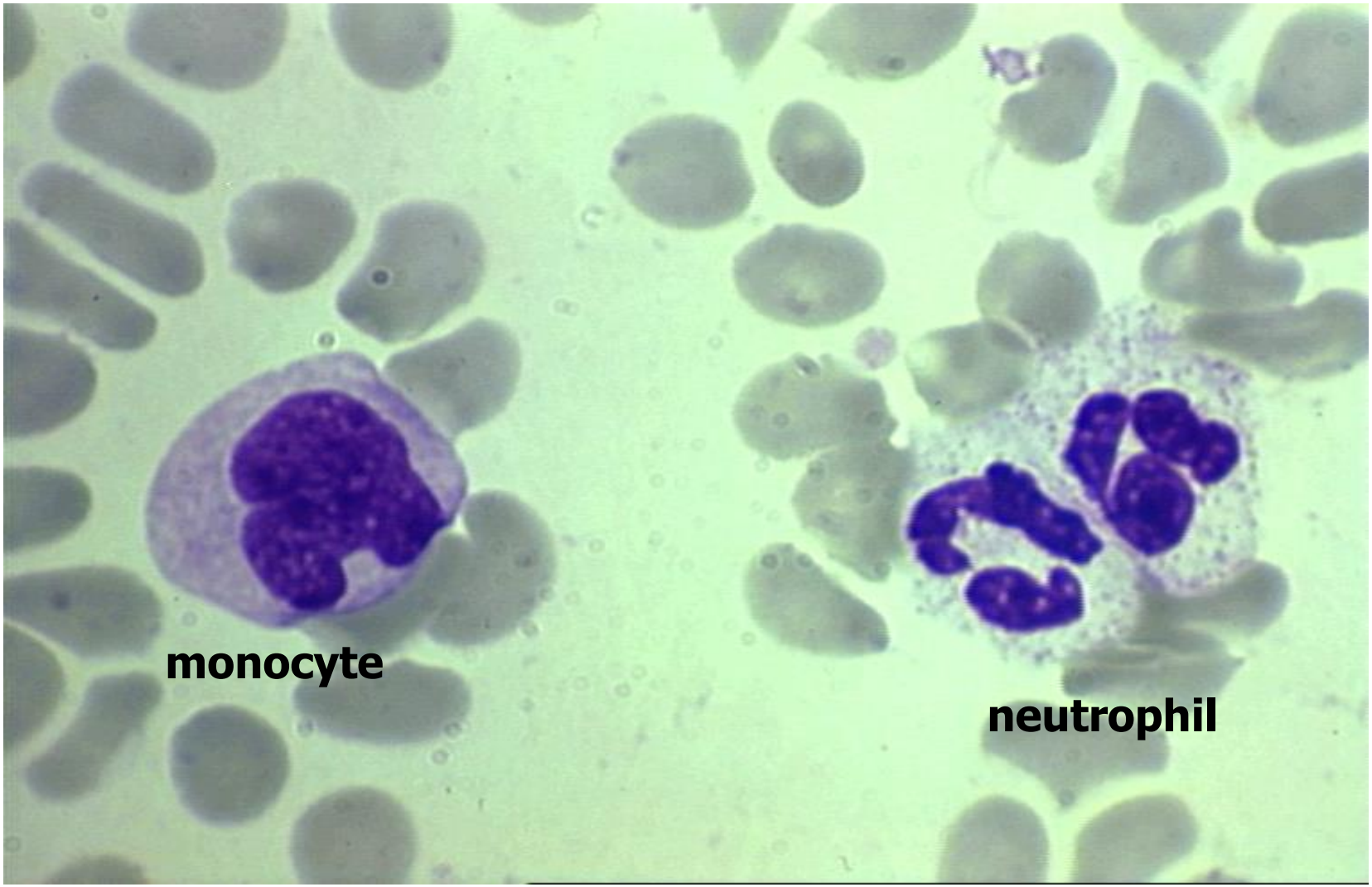
- **Phagocytes**

Phagocytes (macrophages and neutrophils) engulf and then destroy pathogens by process of phagocytosis.

