TDC 5TH SEM MAJOR PAOER 5.3

BASIC IMMUNOLOGICAL CONCEPT

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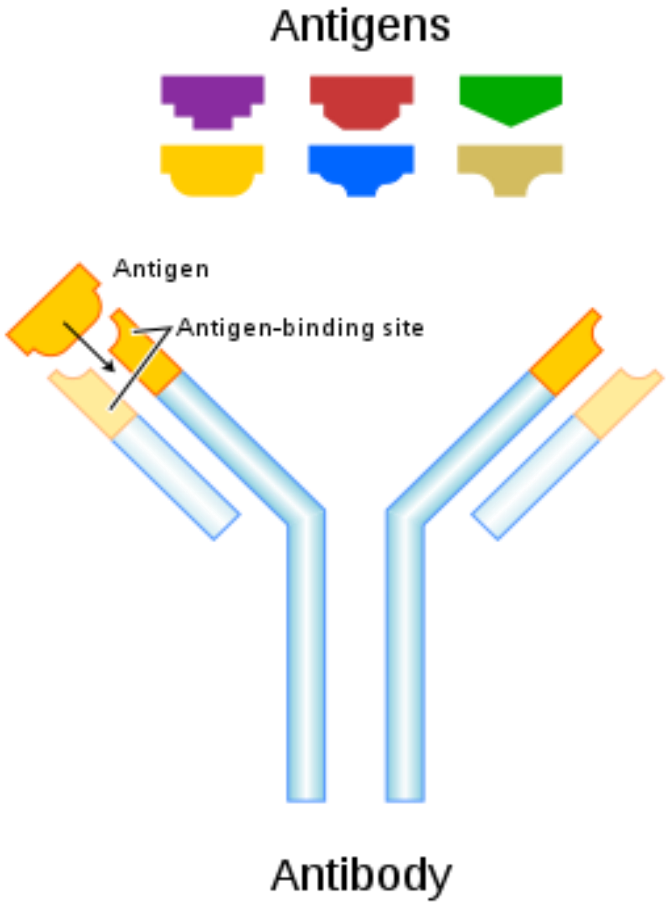
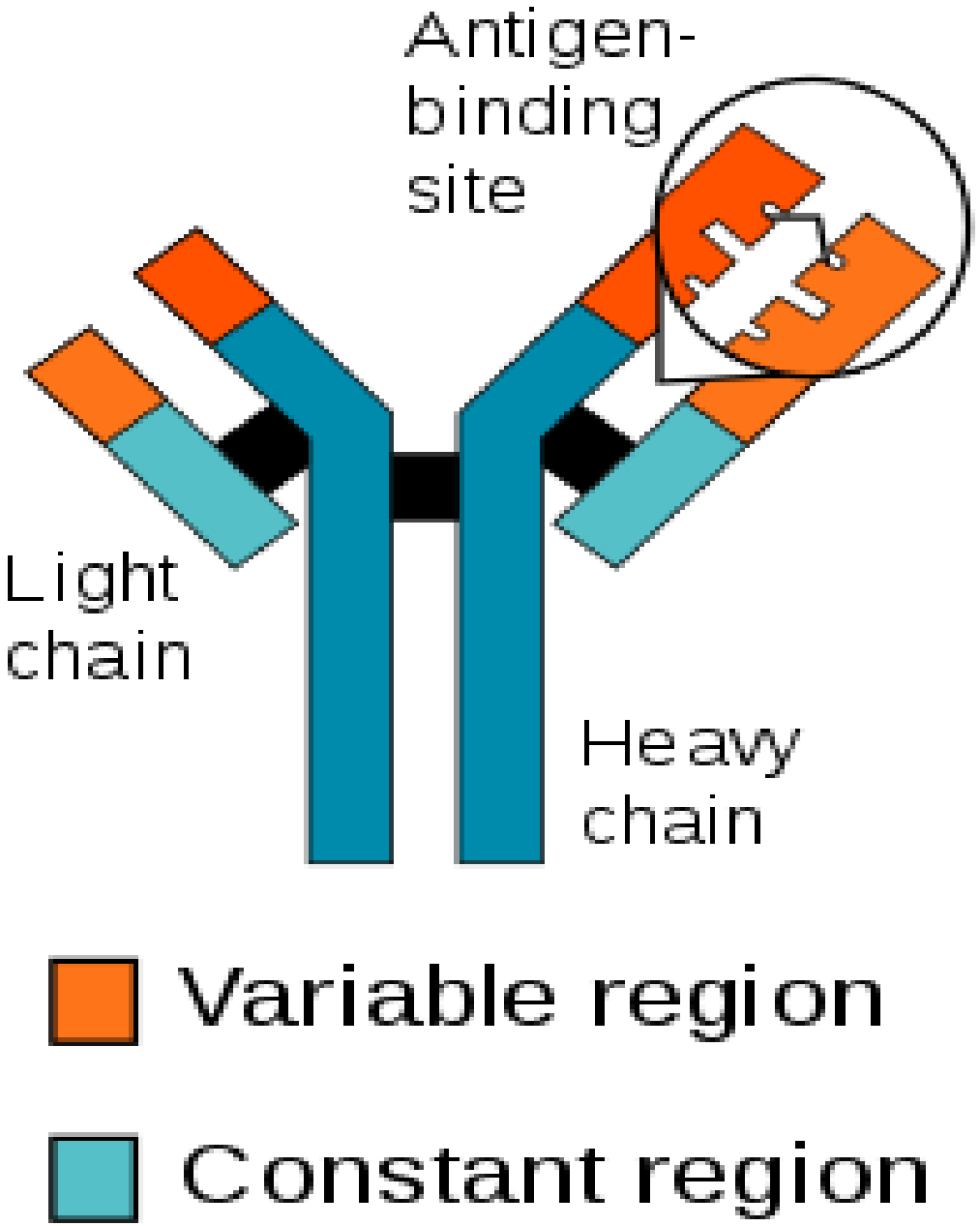


