Al-Mustaqbal University College

Pharmacy Department / Second Stage

PHYSIOLOGY II

HEMATOLOGY ,L2

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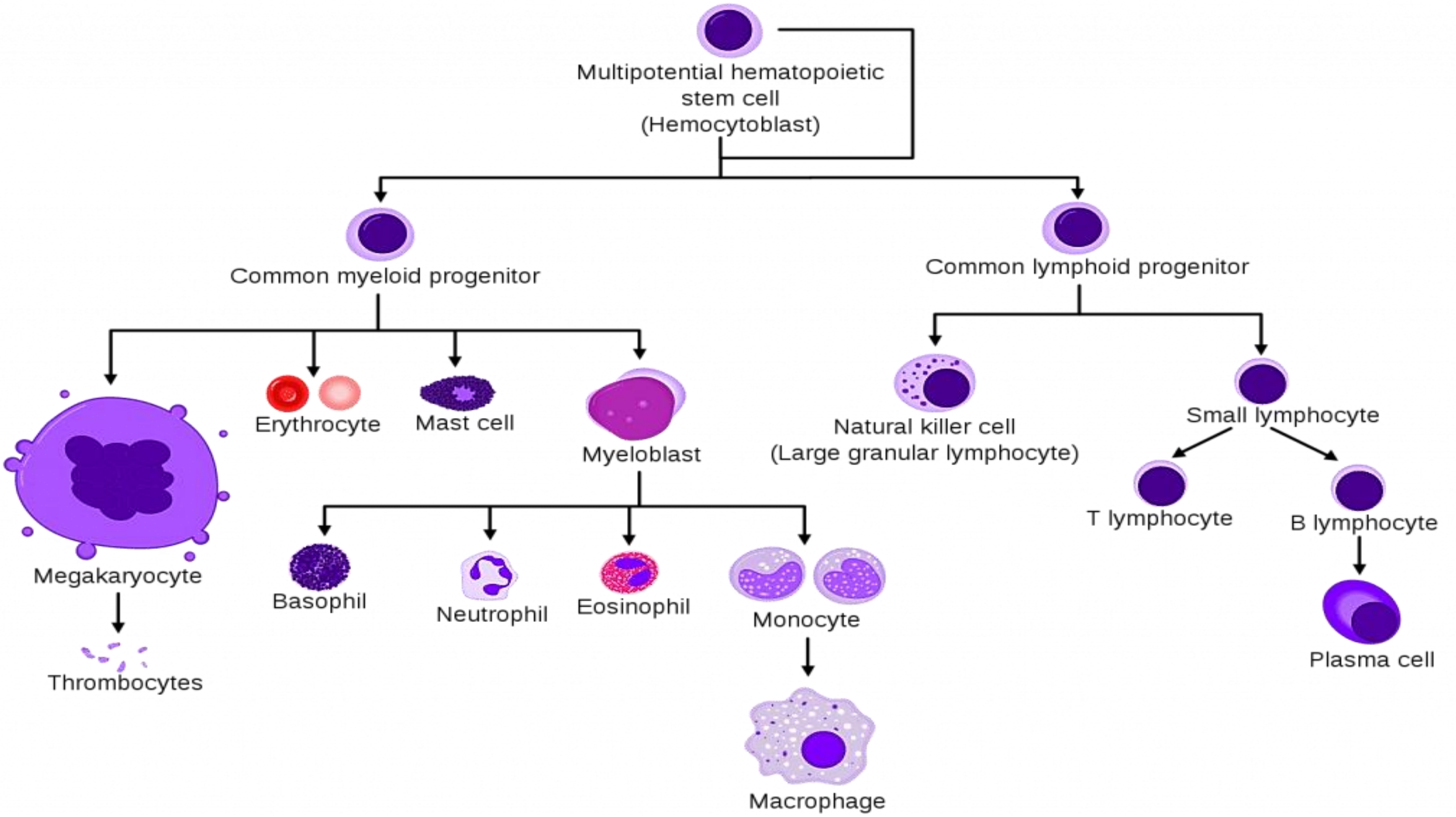
White blood cells, also known as leukocytes, are immune cells that circulate in the blood and lymphatic system.
There are 5 main types:

Neutrophils – main action against bacterial and fungal infections.
Monocytes – main action against bacterial infections.
Eosinophils – main action against parasitic infections.
Basophils – responsible for responses to allergens.
Lymphocytes – main action against viral infections.
Neutrophils, eosinophils, and basophils are granulocytes since they have cytoplasmic granules which can digest microorganisms.

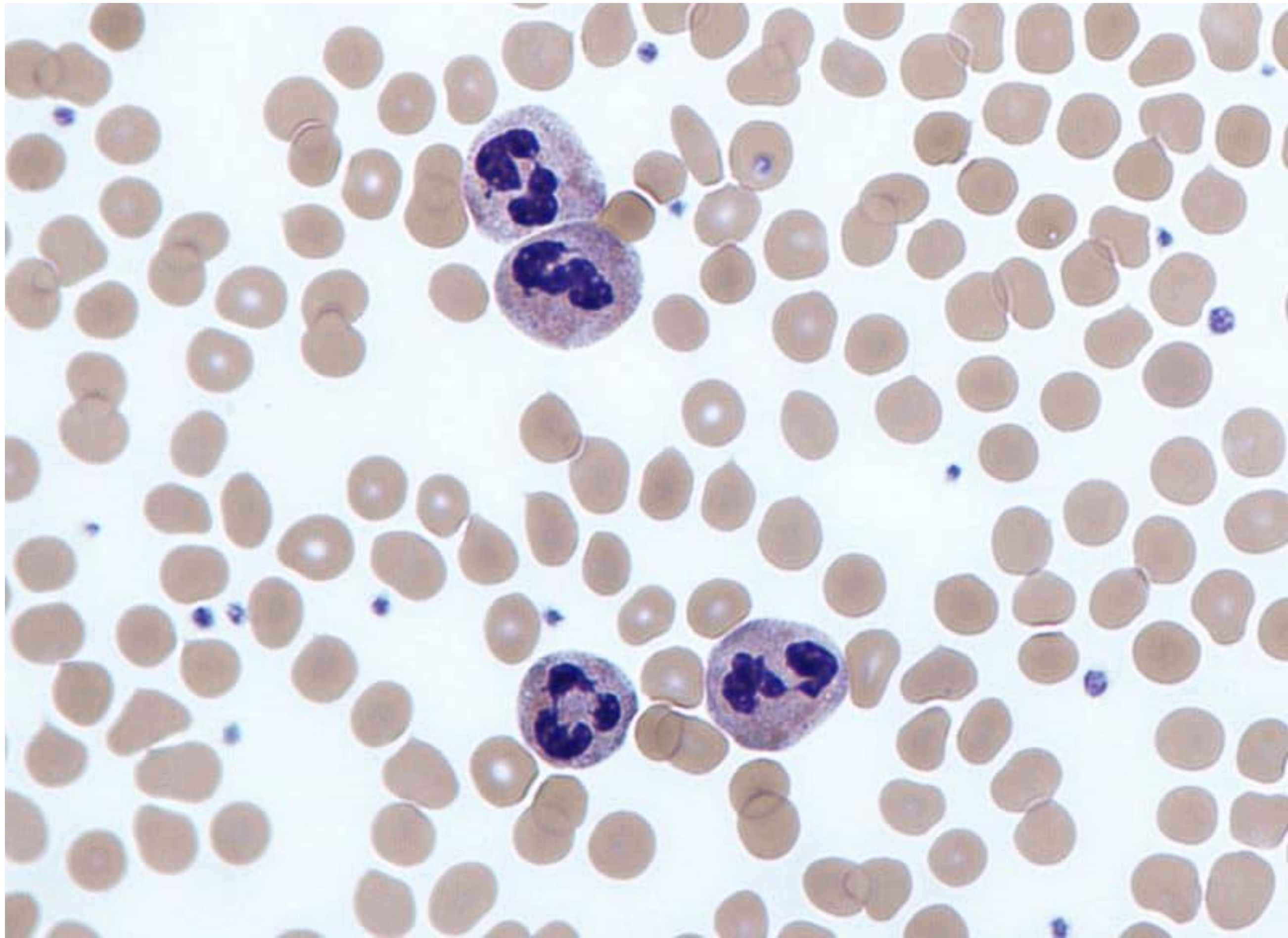
Lymphocytes and monocytes are agranulocytes since they lack granules in their cytoplasm.
WBCs are produced in the bone marrow and circulate throughout the body in the bloodstream. They can also move into tissues to fight infections. The number and type of WBCs in the blood can be used to diagnose infections and other diseases.