Macrophages are long lived cells at sites of infection; they release cytokines that recruit the shorter-lived but more actively phagocytic **neutrophils**.

- Neutrophils comprise 50–70% of circulating white cells. Neutrophils arrive quickly at the site of inflammation and in the act of killing pathogens they die.

Phagocytic cells



Stages of Phagocytosis

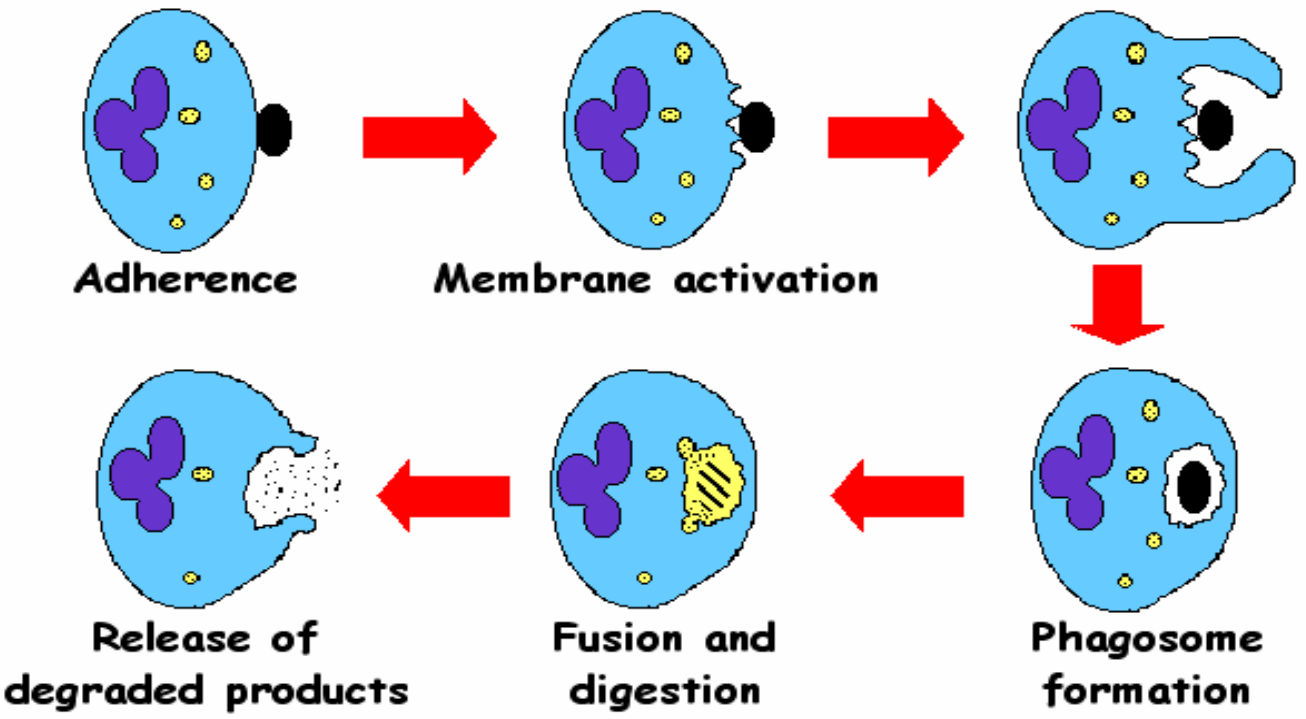
1.Chemotaxis: Phagocytes are chemically attracted to site of infection.

2.Adherence: Phagocyte plasma membrane attaches to surface of pathogen or foreign material.

3. Ingestion: Plasma membrane of phagocytes extends projections (pseudopods) which engulf the microbe. Microbe is enclosed in a sac called phagosome.

