Animal Physiology
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Module - 1
Lecture - 33

Welcome back to the lecture series on animal physiology in NPTEL. So, we are in section 6 which is a blood cells immunity and clotting. So, initially we have dealt with blood cells in the first lecture in the section. And I am just bypassing the immunity section and I am moving out of the clotting and I will come back to the immunity. So, when I was explaining of about the different kind of blood cells I told you that there are proudly speaking. There are three kinds of blood cells red blood cells white blood cells and the platelets and the red blood cells are the cells, which has no nucleus. And I explained you how the nucleus kind of gets degenerated during the formation of these cells and I also mentioned that. These red blood cells have a life of 100 to 100 20 days after which they are engulfed by the macrophages or the white blood cells.

And they are being you know they are being destroyed and all the iron and all other thing which makes the hemoglobin molecule is being reabsorbed by the body. So, that was pretty much about the red blood cells and I have not discussed 1 part which I will be doing in summation once I will be winding up this whole section is how all these cells are developed, but apart from. So, among these 2, 3 kind of blood cells red blood cells white blood cells and the platelets this third type the platelets. They also do not have nucleus, but there is something more interesting about these cells. So, they are not purely really cells they are something they do not have any nucleus other than. So, mark my word there are few invertebrates they have platelets or some other maybe they are some other vertebrates, which have platelet with nucleus.

But in human being the platelets are not having a nucleus they are essentially something like that. They are cellular pieces you can call it suppose there is a huge cell and it kind of you know chopped down into pieces. So, what happens part of the cytoplasm engulfed into a bilipid membrane and those are kind of small vesicle like structure. And they are around 3 to 4 micron or I mean long and they are kind of elongated shape kind of cells. It is kind of if you look it under the microscope if you take a blood smear. And look it

under the microscope it looks more or less like a it is a triangular kind of shape at a low resolution microscope. They look like you know like you know this something like this, this kind of shape of cells. But, these in nucleated or without nucleated nucleus cells are of extreme importance for some one of the very interesting phenomena which is called blood clotting or in other word the repair of the blood vessels.

So, while talking about this let us take a simple system simple physical system say for example, you make a pipe, so say for example, so you see this. So, I role it round like this something like a pipe structure, so you could see this is a see through pipe out here. So, say for example, fluid flows through this pipe and it is all sealed all from the top to bottom ok now, say for example, I you create by sum reason a hole is formed. So, what is ever the fluid flowing through it will start oozing out. And eventually that hole will be become bigger and bigger and bigger and eventually no fluid can flow this whole thing will kind of you know tera apart into 2 pieces fine. But if that happens say for example, in your blood vessel then this is a serious problem the blood would not flow.

And basically we will die oxygen would not be supplied to all parts of the body. And blood will mix up in the outer extra cellular space and we will laws all we will lose all the nutrients and everything will be in a mess. So, and yet we are always prone to injuries you know you fell down what you see essentially is that you fell down. So, blood starts coming out from x y z part of your body and then after sometime it stops. And then what you see is that after few days you see a kind of a hard tissue forms there and eventually that is also wipes off. And you are hail and hearty so there is a self repairing mechanism. And this self repairing mechanism of the blood vessel is initiated by the process called blood clotting which is a very controlled process. It has to be regulated at a very to the very I should say precise fine tuning why is it, so is that if the repair mechanism exceeds certain limit.

Then it will lead to blood clots blood clot means you know globules say for example. The blood is flowing through this these are basically particles these are cells. So, if there is a clot it would form a kind of lump like structure if a huge lump kind of you know gets here. This is going to block the flow of the fluid, so but if there is a damage. Then it has to be repaired, so there will be some degree of clotting, but clotting has to be regulated in a very fine tuned fashion. And this whole clotting mechanism of one of the central player in this clotting mechanism is the platelet cells platelets are you can call them. The in a

simple analogy the tailors of the blood vessels they are just like tailor they go whenever. There is stitching is needed or the stitching elements of the blood vessel they go there and stitch the part which is broken. And this whole cascade of clotting is divided into 3 different stages they are vascular first is the vascular stage.

And I will come to that then there is a platelet movement stage then there is a clotting coagulation state. But it is a chain of reaction which initiates at 0 or the first the exact movement when there is a kind of a rupture in the blood vessels. And within 15 to 30 seconds pretty much all the process comes into play. So, but in order to understand this whole process we need to divide it into different compartments. So phase 1 phase 2 phase 3 but mind it pretty much all the phases overlap with the other 1 it is not like that 1 phase is exclusive .And then the second 1 takes place and then the third 1 takes place, so they are all overlapped with each other. That is something to understand it is not something like you know 1 phase stand alone second phase stand alone.

And third phase stand alone there is another thing which you have to understand why I am telling I will giving you the overview. Because that will help you once I will get in the technical details. There are two major component which are involved in this whole process first component is the blood component the platelets. And all those components red blood cells white blood cells which are flowing through it those, component are called intrinsic components.

And there is another set of components who are not part of the blood. They are in every part of the vessel like you know in the endothelial cells or the surrounding tissue. And those are called extrinsic factors so; this is regulated by extrinsic factor and intrinsic factors and these different intrinsic. And extrinsic factors are responsible for regulating the different feedback mechanism which are involved in it controlling the flow of a controlling. The secretion of different kind of molecules which will regulate this whole process, so it is a very fine tuned very well organized process starting from the formation of the platelets. So, what we will do now I will give you some of the simple details which is essential for you to you know grasp the topic. And then we will go technically 1 by 1 at the different stages and I will try to make it as diagrammatic as possible.

So, that it helps you to visualize this in front of you how this whole process is taking place. So, let us first of all get some of the technical details of the platelet cell how the

platelet is forming. So, diagrammatically how it looks like how small those are what is number you are talking about mind. It this is 1 thing you people wish to kind of retain in your mind that if the half life of a red blood cell is 100 20 days half life of a platelet is very low very, very, very low. That is almost maybe a day or less than that that is the half life of a platelet we will come to those. We will come to those some of those, tick some of those logistically statistical details which you need to know. Then the technical aspect of it, but it has to be very clear in your visualization how this whole process of rupture. And what immediately happens, what are the cascade of your actions has to be very, very clear in your mind.

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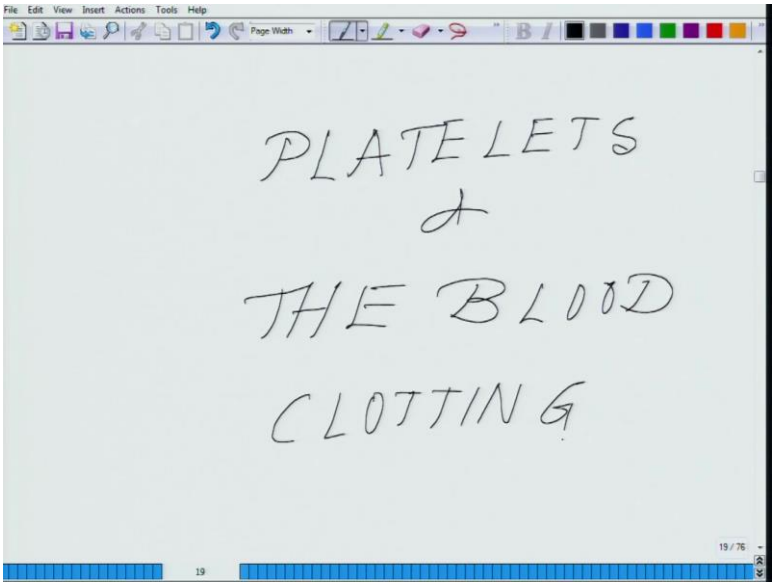

Let us get into the some of the technical details what we are talking about, so here we are talking about the platelets and the blood clotting blood clotting.