An illustration that shows how antigens induce the immune system response by interacting with an antibody that matches the molecular structure of an antigen

In immunology, an antigen (Ag) is a molecule or molecular structure, such as may be present at the outside of a pathogen, that can be bound by an antigen-specific antibody or B cell antigen receptor.[1] The presence of antigens in the body normally triggers an immune response.[2] The Ag abbreviation stands for an antibody generator.



An antibody is made up of two heavy chains and two light chains. The unique variable region allows an antibody to recognize its matching antigen.

The immune system is a host defense system comprising many biological structures and processes within an organism that protects against disease. To function properly, an immune system must detect a wide variety of agents, known as pathogens, from viruses to parasitic worms, and distinguish them from the organism's own healthy tissue.

In many species, there are two major subsystems of the immune system: the innate immune system and the adaptive immune system.

Both subsystems use humoral immunity and cell-mediated immunity to perform their functions. In humans, the blood–brain barrier, blood–cerebrospinal fluid barrier, and similar fluid–brain barriers separate the peripheral immune system from the neuroimmune system, which protects the brain.

Pathogens can rapidly evolve and adapt, and thereby avoid detection and neutralization by the immune system; however, multiple defense mechanisms have also evolved to recognize and neutralize pathogensDisorders of the immune system can result in autoimmune diseases, inflammatory diseases and cancer.

Immunodeficiency occurs when the immune system is less active than normal, resulting in recurring and life-threatening infections.

In humans, immunodeficiency can either be the result of a genetic disease such as severe combined immunodeficiency, acquired conditions such as HIV/AIDS, or the use of immunosuppressive medication. In contrast, autoimmunity results from a hyperactive immune system attacking normal tissues as if they were foreign organisms. Common autoimmune diseases include Hashimoto's thyroiditis, rheumatoid arthritis, diabetes mellitus type 1, and systemic lupus erythematosus.

Components of the immune system

Innate immune system	Adaptive immune system
Response is non-specific	Pathogen and antigen specific response
Composed of leukocytes	Composed of antigens, B cells, T cells
Exposure leads to immediate maximal response	Lag time between exposure and maximal response
Cell-mediated and humoral components	Cell-mediated and humoral components
No immunological memory	Exposure leads to immunological memory
Found in nearly all forms of life	Found only in jawed vertebrates

Both innate and adaptive immunity depend on the ability of the immune system to distinguish between self and non-self molecules. In immunology, self molecules are those components of an organism's body that can be distinguished from foreign substances by the immune system. Conversely, non-self molecules are those recognized as foreign molecules. One class of non-self molecules are called antigens (short for antibody generators) and are defined as substances that bind to specific immune receptors and elicit an immune response

Innate immunity

Innate immunity refers to nonspecific defense mechanisms that come into play immediately or within hours of an antigen's appearance in the body. These mechanisms include physical barriers such as skin, chemicals in the blood, and immune system cells that attack foreign cells in the body.

The innate immune system is made of defenses against infection that can be activated immediately once a pathogen attacks. The innate immune system is essentially made up of barriers that aim to keep viruses, bacteria, parasites, and other foreign particles out of your body or limit their ability to spread and move throughout the body. The innate immune system includes:

Physical Barriers

such as skin, the gastrointestinal tract, the respiratory tract, the nasopharynx, cilia, eyelashes and other body hair.

Defense Mechanisms

such as secretions, mucous, bile, gastric acid, saliva, tears, and sweat.

General Immune Responses

such as inflammation, complement, and non-specific cellular responses. The inflammatory response actively brings immune cells to the site of an infection by increasing blood flow to the area. Complement is an immune response that marks pathogens for destruction and makes holes in the cell membrane of the pathogen. Check out our video that explains inflammation and complement, which we will touch on later.

