Tissue Engineering
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Lecture – 26
Host integration and immune response – Part 1

Good morning everyone. Hi, I am Hemalatha Kanniyappan, doing my research under the guidance of Doctor Vignesh Muthuvijayan. Today, I will be giving a lecture on immunology. The main lecture is based on immune responses to foreign material or biomaterial or any other implant.

Before understanding the immune responses in the presence of biomaterial, we should note a few basics of immunological responses or immunological terms or what is immunology or what are the cells involved in immune responses and all.

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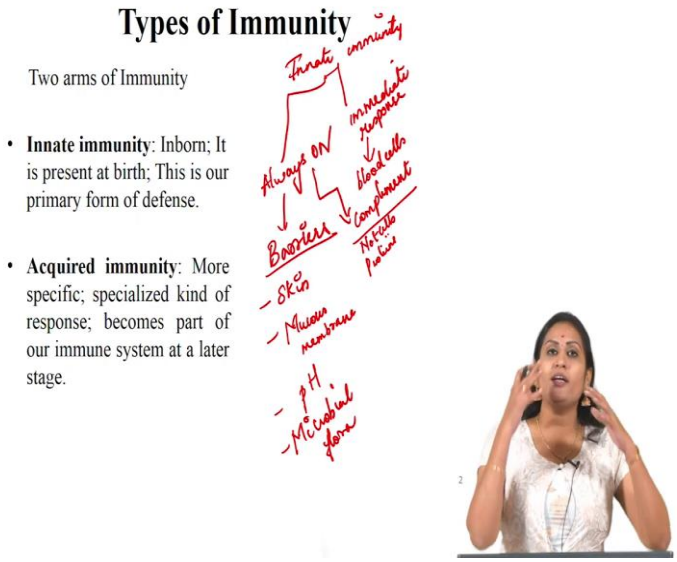

In this lecture, I will be giving a brief introduction about what is immunology or what are the immune responses or what are the types of immune responses or what are the cells or organs involved in the immune system and the major cells which are responsible for immune responses.

We should know what immunology is. So, what is immunology? It is the study of biology that studies the immune systems of all organisms, or what do you mean by

immunity? We say right; you have a very good immune response to this kind of infection and so on. So, what do you mean by that? what is immunity? Immunity is the protection of the body against pathogens or infections caused by pathogens. When I say pathogens; pathogens are viruses, bacteria, fungi, parasites or some proteins. So, this is about immunity and what is a pathogen.

There are two types of immunity; innate immunity and adaptive immunity. When I say it is innate immunity, it is the primary form of defense mechanism in our body. Our body itself has a defense mechanism; it has a very good defense force to act against the pathogens which enter the body. So, it is divided into innate and adaptive immunity.

Innate immunity is like; it is always on. It is present from birth; this is the primary form of defense mechanism. So, always on which means it has barriers. When I said barriers, it means what? What are the barriers that protect our body from the pathogens? The first and foremost is skin. Skin is the largest organ of the body; it protects our entire body from various pathogens entering into our body.

The next one is a mucous membrane, mucous. There are several parts of the body covered by mucous, which protects those parts from the pathogens. Mucous are two or more layers of epithelial cells. And then pH, the acidic pH of our stomach which is like around two to three, kills the bacteria effectively. Then microbial flora, which is present in our body, there are some good bacterias in our gut which protect our body from the pathogens. So, these are the main barriers present from our birth to fight against the pathogens. Then again, in innate immunity, this part of the cells is always present. Always-on, no matter what the pathogen enters, it will go and act against that pathogen.

The next is an immediate response; where the cells present in this are not activated all the time, but once when the pathogen enters, it immediately gets activated and starts acting or fight against the entering pathogen. For example, blood cells. These blood cells, it will be there in the bloodstream, but once when the pathogen enters, it will get activated and fight against those pathogens. And one more thing, in always-on immunity, there are compliment factors. Compliment factors are not the cells; they are kind of proteins that acts against the pathogen. So, this is about innate immunity.

The next one is acquired immunity or adaptive immunity. It is a more specific and specialized kind of response that becomes part of our immune system at a later stage, which means it is not an immediate response; it is a kind of delayed response.

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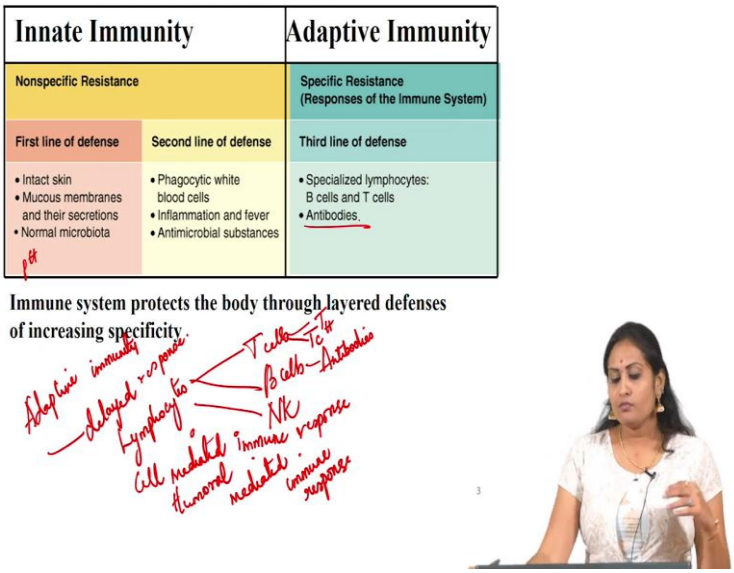

Adaptive immunity is a delayed response. The major cells responsible for this type of immunity are lymphocytes. Lymphocytes again divided into T cells and B cells and natural killer cells. These B cells produce antibodies, which fight against the pathogen. And in T cells, T helper cells and T cytotoxic cells are there. Natural killer cells are distinguished from T cells and B cells with the presence and absence of specialized receptors on the surface. That is a major difference between these cells.

So, in innate immunity as well as in adaptive immunity, when I say the immune response is because of the cells, it is called cell-mediated immune response. The other immune response is mainly based on proteins or these antibodies; they are not cells that are termed as humoral mediated immune response. These are the two major immune responses which act in our body.

In this slide, innate immunity is mentioned as nonspecific resistance, which means no matter what the pathogen is. Once it enters the bloodstream, it will go and engulf, and it will kill the pathogen; that is nonspecific immunity. Whereas the adaptive, it is more specific, it will go and kill the most specific antigen, or it will produce a specific antigen to kill the specific pathogen; specific resistance responses to the immune system.

So, the first line of defense we all know that the barriers. The barriers are nothing but skin, mucous membranes. An example of the mucous membrane is the layer covering the nose, eyes, lips and all. They are covered by mucous membranes and not covered by skin, thereby protects our eyes from the external pathogens. Normal microbiota present in our gut. Our gut will produce good bacteria to engulf the bad bacterias, also the pH.

The second line of defense is the phagocytes, which engulf the microorganisms, mainly made up of WBC cells. And the third line of defense, which are the adaptive immunity specialized lymphocytes. The lymphocytes are the major cells responsible for this. Central cells for the adaptive immunity, which are again divided into B cells and T cells and the B cells, produce antibodies that fight against the pathogen.

