>> Today is October 30th. This is Lecture 20 in Phys. Let's review only briefly the concept of hemostasis, which means literally to stop the loss of blood, which is inherently an important mechanism. There are two ways to do so. One is called "vascular spasm." This means the local constriction of arterioles that have been injured, or cut in a particular incident or wound, this is a reflex triggered by pain, and also chemically supported by the compound serotonin, which as you know is released from platelets. This mechanism may or may not be successful. In other words, it may reduce blood loss, but is usually accompanied by, and supported by, coagulation, which we think of in a more significant way. In other words, blood loss is mainly restricted, or otherwise blocked by coagulation. Coagulation is making a plug, p, l, u, g, which is otherwise known as a "thrombus." This is ultimately an enzymatic reaction triggered in the beginning by some injury to a vessel, which causes platelets to stick to the wound. That's called "platelet adhesion." At the same time, the cells that have been destroyed, that is the cells of the injured vessel, are going to release their own chemical factors. And, so, platelet factors and tissue factors combine to form something called "prothrombin activator." Prothrombin activator is just that. It activates existing prothrombin, a precursor molecule coming from the liver, and converts this pre-enzyme to the actual enzyme thrombin. Thrombin, which incidentally requires calcium, concludes the final step, which is transforming fibrinogen into fibrin. And what's the difference? Fibrinogen is water soluble. Fibrin is water insoluble. This final step is what creates this insoluble network of protein, which is fundamentally a clot. And, so, this process, we'll demonstrate tomorrow in lab, takes about two to five minutes, because it is a multi-step sequence of events. We talked about anti-coagulation, which involves any effort to either reduce clotting, or destroy an existing clot. You see, vessels are injured all the time, and not necessarily appropriate for clots to form in every case. So there is a prevailing anti-clotting system. And the chief, and major natural anti-coagulant, is heparin, manufactured by a lot of different tissues, especially the lungs and liver. Basically, heparin is an enzyme inhibitor. What does it inhibit? Thrombin. Therefore, it reduces, or slows down, the creation of an inappropriate or undesirable clot. Also in our bag of tricks is an artificial compound called "coumarin," also known as "warfarin," and so forth. These are various drugs that are available. And they act mainly on the liver by inhibiting what vitamin that is necessary for the production of prothrombin? Vitamin K. If you inhibit that vitamin, or if you antagonize this action, then the net effect is a reduction in prothrombin. And, therefore, some reduction in coagulation. So people who have a tendency to form clots may be on these medications. And what's the common misnomer that you hear thrown about? What are these called by the lay folks?

>> Blood thinners [multiple speakers].

>> Blood thinners, which, of course, they're not. Water thins blood, but nothing else. Then we have these so-called "clot busters." Mainly tPA. These are used in hospital settings to dissolve existing clots, inappropriate clots that might be obstructing coronary vessels, cerebral vessels, and the like. So there

you go. That's our review of hemostasis. We have one more blood-related issue, which bears heavily on what we'll do tomorrow, because among the things you'll examine tomorrow, or determine tomorrow, is your blood type. How many of you know, or think you know, your blood type? At least half. And half of those who think they know their blood type will probably find that, well, it may be different. That's not that it changes. Blood type doesn't change. Nothing you can do will change your blood type. But very often people are misinformed about their blood type. So we'll see how that works out tomorrow. So what is blood typing? Actually successful transfusion and blood typing is predicated on avoiding a very undesirable blood response called "agglutination." Not to be confused with the "c" word. What's the "c" word that almost rhymes with "agglutination?"

[Inaudible Speakers]

This has nothing to do with coagulation. Instead it's called "agglutination," which is the clumping, and the subsequent hemolysis, of RBCs. Now as a definition, does "agglutination" sound like a desirable thing? Is there anything good about clumping and hemolyzing red blood cells? Absolutely not. So this is not a desirable mechanism, but actually a result of an inappropriate immune response to foreign blood cells typically introduced as a transfusion. So obviously this is a bad mechanism. And it was, in fact, the reason that transfusions were unsuccessful when first conceived, and remained risky and unsuccessful until the discovery of what are called "natural RBC antigens." These antigens are numerous. In fact, they number into the 100s. But the only important antigens, that are the basis of blood typing, are antigens A, B and D. The latter used to be referred to as capital r, lowercase h, which stood for "rhesus." Not the peanut butter cup, but the monkey. And we'll see more about that in a minute. But I think it's interesting, because when somebody has hemorrhage, or blood loss, what's the intuitive therapeutic measure that we know today to be obviously necessary? Somebody's lost a lot of blood. What's the obvious therapy? A blood transfusion. I mean isn't it logical that if you've lost blood, you should replace that blood as soon as possible? But certainly, in the time of George Washington, and even until the mid-1800s, transfusions were not only not done, but they were thought to be bad. And, so, what, in fact, was the therapy for blood loss? Not transfusions. Bloodletting. Isn't that preposterous? A patient's lost a lot of blood. Let's let more out. Yeah. This is an account from 1824. True story. A French sergeant was stabbed through his chest while engaged in combat. Within minutes he fainted from a loss of blood. So he was taken to the local hospital. And immediately he was bled .5 liters to prevent inflammation. During the night he was bled another .6 liters. Early the next morning the chief surgeon bled the patient another .3 liters. And during the next 14 hours he was bled five more times. So medical personnel intentionally removed more than half of his blood volume. Not to mention that which was lost at the time of the injury. So bleeding continued over the next several days. Two weeks later his wound had become inflamed. So the physician applied 32 leeches, 32 leeches, to the wound. And over the next three days more

bleeding's totaling 40 more leeches. Finally, two months after the injury he was released from the hospital. His physician bragged, "That by large quantity of blood loss, amounting to over 4.8 liters, I was able to save my patient." So isn't that crazy that he survived, not because of his physician, but in spite of his physician? And, so, bloodletting, ridiculous as it seems, was the therapy until the discovery of these antigens, which make possible the safe and appropriate implementation of transfusions. So let's get into it. Basically, blood types are based on the presence, or absence, of these three known antigens. And the primary blood groups are thus A, B and 0. Although most people pronounce that not "zero," they pronounce it "oh." So this is not complicated, but it's easy to get lost. So stay with this. If you have the A antigen on the surface of your red blood cells, if you have only the A antigen, then you're obviously type what? A. Now if you have the A antigen, your immune system will manufacture B antibodies, which is not inappropriate, and no problem whatsoever, because, remember, antibodies attach to antigens. And these antibodies will only attach to B antigens. So the presence of these antibodies in your blood do you no harm, and, in a sense, are protecting you from B antigens, should they be acquired through a faulty transfusion. Next, it's possible for your RBCs to have, not the A antigen, but just the B. And what would be the appropriate name for your blood if you have only the B antigens? B. If you have only the B antigens, then it's quite appropriate, quite okay, for your immune system to manufacture A antibodies. This does you no harm, because you don't have the A antigen. So this is natural, appropriate, and perfectly safe. What are the other two possibilities that you can think of? Well, maybe you have them both. Maybe you have both A and B antigens. That's possible. And if you do, what would be the name for your blood type?