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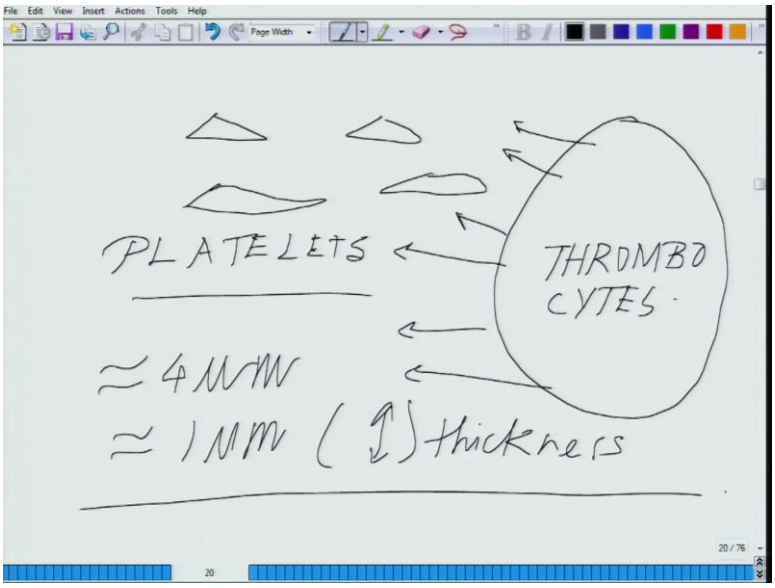

So, in this section, so basically what we are trying to do is, so I told you that with if you look at the platelet they look like this something like you know. This kind of they do not have any nucleus, so essentially how they are formed is basically they huge cells. And these huge cells specially what you see is these are basically called thrombocytes. And from there comes these smaller fragments which forms the platelets and their average diameter is around 4 mm and roughly 1 mm of the thickness.

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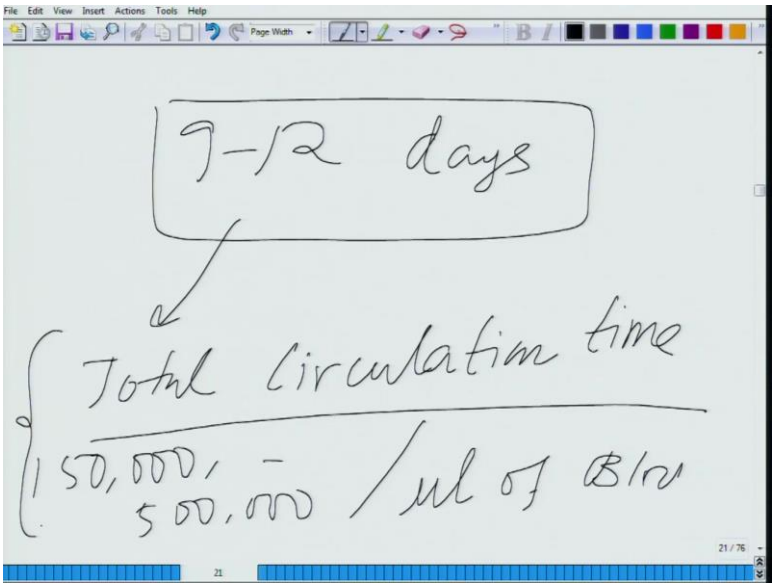

This is essentially is about talking about their size and they are essentially are individual they are different fragments and their half life is 9 to 1 days sorry. This is the total days total circulation time and at times it could be even a day. And each micro liter of blood per micro liter of blood contains they you can call them as particle 100 to... So, this is these are some of the statistics which I would recommend you to remember.

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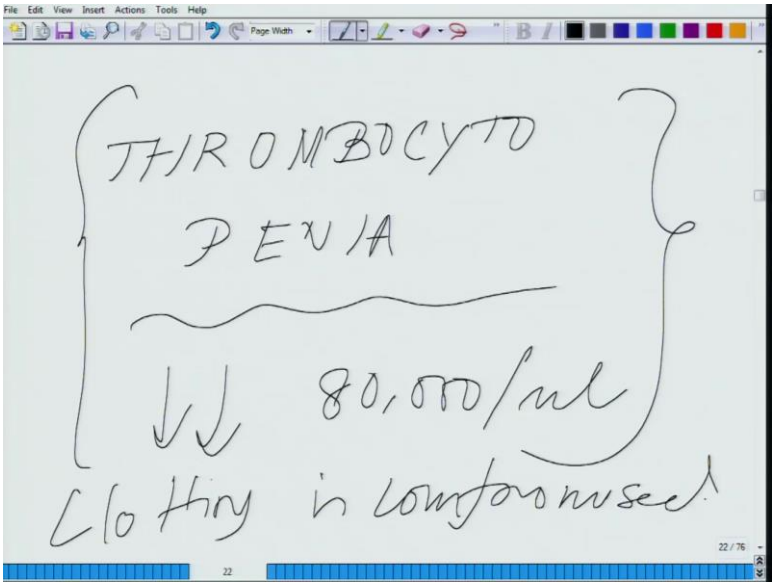

And some of the disease related to platelets are thrombocytopenia t h r o t h r o m b o thrombocyto penia where essentially the platelet count is very low around 80,000 per micro liter. And automatically such patients have clotting it will be compromised this is one of the major problems such patient faces.

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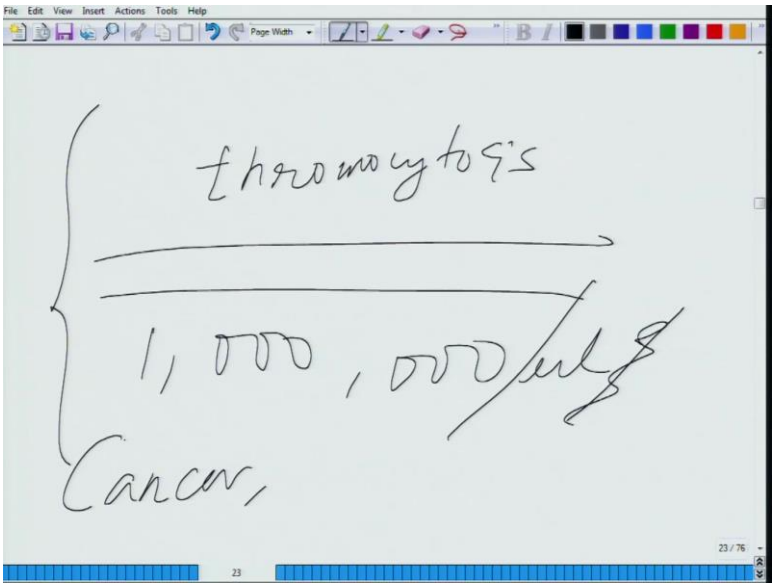

And then you have thrombocytos these are the patient whose platelet count goes extremely high per micro liter sorry. So, these, this this is a situation which happens sometimes in cancer some kind of inflammation disorder and all the things. So, if you look it in terms of the number these are fairly high in terms of the number. And this number has to be regulated very tightly as the number goes up then also. There is a problem as the number goes down then there is a problem. The reason is that your size of a blood vessel or the dimension of your blood vessel is limited and it has a limited degree of elastic feature. So, if the total number of particle goes up as it happens in thrombocytosis automatically. The viscosity of the blood increases big time when the viscosity increases the flow reduces.

So, automatically if the part of the body needs oxygen at a certain period of time. So, the oxygen will be reaching slowly, because the blood has to there are too many particle. It is just like you know a muddy water flowing through think of it a huge amount of muddy water that flows slowly. Because the total number of particles are very huge in that situation where as if it goes low say for example, a the thrombocytopenia where your platelet count has gone down. So, in that situation the problem is that if there is a, damage blood vessel damage then the total number of platelet which has to reach to that spot will be less. And there would not be any significant backup coming, so automatically such patients are prone to excess blood loss, so these are the 2 extreme situation.

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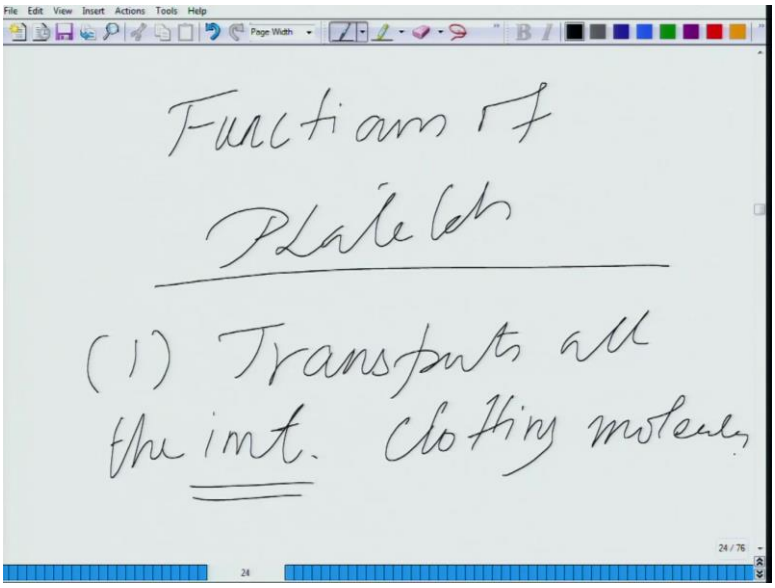

And now what we will do I will enumerate all the different functions of platelets let us get into the functions of platelets, so among the functions. So, basically it is a transporting it transports all the important all the important clotting molecules this is the major function by this time, it is very speculative people.

