Animal Physiology
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Lecture – 35

Welcome back to the NPTEL lecture series on animal physiology. So, we are in section 6 about the blood cells, immunity and the clotting. So, initiated with the red blood cells in the first section, and then in the second section I by pass the white blood cells and moved onto the platelets, and the clotting factors. So, today what I will do? I will tell some of the basics, now since you have fairly good idea about what blood is about some of the basics what, whenever you go to a doctor, and the doctor asks you to get a blood sample, and a blood testing and what you see in the sheet.

So now, the doctor takes the blood or the compounder takes the blood, and then it is being processed, and next day evening or the same day or after sometime you see your report. So, what that report really says, and how you can interpret that report, this is very important for you people to understand, this is a practical aspect of it. And next thing what we will be doing, I promised you that I will be covering, how this different blood cells are formed, how this whole differentiation process, how a one single cell.

So, let me rephrase this sentence, essentially blood is formed from one single form of you can call it a pluripotent or a stem cell or something of that kind. So, from one source, it all divides, some forms following a different path way red blood cells, some forms white blood cells, some form platelets, how that whole thing happens. And one more thing, in my last class well I was teaching you about the platelets, I made a small mistake, just correct it I talked to you about the thermo sites. Thermo sites are not actually the platelets of the human being or mammal, it is for the non mammalians, so thermo sites are those such a slight error.

Basically platelets are formed from mega carrier sites; I will come to that, just correct that small error which I made in my previous class on the clotting aspect. So, talking about the blood, what a doctor does when doctor asks you to a, do a blood analysis. So, blood is a fluid that we all know by this time we know that it is flowing all over the body. And fluid has lot of particles, and those particles could be cells, we have talked about it blood cells, which are carrying the oxygen.

Then we talked about the platelets, there are also small tine tiny particles of four micron, kind of a major diameter or it is kind of triangular shape. So, you cannot call it a major diameter, it is kind of if you take the maximum length of that triangle, the kind of the base of the triangle then ((Refer Time: 03:03)) it will be around four micron, and those are non nucleated, same way the red blood cells and non nucleated they do not have any nucleus.

Apart from I talked about the platelet that is why the thermo sites come. Thermo sites are the platelets of the non mammalian system, which indeed have nucleus in them true; we are not going to deal with that those thermo sites. You will be only dealing with the platelets, which are in the human system. So, and then you have the third cell type, which is white blood cells, the cells for immunity, the microfaches. We talked towards the microfaches, why will talked about, how the red blood cells, which live their lifetime of say 120 days or 110 days, kind of rejected out of the body, how they are being engulf, by the white blood cells in microfaches.

So, the macrofiches, if you do something called a blood smear, so what essential is blood smear is that, say for example, you might I just break it and get a drop of blood and make a smear. So, you take the drop of blood and put it in a glass cover slip, and you just, you know spread it like this, just like you have a drop of water, you do it like this, look at my hand and if this is the glass cover slip you just smear it. And if you look at the smear, then there are several kinds of… One second excuse me.

So, if you look it another microscope, you will see, three distinct features, one you will see I told you about this platelet cells, we do not have any nucleus. So, if you add any nucleus stain you would not find any nuclear staining on them, then you will find some cells, which are circular by concave kind of cell, which also do not have any nucleus, those are your red blood cells or there maybe some red blood cells in the phase of formation, which also does not have any nucleus. Yet you will find a kind of cell or a series of set cells, which will have multiple nucleus connected to each other, which are multi nucleated, those multi nucleated cells are your white blood cells.

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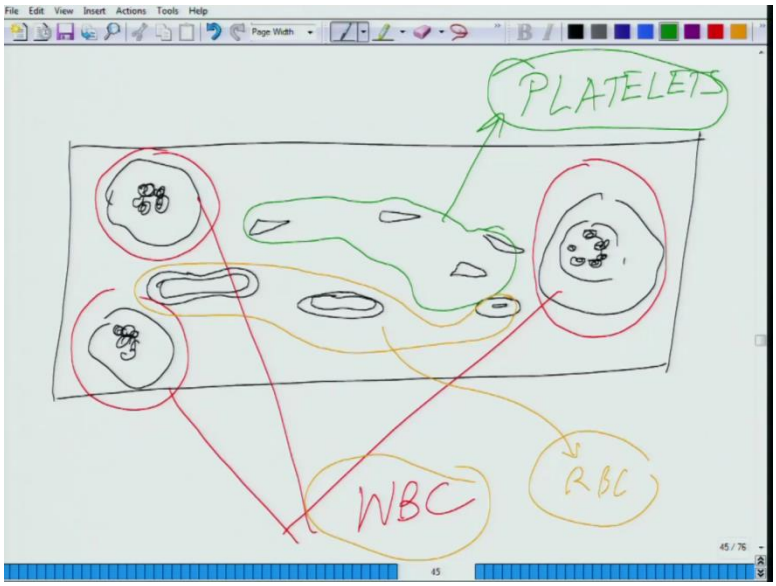

So, if I had to draw this classification of it, it will look something like this, on a blood smear you will see. So, if this is your glass, and if you are looking at a smear, you will see something like this, then you will see something like this, you will see huge, huge cells with something like this. So now, look at this, and going by the dimensions, if you look at it, these huge cells which are now circling in red, these are your W B C (s), these one which I put it in green are the platelets, and the one I am now putting in yellow, are your R B C (s) this is what you can see it another microscope, in a blood smear.

Yet these are the cellular component, but your blood is fluid, then what is the fluid component? So, if see just imagine, then in that smear, if you have a very high resolution microscope you can see proteins, just imagine so the imagine is see give cannot really see it under like that, with the known technologies. Then we will see a series of such proteins which are present there, and they are kind of floating in the fluid, which is mostly water. So, this watery fluid on which this proteins are suspended, and the cell component are two different aspects.