>> AB [multiple speakers].

>> AB. If you have both of these antigens, then it's inappropriate, and obviously self-destructive for you to have either A or B antibodies. And, so, your immune system manufactures neither A nor B antibodies. In fact, if it did, what would happen? What if you had both antibodies, and had both antigens? Then you would have clumping and hemolysis. In other words, agglutination. In other words, death. So certainly the presence of both antigens precludes the possibility of you having either or both antibodies. Now what's the fourth, and only other, possibility? Let's review. It's possible to have A alone. It's possible to have B alone. It's possible to have both A and B. And it's also possible to have neither. And if you have neither A and B, you're said to be type O. But that's actually a misstatement, because it's not "o," as in "Oh, my God." It's what?

>> "Zero [multiple speakers]." "Zero." You see, oftentimes when you give a phone number out and there's a zero in there, you often say what? "Oh" when you meant to say "zero." So like it or not, this is called "oh," but it really means what? "Zero." It means you don't have A or B antigens. And if you do, that is if you don't have either these antigens, then it's quite okay, and, indeed, natural

to have both A and B antibodies. So this is the fundamental framework for the basic description that is the A, B, 0 groups. Now there is something odd, or at least questionable, about this, because considering antibodies and antigens, which was our story last Wednesday, when does the body make antibodies to an antigen? When does your body make an antibody to a particular antigen?

[Inaudible Speakers]

Only when you're exposed. And, so, that makes this a little unexpected, because people who have the A antigen will make B antibodies spontaneously, whether or not they've ever had a transfusion. Appropriate or not. And, so, this fact is something called "spontaneous induction," which means your immune system will make these antibodies, even without obvious exposure to the antigen. And for years and years this was not understood, because it was contrary to this notion. What notion? Normally the immune system never makes antibodies until it's exposed to the foreign antigen. This seemed to be an exception, because these antibodies are actually produced spontaneously within one year of your birth, without exposure to any other blood. And for the longest time it remained a mystery. We now know that in that first year of life your diet, your digestive system, I should say, is much more permeable to bacteria than it is later. And many bacteria in our food contain antigens, which mimic or resemble A, B or both. And, so, not actually knowing it eating a normal diet during this first year of life exposes you to bacteria, which have antigens similar to A and B. And, therefore, cause your immune system to make A and B what?

[Inaudible Speakers]

Antibodies, even though you've not had a transfusion. So this discovery answered that question. And, like it or not, it's the way it is. In other words, if you're born type A, you will automatically within one year make what? You'll automatically make B antibodies. And if you are born type B, your immune system will automatically, and unavoidably, manufacture A antibodies within the first year. Now this forms the basis of what's called the "AB0 blood typing system." And naturally it raises the question then, how can we avoid a bogus transfusion which would ultimately lead to death? Cause of death "a" word–agglutination. So when someone is a candidate for a blood transfusion, obviously his or her blood has to be compatible with the blood that you're giving. And naturally, and obviously, and usually, if you're type A, what type of blood do you think you're going to get? A. But sometimes there might be a shortage or a rush, that is an emergency, which might demand a little different approach. So perhaps you've heard of these expressions. First of all, something called the "universal recipient," which is self-explanatory. What's that mean? The universal recipient? That kind of blood can what?

[Inaudible Speaker]

Receive any kind without fear of the "a" word. What's the "a" word?

>> Agglutination [multiple speakers]. So what type of blood could receive any

other, and not agglutinate those cells? Well, clearly it's AB, because AB has neither A or B what? Anta?

>> Bodies [multiple speakers].

>> Bodies. And, therefore, any blood you give will not be "a" word, not be agglutinated. So quite logically AB blood is considered the universal recipient. That's because it can receive any of the other blood types without fear of agglutination. Now what's the opposite of the universal recipient? That would be something called a "universal donor." And that would mean blood that you could give to what? Give that to anybody without fear of what?

>> Agglutination [multiple speakers].

>> Without fear of agglutination. And look at the list. What type of blood has no antigen, and, therefore, can't be agglutinated by any antibody that it might encounter? Clearly that's type 0. Let's call it type "zero." And it is the universal donor, because these cells have neither A or B antigens. Therefore, they can't be agglutinated. Type 0 then the universal donor, because the cells are compatible with any type of plasma. Now these remarks, these designations, are in quotes. Do you see that? Because when we say "universal donor," it's kind of tongue-in-cheek. Meaning that there is some risk here. And some of you have already detected it. Because, obviously, yes, type 0 has neither what? Has neither A or B antigens. But that blood has both antibodies. And when you give blood, aren't you giving the recipient those antibodies, too? And couldn't they agglutinates some of the cells of the recipient? And if you scratch your head on that, you say, "Well, why then is this called the 'universal donor?' Isn't there some risk from the antibodies that you're giving?" And the answer is "yes." But that risk is very low for reasons that we'll see in a minute. So if someone is considering or in need of a transfusion, obviously, we want to make sure that the blood we're giving is in fact compatible. And, so, upstairs in the laboratory, I'm speaking in a hospital sense, are there laboratories in every hospital which check, among other things, blood that's available for transfusion? And, so, a simple and routine test is called "crossmatching." You might have picked up that word on TV. It's a routine and simple, inexpensive test to make sure that the blood you're preparing to give is going to be "c" word. What?

>> Compatible.

>> Compatible. What's that mean? Compatible? We want to make sure that these cells are not going to be "a" word.

>> Agglutinated [multiple speakers].

>> Agglutinated. And, so, what are the steps in what's called a "double crossmatch?" This test doesn't require any sophisticated instruments, doesn't require a microscope. All it requires is one of those porcelain dishes that we used the very first lab. Remember those white dishes where we put blood in it? In fact, that's all you need. And here's how it works. You take a sample of the donor's cells, in other words, a blood sample, and you expose it to a sample of the

recipient's serum, and you just mix it up with toothpicks. That's all. And you don't need a microscope, because you're looking for the "a" word.

