Animal Physiology
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Lecture - 31

Welcome back to the NPTEL lecture series in animal physiology. Today, we will be initiating the section on blood cells immunity and clotting. We have talked about the cardiovascular system, where we have learnt about how the blood is pumped all over the body. Then we talked about the circulation. We talked about the vessels, the arteries, veins, the capillaries, and arterioles, where all the exchange of different gases takes place and then you can take up disposing of the stuff, which has to be thrown out of the body, along the capillary network and along the lymphatic vessels.

What we have not discussed yet, what are the components, which constitute the blood itself? The major other than water, the major fluid or the fluid which helps us to communicate with rest of the body, and the major medium or the major carrier medium, as well as, the home for the immune system. Overall, whenever you see, I mean like, the broad classification of blood could be like; you have different kind of blood cells. What we will be ensuring in this class? In this first class, we will be outlining all the different kind of blood cells; how they are formed? What are their functions? Wherever the deficiency or excess of those leads to what kind of physiological problems? That is what we are going to discuss. Broadly speaking, you could divide the complete blood. Let us come back and let us start putting them down on the slides.

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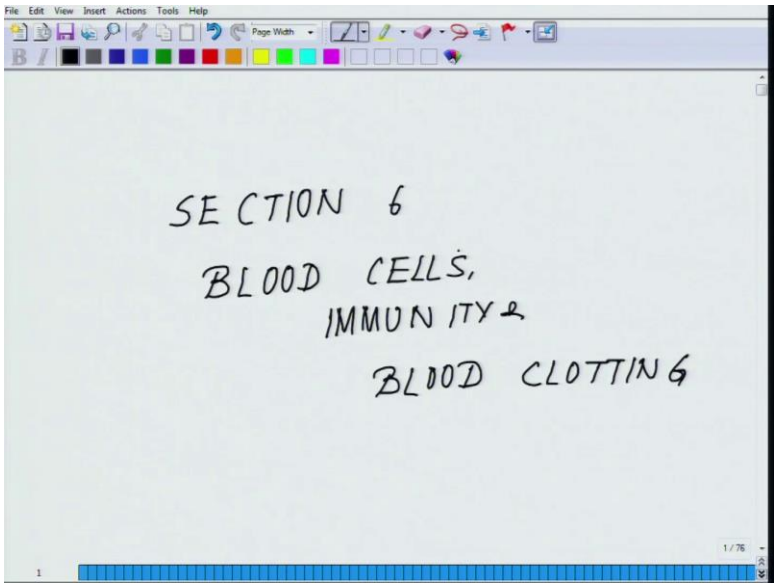

This is the section what we are starting. We are covering three parts; the blood cells, immunity and clotting. Just to clarify, this is the part where, you will be talking about blood cell classification.

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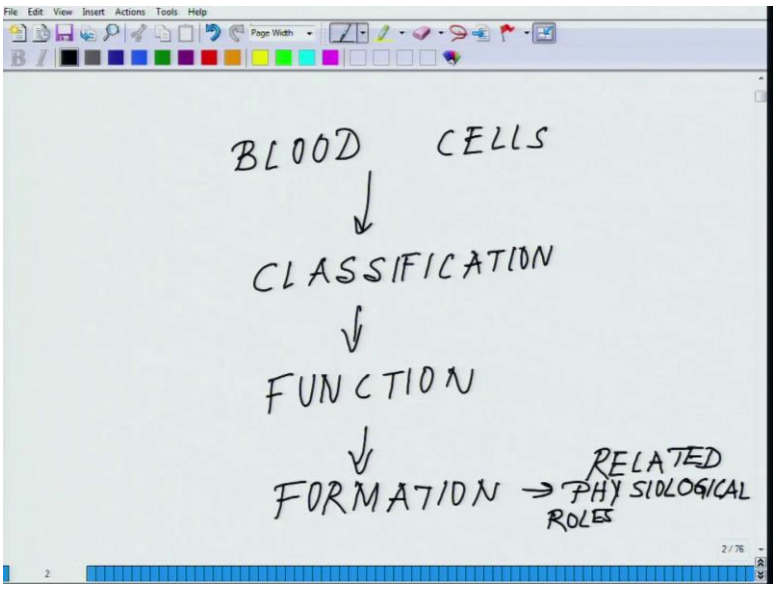

This is the overall outline which will be dealing today; classification, function and formation and related physiological problem. So, these are the headings under which physiological rolls. These are the broad headings under which, we are going to discuss this topic. So, let us go into the classification first.

