Introduction to Complex Biological Systems

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Lecture 46
Introduction to the immune system

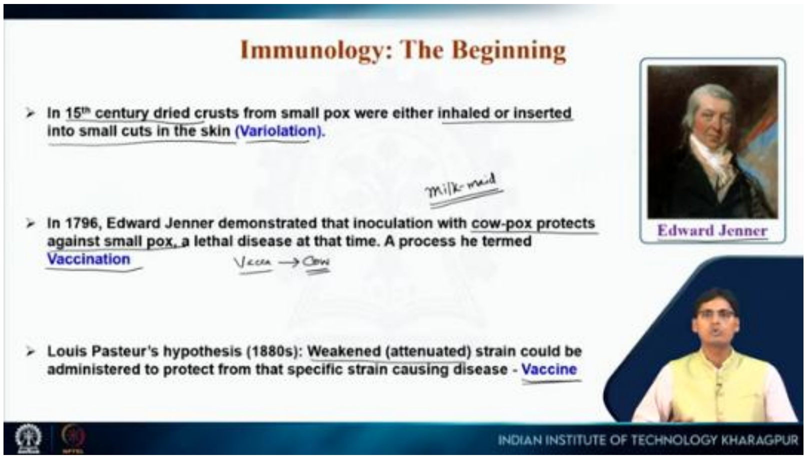
Welcome back to NPTEL online course on Introduction to Complex Biological Systems. I will discuss the immune system, the host defense mechanism, in this module 10, and in this lecture, I will be focusing on our immune system, mostly the introductory part. Here we will learn about the early insights into the mechanism of immunity followed by the origin of vertebrate immune cells. We have different types of immune cells.

So, from where they are coming. So, I am going to discuss that, and I would also like to discuss in this lecture the special features of our immune system and, in the subsequent lectures, I will be discussing in a more focused way about our different types of immune system, including innate immune system and adaptive immune system, but before that, I will explain what is innate and what is adaptive immune response. Here immunology, the beginning, let us start from the very beginning. In the 15th century, dried crusts from smallpox were either inhaled or inserted into small cuts in the skin.

So, I should mention that smallpox is a viral disease and it is a very lethal disease, also highly infectious. Generally, if smallpox starts, the fatality rate is very high. Many people died long back because of this smallpox, and as you can see here in the 15th century, maybe even more, this is a quarter of whatever records are available. So, what they used to do during pox, whatever pox you know now. So this is chicken pox; generally, we say this is chicken pox, but this is not chicken pox; this is smallpox. I am talking about and after smallpox, whatever that dried crust on the skin. So, those crusts kept dried, and maybe one year later it is used to be inhaled or inserted into small cuts in the skin; this process is called variolation. So what I'm trying to say is that there should not be live viruses available. Rather, whatever this dried crust coming from this smallpox infection from that particular patient is being used, and it is somehow protecting the new person where it is being applied. If you see more scientifically and if more records are available, Edward Jenner demonstrated that inoculation with cowpox protects against smallpox in 1796. This is a great discovery. Edward Jenner noticed that particularly milkmaids, people who used to work in dairy farms and they were doing some milking on all those stuff, they found particularly Edward Jenner noticed that those milkmaids are not getting this smallpox disease. So he thought that means during that time, cowpox is another viral disease and the cow is their host. Now this milkmaid is getting this cowpox because they are working with cows and milking them, and somehow this is protecting those people. So, as a result, Edward Jenner demonstrated that inoculation with cowpox protects from smallpox and this process is termed as vaccination, same term we also use now.

Why vaccination? Because this vacca means cow, so vaccination so the idea is that this cowpox virus somehow creates something in this milkmaid, so that they are getting some protection from the smallpox virus and this is the starting point of vaccination.

Later on in the 1880s, Louis Pasteur demonstrated that the weakened or attenuated strain could be administered to protect from the specific strain causing disease, and this vaccine, a lot of vaccines available in the market, and some of the vaccines are mandatory for all of us. We need to take so many of them, as they are attenuated strains, so this way the field developed. So the immunology field developed. But what is the mechanism? How does it work? Those things were not known at that time, but gradually we will learn how it is actually working. So, since I started with smallpox let us see. So, smallpox was officially eradicated in 1980, although you will see that it is mentioned here as 1979; as you can see, this is one year with some kind of issue there. I have taken this from a very standard textbook, which I will refer to at the end. But anyway, that does not create any understanding issues. The idea is if you see here, we are showing from 1965 to 1980, and on the y-axis you can see the number of countries with one or more cases per month; cases here mean smallpox disease.