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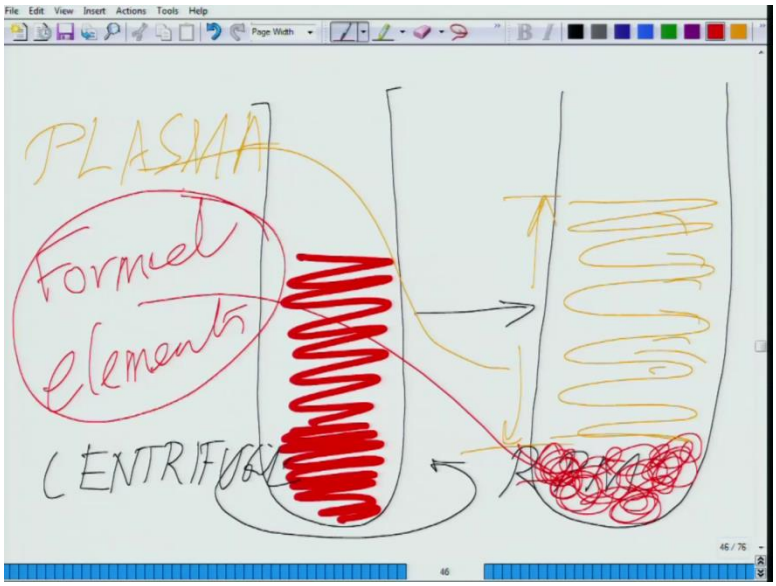

So, there are two different aspects of the blood, so the blood essentially, if you have some way, say for example, you take the blood sample in a tube like this, I will just draw it for your visualization. So, say for example, I give a tube like that, and here you have filled with blood, so this all red is the blood. Now, if you one second, if you take this blood and you spin it, at certain r p m, you put it in a centrifuge and spin it. After sometime what will you see, after spinning down, this is what you are going to see, this is spinning or centrifugation is done to separate out components within a fluid.

So, what will essentially see the fluid component remains at the top, and the cellular component or the solid component comes at the bottom, there will be separation and separation will look pretty much like this. So, what we see is, lot of solid component here, and here you have a lot of fluid component. This fluid component, which is separate out is called plasma and this cellular component or if this we can call it as a cellular component or it is technically it is called formed elements.

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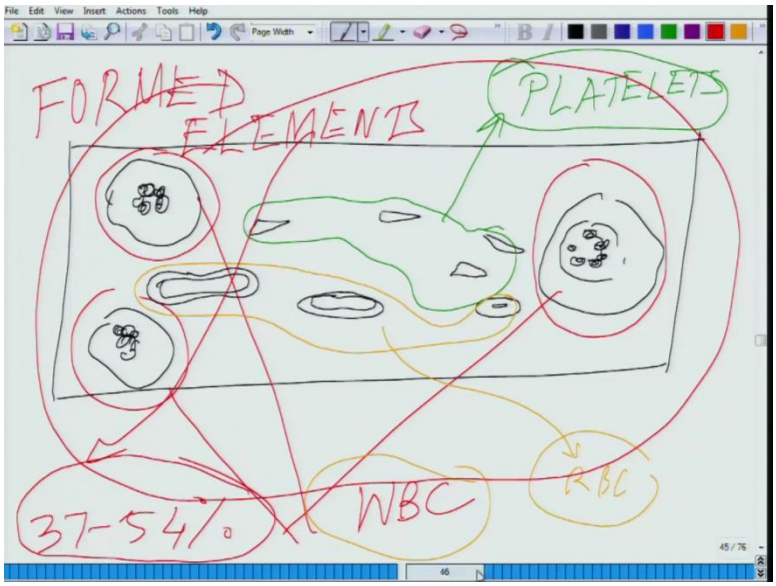

And these form elements are nothing but what I should you here, these are the formed elements W B C (s), R B C (s) and platelets. So now, put the name for that, formed elements, and if I have to do a volume percentage ratio for this, this form elements are around 37 to 54 percent, that is the constituent of the formed element, whereas, the plasma component out here, this plasma component varies from 46 to 63 percent. Now, I talked to you about, the different formed elements, now I will talk to you, about the different proteins which are present there, and these proteins are essentially called plasma proteins.

So, that formed the plasma component consists of protein elements. So, which you can imagine as, it is cell is a bigger particle each, so protein is a micro nano particle. So, microscopic particle at the micron range, and you have an nano particle. So, those nano particles remain suspended in the fluid, in the fluid consists of lot of electrolytes. So, plasma can be now put into two component, plasma protein component, plasma electrolyte component.

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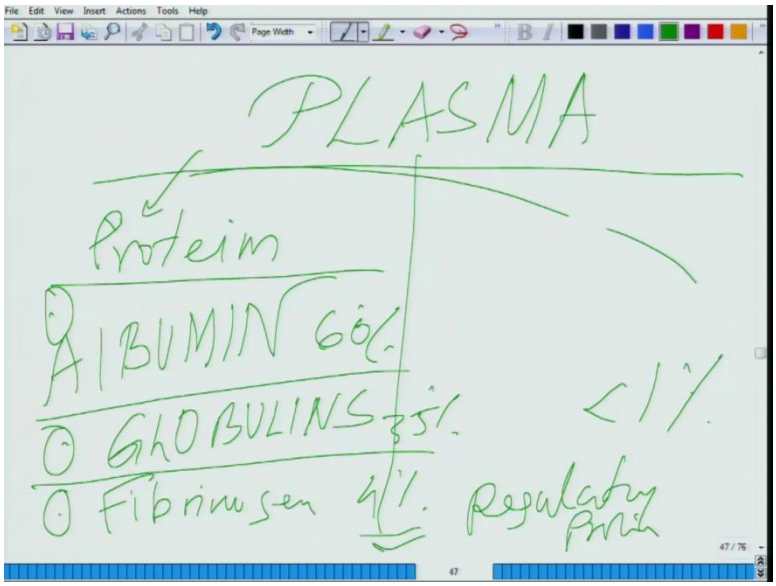

So, that what we will do, now let us classify the plasma, your plasma into parts, one plat is called plasma proteins. This plasma protein the major contribution is meant by albumin, albumin you all of you are aware of that in the, this is one of the major egg protein. You see that in the egg you have this albumin protein ((Refer Time: 10:56)) albumin and all these albumins. So, albumin is one of the major chunk, which is approximately almost I think around 60 percent of albumin, apart from albumin in the clotting, I highlighted that you will be needing fibrinogen.