Multipotential hematopoietic stem cell (Hemocytoblast)
Common myeloid progenitor
Common lymphoid progenitor
Megakaryocyte
Thrombocytes
Erythrocyte
Mast cell
Myeloblast
Basophil
Neutrophil
Eosinophil
Monocyte
Macrophage
Natural killer cell (Large granular lymphocyte)
Small lymphocyte
T lymphocyte
B lymphocyte
Plasma cell

Neutrophils

Neutrophils are **granular** leukocytes and develop within the bone marrow. They are the most abundant leukocyte type, making up 40-70% of those found in peripheral blood. Neutrophils are primarily involved in the immune response against bacterial infections and their presence in tissue is associated with acute inflammation.

They are 9-16μm in diameter and have a **multi–lobed nucleus**. Their cytoplasm contains granules with degradative enzymes which are released during phagocytosis. They have a short lifespan of 2-3 day and are one of the first responders to invading microbes. Bacterial infections, stress, cancers (e.g. leukaemia) and trauma can cause **high neutrophil counts**.

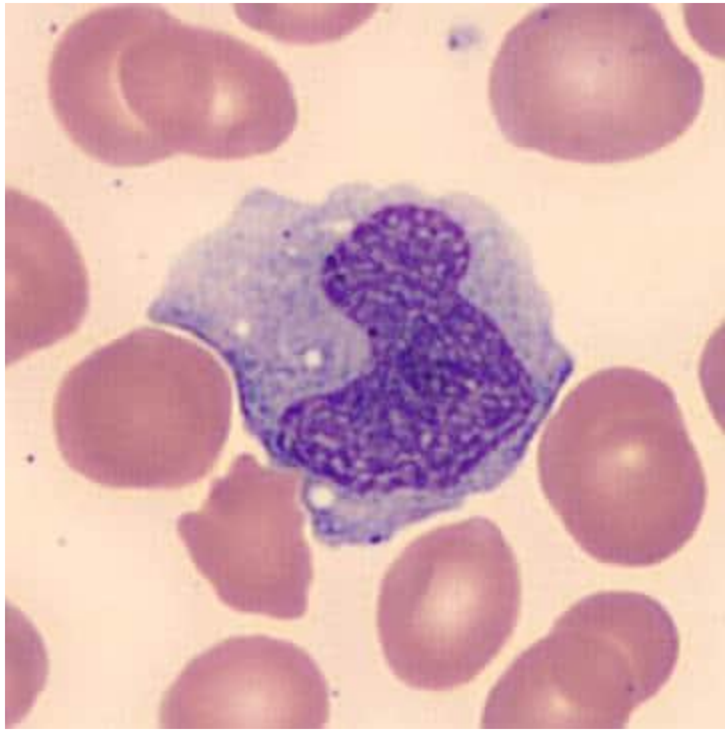


Chemotherapy, aplastic anaemia, Vitamin B12 deficiency and cancer can cause **low neutrophil counts.**

Monocytes

Monocytes belong to the myeloid cell line within the bone marrow. They are primarily involved in the immune response against **bacterial infection** and make up roughly 5-10% of all circulating leukocytes. They have a kidney bean-shaped nucleus.

Monocytes are **circulating leukocytes** which typically remain in the blood for around 8 hours before migrating into tissue where they differentiate into macrophages.



Macrophages then form the main population of phagocytic cells within tissues and have a much longer lifespan than neutrophils, lasting months or even years. In some tissues, resident macrophages have specific names e.g. Kupffer cells in the liver and osteoclasts in the bone.

They are much larger than neutrophils, with a diameter of 25-50µm and have a single-lobed, round nucleus.

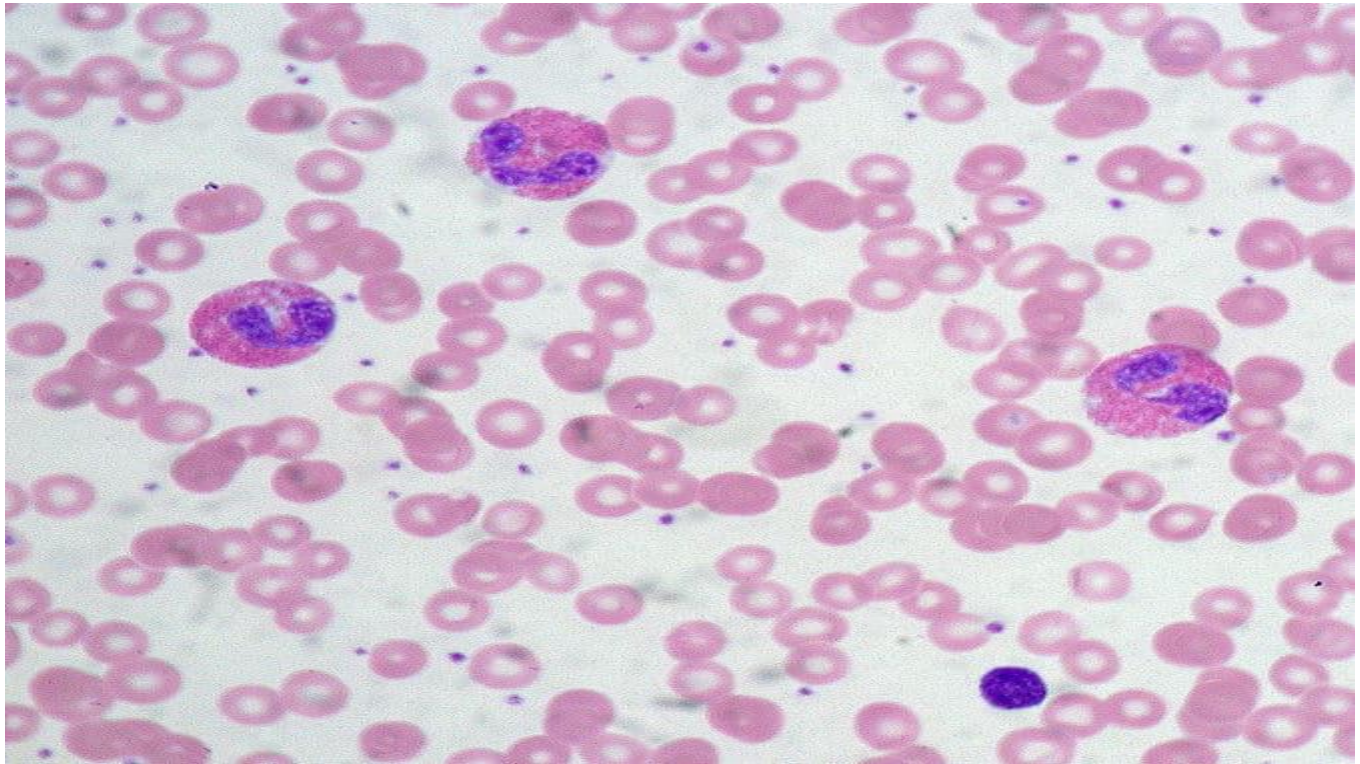
In certain situations, monocytes can also differentiate into dendritic cells. These form an important link between the innate and adaptive immune systems.