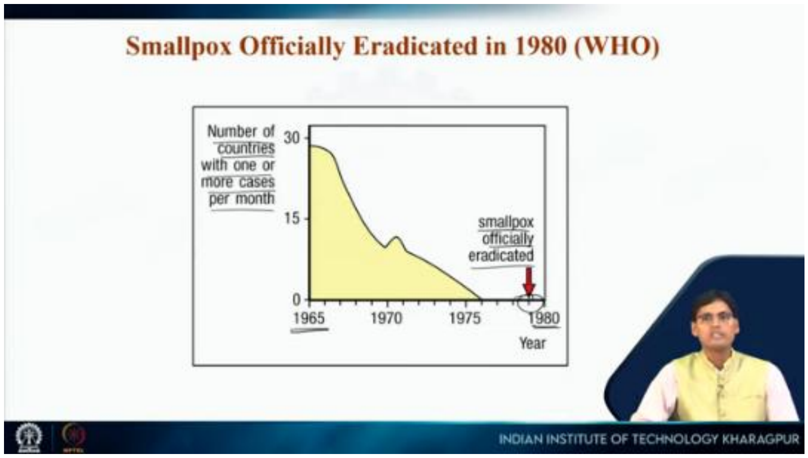


So, as you can see, in 1965 almost 30 countries reported smallpox, and over time by 1976 there was no smallpox reported or the occurrence of smallpox. Therefore, after a few years, the World Health Organization declared that it has been eradicated; the disease has been eradicated and this is the great success of vaccination, I would say. I would just like to mention that smallpox vaccination was so successful. If you are very young and listening to this course, you might not see the vaccination, but if your age is above 40-45 years or you can see it in your parents' arm, generally in the left arm in this region, I also have this. So you will see some scar here, scarification it is called. So that way, this smallpox vaccination was done. So generally you will be seeing on the left arm somewhere here. So as I mentioned, I also have that.

But most of you, if you are first year students so if that is the case, first year or college student, you will not see in your arms. You can check with your parents. This vaccination successfully eradicated smallpox from the world. So that is a great success, I would say.

In this case, I would like to mention that, whatever the stock of this smallpox was at that time, when WHO declared it had been eradicated, all those smallpox virus stocks were destroyed or transferred to two laboratories, WHO-designated laboratories. One is in the United States that is the Center for Disease Control and Prevention, and the other laboratory in Russia, which is called the State Research Center of Biology and

Biotechnology. In these two labs, this virus stock is still there. So anyway, let's see what is happening here, the first insight into the mechanism of immunity.

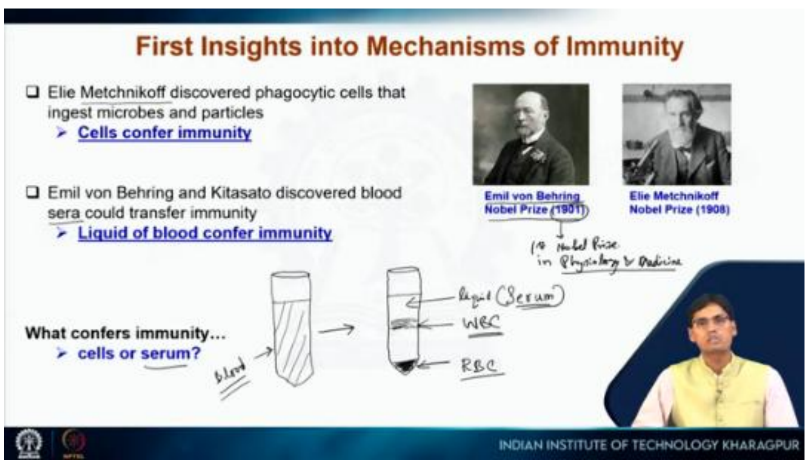


Whatever I discuss until now, this is just how vaccination protects us from a particular disease. But now, how does our immune system work? This is where I am going to discuss. So, Elie Metchnikoff discovered that phagocytic cells that are present in our body, It engulfs microbes and some foreign particles, and that's why we have this immunity, which means the protection power against pathogens against disease. So Metchnikoff mentioned that cells confer immunity.

