

Human Physiology
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Hello everyone, welcome to another brand new class of human physiology. Hope you are enjoying the various episodes of human physiology class. In today's class, we will discuss about various anticoagulants, their process of anticoagulation and also we will also further kind of discuss about various blood related diseases. So, in our in our last class if you remember that we detailed we discussed about like blood coagulation pathways and process of blood coagulation. So, this class will try to kind of dissect about the anticoagulation pathways and anticoagulation mechanism. Hope you will enjoy it.

So, what are the different contents for today's class? We will discuss about blood anticoagulation and then we will discuss about different anticoagulants like EDTA, heparin, warfarin, oxalates. Then after that we will discuss about different bleeding disorders, we will discuss about thrombosis, we will discuss about anemia, sickle cell disease and finally, leukemia. So, what is anticoagulation? So, as you know like during a process of like wound in case of any injury, what is mostly needed? We need to first stop the blood flow and then following the blood flow the injury gets repaired by like endothelial cell formation and tissue remodeling. But now imagine that if our blood is flowing across like arteries and if there is like abrupt coagulation all of a sudden that happens inside of the artery, then what will happen? Basically, the blood flow will get hampered and due to the obstruction of blood flow there would be a region called ischemic area where not enough oxygen would be supplied to that area and also the blood carrying capacity will get reduced due to the reduction of the blood flow that will impact like the cellular health and all our organ health.

So, it is so important that in a normal condition in our body, the blood should be flow without any obstruction. So, there should not be any kind of thrombus formation or any clogging formation that can hamper the proper blood flow. And that is why lot of different natural anticoagulants are present in our body that ensures that our human blood is flowing without any obstruction all the time. So, what is basically anticoagulant? Anticoagulant is a substance that prevent the blood coagulation in the body and they can prevent our internal blood coagulation also and during the blood collection if you remember like we do lot of blood test and we go to the path lab and give our blood. So, there also it is required that when you collect your blood, it should be collected in a anticoagulant so that the blood does not coagulate.

So, during the internal our human blood flow along with the blood collection both cases anticoagulants are so important. Mostly anticoagulants are kind of three types. So, the first types are the anticoagulants which are present in our body and that prevents the blood coagulation inside. Second types are the anticoagulants that prevent blood clotting that is collected from the body which is done like for the path lab test and all. And then the third types are the anticoagulants to prevent blood clotting both in vivo and in vitro.

So, these are like three different type of anticoagulants that can be used commercially. So, as you see in the picture that how the clotting happens, right. So there are like platelet aggregation in your last class if you remember that platelet aggregation can create like a thrombus formation

and then the fibrinogen to fibrin mesh, this conversion happened and the fibrin, so basically if you remember here from the last class that initially there is like platelet clot formation, right. Following the platelet plaque formation then this conversion of fibrinogen to fibrin happens. And then this fibrin gets polymerized and it creates like a mesh formation to hold this thrombus. So, this is like abrupt thrombus formation that can severely kind of impact the blood flow, right.

So, the anticoagulant agent like heparin, like warfarin or other type of anticoagulant agent can prevent this clot formation in the blood so that blood can flow nicely with the proper speed. So, we will discuss some of the anticoagulant today and see like what are their probable mechanism of action. So, first one is the heparin as you can see like heparin was first discovered around in 1916 by J. MacLean and William Henry Howell from John Hopkins University. Heparin is generally secreted from the basophils and the mast cells of our body and which tissues are generally responsible for heparin secretion you can see like liver, lungs and gastrointestinal tract.

So, heparin prevents blood clotting by its antithrombin activity. It directly suppresses the activity of the thrombin. You remember in the last class we discussed what is the thrombin or prothrombin, what is their role? Prothrombin or thrombin, they basically activate this conversion of fibrinogen to fibrin. So, this thrombin and apart from like calcium and other ions, they basically activate this conversion of fibrinogen to fibrin. And what heparin does? Heparin basically suppresses the thrombin activity.