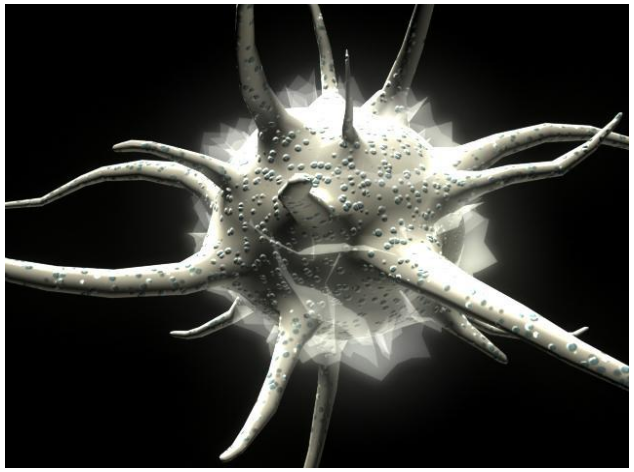
4. Digestion: Inside the cell, phagosome fuses with lysosome to form a phagolysosome. Lysosomal enzymes kill most bacteria within 30 minutes.

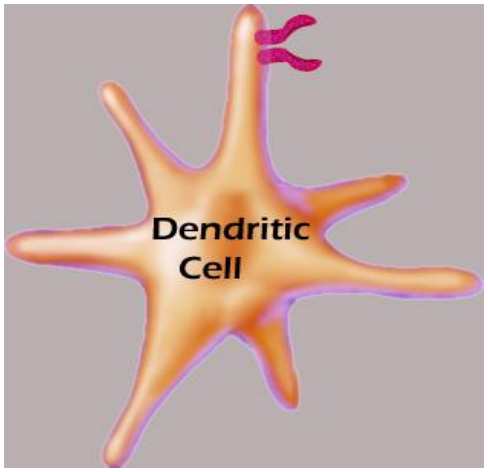
Phagocytosis

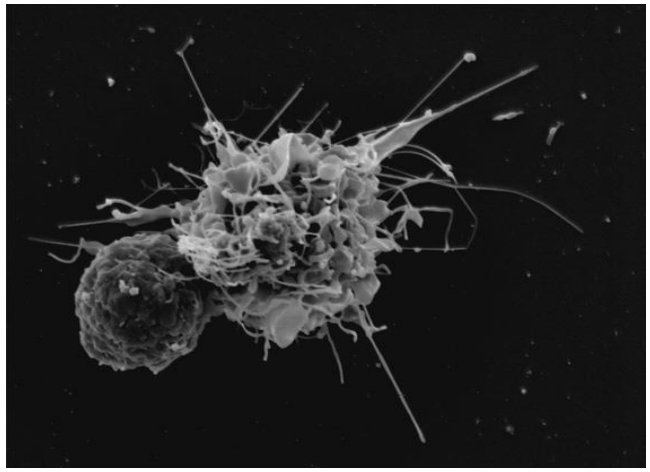


Antigen presenting cells (APC)

- Antigen presenting cells- are cells that mediate cellular immune response by engulfment, processing and presenting antigens to the T-cell receptor.
- **Traditional APC include: macrophages, dendritic cells, langerhans cells, and B- lymphocytes.**



