Survey of Human Diseases
Module 2/Week 5 Blood Coagulation Presentation

>> PROFESSOR: All right. So today's lecture is chapter 9, blood coagulation, abnormalities and circulation disturbances. Okay. Now, hemostasis, the definition of hemostasis is the arrest of bleeding caused by activation of the blood coagulation mechanism. Now, there are certain factors which are required for hemostasis. One is the integrity of the small blood vessels. They have to be normal. They have to be intact. Okay? You also need an adequate number of platelets. Platelets are produced in the bone marrow, and they are produced or they come from large cells called megakaryocytes. And what happens is with the megakaryocytes, bits of the cytoplasm breaks off basically and those are the platelets. So platelets don't have nuclei or anything else like that, and they last about ten days. They survive about ten days. Also for hemostasis, you need normal amounts of coagulation factors, which are produced by the blood and the liver and there are normal a little -- needs to be normal amounts of coagulation inhibitors. Okay? And the typical one is going to be plasmin. And there also needs to be adequate amounts of calcium ions in the blood.

All right. So factors concerned with hemostasis. The small blood vessels, they're the first line of defense in the body. And typically, if they're injured, they constrict or narrow down, and by narrowing down, it helps to facilitate closure by a clot. When they narrow down, blood slows down a little bit, a clot can form and transfer obstruct the injury and -- therefore obstruct the injury and therefore stop bleeding. And when typically a small vessel gets injured, the lining cells are endothelial cells. They're called endothelial cells. When they get injured, they expose the tissue underneath, and that helps to activate the coagulation mechanism. And with vasoconstriction slowing down, platelets have a chance to stick and adhere to the injured area.

All right. So I mentioned that platelets are small amounts of cytoplasm, from megakaryocytes, they survive about ten days, and they typically are removed by the macrophages in the spleen. And three important platelet functions. They plug, or a defect in the vessel wall. They also liberate. They also release vasoconstrictors and compounds causing platelets to stick. And of course vasoconstriction means narrowing down of the blood vessels and they release phospholipids that start the coagulation process. So platelets are very significant. When people have level of platelets below the usual number, that's called thrombocytopenia. Penia
means decreased amount, lowered amount, okay, and a thrombocyte is another word for platelet.
So basically, the coagulation process is a highly complex chain of factors, and it's what we call a waterfall or a cascading effect, and that one factor gets activated and it activates another factor. The activated factor then activates another factor, and that's how the coagulation process occurs. That's why they describe it as a highly complex chain reaction.
The first phase is the formation of thromboplastin, and there's two ways it can be formed. The intrinsic or the extrinsic. The intrinsic refers to the formation of thromboplastin within the blood vessels. Okay? Within the -- it arises from platelets within the blood -- constituents within the blood. So the intrinsic factors are in the blood. It's going to be platelets, plasma factors and that refers to the intrinsic factor. Okay? Intrinsic process. The extrinsic process basically, there's activation of clotting mechanisms from components outside the circulatory system. Connective tissue, injured tissue can also create a coagulation process.
Then the second phase is conversion, basically where there's conversion of prothrombin into thrombin. Okay? And that occurs because of the action of thromboplastin. So extrinsic factors, or intrinsic factors activate thromboplastin. Thromboplastin then acts to convert prothrombin into thrombin.
Now, then phase three, what happens is thrombin acts to convert fibrinogen into fibrin, and the way it works is thrombin splits off part of the fibrinogen to form smaller molecules called fibrin monomers. These fibrin monomers can then be joined end to end and then the fibrin stabilizing factor strengthens the bonds between the fibrin molecules, causes cross attachment and basically forms the fibrin clot. A scab, when you've had an injury and you've had some bleeding at the site, scrape your knee when you were younger, whatever, you formed a scab. The scab was made up of fibrin platelets to form basically an area of healing. So a blood clot, all right, is basically the end stage of the clotting process. That's what we want. Okay? We want the blood to clot.
All right. To plug a leak or an injury in the vessel so people don't keep bleeding from that injury or that defect. All right. And so that clot ends up being made up of an interlacing mesh work of fibrin threats with plasma, red cells, white cells and platelets. All right. So here's the diagram up here. You have your intrinsic on the left, extrinsic on the right and both of them serve to activate thromboplastin. The extrinsic refers to tissue injury. The intrinsic is going to be a factor within the bloodstream,
within the circulatory system. Then thromboplastin acts to convert prothrombin to thrombin. Now, for thromboplastin to activate prothrombin to thrombin, plasma factors have to be present, coagulation factors have to be present. And then fibrinogen gets converted by thrombin into fibrin. You have your lacy network, small fibrin molecules will stick end to end. All right. So disturbances of blood coagulation. There's four categories. Abnormalities of small blood vessels, abnormalities of platelet formation, deficiency of one or more plasma coagulation factors, and of course the most common deficiency of plasma coagulation factors is what?