Eosinophils

Eosinophils, named so because they histologically stain with **eosin**, are granular leukocytes from the myeloid cell line within the bone marrow. They make up 1-3% of circulating leukocytes. Eosinophils generally spend around an hour in peripheral blood and are mainly present in tissues.

They have a diameter of 12-17μm and have a bi-lobed, sausage-shaped nucleus.

Patients with parasitic infections, allergic reactions or some autoimmune diseases (see below) typically display high eosinophil counts.



Basophils

Basophils are **granular** leukocytes of myeloid lineage. They are 14-16μm in diameter and have a bi-lobed, S-shaped nucleus. Basophils circulate through the peripheral blood and have a lifespan of roughly 2 weeks.

They are very similar in function and appearance to mast cells, which are found within tissues.

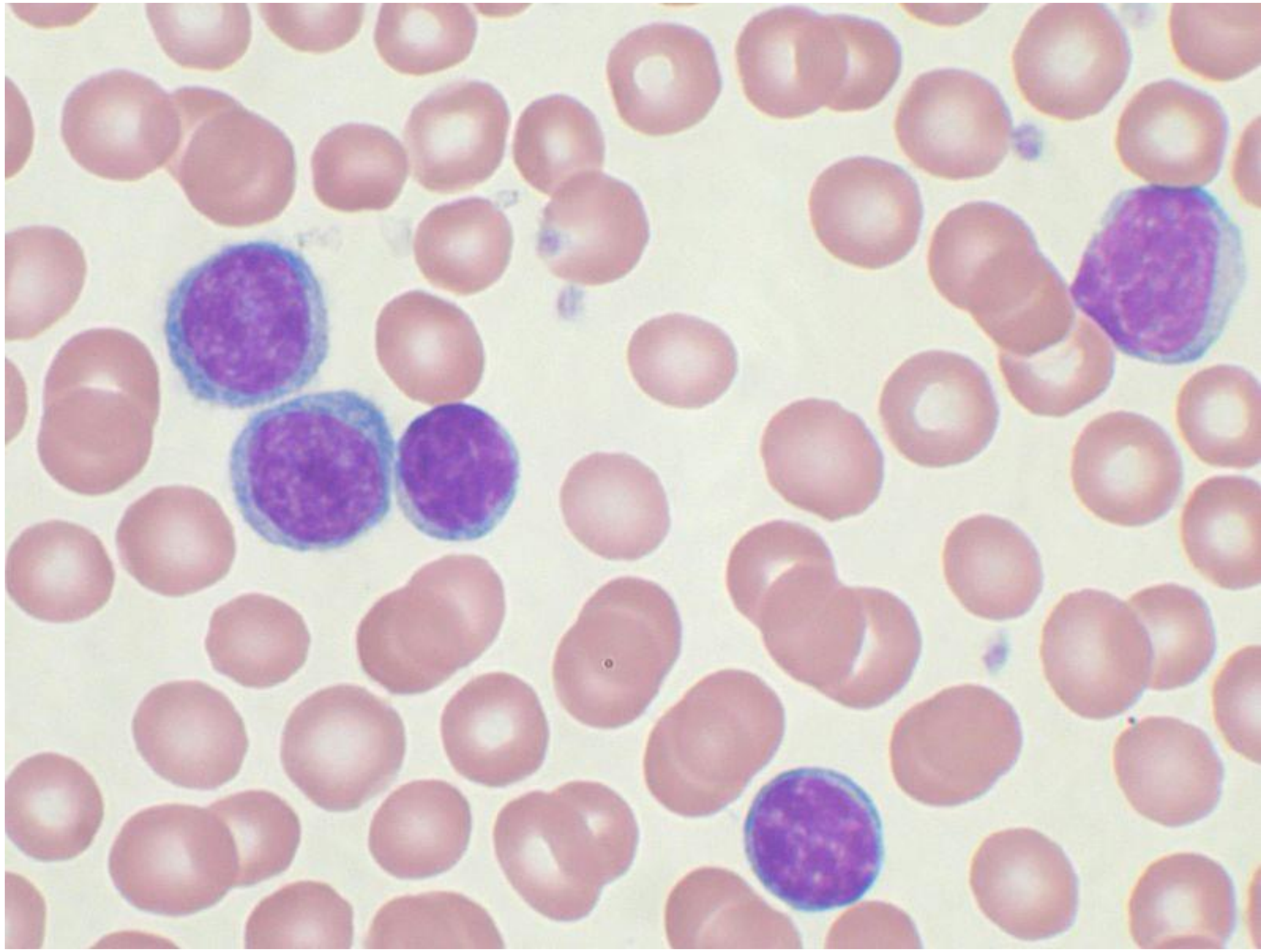
Basophils contain **histamine** granules and cause local inflammatory responses through their interaction with IgE. Patients with allergic reactions typically have **high basophil counts**.

Basophil

Lymphocytes

Lymphocytes are **agranular** leukocytes which form from the lymphoid cell line within the bone marrow. They respond to **viral infections** and are the smallest leukocytes, with a diameter of 6-15μm. Lymphocytes have round, densely-staining nuclei with sparse cytoplasm.

They circulate between the tissues, peripheral blood and lymphatic system. Their lifespan also varies depending on the subtype that they differentiate into. There are three major types of lymphocytes:



- **Natural killer cells**
- **T cells**
- **B cells**

Natural Killer Cells

NK cells provide **non-specific immunity** against cells displaying foreign proteins such as **cancer** cells and **virally-** infected cells. They make up less than 5% of circulating leukocytes.