Fibrinogen is another component, which is present there, then let me enumerate them. Albumin which is approximately 60 percent, then you have globulin proteins, hemoglobulin these are the globulin protein, which constitute 35 percent, then you have 4 percent of fibrinogen. And you have a bunch of enzyme, pro enzyme, hormones. So, which essentially falls under regulatory proteins, which is around less than 1 percent. So, this is pretty much, that the protein component, which is involved in it. So, you have the huge chunk of the albumin, globulins, fibrinogen and a series of hormones and pro enzyme and everything.

And this concentration of this different protein varies, under different conditions of your body, different physiological status of your body, different pathological status of your body. So, by looking at the blood sample, analysis of the blood sample, could tell with what kind of technically speaking, one can predict cancer, by very early diagnostics, but

where is the problem, why we unable to detect it, this is the challenge. The reason we are unable to detect it, lies in that last less than 1 percent regulatory protein, I just telling you.

All the hormones, enzymes, pro enzymes and everything, because it is exceptionally challenging to you know, the I should say estimate proteins, at a very low concentration, it is a big challenge, it is a enormously big challenge. Because on what level is higher than normal is another challenge to figure out, because whenever cancer or any kind of pathological situation happens, it is not that, those proteins, they are already present in the body, but because of some x y z wrong situation, their level either goes up or goes down, but how to make that demonstration.

Because, already these proteins are present in proteins and enzymes are present in such a, such a lower concentration and they work at a, it is a very low concentration chemistry, if you will call about it is a very femto, nano, nano femto likewise that molarity. At that molarity these things are working, so at that concentration, it is really, really tough. And it is across the globe, whether you talk about ((Refer Time: 13:42)) united states, whether you talk about other similar organizations in Europe, back home in India. All the places is still blood always remain one of the hot subject of research, could be analyze all the component.

And far more early, before the, we reached to a point, there is no point, I am no return that I mean you ((Refer Time: 14:05)) best patient do will die of that problem. So, could we diagnostic it is there a way to diagnose, is there a way to diagnose cancer very early; is there a way to diagnose some neurological disorder very early. By just doing a blood sample, could you predict, do you have any mode, how low we can detect. It is all about the detection limit and how accurately we could we can detect at what is the level of accuracy that is very, very important.

So, that is why I highlighted this, that is the reason why I wanted to highlight this point, those less than 1 percent do not neglect them, they are exceptionally important, because that is where live all your diagnostic kits, diagnostic tools, and everything. Now, let us move on to the other component of the plasma. So, we talked about all these smaller particle component, which are then nano not only the nano I mean like the nano sized domain.

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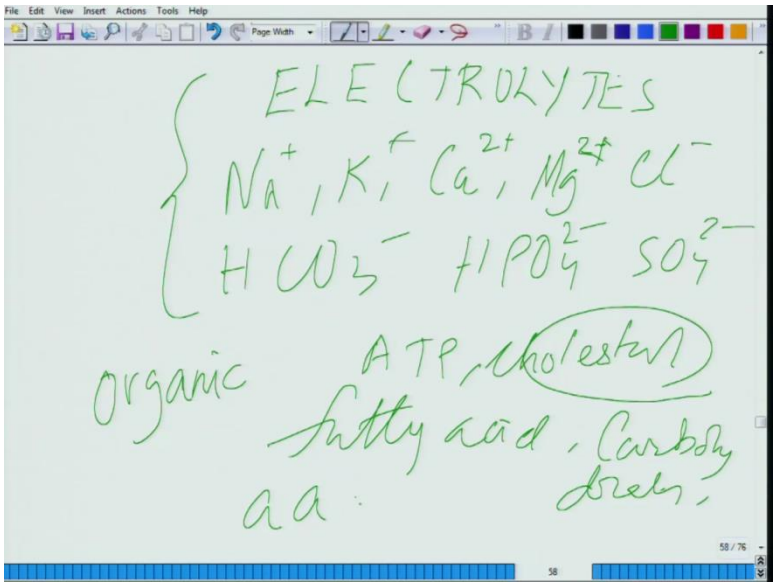

Now, let us talk about, the pure elemental composition in the form of the electrolytes. Let us get back to the slides and once again, the other solutes include electrolytes, which of course, you have sodium, potassium, calcium, magnesium, chloride, bi carbonate, phosphate, sulphates, likewise s two plus minus these are the series of electrolyte, then you have the in this fragment you have the organic nutrients, which includes your A T P cholesterol. So, this is another one, fatty acids then you have a carbohydrate, we have amino acids likewise.

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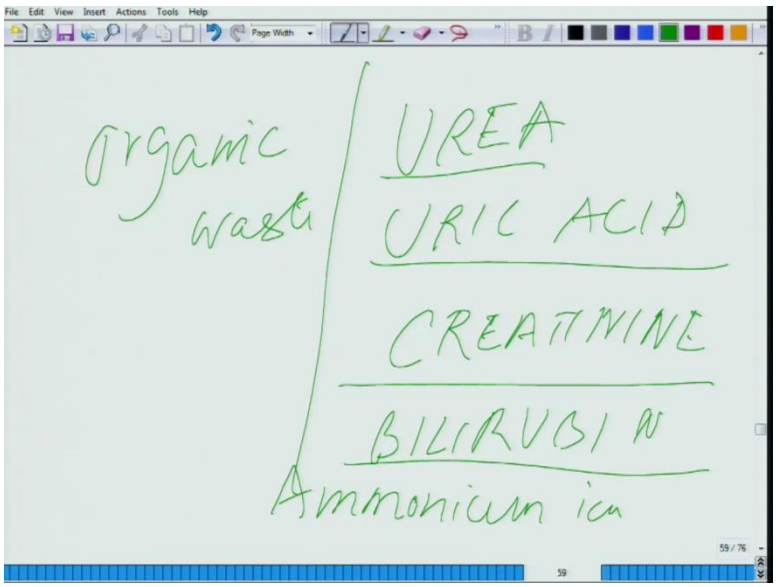

And then you have the organic wasted carries, which includes your urea, uric acid, creatinine, bilirubin, ammonium ion. Now, having enumerated this, I will request all of you, see whenever you get a blood profile check, what all the doctors can tell you, doctors can tell you get me the possibilities, the doctor can tell you, I wanted to see a blood cell profile. If the doctor asks for the blood cell profile what are the possibilities, either the R B C profile they will doctor is asking; or a W B C profile doctor is asking; or a platelet profile doctor is asking.