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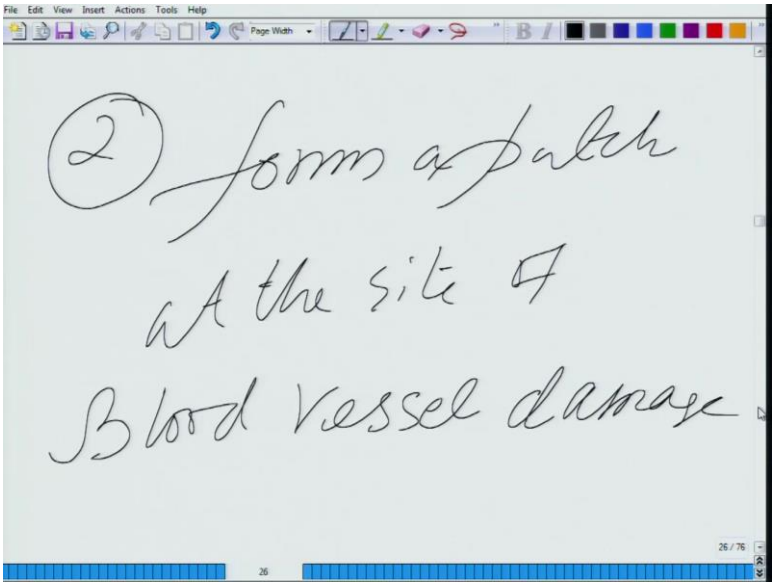

And then apart from it is it forms a patch at the site of blood vessel damage this is the second major function.

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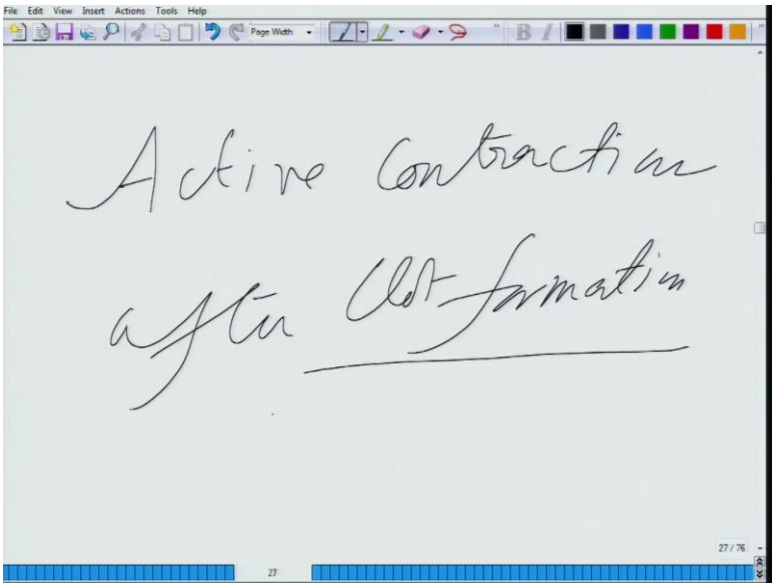

The third major function it has it is it has an active contraction after clot formation in other word what that essentially means is that once. The clot is formed after some time once the whole repairing of the vessel has taken place then it has to retract it back that clot has to retract back. It has to be moved out otherwise you will always say for example, you have a cut here after the cut is kind of repaired. And the clot has to be you know moved out it has to be thrown out of the system otherwise there will be always a scar out there. So, this scar has to be moved out, so that is called clot retraction process. So, these are the 3 major functions which is which is very, very tightly regulated with a optimal number of platelets in your body. And which are regulated by a cascade of chemical reactions what we are going to talk now ok.

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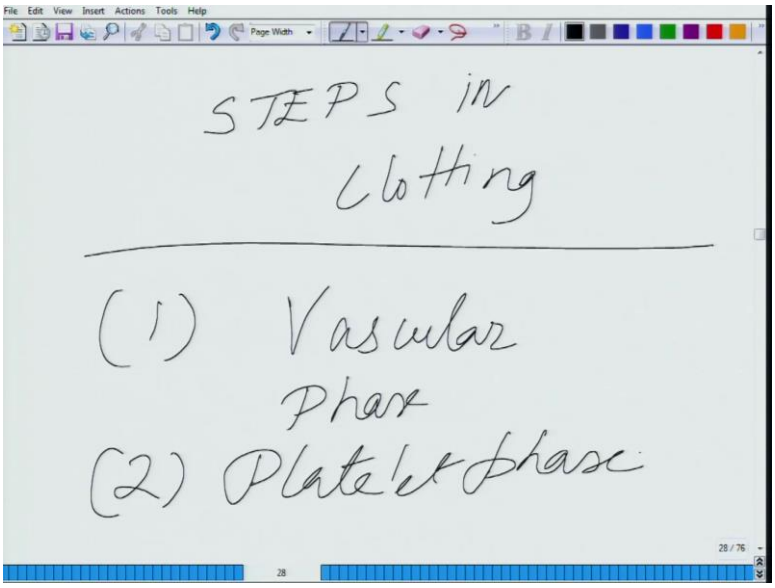

So, let us talk about as I told you in the beginning it is a cascade of 3 step reaction, so now, what we will do I will enumerate first of all I will enumerate all the 3 different states which are involved in the clotting. And then we will pick 1 step after another and we will discuss what exactly happens in those states. So, now I was talking about the stages steps or in clotting step 1 basically is your, so this whole. So, that is 1 step is called the vascular phase phase 1 phase 2 is platelet phase which is phase 2.

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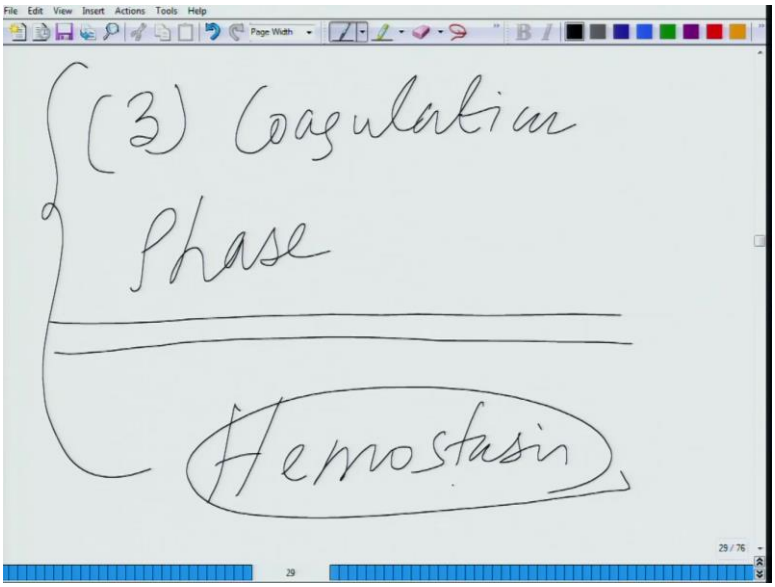

And there is a third phase which is called coagulation phase which is the coagulation phase. These are the 3 phases, which are involved in the whole process of hemostasis, so this whole process is called hemostasis.