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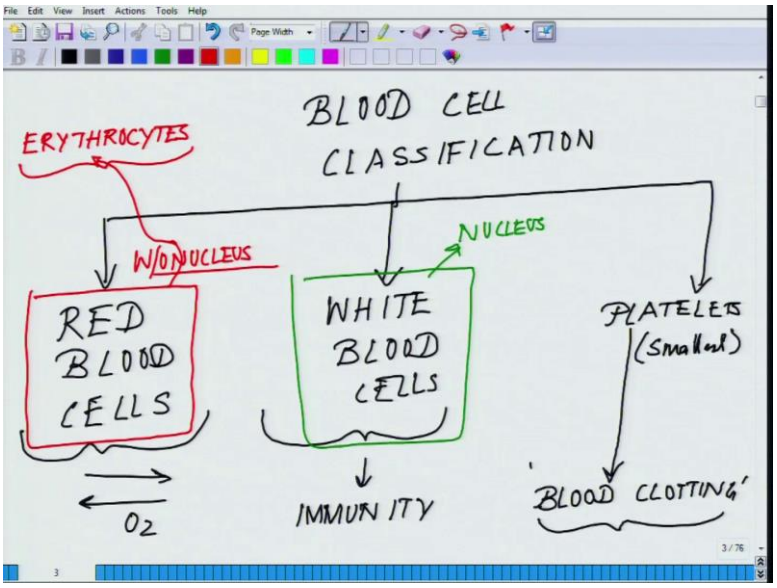

The blood could be classified into three different components; blood cell classification. The major classification falls under red blood cells. These red blood cells get the red color, because of the hemoglobin molecule. I have discussed this hemoglobin molecule, while we talked about the respiration. While we talked about, how the oxygen binds to the hemoglobin molecule in moiety and it has a periphery ring, we have this iron in the center. It is something like this. Let me do the classification, then I will come back to this. Then you have white blood cells and then you have very small cells called the platelets. These platelets are involved, these are the smallest of them as compared to red blood cells; these are involved in blood clotting, which is the third part, what we will be starting in this particular section.

White blood cells are involved in immunity, and we will be talking about the classification of the white blood cells. Red blood cells are our oxygen transporter all over the body. Now, these red blood cells, what you see here, are without nucleus. Why they are without nucleus? We will be discussing it. These indeed have nucleus. These white blood cells are also called erythrocytes. What we will do now, we will talk about overall how this. One more thing which we have to discuss is the location, where red blood cells are synthesized; location of blood cells synthesis.

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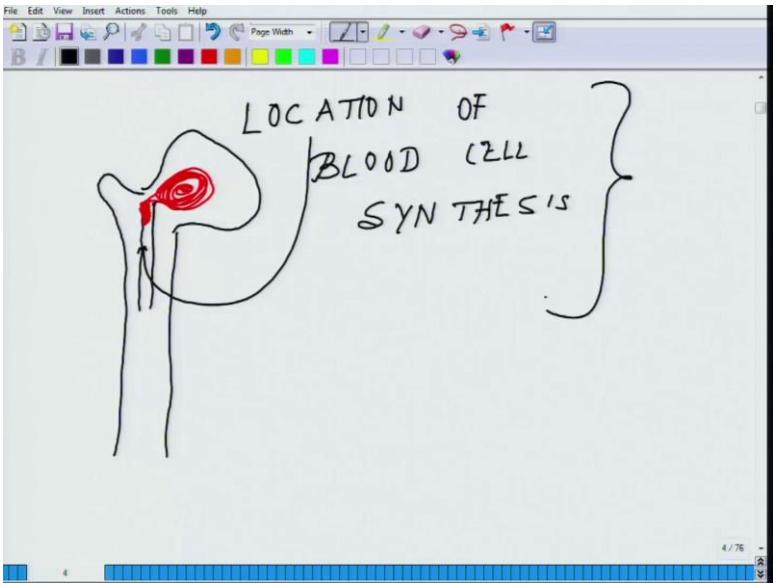

Basically, the blood cell is synthesized in the bone marrow, something like, this structure and where is the marrow region, somewhere inside, deep inside; basically, the site of synthesis out here, somewhere. Whenever, you hear that for people, who are suffering from cancer, blood cancer, you say bone marrow transplantation. Basically, in other words, that if the marrow material is unable to, there is a miss regulation or because of which, production of red blood cells or white blood cells goes in excess. Red blood cells falls down, which leads to cancer like situation or blood cancer leukemia, which is how commonly called. There is a time, when there are medical options of curing that. Thing is that, if you could transplant another bone marrow to the host, from another source, which is kind of very challenging thing, or from other or from the same part from somewhere else, you transplant the bone marrow.

It is that site where, all these blood cells are being formed. It is very tightly regulated phenomena. After this, the location, once we have discussed about location, now, what we will do, what regulates the synthesis of it?