>> STUDENT: [Inaudible].

>> PROFESSOR: Good. Hemophilia, and that's a deficiency of factor 8. Okay?

And then the last one is liberation of thromboplastic material into circulation. That can be injured tissue. That can be cancerous-type tissue.

All right. Now, so disturbances of blood coagulation, we mentioned abnormalities of small blood vessels. You can have abnormal bleeding resulting from failure of the small blood vessels to contract after tissue injury. There can be abnormality of platelet formation, or the term thrombocytopenia. Thrombocytopenia again refers to low numbers of platelets. Thrombocyte is a platelet.

So injury or disease of the bone marrow can damage the megakaryocytes, or the bone marrow becomes infiltrated by leukemic cells or cancer cells that there are can spread within the skeletal system, crowding out the megakaryocytes. Now, what type of injury or disease can damage megakaryocytes? When I was teaching survey, I think I told you this, a couple of years ago, I had two students who are systemic lupus erythematosus, and one of them had depression of her bone marrow, and she had to go on prednisone. She missed school for two weeks and the prednisone was, of course, to reduce the autoimmune damage caused by the systemic lupus on the bone marrow and her platelet count was down. So that's the type of disease that can affect platelets.

Also, you can have antiplatelet antibodies destroy platelets in the peripheral blood. When I was in practice, rarely, but we did have several patients over the years who had what we call ITP. ITP was idiopathic thrombocytopenic purpura and what that was was they had hemorrhagic spots on their skin. Little hemorrhagic spots, what we call petechiae, okay, small spots, we'll mention in the chapter in a little bit, caused by low platelets. Okay? And it was idiopathic in that we didn't know why they developed that. Okay? There's no reason. But it's a syndrome, and it's called ITP.
And any type of trauma to the skin would result in small petechiae, even if there was no trauma, there still would be petechiae present. So you could have abnormal function of platelets despite a normal count. Okay. So petechiae, what are they? Small red or red-blue spots about one to five millimeters. Okay? Now, how many millimeters make up an inch? Anybody? Around? Close. 25. Okay. Actually, 25.4. So as a result, you see that these are pretty small. Okay? They're, you know, quarter of an inch, eighth of an inch. They're pinpoint size hemorrhages of capillaries in the skin or mucus membranes and they're indicative of defective or inadequate platelets and when you press on them they don't Blanch. So some diseases are associated with petechiae and fever. One of them is meningococcemia, and the most common disease associated with meningococcemia is when the meningococcus gets into the blood and we're talking about neisseria meningitidis, all right, or meningococcal inflammation of the spine. So, also dengue hemorrhagic disease, which obviously is not common, but meningococcemia is a concern. All right. Here's an example of petechiae. Okay. This is an example of a large hematoma associated with deficiency of plasma coagulation factors, not petechiae, not platelets. This is coagulation factors. A person with hemophilia may present like that. All right. So disturbances of blood coagulation, Phase I, all right, can maybe be hereditary. Hemophilia, Von Willebrand's disease. Hemophilia we mentioned before is sex-linked, all right, affecting males. It's most common and best known to have episodes of hemorrhage into joints and internal organs. Classic hemophilia is deficiency of factor A. Hemophilia B, similar it's Christmas disease, all right, and that's basically refers to factor 9. Von Willebrand's disease is interesting. It's not exactly deficiency of a coagulation factor, but what it is is it's deficiency of a large protein molecule that is necessary to complex with factor VIII to provide hemostasis, so Von Willebrand's factor adheres to a damaged vessel wall and forms a framework that allows platelets and coagulation factors to adhere, interact and form a clot. So it forms a complex of factor VIII and maintains normal levels of factor VIII. All right. Phase 2, disturbance of blood coagulation would be deficiency of prothrombin or factors required for the conversion of prothrombin into thrombin. And what would be the causes of coagulation disturbances? Well, as I mentioned, it's produced in the liver. Prothrombin is produced in the liver so a disturbance that might involve that. One of the things that's signature is vitamin K. It's
dependent on vitamin K for the synthesis of a lot of the coagulation factors involved here, and when people are placed on blood thinners, their primary action is they inhibit the formation and synthesis of vitamin K coagulation factors. So that's how they work, such as Coumadin. How many here have heard of the medicine Coumadin before? Okay. Coumadin, it's a blood thinner. And the way it acts is it inhibits a synthesis of vitamin K factors. Now, vitamin K also can be synthesized by intestinal bacteria and it's a source of vitamin K. People on broad spectrum antibiotics may affect the intestinal bacteria and therefore levels of vitamin K. Also, bile is required for the absorption of vitamin K. It's a fat soluble vitamin, along with A, D and E. All right. So disturbances of blood coagulation. Administration of anticoagulants inhibits the synthesis of the biochemically active vitamin K dependent factors. Or there can be inadequate synthesis of vitamin K, maybe a prolonged use of antibiotics affecting intestinal bacteria or inadequate absorption of vitamin K due to decrease d bile, or severe liver disease. Now, causes of thrombocytopenia, low platelets. You can have injury or disease to the bone marrow, leukemia, cancer cells infiltrate the bone marrow and crowd out megakaryocytes or you can have antiplatelet antibody which destroys platelets in peripheral blood and that basically is what I talked about previously called ITP, idiopathic thrombocytopenic purpura. Now, liberation of thromboplastic material into circulation. Certain products of the following events that have thromboplastic activity, in other words, they can promote coagulation, and if they're liberated into the circulation, it results in a disseminated intravascular coagulation. And what we call that is DIC, disseminate means to spread throughout the body, intravascular, occurs within the vessels, and it's coagulation. So the diseases associated with shock and tissue necrosis can cause that. Overwhelming bacterial infections, and other causes of tissue necrosis. Dead tissue has thromboplastic activity, okay, can create and initiate coagulation. So DIC. What DIC is an abnormal bleeding state, and there's activation of the coagulation mechanism due to diseases associated with shock, or bacterial infection or extensive necrosis. And these products of tissue necrosis, other substances with thromboplastic activity are liberated into the circulation. So they get into the circulation, and as a result, DIC is initiated. What happens then is platelets, plasma coagulation factors are utilized to form clots, and as a result, their levels
drop, and then the body's counteracting mechanism, there's activation of fibrinolysin to defend the body from widespread intravascular coagulation and as a result this then dissolves clots and the purpose of that is to prevent a lethal obstruction of the circulatory system and the net effect is hemorrhage.