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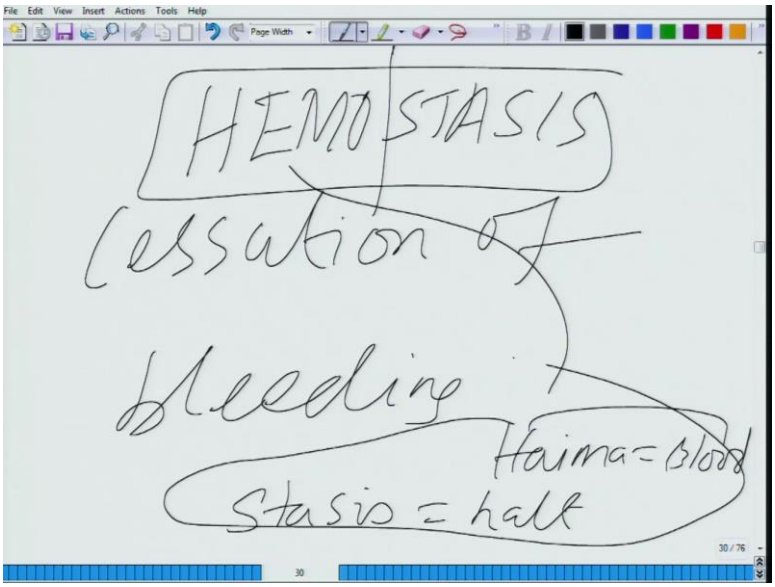

Essentially what does that mean is that hemostasis means cessation of bleeding h e m o hemo stasis where basically if you break. This word haima means blood in in Greek; haima means blood and stasis means halt halting the blood the leakage of blood.

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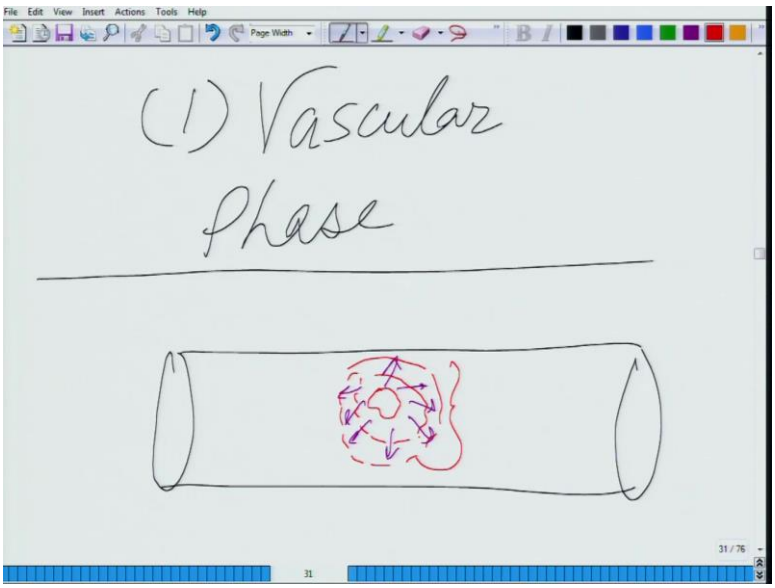

So, now what we will do? We will start with the vascular phase what really vascular phase is about. So, in order to explain the vascular phase I will again take the, this analogy which will help you, so I had this paper, so I roll this paper. So, this is imagine this is a blood vessel now say for example, there is a leakage somewhere or imagine somewhere. So, if there is a leakage here, so essentially what happens as more and more pressure goes the leak the leaky spot goes becomes bigger or something like this. So, so imagine this is the vessel and you have a kind of leak here.

So, essentially this is how it works inanimate object like this this leak goes on increasing. And eventually this leaky thing becomes this big. And then that becomes this big likewise this thing increases but, the case of blood vessels. There is something called a phenomena called vascular spasm takes place whenever. There is a damage what vascular spasm means essentially what vascular spasm means say for example, I have taken extreme example to explain this. So, if this is a blood vessel imagine this is your blood vessel through which the blood is flowing through.

Now, if there is a cut something like this I am cutting it into 2 pieces, so this is the part of the vessel and this is the other part of the vessel. So, what happens is that under this situation these sites these 2 sites become narrows down. So, the diameter of these 2 ends damaged end becomes narrowed something like this. Now, if you look at it they become narrow down the diameter here is more and diameter here is less. And this process is a inherent tendency of the smooth muscles which are forming the blood vessels along. The endothelial coverage, so they contract like this and this contraction process.

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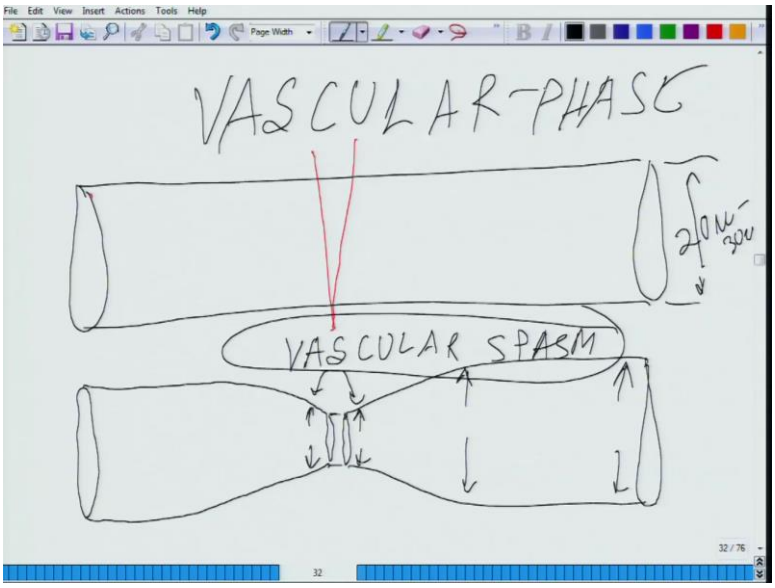

So, essentially if I have to draw this it will be something like this, so imagine this is your, this is your blood vessel fine. So, now there you say for example, you create a cut out here, so then what will happen this vessel this is the vascular spasm situation. So, here the diameter if you look at diameters out here this is all same or their diameter here is far reduced. And this reduction is diameter at times so; imagine if this vessel is like you know some save the thickness of this vessel. If the cross section of this vessel is same say for example, or say 20 microns or say 30 micron. So, at that level there is a significant reduction out here and this whole change is called vascular spasm. This is a very, very critical step in the formation of the vascular phase this is part of the vascular phase.

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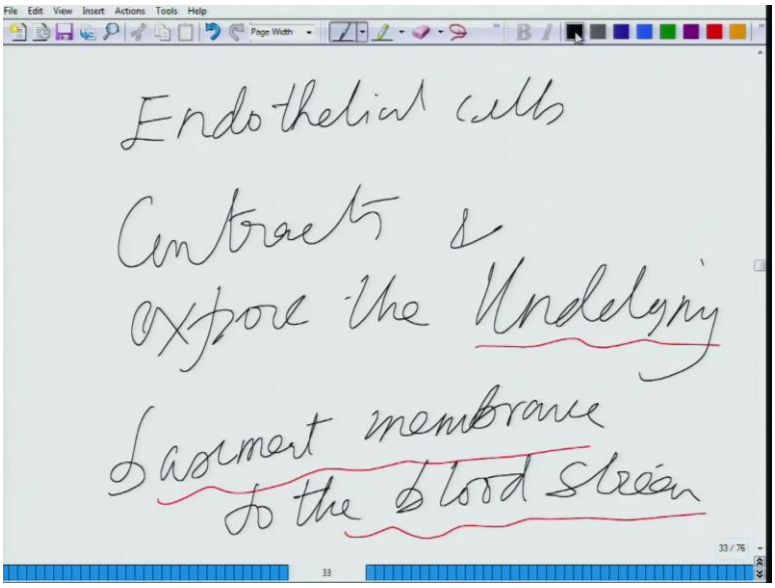

So, next thing what happens in this is that this is regulated by the endothelial cells endothelial cells contracts as I was telling you. And expose the underlying basement membrane to the bloodstream the important part is that this part underlying. The basement membrane to the bloodstream, because this is where another next set of reactions starts to take place in the vascular spasm phase.