>> Agglutinate [multiple speakers].

>> Not coagulation, but agglutination. And if it agglutinates, if the cells clump, then you know you've got a problem, then you know that the recipient's serum must have what?

>> Antibodies.

>> Antibodies against the donor's antigens. And would that be enough to stop, or cause pause in your attempt to transfuse that blood? Yes. Because it would be lethal. Because if the serum had antibodies against the donor's antigens, what would happen to the donor's cells? "a" word.

>> Agglutination [multiple speakers].

>> And what is agglutination? Clumping and hemolysis. Game over. The second part of a double crossmatch is the reverse of this. And if you think about the phraseology here, it's just that. We take the recipient's cells, and we expose them to a sample of the donor's serum, mix them up with a toothpick. We're looking visually for what? Visually for clumping and hemolysis, otherwise known as agglutination. If there is agglutination, then we know the donor's serum has antibodies against the recipient's antigens. And that would be concerning as well. So either one, or both of these. would be cause to suspend, that means discontinue, any attempt to use that blood for given transfusion. But of these two, Step 1 or Step 2, Step 2 is not such a big deal. Now why is that? Certainly the donor's serum having antibodies against the recipient's antigens would seem to be concerning. But two reasons make this less of a concern. First of all, you're giving this blood to a recipient who has a huge volume there. So will this donated blood be diluted by the body you're giving it to? Therefore, those antibodies, even though they are in high concentration here, once you put them in this recipient, they're now going to be in low concentration. That's one reason Step two not a big deal. The second reason has to do with the way transfusions are done these days. In the old days transfusions were whole blood. Meaning giving actual whole blood. But now we realize that when a transfusion is indicated, we don't really need whole blood. What does the patient need? Plasma or cells? Cells. So we get rid of a lot of the plasma. And we pack the blood down. In fact, you may know this is called "packed" blood. Meaning a lot of the "p" word, a lot of the what? Plasma is gone. And with the plasma removed, you're taking away a lot of the antibodies, which would otherwise be carried through. So for these two reasons, the second of these possible conflicts is quite minimal. Because often the volume that we're giving is going to be diluted, and most transfusions today are not whole blood, but packed cells. And, therefore, minimizing the delivery of antibodies, which would otherwise be a potential threat to the person's blood cells. So what's the name of this test? It can be done in less than five minutes. It's called a? Crossmatch. A double crossmatch. And you would assume, and expect and hope, that a double

crossmatch would be routine. It costs almost no money. But yet oddly not. There's an interesting story that dates back to I think 2003, but not really that uncommon. It's attached to the attendance sheet, which is going around. And the story goes like this. There was a 17-year-old girl down in Haiti. She needed a heart-lung transplant. She couldn't afford it. And there were no facilities in Haiti. So a wealthy American benefactor flew her up to the U.S. of A. to Duke University, because he wanted to pay for a heart-lung transplant. A very great, very generous thought. So she came up. A donor was found. Heart, lungs installed. Surgery went well. But then a deadly "a" word, agglutination reaction. Why? Her blood type was 0. The organs that were transplanted came from a patient who was type A. Now you scratch your head, and say, "Well, who would make such a blunder?" Well, fingers started to be pointing. Right? The surgeon said, "Oh, not my fault. I just did the installation." And fingers got pointed on down the line. But what was the problem? They installed lungs from a patient who was type what?

>> A.

>> A. And the recipient was type 0. What antibodies did she have that agglutinated, and, therefore, rejected that organ? She had both A and B. Now they discovered this. And they immediately tried to find a replacement. But they couldn't. And she died. So a simple, very basic, and cheap test was either ignored, or somebody just didn't follow up. And death occurred. And, so, if a transfusion is done in a hospital setting, is crossmatching obviously indicated? Yes. And even if it has been done, when you're hanging blood in a hospital room, do you just hang it, and say, "I'll see you after my lunch break?" No. Nurses always stay what? Right there, because this reaction, what is it, the "a" word, agglutination will happen within minutes. And just because it says "A" on the label, doesn't mean that somebody may be blundered with a basic thing like a crossmatch. So typing is necessary to avoid death through agglutination, and is the basis then for safe transfusions as we know today. But part of our story is still not in place, because we've mentioned only how many antigens? Two. You might say three. But only two. What are the two antigens we've mentioned?

>> A and B [multiple speakers].

>> A and B. 0 is not an antigen. What is 0?

[Inaudible Speaker]

Nothing. So only two mentioned so far. The third one, which you will also assay tomorrow, is the D antigen, which is actually three–C, D and E. And it was first discovered in a rhesus monkey. And, so, for that reason even today it's called the Rh factor. But it's actually three antigens. The most important one is the D. So if that's confusing enough, let's go on. Essentially this so-called Rh factor, which is mainly the D antigen, can be or may be inherited along with the other two. And, so, if it is, it is. If it's not, it's not. And, so, this is even more simple than the A and B story. In short, if you have the Rh antigen, you're

said to be Rh? Positive. Doesn't that make sense? If you have the Rh antigen, you're said to be Rh? Positive. And obviously, I think obviously, it would be stupid for your immune system to make antibodies against your own antigens. In fact, that does happen. And we gave it a name last week. What do you call those syndromes where your immune system manufactures antibodies to your own antigens?

>> Autoimmunity [multiple speakers].

>> Autoimmunity. But, anyway, normally that wouldn't happen. So if you are Rh positive, your body will never make Rh antigens. The other possibility, the only other possibility, is that your cells don't have the Rh antigen. And what name might apply? Rh negative. Now let's be clear, Rh negative is nothing. That means you don't have the Rh antigen. And if you don't, then is it okay, is it permissible for your immune system to make Rh antibodies if you don't have the Rh antigen? Yeah. That's perfectly okay. And, in fact, in this case, the production of these antibodies follows the normal pattern. What is the normal pattern? We mentioned before, your immune system only makes antibodies if you're exposed to the foreign antigen. And, so, the production of these antibodies is not going to occur within the first year, or maybe not ever until, and unless, you're exposed to the Rh antigen, which would have to be the result of a transfusion that went bad, or in this not so uncommon scenario where you've been exposed to the Rh antigen as a result of delivering an Rh what? Positive baby. Now obviously this applies only to females. And not all females. Because what females would ever be able to produce Rh antibodies? Only those females who are themselves Rh negative. And that's less than 15% of the American population. So this is rare. But it's not uncommon. That is to say, it's not something that you should dismiss. And, in fact, it has some personal meaning to me, because my wife is Rh negative. So here's the story, which you may have heard. Here's mom. And let's say she's something. But she's basically Rh what?