Now, I want to explain this. DIC is when there's activation of clotting, the clotting mechanism throughout the body. Okay? And cancer cells, necrotic cells, can do that. All right? When that happens and clots start to form, then what requires -- if a clot's going to form, what's it going to do? It's going to require clotting factors, coagulation factors and fibrinogen, so these clots start to form. Then it lowers the level of coagulation factors. It lowers the level of fibrin, and then the body counteracts by having the conversion of plasminogen to plasm which breaks up the clots. When it breaks up the clots, then there's no more fibrin or coagulation factors present to counterbalance that effect, and you end up with bleeding.

All right. And I've seen this in patients. One of the things that can happen, it was a really a very dramatic situation, is that I told you necrotic tissue can cause DIC. And when I was a resident, okay, I did my residency in Washington, D.C., and we had a patient come in and she was the ambassador's wife from a foreign country, and it was an emerging country, and medical standards and medical care certainly was not at our level. And she had been pregnant, okay, and what happened is the pregnancy stopped growing in the first trimester. However, even though it stopped growing, okay, the body really, the uterus did not abort the pregnancy. It wasn't a spontaneous miscarriage. Typically when pregnancies stop growing, what happens is that the uterus realizes, or the body realizes that the pregnancy has stopped growing, it's not healthy, and the uterus will then miscarry, cramp and miscarry, pass the tissue. Occasionally, what happens is pregnancy stops growing but the uterus doesn't reject it, doesn't pass it. So in this woman -- and this woman was from a third world country. She didn't want to have a D & C, which is where the cervix is dilated a little bit and we scrape the tissue out of the uterus. She didn't want to have that done in her country. She wanted to come to the U.S. well, it took two or three months for her to get here. So when she came here, the diagnosis was confirmed. She went in for a simple D & C, where the cervix was dilated and the tissue was curated out and what happened the D & C was done and everything was unconventional, she went back to the recovery room and then she started to hemorrhage and she then started to bleed from the IV site and she started to bleed from her nose, and the reason being is that the tissue from inside the uterus was
necrotic, was old, was dead, it was infected to some degree, and some of it, a small amount of it, got into the circulatory system, so she was starting into DIC. That necrotic tissue that got into the circulatory system initiated coagulation, and it disseminated, and then what happened is used up all the coagulation factors, and then plasminogen got activated into plasmin and started to break up the clots and as a result she went into severe DIC. So she had to be transfuse add lot of blood and coagulation factors. She was in ICU for several days, and she recovered. However, it was a very dangerous situation. So that's a dramatic situation of DIC, but I want you to understand that there's a balance here. There's a balance of coagulation and then there's the balance of dissolving the clot, and it's the healthy balance that keeps us healthy. If we don't have a healthy coagulation mechanism, we can lose blood. If we have too healthy a coagulation mechanism and not counteracted by plasmin, which can break up a clot, then our bodies would form clots and if our bodies formed clots, then those clots would be in the vessels and they would obstruct blood flow. We'd end up with infarctions and die.