If the doctor is asking for a platelet profile, it is doctor has a suspicion about your clotting, maybe there is excessive clotting, or you know there is a lesser clotting, maybe something related to hemophilia or blockage in somewhere in the vessels. If the doctors talks about, W B C (s) then it has something to do with immunity fine. If the doctor talks to you about R B C, it has something to do with oxygen carrying capacity; or in anemic; or you are hyperactive; or you are carrying more oxygen. So, look at, from one simple fluid, these are the three aspect.

Now, if the doctor ask you, I want an uric acid profile or I wanted to know, what is the urea or ammonia, that essentially means doctor is doubting, you know how your kidney function is, because urea and uric acid this is all secreted by that whether through the kidney. Now, if the doctor ask, get me the potassium profile, this is very interesting, when the doctor asks for potassium profile, doctor may suspect that you may have some clotting problem. Because if you remember, I was telling you that potassium plays a very critical role in all kind of clotting mechanism.

If the doctor asks you, that I want like you know, profiles like electrolyte profile and doctor is may suspect, that you know your electrolyte exchange is being compromised. Then doctor may ask you, I want a lipid profile, this is also doctors will ask you, just give your blood sample will get a lipid profile. Then the doctors are aware of, is your cholesterol, is within control or is the good cholesterol and proportional our good and the bad cholesterol, are they balanced in an optimum zone or you are at the danger zone, you are at the susceptible zone for heart attacks or any kind of other disorders.

Then may ask for a lipid profile, so look at it, from one blood sample, you can predict almost just I mean randomly, I could tell you, at least fifty different situations, which could happen in your body, because always realize, whenever you study physiology

((Refer Time: 19:30)) very holistic thing, this whole blood is flowing all over your body. It is not only picking up the element which it has to through away from the body organic waste, it is also circulating the important compounds, which the body needs, for it is growth survival and maintaining the homiest cases.

As well as hemoeostasis, is the clotting, and homoeostasis is the complete balance of the body. So, that is why blood analysis and blood sampling is so very important, that a first thing doctor will say or if the doctor suspect diabetes, I want the fasting sugar, non fasting sugar. So, try to look through any of those risk like the blood report, and see on one column you will see, what that what the analysis as told you. And the other column they will see, this is the control, this is the maximum allowed, minimum allowed zone, and this is the normal zone.

And then you have to co relate, where your value falls, in terms of you know, the blood cell count or carbohydrate, urea, what is ever. Then doctor may tell you, I want bilirubin profile or the bilirubin concentration that is why doctor is basically essentially indicating, doctor is suspecting, you suffer from jaundice you know. So, these are some of the things, which a blood analysis can tell you, and that is why after giving some better for introduction about the blood, red blood cells and the platelets. I came to this topic that will help you to appreciate, why are we studying it in depth.

Now, what I will do after covering this part of the basic, the whole idea of blood testing and diagnostics and everything, what I will do, I will move on to the way the blood cells are formed. So, I will try to cover it in one slide with a pictorial representation, how within the bone marrow, from one single cell type, all the different cell types are getting differentiated, the left most column. We will be talking about red blood cells, only talking about the white blood cells; then we will be talking about the platelets. So, you know one slide, this is how I am planning that, that will take care of all your doubts, how these are being formed.

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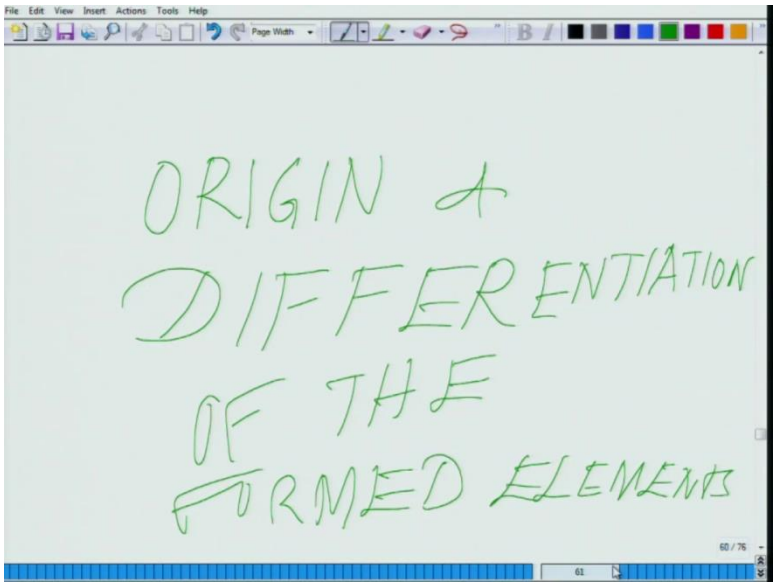

So, let us get back to the slide, and talk about the origin of the ((Refer Time: 22:04)) basically the origin and differentiation of formed element. Origin and differentiation the process by which a cell attains it final state, and differentiation of the formed elements ((Refer Time: 22:39)) back to it fine.

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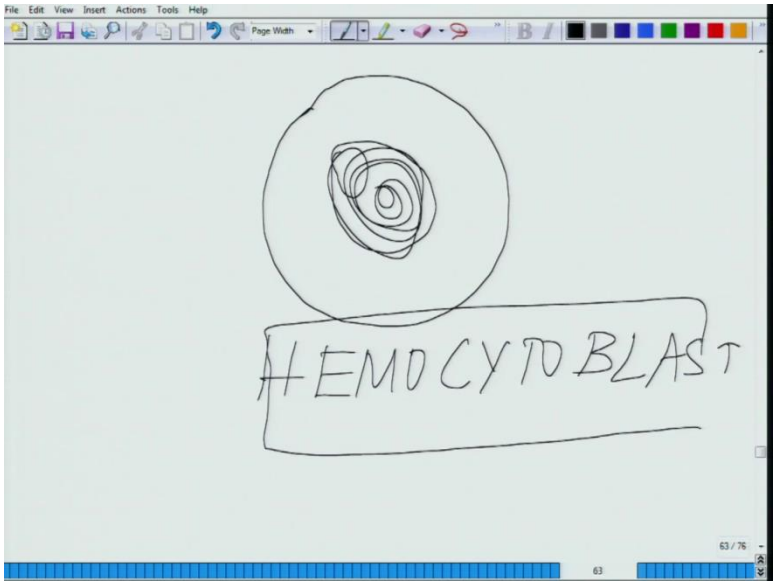

So, it starts with something called hemocytoblast, it is a huge cell though, this is the nucleus, hemo means blood, hemocytoblast this is the beginning point in the blood marrow, in the bone marrow.