>> Negative.

>> Negative. So she might be 0 negative, A negative, AB negative, whatever. The thing is she's what? Rh negative. Now here's her baby. You can call it a fetus if you want. And is it possible for this fetus to be conceived, and actually have a blood type which is Rh positive? That's entirely possible. Because, remember, baby's not made just by mom. Baby's made also by dad. So is that possible? Sure. What's the big deal? Nothing so far, because these bloods do not mix during gestation. Does baby's blood ever get into mom's blood, or vice versa? No. That doesn't happen. But here's what does happen. At birth the baby's born. Yes? Okay, fine. But what's born after the baby?

>> Placenta.

>> The placenta. And does the placenta contain a lot of baby's blood? And is the uterus of the mom bleeding at the same time? So now you have what you didn't have throughout nine months. You have baby's blood mixing with

mom's blood. And, so, mom sees this blood as not hers, right, because she's Rh negative, this is Rh positive. What does mom's immune system do? Mom's immune system does the right thing. Mom's immune system makes anti-Rh. Okay? Fine. Any problem? None whatsoever, because this baby's already in the crib, and maybe off to daycare, who knows. My point is that first baby got off clean. But let's say nine months later a second baby comes along. A little early. But okay. It's possible. Second baby also Rh positive. Well, okay, let's do it this way. Second baby Rh negative. Any problem? No, because, well, let's answer this. Do these antibodies get into fetal circulation? The answer is "yes." Not only do they, they should. Remember, our baby's born with antibodies that the baby himself/herself actually didn't make. Is that a kind of immunity? Yes. So is it okay for antibodies to get into the baby? Sure. Are these antibodies going to be welcome? Well, not a problem here, because second baby was what? Rh?

>> Negative [multiple speakers].

>> But what if second baby turned out also to be Rh positive? Now these antibodies are going to get into baby, and do what to these cells? "A" word.

>> Agglutinate [multiple speakers].

>> Agglutinate them. Would this baby be killed on site, or otherwise have a massive problem? Yes. This is called "erythroblastosis fetalis," and it doesn't affect the first baby. It affects the second baby, only if that baby is? And only if the mom, of course, from the very get go was Rh negative. Now this may take a while for you to actually come to complete understanding of. But clearly if this is a problem, the obvious strategy medically would be to prevent the mom from making what? Somehow prevent her from making anti-Rh. Because if you think about it, this does her no good. And it does a potential second or third baby harm. So is it okay to somehow prevent her from making those antibodies? And how do you do that? Can you prevent the blood from the baby getting into the mom? That's not possible. That's going to happen. But here's the interesting thing. What if you give the mom anti-Rh before she gives birth? Hmm. Now that seems odd, because, wait a minute, you want to give her anti-Rh so she doesn't make anti-Rh? Well, hold on. If you give her an injection of what? Then these cells that come over are going to be "a" word. Right on the spot. They're going to be agglutinated. And, therefore, it's as if her immune system never saw those, because those cells are what? Stopped right in their tracks. And you say, "Well, what about this anti-Rh? Won't that be around?" Well, not very long, because the next baby's not due for at least nine months, and those antibodies will disappear. Remember, injecting antibodies doesn't cause new antibodies to be made. Now if you're aware of this overall situation at all, there is a name for this treatment. It's called RhoGAM. And it's nothing more than a solution of what, anti, Rh, given to the mom when? Before delivery. To do what to the cells, which we know are going to come over?

>> Agglutinate [multiple speakers].

>> Agglutinate. And, therefore, prevent her system from making anti-Rh. Would RhoGAM be necessary for all pregnant women? No. Only women who are pregnant and happen to be what?

>> Rh negative.

>> Rh negative. And only if they plan to have a second baby, which you never know. Now back to my story. My wife is Rh what?

>> Negative.

>> Negative. And our firstborn, Natalie, was also Rh negative. And incidentally this is determined right there at the moment of birth. It's not like a day later. So as soon as the baby's delivered, what's one of the first things that's done? Type that baby. So Natalie came out. She was what? Rh negative. So I said, "Great. We can save money on the RhoGAM." I didn't actually say that. But even though I was thinking that, because you don't have to give RhoGAM if the baby's Rh negative. Only if the first one was Rh what?

[Inaudible Speaker]

And, so, I noticed that I got billed for RhoGAM. No. And, so, I said, "Wait a minute. Why did we give the RhoGAM there? It doesn't make any sense." They said, "Oh, well, yeah, we know that physiology stuff. But we give it anyway." I said, "Why? Is this just a ripoff or something?" "No. It's a very good reason. Yes, your daughter was what? Rh negative. And, yes, there was no need to give RhoGAM. But do laboratories make mistakes? And what if the next day they said, 'Whoa, Mr. Langjahr, Natalie turned out to be Rh positive. Sorry about that.' Well, we missed the boat, because RhoGAM wasn't there." And, so, RhoGAM is almost always given just to cover, you know, what is it, "CYA," just to cover things, so to speak, in this case of a possible mistake. So in summary, tomorrow you're going to measure your blood type. And if you have all three antigens, what then will your blood type be? What are the antigens? They are A. They are B. And they are D, which is also called Rh. If your cells have all three, what is your final declaration?

[Inaudible Speakers]

You're AB Rh positive. What if you have none of them? Is that possible? Yes. If you don't have A, don't have B, and don't have Rh, then your final description is 0 what? 0 negative, which means zero and nothing, which is exactly what it in fact is. Is it possible to have any combinations thereof? Can you have this, but not those? This, but not those? Yes. And, so, that's what you'll be searching for–your blood type. And, incidentally, in case you don't know, the most common in the U.S. of A. is right there. 0 positive. That means no A, no B, but definitely the Rh. I'm a member of that club. And probably 50% of you are members of that club. Now don't get me wrong. I'm not saying this is a distinguished or somehow exclusive, or you're better or healthier. It's just what you are. Nobody's going to say that blue eyes are better than brown, or that 0 is better than A. It's just a fact. But you'll

discover that tomorrow. And, hopefully, it'll agree with what you know, or think you know about your blood type. Blood typing. Basically a method to check for antigens, and, therefore, avoid that embarrassing deadly possibility. What's the "a" word? Agglutination, which might be the result of a faulty or a necessary transfusion. Tomorrow's lab then exciting, because you're going to be measuring your blood type. Also be counting red cells, white cells, measuring coagulation, hemoglobin, hematocrit. A lot of fun stuff. Now with no fanfare or drum roll, let's switch into a different system, because we're closing the book on the circulatory system, and linking up all of this information to the respiratory system. It's easy to think of these systems as separate. But hardly. Because what's one of the obvious first and most important functions of the circulatory system? It's to get that gas what?