In that way, it does not convert the fibrinogen to fibrin. In this way, heparin acts as an anticoagulant. It also inactivates different other blood clotting factors, for example, like factor 9, factor 10, factor 11 and factor 12. So, all these clotting factors are also very much important. You remember both intrinsic and extrinsic pathways.

So, heparin also inactivates some of these blood clotting factors and inactivates blood coagulation. Okay so what are different uses of heparin, heparin can be used to prevent and for the treatment of deep brain thrombosis and also pulmonary embolism they can use for like prevent prevention of any type of clot formation during like cardiac surgeries after the stroke also if there is a high risk of clot formation post following like stroke heparin can be used to prevent any type of like blood clot formation because after the stroke there is a high risk that the proper blood flow gets kind of hampered and then it is also used in the hospitalized patient who are kind of immobile due to like various sort of clot formation. But there are certain limitations or side effects that can be there for this heparin reagent. First of all it is a biological reagent right. So any biological reagent there is a risk that if you are preparing a biological reagent if it is not properly pure or purified then there is a risk of like immune rejection or any type of like allergy or complications.

So, that is always a high risk with any type of biological reagent that if it is not properly made immune rejection or allergy symptoms can be developed and that can also cause like severe other trouble like breathing trouble and all. And there is also a risk of like bleeding kind of excessive bleeding. So, if too much of heparin is also used to prevent the bleeding, internal bleeding can happen and that can be very detrimental. So, too much of heparin usage is not recommended. You should be always like you should not take heparin without the proper prescription and without proper observation of without the doctor.

You should always take like recommended dose in case it is required. And also another last one is like the osteoporosis. So, osteoporosis can also be a problem for prolonged use especially

in case of the pregnancy. So, the next anticoagulant what we will discuss is the EDTA. So, in the last one heparin is mostly used for the internal application, but EDTA is one of the very common one along with the sodium citrate that are used for the blood collection while in the path lab.

So, what is the EDTA you know like EDTA is like the ethyl diamine tetraacetic acid and it has this tetraacetic component because of this four arm. So, because of this 4 tetraacidic arm it can bind with like 4 calcium ion. This EDTA is very highly like strong, it has a strong binding affinity with calcium. And as you remember in our last class that calcium is very important both for intrinsic and extrinsic pathway for the both for clotting purpose. So, without the calcium if the EDTA is basically chelates the calcium out of the blood, calcium ions get depleted in the local blood that contributes the anticoagulation property.

So, it is a very simple type of clotting, anti-clotting mechanism that you remove out the calcium from the blood that contributes the depletion of calcium concentration resulting the anti-coagulation. So, you can see EDTA is a very good chelating agent that can bind with the calcium which form like a EDTA calcium complex and as the calcium gets depleted, you can understand that how the coagulation prevention happens. But EDTA is also very toxic EDTA cannot be used for our internal applications it can be only used for external path lab like for blood collection vial purpose because there are so many toxicities you can see like EDTA can cause like hypocalcemia because so much of calcium is removed out of your body that it can cause osteoporosity it can cause hypocalcemia and calcium also contributes for muscle contraction property, right. So, if lot of calcium is coming out or getting removed from your blood, then all the muscles including your heart will not be able to properly contract and that can be very significant because you will not be properly able to kind of breathe, will not be able to do your right functions including compromisation of your heartbeat. So, that is very dangerous.

So, that is why EDTA cannot be used for internal application. Next another very important anticoagulant which is warfarin. This is warfarin is discovered around like 1954, it is clinically approved for the clinical use. and warfarin it can be used as a oral anticoagulant. So, mostly for heparin it is used generally as a IV dose, but for warfarin it can be used as a oral tablet.

It prevents blood clot by inhibiting vitamin K dependent clotting factor. So, what happens basically vitamin K is responsible for different type of clotting factor synthesis so you can see here like clotting factor 8 9 10 and all of them get mostly synthesized in our liver so vitamin k if it kind of get hampered by this warfarin, it basically directly inhibits the clotting factors synthesis like clotting factor 7, clotting factor 9, clotting factor 10. So, you can understand that warfarin inhibits vitamin K and associated clotting factor synthesis that can be a possible mechanism for anticoagulation pathway. There are other mechanism also like warfarin inhibits vitamin K, epoxide reductase which is a very important enzyme for regenerate active vitamin K and this reduces the production of this all this clotting factor as well as anticoagulant proteins like C and S. So where are the most frequent uses of warfarin? You can see like warfarin can be used for prevention and treatment of thrombosis.