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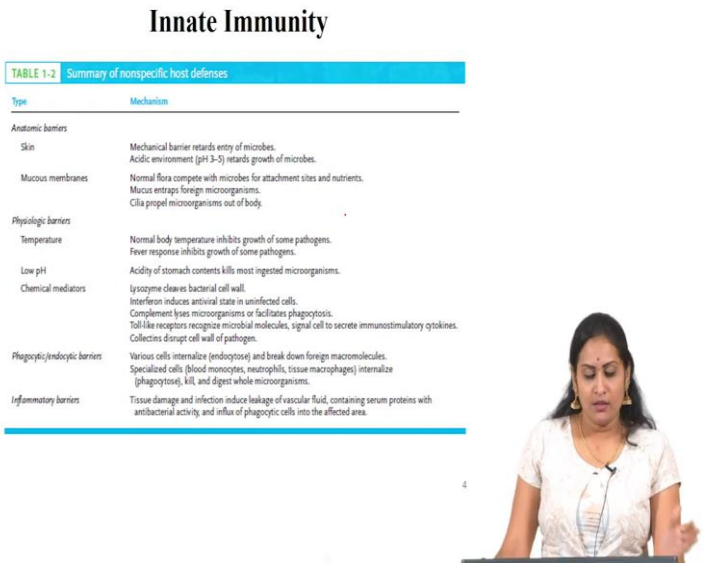

There are specific, nonspecific host defenses; these are the summary of nonspecific innate immunity. Anatomic barriers which are skin, mucous membrane. The skin is the largest organ of the body. It plays a very important role in our defense mechanism and mechanical barrier, which stops the entry of microbes on the first step itself. The acidic environment, stomach, which digests the bacteria. The mucous membrane again helps to protect the entry of microbes into the internal organs.

The physiological barriers like temperature, low pH, which I said already, the acidity of the stomach and chemical mediators or the complement factors.

Phagocytic or endocytic barriers contain all the various types of cells, which will endocytose. Endocytose is the process of engulfing cells and breaking down into foreign macromolecules. The cells responsible for those are macrophages, neutrophils, monocyte, and tissue macrophages. Inflammatory barrier occurs during the tissue damage, and infection inducing leakage of vascular fluid containing the serum proteins which has the antibacterial activity and into the affected area.

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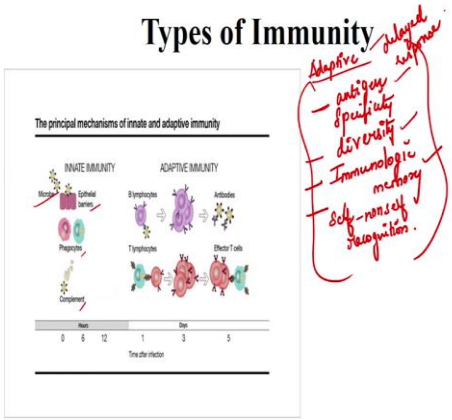

This is the principal mechanism of innate and adaptive immunity. In terms of adaptive immunity, the adaptive immune system has four important characteristic attributes. The first one is antigen specificity, the second one is diversity, the third one is immunologic memory, and the last one is self, non-self recognition.

The first characteristic attribute is antigen specificity. It permits the immune system to distinguish even a small difference among the antigens. So, it will be more specific in recognizing the antigen. Diversity allows the adaptive immune system for generating tremendous diversity of recognition molecules, thereby allowing that to recognize billions of unique structures present in the foreign antigens. That is diversity.

In immunologic memory, once the immune system recognizes the antigen and responds to the antigen. When the same antigen it encounters for the second time, it will develop a high level of an immune response to that specific pathogen. It keeps that in its memory

that we have encountered this already, and we became immune to that. This attribute is a very important attribute in adaptive immunity.

Finally, once it is responded to and the immune system should be able to differentiate from the self and the non-self components in order to act on the non-self components. What will happen when the immune system fails to recognize or differentiate between the self and non-self components? Yes, obviously, it will lead to some other responses, and it could be fatal. So, these are the major four important characteristics of adaptive humanity.

In the principal mechanisms of adaptive immunity, the main is microbes, epithelial barriers, phagocytes and compliment. In case of adaptive immunity, B lymphocytes and T lymphocytes. B lymphocytes produce antibodies, and T lymphocytes are the effector T cells Th cells and Tc cells. So, this is all about the types of immunity.

To summarize that innate immunity and adaptive immunity. Innate immunity is non-specific resistance; like whatever the pathogen enters the body, it will go and act against that pathogen. Whereas adaptive immunity is completely specific to the pathogen and fight against that pathogen, and it is also termed as a delayed response immune system immunity. Whereas innate immunity acts immediately, there is an immediate response as well as always-on responses; there will be some barriers that are always on in the innate immunity. Major cells present in innate immunity are skin or the epithelial cells; then microbes and few other chemical factors or physical factors that are also involved like temperature or pH and chemical cytokines. Major cells in adaptive immunity are lymphocytes. So, this is all this all about immunity.

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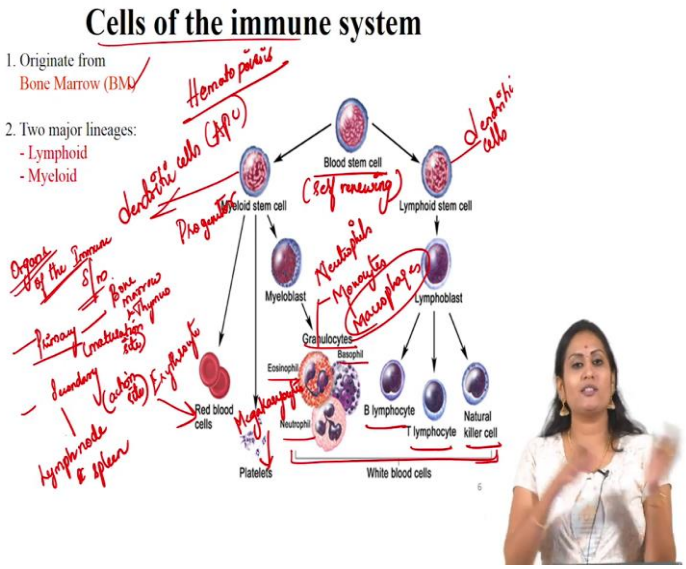

Now, we will go to the cells present in the immune system. This picture is the process of hematopoiesis. Hematopoiesis is nothing but the formation of blood cells. Any blood cells will originate from the hematopoietic stem cell. The blood stem cell is nothing but hematopoietic stem cell which is self-renewing cells. This self-renewing cell will give rise to either of myeloid progenitor cells or lymphoid progenitor cells. When I say, they are progenitor cells, which means it loses the self-renewing capacity and it will be specific to a particular cell lineage. The hematopoietic blood cell originated from bone marrow. So, that is the place where this hematopoiesis takes place. So, two major cell lineages are lymphoid cell lineage and myeloid stem cell lineage.

Myeloid stem cell progenitor cells will give rise to granulocyte progenitor cells, basophil progenitor cells, and eosinophil progenitor cells. From the granulocyte, it will give rise to neutrophils, monocytes. These monocytes give rise to macrophages, which are very important cells responsible for immune system. Neutrophil progenitor cells give rise to neutrophils and basophil progenitor cell gives rise to basophil, eosinophil progenitor cells give rise to eosinophils. Also, erythrocyte progenitor cells give rise to red blood cells and megakaryocytes which gives rise to platelets. It also gives rise to dendritic cells. Dendritic cells are antigen-presenting cells they are APCs. So, this all about the myeloid lineage.

Whereas in lymphoid stem cell lineage, it gives rise to lymphocyte. Lymphocyte, which is again divided into B lymphocyte, T lymphocyte, and natural killer cells; also, it gives rise to dendritic cells.

This natural killer cells mainly differ from B lymphocyte and the T lymphocytes with the presence or absence of surface receptors. Where in B cell and T cell have the surface receptors whereas in the natural killer cell, it does not have. And it is called as the cell and whereas B and T are small naive cells. These are about the cells of the immune system.

Before going in-depth with the cells, We should know about the organs of the immune system. It is divided into primary and secondary. In primary, bone marrow and thymus, these are the organs responsible for the production of these cells and in secondary, lymph node, and spleen.