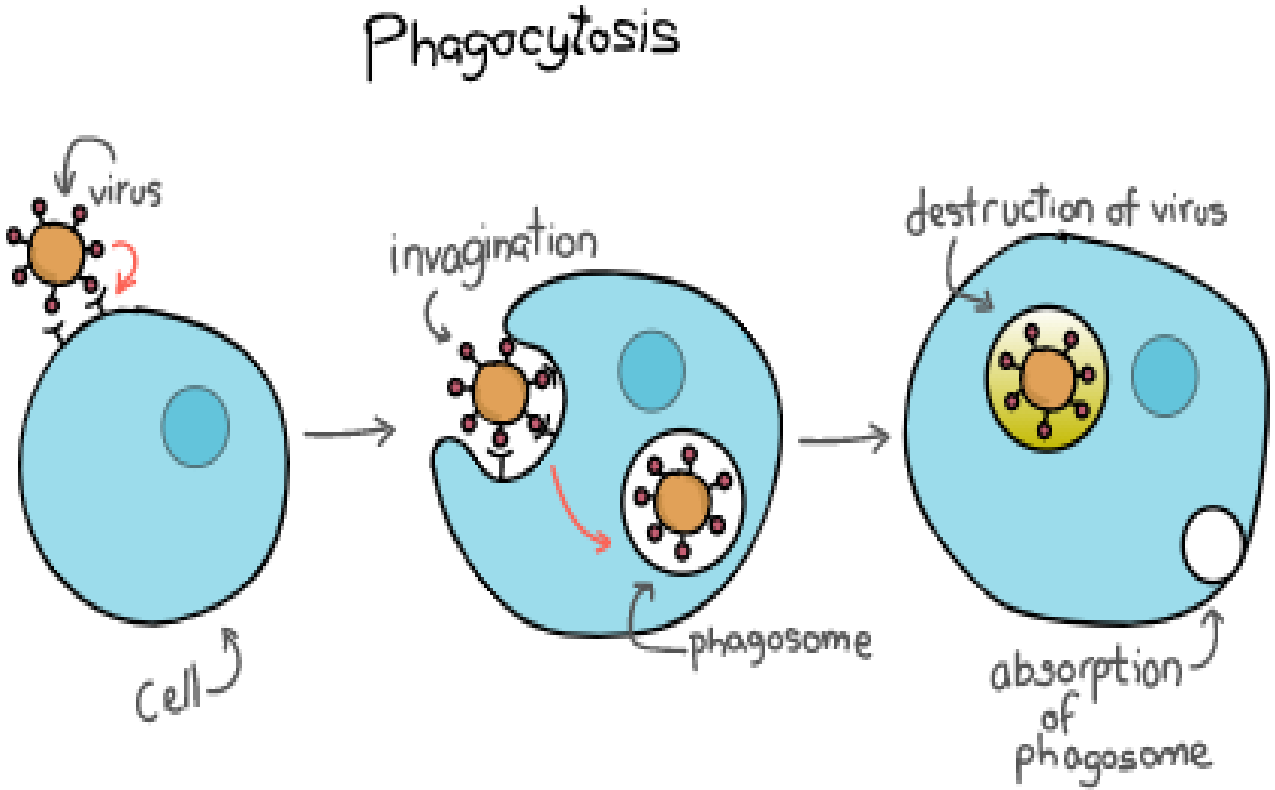
The innate immune system is always general, or nonspecific, meaning anything that is identified as foreign or non-self is a target for the innate immune response. The innate immune system is activated by the presence of antigens and their chemical properties.

Cells of the Innate Immune System

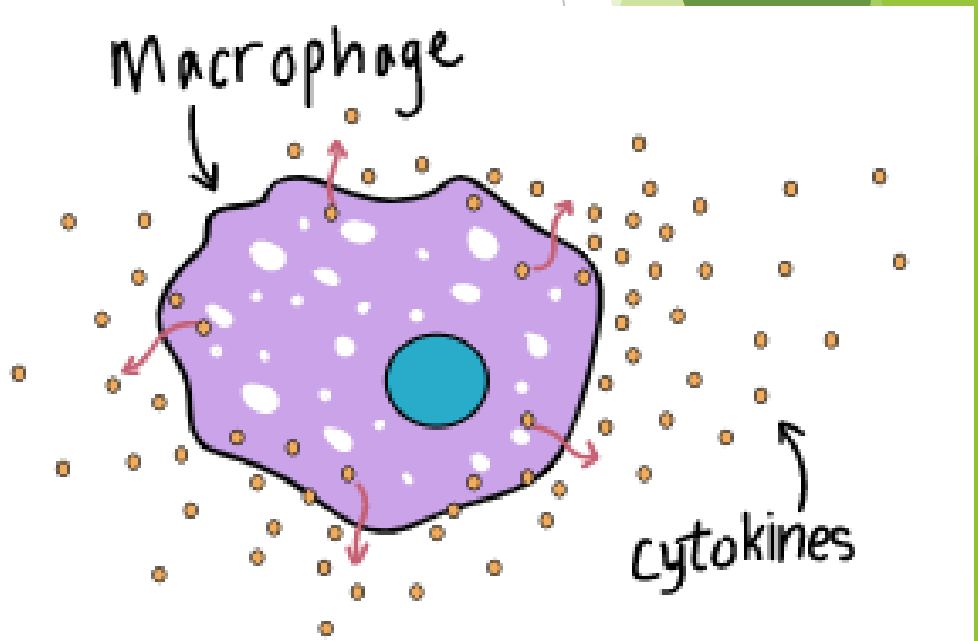
There are many types of white blood cells, or leukocytes, that work to defend and protect the human body. In order to patrol the entire body, leukocytes travel by way of the circulatory system.