All right. Let's move on. So anyway, the pathogenesis of DIC of activating the clotting mechanism, thrombosis, then the clot breaks down, and then there's consumption of platelets and clotting factors, and what happens is there's the formation of fibrinogen in the fibrin. Fibrinogen is converted into fibrin, and fibrin split products. They have fibrin degradation products. The fibrin split products help to break up the clot, serve as a source to dry the plasminogen. Here's an example, and it's a poor example, but here's a clot in a small blood vessel.

All right. So laboratory tests. I'm going to go over these. Sometimes this book gets a little clinical, okay, a little too clinical for basically undergrad course, but I will go over this. So you're going to evaluate the overall efficiency of coagulation process, what are you going to look at? Platelet count, right? Roughly the platelet count. They do bleeding times. And what they do is it's nicking the skin and they measure the time it takes for a small skin lesion to stop bleeding. Basically evaluates the function, the capillaries, the hemostatic process. They also do a clotting time. They take a sample of the blood and they time how long it takes for the blood to clot in the test tube. All right?

Basically, to evaluate the overall efficiency of the coagulation process. Partial thromboplastin time. That's the time it takes for blood plasma to clot after a lipid substance is out to the plasma sample. Basically, it measures the time of the first phase coagulation.
Prothrombin measures the time of the combined second and third phases. All right. And the partial thromboplastin as I mentioned measures the time it takes for blood to clot. All right. Let's see.

So I'm not going to do these discussions because of the fact that these lectures last a long time, and they're hard to get done within an hour.

All right. So normally, blood does not clot within the vascular system. All right? And for the process, of intravascular clotting, if blood slows down, all right, if there's stasis of blood flow to a vessel, if there's injury to a vessel wall or increased coagulability of blood, then blood will clot within the circulatory system. The terms, thrombus is an intravascular clot. It can occur in any vessel or within the heart. Embolus is a clot that detaches. It detaches and then it is free within the circulatory system. Okay? And it tends to travel in the circulatory system, and then it will plug or occupy or block a vessel of smaller caliber. So when it occurs, what happens is it breaks off. It travels and eventually it finds a vessel that can't get through. For example, you know, the traffic, or the highway system in the U.S.. 75 is the really main road around here, right? So then you get the lower roots and then you break off the roots and you go into the roads and then you go into a dirt road and then a driveway. Everything gets smaller and smaller and smaller and what happens is the clot breaks off and eventually it finds a vessel it can't fit through and then it blocks blood flow. When it blocks blood flow, you get tissue death, necrosis. Okay?

An infarct refers to tissue necrosis from interruption in the blood flow.

Embolism. There's different types of embolisms. Okay? Fat, air, amniotic fluid and foreign particles. Fat embolism, how does fat cause an embolism? Bone fractures. Okay? Fat is present in bone marrow. In a severe bone fracture, it disrupts the fatty bone marrow and also the surrounding adipose tissue. Then these fat globules, all right, they get sucked into veins, they go -- and when they're -- when blood within the veins, where does it go? It goes to the heart. All right? Blood in the veins, is that high in oxygen Ohio low in oxygen? Venous blood? Good. It's low. So that means if it's low in oxygen, it's going to the heart. So the heart then gets the blood and pumps it into the lungs. So if you have a fat embolism within the venous system, as it moves closer to the heart, the vessels get larger, they don't get smaller, so it travels very easily through the heart, and then it goes to the lungs. Once it's in the lungs, what happens is that the vessels start to narrow, narrow, narrow, and finally it
obstructs. Okay? And it blocks the smaller blood vessels. Now, let's see, air embolism. A large amount of air can be sucked into a circulation from a lung injury due to a chest wound. When we talk about chest trauma, one of the things that occurs in chest trauma is a pneumothorax, and we'll discuss that more in the respiratory chapter, but that's when air gets into the small little space in between the rib cage and the lungs. All right? And what that space is is it's a slight vacuum. That vacuum serves to keep the lung tissue expanded, sucked open. So when there's chest trauma or chest wound, for example a knife stabbing or an auto accident, someone hits -- they're crushed into their steering wheel, you then can puncture that space and you can injure the lung, and sometimes air gets into the lung. Or it can be accidentally injected into the circulation, and so the air embolism then is carried into the right heart chambers, and what happens then is prevents -- it can stay in the heart chamber and prevents filling of the heart by returning venous blood. And then what happens is the heart's unable to pump blood well, and the individual can die a circulatory failure. It all depends really how much air gets into the circulatory system.