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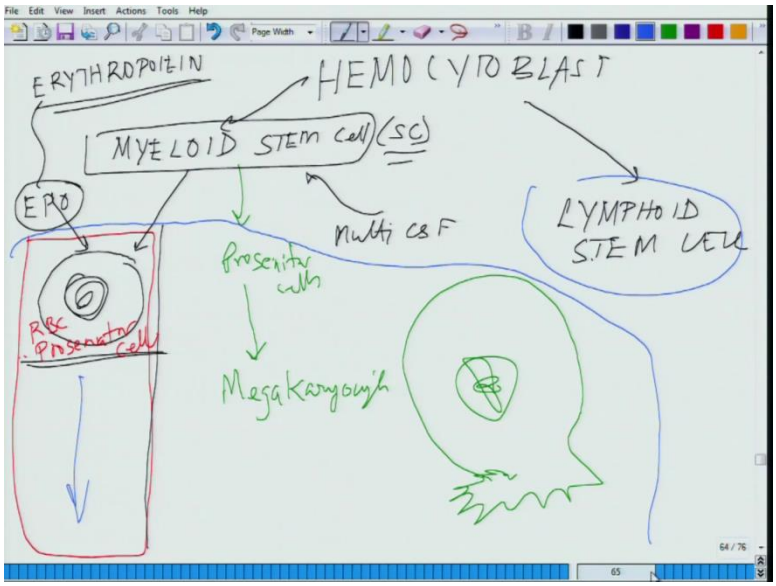

Hemocytoblast divides into two parts. So, hemocytoblast part of it from lymphoid stem cells, lymphoid stem cell and part of it from myeloid stem cells, myeloid stem cell I will just put s c henceforth, because that will help me ease. So, then this myeloid stem cells under then fence of factor called multi c s f, they form certain elements called and of course, there are few other molecules which are involved in it, which is called erythropoltin E P O, erythropoltin the influence of E P O, some of these myeloid cells, from the picker cells for, so this is the zone where, we talking about all the R B C formation.

So, let me put it in red. So, these are the progenitor cells for the R B C, this is and I put it like this R B C progenitor cell. So, this what the R B C progenitor cells are forming. And there is another series of progenitor cells from myeloid they are forming I am putting them in green progenitor cells. These progenitor cells form something called mega karyocytes and these mega karyocytes are cells like these huge, huge cells like this.

So, what we will do, before I come back to the right side like all the lymphoid stem cells, and all other things, what I will do I will just talk about these two elements, I am just putting them in, these two elements, we will talk about first. Otherwise it will become very complex, we will talk about these two elements, what is happening here.

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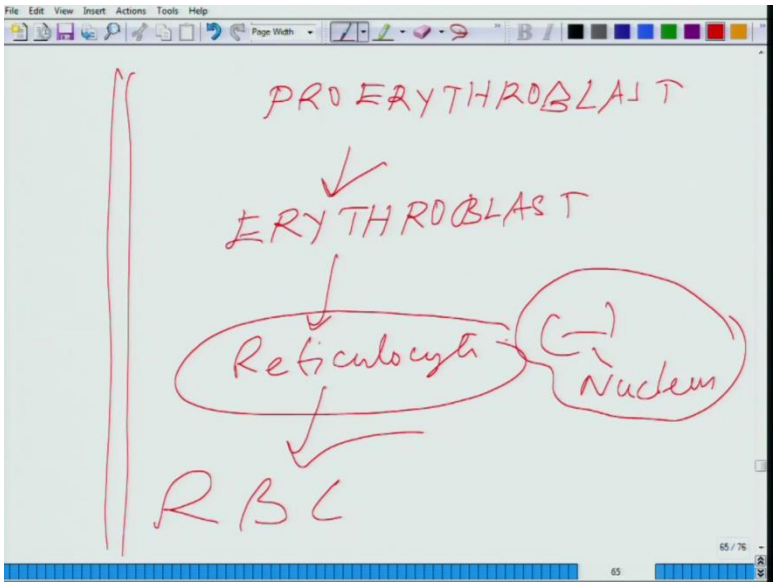

So, let us first of all talk about, what is happening to the R B C progenitor cells. So, we start with after the… So, the first series of cells are called pro erythroblast, this pro erythroblast reached into erythroblast stage, erythroblast is the other name for the R B C erythroblast. And from here, it forms something reticulocyte and reticulocyte is the phase, when it starts loosing the nucleus, which you remember I was showing in the first class, how there are losing the nucleus, because of fifteen lypoxyginous activity.

So, this is the zone, where the reticular site is the stage, when from erythroblast to reticular site formation, this is the stage when there is a sharp peak within the cytoplasm of fifteen lypoxyginous enzyme, which I have already discussed in the first class. And because of that fifteen lypoxyginous enzyme, all the different cells organelles and the nucleus completely get us damaged. So, the cell is only filled with hemoglobin molecule, with as for rest of it is life of 120 days, to carry oxygen. Farm reticular sites, what do you get is essentially, the R B C (s).