[Inaudible Speakers]

And circulate that gas. And return and get rid of that other gas.

[Inaudible Speakers]

So clearly the circulatory and the respiratory system are basically working for at least that common goal. And, so, failures of the respiratory system, failures of the circulatory system, have repercussions on these gases. That is, effects on blood gases. Before we get to the physiology, we'll review quickly the anatomy. And certainly the fundamental function of this system, which is to acquire, to exchange, and to bring about the utilization of these two important blood gases. That is, exchanging them from the environment and the organism, and from the organism back into the environment. It's too simple to think of respiration as just breathing. Breathing is only a part of what this system does. So before going into the fizz, or even the anatomy, what are the basic elements, the sub-processes, that are involved in the operation of this system? First, ventilation. It's a familiar enough word. You open the window, what do you call that? Open the window. You're what? You're?

>> Ventilating [multiple speakers].

>> Ventilating. Ventilation is the physical act of moving air in and out of the lungs. In other words, the "b" word–breathing. Now this process is a mechanical one. It's a physical one. It's a muscular one. And actually has almost nothing to do with the lungs. Ventilation almost nothing to do with the lungs, because moving air is not a function of the lungs. It's a function of the ribcage and the diaphragm, and the air pressure changes that occur around the lungs. But no one's saying that ventilation is not important. In fact, if you're not ventilating, you're soon to be what?

>> Dead.

>> Dead. So ventilation, important. But one of three processes. The second of these three is really, you could argue what it's all about, it's called "gas exchange." Now the word "exchange" may have different meanings. But it's not

terribly outside your vocabulary. When you go to the grocery store, what do you exchange for what?

[Inaudible Speakers]

You exchange money for groceries, food. Right. So that's what it is. But what's being exchanged here? And by what means? Essentially, there are two sites for what is gas exchange. The first site, or location, occurs at the lungs. And what gas is being acquired from the environment? And what gas is being given back to the environment? You got it. So we're basically exchanging what? What are we getting from the external air, and putting into the blood? Oxygen. And what are we taking out of the blood, and putting back into the external air? Oxygen. So notice that this process of gas exchange is a two-way street. So already you wrote what up here? Oxygen. And what did you write there? Carbon dioxide. It's easy, but oversimplified to emphasize oxygen. In fact, that's what you hear most about. Oh, the lungs are forgotten. You're forgetting what? Oxygen. Is it equally important to get rid of CO2? In fact, we're going to make the case that it's even more important to get rid of the CO2. And that'll be clear later. So gas exchange is a two-way street, which doesn't conclude here, but also also occurs at the second site. In other words, between the blood and the tissues. What gas is going to come out of the blood, and go into the tissues we assume? Oxygen. And what gas is going to come out of the tissues, and go into the blood? CO2. Now this process is gas exchange, but it's not magic. It's, in fact, the "p" word. What's that? Passive. What causes oxygen to leave the blood, and go into the tissues? It's not because the tissues want blood, or they're paying for oxygen, or anything like that. The reason oxygen is leaving the blood, and going into the tissues, is simply the rule of passive diffusion. From a high to a?

[Inaudible Speakers]

Now instead of using the word "concentration," we're going to use the word "pressure." But still it's the same notion. It's passive diffusion from a high pressure to a low pressure. Obviously, there are lots of details here, which we won't even get to today. But this is, of course, the meaning of gas exchange. And clearly it depends upon the health of what? What are the organs that make this possible? Obviously, the lungs. But also, obviously, the circulatory system, because we've got to circulate blood through the lungs, and then we've got to circulate that blood out to the body. So to put it simple, if the lungs fail, is gas exchange going to suffer? Obviously. If the heart fails, will gas exchange suffer? Sure. So we see this unification, this cooperation, between circulation and respiration. They work hand-in-hand. And the failure of one dooms the overall process of gas exchange. What's the final element? It's something we spent a whole unit on. And that's cell respiration. This is all about glycolysis, aerobic or anaerobic, and the citric acid cycle. Because, remember, what's the point of getting oxygen is to provide for that function. What is the one and only function of oxygen? One and only function of oxygen is to be the final electron acceptor at the end of the ETC. Is that pretty important? Yeah. If you don't have that, the rest is all moot. So cell respiration depends upon, obviously, good

ventilation, and good gas exchange. But clearly we're not going to talk about C at all. Because we already did. Our focus then ventilation and gas exchange. And ventilation will be today. In fact, also Wednesday, because there's a lot to talk about there. Then a whole lecture devoted to gas exchange. So that's our agenda or previews of coming attractions. Now we should assume this, but we won't. In other words, we have to talk about anatomy of this system. So a little review. We know that air is taken in, and passed out of the nose, or maybe the mouth. So the nasal cavity is certainly mentioned, as is the oral cavity. Air then will pass into the "p" word. Maybe that's legible. The pharynx. Then through the "l" word. Larynx. Then down into the "t" word. Trachea, which then bifurcates into primary bronchi. You remember this? Primary bronchi bifurcating into secondary bronchi, tertiary bronchi, and so forth. Eventually down to what are called, not bronchi, not bronchus, but "bronchi" what? Oles. Now that suffix is not unfamiliar. What do we call big, big vessels that carry oxygenated blood?

>> Arteries [multiple speakers].

>> Arteries. The smaller ones are called arteri?

>> Oles [multiple speakers].

>> Oles. So big tubes that carry air are called "bronchi." Tiny ones are called "bronchioles." It's a very familiar enough suffix. And bronchioles divide even further, you might remember, into what are called "respiratory bronchioles," ultimately, I should say, "terminal bronchioles," eventually into "respiratory bronchioles." But finally, and ultimately, the tiniest of microscopic air sacs that I'm sure you know are called "alveoli." Now everything from this point up, all of that stuff, is basically just airway. That is, tubes for air to move through. Everything from this line down does more than move air. It allows for this process, the "e" word. Gas exchange. So for that reason, these larger conveyances are called "conducting units." And all of these are called "exchange units." What's that mean? What are we exchanging? What are the gases that are being exchanged? Carbon dioxide and oxygen. So that's an anatomical review of terminology. And before we get down to physiology, let's at least pay some respect to the conducting units, which the name tells you, move air. And, as you know from Anatomy, the big airways are lined with simple ciliated columnar. "E" word.