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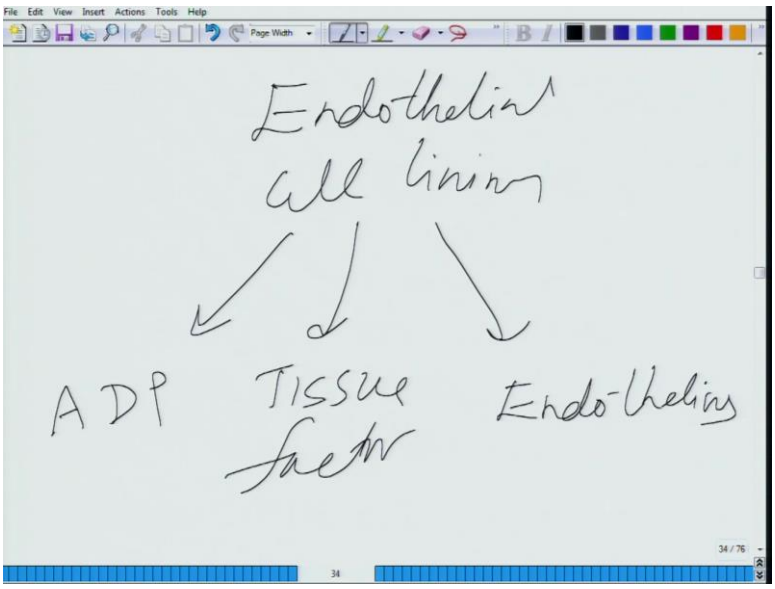

So, what essentially happens is this then this endothelial cell lining cell lining secretes certain compounds which includes your a d p tissue factor. And endothelins these are the

different factors which are secreted endothelins these are different factors which are being secreted at that point.

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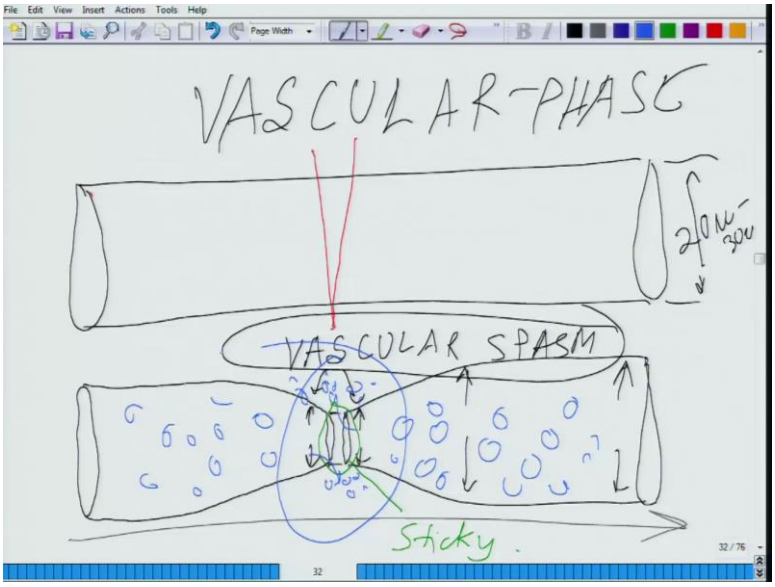

And this one more thing what happens at this phase these 2 zones these 2 zones become fairly sticky. So, in other word if I have to again take the paper analogy out here which will help you to understand let me get it. So, these 2 big ends start to secrete certain things which makes it really more sticky, so they try to you know glue together. It is just like there you put some glue and they started to glue together slowly. So, these are some of the reactions which takes place in the endothelial phase. And what we will do now I will just put them in a drawing in a in a diagram.

So, that from there we could guide you to the next level which is the, which essentially is the platelet phase, because as soon as there is. So, for example, if imagine these are the blood cells which are moving these the blue ones are the blood cells blood cells which are travelling along it. And just imagine that the direction of this thing is like this, so as soon these are damaged here. So, these cells are coming out and this is what is the blood is flowing out, so at this stage certain thing happens.

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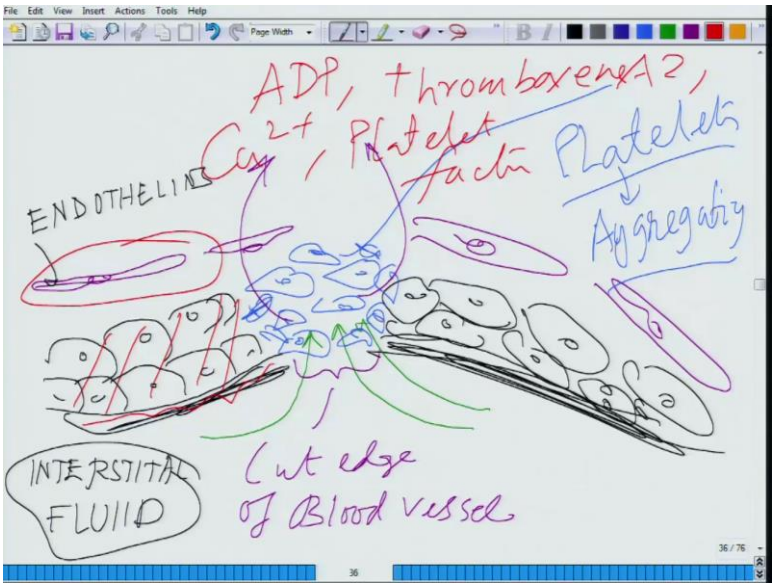

And this is I will put it diagrammatically that will help you to appreciate what exactly happens at that point, so if I have to draw it really in terms of. So, now, I will put all the cells in place likewise these are the endothelial cells of the basement membrane. And something like this are the nucleus see these are the cells all over the place and this is the blood vessel, so I am putting all the cellular structures in place. And this is the basement membrane and this is the zone where this is the zone cut edge of blood vessel. And here you have the the blood the upper part of the blood vessels and here you have the let me pick up another color endothelial cells out here likewise. And here you have the interstitial fluid on this side interstitial fluid and these are endothelins. And this is what essentially happens so; as soon as there is a breakage here the platelet starts to come out at the zone, because they are the smallest one. So, now, in the blue you see the platelets all over the place these are the blue cells are the platelets.

And platelets tries to aggregate at this spot, so these are the platelets, so what is happening is that they are aggregating at the site of injury while. They are aggregating simultaneously from the platelet as well as from the surrounding there are secretion of certain factors. And the secretion could take place either from these cells what I am just shedding in red. Now, from these cells as well as from these cells as well as from these cells what I circulated put the circle. So, this leads to the secretion of a d p thromboxene A 2 thromboxene a, 2 calcium and platelet factors. So, at the site of injury these are the different compounds which are being secreted out.

And next phase comes is the platelet phase, so and mind it these are all happening like you know fraction of a moment like within 15 seconds of the injury. The platelet started to accumulate at the site as drawing with all the blue cells. What you see those are accumulating at that spot and that initiates the platelet phase. So, there is a overlapping and mind it vascular phase is continuing, because it is still there is secretion of chemicals which will continue for few more hours. So, it is not as I was telling in the beginning it is not a water take compound phase 1 phase 2 phase 3 no phase 1 phase 2 and there is a phase 3, they are all overlapping on one another.

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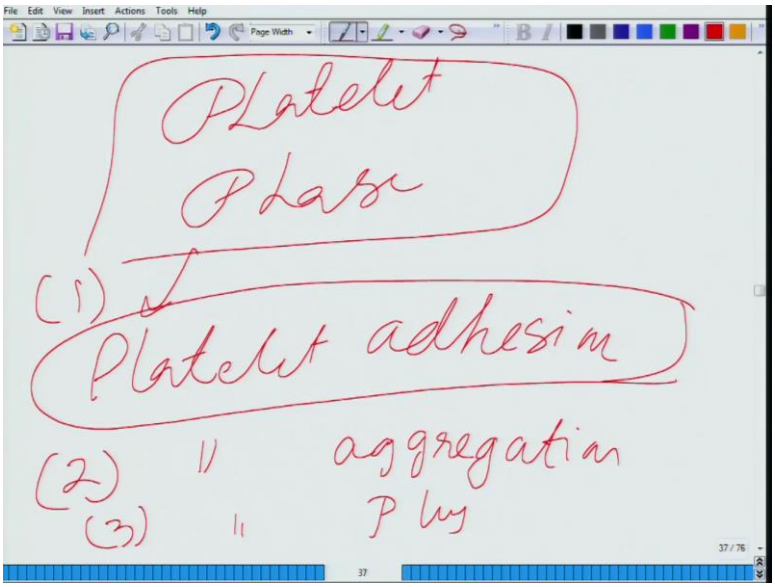

So, now we will diagrammatically show the platelet phase the phase 2 coming back to the slides, so now, you are into the platelet phase. So, platelet phase is shown by first is first reaction is platelet adhesion as I told you that at that site at the site of injury. There is an adhesive sticky situation then this form platelet aggregation, because of that aggregation platelet aggregation. And third phase is forming platelet plug these are the 3 things which happens at that phase.