It can be like deep vein thrombosis or pulmonary thrombosis even like cardiac thrombosis also it can be used. Atrial fibrillation for that like mainly prevents like stroke by reducing the clot formation risk. It can be also used like in the mechanical hard valves because if there is a coagulation happens in the artificial hard valve, then it can cause improper blood flow and further formation of further thrombus in contact with the previous thrombus. So, warfarin

coating can be used like in the hard valves and also post myocardial infarction also warfarin uses are very common. But warfarin also has some side effect.

The first and foremost is it increases the bleeding risk. So, excessive amount of use of warfarin or heparin, these are not recommended. Of course, you should use it only with proper observation and proper recommended dose. Apart from that, skin necrosis, purple toe syndrome can be observed. Birth defect is of course not like it is common, but frequent use of warfarin can cause like tetrazonic type of birth defect, which is rare, but it is also observed.

So, as you can see like there are lot of like different type of challenges with the current coagulant. These are like another one sodium citrate. It is not being used for internal use. Sodium citrate can be used for external blood collection purpose. In 1900 only sodium citrate has been discovered by the scientist.

And citrate also as you know like it binds with the calcium. So, by binding with the calcium, it acts as a strong calcium binder which kind of reduces the calcium concentration from the blood causing the anticoagulation. Same way oxalate. Oxalate is also a very important like, you can use like calcium oxalate. you can use like other different type of oxalates.

So, oxalates are also strongly it can bind with the calcium like zinc oxalate, iron oxalate. So, different type of oxalate can be used. These oxalates strongly bind with the calcium, same way deplete the calcium concentration from the blood resulting in the anticoagulation mechanism. But this oxalate and citrate, these are not generally properly used for internal application, but they can be used for external blood collection purpose. So, I hope like you kind of went through different type of anticoagulants.

Now, let us discuss about some of the bleeding disorder. So, very common bleeding disorder which happens like in general, these are not of course very frequent, some of them are really rare and some of them are also genetic disorder which can be called as rare genetic disorder. So, some of them are called like hemophilia, purpura or von Willebrand disease. So, hemophilia is a rare genetic disorder. right so let's see how it happens hemophilia is a sex link inherited like rare genetic blood disorder which is mostly characterized by the by the prolonged clotting time right and usually it affects the males mostly females are the carrier and males can get affected by this genetic this deadly genetic disorder and because of the prolonged clotting time what happens like there is a high risk of internal bleeding after any injury or without even injury also there is a high risk of internal bleeding and that can contribute to a significant blood loss.

And if like significant blood loss happen you can understand that oxygen delivery to your cells including brain will get severely hampered and that can contribute to a hypoxic condition and even like coma or brain death. So, what are the causes of hemophilia? Hemophilia mostly occurs due to lack of formation of the prothrombin activator. So, what prothrombin activator does it converts prothrombin to thrombin and then thrombin converts fibrinogen to fibrin. So, basically it the genetic mutation or the genetic disorder eventually affects the formation of this prothrombin activator. And that is why like this intrinsic and extrinsic pathway gets like prolonged and blood clotting gets severely delayed.

So, this is like a that is a severe kind of case where clotting situation kind of prolonged causing like severe internal bleeding. And this is also happens due to different deficiency of the factor like factor VIII, factor IX or factor XI. So, you can see like a normal blood vessels, it should not be like ruptured or you should not observe like any excessive bleeding out of the normal

blood vessel. But if this genetic mutation happen maybe in some cases of any like cells, if you consider like certain genetic mutation happens here, that will cause like this deficiency of factor 8, 9 and 11 and that will cause like bleeding internally and ruptured blood vessels. This is a very serious life threatening situation.