On the other hand, almost at the same time, von Behring and Kitasato discovered that blood sera could transfer immunity. What is blood sera? So blood sera is the liquid part of the blood. So the liquid of blood confers immunity. See, these two are contrasting.

One group is mentioning the cells confer immunity, some cells, particularly phagocytic cells and another group is saying the liquid of blood confers immunity. So, then what is the correct one? Whether immunity is conferred by cells or serum? This is a long time back as you can understand, but now we came to know both are very important sera, that means serum and cells both are indispensable for this immunity, and they protect us. So first I should mention what cells and serum because that will be clearer to you so for example, if you take in this tube. If you take a blood sample by drawing some blood from an individual, this is nothing but this is a blood sample. Now, if you centrifuge this tube at a proper speed, then what will happen is you will see that some cells are at the bottom. So, these cells are much heavier, and this is our RBC red blood cell RBC, and then it is all liquid. So, here you have a solution you will get some cells here also those cells are white blood cells. At that speed, the RBCs only settled at the bottom. These are white blood cells, which are mostly immune cells present in our body, in our blood, and on top of that, you have this liquid. This is serum whatever I am saying that this serum or this sera, the same thing serum. So, as a result of what I am trying to say at the beginning, this group of scientists mentioned that cells and the other group said serum confers immunity. I would like to mention here that both of these groups received Nobel Prize in Physiology and Medicine.

Particularly I would like to mention that von Behring received the Nobel Prize in 1901. This is the first Nobel Prize in physiology and medicine. This Nobel Prize started in 1901. So, this is in that category. This is the first one and Metchnikoff also got the Nobel Prize in 1908 for their work.



So, this is beautiful work, but let us sees what is happening in more detail. Now I just mentioned what serum and what are those cells present in our body, as I discussed in different modules, different types of cells are present, and all those cells started from a zygote; particularly, I am talking about our system right from the zygote. Then followed by those zygotes are proper stem cells, pluripotent stem cells, and it is differentiated into many different types of cells; different types of organ systems are actually formed in our body. Let us see from where these immune cells are arising. So, now all these immune cells, or I would say the cellular components of the immune system, are coming from bone marrow and bone marrow are multipotent stem cells.

Although this is mentioned here regarding pluripotent cells, as I mentioned before, too. Pluripotent generally refers to cells which can give rise to all cell types present in our body. So, for example, the zygote or at the very early stage of division; those cells have the potential to make anything in our body. So those are, in true sense, the pluripotent cells, so here it will be better to say multipotent stem cells because this stem cell, these bone marrow cells, will give rise to only different types of immune cells, blood cells particularly, I would say, and this is called hematopoietic stem cells, and they are multipotent in nature and those are present inside the bone marrow. Now, if you see over time, they will be differentiated and they will form different types of blood cells present in our blood. What are the different types of blood cells; immune cells as well as red blood cells all are present there? Let us see.

So, now initially they can get differentiated into lymphoid progenitors and the other one is myeloid progenitor. So, a lymphoid progenitor means they will mostly define types of immune cells like T cell, B cells, NK cells. So there are many things. If you do not remember all those things, that should be fine, but our basic idea here is that all those cells are originating from our bone marrow followed by some differentiation and finally we get erythrocyte.

This is a red blood cell which carries oxygen, and platelets, which help in blood clotting. Apart from that, a few very important things you have to remember, so that I can discuss the other lectures here, is that from this lymphoid progenitor we get a B cell here, T cell and NK cell are all very important to remember because they play a very important role in our immune system. So, as you can see, this is a B cell, T cell, and NK cell, particularly this B cell when they get expanded; they are actually making antibodies called plasma cells. So that is why I just mentioned this, so that we can discuss later parts like B cell, T cell, NK cell and plasma cell. Those are the major immune cells; in addition to that, we have to be very careful about these two cells also. They are also very important: macrophage and dendritic cells.

