Human Physiology
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Lecture - 02

Hello, welcome to another new class in Human Physiology. In the last few classes, we have been discussing topics such as blood, its various components, and their functions. In this class specifically, we will discuss the immune mechanisms of blood and lymph. So, let us start with that. So, what different content will be covered in this class? We will discuss what an antigen is, and then we will see what different organs are associated with our immunity. We will briefly describe different types of immune cells that are present in our body.

We will see what the different forms of immunity are, for example, innate immunity and adaptive immunity, and we will also briefly discuss antibodies and immunoglobulins. So, to start with, first we have to understand what immunity actually is and why the immune system works this way in our body. So, before that, let us first discuss what an antigen is, right? So, an antigen is a type of substance that can stimulate an immune response in our body, and it can be any foreign particle or object. It can be either a living foreign object or a non-living foreign object.

For example, an antigen can be like bacteria; it can be any type of microbe, it can be a virus, or it can be another foreign particle like dust or any other toxins or toxic substances. And whenever this type of antigen comes into our body, there is a certain immune response or foreign body response that is initiated. What is the main reason for this? Because our body wants to first understand whether those antigens are harmful or not. If our body understands that those antigens are not harmful, then the human body may not trigger any type of reaction, which is called an immune reaction. But if our body determines that these antigens are harmful, for example, in the case of any bacterial or viral infection, then there is a cascade of reactions that would initiate, called immune reactions, to eventually eliminate those harmful antigens from the body.

So, in short, an antigen is mostly like a foreign object that can either be harmful or not. Then, we also briefly have to understand that there are different types of antigen-presenting cells in our body. So, once the antigen comes, certain components of our body cells have to present that antigen to our overall immune system, and a few cells participate in this. For example, you can see here macrophage cells, dendritic cells, and B-lymphocyte cells. So, these are some of the antigen-presenting cells that eventually present those antigens and then determine if those antigens are harmful or not.

So, we will further discuss these cells in detail in the consecutive slides. But before that, let us briefly discuss different types of immune organs or the organs that are associated with our immune system. So, as you can see, there are some primary lymphoid organs; these are very important, like bone marrow and thymus. Bone marrow, as you know, produces all types of blood cells, including immune cells like lymphocytes. And in the case of the thymus, it is highly important because the T cells, which are one of the most important components of immune cells, eventually mature in the thymus.

Then there are also certain secondary lymphoid organs. For example, the main role of the spleen is to filter the blood, but the spleen also contains immune cells that help to fight different types of infections. The second most important secondary lymphoid organ is the lymph node. As you know, lymph nodes are very small, bean-shaped organs, and what is their function? They filter lymph fluid. So, we will discuss the lymph, as you know, lymph is another parallel circulation that happens alongside the blood, and it mostly filters the tissue fluid or lymph fluid.

But this lymph node also had different immune cells. So, whenever any foreign objects or antigens like bacteria and viruses come to the lymph node, the immune cells present in the lymph node participate in the destruction of those antigens. Then we have another important lymphoid organ, or rather another important immune organ, which is the tonsil, and this is located near our throat. It also helps to trap the pathogens that enter through the mouth. So, tonsils are also one of the very initial immune-related organs.

So, because we eat a lot of food and eventually, many of our drinks may also contain different pathogens and antigens. So, tonsils can trap those antigens and start the immune cascade. Then other immune organs, for example, include skin and mucous membranes, which act as a physical barrier. It can be like gut-associated lymphoid cells. They are present mostly in the lining of the intestines, and the liver also has an important role to play.

For example, the liver also filters the blood and removes some harmful substances. So, these are all associated secondary lymphoid organs. Now, let us discuss different immune cells that are present in our body and briefly discuss their role. The first one we will discuss is related to the neutrophils. So, as you see, neutrophils are generally synthesized or produced in the myeloid lineage in the bone marrow, and they can be stored in the bone marrow; whenever required, they can be released into the blood.

So, basically, the synthesis, along with the maturation, both happened in the bone marrow, and neutrophils play an important role in maintaining innate immunity. So, this is very important that neutrophils participate in our innate immunity. And what are their functions? They are one of the first responders. They basically phagocytose the bacteria, fungi, or any microbes. They also release different types of enzymes; for example, neutrophil extracellular traps.

These enzymes can also destroy the antigens. Their lifespan is generally very short, around 1 to 2 days. The next most another one of the important macrophage and this is also like our largest immune cell. So, this is like a macrophage, which is the largest immune cell in our body. They generally get produced from the monocytes mainly in the bone marrow, right? So, they can be stored or circulate like monocytes, and eventually, when their function is required, they can migrate to the tissues and differentiate into macrophages.

