Animal Physiology
Prof. Mainak Das
Department of Biological Sciences and Bioengineering
Indian Institute of Technology, Kanpur

Lecture - 40

Welcome back to the NPTEL lecture series on animal physiology. We are in section 6. We have covered four lectures and today is the concluding lecture on section 6 on blood cells immunity and clotting. As of now I have covered the red blood cells or erythroblast. Then from there we went ahead and talked about the clotting, which involves all the platelets and the clotting factor, intrinsic factor, extrinsic factor, role of the endocervical cell and the surrounding tissue role of the platelet cells.

Then we talked about the genesis by which all the different blood component or the formed elements of the blood; the red blood cells, white blood cells and platelets are formed from the stem cell origin. In that process of course, we have discussed how RBCs looses their nucleus, the whole process of pipetine lypoxygen; sharp rise of pipetine lypoxygen, and followed by a fall in a very narrow time window. Then in our 4th lecture we discussed about immune cells, which are our white blood cells, we talked about the myeloid origin, neutrophill, basophile, eosinophill and monocytes.

We talked about the lymphoid origin, which leads to the lymphocytes. Among the lymphocytes we talked about the B cells, T cells, and the nature killer cells, and the origin of a selmidaited immunity and humeral immunity, and within that we talked about the origin of how all these antibodies are getting originated.

Among the miller origin like, monocyte, neutrophill, basophile, we talked about. The way these are being identified using acetic dye, basic dye, likewise. Today, we will be concluding with one aspect, which I purposefully did not touch, I told you at the end, I am going to touch that. That is, we will talk about couple of disease and we will talk about the blood grouping; I have not talked to you about the blood grouping; how the blood.

You must have heard, that sometimes, they say, what is your blood group? Somebody will say A positive; somebody will say O negative. I mean to say, O positive or AB or B positive. What essentially… That means, what how we call it something A, and a

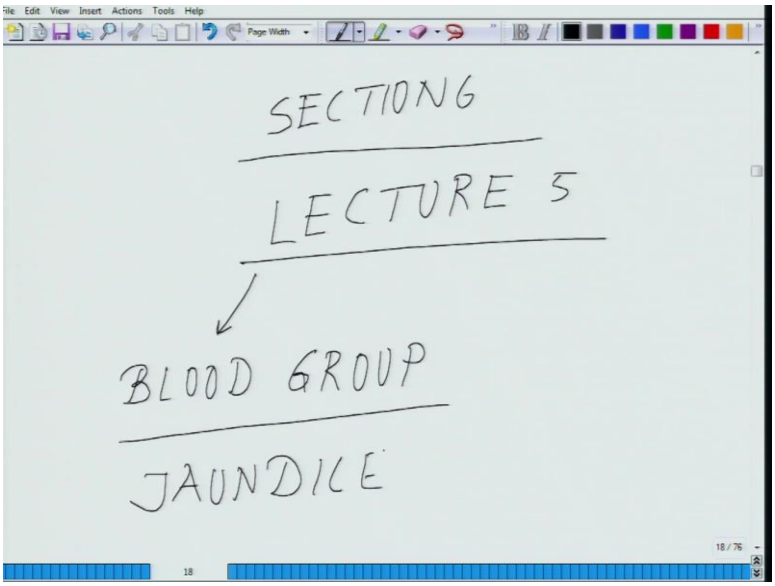
positive sign or A, a negative sign O. And then a positive sign. What are these groupings? This is one aspect what we are going to deal.

Second, we are going to deal, that how that could influence the birth of a new child in terms of pregnancy, that is the second thing we are going to deal. The third thing, what we are going to deal is what is jaundice? We hear about this; someone is suffering from jaundice; what really jaundice is all about? Though, I have covered a part of it, in the first lecture, while talking about the RBC and degradation, but I did not go in depth on the jaundice, what I will be doing.

So, let us start with the blood grouping. Essentially, we know that you cannot like, if somebody needs blood, I just cannot draw my blood and put it in that person. The first thing the doctor tells, they check my group and they check the group of the recipient. What that essentially means? That is essential for a lien man; it sounds like my blood, when I am drawing blood, basically I am drawing blood from my blood vessels.

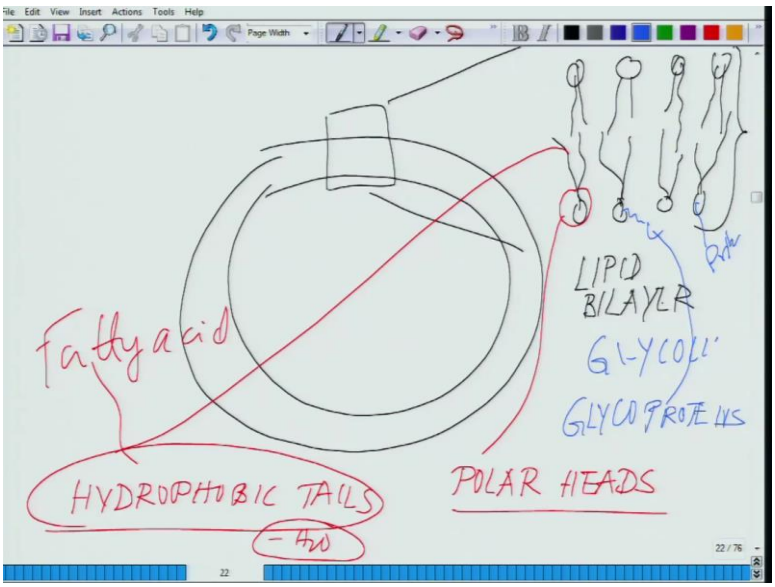
What is going to the other person, has the formed elements, which includes RBCs, WBCs and the platelets, and all the electrolytes and everything; plasma, all the fibrinogen, everything. If I cannot transfer like, if I cannot just as it is, put the blood to another person; that means, either the formed elements or the liquid component has some signature. If that signature is not tallying, the recipient will not accept the blood. Where lies the signature? To the best of our understanding, what we have, because this is another hot area, where still enormous work is going on. The signature lies in the red blood cells. What kind of signature is that? If you remember the first series of lectures, when I started in the introduction, I talked to you about the bilipping membrane of the cells; every cell has a bilipping membrane.