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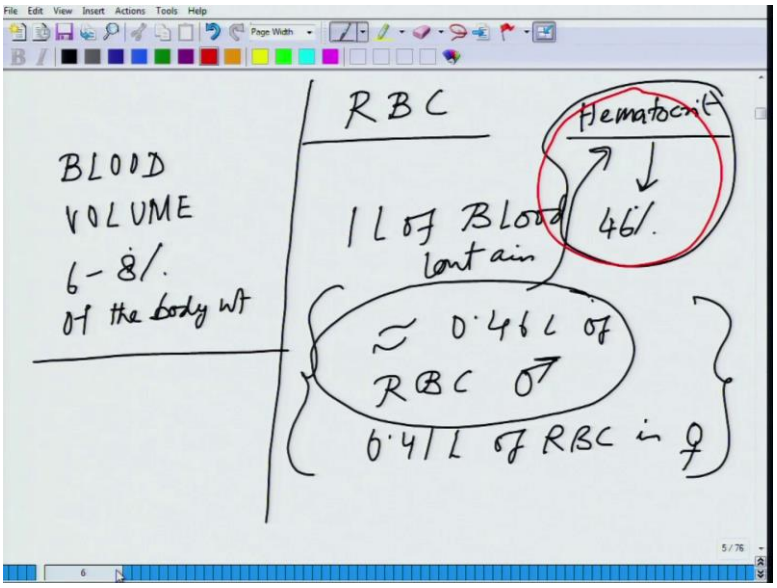

First of all what we will be dealing with, we will be dealing with the RBCs. Before we get into the RBCs, there are some facts, which we will need to, like, it will help you to appreciate the blood factor. Blood volume is approximately, of the whole body, approximately, 6 to 8 percent of the body weight. These are some of the facts which will help you to appreciate. One liter of blood contains approximately, 0.46 liter of RBCs in males and 0.41 liter of RBCs in females. It varies and varies according to the physiological status.

This is basically, essentially, this value what you see here is essentially, called hematocrit. If you see any prescription given in the clinic, they say 46 percent hematocrit, which is essentially nothing, but the red blood cell concentration. So, this is very essential, that you will understand, what is matocrit and how the matocrit is being shown in the complete blood profile, whenever you take the blood profile. Next, what I will do, I will draw the overall control or the synthesis distraction of erythrocyte in adults.

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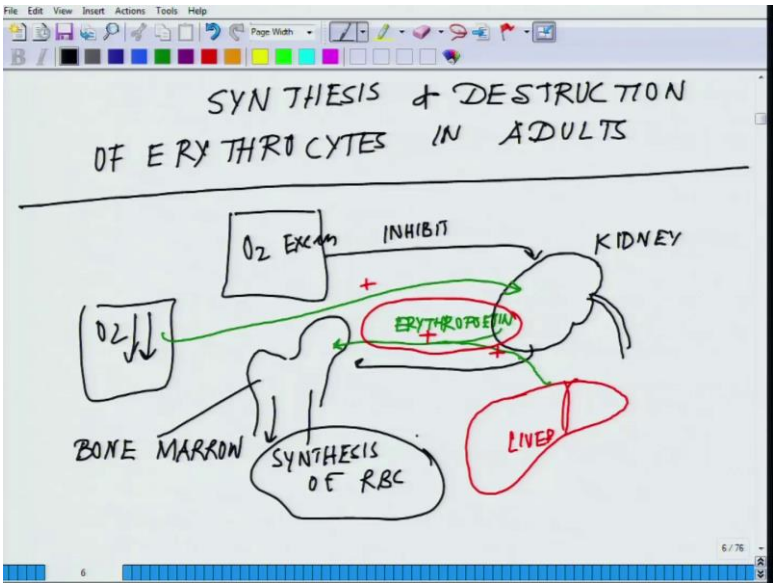

Then, we will talk about why these erythrocytes or red blood cells are without nucleus. What I will do, I will give you in a diagrammatical manner that will help you to understand this whole process. Say for example, a situation, when there is oxygen in excess in the body; this sends an inhibitory signal to the kidney. Here, you have the kidney. So, this is inhibitory signal, the first face. This inhibitory signal sends another inhibitory signal to the bone marrow, whereas, if the body is having deficiency of oxygen; oxygen is fairly low; and there is a positive signal which is being sent to the kidney. From there, another positive signal is being sent to the bone marrow. This is done by erythro poetin. These are the factors which are responsible for it.

There is one more signal which comes from the big organ, called liver, which we have already covered in the digestive system; second signal comes from the liver. Now, these two signals, essentially it does is, that these are all, let me give a mark. These are all positive signals, going all the positive signal; positive signal coming from here. Then, these positive signals are being conveyed by erythropoietin. Erythropoietin tells the bone marrow to start synthesizing the blood specially, the red blood cells. Then begins the synthesis process; synthesis of RBCs. Let us just go to the next page.