[Inaudible Speakers]

Epithelium. Remember that? Simple ciliated columnar epithelium. Which are also punctuated by those cells called "goblet cells." Remember those? Okay. The goblet cells make the "m" word. What's the "m" word?

>> Mucus [multiple speakers].

>> Mucus. And the cilia, of course, move constantly, 24/7. And, therefore, the combined function of this mucus membrane is to trap airborne stuff, and then move that stuff, not down into the lungs, but move it back up from where

it came, so that you can spit it out, or swallow it, or put it into a Kleenex, or whatever you want to do. So the conducting units have the function of cleaning the air, cleaning the air. At the same time, they moisten the air. They add water vapor to the air. At the same time, they heat the air. So as a result of these three functions, by the time air reaches the alveoli, is it body temperature? Yes. Is it humidified? Yes. Is it clean? Yes. Unless you're smoking cigarettes. But with that exception, this works pretty well. And its function is to condition the air, so that it's free of impurities, so that it's proper temperature, and also proper moisture content. Now the conducting units also make possible what we love to do. And that's talk. That is, permits what? Vocalization. And that's mainly because of the vocal cords, which are located in the larynx. And human beings, obviously, have refined that. We're not just squeakers and barkers. But we can create words that others understand. So it's an amazing development that is made possible by the functioning larynx. But let's skip down to the exchange units, which, basically, include or mainly are represented by the 100 million alveoli. If you look at lung tissue, and all of you did at least in Anatomy, you were probably struck by the fact that lungs are not like balloons. Sometimes they're shown or represented as balloons. They're more like bread. They're more like a sponge. They literally are an air sponge made up of, well, lots and lots of alveoli. And if you could spread those alveoli out on a flat surface, it would amount to anywhere from 800 to 1,000 square what? Which is half a tennis court. Just for reference. Now that's incredible, incredible surface area, which makes possible and improves what process? What process did we say is contingent on passive diffusion, and intact healthy lungs?

[Inaudible Speakers]

All right. Gas exchange. Do you need all this surface area? Well, you could argue either way. Right now you're not using all that surface area at all. Can you live with one lung? Can you live with half of one long? Yeah. Then why all this extra? Well, are there times when you need all that surface area? I never go there. But there are people who exercise. I know. I've seen them on TV. And they use what? Not just some, but pretty much all of that surface area. So can you get by with less? Yes. Are many people getting by just fine with less? Yeah. But when you're out there doing something like exercise, then, obviously, you need all of this. And speaking of that, can this surface area be compromised? Are there ways of gumming up, or otherwise destroying, the surface area? Emphysema, asthma, bronchitis. The list goes on. So the surface area is there. And its function is to permit efficient, rapid gas exchange. That is, in and out of the alveoli into the pulmonary bloodstream. None of this would be possible if it weren't for muscular effort. And let's be clear. Lungs have no muscle. Lungs are just, basically, air sponges. The muscular units, which make possible ventilation, are, basically, divisible into two types of muscle. Those that are involved in inhalation are called "inspiratory muscles." And their job is to increase the chest size, and, therefore, lower the intrathoracic pressure. The intrathoracic air pressure. As you know from Anatomy, what is the most important skeletal muscle which leads to expansion of the thoracic volume, and,

therefore, lowering intrathoracic pressure accordingly?

>> Diaphragm [multiple speakers].

>> Diaphragm. You might think, incorrectly, that the diaphragm is smooth muscle. But it's what?

>> Skeletal [multiple speakers].

>> Skeletal muscle. Absolutely dependent on a nerve, that you might recall, called the "phrenic nerve." The diaphragm does almost all the work of inspiration. It's innervated by the phrenic nerve. And it's assisted by some other muscles, which are located from rib to rib. And these, you recall from Anatomy, are called the "external intercostals." Their job is to pull the ribcage up. Something we call "elevation of the ribs." And when you think about it, if the ribs are elevated, your chest protrudes. Does it not? And when your chest protrudes, it's getting bigger. And that's going to do what to the pressure of gas inside? Decrease it. So in any given breath your diaphragm is the key player. But there may be instances where your external intercostals get involved. And when would you need that extra, extra inspiratory effort? "E" word. Exercise. Now the opposite of the inspiratory muscles are those that are involved in shrinking the chest. And in doing so, they raise the intrathoracic pressure. Therefore, as we'll see, force air out. There is no dedicated muscle to this effort. In other words, most of expiration is just relaxation of the muscles we've already named. But, on occasion, do you exhale more than you are now? Your normal exhalation is rather minimum, and certainly not very demanding. But can you exhale more than you just did? Yes. And you find yourself, you know, bending over, and your abdomens getting tight. So when it comes to birthday celebrations, and you have to blow out those candles, you're going to have to bring in the big guns, or something that, you know, stands in for those. The abdominal muscles. Wait a minute. How can the abdominal muscles have anything to do with what's going on up here at the chest? The abdominal muscles are down here. But when they contract, they compress the abdomen, and the liver and other organs go which way? Up. And, therefore, push the diaphragm what? Even higher. Therefore, serving to raise further the intrathoracic pressure. So by elevating the viscera, mainly the liver, they help. The other, synergists, are the internal intercostals, which are the antagonist to the external intercostals. Logically then, if the externals do what? Hmm. If the external intercostals elevate the ribs, then these are serving to depress the ribs. That compresses the chest more. And, therefore, raises even more the intrathoracic pressure. So we'll get to these muscles in a moment. But, obviously, these are the ones that move air. These are responsible for the "v" word. What's the "v" word? Moving air in and out of any place is called "ventilation." Now there are other muscles which are worthy of a remark. And these don't so much bring about inspiration and expiration, but they do facilitate movement of air, because they create or remove resistance. Resistance to airflow. And we speak of that word in blood terms. But is there friction in airways? And if this is an airway, and we make it bigger, does that reduce or increase the friction of air that's moving

through?