(Refer Slide Time: 05:32)



There, I talked about the presence of finger lipids, cholesterol, several other lipids. There also, I talked about the glycolipids and glycoproteins; presence of all these things. Just for the recap, we talked about. Let us take it back. Formally, let us start the lecture. This is section 6, and this is lecture 5. And here we will be talking about blood group and jaundice, mostly.

(Refer Slide Time: 06:10)



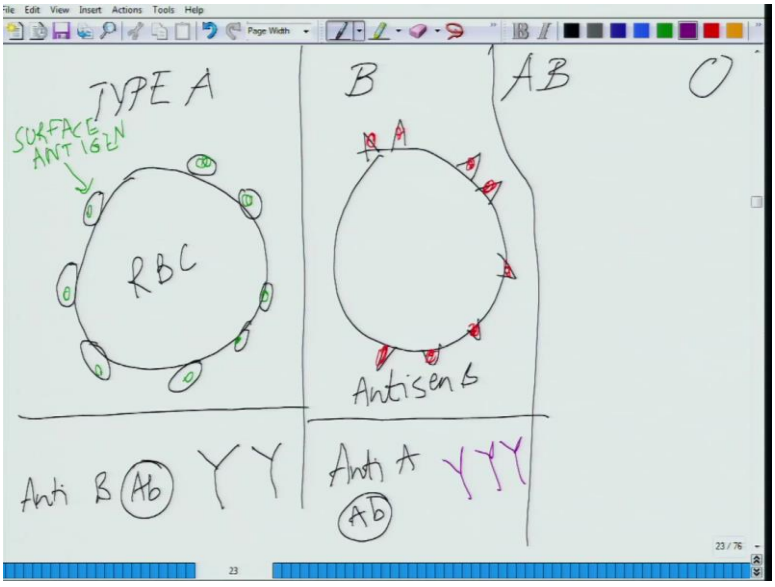
Now, talking about what I was trying to tell you. Whenever, I drew a cell I drew it like this. I told you that this is the membrane; this box type. This membrane looks like this. If

you go back to the first lecture, initial lectures, I spent significant amount of time on this. I told you that these are the lipid bilayer; this is. Within the deep lipid bilayer, I told you this, they have these; these are the polar heads and these are the hydrophobic tails. These tails mostly consist of fatty acids; fatty acid tail. They are water hating tails.

There, I highlighted one point that these polar groups are modified, sometimes with carbohydrate, sometimes with some other proteins, and based on that, there are glycoproteins and glycolipids. After giving this kind of reaction, what I have already taught you, it is in those lipid bilayers, some of the signature lies. Those signatures determine, whether you will have blood group A, blood group B or blood group O or blood group AB.

Let us first of all classify the blood groups; first system. After classification of the blood group, we will talk about the antigen and antibodies against it. Then, we will come back and determine the molecular identity of this. Then from there, we will move on to another factor called RH factor for which, you get positive or negative sign with your; whenever the blood group is recruited.

(Refer slide Time: 08:34)



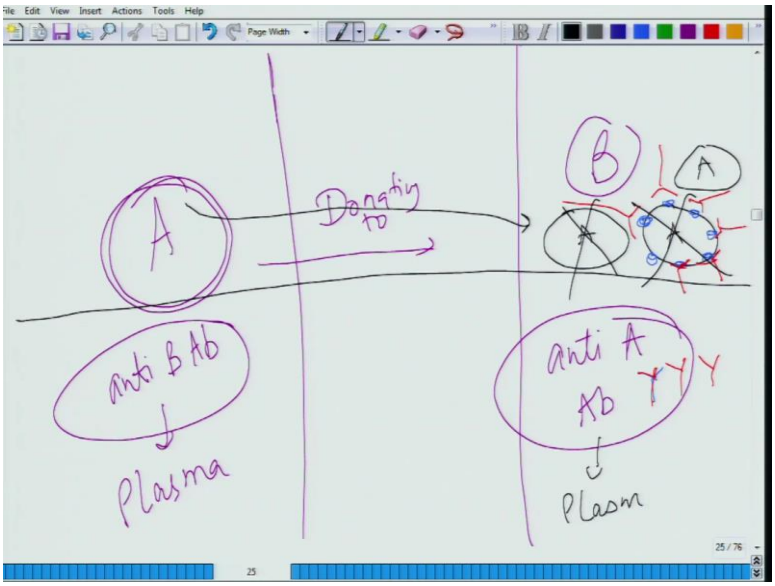
Coming back, we essentially have four blood types; type A; type B; type AB; and type O. If you look at an RBC, which is something like this biconcave disc; they have these surface antigens, likewise. For type A, they have a surface antigen A. What are antigens? This is something, which I have not discussed, if I remember correctly. Antigens are the

molecules, in whose response, antibodies are produced. Body has its own antigen. If body has its own antigen, technically, body should produce antibody against it. But, if it is of your own body, they do not produce antibody, against those antigens. Those are the surface antigens which are present in our cells; in top of our cell. But, there are diseases which are auto immune. Body produces anti body against its own member. It tries to, it could not identify, that this is your own. Some auto immune diseases like, (( )) likewise, there are whole range of auto immune diseases which are in part, these surface antigens are identified by the individuals, that is, its own antigen. That is its identification hallmark. Similarly, if you have a type B cell; type B of RBC; this is the RBC. On top of that, they have another set of antigens, which are called antigen B. Just for your understanding, these are the antigens; I am putting them in red and these, I am putting them in green.

If you have type A, and what you produce is that, you produce antibody in your plasma. I have already discussed about plasma. Let me just rub this off. Just put the surface end here. These are the surface antigen. Against this surface antigen, body has antibodies, which are called anti B antibodies; AB stands for antibodies. They are something like this.

Similarly, for people having blood group B, have anti A antibody. Those are maybe, you know something like this. If a person who is having blood group A, donates the blood to a person having blood group B, what will happen? As soon as they donate the blood, the anti A antibodies will come, and will start hit upon the RBCs, which are coming from blood group A. Let me draw it for your understanding.