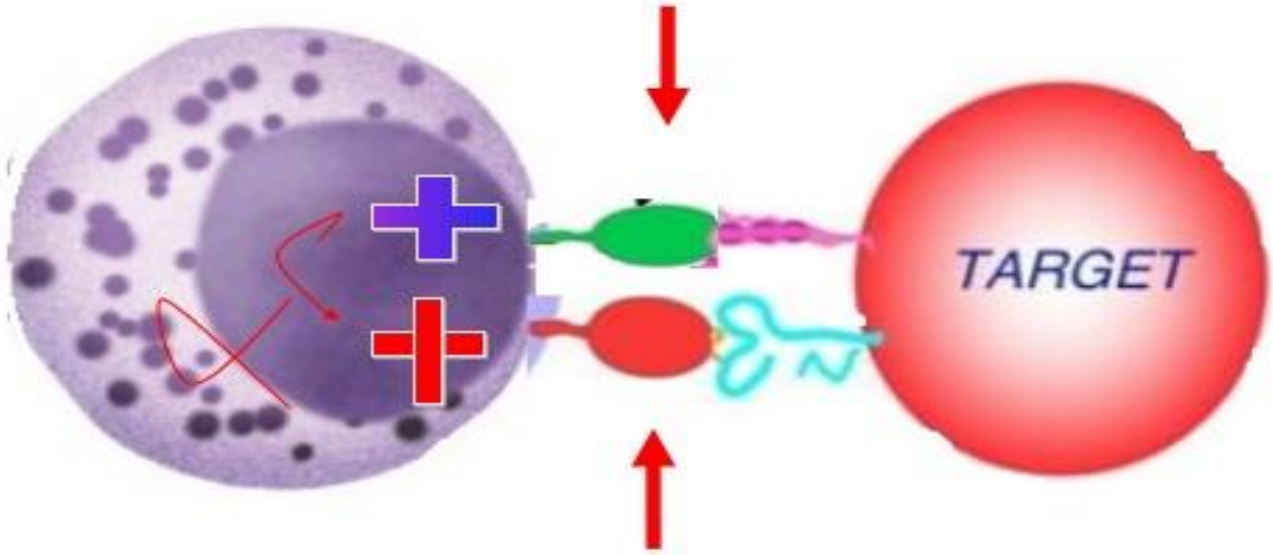




Natural killer (NK) cells

Large granular lymphocytes (not B-cell or T-cell) Kills tumor cells & viral inf. cells (intracellular pathogens) NK cells do not require prior immunization or activation They attach to ‘target’ cells, then cytotoxic granules are released onto surface of cell and effectors proteins penetrate cell membrane and induce death.

Activating receptors



Inhibitory receptors

SANA ISAA SOULIMAN

- **Inflammation:** Triggered by tissue damage due to infection, heat, wound, etc.
- **Major Symptoms of Inflammation**

1. Redness
2. Pain
3. Heat
4. Swelling

May also observe:
5. Loss of function

- **Functions of Inflammation**

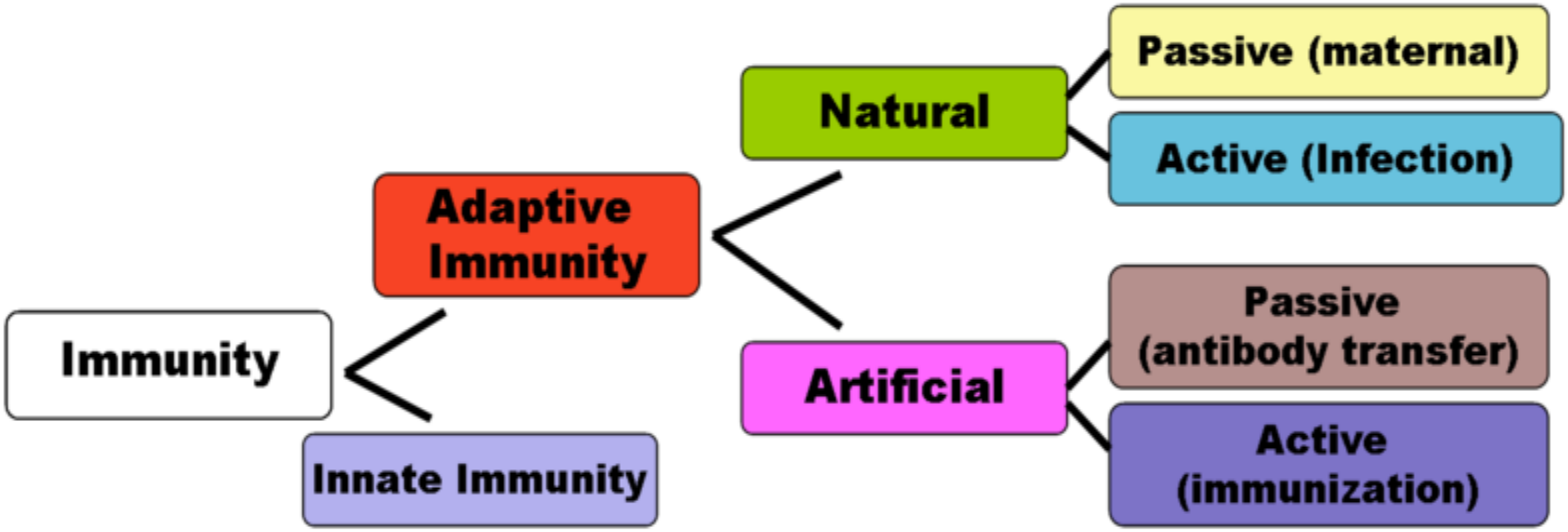
1. Destroy and remove pathogens
2. If destruction is not possible, to limit effects by confining the pathogen and its products.
3. Repair and replace tissue damaged by pathogen and its products.