So I am just summarizing here, B cell, T cell, NK cell and then macrophage and dendritic cell. So, these are very important immune cells; other cells are also important, but without discussing these cells, I will not be able to explain innate and adaptive immune response that is why. So, this macrophage and dendritic cell are particularly phagocytic cells and B cell as I already mentioned it produces antibodies ah later on we will learn all those things.

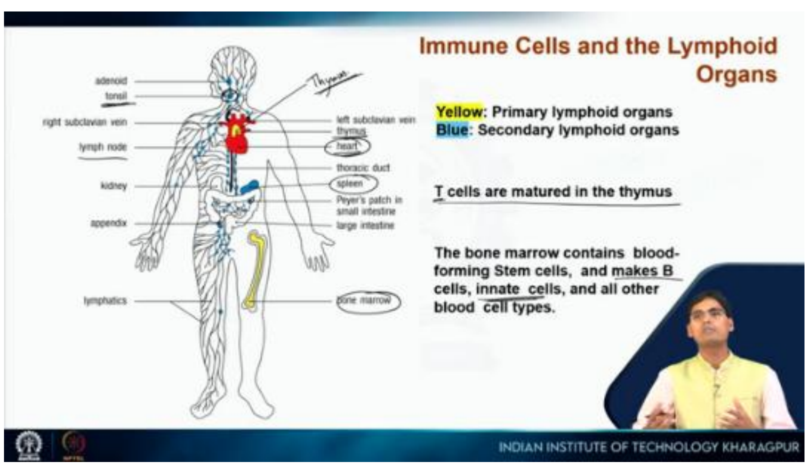
Now let us see where these immune cells are present in our body. I told you that all of them originate from the bone marrow and after that what is happening. So, immune cells and the lymphoid organs we are going to discuss here now. So if you see whatever in red color, as you can see, we are just referring to this is our heart, so that this is a reference point from where you can see all these things, and in yellow color, two things are mentioned here: bone marrow and the thigh mass. These two are our primary lymphoid organs. So, primary lymphoid organs mean particularly here bone marrow as I already mentioned all sort of immune cells they are getting generated from the bone marrow.

Here, that is why I mentioned that all blood-forming stem cells are present in bone marrow and make B cells, inert cells. Inert cells here mean dendritic cells, macrophage and all other blood cell types. So, those are coming from the bone marrow. Then why are we mentioning that the thymus is also a primary lymphoid organ? Because here, I am not particularly mentioning the T cells if you see.

T cells also originated in the bone marrow, but they mature in the thymus. So, this is the thymus. This is very close to our heart. So, this is the thymus. So, here those cells are maturing.

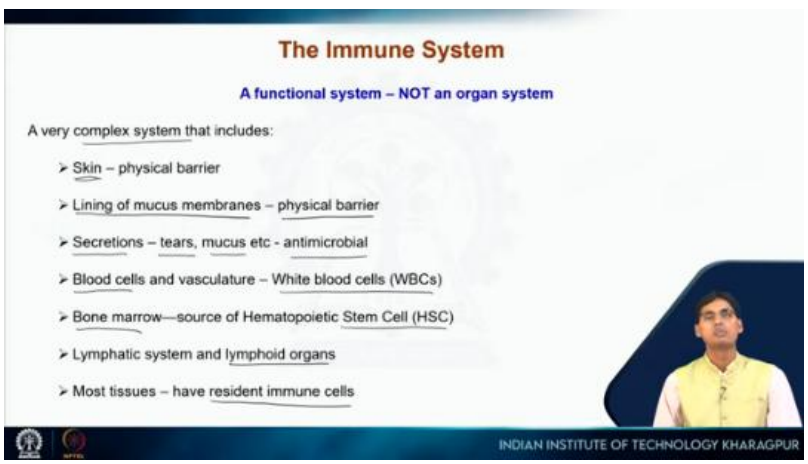
So, that is why they are called T cells. Just remembering that T stands for thymus and although B cells have an initial designation that was different, but remembering the thing that you can imagine because they are coming from bone marrow directly. But that way the name was not given at the initial point of time, but here, if you see many other small organs which are colored in blue, particularly I should mention here that it is the spleen. This is a very large secondary lymphoid organ; it stores a huge amount of immune cells and apart from that, you will be seeing there are many, for example, tonsil, lymph nodes. There are many things that actually store or keep all those immune cells, and we have lymphatic ducts, just like our blood vessels which carry only blood, so we have lymphatic ducts where we have some fluid as well as this, which is called lymph; the fluid is called lymph, and these immune cells travel through our lymphatic ducts. Particularly, I would like to highlight here, for example, the tonsil, as you can see, the tonsil gland which is present somewhere here, the tonsil gland. So, when someone is suffering from fever, for example, and the fever is there for a long time, and if you go to check with your doctor's office, then sometimes you will see that most of the doctors are trying to examine by pressing somewhere here whether the tonsil gland is swollen or not. So this kind of infection like viral fever for example, tonsil gland might be swollen, that is not a bad thing.