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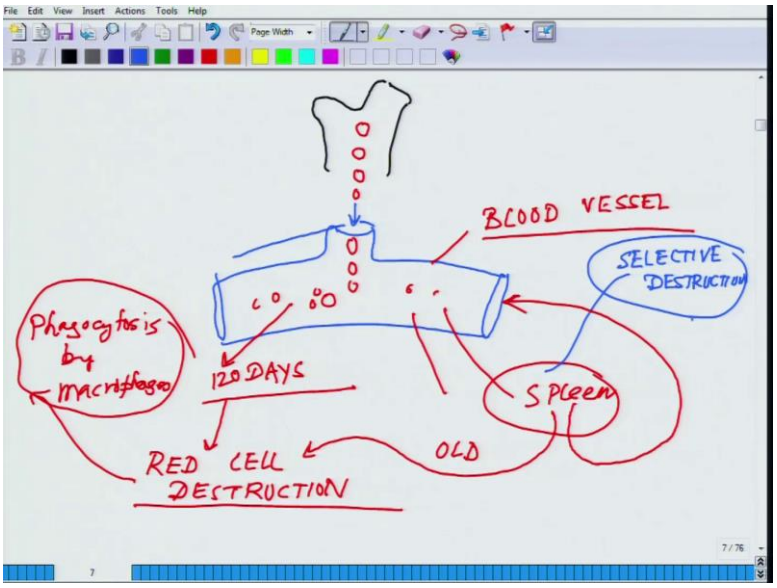

Once these are synthesized, this is continuing from the previous page, from the bone marrow here, basically, here the red blood cells are forming now. These red blood cells from here, moves on to the blood vessels. Now, these are suspended onto the blood vessels. In the blood vessel, lifespan of these red blood cells is approximately, 120 days; they die out after 120 days. Once they die out, then these red blood cells have to be destructed. These are done by a couple of processes, which we will be discussing now; red cell destruction.

Red cell destruction takes place by phagocytosis, by macrophages. What does that mean? This is also called; this is one route by which they are being destroyed; there is another route where, they go to the spleen and the spleen, there are selective, the one which is old, they are phagocytosized, the old ones. The new ones are being, or not that old ones, are being retained and put back into the blood vessels. In the spleen, there is something called a selective destruction process, takes place.

This is kind of a scanner where, if the blood cells are older, then they are sent for red blood cell destruction process. If still they have possibility, which they can carry on the whole process, then they are being sent back to the blood vessels. If you summarize the whole process, it is a very tightly regulated process. What essentially is happening is that body is running out of oxygen; body has a lesser concentration of oxygen.

Automatically, there will be a signal, which will be sent to the kidney. From the kidney, another signal in the form of erythropoietin, will be sent to the bone marrow, along with certain signals, which will be coming from the liver. Then, the bone marrow will start synthesizing the blood. Then, the bloods which are synthesized are now channelized to the blood vessels. Now, within the blood vessel they have a life span of 120 days. After 120 days, when their capability to carry oxygen is, kind of getting dwindle, then those have to be destructed.

In order for the destruction, there are two routes. A part of it goes to the spleen. In the spleen, there is a selective scanning. The one which are very old and what to be discarded out from the body, are being sent for red blood cell destruction. Whereas, some of those, which are still active, are being retained by the body, till they finish their life term. What exactly happens in the form of destruction is that, there is phagocytosis taking place, where the macrophages are. Macrophages are nothing, but the white blood cells, basically. What they do is, the way it works, if this is a red blood cell then these macrophages will come, and they will engulf it inside them. It is something like this.

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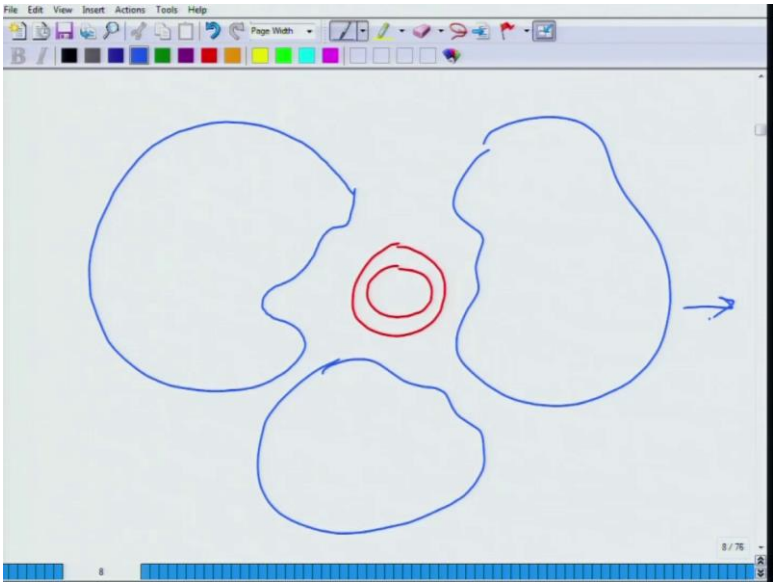