Amniotic fluid embolism. As an obstetrician, this was a concern for us because amniotic fluid has thromboplastic activity, and what it does is it creates DIC: It can create DIC. And it's a devastating complication of pregnancy. Amniotic fluid enters the maternal circulation through a tear in the fetal membranes. You have fetal hair, cells, maybe fat, amniotic debris, blocks of pulmonary capillaries causing severe respiratory distress. So you have obstruction of the pulmonary capillaries, and the thromboplastic material in the fluid activates the coagulation mechanism, leading to DIC. Thankfully, when I was in practice, our group never had a patient that died from DIC. Okay? But we did have one or two patients who did have DIC after delivery. And they were always a very complicated delivery.

All right. Foreign particulate matter, embolism. Various types of particulate matter may be injected by a substance user, basically illicit drug use. All right? Some drug users will actually take medication they get in tablet form, crush it and inject it. And when it was just intended for oral use. And as a result, this medication that gets crushed can be trapped in the small capillary vessels, obstruct blood flow and cause respiratory distress.

All right. Septic emboli. Thrombi formed in the pelvic vein following uterine infection. That was a concern. Not so much now, but when I first was doing my residency, what happened is -- and once again, you know, this dates me. I
always tell you I'm really old, but when I first, in my residency, abortions were not legal. Okay? So abortions not being legal, they were legalized during my residency, but when I first started, they were not legal, so we would have patients who would come in with a, quote, back alley or backyard abortion, all right, done by basically relatively untrained people. Sometimes they were very unsterile and as a result the pregnancy may be terminated but they had a uterine infection and it was a severe uterine infection. So these people are very sick, and what happened is because of the infection, it was -- and the pelvic veins were involved, they had a pelvic vein infections, they had to go and they became septic, had to go on IV antibiotics and lots of times we had to place them on heparin, too, all right, because of the risk of developing a pelvic thrombophlebitis. And of course if they had formed an embolus, if that broke off, then you had a septic embolus going to the lungs, so you'd have a pelvic infection. Then you'd have the risk of the infection in the lungs, and the embolus causing necrosis. It was just very complicated.

All right. So emboli from infected thrombus travel to the lungs causing a pulmonary infarct. The bacteria in the clot then invade the pulmonary infarct causing a lung abscess. Venous thrombosis. All right. So what's that? Basically predisposing factors that cause clot formation in the leg veins. What causes that? The most common is prolonged bed rest. Cramped position for an extended period. And these two things occur, for example, cramped position for an extended period, if you've been on a long air flight, okay, you sit in the same position for a long time if you don't get up and walk around. Maybe you visited someone in the hospital after they've had major surgery, and when, if they've had major abdominal surgery, very often they have those white stockings on. What are those white stockings do? They compress the leg veins. They, by putting pressure on the leg veins and compressing them it encourages circulation throughout the legs. The normal way leg musculature works is that when you walk, okay, your calves contract, and that contracting of the calves, all right, pushes blood down the veins. When you stop walking, how come blood in your legs doesn't get pulled down to the floor? Well, part of that is because there are valves in the veins, all right, and they're along the side of the vein, has blood, it's flowing up the vein. They're open. And when you stop walking, then there's a change in pressure, a little bit of the blood then starts to fall down towards the feet, towards the floor. As it does, it catches the valves, and the valves meet. When it catches the valves and the valves meet, it seals the vein and prevents more blood from going down. Okay?
So therefore, the milking actually the leg musculature normally promotes venous return, and if it's impaired then it promotes stasis of blood in the veins, or varicose veins or any other condition preventing normal emptying of veins. Varicose veins are dilated veins. They're tortuous, and blood return can be impaired through them. So the outcome is leg swelling from partial blockage of venous return in the leg, and the result is if you get blockage due to a clot, the risk is that the clot breaks off, becomes an embolus, and ends up in the lungs because remember, this all is occurring in veins, and blood in the veins goes to the heart, right side of the heart, and then to the lungs for oxygenation.

Pulmonary embolism, basically, the clinical manifestations depend on the size of the embolus and where it lodges in the pulmonary artery. Large pulmonary emboli may completely block a main pulmonary artery or major branches and obstructing blood flow to the lungs. If the embolus is really large and blocks a large pulmonary artery, it can cause death. Instantaneous death. And I've seen that. We had one patient who had that.