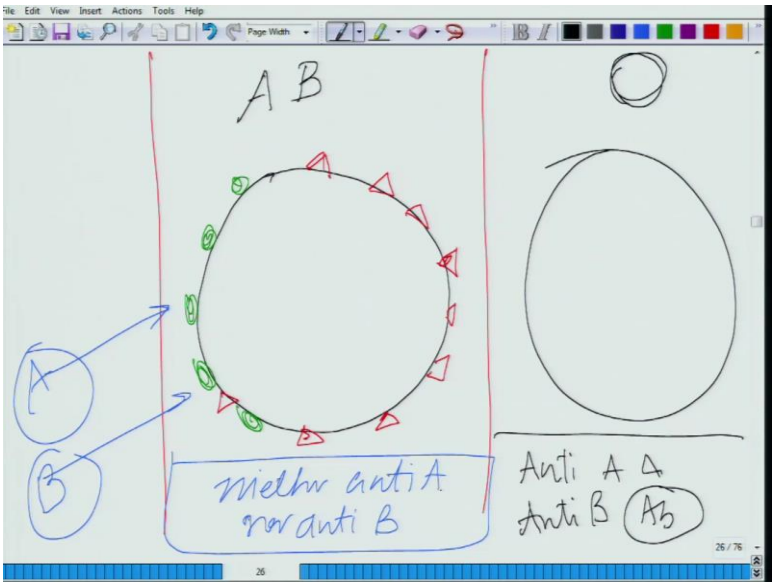
(Refer Slide Time: 11:58)



For example, here is a person having blood group A. If this person has blood group A, so this person has anti B antibody in its plasma; in this person's plasma they have anti B. Now, this person is donating to a person who has B blood group. So, in this person's plasma, he or she has anti A antibody; it is already present there. Nature has designed us for some reason or other, like that.

Now, this is present in the plasma. As soon as this A comes into game, this A blood is coming; RBCs of A; these are A, A. Immediately, imagine these are the surface antigen for A, and antibodies against that which are, I am putting them in red, they will come and bind here. What they will do essentially? They will rip the cell apart and will kill the cell. Whatsoever blood is being transferred or transfused to the other person, will be of no use or will be all destroyed. This is what happens, when it does not match. Then comes a blood group called AB, which is the third one.

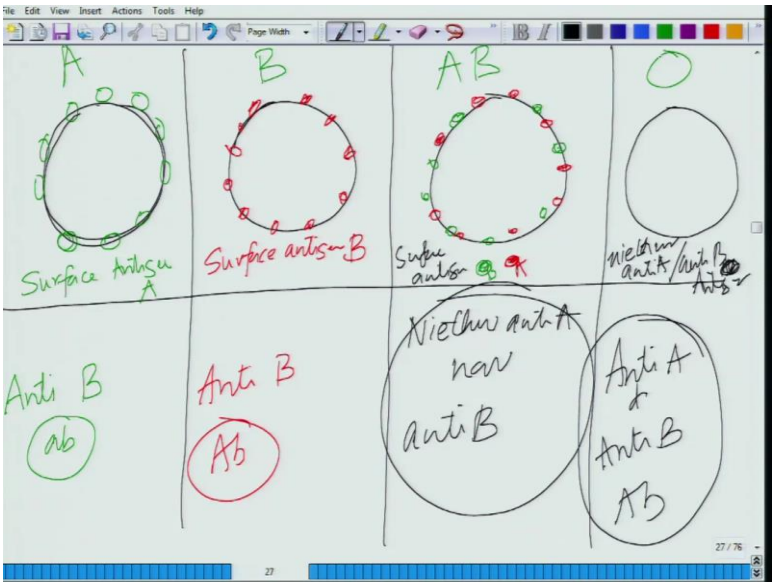
(Refer Slide Time: 13:36)



I talked about A and I will talk about group AB. AB is a person, whose blood cells have both, I showed you in the green, the anti B antibody; this thing, and you have the both, likewise; all distributed all over the place, randomly like this. That is why a person having AB could accept blood from both A as well as B. Because, this person is equipped with, they do not have any; they have neither anti B or nor anti B. They do not have any of these; neither have they anti A, nor they have anti B.

So, these persons are universal acceptor; they can accept blood from anybody. Of course, I have not introduced the RH factor, I will introduce it very soon, as soon as I finish this. Then comes a group called blood group O. Blood group O is somebody like, imagine a cell like this, which does not have any surface antigen. They do not have any surface antigen, yet, they have anti A and anti B antibodies in their blood, in their plasma.

(Refer Slide Time: 15:13)



Let me just, for your better understanding, draw it in such a way, that you understand all the groups clearly; a, b, c, d. Here is single red blood cells, I am showing and here, you have, these green colors are showing your surface antigen A. So, this is blood group A; this is B; this is AB; and this is O.

Surface antigen A, and within the plasma you have anti B anti body. Now, blood group B they have this. They have surface antigen B and they have anti B antibody. Now, you have the third group of person, who has both the surface antigens present, and they do not have, I am just, they have neither anti A nor anti B. And now, you have the O; they have surface antigen; both the surface antigens are present for A as well as B.

This is the A and this is the B. These persons have neither anti A, nor anti B body, yet, they have anti A and sorry, antigen, sorry, I am sorry, antigen anti B antibodies. That is why, the blood group with O is called universal acceptor, sorry blood group O is called universal donor. They could donate blood to anybody, and they can only accept blood from somebody, who is having O. You have this AB, which is universal acceptor. They can accept blood from anybody.

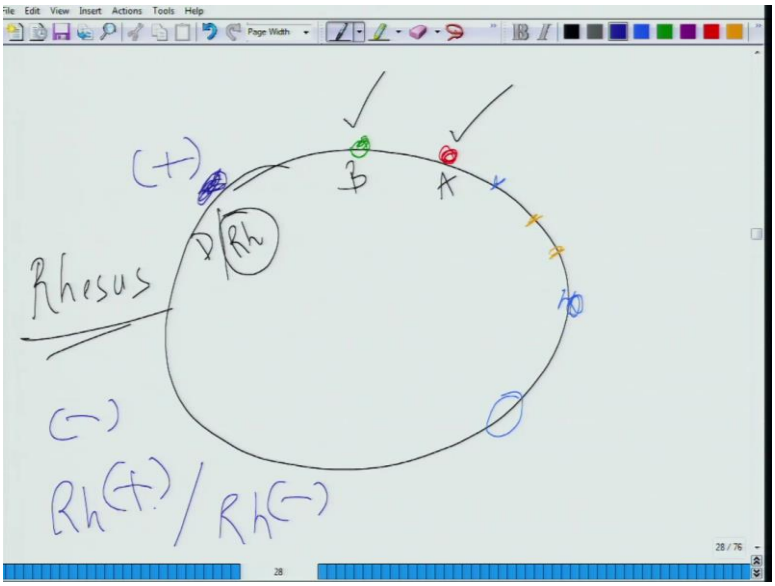
So, this is the first set of factor, and mind it here for those might wonder is the only thing; there are at least 50, 60, 50 to 60 odd identification markers on the surface of red blood cells, but it is only 2 or 3 or maybe 4, which are of extreme significance, but that does not rule out, what will happen with the other factors? Be aware, these in the

population are most significant one, as of now. There is lot of research going on. We do not get these cases at times; these are rare happenings. But other, say for example, if total we assume, there are 50 such identification marker. For 50 such identification marker, in the sense, surface antigen on top of it, we are only talking about two surface antigens; A and B, their presence, absence. But that does not mean, there cannot be on tomorrow; f, g, h, i, j, k, likewise. There are at least known 50; this is known this is last time I was reading through, it was 50.