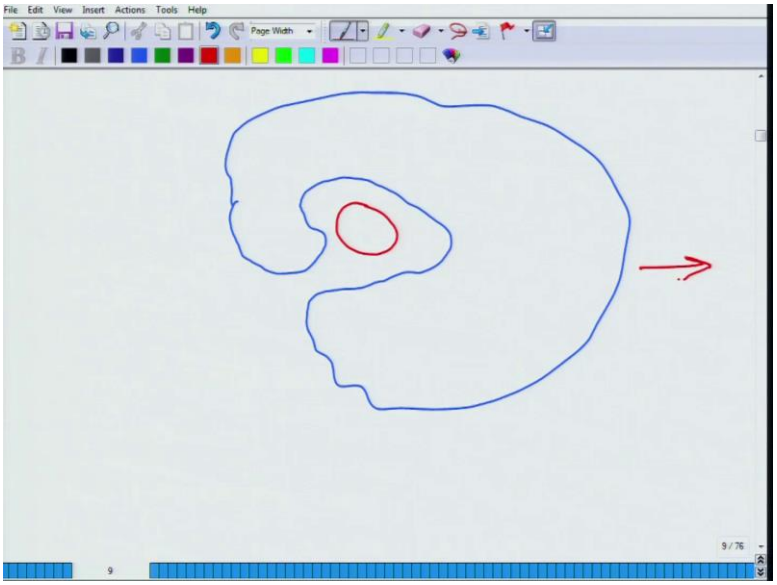

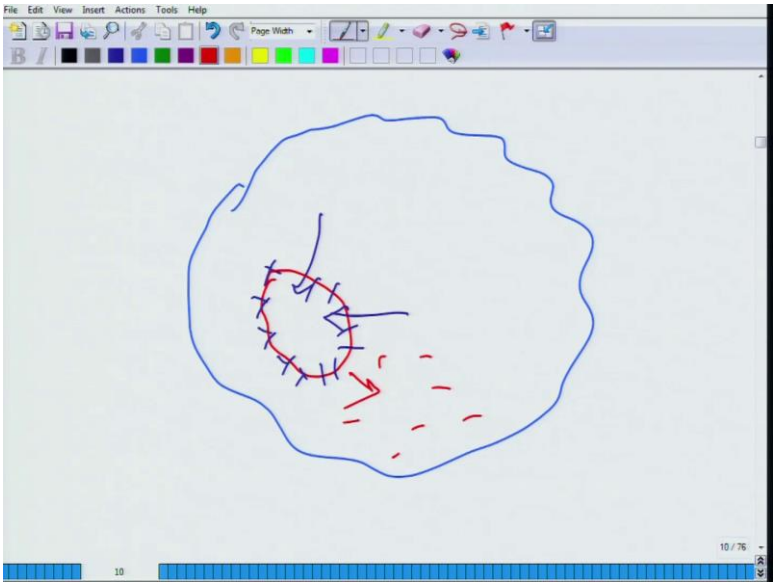

If, these are the macrophages and here, you have a red blood cell. What they will do essentially is this. This macrophage will engulf this. If you go the next slide, it will make more sense. It will be something like an event will happen like this. Now, they are entrapping the red blood cell inside it. Then, move to the next page to explain it. Eventually, what happens, here you have the macrophage and you have the red blood cell inside and then there are series of enzymes, which come and chop it off. This whole process is basically called phagocytosis by the macrophages. Not only are the red blood cells which are being processed like that; anything which body has to break down, they phagocytosized like this. They are engulfed inside the white blood cells and then they chop it off using different kind of enzyme, different kind of other molecules, which are present there. So, this is the overall geometry or overall schematics of the red blood cell

formation. But I told in the beginning, there is something very interesting about the red blood cells; that red blood cells do not have a nucleus. How that happens? This is a very interesting thing.

When the red blood cell starts forming, they indeed have a nucleus. It starts like this. I will tell you the story and then I will draw it so that, it gets into your understanding properly. When the red blood cells are forming, there are progenitor cells which lead to the formation of all kind of cells. Same way, there are progenitor cells which leads to the formation of the red blood cells. Once the cells are formed, they have a nucleus. This is all intact. Then, what happens? As it gets matured like, all the organals inside the cells are forming, mitochondria, it has everything; it has mitochondria; endoplasmic redicula; it has nucleus; it has all the cytoplasmic components.

Then, at a specific point of time, there is an expression of a particular enzyme, and that particular enzyme with respect to other cells, as compared to the other cells, is expressed higher in these red blood cells. When this concentration goes up, that particular enzyme chop off the nuclei membrane, get rid of all that DNA and get rid of most of the organals inside the cell. Then, almost would, like, it has the ability to chop off the membrane of the cell itself, but it does not do so because its concentration falls down and due to that process, then the cell is nothing, but it has a bilipid membrane and a fluid filled cavity, which is filled with, in the case of red blood cell, it is filled with these he molecules; hemoglobin. So, you have a globulin protein, on with you have the he moiety. This is how the red blood cells are being formed. Then, I will tell you, which is that enzyme. Let us get back to the schematics of it.