And there is mostly two types of hemophilia, hemophilia A and hemophilia B. In case of hemophilia A, it happens due to a lack of clotting factor 8 and hemophilia B, it happens due to a lack of clotting factor 9. And there is not enough treatment for the hemophilia disease, but you can give the supplement of factor 8 or factor 9 from outside. But the problem is like these are also biological reagent. So, if those biological reagent like clotting factor 8 or 9 is not properly purified that can cause lot of allergic reaction or immune reaction to your body.

A lot of new type of therapies are also being tested nowadays like gene therapy, gene therapy using maybe like CRISPR based Cas9. So, you can kind of directly correct, directly cut those faulty genes which were present in our body and insert the right genetic sequence to your like genetic cell, to the cell causing like the proper production of factor VIII or IX. Also, you can use like another therapies getting very popular, but which is not yet in the market, which is the cell therapy. What you can do in this case? You can engineer a cell of course in your nucleus. So, what we will do like we will insert the genetic, write genetic sequence that can produce this factor 8 and then the factor 9.

so that the genetic sequence get inserted to a cells and then they can secrete this factor 8 and 9 clotting factor. And these cells can be injected to the body, these cells can be encapsulated in a polymeric component like a capsules. These cells can be encapsulated and then implanted to the body, so that the cells can keep on producing the clotting factor and in cases of excessive bleeding they can help to clot the blood. So, new different type of new therapies like gene therapy, cell therapy are being explored, but some of them are still yet to come in the market. This is an example you can see like generally mother is the carrier of the faulty gene.

So, if you can see like the mother is carrying this faulty gene here and there is like this father, this is the father and it is the mother. Mother is carrying the faulty gene, so it can either go to one daughter and also it the son so if it goes to the daughter then what will happen the daughter will become the carrier but if it is go if it if it goes to the son then the male child will become the hemophilic so mostly in this case female is the carrier it will not affect because of the excess condition it will not affect the female will be the carrier but the female can give their active fault gene to a male and in that case the male can become hemophilic. This is the case if the female is the carrier of the thing but it can also happen that both female and both male can be the carrier. So, what will happen in that case, if both female and both male has a faulty gene for the hemophilia, you can see that 25% of the female can become hemophilic along with the 20 percent male can become hemophilic. But mostly another 20 percent of female become carrier.

So, there is a been high risk that both the one daughter and one son can become hemophilic in nature. And in case you see like the male or the father is carrying the genetic faulty gene, there is a chance that 100 percent of the daughter or the offspring like both the male or female can be the carrier, mostly the daughter. So, 100 percent daughter will be the carrier and in cases of the male 100 percent will be the healthy case. So, this is like mostly you can see this can happen where it get like if the father is carrying like a faulty gene, then 100% daughter becomes a carrier and 100% son becomes the healthy. So, these are several scenarios you can kind of go through.

Then the next genetic like the next blood disease related disorder is the purpura. Purpura is the rare blood disorder that is characterized by the prolonged bleeding time mostly if it affects the platelet platelet plaque formation and you can see like purpura has like different type which is like thrombocytopenic purpura. This happens due to the deficiency of the platelet which is also called as thrombocytopenia. Or there can be like idiopathic thrombocytopenic purpura. So, that platelet count decreases in this case causing like lack of platelet plug formation and lack of coagulation.

Also, it can be like thrombasthenic purpura which can happen due to the structural functional abnormalities of the platelet. So, different kind of scenarios can happen mostly this is the abnormality with the platelet. Genetic component you can see like some forms of thrombotic thrombocytopenic purpura like congenital TTP are caused by the genetic mutations. And there are some time like autoimmune component also for this case like you can see this ITP or immune thrombocytopenia and HSP or the henochycoline purpura, these are some autoimmune disorder. And what happens in case of autoimmune disorder you know like our immune cells of the body mostly the T cell it attacks like our healthy tissues and that can causes like significant damages to the platelet causing like lack of platelet plug formation.