So, the immune system is working; there are a lot of immune cells there, and those are correlated between the symptoms, and all this is important. Now if you see our immune system, I just mentioned from where our immune cells are formed and then where immune cells go, different types of lymph node and as I mentioned the lymphatic duct and also there are many different types of immune cell those are called tissue resident immune cells they are traveling and they are going into tissues. So, whenever some infection comes, they can act on it. The immune system is a functional system, not an organ system, not like kidney or lung, not something like that.



It is a functional system. It is present everywhere in our body so that we are protected. As you can see this is a very complex system, which includes different parts, for example skin I would say skin is also part of our immune system because it is making some kind of physical barrier. So any pathogens like microbes are not able to enter directly in our body. We have almost everywhere covered by skin and whenever you will see some person, for example this eye. So you will not see it covered by skin, but even in tears, some secretions are present, some kind of enzymes present, which will protect us. Those secretions from the eye are killing these microbes directly.

Now, the lining of the mucous membrane is also a physical barrier, and from this mucous membrane or mucous layer, different types of antimicrobial peptides are also secreted. So this also somehow gives us protection from microbes. Then secretion, as I already mentioned, for example tears and mucus, are antimicrobial, and those are all part of our immune system, and then blood cells, particularly I mentioned different types of white blood cells, bone marrow from where all these cells are generated, and then lymphatic system and lymphoid organ and at the end, most tissues have tissue-resident immune cells. So, everything together makes up our immune system.



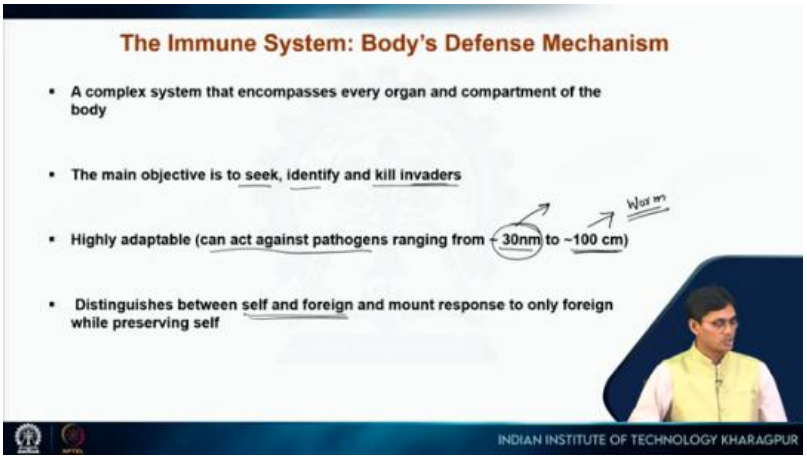
Now, the challenges of our immune system are that it must take care of many things. Let us see: this is a complex system that encompasses every organ and compartment of the body. We have to protect our whole body; so as a result, it should take care of the entire system. The main objective is to seek, identify, and kill invaders. This is very important.

So, find out and then identify and kill invaders because this is one of the most important functions. These immune cells should not destroy our own tissues, so it is crucial that they properly identify targets. Another important feature is that they are highly adaptable in nature. So, as you can see, our immune system can act against pathogens ranging from 30 nanometers. So, what is 30 nanometers? In the last module, Module 9, I discussed that 30 nanometers can be the size of a very small virus.