Adaptive or acquired or specific immunity

is a type of resistance that is characterized by **specificity** for each individual pathogen, or microbial agent, and the ability to **remember** a prior exposure, which results in an increased response upon repeated exposure.

- Adaptive immunity is often sub-divided into two major types depending on how the immunity was introduced:
- **a. Naturally acquired immunity:** is occurs through contact with a disease.
- **b. Artificially acquired immunity:** is develops only through deliberate actions such as vaccination.
- **Both naturally and artificially acquired immunity can be further subdivided depending on whether immunity is induced in the host or passively transferred from an immune host.

- Naturally acquired ⟶ Placental transfer of antibody (Passive)
- Recovery from disease (Active)
- Artificially acquired ⟶ Administration of antitoxin (Passive)
- Vaccination (Active)



- **Adaptive immunity is mediated by B or T lymphocytes and stimulated by exposure to infectious agents.**

I- Humoral Immunity (Antibody Immunity):

- Type of immunity that is mediated by secreted antibodies produced by the B-lymphocyte cells. Secreted antibodies bind to antigens on the surfaces of invading microbes (such as viruses or bacteria), which exposure them for destruction.
- Humoral immunity is called as such, because it involves substances found in the body fluids.

II- Cell-mediated immunity (Cellular Immunity):

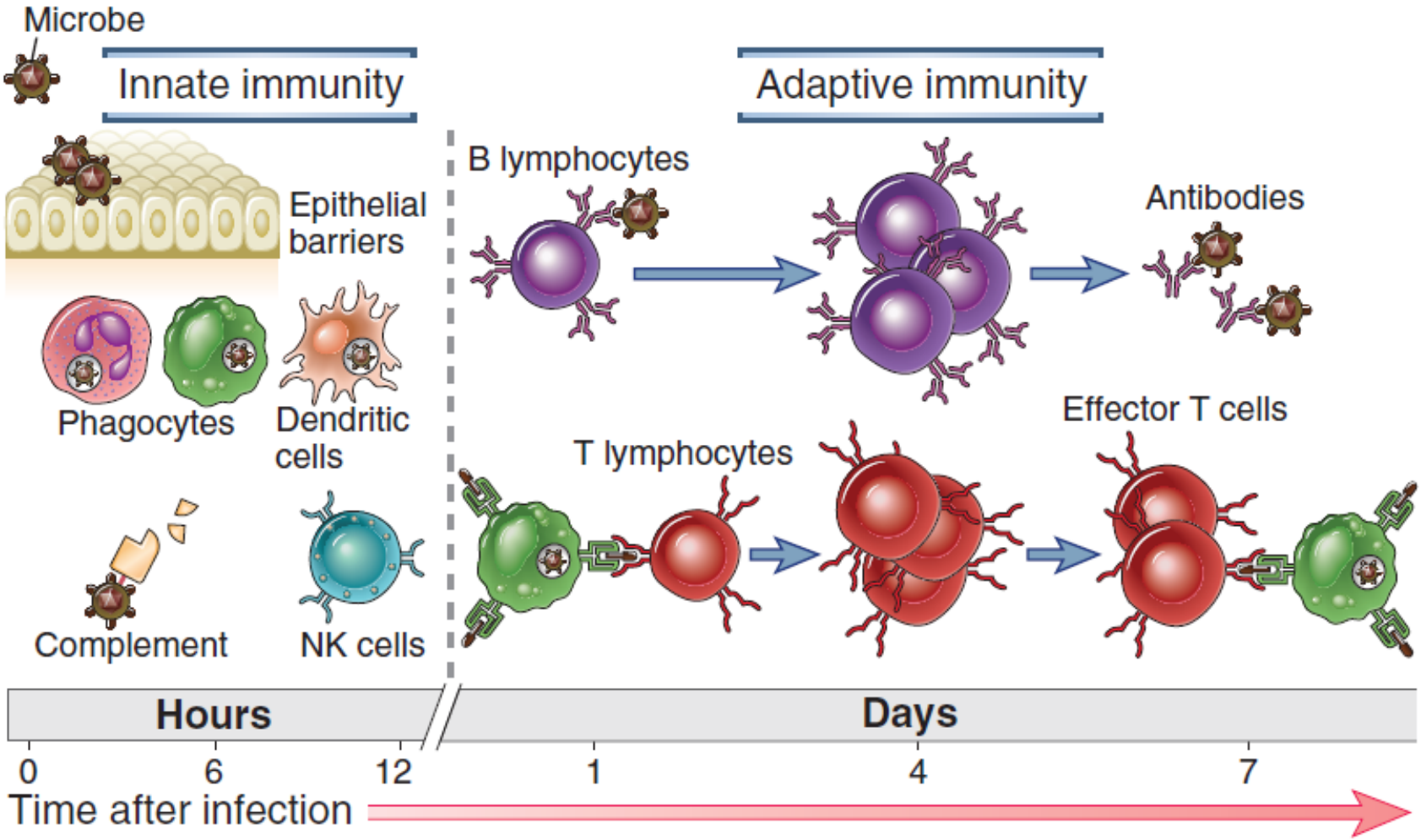
- Since antibodies are useless against intracellular antigens, cell-mediated immunity is needed. Two major populations of T cells mediate cellular immunity:
  1. CD4 cells are helper T cells (T_H).
  2. CD8 cells are cytotoxic T cells (T_C) that destroy cells harboring foreign antigens.