This primary organ, it is the site for the maturation of the cells B cells or the T cells. This is the maturation site. Once it got matured, it will go and fight against the pathogen; that will act in the secondary organs, which are action sites. These basic few points you should know when you study about the immune system. So, this all about the organs and the cells of the immune system.

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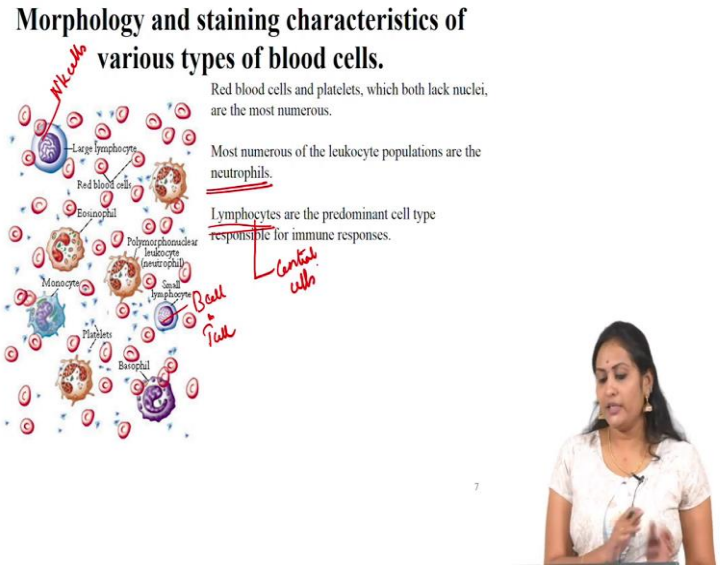

Then morphology and staining characteristics of the various type of blood cells. From this, as I said in the previous slide the large lymphocytes are nothing but natural killer cells and the small lymphocytes are nothing but B cell and T cell. These small red cells are red blood cells. Monocytes and basophils, eosinophils are also present.

Both red blood cells and platelets lack a nucleus, and they are the most numerous cells present. Most numerous of the leukocyte population are neutrophils. In the next slide, you will see the percentage of different cell types present in the WBC. And lymphocytes are the predominant cell type responsible for the immune response. They are the central cells responsible for the immune response.

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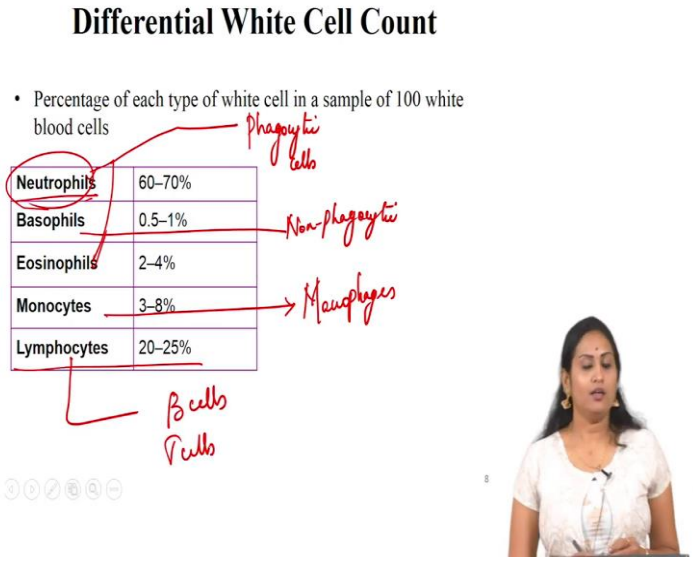

This slide will tell you about the percentage of cells present in the white blood cells. In this neutrophils occupies like 60 to 70 percent, basophils 0.5 to 1 percent, eosinophils 2 to 4 percent, monocytes 3 to 8 percent, and lymphocytes 20 to 25 percent. In this, neutrophils and eosinophils are again phagocytic cells. Basophils are non-phagocytic. Monocytes give rise to macrophages. B cells T cells are the lymphocytes.

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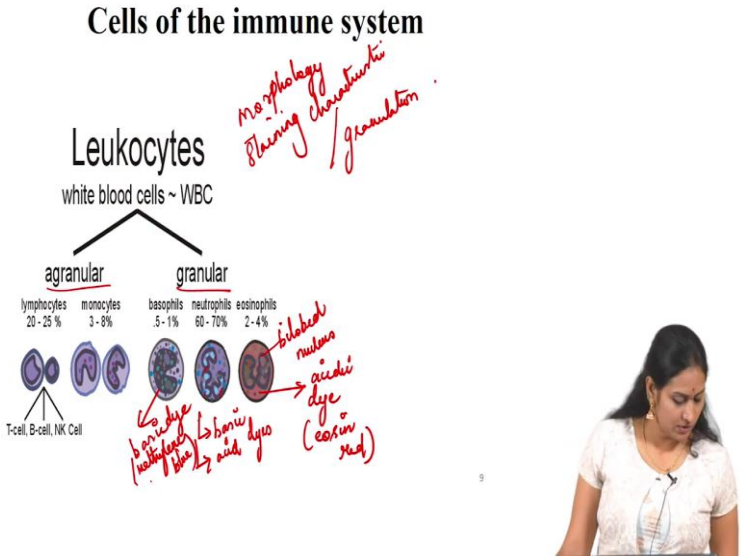

This classification is mainly based on the granulation and the staining characteristic of cells. So, agranular and granular, it is based on the presence of granules in the cytoplasm, also, based on the classification of the nuclei. Based on the classification of morphology, based on the difference in morphology and staining characteristic or granulation. Lymphocytes and monocytes are agranular; it does not have granules in the cytoplasm. Whereas basophil, neutrophil, and eosinophil have granules in the cytoplasm.

Neutrophils have multilobed nuclei, and it will stain with both acidic and basic dyes. And eosinophils have a bilobed nucleus, where it stains only with the acidic dye, eosin red; that is why its name as eosinophils. Whereas, basophils stains only with basic dye methylene blue. These all about the classification based on the morphology and staining characteristics or granulation present in the cells.

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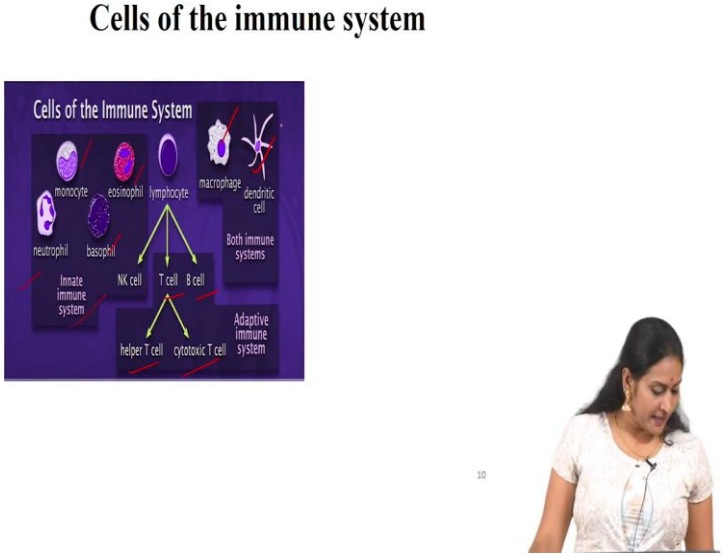

This picture summarizes all the cells present in the immune system, which are responsible for the immune responses. So, cells of the immune system, for the innate immune system, for the adaptive immune system and certain cells which are produced in both.