But that number maybe increasing day by day, with the explosion of genomics and proteomics, and is exploding big time. It is just statistically, that concentration of the title is low, but you never know. Maybe tomorrow or maybe 20 years, down the lane, we may discover other factors and the blood transfusion again, become more complex as what it is today.

So, we talked about two surface antigen; A and B, and we have not talked about the chemical nature of this. That we are going to talk just soon after this. There is a third surface antigen factor, I will be talking about; that is RH. It is also sometimes called D factor. RH factor is again, it is a protein on the surface.

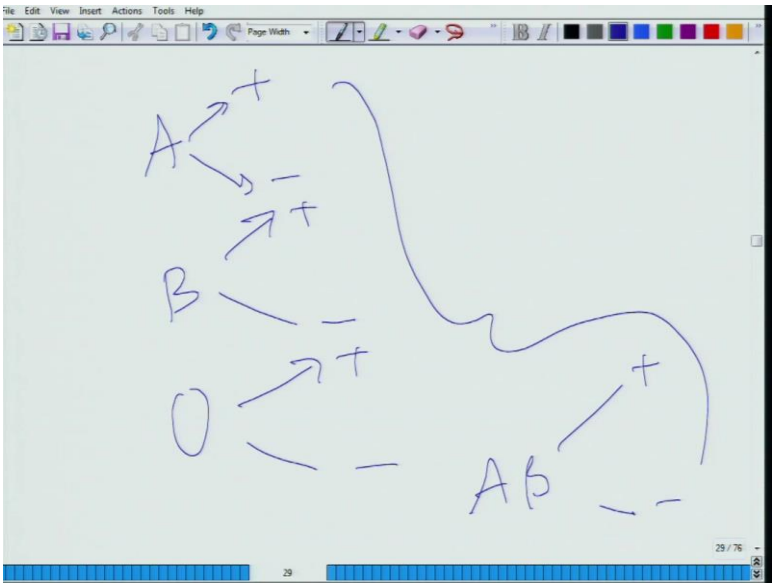
(Refer Slide Time: 19:53)



While I was drawing, you say something like this. If this is the RBC, we talked about these surface antigens, likewise, and I told you that there are other surface antigens which we are not aware of… I am just putting them in different colors, so that you

appreciate it like or likewise. Only the major ones, which you were dealing with, is this one and this one, which is for A and for B. There is one factor which is called D or which is also called RH. It is called RH because it has been discovered in one of the monkeys in Africa, called rhesus monkeys. This was discovered in the rhesus monkeys, that is why, it is called RH, and it is a protein on the surface. So, it is something like this, something, like a protein sitting there. If this protein is present, we call it positive and if this protein is absent, we call it negative. based on that we have RH positive and RH negative.

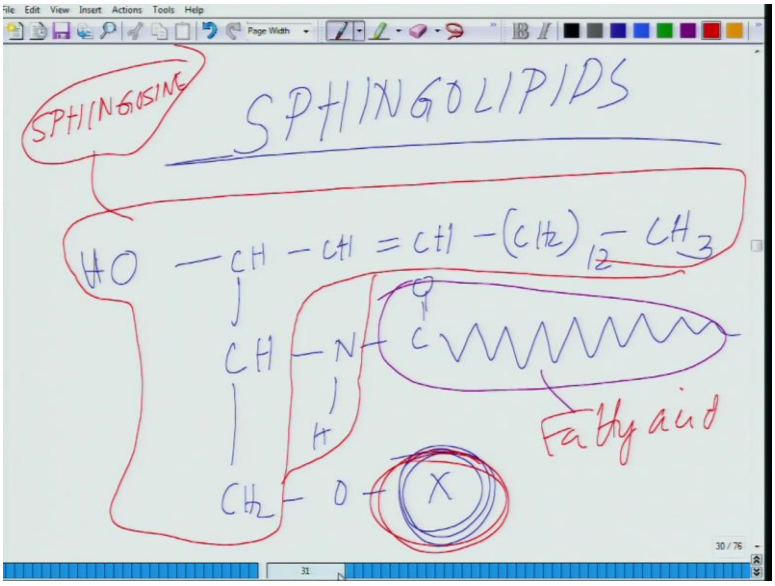
(Refer Slide Time: 20:59)



On top of what I have taught you, as of now A positive, A negative, B positive, B negative, O positive, O negative, and then you have AB, they have both; they could have positive or negative. So, these are the broad classification, as of now. But tomorrow, you may hear some other factors, which add up to this. We may have a different kind of nomenclature, actually, there are because, if you go through the research papers and different people, write, and like they analyze bloods, you will see there, many others, those classifications are way to complex, but I am not getting you the complexity, but I am giving you feel of the complexity. It is just like, think of a crowded street and there, you have to identify a house. It has its all bar coded, as this blood belongs to this individual and it is so very unique.

It is just in the population, as of now and those antigens; surface antigens, are present in such a low concentration, such as you are talking about a fintomolar, picomolar; it is really tough to identify them. So, we always identify the one which are in larger concentration. Those which are in smaller, but tomorrow, when mankind will have much sharper tools; much better tools; to identify all these things. I am pretty confident that we will come to know many other factors, which ensures and maybe, blood transfusion will take a quantum jump out there, which identification of these different antigens on the surface of RBCs. So, after introducing this, RH factor and everything, now, we will come back; what happens? How that influences? Before I do, let me just take a detour and tell you that what are the as of now I have not talked about the chemical nature of this.