The following cells are leukocytes of the innate immune system:

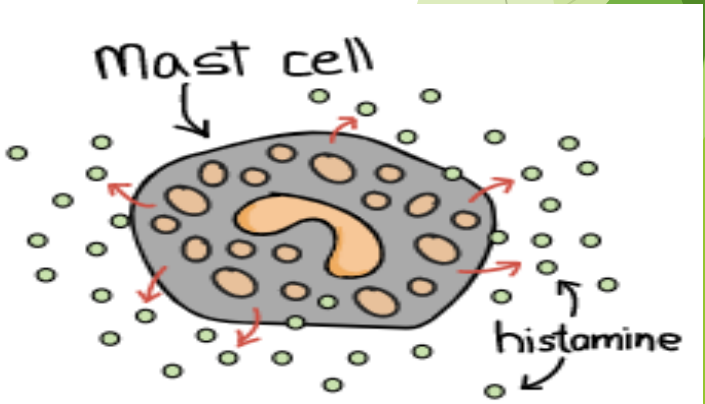
Phagocytes, or Phagocytic cells: Phagocyte means “eating cell”, which describes what role phagocytes play in the immune response. Phagocytes circulate throughout the body, looking for potential threats, like bacteria and viruses, to engulf and destroy. You can think of phagocytes as security guards on patrol.


Phagocytosis
virus
invagination
destruction of virus
cell
phagosome
absorption of phagosome

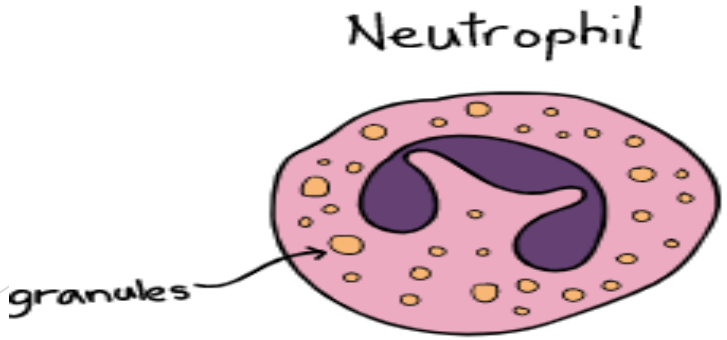
Macrophages: Macrophages, commonly abbreviated as "Mφ", are efficient phagocytic cells that can leave the circulatory system by moving across the walls of capillary vessels. The ability to roam outside of the circulatory system is important, because it allows macrophages to hunt pathogens with less limits. Macrophages can also release cytokines in order to signal and recruit other cells to an area with pathogen



Mast cells: Mast cells are found in mucous membranes and connective tissues, and are important for wound healing and defense against pathogens via the inflammatory response. When mast cells are activated, they release cytokines and granules that contain chemical molecules to create an inflammatory cascade. Mediators, such as histamine, cause blood vessels to dilate, increasing blood flow and cell trafficking to the area of infection. The cytokines released during this process act as a messenger service, alerting other immune cells, like neutrophils and macrophages, to make their way to the area of infection, or to be on alert for circulating threats.



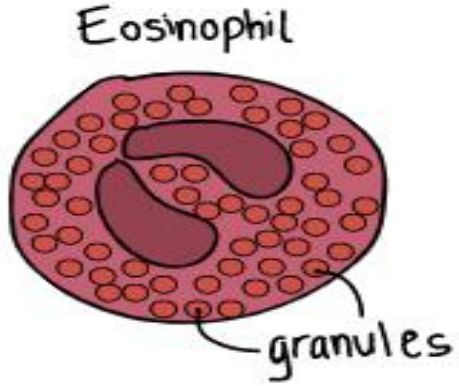
Neutrophils: Neutrophils are phagocytic cells that are also classified as granulocytes because they contain granules in their cytoplasm. These granules are very toxic to bacteria and fungi, and cause them to stop proliferating or die on contact. The bone marrow of an average healthy adult makes approximately 100 billion new neutrophils per day. Neutrophils are typically the first cells to arrive at the site of an infection because there are so many of them in circulation at any given time.



Eosinophils: Eosinophils are granulocytes target multicellular parasites.

Eosinophils secrete a range of highly toxic proteins and free radicals that kill bacteria and parasites. The use of toxic proteins and free radicals also causes tissue damage during allergic reactions, so activation and toxin release by eosinophils is highly regulated to prevent any unnecessary tissue damage.

While eosinophils only make up 1-6% of the white blood cells, they are found in many locations, including the thymus, lower gastrointestinal tract, ovaries, uterus, spleen, and lymph nodes.



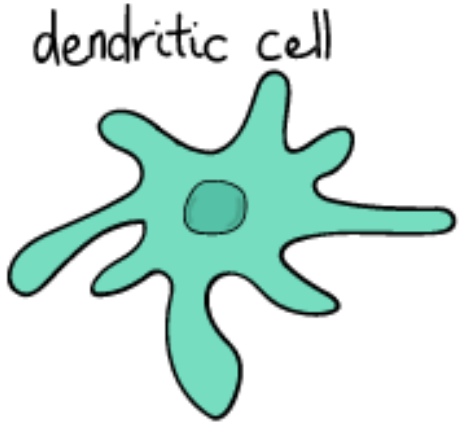
Basophils:

Basophils are also granulocytes that attack multicellular parasites. Basophils release histamine, much like mast cells. The use of histamine makes basophils and mast cells key players in mounting an allergic response.

Natural Killer cells:

Natural Killer cells (NK cells), do not attack pathogens directly. Instead, natural killer cells destroy infected host cells in order to stop the spread of an infection. Infected or compromised host cells can signal natural kill cells for destruction through the expression of specific receptors and antigen presentation

Dendritic cells: Dendritic cells are antigen-presenting cells that are located in tissues, and can contact external environments through the skin, the inner mucosal lining of the nose, lungs, stomach, and intestines. Since dendritic cells are located in tissues that are common points for initial infection, they can identify threats and act as messengers for the rest of the immune system by antigen presentation. Dendritic cells also act as bridge between the innate immune system and the adaptive immune system.