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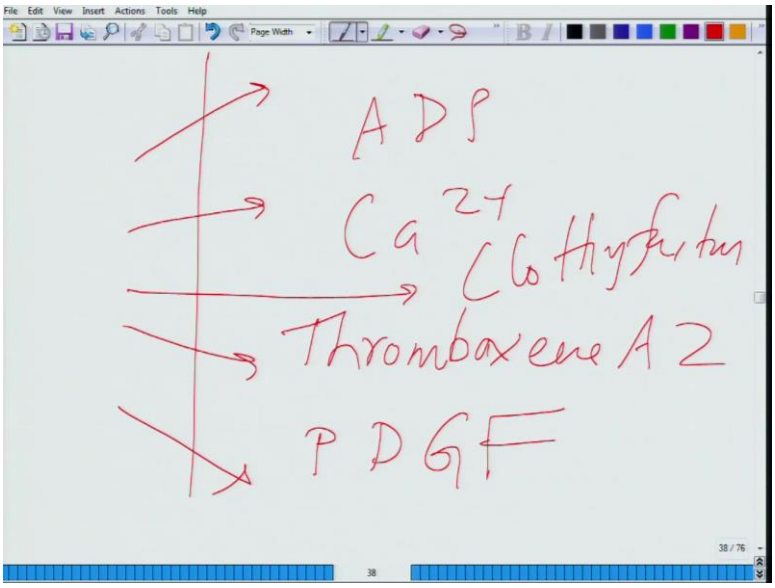

And apart from it as I was enumerating there are secretion of a bunch of compounds which takes place which includes ADP calcium thromboxene A 2. And you have PDGF platelet derived growth factors and you have the calcium ions. And you have few there clotting factors, these are different factors which are secreted at this phase.

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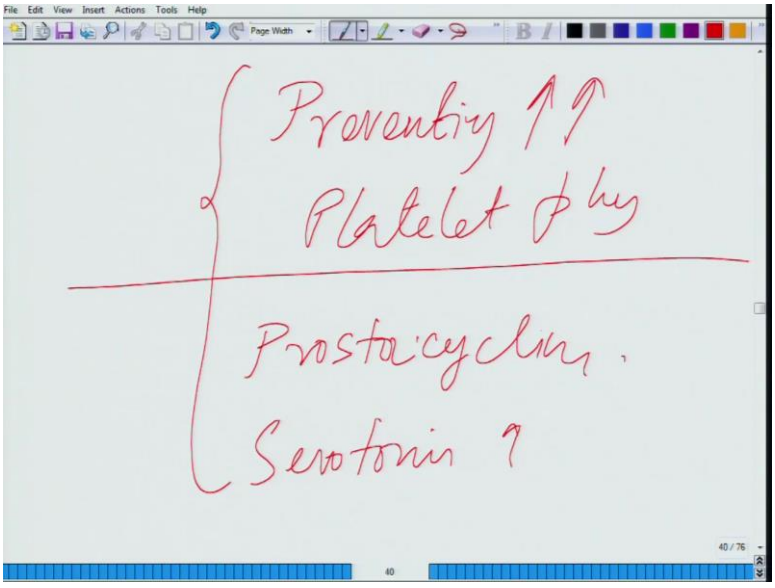

And apart from it, there are few other compounds which are secreted which basically limit the formation of platelet plug which includes preventing excess platelet plug. And why it is important I will just explain is done by molecules like prostacycline and few

other inhibitory molecules which include sometimes serotonin. And few other molecules which are known, so there essentially what happens if the plug is becomes. So, again I will take this paper example if the plug becomes too sticky out there. So, what will happen the blood would not be able to flow from this side to this side. So, in order to ensure the blood continues to flow maybe at a slower velocity at that point, because it is kind of you know lesser amount of blood will move. Because it will slow down, because the diameter has reduced down, but if it is become too sticky.

And there are too many plugs of a platelet starts forming then automatically what will happen is. That that the blood flow will be interrupted for longer, so you have to ensure that this whole process of plugging in. So, adhesion aggregation blood formation has to be very, very tightly regulated if there is a little error in that. Then there will be a problem and this is the hallmark of the body it is a very smart machine it. It is a it is one of the it is build with probably some of the most smartest material you can ever think of on the floor of earth. And it just very tightly regulated as soon as that blood formation and still these are some of the mysteries what really determine. That this much sufficient plug has formed what is that feedback loop to say we do not need to recruit any more platelets out. There because you are recruiting platelet at the site of injury ok, so now who says that I do not need more platelet? These are falls under the most beautiful idea of biology called the signal transduction or the signal processing or feedback loops.

So, there is a inbuilt feedback loop which says that we do not need any more of this platelets out. There fine now we can proceed with the phase 3 of the game which is the clotting factor or the clotting phase or coagulation phase which, so ever you call that ok. So, now, form here we will move on to the coagulation phase and this is that coagulation phase here. We will be talking about almost twelve different clotting factors and how they regulate this process. So, in this clotting the coagulation phase or the clotting phase there are 2 sets of chemical reactions which are involved one is called extrinsical reaction. The other 1 is called intrinsic reaction intrinsic reaction are the one's which are carried out by the blood cells as I was mentioning in the beginning of the talk by the platelets.

And all other cells which are involved the blood cells blood vessels involved in this whole thing all the blood components are secreting factor they regulate the intrinsic pathway. And then there is an extrinsic pathway which is regulated by the vessels around

or the surrounding tissue or the endothelial cells which you component about blood. It is just form in the vessel those are called extrinsic pathways. So, these 2 pathways merge at 1 point and results in the whole clotting process and that is what we are going to regulate at. What are the regulatory mechanism, which says clotting is done no further clotting is needed otherwise there will be a blood aggregation. And the fluid flow the dynamics of fluid flow of blood will be hindered. So, now what you will do in the in the coagulation phase we will diagrammatically see the extrinsic factor. And the intrinsic factor how they are regulating this whole process of clotting. And then what I will do I will put a table for you of all the factors and the regular names and where they are being produced.

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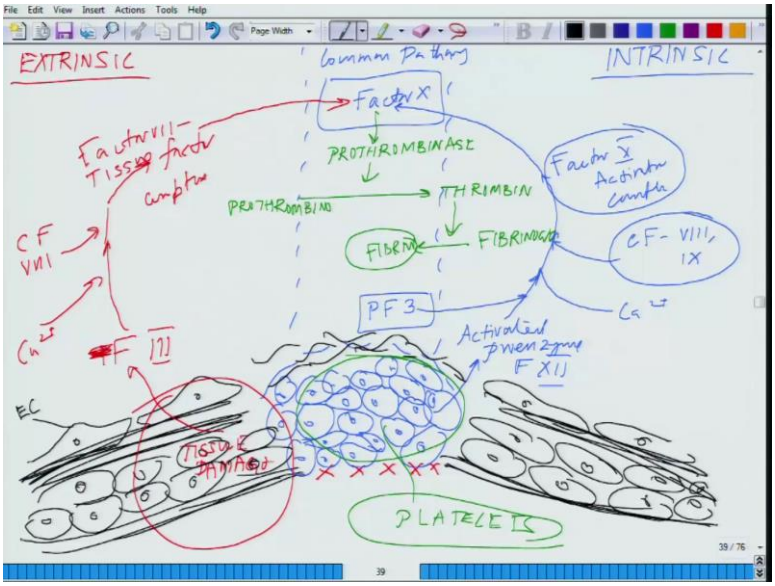

Let us move on to the phase 3 of it, which is the clotting phase or the coagulation phase the coagulation phase in the coagulation phase. So, this is what essentially happens, so I will again redraw what I was drawing just the last diagram all I was drawing the injury site. So, that will help you to understand it much better, so these are different cells which are forming the basement cells if you follow the previous diagram. And this is the site where the let me redraw it that will help you to sorry for this mix up fine. So, here is the basement layer basement layer and here is the injury site, so I am just putting the injury site like this with a cross this is the injury site. And these are the cells of the blood vessels which are forming the blood vessels likewise and we will draw the endothelial cells. And then we will again make the platelet plug and from there we will initiate the

process of. So, and here you have the endothelial cells, which I am drawing now these are the e c endothelial cell endothelial cell this much cells.