Let's see. Now, sometimes what happens is when there's an infarct or an obstruction, all right, due to an embolus, infarction does not occur because there can be collateral blood flow from other blood vessels. In the lung you have the bronchial arteries. Blood -- arteries that bring blood to the bronchi, not really via alveoli and as a result they have a different path. They are part of the descending aorta, and they connect with the pulmonary arteries. Symptoms would be cyanosis, where you turn blue due to lack of oxygen and shortness of breath. Okay?

Now, so large pulmonary emboli. If you have a large pulmonary embolus, all right, the right side of the heart becomes distended because one of the main vessels that takes blood from the right side of the heart becomes blocked. The pulmonary artery becomes over-distended with blood, causing increased pulmonary pressure. The left ventricle therefore becomes unable to pump blood adequately to the brain and vital organs because it's not getting adequate blood back from the lungs. And as a result, blood pressure drops in the system, and the patient can go into shock.

All right. Small emboli. What happens with small emboli is they pass through the main pulmonary arteries and they become impacted and peripheral arteries. All right? And what it does is raises the pulmonary pressure, and there's inadequate collateral circulation. The word collateral means it basically supplies, or the blood comes in from a different area than usual. Okay? So collateral circulation. And an example would be if there's a blockage on 75, okay, and the blockage, you're heading South --
actually, you're heading North on 75 and the blockage is right after Fowler, and you really want to get to Fletcher. Well, what can you do? You want to get to Fletcher. You can get off at the Fowler exit and take, you know, a larger route, and then some of the cross roads, and you can get to Fletcher that way. Well, that's a way to get to Fletcher, and that's an example of collateral travel. All right? Where your main pathway is blocked and you get a circuitous type route. Okay?
So then let's see, and if there's inadequate collateral circulation, the pulmonary pressure raise and the affected lung segment that's affected undergoes necrosis. It tends to be a wedge-shaped pulmonary infarct, and then it blocks the vessel. The vessel is blocked, and then it fans out, the damage to the tissue fans out. And if you have an infarct, then symptoms typically are dyspnea, difficulty breathing, pleuritic chest pain, you get pain in the chest when you take a deep breath. Pleuritic chest pain refers to the pleura. The pleura covers pulmonary tissue. It's a thin layer, okay, one cell thick. It's like saran wrap, and it becomes very, if there's an infarction, it extends out to the pleura. Then when you take a deep breath, the pleura is inflamed, and as a result, causes pain. You can get a cough. You can bring up bloody sputum.
All right. So here's an example of an embolus, and then right to the right, you see the bronchial artery which provides collateral circulation to the pulmonary capillaries.
This arrow shows the embolus within the artery. And there's an infarction on the right, wedge-shaped.
All right. So pulmonary embolism. How do you diagnose it? You can -- a chest x-ray may detect the infarct, but not the embolus. Okay? Radio isotope lung scans. Lung scans detect the abnormal pulmonary blood flow caused by the embolus, so there would be a defect or deficiency in the radio isotope being disseminated through the entire lung tree because there's going to be obstruction of the blood vessel. The gold standard is the pulmonary angiogram, where dye is injected into the blocked pulmonary artery and it's proven. The problem is the pulmonary artery is invasive. You have to put a catheter. Basically, it's done, they'll put the catheter into the groin in the femoral artery and then they snake it up through the heart, okay, or there's other ways to approach it. But it is an invasive procedure. Then also the CAT scan, all right, the CAT scan works by detecting the pulmonary embolus, indicated by the flow of contrast media. Information comparable to the pulmonary angiography without requiring insertion of the catheter. The CAT scan, they inject dye, they can inject it peripherally into the vein. They don't have to use a
catheter.

>> STUDENT: What does the gold standard mean?

>> PROFESSOR: Gold standard means the best, okay? Gold standard means, like, if it's demonstrated on a pulmonary angiogram, it's present. And if it's not on a pulmonary angiogram, then it's not present. Even if a chest x-ray's borderline, even if a lung scan is borderline because sometimes that happens.

>> STUDENT: [Inaudible].

>> PROFESSOR: No. It's definitive. In other words, if you get someone who has a lung scan, that's indefinite. That's not really definitive. And you need to nail down the diagnosis. You can do the pulmonary angiogram. Okay? All right. So here the arrows point to the obstruction of blood flow through that blood vessel. Notice just superiorly to it, you see the diameter and then there's a big clot that obstructs blood flow.