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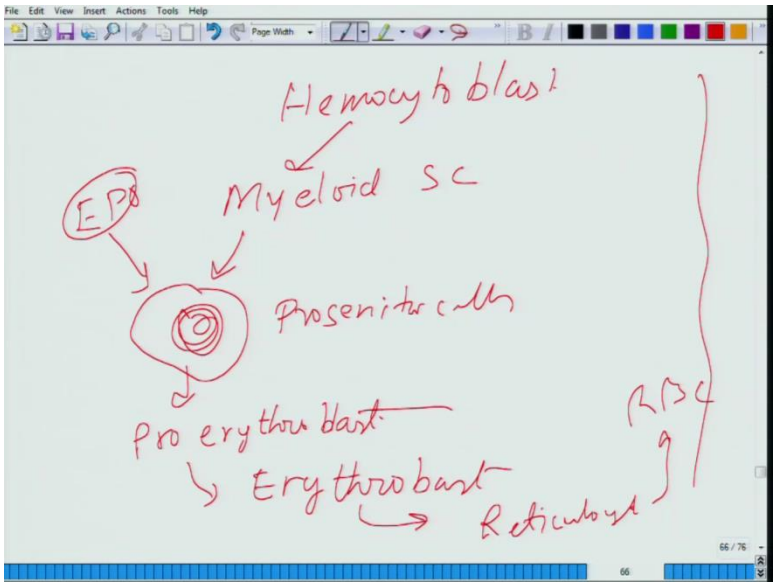

So, this is the pathway which is followed, which started with, if I summarize it, started with hemocytoblast; then you have myeloid stem cells, from myeloid stem cells, because of the influence of erythropoltin. Some of these progenitor cells, these are the progenitor cells, form pro erythroblast; and pro erythroblast becomes erythroblast; and then erythroblast becomes reticulocyte; and that becomes R B C. So, we have done with one set of reactions, which leads to the formation of the RBC (s). Now what we will do, will talk about the second one, which is the formation of the platelets or the clotting elements of the body.

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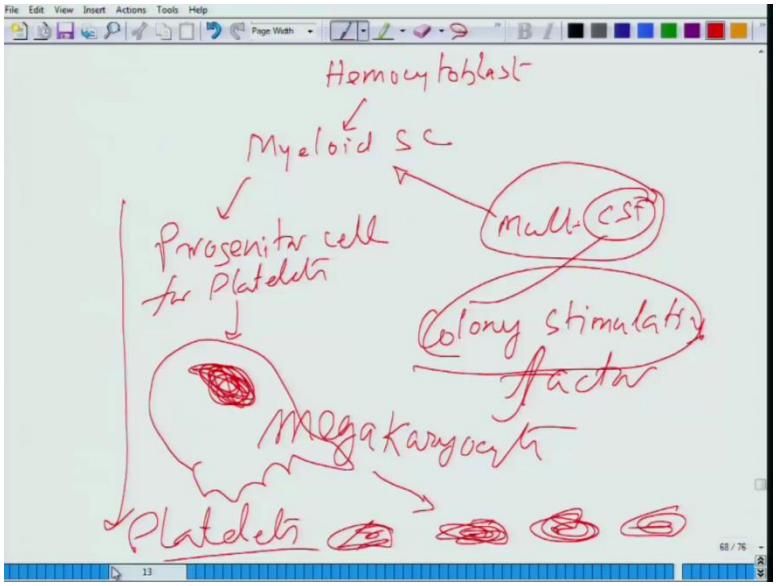

Let us get back to that, so what is happening here. So, same again, starting with hemocytoblast, hemocytoblast to myeloid stem cell, myeloid stem cells under the action of multi c s f which is multi c s f, stands for colony stimulating factor. This myeloid stem cells from a progenitor cells for progenitor cell for, which a destine to become platelets, the progenitor cells for platelets. And then they form a structure huge structure called mega karyocytes; of course, mega karyocytes has nucleus mind it. Mega karyocyte and this mega karyocytes then divide into small cells the platelets.

So, this is the second root, by the stimulation of the myeloid stem cells by colony stimulating factor, these cells form a huge cells called mega karyocytes then mega karyocytes started fragmenting. The basically, as I told you, platelets are fragments of a bigger cell, they do not have any nucleus, at least in our mammalian system a non mammalian; of course, in the thermo site they do, in need have, that is a ((Refer Time: 30:12)) different mechanism. We are not going discuss this here, so these fragments of the cells from the platelets.

Now, we come to the much bigger and the tougher one, which is how our immune cells have formed, because as of now we bye passed all that, we talked about the R B C (s), we talked about the platelets. Now, let us get back to that whole hemocytoblast; and we talked about the lymphoid stem cells; and I have not talked about. Now, I am going to talk about, part of the lymphoid stem cells, and part of the myeloid stem cells, and how they are leading to the formation of the different white blood cells, which are almost five types eosinophil, basophil, lymphocyte, lecocyte likewise, thus get into that. So, let us go to the next slide.

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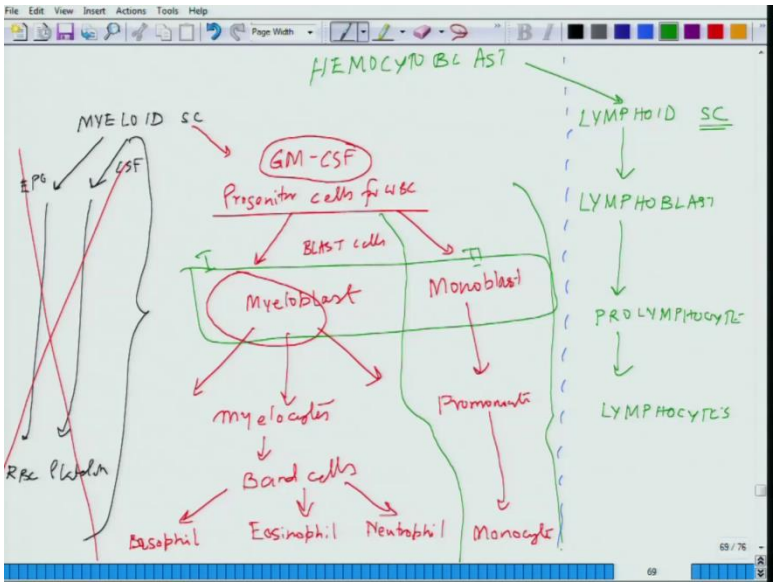

So, again we start with, hemocytoblast, under color hemocytoblast. So, I showed you the one classification on the one division on the side, they form lymphoid stem cell. Then lymphoid stem cells form something called lymphoblast; and lymphoblastform something called pro lymphocyte; and pro lymphocyte forms lymphocytes, this is one root. There are multiple root, which I am coming the next, so this is where, all the lymphocytes are forms. So, white blood cells could be classified into two groups, one group which has the lymphoid linage, they form from hemocytoblast to lymphoid cells.