The Complement System

The complement system (also called the complement cascade) is a mechanism that complements other aspects of the immune response. Typically, the complement system acts as a part of the innate immune system, but it can work with the adaptive immune system if necessary.

The complement system is made of a variety of proteins that, when inactive, circulate in the blood. When activated, these proteins come together to initiate the complement cascade, which starts the following steps

Opsonization: Opsonization is a process in which foreign particles are marked for phagocytosis. All of the pathways require an antigen to signal that there is a threat present. Opsonization tags infected cells and identifies circulating pathogens expressing the same antigens.

Chemotaxis: Chemotaxis is the attraction and movement of macrophages to a chemical signal. Chemotaxis uses cytokines and chemokines to attract macrophages and neutrophils to the site of infection, ensuring that pathogens in the area will be destroyed. By bringing immune cells to an area with identified pathogens, it improves the likelihood that the threats will be destroyed and the infection will be treated.

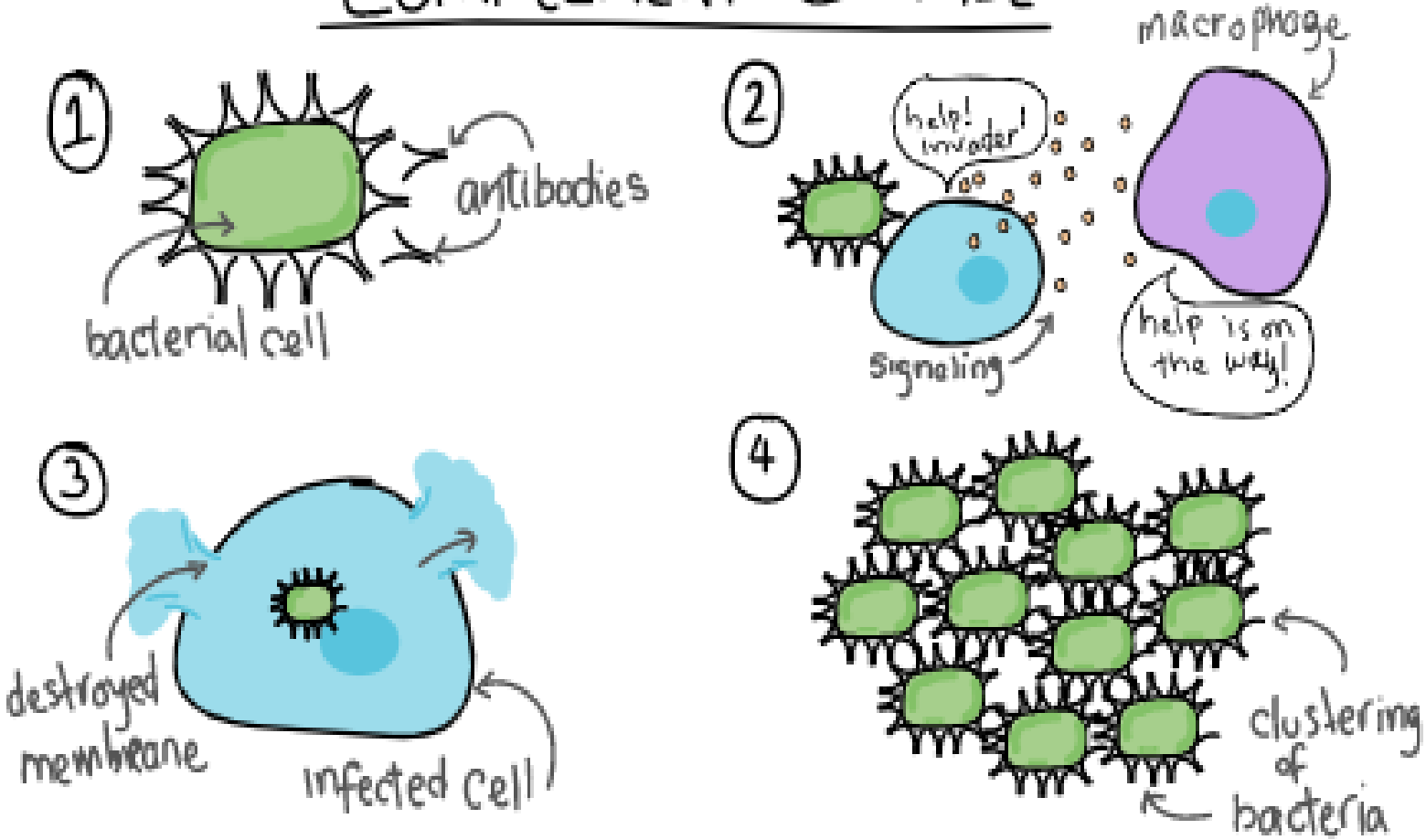
Cell Lysis: Lysis is the breaking down or destruction of the membrane of a cell. The proteins of the complement system puncture the membranes of foreign cells, destroying the integrity of the pathogen. Destroying the membrane of foreign cells or pathogens weakens their ability to proliferate, and helps to stop the spread of infection.

Agglutination: Agglutination uses antibodies to cluster and bind pathogens together, much like a cowboy rounds up his cattle. By bringing as many pathogens together in the same area, the cells of the immune system can mount an attack and weaken the infection.