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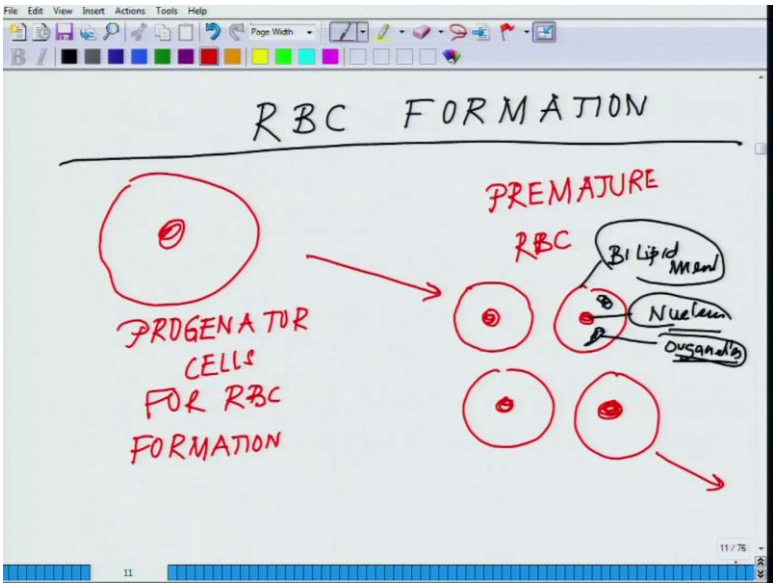

RBC; red blood cell formation. The first step is, these are the progenitor cells, are the ones which will form red blood cells for RBC formation. Here, the RBCs are formed. So, lots of RBCs are formed. These are the RBCs or most premature RBCs; they are in the maturation phase. They have all the organals like, in a bilipid membrane, nucleus, mitochondria, likewise, all the organals. So, they are all present. Then, what happens?

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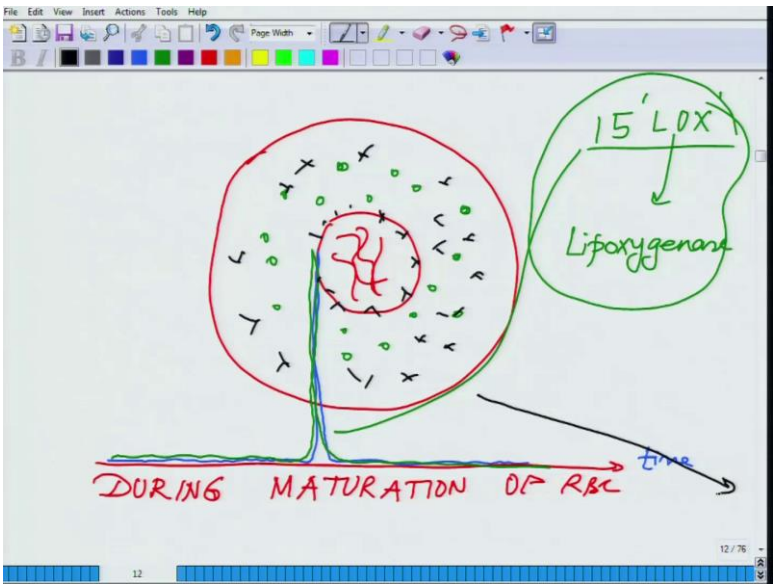

Here is the nucleus with the DNA and everything. As they are maturing, during maturation of RBC at specific point of time, it is very tightly regulated. If this is showing

time, that is very specific time, a particular enzyme, that enzyme remains at a baser level. At a specific time, there is a sharp peak of that particular enzyme and it falls down, like this. This particular enzyme is called 15 Lox. Lox stands for lipoxygenase; fifteen lipoxygenase. This enzyme, generally remain in the baser level; this blue color is showing it is in the baser level during maturation. But there is a specific point, when there is a sharp peak of this enzyme, and it falls down, like this.

When there is a sharp peak, during that time, what essentially is happening, let me represent lipoxygenase molecules like this; lot of lipoxygenase are in the green color; green dots are lipoxygenase. What they do generally, what they essentially do is that, they start chopping off this. They even have the ability to chop off the main membrane. They chop off all other organals.

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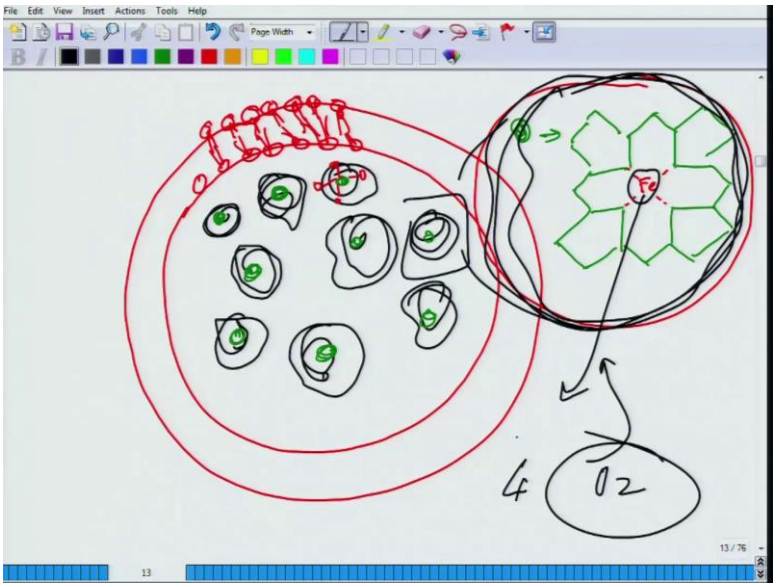