And then through a cascade of lymphoid stem cells to lymphoblast, to pro lymphoblast and reaching all the way to lymphocytes. The lymphocytes are further classification, which all be coming soon, lymphocytes could be b cell t cell likewise, I am not getting to that at this point. So, this is one root which is the lymphoid root, but I showed you, that this is another route which is myeloid route, what is happening in the myeloid route, what they are responsible for, because already you have seen, when hemocytoblast is divide into myeloid route, it leads to the formation of W B C (s) RBC (s) and the platelet. Yet a part of these myeloid stem cells, do form other components of the white blood cells.

So, we will now discuss that is second route, which is, so hemocytoblast to, what I will do, I just pick up another color, so that, will make your slide easy to understand. We have already talked about two routes, so hemocytoblast let us do it like this; this is a

wrong way to show it fine. Here, let us put the myeloid stem cells, myeloid stem cells, from myeloid stem cells, I talked to you, that through erythropotlin something is form R B C (s), this part is all taking care. Then through colony stimulating factor, some of the cells are forming platelets, this part is all done. So, we are not going to deal with this part.

Now, we will talk about, what is happening to myeloid stem cells, then out here, some of the myeloid stem cells are, and this ((Refer Time: 34:22)) influence of g m and c s f colony stimulating factors, to progenitor cells which are distinct to become white blood cells, progenitor cells for W B C white blood cells. These progenitor cells then divide into two parts, these are called one part, they all fall under one part which are called blast cells, these are called myeloblast. This myeloblast further form three kinds of myelocytes, these myelocytes then form something called band cells, and these band cells form three different white blood cells, one is called basophil, the other one is called eosinophil, third one is called neutrophil.

Whereas, there is another route I showed you, is something which form, there is some myoblast is form, monoblast. This monoblast form then called promonocyte; and promonocyte form monocyte. So, this is the other route, which is of course, let me separate it out at this point, this is the demarcation taking place. This is where the two different cell types are getting separated from here, this is one type one separation, this is the second separation and this is the second route, so in some total, your basophile. So, if you look at it, what are the different kinds of white blood cells, you have basophile; you have eosinophill; you have neutrophill; you have monocyte, which are coming from myeloid lineage.

And your lymphocytes, which is coming from lymphoid lineage, so some in somewhere in some total and they are five different kind of W B C (s). Now if you in the light of this information, if you look at the blood chart, when the doctor ask you that, get me the blood report, they will say eosinophill concentration is higher. Generally, whenever you have persistent sneezing or something doctor told you are suffering from eosinophiliya, what does that mean; that means, your eosinophill cell number has gone up, these eosinophill what you see, I which I draw, which has coming from myeloblast and myelocytes and the band cells.

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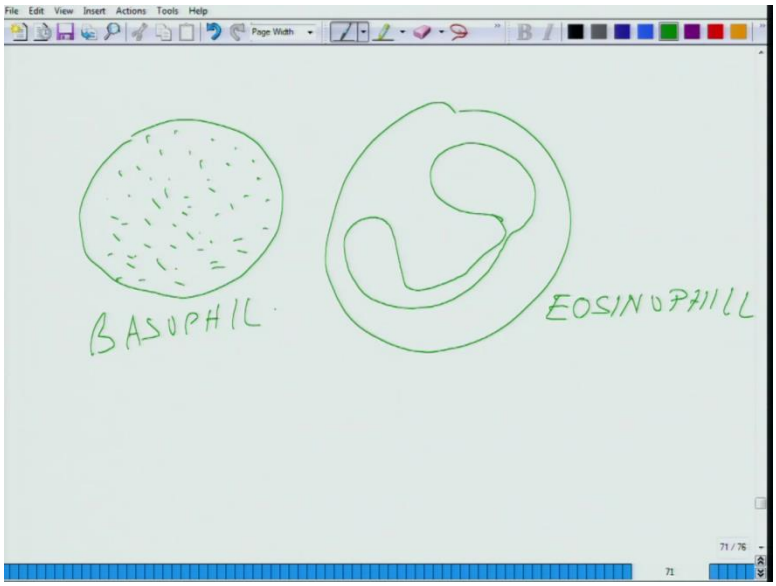

And if you look under the microscope, how they look like, they look something like this. All this different now under, so basophile looks like this, there are a lot of pigments all over the place. And if you look at eosinophill, eosinophill cells will look like this, something like this. So, this is eosinophill, this is of course, they have to be puts different kind of dyes, in order to color them.

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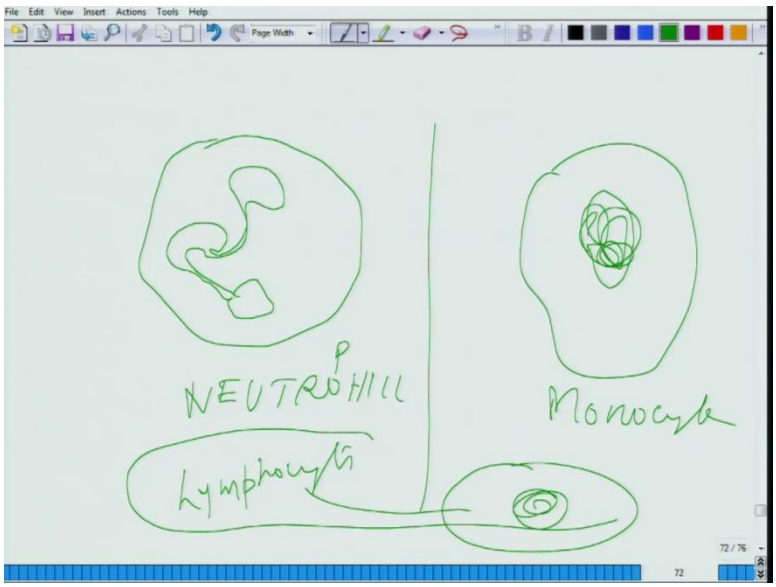

Then if you look at the neutrophill, it sizes are fairly close to each other I mean. So, these are all multi nucleated cells. So, this is called neutrophill, then you have monocytes,

which is more compact kind of you know, this is monocyte and of course, lymphocytes also slightly smaller though like this, which is lymphocyte, so coming back, so in if I had to summarize it. So, we talk about hemocytoblast, myeloid origin, where hemocytoblast divided into myeloid lineage, lymphoid lineage; myeloid lineage leads to the formation of R B C (s) platelets and basophile, eosinophill, neutrophill, monocyte, which are all clubbed under the category of white blood cells.