Neutrophils, monocyte, eosinophils, basophils are present in the innate immune system. So, when I say it is an innate immune system, these cells will be there always, always-on. When a pathogen comes, it will go and act against the pathogen, no matter what the pathogen is or what the antigen is. Whereas, when I say the cell of the adaptive immune system, they are the delayed response system. They act against the specific antigen by T cell B cell and T helper cell and T cytotoxic cells. Both immune systems have macrophages and dendritic cells; macrophages for the phagocytic activity.

With this slide, we knew about what are the immunity and what are the immune responses and what are the cells present in the immune system and what are the organs of the immune system.

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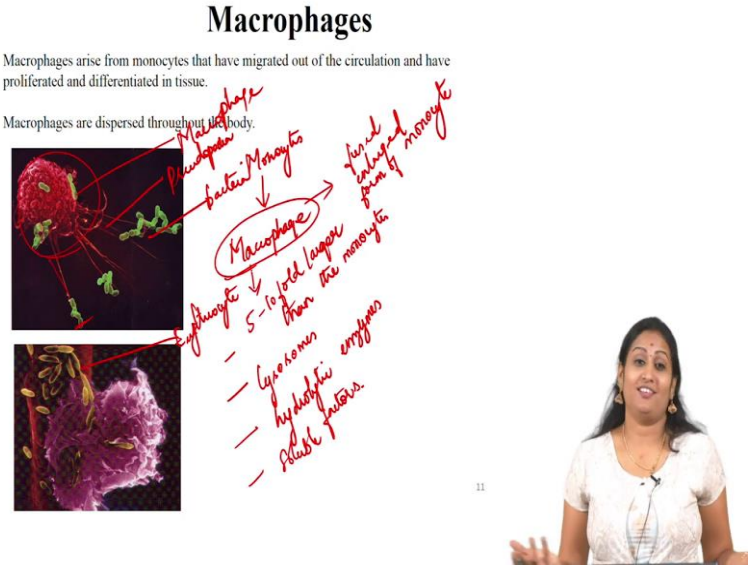

Next, I will talk about macrophages. So, we can say that the macrophages are nothing but the enlarged monocytes. Monocyte circulates in bloodstream for a period of 8 hours, during which they become enlarged and go to a specific tissue where they fuse together and enlarge and become a macrophage. The main difference between monocyte and macrophage is in the structure. The structure of macrophages is 5 to 10-fold larger than the monocytes. Also, the number of organelles and their complexity is increased than the monocyte, especially lysosomes. The number is increased a lot as well as its complexity; also, it produces hydrolytic enzymes.

So, this is the major difference between macrophage and neutrophils. Neutrophils will not produce hydrolytic enzymes. Other than that, it will go and phagocytize in a similar way how the macrophage does. But the macrophage secretes hydrolytic enzymes and some soluble factors as well as. So, the macrophage is the fused enlarged form of monocyte. When it migrates and goes and deposit to a specific tissue, it becomes a tissue-specific macrophage.

These are the SEM images of the macrophage. The first is the macrophages SEM image where it has a very long pseudopodia, and it acts against the bacteria. And this is the macrophage, pseudopodia, bacteria; the same is here, but these ones are erythrocytes.

So, how beautiful it is the macrophages are, right? macrophages are very beautiful to know, because they are very important to our immune system to fight against the pathogen, we should praise them of course.

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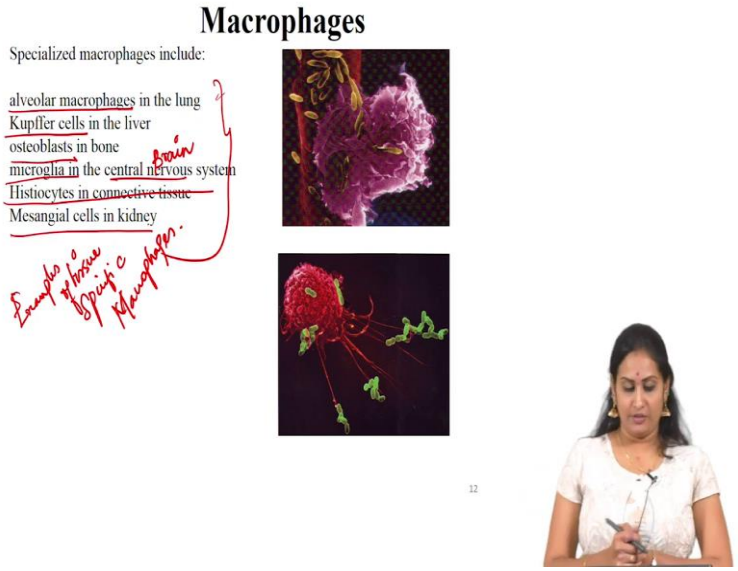

Specialized macrophages go and deposit in the tissue, and it would become the tissue-specific macrophages, and here we have given the few examples of tissue-specific macrophages. So, the macrophage in the lung is alveolar macrophages and kupffer cells in the liver, osteoblast in the bone, microglia in the central nervous system which is in the brain. Histiocytes in connective tissue, mesangial cells in a kidney, these are the tissue-specific macrophages.

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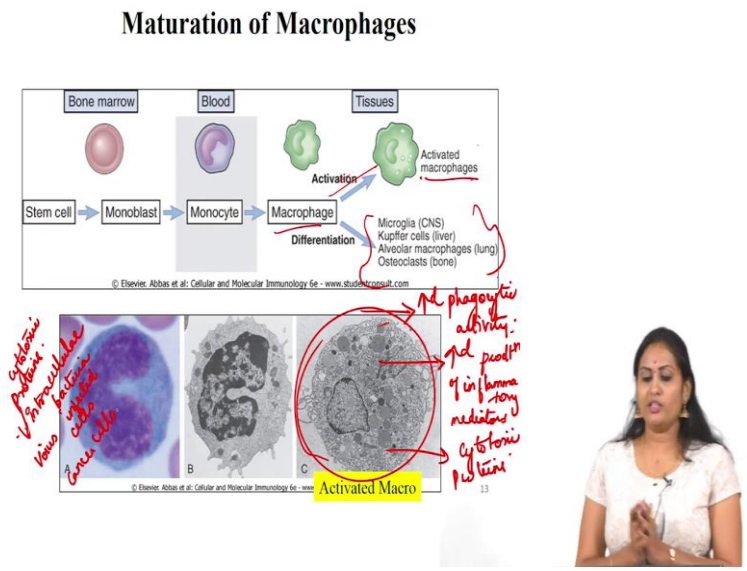

This diagram shows the maturation of macrophage. First, the stem cell and then monoblast, then monocyte, and that monocyte fuses and forms an enlarged macrophage. There are two types of macrophages, like resting macrophages and activated macrophages. Resting macrophages, it will go and sit in one place, it will take rest. Once someone calls it, like when it gets some signal, then it will act against the pathogen, but certain macrophages are active throughout. Activated macrophages are more effective than the resting macrophages; obviously, right when a person who is very active is more effective than a person who sits in the same place all the time. And these are the tissues specific macrophages.

The lower panel shows the activated macrophages; you can see how large it is. The activated macrophage in terms of morphology, also the presence of organelles in number as well as its complexity.

Activated macrophages are more effective than the resting macrophages in killing pathogens for several reasons. It has increased phagocytic activity, and it produces increased production of inflammatory mediators. Also, it produces special cytotoxic proteins; these proteins can act against several pathogens like specific pathogens, like cytosolic proteins. This cytotoxic protein acts against the broad range of targets; including intracellular bacteria, virus-infected cells, or cancer infected cells. So, these all about the activated macrophages.