All right. So treatment, what do they do? Initially they give heparin. Heparin is given intravenously and it works right away to dissolve a clot, and it can be given every four to six hours. Coumadin, do you remember what Coumadin does? What's it inhibit?

>> STUDENT: [Inaudible].

>> PROFESSOR: Good. Coagulation factors that are dependent on vitamin K. All right. So obviously that's going to take a little bit of time. So you start them on Coumadin at the same time you start the heparin, but the Coumadin's not going to have an effect for a little while, and then the Coumadin dose has to be titrated. Can't give them too much or they're going to bleed spontaneously. It has to be given appropriately, and that's why people on Coumadin have to have their bleeding times monitored. Or there's thrombolytic drugs. All right? That can be used if there's a massive embolus. A thrombolytic drug, one is Streptokinase and what that is, that's tissue plasminogen activated factor and it basically serves to dissolve clots and it's given to people who have had an MRI. Or they've had an obstruction of a coronary artery by a clot, and if it's given soon enough after the event occurs, then it prevents cardiac tissue necrosis.

So angioplasty, a balloon or stent to widen a vein is one way of dealing with it. Thrombectomy is one way of removing the clot. That's going to be surgery. All of these are ways of dealing with a pulmonary embolus, depending on the clinical situation.

Arterial thrombosis. Remember, these are clots within the embolus. Now we're talking about within the artery. All right. Stasis is not a factor, all right, with clots forming in the arteries because of the rapid blood flow and high intravascular pressure. Blood pressure is higher in
the arteries than in the veins.

>> STUDENT: Are angio plasties only in veins?
>> PROFESSOR: No. No. Angio plasties can be in arteries, too.
>> STUDENT: Okay. That's what I thought.
>> PROFESSOR: All right. So basically, the concern with arterial thrombosis is that it blocks blood flow. The coronary artery, as I just mentioned, can be blocked by a clot, and causes infarction of the tissue, necrosis, and we'll talk about this more when we get to the next chapter, chapter 10.

If you obstruct blood flow in a leg artery, you get gangrene, and there's a picture of that in our text. And if it's a cerebral artery, artery of the brain, you obstruct blood flow, you get a stroke.

So here's someone who has gangrene of the toe. Actually, toes. And the other thing is so the black area is the gangrene. But there's also a subsequent cellulitis in the area. See how red it is. And you hear about people who have to have amputation of a limb, a foot, or whatever, because of gangrene. If there's tissue death and obstruction of blood flow, it's not going to come back, and it becomes gangrenous, and the best treatment may be amputation.

So arterial thrombosis. Now, they talk about intracardiac thrombosis. I don't consider that that significant. The concern is that a blood clot can form within the atrium and cause heart failure. We'll talk about the cardiac atrium in the next chapter. It also can form on a valve of the heart and cause valve injury. It also, what happens if someone has a heart attack, all right, and the necrotic area extends into the chamber of the heart so that the actual inner portion of the chamber, the wall of the heart, is affected, the interior wall. That gets roughened. It's scar tissue. Platelets can stick there, and a clot can form.

And then if that clot breaks off in the left ventricle, where is it going to go? It goes into the aorta, and the aorta then brings oxygen-rich blood to different organs in the body such as the spleen, the kidneys or the brain. All right. Thrombosis. All right. What increases thrombosis, all right, or increases coagulability, coagulation. An increase of coagulation factors, okay. Estrogen. Now, they say estrogen, and that is a warning on birth control pills. When you get birth control pills, you read the little packet. However, with the low-dose birth control pills, estrogen is a very, very low risk factor. And I do believe that the pill is an excellent form of contraception. That's why it's so popular. Yes?