[Inaudible Speakers]

And if we make them tinier, that's going to raise resistance, and reduce flow. So certainly we're talking about, not skeletal muscle, but smooth muscle. And these are found, not on bronchi, but bronchi?

>> Oles [multiple speakers].

>> Oles. As you recall from Anatomy, the bronchi have rigid, rigid tissue, which holds these airways open. What is that stuff that holds the trachea and bronchi open?

>> Cartilage.

>> Cartilage. Hyaline cartilage. But that's almost entirely replaced by smooth muscle by the time you get down to the bronchioles. And is smooth muscle innervated by sympathetic and parasympathetic fibers? And does smooth muscle have a normal tone, t, o, n, e? And could that tone be relaxed or increased? And what would that be called if bronchioles get smaller? That's the "c" word.

[Inaudible Speakers]

If they get wider, that's the "d" word. And you get the picture. So we're talking about dilation and constriction, which interferes or improves air flow along the way. And, so, certainly what is the most familiar, inappropriate response of this smooth muscle, which can be for some life-threatening? What's the most common case of air hunger and panic?

>> Asthma [multiple speakers].

>> Asthma. Right? And asthma is not a lung problem. Not fundamentally. It's inappropriate "c" word.

>> Constriction [multiple speakers].

>> Constriction of bronchial smooth muscle. And that can be devastating, not just because you're not getting air in, but you're also not getting air what? Out. And, therefore, you're not getting oxygen, you're not getting rid of carbon dioxide. Speaking of that, what is the quickest intervention for bronchial constriction due to asthma attacks of one kind or another?

>> Inhale.

>> You inhale something called a "puffer" or a "rescue inhaler," which is, basically, a vapor of epinephrine. Epinephrine. Why would that be appropriate? What does epinephrine do to this kind of muscle? It dilates. Therefore, relieves this congestion, or, otherwise, opens up these airways. And I'm sure that's familiar. So here we have the muscular story in summary. The biggest, and most important, the prime mover, is the diaphragm, assisted by these other muscles, which are involved on occasion. Especially with exercise. But to say it as simply as possible, if your diaphragm is arrested, or not working, you're

soon to be dead. Right? And we mentioned that more than once. Did we talk about Botox? Did we talk about Curare? Did we talk about these other things? Because, remember, fundamentally the diaphragm is not a smooth muscle. Its skeletal muscle. And respiratory arrest is synonymous with soon-to-be cardiac arrest. And, therefore, soon to be death. So the movement of air is a 24/7 thing. And clearly fundamental for gas exchange. So now let's do what we need to do to understand how that is, by what means, air moves into and out of the lungs. This is very troublesome, or at least prone to misconception. Because very often I hear this. Students will say, "Oh, air goes into the lungs, and then they inflate." Does that sound right? Air goes into the lungs, and then they inflate. That's exactly opposite. What? They inflate. And then what? Air goes in. Now you might not think that's a big deal. But that's putting the cart before the horse. Air doesn't go into the lungs, and then they inflate. No they what? They inflate, and then air goes in. And this is all the result of pressure gradients. So to understand how air moves in and out, we have to understand pressure. And it really is not that complicated. When you take an ice pick and drive it through the tire of somebody's car, I'm sure you've done that, no, imagine it being done, does air go into the tire or out?

>> Out [multiple speakers].

>> Well, of course, it goes out. Why? Because the tire wants to give up the air? No, don't say that. It's because air is moving from a high pressure to a what? That's it. We don't have to have any need or want or anything else. Why did air leave that tire? It went from a high pressure to a? And that's what air does. It always does that. So if we're going to get air into the lungs, we have to show that there's a high pressure here, and a relatively?

[Inaudible Speaker]

And if we want to get air out, we have to show there's a high pressure here, and a relatively low pressure out there. It's just that simple. So we have to talk about pressure. And pressure is measured in millimeters. Hg. What's that? Millimeters of mercury. The same units that we'd use for blood pressure. And, so, there's a lot of acronyms or abbreviations here. The first one is Pa. "P" stands for "pressure." "A" stands for "atmosphere." And that means just that. The pressure of air right now in this room. And that tends to be around 760 millimeters of mercury at sea level. Are we at sea level?

>> No [multiple speakers].

>> No. I don't see any surf out there. So we're not at sea level. In fact, we're pretty high up here. And we call it after all the high desert. You probably know we're at about 2,500 feet, plus or minus. My point is what? As you go up on this planet is the air pressure getting more or less? As you go up mountains is the pressure getting less or more? Less. Because there's less air on your shoulders. Right? So, anyway, would that number be higher or lower than 760 here in the Antelope Valley on a given day? Less. Not a lot less, but just to give you some facts. The next pressure will give an abbreviation to is Pt. Now "Pt"

stands for "pressure in the chest." So-called "intrathoracic pressure." Sometimes synonymous with intrapleural pressure. That pressure, we're not going to give a number to, because it's not a fixed number. It's a number that fluctuates above and below Pa. But it is the pressure, not in the lungs, but outside the lungs in that space called the "intrathoracic space." Then there's the pressure of air actually in the lungs. And that's called "Palv." "Alv" stands for "alveoli." And that pressure, we're also not going to give a number to, because it, too, changes. Rises above and below 760, as it must. Because, remember, how do we get air into the alveoli? The only way air's going to go in is if we create a low what?

[Inaudible Speakers]

And the only way it's going to come out is if we create a high pressure. So no numbers are given to these, because there is no fixed value. They constantly change around this atmospheric level in ways that we'll see. So here's some diagram that may help with these ideas. The pressure outside your body is called "P what?" Pa. The pressure here in yellow, that space, that space is not in the lungs, but outside the lungs, in that compartment called the "intrathoracic space." Which, incidentally, is airtight and sealed from the exterior. And the black space here is, of course, the space in the alveoli in themselves. So let's discuss how ventilation occurs. The first phase is getting air in. And what was the obvious prerequisite? If we're going to get air in there, we have to create what pressure in there?

[Inaudible Speaker]

Lower than the atmosphere. Okay. How is that done? Well, the first thing that happens is the diaphragm contracts. And it's important to know what that means. The diaphragm is, basically, a dome-shaped muscle, like this bent piece of paper. And when the diaphragm contracts, it does this. It flattens out. So this is the what position?

[Inaudible Speakers]

Relaxed. This is the contracted. Relaxed. Contracted. It's as if this floor were to suddenly fall ten feet. What would happen to the volume of this room if the floor were to fall ten feet down? The volume would increase. But the air in here would be the same, except that it would be spread out over a greater volume. What would happen to the air pressure in this room if the floor were to sink ten feet?