So, what is left after this, at the end of the maturity is biconcave red blood cells without, just this destruction is almost like, if you see the 3-dimensional structure, it is a bi concave structure, and it is has absolutely no organal left in it. What you essentially see is a bilipid membrane, which remains intact, like this. Here is the bi lipid membrane out here and with, if you go back to your first membrane class, what we have tried to, something like this. This whole cavity is filled with these hemproteins, which are like this. These are globulin protein and on that, you have this iron center, a green one

showing the irons. Each one of the hemolecule has ability to bind to four oxygen. So, it is something like this; four sides.

Essentially, the green stands for, kindly look for the structure of the por pherene. I am just drawing the skeleton of it, but if you go online you will see the structure of the por pherene, pretty much in every, and here you have iron. So, this is how, this is sitting surrounded by the globulin protein. This is basically, the blow up of this image. This is the one which has the ability to carry the oxygen. So, if you look at this structure, there is one more thing which will come. Basically, there are four oxygen molecules which are coming to bind to this.

If you logically think of it, the last major protein which is synthesized by the red blood cell is hemoglobin. Because that is, which is in highest concentration. This particular process or this kind of event is seen in the body in physiology; only two places. It is very fantastically well regulated mechanism. The other place where you see this, with slight digration, is in the formation of the lens cells; lens of the eyes. Those lens of the eyes; think of it. All the light process through the lens, people thinks inanimate things. Actually, lens cells are nothing; they exactly follow the same pattern, if I draw that.

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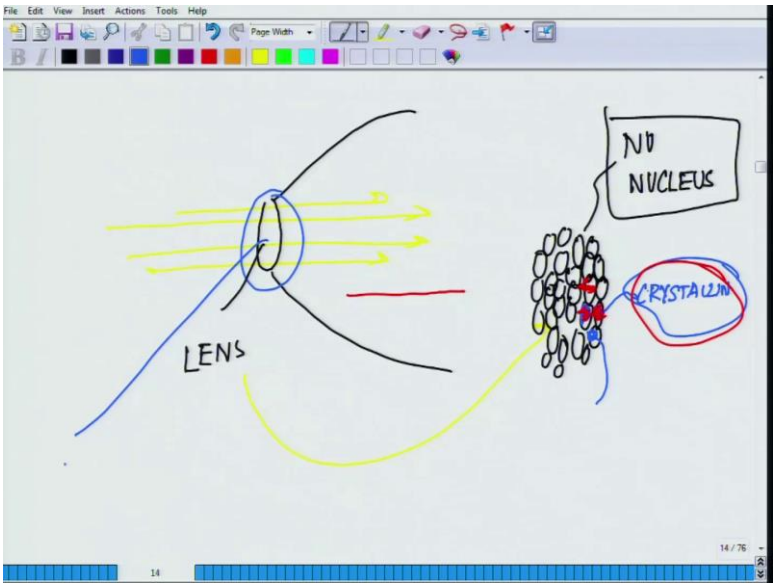

If you just go back and see the structure of the eye, it is something, like this. You have this lens, what lens is, because all the light passes through it without any problem. They pass through it, because this lens structure is formed by individual cells, which are

arranged like this. None of these structures have any nucleus; they have no nucleus. In the case of lens, they are filled with a fluid, a kind of a gelatinous protein called crystalline.

So, this is how the lens cells are formed and whenever, and what is cataract? This I did not discuss, I am just coming since. Cataract is, the cells either, start dying out or the crystalline protein, which is present inside those cells are folded wrongly; their folding pattern changes and they started occluding the path of light. What we essentially do is that, we remove this lens and put an artificial lens out there. But this is the same thing. The reason why, I brought you back to the lens is that, this is exactly the same mechanism by which red blood cells are formed. They follow the same enzyme; 15 lipoxygenase has this ability.

There is some profound implication of this, because there are pharmacologist who are trying to use this 15 lipoxygenase or this mechanism; they are trying to figure out whether this could be used for against cancer. Could we make, could we program a cell that it get rid of all the organal, kind of, its metabolic activity goes down all of a sudden; could we really master that pathway, by which cell is following this? Wonderful thing and mind it. Again, this does not happen in any other cell. These are the two very different kind of cell types in our body. They all originate from the same cell, but they follow a different route for of course, different path, different reasons.

As you are seeing this, there are such some of the things, which are very important here for us to understand. One of the major things is that, you hear about people suffering from anemia. In other words, they lack red blood cells. That happens when? One of the reasons for formation of anemia could be, when your iron metabolism is being compromised. This essentially brings us to the fact, that iron metabolism is extremely essential for the formation of the red blood cells. Iron has to be absorbed at different levels. Without the absorption of iron, the formation of the hemoglobin or the hemoity is being challenged.