Now, So, this is the site now what you see essentially here a lot of platelets and when the platelets move at the injury site they change their shape. They become more circular from triangular they become more and more circular and more. And more spherical, because they have to accommodate in large number and as you know. The spheres does it better in terms of the maximum number of spheres could be accommodated in 1 spot. So, this is where the plug has to be formed, so now the 2 pathways start to function, so on a right what we will do on this right. We will talking about the intrinsic pathway on the left we will talk about the extrinsic pathway extrinsic. And the red will show the extrinsic with red and intrinsic with blue, so the first thing intrinsic means these are all coming from the platelets.

So, platelets all other blood vessels which are involved in it, so the first thing happens is activated pro enzymes usually factor 12 activated pro enzyme which is also called factor 12. So, there are 12 different factors I was telling you this particular factor reacts with platelet factor p f factor 3 PF 3 platelet factor 3. And further a reaction with calcium leading an further addition of clotting factors c f stands for clotting factor 8. And clotting factor 9 clotting factor 8 and clotting factor 9 further with clotting factor 10 activated complex initiates the reaction. And this eventually leads here the common pathway comes again the role of factor 10. So, factor 10 activated complex comes here and that factor 10 activated complex leads to the formation of the activation of the factor 10.

So, now, here this is the part which is the system things to the common pathway from here. It is all common from the left end one's I come to the extrinsic from the extrinsic side you will realize that common pathway. So, factor 10 activated, so again to summarize, so activated pro enzyme factor twelve secreted by the platelet reaction with platelet factor 3. And calcium it leads to formation of clotting factor and the reaction of clotting factor 8 and 9 activates something called platelet 10 activating factor activating platelet where the factor 10. Now, the factor 10 simultaneously what is happening from this damaged tissues out here from this tissue damage and endothelial cells and the basement cells. These secrete something called tissue factor, so on that side you saw the you saw the platelet clotting factors or the platelet factors on the other side you see tissue factor 3.

This tissue factor 3 moves on react with calcium then clotting factor 7 then that goes to factor 7 tissue factor complex. And then this activates to factor 10, so now, the common pathway starts. So, if you look at it on your left on the extrinsic pathway and the intrinsic pathway and the source of extrinsic pathway are all the damaged tissue out here. And the source of intrinsic pathway, are all the platelets which are present here and these are the platelets. So, now there are series of reaction taking like this stage I am putting in green now, so that activates something called prothrombinase prothrombinase. This prothrombinase leads to a reaction of prothrombine to thrombin prothrombin to thrombin.

And this thrombin then leads to the conversion of fibrinogen to fibrin and this fibrin is the 1 which essentially forms the clot. And coming back while summarizing the whole process, so when you are kind of creating a stitching, so you need thread to stitch. So, the thread component in this game is the fibrin it is the fibrin thread which forms. The mesh out like this you see consider these my fingers as fibrin, but they do not get activated till. There is this thrombin coming into play, which breaks down the fibrinogen to fibrin that conversion. And thrombin never gets activated, because it remains in a prothrombin state till it gets thrombinase and thrombinase never get activated till factor 10 comes into play.

And factor 10 would not get activated till both extrinsic and intrinsic pathways form factor like tissue factor 7 from the extrinsic pathway factor 10 activating complex from the intrinsic pathway comes and activated. So, this whole cascade is a function of injury if by chance this cascade gets activated all by itself we would not be alive. Because all our bloods will start getting clotting in the vessel and blood would not flow. So, you have to realize that this has to be very very temporally very tightly regulated. If there is a little problem in this whole thing there will be some serious issues you will be facing. Now, let us look at and I will be enumerating all these factors what I have just drawn for you people. And let us talk about some of the control pathways which are controlling this whole process.

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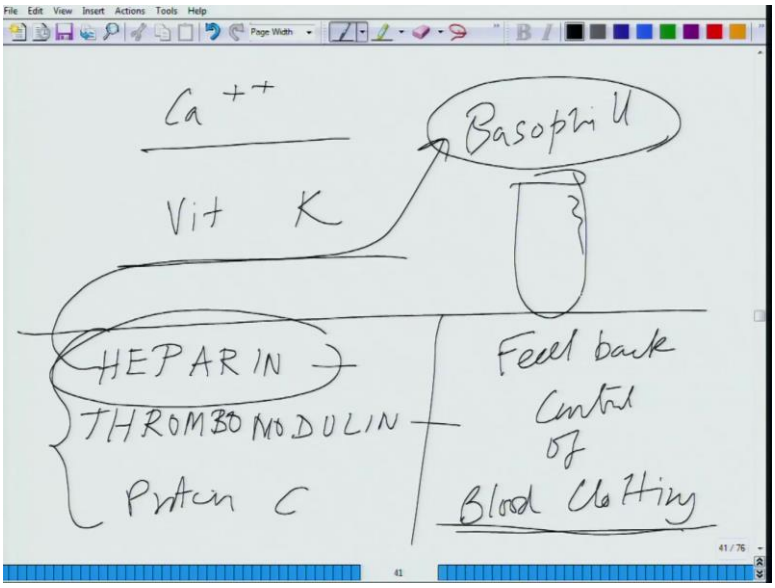

Coming back to the slides, so slides let me go to afresh slide to explain, so this is, so if you look at it. So, there are different the different feedback loops which are involved in it and these are controlled some of these are controlled by the calcium's vitamin k. And we will be coming to that how this different factors apart from it. There are certain other factors which needs we talked about is called heparin these are the 1 which are controlling. The feedback control of blood clotting feedback control of blood clotting this is done by heparin thrombomodulin t h r o m b o thromobomodulin. This is done by protein c, so these are the one's which are this heparin is being released by basophil. And I will be coming to basophil while I will be talking about the white blood cells these are part of that.

So, they basically ensure that you know this whole is basically it is it prevents clotting. So, if you see there are there are vacutanors where the blood is being collected they are called heparinized. So, what you essentially do on the on glass you coat heparin and if you collect the blood the blood would not clot. So, blood clotting could be prevented if you have the heparin because heparin does not promote the clotting of the blood. So, you need these factors to be present there which ensures, but they get activated once the clotting process gets initiated. So, they are the kind of the control check points which ensures that the blood does not get clotted up excessively. So, that the blocks start forming and the blood cannot flow, so there is this heparin which is produced by the basophil.

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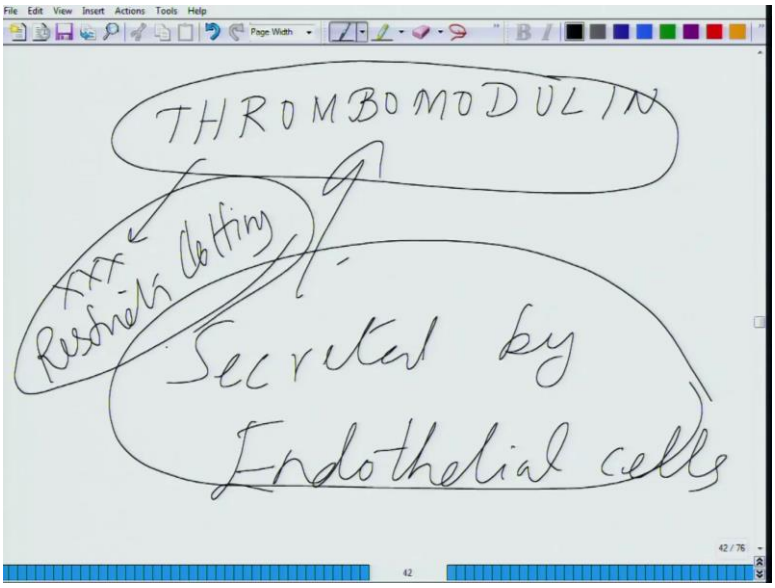

Then you have thrombomodulin t h r o m thrombomodulin this thrombomodulin is secreted by by endothelial cell secreted by endothelial cells. And this essentially also ensures that the blood clotting does not you know continue like forever it has to be. So, they restricts clotting that is their role these are the one's which are involved in restricting the clotting process.