T Cells

T cells form in the bone marrow but mature in the **t**hymus. They are part of the adaptive immune system and are involved in cell-mediated immunity.

Once active, Cytotoxic T cells can directly attack infected cells. In addition, helper T cells have many functions including activating B cells and forming memory T cells which respond on re-infection

B Cells

B cells form and mature in the **b**one marrow. They are part of the adaptive immune system and involved in humoral immunity by secreting antibodies. Once active, B cells mature into **plasma cells** which secrete antibodies, and **memory B cells**.

Phagocytosis is a type of endocytosis whereby a cell engulfs a particle in an internal compartment- the **phagosome.** The cell rearranges its membrane to surround and internalise the target particle.
Phagocytosis is a major mechanism for detecting and removing potentially pathogenic material. Phagocytes also have lysosomes which are membrane-bound organelles containing hydrolytic enzymes.

Phagocytic Cells of The Immune System

Many cells are capable of phagocytosis, but these are specialised for this role:

•**Neutrophils** are abundant in the blood and essential in acute inflammation, as they are the first immune cells to arrive at the infection site.
•**Macrophages** are tissue-resident cells that act as an initial defence mechanism and serve to activate the adaptive immune response.
•**Dendritic cells** – these cycle through the bloodstream, tissues and lymphoid organs, sampling potential pathogens and acting as a major link between the innate and adaptive immune systems.

Stages of Phagocytosis

Activation

Resting phagocytes become activated by inflammatory mediators (e.g. bacterial proteins, capsules, peptidoglycan, prostaglandins, complement proteins). Consequently, they gain the ability to leave the capillaries, enter tissues and move towards the infection site **(chemotaxis).**

Chemotaxis

Chemotaxis is the directional movement of the phagocyte towards a chemical attractant (chemotaxins). **Chemotaxins** include bacterial products (e.g. endotoxin), injured tissues, complement proteins (C3a, C4a, C5a) and chemical substances produced by leukocytes (leukotrienes). Chemotaxins both activate phagocytes and attract them to the target site to mediate their effect.

Margination, Rolling and Adhesion

In margination, leukocytes assume marginal positions in the blood vessels. They intermittently stick to the walls of the venules and roll along them until they become firmly attached to the vessel wall **(adhesion).** At this point, they begin to move out of the vessel.