(Refer Slide Time: 23:36)

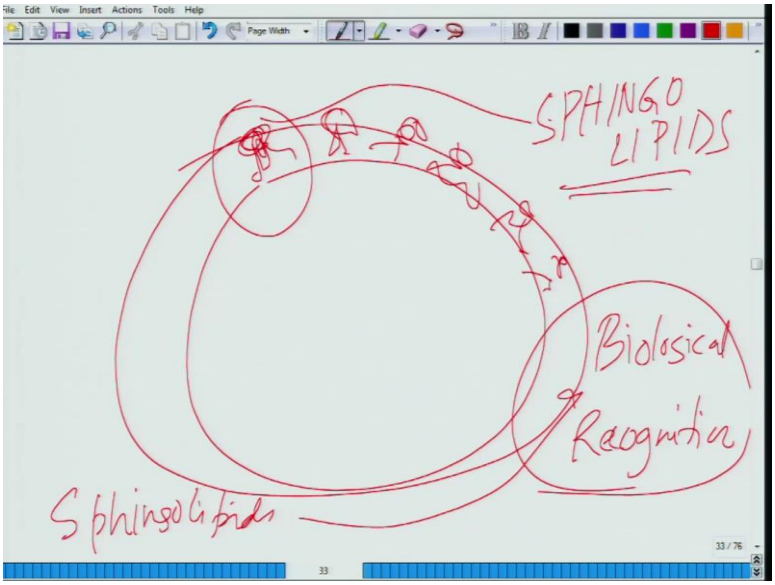


Now, what I will do, I will talk about the chemical nature of these molecules and then I will move on to the pregnancy and related issues with it. The chemical nature of these, if you remember, I talked to you about sphingolipids. While I was talking to you about the lipids, I talked to you about sphingolipids. What I will do now, I will draw as sphingolipid, just to rehearse, if you have forgotten and from there, I will draw the story.

Sphingolipids essentially looks something like this. So, it has a sphingo scene moiety, just you have to go through my previous lectures on, then you have the OH group out here, and this is attached to CH and H and from here, it is a huge chain of fatty acid

going through, and out here, this is the third moiety which is CH2 O. Here is a X group as important. Here, this part, what you see is this part is called sphingosine part, and this is basically, sphingolipids. This is your fatty acid components sorry, I just drew it slightly wrong, this is included. So, this is the fatty acid component, and this X is the critical one.

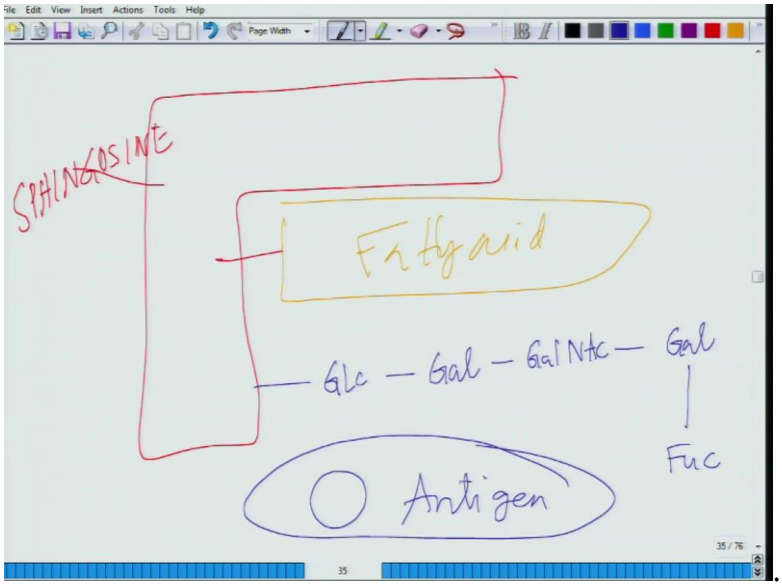
(Refer Slide Time: 25:02)



These sphingolipids, if I have to draw the membrane again, if this is the membrane, there is sphingolipids, which are present like this, out here, along embedded within the lipid bilayers, with other lipids. These sphingolipids, what I draw has a wide range of modification. These sphingolipids at self surfaces are site of biogoligcal recognition.

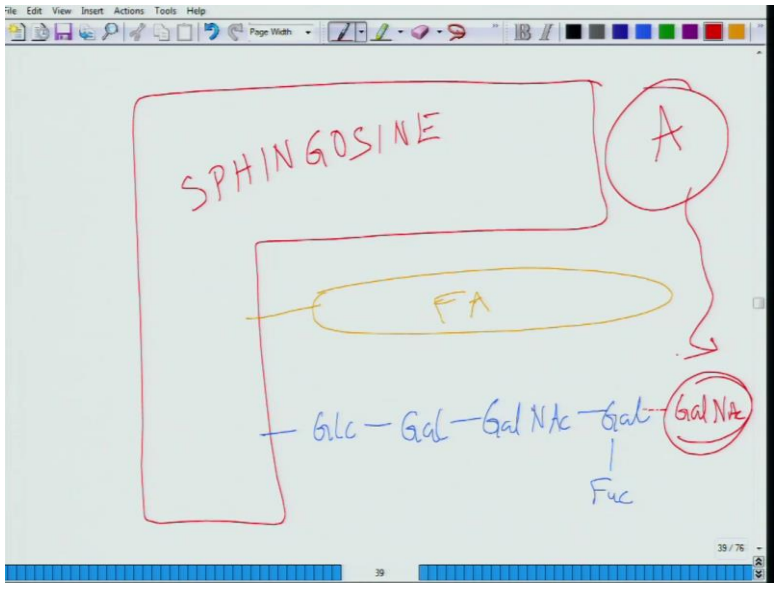
So, sphingolipids for biological recognition. How they do so? I have highlighted that X part to you. Now, I will show you what, I will not draw, what I will do is keep the fatty acid, I will keep the sphingosine moiety intact. I will keep the fatty acid and I showed you, that X now you see the variation in the X determines, whether somebody has A or somebody has B or somebody has AB.

(Refer Slide Time: 26:12)



Now, let us draw it. Here, you have the sphingosine moiety. Here, you have the fatty acid. Now, start the game. Now, this is the case of antigen O. You have a glucose; glc is the glucose. Then, you have a galactos; another fatty acid. Then, you have galactos NAC; acetyl numeric acid. Then, you have another galactos sitting here and then you have a fucose, which is another carbohydrate. So, this is the structure of O antigen which has both A and B. If you know O then what I ensure that, always try to recollect the structure O. If you know O, then you can diverge and say, this is A and this is B, because O contains both of them.