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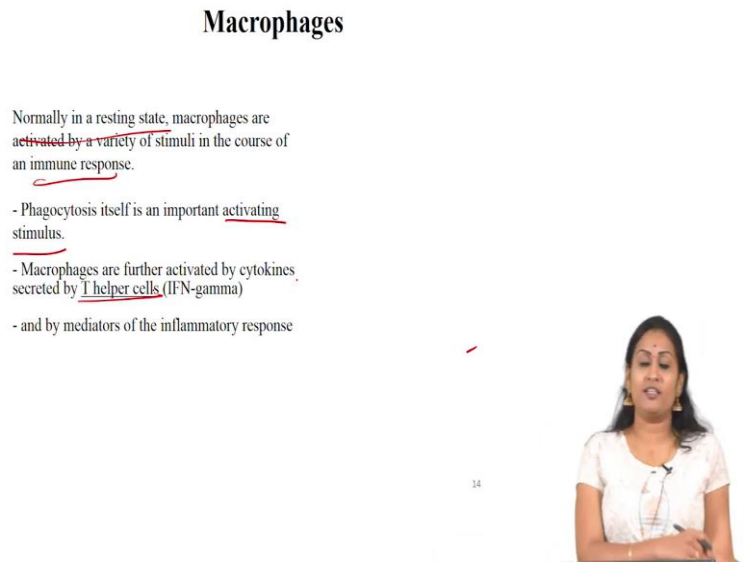

Normally in a resting-state, macrophages are activated by a variety of stimuli in the course of the immune response. So, there are certain macrophages that will be in a resting state, which starts to activate once it gets the signal from the other cells. And phagocytosis is an important activating stimulus. Phagocytosis is nothing but the engulfing of the pathogen. Again, the macrophages are further activated by cytokines secreted by T helper cells. In the entire immune system, these macrophages and T helper cells facilitate with each other. Also, it activates mediators by the inflammatory response. These are a certain stimulus for the resting macrophages to get activated.

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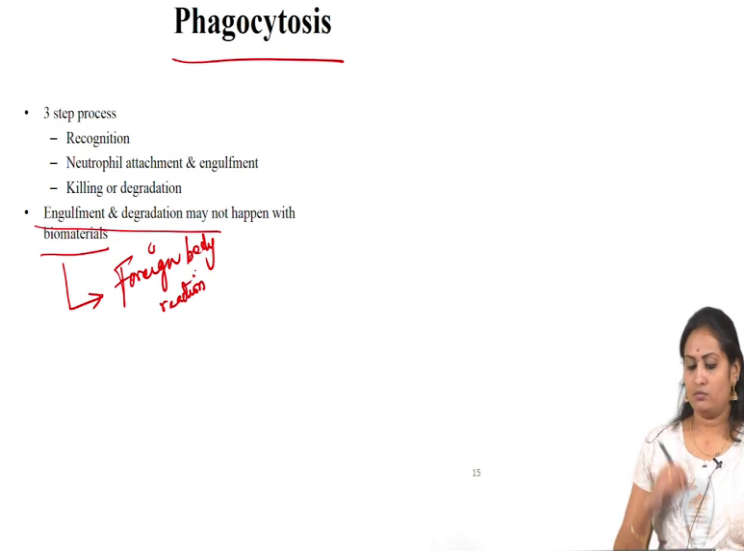

Next is the phagocytosis. Phagocytosis is nothing but the engulfing of the foreign material ok. There are 3 steps; first, it has to go and recognize what is the pathogen. Then the neutrophil gets attached and engulf. Once it engulfs, the lysosome and everything, all enzyme acts on it, kills it and degrade it.

Engulfment and degradation may not happen with the biomaterials. The biomaterials will be too large for that the phagocytes to go and engulf it. So, it cannot do that for the biomaterials. It will have a different type of foreign body reaction in the presence of biomaterials.

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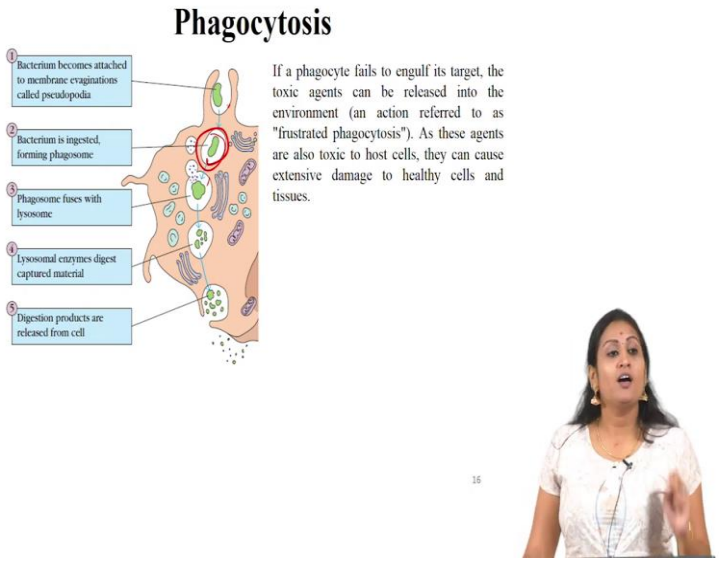

These are the steps of phagocytosis for the engulfing the pathogen. First, the bacterium becomes attached to a membrane called pseudopodia. Once it is attached, it is ingested to form a phagosome. Then phagosome fuses with the lysosome. And this lysosomal enzyme digests the captured material. Finally, the digestive products are released from the cells. But if this target during phagocytosis fails to be engulfed, phagocyte will become more frustrated.

See, if I have given some work to do and if I did not do that; obviously, my senior or the guide who gave me this work will become frustrated or even me as well, I will become frustrated, right. So, the same thing will happen to phagocytosis. Because it cannot do the work that is given to it. So, that is why it is termed as frustrated phagocytosis.

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Now, I will be showing a small video about the process called phagocytosis. What is phagocytosis? The engulfing of the bacteria by the immune cells. So, what are the immune cells which play a very important role in phagocytosis? Macrophages. Now look into the video, you will understand even more better. Those cells are macrophages that engulfing the bacteria; they eat and destroy the bacteria.

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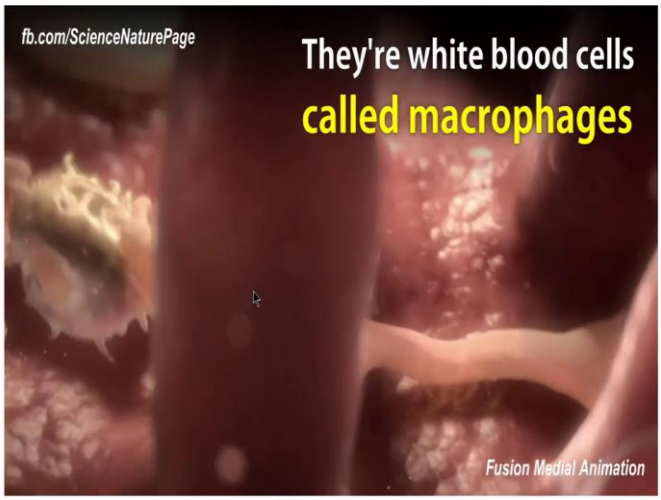

They are the white blood cells, which are called macrophages. See how they are invading, it is very beautiful, right.

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So, the main job is to eliminate foreign entities that invade your body, which is through the process called phagocytosis.

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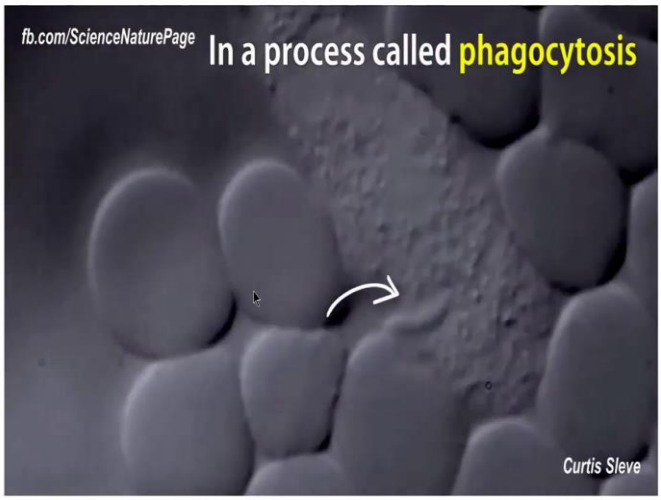

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See these bacteria, as soon as it enters; it releases some proteins which go and alert the macrophages to start its function.