Other innate immune system cells continue to circulate throughout the body in order to track down any other pathogens that have not been clustered and bound for destruction. The steps of the complement cascade facilitate the search for and removal of antigens by placing them in large clumps, making it easier for other aspects of the immune system to do their jobs. Remember that the complement system is a supplemental cascade of proteins that assists, or "complements" the other aspects of the innate immune system.

The innate immune system works to fight off pathogens before they can start an active infection. For some cases, the innate immune response is not enough, or the pathogen is able to exploit the innate immune response for a way into the host cells. In such situations, the innate immune system works with the adaptive immune system to reduce the severity of infection, and to fight off any additional invaders while the adaptive immune system is busy destroying the initial infection.

Complement Cascade



ACQUIRED IMMUNITY

The adaptive immune system, also referred as the acquired immune system, is a subsystem of the immune system that is composed of specialized, systemic cells and processes that eliminates pathogens by preventing their growth. The acquired immune system is one of the two main immunity strategies found in vertebrates (the other being the innate immune system).

Acquired immunity creates immunological memory after an initial response to a specific pathogen, and leads to an enhanced response to subsequent encounters with that pathogen. This process of acquired immunity is the basis of vaccination. Like the innate system, the acquired system includes both humoral immunity components and cell-mediated immunity components.

Types of acquired immunity

Immunity can be acquired either actively or passively. Immunity is acquired actively when a person is exposed to foreign substances and the immune system responds. Passive immunity is when antibodies are transferred from one host to another. Both actively acquired and passively acquired immunity can be obtained by natural or artificial means.

Naturally Acquired Active Immunity – when a person is naturally exposed to antigens, becomes ill, then recovers.

Naturally Acquired Passive Immunity – involves a natural transfer of antibodies from a mother to her infant. The antibodies cross the woman's placenta to the fetus. Antibodies can also be transferred through breast milk with the secretions of colostrum.

Artificially Acquired Active Immunity – is done by vaccination (introducing dead or weakened antigen to the host's cell).

Artificially Acquired Passive Immunity – **This involves the introduction of antibodies rather than antigens to the human body. These antibodies are from an animal or person who is already immune to the disease.**

The cells that carry out the acquired immune response are white blood cells known as lymphocytes. Two main activities—antibody responses and cell mediated immune response—are also carried out by two different lymphocytes (B cells and T cells). In antibody responses, B cells are activated to secrete antibodies, which are proteins also known as immunoglobulins. Antibodies travel through the bloodstream and bind to the foreign antigen causing it to inactivate, which does not allow the antigen to bind to the host.

In acquired immunity, pathogen-specific receptors are "acquired" during the lifetime of the organism (whereas in innate immunity pathogen-specific receptors are already encoded in the germline). The acquired response is called "adaptive" because it prepares the body's immune system for future challenges (though it can actually also be maladaptive when it results in autoimmunity

Functions

Overview of the processes involved in the primary immune response

Acquired immunity is triggered in vertebrates when a pathogen evades the innate immune system and (1) generates a threshold level of antigen and (2) generates "stranger" or "danger" signals activating dendritic cells.

The major functions of the acquired immune system include:

Recognition of specific "non-self" antigens in the presence of "self", during the process of antigen presentation.

Generation of responses that are tailored to maximally eliminate specific pathogens or pathogen-infected cells.

Development of immunological memory, in which pathogens are "remembered" through memory B cells and memory T cells.

In humans, it takes 4-7 days for the adaptive immune system to mount a significant response.

Lymphocyte

The cells of the acquired immune system are T and B lymphocytes; lymphocytes are a subset of leukocyte. B cells and T cells are the major types of lymphocytes. The human body has about 2 trillion lymphocytes, constituting 20–40% of white blood cells (WBCs); their total mass is about the same as the brain or liver. The peripheral blood contains 2% of circulating lymphocytes; the rest move within the tissues and lymphatic system.

B cells and T cells are derived from the same multipotent hematopoietic stem cells, and are morphologically indistinguishable from one another until after they are activated. B cells play a large role in the humoral immune response, whereas T cells are intimately involved in cell-mediated immune responses. In all vertebrates except Agnatha, B cells and T cells are produced by stem cells in the bone marrow.

T progenitors migrate from the bone marrow to the thymus where they are called thymocytes and where they develop into T cells. In humans, approximately 1–2% of the lymphocyte pool recirculates each hour to optimize the opportunities for antigen-specific lymphocytes to find their specific antigen within the secondary lymphoid tissues. In an adult animal, the peripheral lymphoid organs contain a mixture of B and T cells in at least three stages of differentiation:

naive B and naive T cells (cells that have not matured), left the bone marrow or thymus, have entered the lymphatic system, but have yet to encounter their cognate antigen,

effector cells that have been activated by their cognate antigen, and are actively involved in eliminating a pathogen.