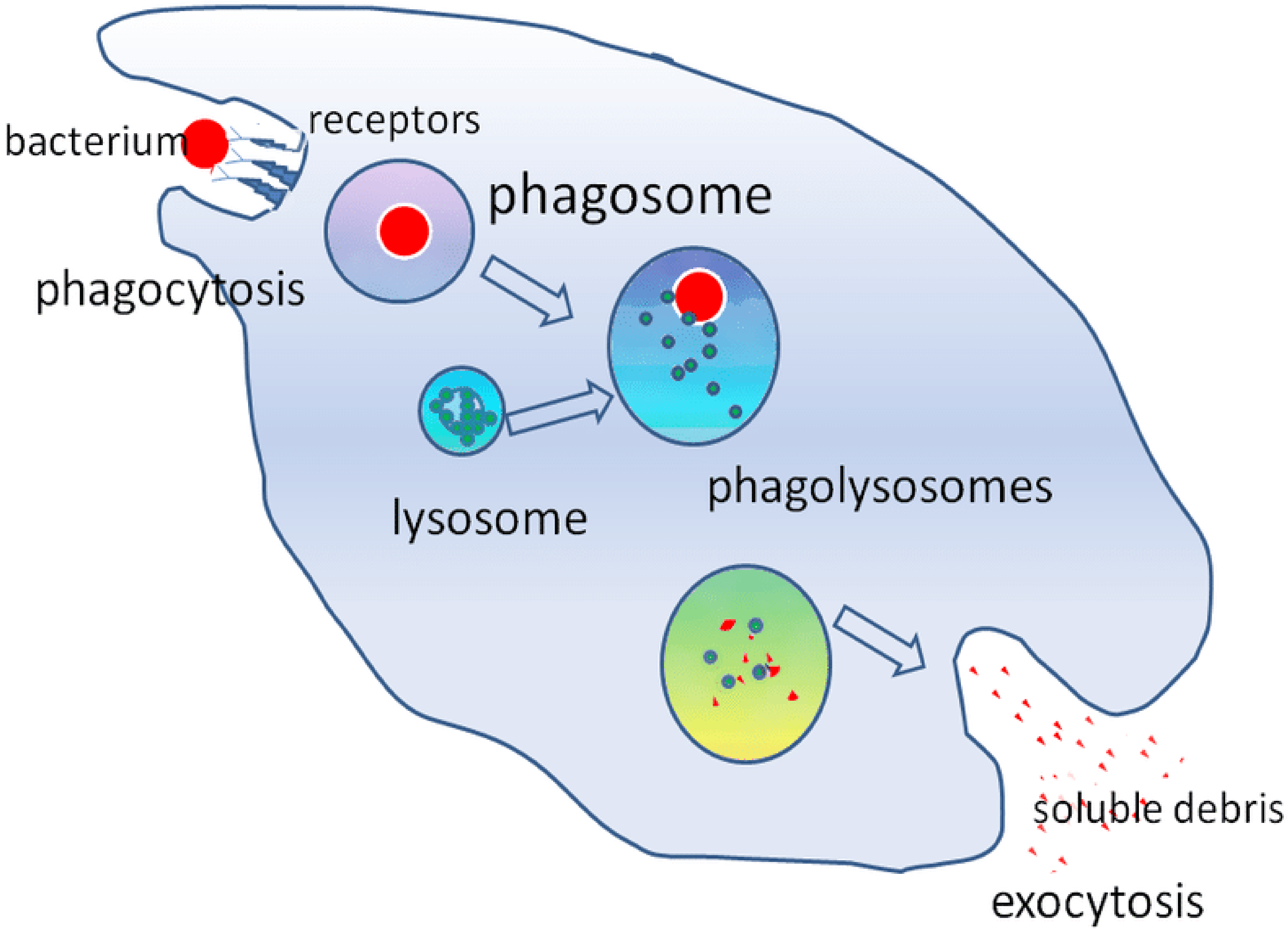
Diapedesis

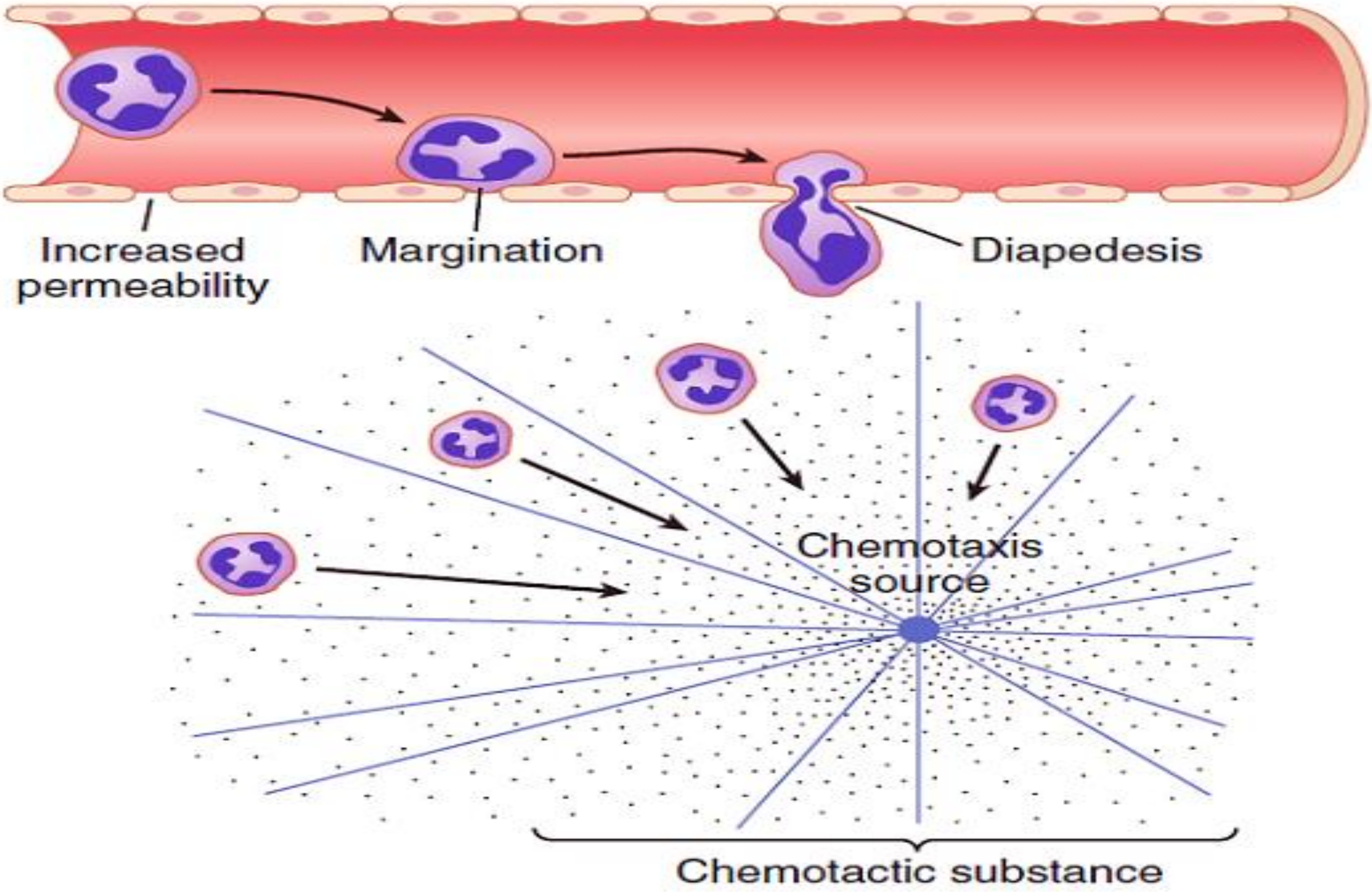
This refers to the process where leukocytes ‘dig’ their way out of the venules..

Recognition-Attachment

Phagocytosis

After attachment,
the phagocyte internalises the microbe into a phagosome.
The phagosome then fuses with a lysosome which contain digestive enzymes to destroy the internalised material.




Increased permeability
Margination
Diapedesis
Chemotaxis source
Chemotactic substance

IMMUNITY : Innate and adaptive immunity are two types of immune responses that work together to protect the body from infections and diseases.

The innate immune response is the first line of defense against pathogens and is a non-specific response. It includes physical and chemical barriers, such as the skin and mucous membranes, as well as cells such as neutrophils, macrophages, and natural killer cells. The innate immune response is rapid and is able to recognize and respond to a wide range of pathogens, but it does not provide long-lasting protection.

The adaptive immune response, on the other hand, is a more specific response that develops over time. It involves the activation of B and T cells, which can recognize and remember specific pathogens. B cells produce antibodies that can recognize and bind to specific pathogens, while T cells directly attack infected cells. The adaptive immune response is slower to develop than the innate response, but it provides long-lasting protection against specific pathogens.

Innate and adaptive immunity work together to provide comprehensive protection against infections and diseases. The innate immune response provides a rapid, non-specific response to pathogens, while the adaptive immune response provides a more specific response that can recognize and remember specific pathogens for long-term protection.

Cellular and humoral immunity are two types of adaptive immune responses that work together to protect the body from infections and diseases.

Cellular immunity, also known as **cell-mediated immunity**, involves the activation of **T cells**, which directly attack and destroy infected cells. T cells are able to recognize and bind to specific antigens on the surface of infected cells, and destroy them. Cellular immunity is important for protecting against **intracellular pathogens**, such as viruses and some bacteria.

Humoral immunity, also known as **antibody-mediated immunity**, involves the activation of B cells, which produce antibodies that can recognize and bind to specific antigens on the surface of pathogens. **Antibodies** are proteins that circulate in the blood and can neutralize or eliminate pathogens by binding to them and marking them for destruction by other cells of the immune system. Humoral immunity is important for protecting against **extracellular pathogens**, such as bacteria and fungi.

Both cellular and humoral immunity are important for protecting the body from infections and diseases. Cellular immunity is important for protecting against intracellular pathogens, while humoral immunity is important for protecting against extracellular pathogens. The two types of immunity work together to provide comprehensive protection against a wide range of pathogens.

There are some **key differences** between the innate and adaptive :

1. **Specificity:** Innate immunity is non-specific and responds to a wide range of pathogens, while adaptive immunity is highly specific and responds to specific antigens.
2. **Memory**: Innate immunity does not have a memory component, while adaptive immunity has a memory component that allows the immune system to remember specific pathogens and respond more quickly and effectively in the future.
3. **Speed of response:** Innate immunity is the first line of defense and responds rapidly to pathogens, while adaptive immunity takes longer to develop but provides a more specific and long-lasting response.
4. **Components:** Innate immunity includes physical and chemical barriers such as the skin and mucous membranes, as well as cells such as neutrophils, macrophages, and natural killer cells. Adaptive immunity includes B cells, which produce antibodies, and T cells, which directly attack infected cells.
5. **Activation**: Innate immunity is activated immediately upon exposure to a pathogen, while adaptive immunity requires the recognition and activation of specific immune cells.
6. **Range of response:** Innate immunity provides a general response to a wide range of pathogens, while adaptive immunity provides a specific response to particular pathogens.