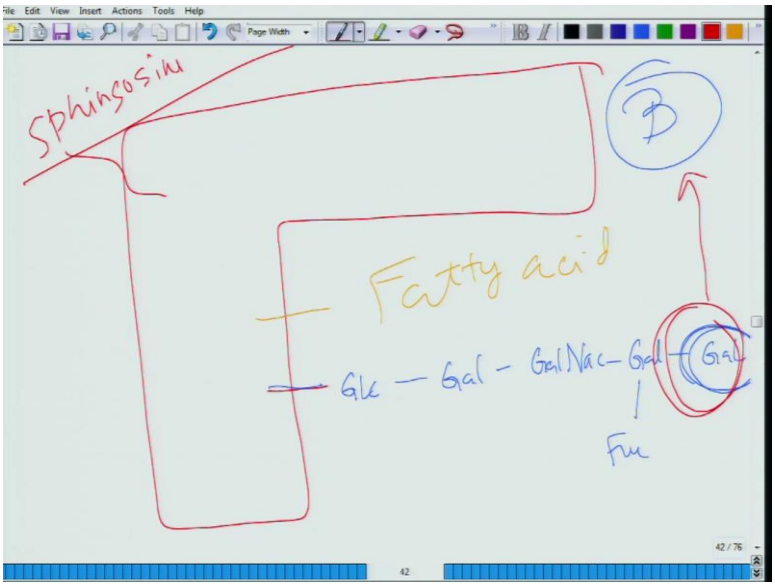
(Refer Slide Time: 27:46)



Now, let us draw, what is the A and B. So, O antigen we have drawn. This is what is essentially, present on the surface of our red blood cell; this structure. Now, for O, there is one modification. Everything remains, sorry, for A, there is one modification and everything remains the same. Nothing changes except, there is one addition here, which you draw that. Again, here is your sphingosine moiety, fine. Here, you have the fatty acid, here you have the sphingosine.

Now, you have this, I taught you this glc; your galactose; glucose; galactose NAC. Then you have galactose and then you have the fucose and here is that addition for A. Now, you are talking about A. Here is that addition. You have another gal NAC. This one small galactose in numeronimic acid, changes the fate. So, that determines that you have A; A blood group; A antigen; A surface antigen. Then, what is B?

(Refer Slide Time: 28:54)



Now, let us draw the b. Again, you have this sphingosine moiety. You have the fatty acid tail out here and then starts your. You have glucose, galactose, gal NAC. Then, you have after gal NAC, you have galactose and then you have the fucose and so here. In the case of A, you have a gal NAC and in the case of B, you have just a galactose present here.

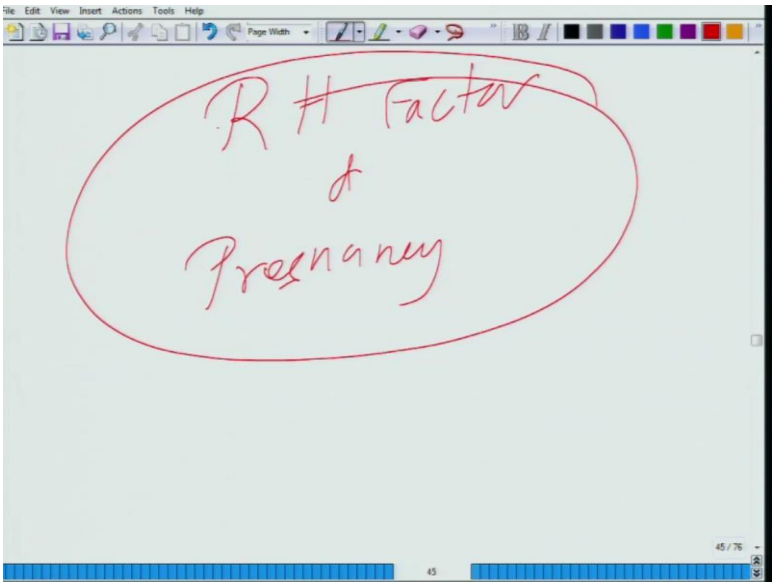
So, this is the one which determines that you have B. In one case, you have galactose in acetyl numonic acid. In one case, you have just a galactose residue. This chemical signature; it has been very nicely highlighted. Those of you are interested for extra reading, you should go through lehninger. In the lehninger fatty acid section, it has been

highlighted very nicely, very beautifully, shown in picture and that will help you to understand this structure much better. But, that is what is where, essential for you to understand, that these blood groupings are molecular recognition tools of biology. They are determined by different kinds of lipids; glycolipids; glycoproteins.

RH factor, similarly is a protein, which is just like, what you see here, a glyco, I should say glycolipid. Because you have lipid group on which you have this carbohydrate moieties, which are attached, like galactose, glucose, gal NAC, fucose, likewise. In the case of RH factor, it is a protein. So, you have these lipid polar groups in which, there are proteins which are tagged, which are essentially, lipoprotein; protein adhered to a lipid.

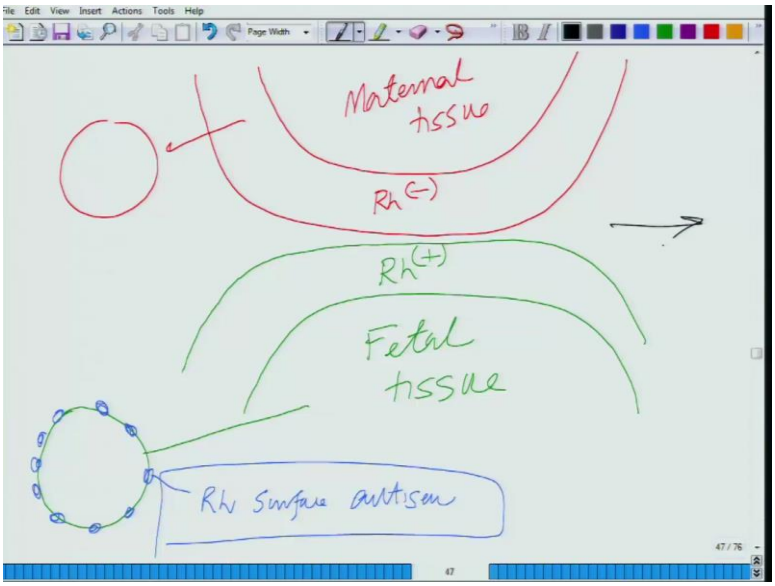
These proteins act as those barcodes, which make you positive or negative. From here, I will come on to what happens in a pregnancy situation. For that, you have to understand, when a woman is pregnant, a baby is growing in the womb. So, essentially, the blood circulation is slightly separated, from the baby and the mother.