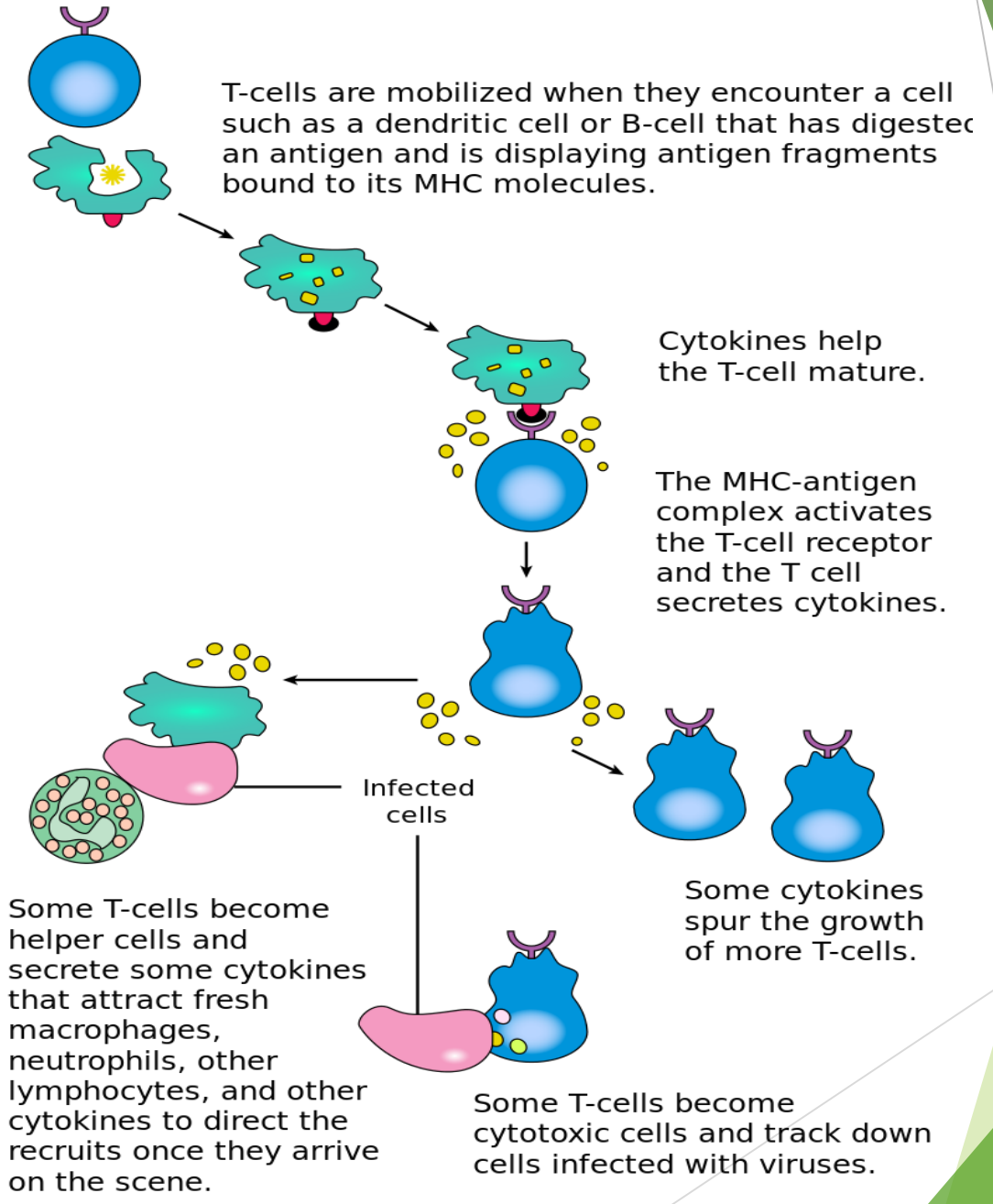
memory cells – the survivors of past infections.

Helper T-cells

The T lymphocyte activation pathway. T cells contribute to immune defenses in two major ways: some direct and regulate immune responses; others directly attack infected or cancerous cells.
CD4+ lymphocytes, also called "helper" T cells, are immune response mediators, and play an important role in establishing and maximizing the capabilities of the acquired immune response. These cells have no cytotoxic or phagocytic activity; and cannot kill infected cells or clear pathogens, but, in essence "manage" the immune response, by directing other cells to perform these tasks.

Helper T cells express T cell receptors (TCR) that recognize antigen bound to Class II MHC molecules. The activation of a naive helper T-cell causes it to release cytokines, which influences the activity of many cell types, including the APC (Antigen-Presenting Cell) that activated it. Helper T-cells require a much milder activation stimulus than cytotoxic T cells. Helper T cells can provide extra signals that "help" activate cytotoxic cells

The T lymphocyte activation pathway. T cells contribute to immune defenses in two major ways: some direct and regulate immune responses; others directly attack infected or cancerous cells



B lymphocytes and antibody production: B cell and Humoral immunity

The B lymphocyte activation pathway. B cells function to protect the host by producing antibodies that identify and neutralize foreign objects like bacteria and viruses.

B Cells are the major cells involved in the creation of antibodies that circulate in blood plasma and lymph, known as humoral immunity.

Antibodies (also known as immunoglobulin, Ig), are large Y-shaped proteins used by the immune system to identify and neutralize foreign objects.