Those small viruses can be in this range, 30 nanometers in diameter and this is surprising. We are mentioning that some pathogens are approximately 100 centimeters long, although this is rare. But yes, for example, some worms could be around 100 centimeters long, I would say. But still, our immune system can take care of it. So, it will destroy this also in a properly functional system. That is why I am mentioning this is highly adaptable, and this is the most important thing; it distinguishes between self and foreign and mounts a response only against foreign while preserving self.

So, our immune system should not act against our own body parts, our own molecules present in our body, or physiologically relevant molecules. Then we will develop another type of disease, which is called autoimmune disease. So, as a result of that, it should properly recognize which one is self. The immune system should not work against those cells so it should only act against foreign things.

So, this is one of the major things for our immune system. Now, I will go into a little bit more of a complex thing that the immune system generates almost an infinite variety of cells and substances. See, for example, in the case of humans, we have a very long lifespan. If I say 80 years, 90 years, over time, we get different types of diseases, different types of challenges day to day happening.



So our immune system can adapt, learn, and mount a response against that. and most of the time, we don't even understand that. Only a few times do we get the disease because we have a proper immune system. The immune system is dealing with this pathogen all the time, so most of the time we are very healthy with no problem there; and when the immune system is not able to tackle the problem smoothly, that's when you might get some disease, depending on the pathogen as well. But after some time, our immune system will learn; it will make a variety of molecules and substances and clear the infection from our body. Let us see how it happens. The first thing is foreign recognition.

As I already mentioned, the immune system should work against the foreign stuff, foreign pathogens, for example and there could be two different types of responses. One is called the effector response, and the other one is called memory. So, effector response means here to eliminate or neutralize foreign particles so that they cannot cause disease.

This is called the effector function. It is mediated by our immune system, immune cells, and the other one is memory. This is very important. This is not the memory that I can remember now. I am talking about immunological memory. So that means upon second exposure, it produces an enhanced response. For example, if I am infected today by some particular virus or bacteria, my immune system acts against that virus or bacteria, and after four, five, or six days, I get well. I am fine now, but after six months or one year later, Again, if I am infected with the same virus or bacteria again, my immune system will act very fast against that particular pathogen and at that time, I shouldn't have any symptoms.

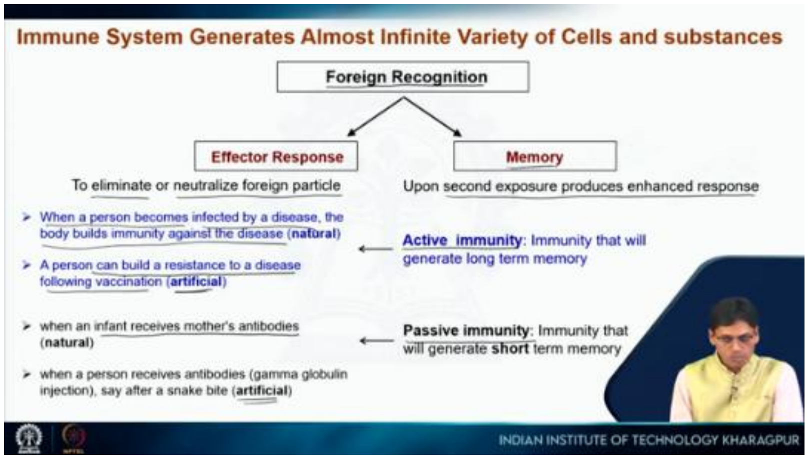
This is because of the memory. Because my immune system actually remembers whatever happened six months or one year before. They remember those things; they have some components, and next time when I get the same infection, the immune system acts very quickly and can clear the infection so I will not have any symptoms, I will not have the disease also. This is because of the immune memory and this can be two types. This immune memory can be developed because of either active immunity or passive immunity. I will go step by step. So, active immunity means immunity that generates long-term memory, and in case of passive immunity, it will generate short-term memory. Let us see with an example. In the case of active immunity, whatever I explained, the natural one is that when a person becomes infected by a disease, the body builds immunity against the disease. This is the natural active immunity. This is naturally happening. We are infected by some pathogen, and our immune system is fighting against it; over time, immunity and memory will be formed.