(Refer Slide Time: 31:47)



Let us draw it, which makes more sense to you. What happens? Now, we will be dealing with RH factor and pregnancy.

(Refer Slide Time: 32:04)

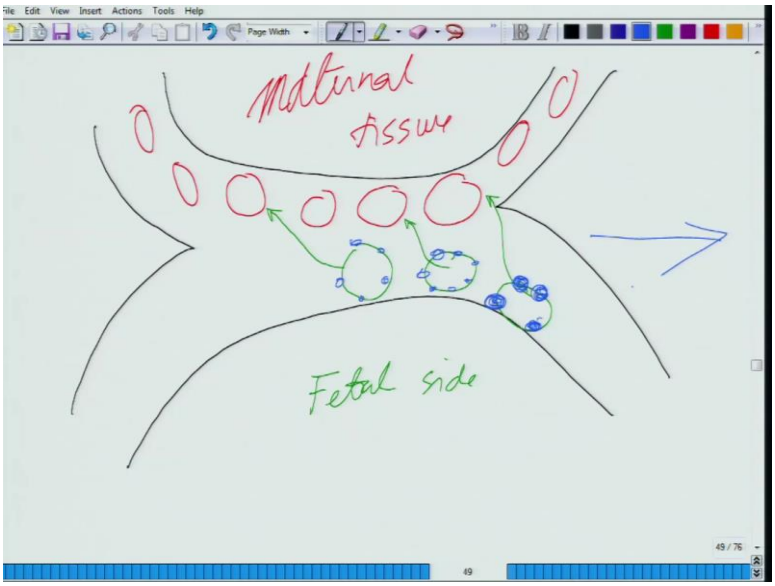


Think of a mother whose, let us draw the two blood vessels. Here, in the mother's womb, the baby is growing and a mother is RH, irrespective of any, RH negative.

This is maternal tissue and now, let me draw the fetal tissue, which I will put in green, just for your understanding. This is like this and imagine, the fetus is RH positive. It has a positive RH factor and here, we are in the fetal tissue. This woman is going through her first pregnancy; this is not a second pregnancy; this is here first pregnancy. This woman does not have any antibodies as of now, because it is RH negative; does not have any antibodies against the RH factors. Because, it has never been exposed to RH positive situation.

So, essentially, what it bounds down; the blood which are present in the mother side, do not have any such marker, whereas, in the case of fetus side, the baby whom she is going to give birth, has these RH proteins, RH antigen on surface of the protein or on the surface of these RBCs, fine. These are RH surface antigen. During her first pregnancy, during the child birth, zone comes. Again, I have to show you through the drawing that will make more sense.

(Refer Slide Time: 33:50)

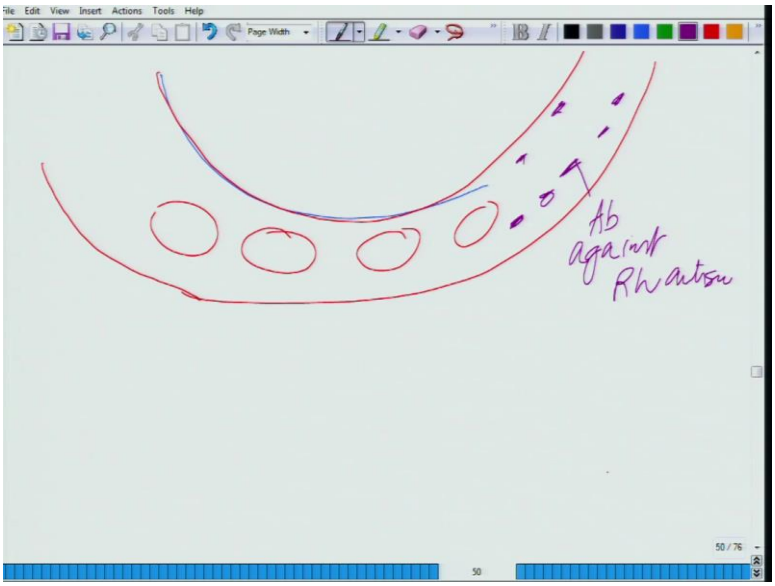


During delivery, basically this is what happens; cutting the umbilical cord and there is a bit of a blood exchange, which takes place. So, what essentially happens are, this the fetal side and this is the maternal side; maternal tissue. These are the fetal RBCs with these factors; with these RH surface antigens on them. Whereas, these are the mother tails without any RH surface antigens.

Some of these RH positive cells get into the mothers circulation. As soon as it gets into the mother's circulation, because of the presence of these, what you see, this blue color and surface antigens, which mother is never exposed to, it starts producing antibodies against it. It produces series of antibodies. It is just like, as if mother is getting vaccinated; almost equivalent to that. The mother is getting vaccinated because, there is a low tighter of it is going.

Now, for the first pregnancy, it will be fine. The child will have no problem. Child will survive, but if this mother goes for second pregnancy, what will happen? Already, the mother has and imagine the second pregnancy, again the fetus is RH positive. Let us draw it, which will make more sense. So, already mother has produced antibodies against it.

(Refer Slide Time: 35:43)



Now, the mother's follow the same color code. So, mother has now these are mother cells and on top of that, they have antibodies against the RH positive. These are the antibodies against RH antigen. Now, if again the fetus becomes RH positive, as soon as the RH positive, from the mother's blood, the RH antibodies will come and will start breaking down the cells of the fetus; blood cells of the fetus. Essentially, what will happen? Either, the child will have premature death inside mother's womb or the child will be produced very anemic. So, these are the situations for where, doctor has to take a special care; very special care.

These are the reasons, why the understanding of the blood grouping and all the surface antigen, on top of the blood on the red blood cells, is so very essential. Because, these are the signatures, which make all the difference, whether it is a pregnancy or whether it is blood transfusion or any other situation. Just to rehearse, this mother was RH negative; fetus was RH positive, and there is a blood exchange. During the blood exchange, mother started producing antibodies against RH factor; RH surface antigen. Because of that antibody production, what happens essentially, the first child will have or maybe, born with a bit of jaundice, which I am going to come now.