So, basically, macrophages are a differentiated product of the monocytes, and where they mature, they can mature in different types of tissue. So, whenever there is a reaction from the antigen in our body, these monocytes can circulate to different tissues, and eventually they become macrophages for further antigen presentation roles, or macrophages can also cause phagocytosis. So, in terms of immunity, these macrophages play a very important role in innate immunity, and these macrophages can have a crucial role in bridging the gap between innate and adaptive. And what are the different functions, as you see, that macrophages play an important role in the phagocytosis of different antigens? They also have an important role in presenting antigens to the T cells. So, macrophages have the role of antigen-presenting cells that present antigens to T cells.

And various tissue-specific types of macrophages can also develop. For example, microglia in the CNS are like copper cells in the liver. To remember, macrophages are very important immune cells in our body. So, the next one is dendritic cells, or DC. This is also an antigen-presenting cell.

They are produced in our bone marrow, and in terms of storage, they can circulate in the blood and reside in the tissue. In terms of maturation, it happens basically in the peripheral tissues and lymph nodes. Immunity, if you see, these dendritic cells play an important role in both innate and adaptive immunity. So, the main role of dendritic cells is that they act as antigen-presenting cells. So, it is very important that the primary role of dendritic cells is to act as antigen presenting cells.

It also bridges the gap between innate and adaptive immunity; it also activates like naive T cells. So, dendritic cells, similar to macrophages, are very important not only because they play an important role in terms of antigen presentation, but they also bridge the gap between innate and adaptive immunity. Then another very important immune cell is a natural killer or NK cell. The production occurs in the lymphoid lineage in the bone marrow. They can be stored in the blood, spleen, or lymph nodes, and basically, the maturation also happens in the bone marrow, and they have a very crucial role to play in maintaining innate immunity.

What are the various functions? As you can see, NK cells can kill either virus-infected cells or tumor cells. They can recognize cells via the downregulation of MHC 1 or major histocompatibility complex 1. We will discuss what the major histocompatibility complex is. They also release various types of enzymes and molecules; for example, perforin and granzymes. These all together play a very crucial role in destroying this virus or tumor cell.

Then eosinophils, you can see that they are generally produced in our bone marrow. They have an important role to play in innate immunity. So, eosinophils have a crucial function to basically destroy the parasites. So, these are very specific to whenever a parasitic infection occurs in our body; eosinophils can act as fast responders to kill these parasites. They also initiates allergic type of responses.

So, in terms like after the initial killing of the parasites, if some infection is still left, they can also generate some allergic or inflammatory response through which other immune cells can sense where the infections are present in our body and eventually get activated to work against those antigens. Then basophils also get produced in our bone marrow, right? They also play a very important role in terms of our innate immunity. Basophils are also very important. Why? Because they also generate this type of allergic or initial inflammatory signals by releasing histamines similar to mast cells, this can also circulate in our blood. Then what is a mast cell? A mast cell is also a similar type to basophils.

They are produced in the bone marrow and can be stored in tissues. As you can see, they play a very important role in our innate immune cells. Similar to basophils, these cells can create allergic reactions, and they can also secrete histamines. So, basically, basophils and mast cells have a very important immune role to play against the parasite. Now, let us see the different types of T lymphocytes or T cells.

These are part of adaptive immune cells and where T cells are generally produced in the bone marrow. They can be stored in the blood and lymph nodes, but very importantly in the bone

marrow where the T cell is produced; there it does not mature. Where does it mature? It matures in the thymus. So, the thymus is very important to remember because it is like an endocrine gland; also, T cell maturation happens in the thymus. So, what happens in the thymus during T cell maturation? And they play a very important role in terms of adaptive immunity.

And different types of T cell classifications are there. For example, there are helper T cells, or CD4-positive cells. They activate the B cells and the cytotoxic T cells. T cells are also very important for secreting different types of cytokines, mainly pro-inflammatory cytokines like IL-2, IL-4, and IFN-gamma. And these cytokines can eventually act to destroy different types of antigens.

There are different roles of cytokines. We are not going into too much detail, but just remember that T cells have a very crucial role in secreting cytokines. These are some sort of protein molecules, and they can trigger either a pro-inflammatory cascade or an anti-inflammatory cascade based on the situation. There are different types of helper T cells like Th1, Th2, Th17, and T regulatory cells, and each of these has specific functions. For example, T regulatory cells participate in immunoregulation and also prevent autoimmune destruction.

Then there can be cytotoxic T cells or CD8+ cells. Mainly, they kill like viral infections or cancer cells, right? They are all like regulatory T cells or T regulatory cells. As you remember, T regulatory cells help in suppressing the immune response and maintaining tolerance. Then another important type of T cells present in our body is the memory T cells. It can recognize previous antigens, help in terms of cytokine production, and also act as immune surveillance.