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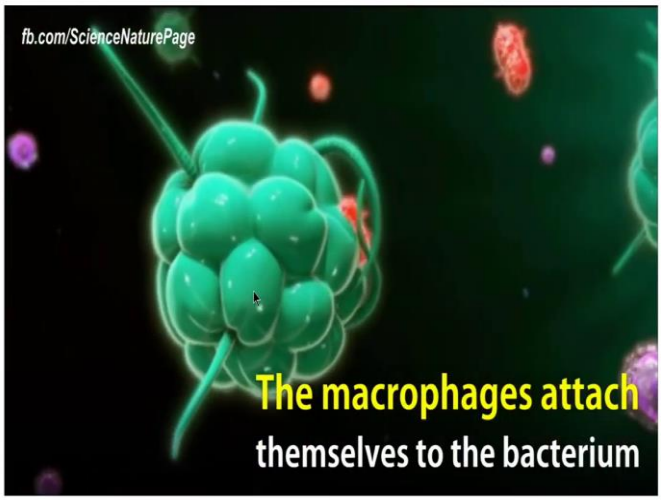

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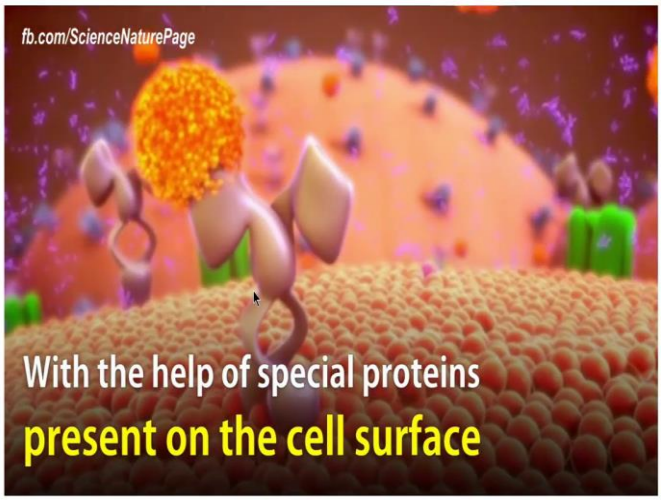

These macrophages attach to that bacterium with the help of special proteins that are present on the cell surface.

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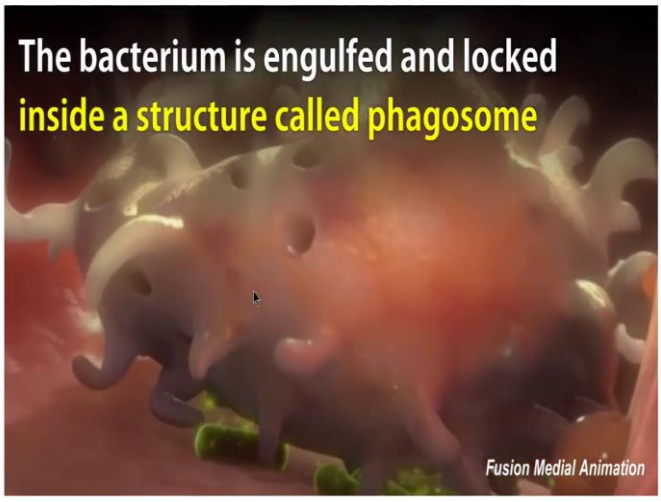

Then the bacterium is engulfed and locked inside a structure called phagosome; then it is cleaved and destroyed by the digestive enzymes into pieces.

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And these resulting particles can be either used by the cell or released out of the cell.

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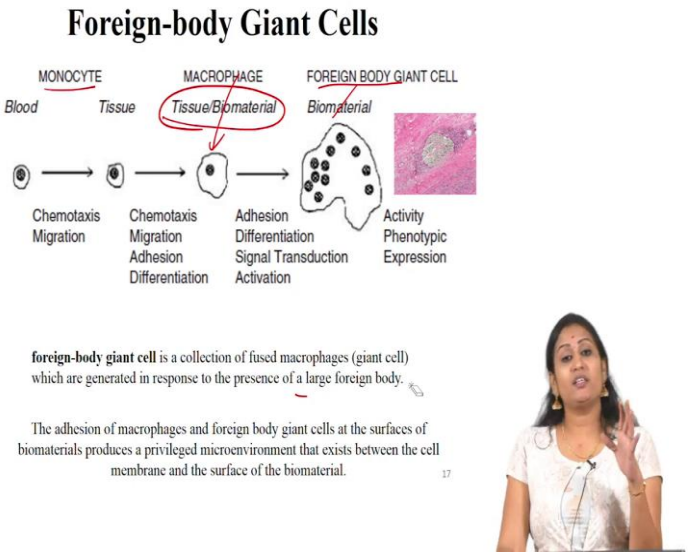

And there it leads to the foreign body giant cells. The foreign body giant cells are the large cell, which are formed as a result of the fusion of macrophages; that happens in the presence of biomaterials. As I explained before, the biomaterial cannot be engulfed by phagocytosis. If an implant or any biomaterial is placed inside, there are a series of reactions will happen. In that reaction, the foreign body giant cell plays a very important role.

So, if I say foreign body reaction, it is mainly due to the presence of macrophages and the foreign body giant cells. The reaction flow is the blood, tissue, tissue-biomaterial interaction, and biomaterial. When they place a biomaterial, there will be some interaction between tissue and biomaterial, right. So, macrophages will there. And in the biomaterial, foreign body giant cells will form. So, we have a huge mass surrounding the biomaterial with the presence of macrophages and foreign body giant cells. So, a foreign body giant cell is the collection of fused macrophages because of the presence of a large foreign body.

The adhesion of macrophages and foreign body giant cells at the surfaces of biomaterial produces an environment that exists between the cell membrane and surface of the biomaterial. So, I will ask you one question. If I want to place a biomaterial, what are the factors you need to consider for an immune response? for a favorable immune response?

See, we cannot directly place a biomaterial inside our body without a proper understanding of the immune responses or the properties of the biomaterial, right. So, what are the properties you need to think a lot for an in vivo application or as an implant? The main thing is size and surface chemistry. Surface chemistry of any biomaterial while placing inside our body or placing in vivo, it is very important.

There should be some compatibility, right; compatibility between tissue and biomaterial. See, there are two interaction majorly takes place, cell-cell interaction, and the cell/tissue-biomaterial interaction. Tissue biomaterial interaction should be proper, then only it becomes nontoxic; otherwise, compatibility will be of a question mark; compatibility represents the safety.

So, you need to consider the surface chemistry, degradation, whether the degrading products or leachate from the biomaterial should be nontoxic. And the size, surface chemistry, geometry, everything you need to be considered for understanding the immune response.