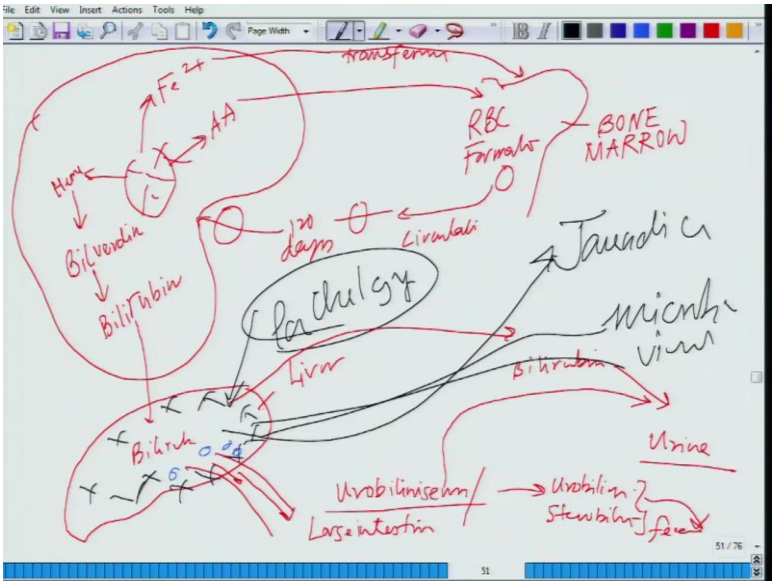
The second child survival will be a big question, because mother will have a very high tighter of RH antibodies. Because, mother is herself negative for RH. So, that is where, lies the whole classification; A positive means A, RH positive; A, RH negative; B, RH

positive; B, RH negative, likewise O, RH positive; O, RH negative. One of those very rarest of the rarest individuals, for whom you really needed another O negative.

Now, I will move on to the jaundice, which is the tail piece of this whole circle, which we covered; just like a blood circulation, it will be just coming back to the point, where we started RBCs. So, that was the sole reason why, the reason for not introducing jaundice at that time, because now, you will be able to appreciate jaundice much better. In the light of red blood cell, white blood cells, platelets, blood grouping, RH factors, we will be able to appreciate jaundice far better.

Now, let us get back. I will just draw a very overall flow chart to explain what exactly, happens in jaundice. If you remember, while I was talking about how RBC is getting, let us start from basics. RBC has a life span of say, 120 days, fine. Now, after 120 days, the RBCs have to be destroyed and that is done by the microphages. So, I will pick up the story from there; production of RBCs; what happens after 120 days; how it is getting broken down, and what happens to those broken down products; and how they are being regulated.

(Refer Slide Time: 39:48)



Coming back to the slides, this is, you are into the bone marrow now. Within the bone marrow, the RBC formation; this is the bone marrow, and here you have the RBC formation. These RBCs, once they form they are in circulation and after their 120 days

life span, and they are being engulfed by the microphages. This is one reaction which I have shown you.

These are the RBCs. Inside the macrophages, what happens? Here, have been chopped off into pieces, and it generates iron; Fe 2 plus, and you have the amino acids. These amino acids are brought back to the bones, iron using transfer in iron by protein is brought back to the bones.

Now, we have the hemmoitem which is converted into biliverdin and biliverdin is converted into something, called bilirubin and this bilirubin, from these macrophages moves to the liver, which we are discussing in the digestive system. In the liver, this bilirubin, through the duct of the liver is sent for excretion. So, there are two routes from here; either, this goes to the kidney where, basically bilirubin is directly put into the urine; it is one route. There is another route; this bilirubin reaches the large intestine. In the large intestine, bilirubin is converted into a molecule called urobilinogens and sterico bilinogens. These molecules further converted into urobilins and stereobilions and part of this urobilinogens, are excreted via urine.

And these urobilinogens are eliminated in the feces, and that is why, you will see the color of the feces is yellow; whitish yellow. It is yellow because of these different compounds, which are present there, whose dye signature is yellow.

Now, imagine what will happen, if the duct from where the bilirubin, is being thrown out from the liver is blocked or liver has problem. That is exactly the situation what happens in jaundice. When the liver ducts through which, coming back to the flow chart, which I was drawing for you guys. There are ducts through which, here in the liver, these ducts get blocked, because of the malfunctioning and this, leads to a state called jaundice. This could happen by multiple routes; there are multiple routes for this to happen. This could happen because of some pathology here; some microbial attacks, some viral attack, which leads to the damage in the liver.

So, that the ducts which are suppose to vent out the bilirubin, fails to do so. What you see on your skins and everything, it becomes yellowish. Because, your bilirubin concentration in the blood goes up, and that could be detected not only from the blood sample; it could be detected from your urine. You will see that there is enormous amount of yellowish, you see your skin colors, along the nails and everything, you see yellowish.

Because, it is this bilirubin concentration goes up, and this is how it all happens. It is from that he molecule, which converts it into biliverdin, biliverdin to bilirubin. From there, the bilirubin has to be sent partly to the kidney, and partly to the large intestine where, erobillunogens, stereo billiogens, stereo billions, eurobillions, likewise. This is a whole complex set of reactions, which takes place and when, it fails to do, so this is what you see is a case of jaundice.

Just to summarize, what all we have covered, we started with the RBC. So, we covered almost 5 lectures on this. We started with the RBCs and we talked about the oxygen carrying capacity using hemoglobin, where I requested you people to look for the structure of the hemoglobin. From there, we moved on to the blood clotting. We talked about the platelets and how from the megakaryocytic, these things are formed. After that we talked about the WBCs. In the WBCs, we talked about how they are formed, and in between, of course we talked about the formation of all the different blood cells. We talked about the WBCs and we talked a very little bit about the immunity; immunity and occlude immunity where in the immunity, we talked about all the different organs of our body which prevents using different kind of toll like receptors, does not allow the entry of the pathogen or occlude the entry of the pathogen. Then we talked about the occlude immunity in the form of T and B cells, and in the form of antibodies, which are produced by the body. Lastly, where we started with the RBCs and we ended with the RBCs. We talked about the identification signature of the major component of the blood, which is RBCs.

How they are being identified in terms of their surface antigens A, B, AB and O. Then, we talked about the RH factor, how RH factor affects the pregnancy of woman, and lastly we exactly ended where we started in the first class talking about jaundice what jaundice is all about.

Thanks a lot.