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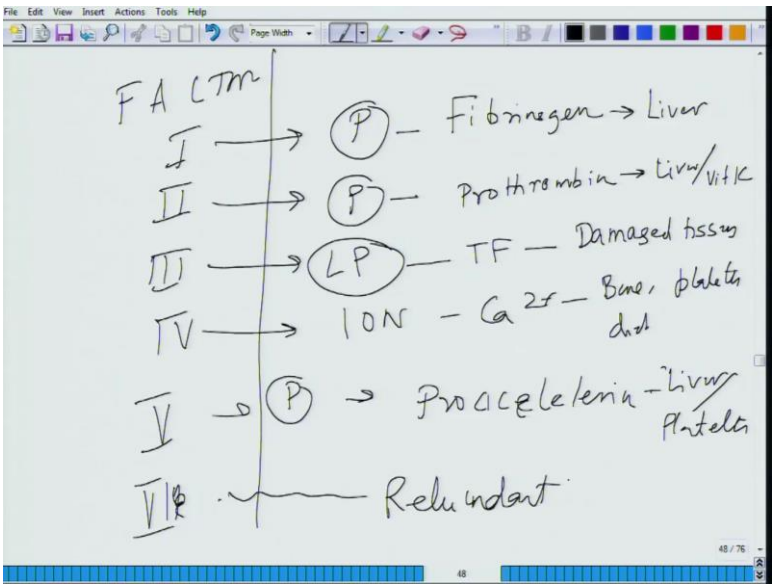

Now, what I will do? I will just enumerate all, the all the different factors which are involved there. So, you have this factors 1 factor 2 factor 3 factor 4 factor 5 factor 6 no

sorry 6 the different factors which are involved in this. So, this is protein, so p stands for protein these are all pretty much protein factor 3 is a lipoprotein factor 4 is an ion which is basically calcium ion which is factor 4 factor 5 is a protein which is basically proacelelerin proacelelerin proacelelerin proacelelerin.

And this one is fibrinogen this one is a prothrombin this lipoprotein is a tissue factor, so fibrinogen is produced by the liver c how all these things are regulated. Then this is also produced by the liver in the presence of vitamin k this tissue factor is produced by the damaged tissues. Then your calcium is being produced by the bone and the platelets and of course, you get it from the diet. Then you have proacelelerin produced by liver and platelets produced by both then you have factor 5 then factor 6. So, factor 6 this basically I mean old literature found you will find this is no longer being used this is kind of a redundant 1 in the old literature you will find factor 6.

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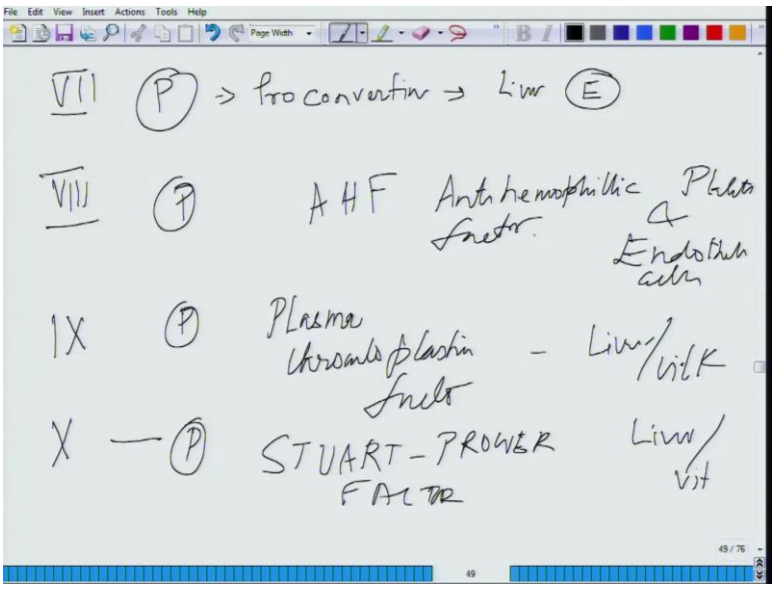

Then we move onto factor 7; factor 7 is essentially it is also a protein it is called proconvertin proconvertin and this is produced by liver. And this is also an extrinsic in the extrinsic pathway I am just leaving it for you guys which is the extrinsic which is the intrinsic. And you have the factor 8 factor 8 is called AHF it is also protein by the way and to anti hemophillic factor anti hemophillic factor. This anti hemophillic factor is produced by the platelets and endothelial cells endothelial cells.

Then you have factor 9, which is plasma thromboplastin factor which is again a protein plasma thromboplastin factor. This is produced by the liver in the presence of vitamin k vitamin k plays a very critical role in most of them this is your factor 9. Then you have factor 10 this is also called this is also protein, but there is a special name for this. This is called staurt prower factor staurt prower factor and factor this is also produced by the liver in the presence of vitamin k.

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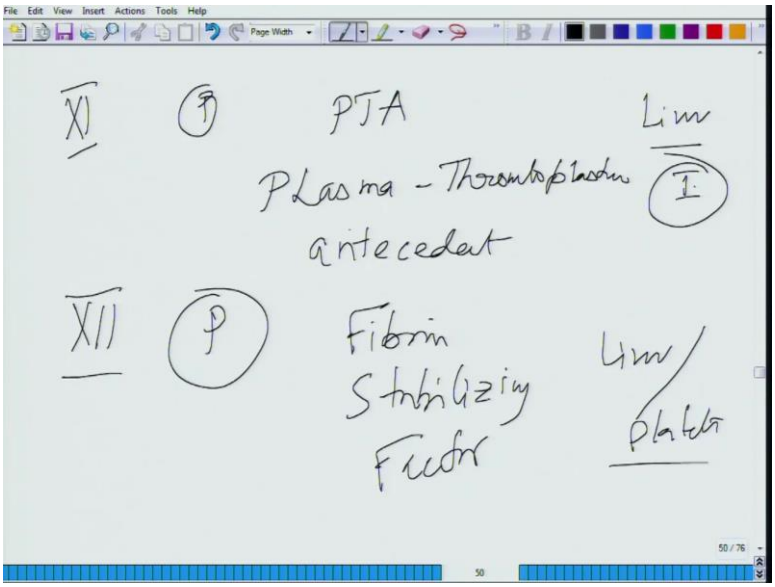

Then you have factor eleven which is also protein this is in short this is called p t a, or plasma thromboplastin plasma thromboplastin antecedent. And this is also produced by the liver and this is essentially an intrinsic factor. And then you have the last which is the factor twelve which is called fibrin stabilizing factor which is produced by the livers and the platelets. So, if you essentially look at all the different factors which are involved in it it is a fairly big list of 12 different factors. And many more understanding we are gaining with more and more research on the blood. And the blood factors which are involved in this whole process, but what is essential to understand is that. It is a very very tightly regulated process where platelets endothelial cells liver blood calcium damaged tissue everybody plays a very critical role.

And it is very, very tightly regulated a little bit of here and there in this whole game could lead to severe problems in our body. So, the overall understanding in summary what I expected from you to understand the nature of the platelet cells. They are formed

in case of human being of course; they are formed by breakage of breaking away from a bigger cell from a mega karyocyte mega means huge karyocyte cell from a mega karyocyte. This they form a small triangular kind of you know shape which changes their morphology when they reach to a, the wounded site or the site where the blood vessel gets ruptured. And they have a certain optimal number you know about if the number goes up the blood viscosity will go up.

And that such thing happens in extreme inflammation like cancer and other situation and if the level goes down then there is a chance will be hemophilic. We would not be able to prevent the blood loss, because there would not be any stitching stitching mechanism out. There or the stitching mechanism will be inefficient when we talked about the 3 phases by which the stitching of the ruptured blood vessel takes place. We talked about the first phase, which is the vascular phase and we talked about the platelet phase. And then we talked about the coagulation or the clotting phase and all and within the clotting phase and in the vascular phase initially. We talked about the vascular spasm how the inept nature of the tissue kind of helps it to you know glue to the other.

And we ensured and we talked about the factors which prevent the complete gluing. It should not be a blockage like this it should be slightly like this something like this. And then eventually the blood vessel again expands and becomes like this original, so the vascular spasm. Then we talked about the migration of the platelet cells and their degradation and everything out there and ensuring that. There should not be too much adhesion aggregation and you know the formation of the stitching. And then we talked about the clotting where you talked about the intrinsic pathway extrinsic pathway. And we and finally, we enumerated all the different factors including from factor 1 to factor 12 which are involved in this whole clotting process. So, kindly go through it carefully it is a very straight forward thing, but you have to kind of visualize to day to day example how that is happening.

Thanks a lot.