>> STUDENT: So if you take, like, Plan B, where it has, like, higher estrogen levels are there increased risks for a
clot?
>> PROFESSOR: No. And what is Plan B? Is Plan B for the termination?
>> STUDENT: Yeah, both before implantation.
>> PROFESSOR: No. Because you're not -- you don't take it long enough.
>> STUDENT: Oh, okay.
>> PROFESSOR: So the higher estrogen levels don't put you at risk because it's only for a couple of days, right?
>> STUDENT: I think it's like one pill.
>> PROFESSOR: And it lasts a little bit longer. Right. Now, years ago, when pills first came out, they had a much higher estrogen content, and that was then the risk of coagulation. Not deep vein coagulation, but superficial venous coagulation. So let's see. Or hereditary gene mutations. And they don't really go into that. All right. So thrombosis in patients with cancer. All right? That can result from increased platelets and coagulation factors, and obviously that will predispose to thrombosis in both the arteries and veins. Hypercoagulability due to rapid release of thromboplastic material and circulation of tumor deposits. Tumor tissue, cancer tissue, can have thromboplastic activity. All right. And then what happens sometimes is platelets and coagulation factors are consumed faster than they can be replenished and you have leading to bleeding. I mentioned that that is one of the problems with DIC. And large tumors release thromboplastic materials slowly but continuously, and therefore the production of coagulation factors exceeds destruction, leading to hypercoagulability. Edema. Edema is accumulation of fluid in the interstitial tissues. And typically it occurs in ankles and legs due to gravity. And it results from disturbance of the balance between the outside the cellular fluid between capillaries and interstitial tissues. Pitting edema is a description, basically how severe is it. All right? If you can depress it or indent in the foot of their ankle, we call that pitting. Hydrothorax refers to fluid in the lungs, and ascites refers to fluid in the peritoneal cavity. All right. So edema, what can cause it. One thing can cause, increased capillary permeability. Easier for fluid to leave the capillaries. We talk about capillary impenetrability with inflammation, inflammatory response, capillaries become more permeable. If there's increased capillary permeability, then that means it's easier for fluid to leave the capillaries and go into the interstitial tissue. All right. Now, low plasma proteins. Proteins exert osmotic pressure, all right? Proteins stay within the
capillary and they exert osmotic pressure, so if someone has low plasma proteins, then their osmotic pressure is going to be less. For example, kidney damage. We'll talk about the kidneys in another chapter, but when people have diseased kidneys, damaged kidneys, what happens is they can spill more protein than urine than they should. If they spill more protein in the urine, there's going to be less protein in the blood and less osmotic pressure. Okay?

Increased hydrostatic pressure from heart failure, all right? When the heart doesn't function well, one of the ways the body compensates is increases blood volume and increases, therefore, the pressure within the capillaries.

Or obstruction, venous obstruction. And another one is lymphatic obstruction. Interstitial fluid will be carried out of the interstitial tissue by the lymph system, and if you obstruct the lymph system, if it's infection, viruses, parasites can invade the lymph system, lymph nodes, and as a result cause obstruction.

>> STUDENT: [Inaudible].

>> PROFESSOR: Obesity can, through different reasons. Really probably not lymph obstruction, okay? All right. So let me see. Factors regulating the fluid flow between capillaries and interstitial tissue. That's the balance. The capillary hydrostatic pressure, what that does is push the fluid out of the capillaries into extracellular space. The space outside the capillary, in between the cells. All right? Capillary permeability determines the ease of fluid flow through the capillary endothelium between the capillary and the extracellular space. Osmotic pressure, all right, is exerted by proteins, and attracts water. So it sucks water back from the interstitial space into the capillaries. And then you need open lymphatic channels for some of the interstitial fluid to gain access into the lymph system. Okay?

So here we have some edema. Okay? Abdominal edema on the left. Here we have some edema here, in the lower picture left leg over the right.

All right. Shock, and then we're done. Basically, what is shock? Low blood flow, low blood pressure to adequately supply the body. It can be life threatening, and shock can be from a decrease in circulatory blood volume. All right? The vascular system can be pumping and working effectively, but you can have decreased blood volume. Categories according to pathogenesis are how do we categorize shock. One is hypovolemic shock. Someone loses a lot of blood right away, okay? Major accident, whatever, they lose tremendous amount of blood. It's called hypovolemic shock. Cardiogenic shock reduced cardiac output, a heart attack. Septic shock is excessive vasodilation secondary to the release of microbial toxins and inflammatory mediators.
Okay?
And then anaphylactic shock is excessive vasodilation from the release of inflammatory mediators. We talked about anaphylaxis before, and septic shock is basically with an overwhelming bacterial infection. Yes?

>> STUDENT: What blood pressure is too low?

>> PROFESSOR: Depends on the person. Depends what you're used to. You know, say someone's hypertensive and not treated, okay? Say their blood pressure is 160 over 110. Someone -- and then they come in and they're 90 over 60, they could go into shock because of the relative drop.

>> STUDENT: Usually when I take my blood pressure, it's pretty low.

>> PROFESSOR: Well, I was going to say, you know, I bet there are people in this room whose blood pressure is 90 over 60. Right. So that's fine. And so someone who's -- you know, it's hard to say, but someone who's 90 over 60 normally, if you're 70 over 40, 70 over 30, then you get a little dizzy, the potential of getting dizzy or if you stand up, you could fall, that type of thing, you know, that's a generalization I don't like to make.

>> Right.

>> PROFESSOR: All right. Let's see. So the prognosis of shock depends on the early recognition and rapid treatment. Drugs that promote vasoconstriction, use of intravenous fluids if you're dealing with hypovolemia. Okay?