This is the memory because of the natural active immunity. On the other hand, a person can build resistance to a disease following vaccination that is artificial active immunity. So what is an example? For example, when I was a kid, I had chickenpox. So chickenpox is a disease, not that much of a severe disease. It's a mild disease. But because of that suffering, my immune system developed the memory, and I didn't have chickenpox anymore.

This is an example of natural active immunity. But nowadays, you will be seeing those small kids getting vaccinations. They are getting a vaccine against chickenpox. So as a result of that, they are bypassing the disease. They are not developing the full-fledged chickenpox disease.

But their immune system learned how to tackle this disease. So they will not have the disease in future but this is called artificial active immunity, the memory is formed because of the artificial active immunity. This is because of the vaccination, and now there are many vaccines available that are mandatory in different countries, in India also, for example, for kids there are different types of vaccines available. Then passive immunity occurs when an infant receives the mother's antibody that is natural Immunity but that is passive so the mother's antibody. How? I would say infant when depending on mother's breast milk so through breast milk the antibodies are also coming to the infant. So that antibody is also giving protection to that baby. So this is passive immunity and artificial passive immunity.

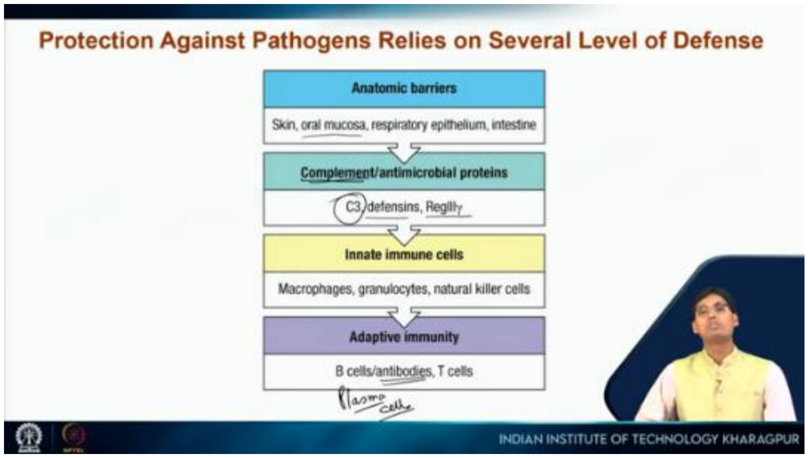
When a person receives antibodies, for example, gamma globulin injection after a snake bite, this gamma globulin injection provides some passive immunity, but this is artificial, not the natural one, so this is some overall idea about our effector response and memory. Now for today's lecture this is the last slide. So, as I mentioned that today I am just discussing the introductory part of our immune system. Now, if you see, the protection against pathogens relies on several levels of defense mechanisms, the first one is anatomic barrier.



As I already mentioned that skin, which is covering our body, is an anatomic barrier. Oral mucosa so in our oral cavity, as well as intestine, everywhere in the inner lining, we have the mucus layer. In this mucus layer, we have immune cells, antimicrobial peptides, and many other things present. Then we have respiratory epithelium, intestine epithelial layer; all those things are part of our anatomical barrier, and they are helping us.

Then we have a complement system and antimicrobial proteins. So, all of you know about antibodies. They are part of our adaptive immune system. I will discuss it later. A complement is also very important. We have around 30 different types of proteins that are together called the complement system, and C3 is one of the key complement proteins which play a very important role in our immune system. Apart from that, there are many antimicrobial peptides present, including Defensins and RegIIIγ.

All those are very important. I would say response against some infection or pathogen and after that, we have different types of innate immune cells, so those are phagocytic cells mostly, for example, macrophages as I already mentioned, and also some granulocytes, some natural killer cells; they are also part of our innate immune system. Those are the different layers. Whenever we are getting infected first, the innate immune system tries to protect us and over time, if it is not taken care of, our adaptive immune system will come into play, and particularly T cells and B cells will take over and B cells will make antibodies; plasma cells also do. When B cells get differentiated and matured, they will make some antibodies; those are called plasma cells. So together all these things, the innate immune system and adaptive immune system will protect us from the infection, and this is all about the introductory part.



In the next class, I will be discussing our innate immune response, and you can follow this textbook. This is a very good textbook, Janeway's Immunology, and thank you very much.