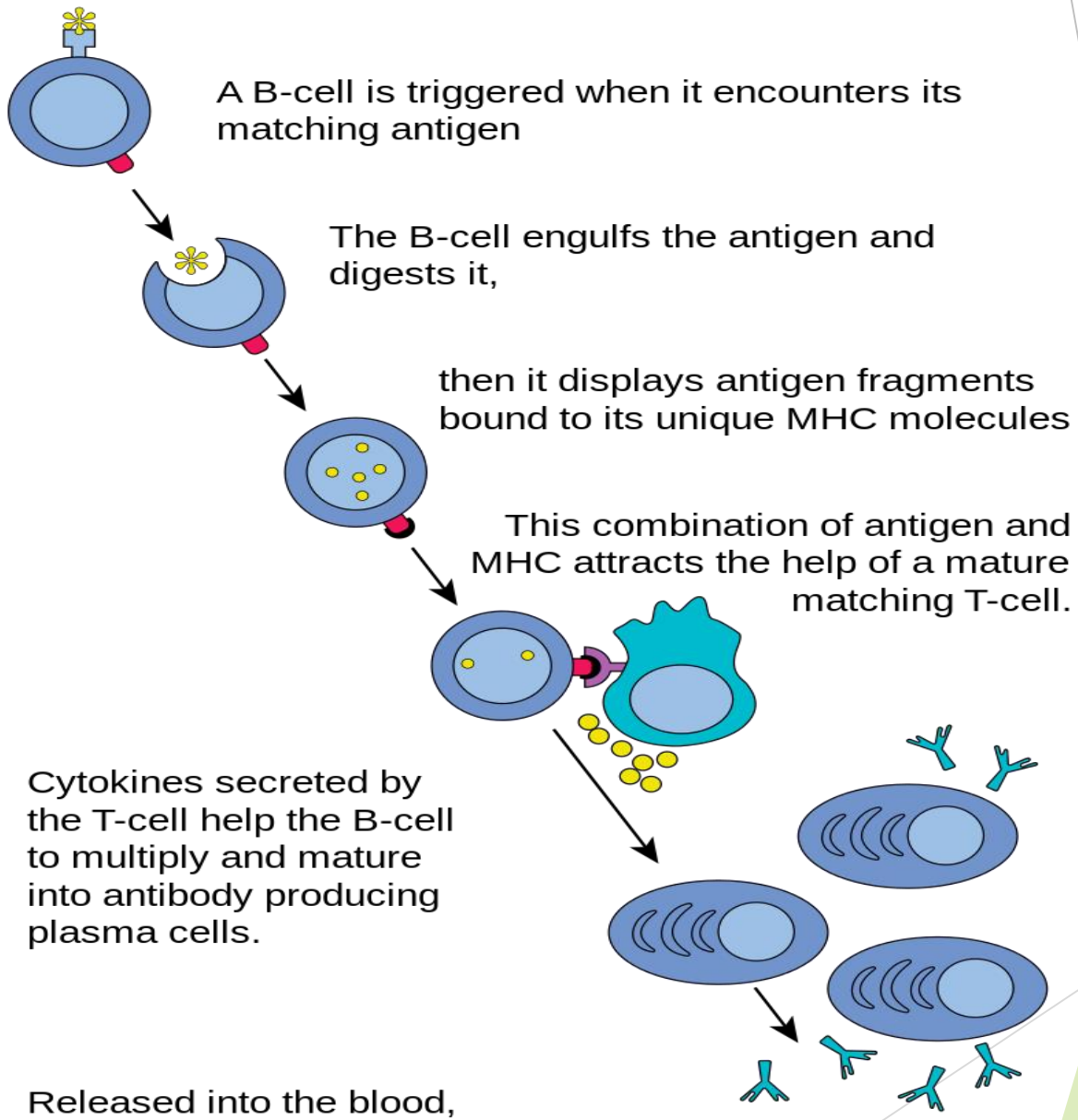
In mammals, there are five types of antibody:

IgA, IgD, IgE, IgG, and IgM,

differing in biological properties; each has evolved to handle different kinds of antigens.

Upon activation, B cells produce antibodies, each of which recognize a unique antigen, and neutralizing specific pathogens.

The B lymphocyte activation pathway. B cells function to protect the host by producing antibodies that identify and neutralize foreign objects like bacteria and viruses



Antigen and antibody binding would cause five different protective mechanisms:

Agglutination: Reduces number of infectious units to be dealt with

Activation of complement: Cause inflammation and cell lysis

Opsonization: Coating antigen with antibody enhances phagocytosis

Antibody-dependent cell-mediated cytotoxicity: Antibodies attached to target cell cause destruction by macrophages, eosinophils, and NK cells

Neutralization: Blocks adhesion of bacteria and viruses to mucosa

Like the T cell, B cells express a unique B cell receptor (BCR), in this case, a membrane-bound antibody molecule. All the BCR of any one clone of B cells recognizes and binds to only one particular antigen. A critical difference between B cells and T cells is how each cell "sees" an antigen. T cells recognize their cognate antigen in a processed form – as a peptide in the context of an MHC molecule, whereas B cells recognize antigens in their native form. Once a B cell encounters its cognate (or specific) antigen (and receives additional signals from a helper T cell (predominately Th2 type)), it further differentiates into an effector cell, known as a plasma cell.

Plasma cells are short-lived cells (2–3 days) that secrete antibodies. These antibodies bind to antigens, making them easier targets for phagocytes, and trigger the complement cascade. About 10% of plasma cells survive to become long-lived antigen-specific memory B cells. Already primed to produce specific antibodies, these cells can be called upon to respond quickly if the same pathogen re-infects the host, while the host experiences few, if any, symptoms.

THANK YOU