Automatically, if there are less number of hemoglobin, your oxygen concentration goes down. Because your total number of oxygen which you needed to be bound, is reduced, because they do not have any binding site. Next, what we will do is that, we will come

back to the iron metabolism, and how iron is being regulated. Let me go back to the iron. What are the different routes of iron being regulated?

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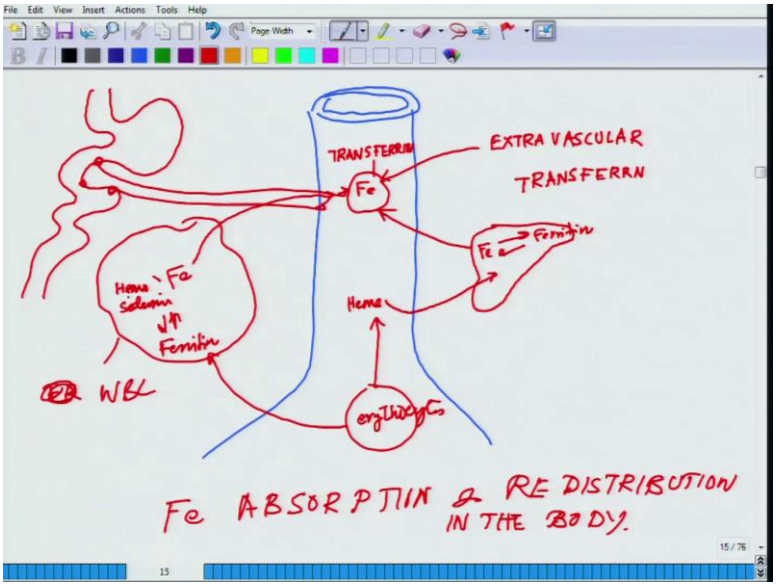

Again, what I will do essentially is that, I will show it diagrammatically. That will help you to appreciate this process much better. There are different molecules in our body, which helps in binding to iron. One of them is called transferrin, and this coming from different sources. This transferrin comes from extra vascular; they are not in the vasculature; or not in the blood vessel; extra vascular transferring. Then, you have ferritin molecule which are present in, which are continuously getting trans changes. Then is coming to the blood vessel and you have the hemoity, which is, when it gets broken down, as I told you. Then, the iron is being absorbed by the liver especially, in the, we have to ensure that none of the iron is being lost. They are all being absorbed by the body.

Then, you have these macrophages. I showed you the macrophages. What they do is, when they chop off the red blood cells, these iron is being absorbed by the blood. Basically, what happens is this. There is something called hemo siderin to ferritin. These are the conversions which are taking place, and this iron is being reabsorbed by the body, which is being basically, eaten away by the erythrocytes; these are the erythrocytes, sorry, these are the WBCs, which eats away the old erythrocytes. Apart from it, along the

digestive system, there are different sources from where, different zones from where, all this iron is being assimilated.

Basically, what is highlighting feature is this iron absorption and redistribution in the body. What essentially that means is this, that whenever red blood cells are being broken down, the old red blood cells are being broken down by their WBCs, the iron is being stripped off and sent to the blood vessels, or to the liver, where the synthesis of the, from there, it is being sent to the bone marrow, where the synthesis takes place. Same way, from the food what we are eating along the digestive tract, iron is being taken out for the blood formation. Apart from it, liver has a significant storage of it in different form of different.

Basically, the way iron moves in the body is that, it does not generally move freely. It is kind of bound to certain protein and which are called cellulophores mostly. You see transferring, hemosiderin, ferritin, these are the different molecules which bind to the iron, and keep the iron intact in the body. So, this has to be really regulated very thoroughly, in order to ensure that RBC formation remain intact. This is the overall, I wish to talk to you about RBC. Few other details which I will be coming up in the next class, while we will be talking about the immunity; briefly about the immunity and then we will go to the clotting.

Clotting process, where basically, we will be talking about, if there is a rupture in the blood vessel, how that rupture is being meant. It is just like, you have a hole in a cloth; you just ensure that you stitch it and get it back. These are the things, which I will be discussing in this section. This is the first class, where you talked about, let us summarize. We talked about the classification of different blood cells; red blood cell white blood cell; platelets; their functions. Red blood cells involved in the oxygen as oxygen carrier. White blood cells in the immunity, and the platelets in the blood clotting. Then, we talked about the location in the bone marrow and then from there, we talked about how the RBCs being formed specially, in terms of the shooting of an enzyme called 15 lipoxygenase, for a very brief span of time, during which all the organals and the nucleus is being destroyed in the RBCs, and which is the same mechanism, which is following in the lens cells of your eyes. Then, we talked about how iron has to be taken back by the different organals of the body, in order to ensure that the RBC formation

goes on uninterrupted. So, I will close in here, and in next class, we will talk about the immunity forward and we will talk about the blood clotting.

Thank you.