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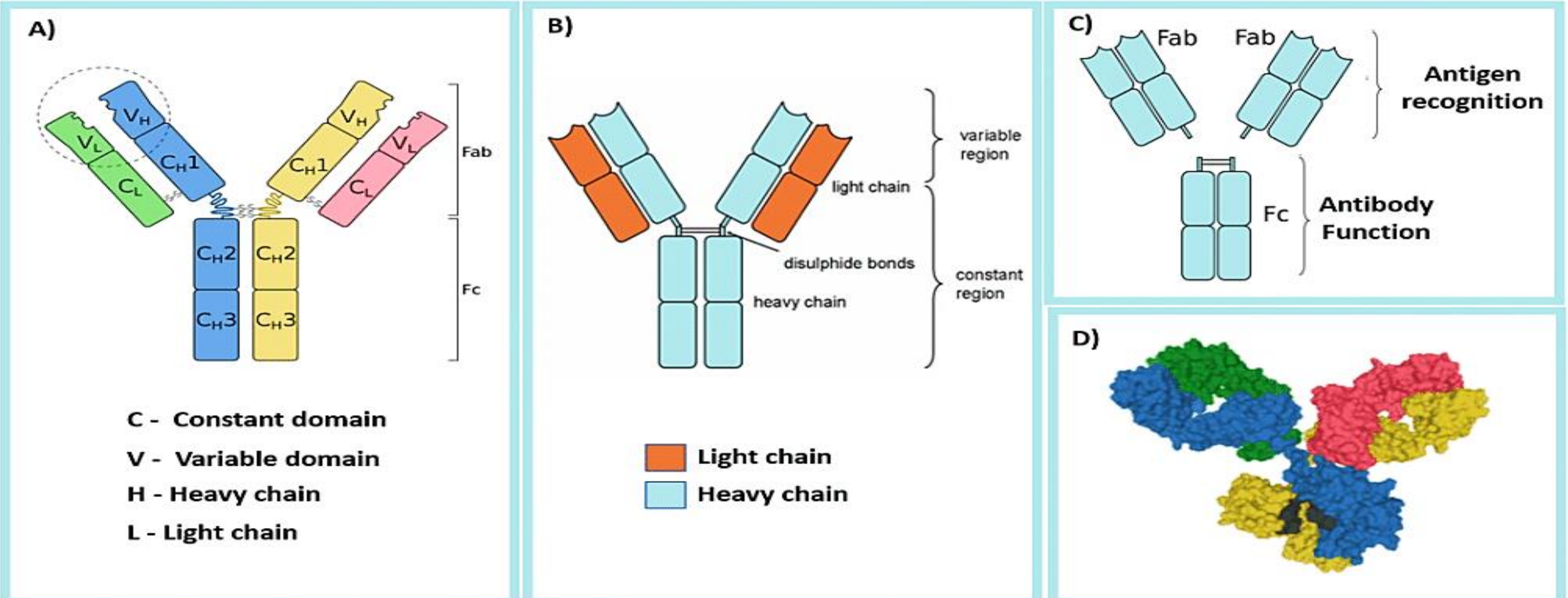
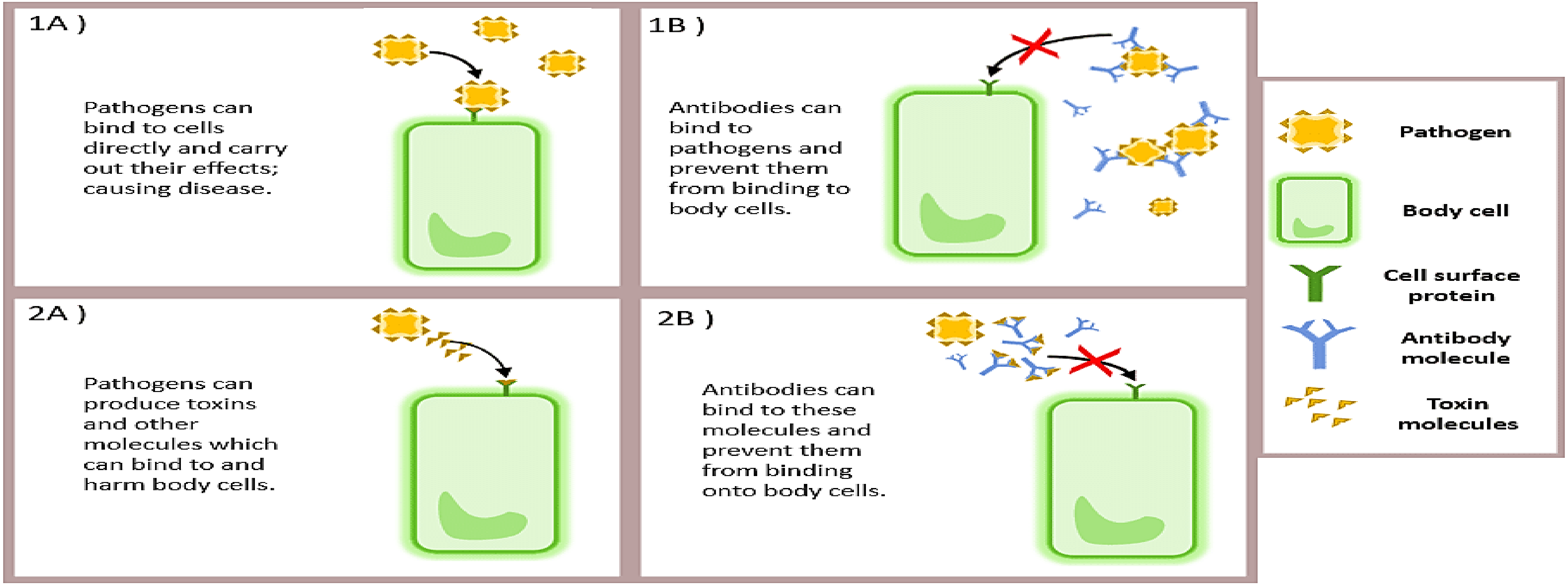
Antibodies : or immunoglobulins, are Y-shaped glycoproteins produced by differentiated B-cells called plasma cells. They are present in bodily fluids, secretions and on the surface of B-cells.

Antibody molecules consist of two identical **heavy chains** and two identical **light chains**, which consequently give the antibody two **antigen-binding sites**.



Classification

Antibodies are classified according to **heavy chain** type. The different classes are IgG, IgA, IgM, IgD and IgE; in **descending** order of abundance in serum.