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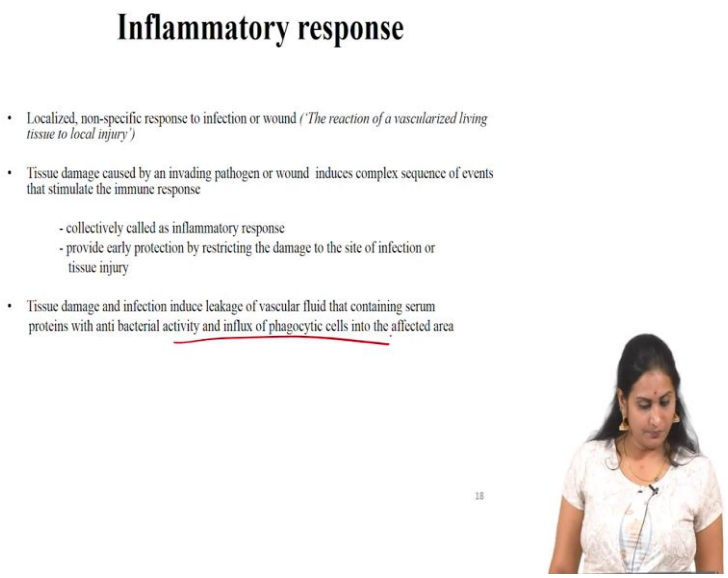

The inflammatory response is the localized nonspecific response to an infection or wound. It is just the physiological response as a result of infection or injury; the immediate response in our body. Tissue damage due to the invading pathogen or a wound that induces the complex sequence of events that stimulate the immune response. That is collectively termed as an inflammatory response.

If my tissue is getting damaged, there will be a sequence of events takes place in order to repair this tissue. Because our immune system is more effective by its own to repair tissue. So, the inflammatory response is this complex sequence of events that happens when the tissue is injured or damaged.

And this provides an early stage of protection by restricting the damage to the site of infection or tissue injury. So, tissue damage and infection induce the leakage of vascular fluid containing serum proteins with antibacterial activity and the influx of the phagocytic cells into the affected area.

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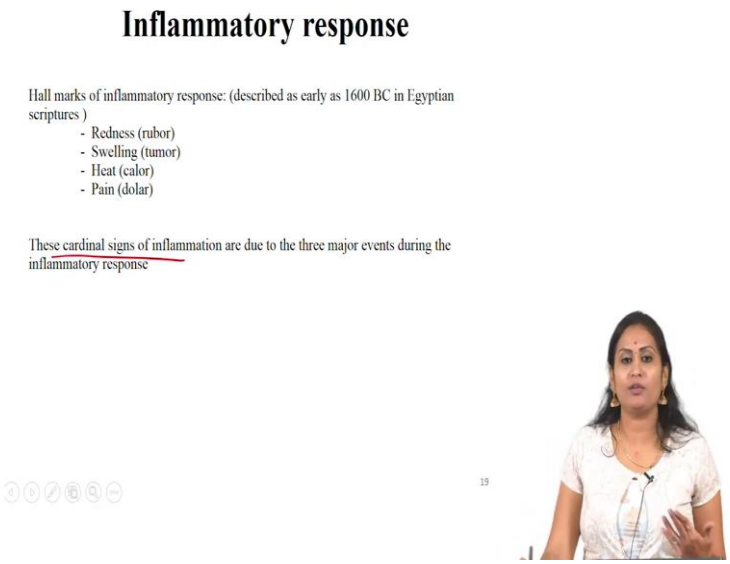

When there is any injury or infection, the first and foremost inflammatory response will be the swelling. The redness or swelling or heat or pain, we would have felt it many times. For a small example, when a mosquito bites you, it swells immediately, and you will get kind of pain; again, it is an inflammatory response.

The redness, swelling, heat, and pain are the cardinal signs of the inflammation resulting due to three major events. These are the signs of the inflammation of the inflammatory response.

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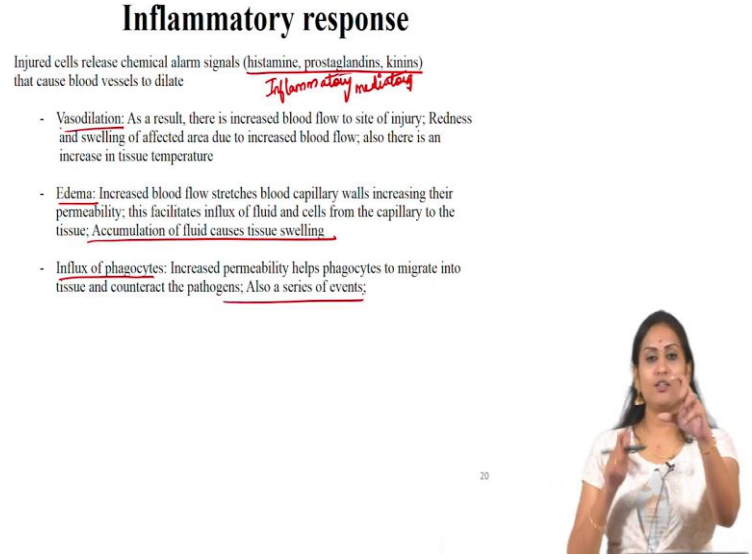

Once the cells got injured, immediately it starts secreting some cell signals; it is the kind of signal for the others to get activated. These chemical alarm signals are called inflammatory mediators; histamines, prostaglandins, and kinins. These are the medical indication to say that there is some injury or infection.

Histamine, prostaglandins, or kinins causes the blood vessels to dilate, which is the vasodilatation. As a result, there is increased blood flow to the site of injury. Once the site got injured, there will be increased blood flow, which is vasodilatation. Again redness and swelling of the affected area due to increased blood flow, also there is an increase in tissue temperature. We would have felt it; there will be some heat generation if there is some injury, right. That is because of the increased temperature, tissue temperature at the affected site.

Edema is the accumulation of fluid. Increased blood flow stretches blood capillary walls increasing their permeability; this facilitates the influx of fluid and cells from the capillary to the tissue. So, the accumulation of fluid causes tissue swelling. So, edema is nothing but the accumulation of fluid

And the influx of phagocytes; Increased permeability helps influx of phagocyte to the affected area. Increased permeability helps phagocyte to migrate into the tissue, and counteract with the pathogens; also a series of events.

Once the site got injured, immediately it starts secreting the inflammatory mediators of histamine, kinins or prostaglandins. And three major events occur in the inflammatory response; vasodilatation, edema, and the influx of phagocytes. Vasodilation is nothing but the increased blood flow to the site, and thereby redness or swelling or an increase in tissue temperature will happen. Edema is nothing but the accumulation of fluid, which causes the swelling, and the third is the influx, they are inviting the phagocytes to counteract with the pathogen.

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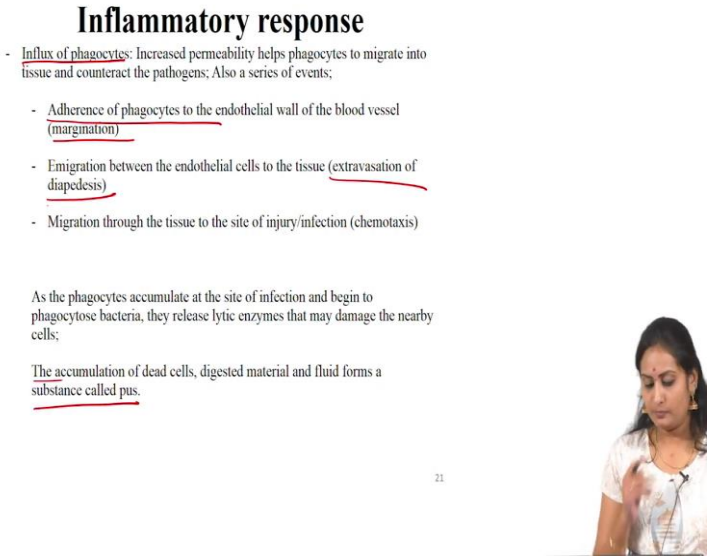

The influx of phagocytes. So, they want phagocytes to come and act against the pathogen. Increased permeability helps phagocyte migrate to the affected area and counteract with the pathogen. This picture gives a series of events happening during the influx of phagocytes. First, the adherence of phagocytes to the endothelial cell wall of the blood vessel; that is margination. And next is the extravasation. Extravasation of diapedesis, the emigration between the endothelial cells to the tissue.