- Regulatory T cells that release cytokines, which suppress the activity of both T cells and B.

Cellular Immunity .vs. Antibody Immunity

Cellular Immunity	Antibody or Humoral Immunity
• Carried out by T-Cells • Infected cells are killed by Cytotoxic T –Cells.	• Carried out by B-cells • Antibodies are produced and dumped into blood stream. • Antibodies bind to antigens and deactivate them.

The innate and adaptive immune response

Characteristics	Cells	Molecules
Innate immunity		
• Responds rapidly • No memory • No specificity • No prior exposure is required	• Physical barriers • Phagocytes (PMNs and macrophages) • Natural killer cells	• Humoral factors • Complement • Acute phase Proteins • Cytokines
Adaptive immunity		
• Responds Slowly • Memory • Highly specific • Present after exposure to an Ag	• T cells • B cells • Dendritic cells	• Antibodies • Cytokines • Granzymes


Microbe
Innate immunity
Adaptive immunity
B lymphocytes
Antibodies
Epithelial barriers
Phagocytes
Dendritic cells
T lymphocytes
Effector T cells
Complement
NK cells
Hours
Days
0
6
12
1
4
7
Time after infection

- **Immunogens:** substance that induce specific immune response.

Antigen: substance that react with the product of specific immune response.

- **Hapten:** substance that are non-immunogenic, small molecules and can never induces immune response by themselves unless coupled to a carrier molecules, but can react with the specific immune products therefore haptens have the property of antigenicity but not immunogenicity.

- **Antibody:** specific protein which is produce in response to immunogen and reacts with an antigen

Epitope or antigenic determinant:

- the portion of antigen (Ag) that combines with antibody (Ab).

Adjuvant: substance that can enhance the immune response to an immunogen.

Paratope: the portion of antibody (Ab) that combines with antigen (Ag).