So, basically, these memory T cells are very important. These memory cells develop to act as immune surveillance in the body. And whenever these cells store the memory of previous antigens and if they see that those antigens are harmful to our body, they can then secrete a lot of cytokines. So, basically, you can also say that these memory T cells act as natural vaccines in our body, right? So, this has some sort of vaccine-type mechanism, although they do not produce antibodies, but they act as cellular vaccines in our body. Then there are other classes of important lymphocytes, which are B lymphocytes.

These are mainly those cells that can actually generate the antibody response against those antigens. So, as you can see, B cells can differentiate into different types of cells, for example, memory B cells or plasma cells, and they are generally produced in the bone marrow, where maturation also occurs. All these B lymphocytes have a very important role to play in the adaptive or humoral immunity of our body. And as you know, B cells generally produce antibodies in response to those antigens. And there are several classes of antibodies, such as IgM, IgG, IgA, etc.

These act to neutralize those antigens and remove the infection from our body. And as I already said, these cells differentiate into either plasma cells or memory B cells. Plasma cells mostly act as antibody factories. So, plasma cells have a very important role to play as antibody factories, while memory B cells can maintain long-term immunity. So, in the last slide, you remember, we discussed the memory T cells.

So, both memory T cells and memory B cells actually work as immune surveillance and maintain the long-term immunity of our body. So, these are basically like natural vaccines, right? These cells are already present in our bodies. And if they fail, then we will observe different types of symptoms, and then we have to go to the doctor. But you have to understand

that our human body is such a powerful machine where the immune system is so strong because we are always covered with so many microbes, so many parasites, and so many pathogens, and eventually, when all these immune systems fail, then only do we become sick. So, we should be really thankful to all our immune cells, as they work continuously and tirelessly to maintain our immune system and to keep us healthy.

Finally, as you see, the plasma cells that are differentiated from the B lymphocytes maintain the adaptive immunity and function by producing large quantities of antibodies, right? Memory B cells we already discussed; they have a very important role in terms of rapid antibody production. They produce high-affinity, highly specific antibodies, and overall, they work in terms of vaccinal efficiency as well. Briefly, we will also discuss the major histocompatibility complex and the AMHC. So, what is the major histocompatibility complex? Like a group of genes that encode the protein found on the surface of the cell. These are highly crucial for the immune system's ability to distinguish between the body's own cells and foreign invaders.

These proteins together are called the major histocompatibility complex molecules that are present in terms of small peptide fragments to the T cell. And what is the function of the MHC molecules? MHC molecules are essential for the adaptive immune system to function properly. They can also act as antigen presenting cells. MHC is also important for organ transplantation compatibility because a mismatch can lead to organ rejection or organ failure. And there can be different classes of MHC, as you can see, like MHC class I and MHC class II.

So, MHC class 1, as you can see, the molecules are generally found on the surface of all the nucleated cells. And MHC class 2 in this case are the molecules found on the antigen presenting cells. And what it does, as we already told, is that it presents the peptides derived from the protein outside the cell to help a T cell. So, there are different areas where the MHC class 1 and 2 are present. So, as we said, what is immunity in general? In cases of any infection, our human system develops a response against that infection or the antigen that is called immunity.

Immunity is mainly of two types: one is innate immunity, which is mostly quick and very non-specific, and the other type of immunity is called adaptive immunity, which is long-term and very specific. So, see how this immune system performs in cases of innate immunity whenever there is an antigen or infection that can be recognized by our body, identifying what type of pathogens they are. Non-specifically, different types of cells that are part of innate immunity, such as macrophages and other types like neutrophils and eosinophils, can immediately perform phagocytosis on these antigens or pathogens. But in the case of adaptive immunity, whenever any infection or antigen enters our body, it generally gets presented by the antigen-presenting cells, and it can either activate the T cells or B cells, either through an antibody-mediated mechanism, cytotoxic T cell mechanism, cytokine production, or the overall immune system takes care of those foreign particles or infections and destroys them. So, one more time, innate immunity is mostly like an inborn capacity of our body to act against pathogens.

That is why it is mostly called natural or non-specific immunity. While you can see that this is, in general, a very nice chart where you can see different cells that actually participate in the immune meeting for the innate case. So, how do these cells generate? You can initially see that there are multipotentials like hepatopoietic stem cells or hemocytoblasts, and through the differentiation process, they can either generate myeloid progenitors or they can also generate lymphoid progenitors. So, from the myeloid progenitor, further differentiation can happen, and you can see that megakaryocytes can form. which can eventually generate thrombocytes or, alternatively, they can form erythrocytes, mast cells, or myoblasts.

Furthermore, myoblasts can undergo the granulopoiesis mechanism and develop different innate immune cells, for example, neutrophils, basophils, eosinophils, or monocytes. Monocytes, as we remember, whenever monocytes distribute in the tissues, and in case there is an infection or the appearance of a foreign body, these monocytes further get differentiated and become macrophage cells. And the lymphoid progenitor can further undergo differentiation and other conversion mechanisms to form natural killer cells, or NK cells. So, all these different cells participate in maintaining the innate immune system of our body. And as we already told you, in terms of adaptive or specific immunity, there is acquired immunity.