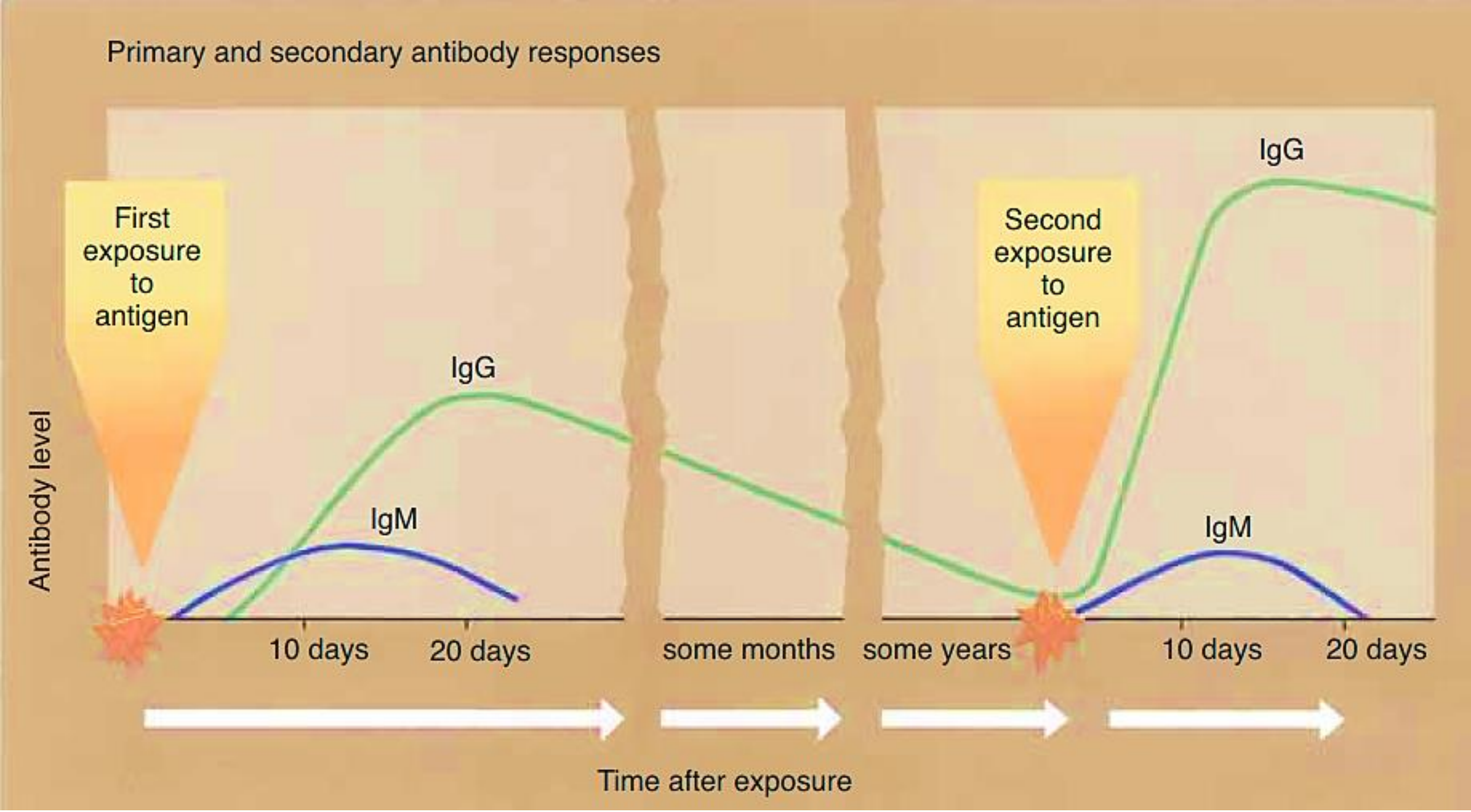
The complement system :

also known as the **complement cascade,** forms a part of the innate immune system. Complement components are generally made in the liver and circulate in their inactive form until they are needed.

The overall aim of the complement system is to support other parts of the immune response by **opsonising** pathogens and triggering inflammation.

Once activated the complement system has several effects, including:

•**Opsonisation**
•**Lysis** of pathogens
•**Chemotaxis**
•**Inflammation**



Primary and secondary antibody responses
First exposure to antigen
IgG
IgM
Second exposure to antigen
IgG
IgM
Antibody level
10 days
20 days
some months
some years
10 days
20 days
Time after exposure

Passive and active immunization are two ways to acquire immunity to a specific pathogen.

Active immunization involves the administration of a vaccine, which contains a weakened or inactivated form of the pathogen or specific parts of the pathogen. The immune system recognizes the pathogen and produces an immune response, including the production of specific antibodies and the activation of T cells. This response allows the immune system to remember the pathogen and produce a more rapid and effective response if the person is exposed to the pathogen in the future. Active immunization can provide long-lasting protection against the pathogen and is often used as a preventive measure.

Passive immunization involves the transfer of pre-formed antibodies to an individual, which can provide immediate but temporary protection against a specific pathogen. Passive immunization can be achieved through the administration of immune globulin, which is a concentrated solution of antibodies that have been collected from the blood of individuals who have recovered from the disease or have been immunized against the pathogen.

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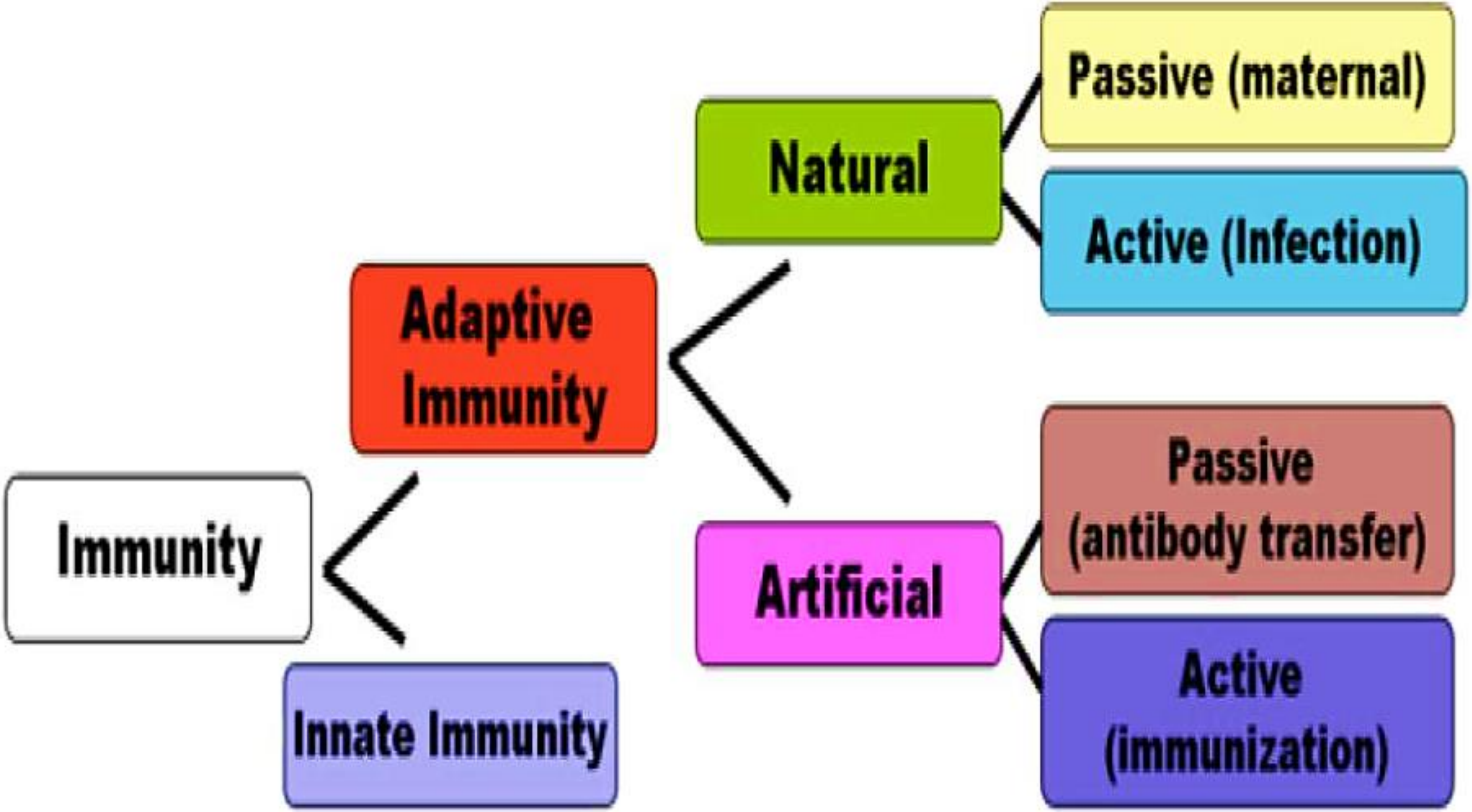
Vaccinations are a way to stimulate the body's immune system to produce an immune response to specific pathogens, without causing the disease itself.