And there is another set of white blood cells, which are of lymphoid origin, which are formed by the, from the lymphoid lineage, which are called lymphocytes. And lymphocytes are further divided, whatever we will do now, after telling you this, I want you guys to visualize, whenever you heard about somebody has a blood cancer, what really happens? Now, in the light of this whole differentiation what I highlighted, in the bone marrow what is happening from hemocytoblast, think of it how tightly this whole process is regulated, each cell number has to be right; if it is wrong then there is a problem.

It is cell number has to be, has to be twit in such a way that if something goes bad, you may suffer from hemophilia; you may suffer from clotting disorder; you may suffer from anemia; oxygen or you may suffer from or you may have higher oxygen carrying capacity, if you are fortunate. Then you will be very hyper, hyperactive you may have more number of, more you may be immune compromised aids, you are immune compromised. So, immune compromisation means, you have problem with your white blood cells.

So, in the light of this whole differentiation process from how from the hemocytoblast, this whole differentiation of blood cells is forming, all throughout your life, within the bone marrow; that means, there is enormous researches taking place across the world. To understand this process, because this is that zone where lies, some of our answer to cancer, because you have to understand cancer, this is where we have to hit upon, one of the of course, related to the blood cancer, this is why it is.

Because, this whole differentiation is very, very tightly regulated, I mean like you know, there is one flow from it is the patient suffers. So, that was the so reason why I took this whole class single like in a exclusively to give you in the light of this, when you look at the whole thing, that will make more sense to you, then looking them at you know, small

fragment ((Refer Time: 41:38)) pieces. So, that is why the blood analysis are is so very important that you know, what are you analyzing in the form of blood, that is the sole reason, why I just started with your R B C (s) talk to about the clotting.

And then came to an introduce you to the whole lineage of W B C (s), how they are formed is from the same cell. So, what regulates, some of the open ended questions, which remain, which are to be answered by mankind is that, what is so unique from the same population of cell; some becomes R B C (s); some became neutrophill; some became platelets could we. So, the future of tissue engineering, future of differentiation development biology is that, could I pickup any cell, any blood cell or those kind of proginated cells like hemocytoblast.

And say, I need more number of platelets or I need more number of R B C (s) and could we put it back, that is the translation medicine where it is all heading, could you do that, that is the future where it lies, could we control the differentiation in the development of these different kinds of a formed elements. And if we could, and how we could, this is what lies, some of the very, very challenging questions of next century or this century as a matter of fact, that could we really do that, could we cure, a patient of blood cancer, that you know, we know do not worry, we can take out a cell or there is another way, could we take any kind of stem cells, and transform them into blood cells or any other cell type.

So, these are some of the very open ended questions, which for which ((Refer Time: 43:23)) thriving all over the world, the scientist are working day and night to figure out, some of these answers. Because, it is very easy to see the chart, and ((Refer Time: 43:32)) the fact is physiology is far beyond those charts, how really to do that; of course, this is only bits and pieces. And may if you look at, if you go back to this, go back to this chart what I was trying to draw and show you guys, like think of it, there are so many factors, which are involved, which about which you have no idea, which are really leading to this, what is leading to this, what are the signal.

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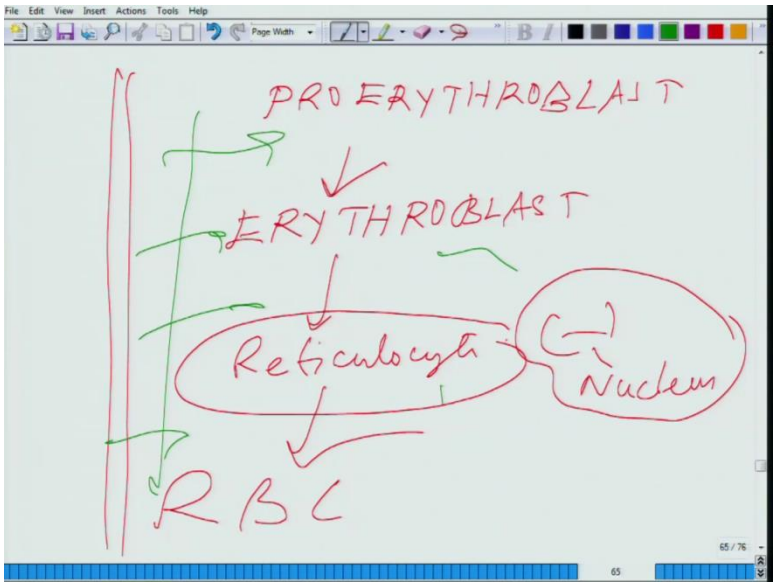

So, that is where lies a lot of unanswered questions out here or say for example here, proerythroblast, erythroblast, reticulocyte there are so many factors, what are those factors, and those are happening at those are very small molecules. There expressed for a moment, and that is it removed out, how we can control differentiation, these are some of the questions. And that is why, that whole chart I wished you guys to redraw that chart in a bigger paper, so that because there is a size and limitations of this screen the I cannot draw everything, unless I am in a black board, where I can have the whole end.

So, I want you guys to you know redraw this whole thing, what I have covered now, as of now that will give you a kind of understanding, how this whole process is taking place. So, what I will do now, probably in the next class, what I will be doing is that, will be talking about the function of the different W B C (s) and will talk about little bit of the immunity and little bit about the r h factor. There couple of things which I have not touched. So, let me tell you, what are we touching in the next class, I will be talking about the blood groupings, the you guys have heard this, a plus b plus o and what is blood grouping really, that is one aspect what I am going to touch.

Second I am going to touch about little bit of immunity, third I am going to touch about all the different kinds of W B C (s) which are present. So, all the different kinds of W B C (s) blood grouping and bit of an r h factor, r h positive, r h negative, and how that

influences the pregnancy will talk about all these things. And little bit of immunity, and that is where will close in, with this section of blood cells, immunity and clotting.

Thanks for your attention.