[Inaudible Speaker]

So if the diaphragm contracts, the chest size is increased. And with it what happens to Pt? What's Pt? Intrathoracic pressure. So here are the steps. Diaphragm contracts, which means that it descends, it flattens out. What does that do to the overall volume or size of the chest? Increases it. What does that do to the pressure of air in this now larger chest? The Pt is going to go which way?

>> Down [multiple speakers].

>> Down. And what will the lungs do? Remember, the lungs are hanging inside this space. And if the pressure outside the lungs goes down, the lungs now will increase in size. That is, they will expand as the pressure around them goes down. Okay? So what follows from a lowered Pt is simply lung expansion. In other words, the alveoli individually and collectively are getting larger. What happens then? If the lungs have gotten larger, what happens to the pressure of air in the alveoli accordingly? That goes down. And are the alveoli connected to the outside world? Are the alveoli connected to the outside world? Yes. So if Palv goes down, then that will be less than, hopefully, less than Pa. In other words, it will fall below this number of 760. Now what? Now the pressure outside is greater than the pressure inside. Which way is air going to go? High pressure to low pressure. And what is that called by any other name when air goes into your lungs? That's called? That's the word. Inhalation. So just to repeat. Did air go in the lungs, and then they expanded? No. Here are the steps. Diaphragm contracts, chest size increases, Pt goes down, lungs expand. Therefore, Palv goes down. Therefore, less than, or becomes less than, what? Less than? Therefore, air flows in. It's just that simple. How's the opposite occur? Well, the opposite. In other words, we start, not with the diaphragm contracting, but now the diaphragm is what? Here we go. This is the diaphragm. It's now what?

>> Contracted [multiple speakers].

>> Contracted. Now it's going to?

>> Relax [multiple speakers].

>> Relax. What did that do to the chest size if the diaphragm relaxes? Chest size relaxes or shrinks. And, so, what? What does that do to the Pt? Pt is the pressure outside the lungs. Hmm. That's going to go, not down, but?

>> Up [multiple speakers].

>> Up. That will force the lungs to shrink a little bit. And if they shrink, what happens to the pressure of air in the lungs? That increases, and, hopefully, becomes at some point greater than what? We want it to be greater than?

>> Pa [multiple speakers].

>> Pa. And when that happens, which way will air move?

>> Out [multiple speakers].

>> Out. And what's the name for that?

>> Exhaling.

>> Exhalation. Now all of this works provided the diaphragm is doing its thing, provided the chest is intact, and provided, incidentally, there's no obstruction to air movement. What did we mention, what condition, what common respiratory ailment can interfere with air movement in or out?

>> Asthma [multiple speakers].

>> Asthma. But never mind asthma. It's not uncommon for people, especially at restaurants when they're having fun, and they've had a few drinks, to be inhaling their food. Ever heard that expression? And sometimes that's exactly what happens. What do I mean? Food gets trapped in the airway. Namely the trachea. And, so, is the diaphragm still working? Is everything good? Well, yes, but no. Everything is working diaphragm-wise. In other words, the diaphragm is relaxing, chest size is decreasing, and Palv is definitely up. But why can't air flow out? There's a blockage there. So this is a big deal. Right? And it is a big deal because, not only is air not moving out, and because air's not moving out, you're not able to make any sound. Right? Because think about it. Making words is not inhaling. It's what?

>> Exhaling [multiple speakers].

>> Exhaling. If you can't exhale, you can't make any noise. So what? You're gesturing in pantomime. And people saying, "Ah, he's having a great old time." And he's going. And some bright individual's going to come over, and do what?

>> The Heimlich maneuver.

>> Do the Heimlich maneuver. Now what's that all about? You don't go down there with a fork, and fish out the chicken bone, or something. You just come around behind, you know it, right? So I don't have to tell you this. But you take your fists, and you press, not on the chest, but on the?

[Inaudible Speaker]

And actually in and up. That's doing as we said, because it's compressing the abdomen, forcing the liver. And, therefore, helping to raise this even more. Therefore, raising that even more. Therefore, hopefully, blowing out, you know, the blueberries, or whatever it is in there, which is a big deal. So my point is that this works provided you have no obstruction, provided the diaphragm is intact, provided the chest wall is intact. Now this is the qualitative story. This is the quantitative story. That is, we've got to give some numbers to this. And I see we're out of time. So we'll save this for next time. But at least let's preface this. In order to get air in, we've got to bring the diaphragm down. That's going to decrease Palv. Remember that. And that will cause air to flow in, which accomplishes inhalation. The opposite is the diaphragm relaxing, which raises Palv. And, therefore, moves air out. But as a final remark, this all is contingent on changes in, what's this right here?

[Inaudible Speaker]

Pt. What if the diaphragm contracts, but what if the chest wall is violated with some hole? Now this is a model you've seen in Biology. And clearly this is the chest wall. Yes? The balloons represent what?

[Inaudible Speaker]

And down here we have the diaphragm. So you played with this in Biology. You can see as the diaphragm moves, the lungs inflate and deflate. That's really great. That's as it's supposed to. But what if you have a hole in your chest wall as a result of a gunshot wound? Hmm. What happens? Is the diaphragm still going to contract? Yes. Is the pressure in here going to go down? Yes. But immediately what's going to happen because of that hole? The pressure went down, and air out here is anxious, don't say that on the exam, the air out here will go through that hole. Right? Because you created a low pressure there. Now is the diaphragm still working? Yes. Is air moving? Yes. But it's not moving in and out of the lungs. It's moving in out of that what? And that's going to cause the lungs to collapse entirely. Worse than that, they're not inflating or deflating. So you have respiratory arrest, even though what's working here?

[Inaudible Speakers]

All right. So this is called, maybe you know, it's called "atelectasis." And the usual cause of it is a pneumothorax. Which as a word means "air in the chest." And what's the most common reason for that? Especially in Ancaster, in Palmdale, in surrounding communities? It's no joke. But there's bullets all over the place. It's a sad commentary. So when you come up to somebody who's got a gunshot wound to the chest, are they bleeding? Yes. And that's probably part of their problem. But are they also in respiratory arrest? Yes. So that's why you should always carry one of these. It's a plug. And stick it right in the hole. Now you say, "I never carry one." But reach into your purse and grab a tampon. If you don't have one, grab something. Stick it in the hole. Okay.

[Background Conversations]