Vaccines contain weakened or inactivated forms of the pathogen, or specific parts of the pathogen, which are not capable of causing disease but are able to trigger an immune response.
When a vaccine is administered, the immune system recognizes the pathogen and produces an immune response, including the production of specific antibodies and the activation of T cells. This response allows the immune system to remember the pathogen and produce a more rapid and effective response if the person is exposed to the pathogen in the future.

Vaccinations can provide immunity to a wide range of infectious diseases, including viral infections such as measles, mumps, rubella, hepatitis B, and influenza, as well as bacterial infections such as pneumococcal disease, meningococcal disease, and tetanus.

Vaccines are an effective way to prevent the spread of infectious diseases and protect individuals and populations from serious illness and death.


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

The lymphatic system and Immunity

The lymphatic system plays an important role in the body's immune system. It is a network of vessels, tissues, and organs that work together to transport lymph, a fluid containing white blood cells and other immune cells, throughout the body.
The lymphatic system helps to defend the body against infection and disease in several ways:

1. **Production of immune cells**: Lymphoid organs, such as the thymus, spleen, and lymph nodes, produce and store immune cells, including lymphocytes (such as B cells and T cells) and phagocytes (such as macrophages and dendritic cells).

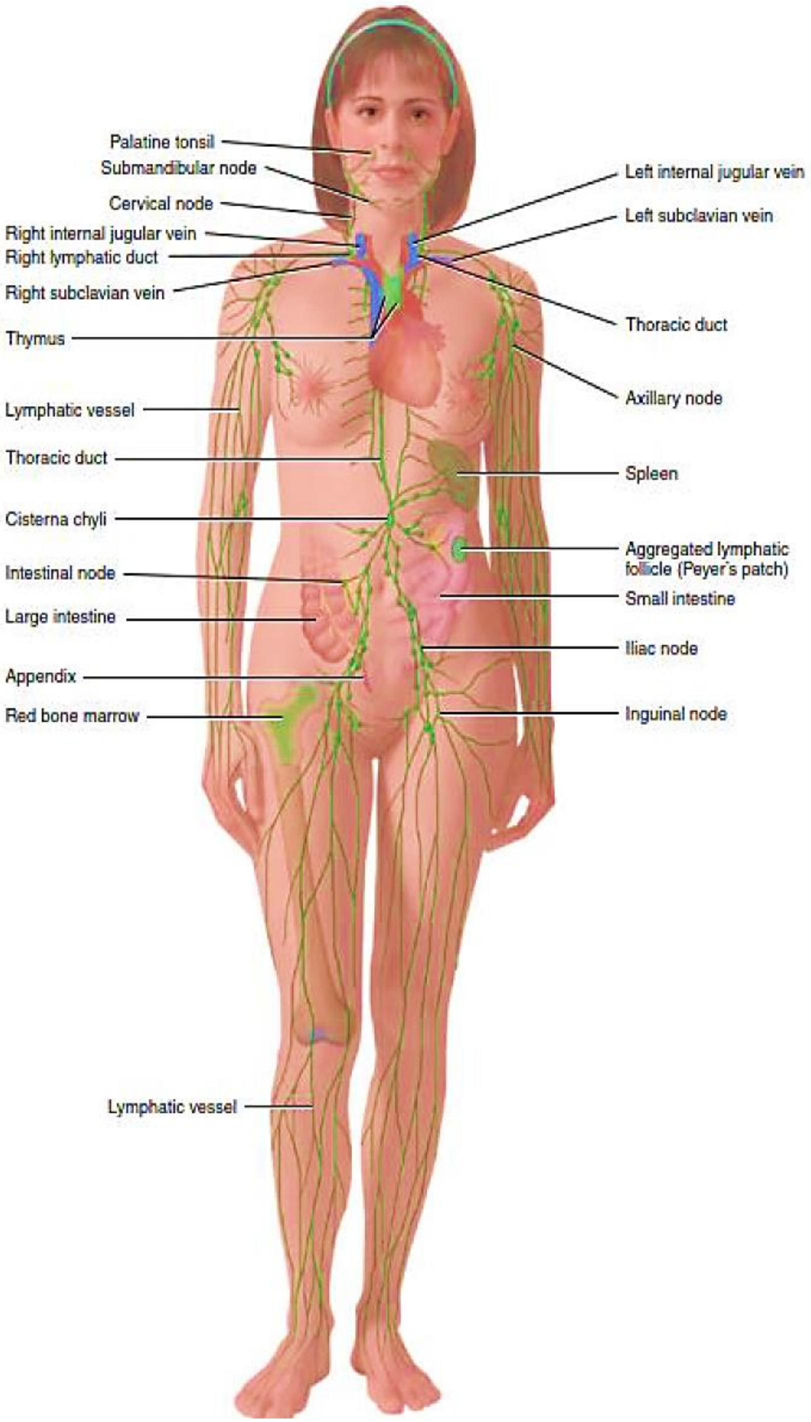
2. **Filtering of foreign substances**: Lymph nodes act as filters for foreign substances, such as bacteria, viruses, and cancer cells, that enter the body. Immune cells within the lymph nodes recognize and attack these foreign substances, helping to prevent infection and disease.

3. **Transport of immune cells**: The lymphatic vessels transport immune cells and lymphatic fluid to areas of the body where they are needed. For example, if an infection occurs in the body, immune cells will migrate to the affected area via the lymphatic vessels to attack and eliminate the infectious agent.

4. Absorption of fats: The lymphatic system also plays a role in the absorption of dietary fats and fat-soluble vitamins from the digestive system.

Overall, the lymphatic system helps to support the body's immune system by producing, storing, and transporting immune cells throughout the body, and by filtering foreign substances and attacking infectious agents.

Dysfunction of the lymphatic system can lead to a variety of immune disorders, such as lymphoma, lymphedema, and autoimmune diseases



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