And the last one is the Von Willebrand disease. So you remember in the last class we discussed that VWF or Von Willebrand disease is an important kind of blood coagulation factor. This basically attracts the platelet towards the injured area causing like plaque formation and eventual stopping the blood like loss. So, this is like a disease where von Willeweine factor is not properly kind of secreted from the damaged cells and that can cause like the lack of proper blood clotting. So, this is very important all these blood related diseases. And finally, like thrombosis, thrombosis as you know like there is abrupt clot formation in the blood that can hamper the proper blood flow.

What are different causes of thrombosis? It can happen due to like internal blood injury, injury to the blood vessels. It can happen to the roughening of the endothelial cell lining or agglutination of the RBCs or even sometime toxic like chemical exposure based like thrombus also can form or even like sometime congenital absence of protein C can also cause the thrombosis. Anemia is also an like very normal like blood related disease as you know like lack of proper RBC formation or red blood cell formation from our bone marrow specially to the pregnant woman or it can mostly observed during like the period cycles of the woman. It can cause like anemic formation which is like lack of RBC or lack of hemoglobin to the body due to the lack of rbc formation what happens is like lack of oxygen supply to the cells and like patients become like nausea nausea patients experience like vomiting their skin becomes like pale and sometimes more often they also experience like breathing trouble okay So, anemia is a significant issue, especially countries like India and other part and iron supplements are sometime kind of recommended by doctor because iron basically influences the red blood cell formation.

B12, vitamin B12 or folic acids are also important. These are all these also helps like proper differentiation of the bone marrow cell lines. So, both iron supplement and vitamin B12 or folate, folic acid supplements are recommended for the treatment of anemia. This is another important like blood related disorder, which is sickle cell disease. This is also kind of a genetic disorder. What happens is like in normal our hemoglobin, which is like HBA or HBB, they are mostly like it cause the RBC is like a biconcave type of shape.

But if there is a genetic mutation to this hemoglobin protein, which becomes like the HBS, In this case, the RBC become like more of this sickle type of shape, right. So, due to genetic mutation, the biconcave RBC kind of becomes like a sickle type of shape. And you can see like biconcave RBCs are, it is designed in a way that they do not hamper the natural blood flow. But the problem with this sickle type of shape of the RBCs are they can kind of create a clogs and they hamper the proper blood flow. And if the proper blood flows are obstructed, you can understand that you can experience anemic like of situation, you can experience lack of oxygen supply and breathing trouble, right.

So, due to this genetic mutation, this changing of the shape of the RBC cells contributes to significant anemic type of situation and like oxygen delivery problem. And finally, another very important and more common like disease related to blood is the leukemia which is the cancer, cancer of the blood. Mostly what happens is like abnormal like development of the white blood cells and if it happens sometime it kind of deposits on the red bone marrow that hampers the formation of properly like the red like RBCs. And it creates a problem like lack of RBC formation as you know like it can cause anemia.

It can also cause like other immune related issues. So, blood cancer which actually contributes abnormal formation of white blood cells, the WBCs is a significant cause or significant kind of challenge in form of leukemia. And there are various treatment of course, you can give like radiation treatment, you can give like chemotherapies or more modern way you can also replace the bone marrows right with a proper bone marrow. You can also use like immunobase therapy, immune therapies. So, different type of therapies are there in the market. We are not going too much in details, but leukemia if it is detected in early stage can be cured and if needed the patient can be also transfused with the blood for proper like their lifestyle maintaining and recovery.

So, I hope like you enjoyed the classes of anticoagulation. So, think about this question like what is the primary function of anticoagulant medication, how do anticoagulants differ from the antiplatelet drugs, what is the main risk associated taking the anticoagulants and what is the antidote for heparin overdose. So, you can google this question, you can read some textbook and let us try to figure out some of this question. And you can refer some of these books, of course, like medicinal physiology textbook, essential of medicinal physiology book, the Gaitan textbook and different like you can also refer different like web based like content. So, thank you again. Thank you again for attending another interesting class of the human physiology where we thoroughly discussed about anticoagulants, various like mechanism of anticoagulant.

After that, we discussed like different blood related disease and some of their therapy, some of their like challenges related to those blood related disease. Thank you again. We will meet with you with another new class of human physiology. Thank you.