And these T cells and B cells, like most lymphocytes, are part of this acquired or adaptive immunity. It can either be active or passive. So, you can see the chart of the adaptive or specific immunity, where in the same way as the multipotential hematopoietic stem cells, it can undergo differentiation and make lymphoid progenitor cells. Then further differentiation occurs; it can either form natural killer cells or this type of small lymphocyte that can further undergo a conversion and differentiation mechanism to generate either T lymphocytes or B lymphocytes. And as you know, B lymphocytes can further generate this type of plasma cells or memory B cells.

And for T lymphocytes, there are also different categories; you remember, right? Helper T cells, cytotoxic T cells, memory T cells. So, these different classes of T cells can also develop. So, as you see how adaptive immunity works, if there is any infection, virus, or bacterial particle that enters our cells or infects them, then dendritic cells, which are the antigen-presenting cells, or sometimes macrophage cells, which are the largest immune cells, basically act as antigen-presenting cells and present these antigens to different types of immune cells. So, whenever these antigens come, this type of dendritic cell gets activated and eventually dendritic cells carry this infection and present it either to the B cells or to the T cells. When the T cells get activated, you know, like either by the performance of the cytotoxic T cells, it can immediately trigger the killing of those antigens, or it can also generate different types of cytokine actions.

In the same way, beta cells, when they convert to plasma cells, develop a lot of antibodies in response to those infections, and they act to neutralize those antigens. So, we already discussed what active immunity is like. So, you can see that active immunity mostly occurs naturally. There can also be artificial active immunity. But mostly active immunity is acquired by the synthesis of antibodies, and that is why it is also called humoral immunity.

So, in the case of natural active immunity, this results from a subclinical or clinical infection. What is basically like artificial active immunity? In the case of artificial active immunity, this occurs through the introduction of antigens into the body, primarily in the form of a vaccine. And then there can be passive immunity, which is not typically present in our body, basically like from mother to daughter or son; passive immunity can be passed, or during COVID you have heard of plasma-based therapy as well. So, we can also kind of supplement another person with the active plasma from a healthy person, and the plasma may carry various antibodies.

So, in this way, immunity can be passed from one person to another. This is also called artificial passive immunity. And what are the basic differences between active immunity and passive immunity? We can see that active immunity is generally produced in the host immune system, but in the case of passive immunity, it is basically passed from one person to another. This active immunity can be induced by either an infection or an immunogen, but passive immunity

is already present in another healthy person's body and can be transfused to another disease patient. Mostly, this type of active immunity is effective only after a certain time or lag period, but passive immunity can respond in a very quick manner.

So, it kind of shows an immediate action. Immunological memory can be present in the case of active immunity, but there is no immunological memory that can be passed from passive immunity. So, these are the different differences between active and passive that you can go through further. And lastly, a little bit, we will touch base on the antibody. So, as we said, the B lymphocyte cells develop this antibody which has a very specific structure. For example, you can see this IgG type of structure; these can also be called immunoglobulin.

So, an IgG is like a Y-shaped molecule. So, you can see this is like a Y-shaped molecule made up mostly of four polypeptide chains. There are like two heavy chains and then two light chains. So, you can see that there are light chains and a heavy chain. So, basically, two heavy chains and two light chains are all polypeptide chains, and they are held together by disulfide bonds.

There are different classes of antibodies that we also discussed. For example, IgA has a very crucial role to play in the localized defense mechanism. Like IgD, these are also involved in the recognition of antigens by B lymphocytes. Then IgE is involved in an allergic reaction. IgG is very crucial. It is responsible for this complement fixation and many of these neutralization reactions of viruses and bacteria; all this happens by the production of IgG.

IgM is also responsible for complement fixation, and in some cases, IgM can also be delivered from mother to baby. So, these are different classes of antibodies. Overall, the role is still more or less the same, but there are certain specifications that can vary for all these different antibodies. Eventually, the antibodies' role is to maintain our adaptive immunity, and whenever there is a memory presented to them from the antigens, they will develop these antibodies, which are like immunoglobulins, and eventually those immunoglobulins or antibodies will bind with the antigen and create a destruction mechanism or neutralize them.

So, I hope you enjoyed the immune system class. Please see some of the questions and try to answer what the differences are between innate and adaptive immunity, how immune memory works, why autoimmune diseases develop, and how allergies arise. So hopefully you like the class. You may refer to different books or web content. If you have further questions, please drop us those questions via email, or you can also discuss them with us during the live sessions.

Hopefully, you are enjoying the human physiology class. Thank you for attending another class. Hopefully, we will meet very soon with another new class on human physiology videos. Thank you very much.