First, phagocytes go and attach to the walls of the endothelial cells. Next, this is the extravasation; between the endothelial walls, it migrates to the tissue. The third one is migration through the tissue to the site of infection. These are the three series of events happening at the influx of phagocytes.

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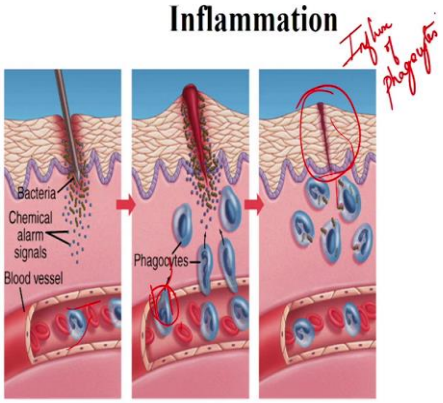

As the phagocytes accumulate at the site of action, and begin to phagocytose the bacteria, and releases the lytic enzymes that may damage the nearby cells. The accumulation of dead cells or digested material and fluid forms a substance called pus, and this is the image of the influx of phagocytes.

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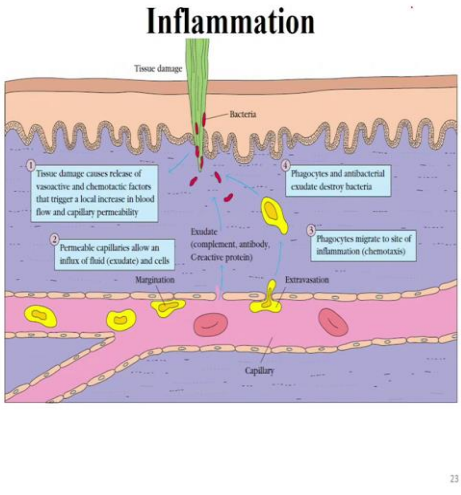

And this is the very detailed image of an inflammatory response.

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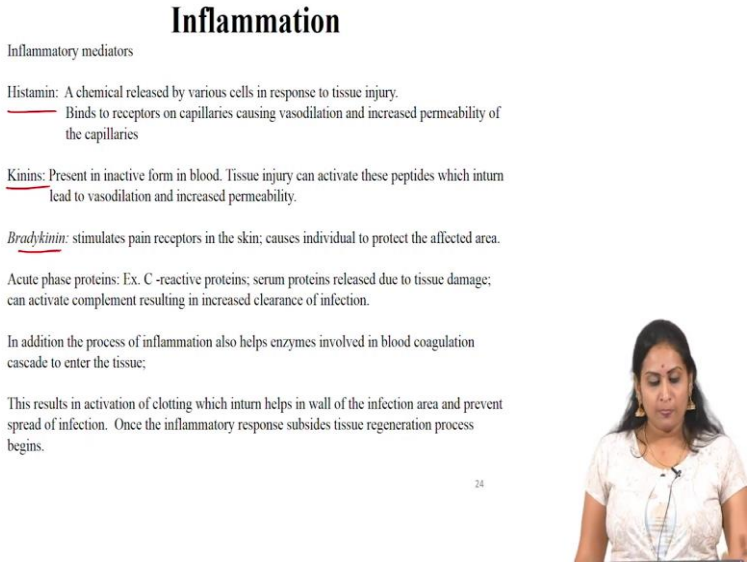

These are the inflammatory mediators that I mentioned earlier. Histamin, kinins, bradykinin, prostaglandins, these are the major mediators involved in the inflammatory response

In addition to the process of inflammation, it also helps enzymes involved in blood coagulation cascade to enter the tissue. So, this results in the activation of clotting which in turn helps in the wall of infection area and prevents the spread of infection. Once an inflammatory response subsides, the tissue regeneration process begins.

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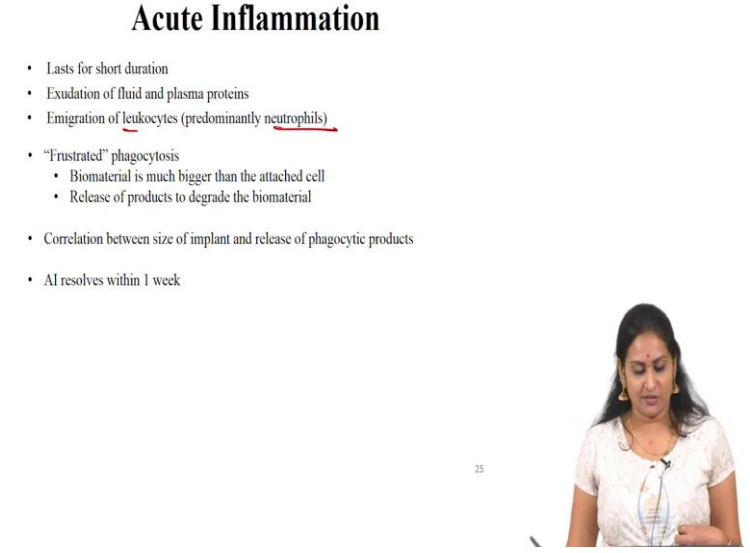

So, there two types of inflammation; acute inflammation and chronic inflammation. Acute inflammation happens only for a shorter period of time, whereas chronic inflammation occurs for a prolonged period of time. The main cells involved in acute inflammation are leukocytes in which predominantly neutrophils again. Frustrated phagocytosis; it is the biomaterial is much bigger than the attached cell, the release of products to degrade the biomaterial. So, this acute inflammation resolves within 1 week.

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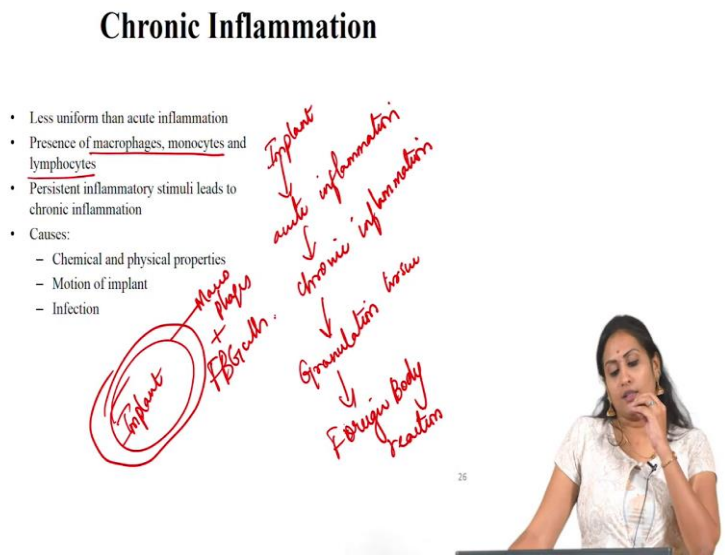

Whereas chronic inflammation, it is less uniform than acute inflammation. Macrophages, monocytes, and lymphocytes are the major cells involved in chronic inflammation. If you place a biomaterial inside our body, there are a series of inflammatory responses. When an implant is placed inside the body, first acute inflammation, chronic inflammation, granulation that is the formulation of granulation tissue, and the foreign body that is the fibrous tissue under foreign body reaction. This foreign body reaction is mainly composed of macrophages and foreign body giant cells. So, this forms a layer outside the implant; it is a thick layer outside the implant, which is macrophages and foreign body giants cells. The detailed explanation of inflammatory response with respect to the implant will be explained in later sessions.

In this session, we learned about what is immunity and what are the cells involved in immunity and what are the organs of the immune system as well as the few basic steps of inflammatory response. Thank you.