>> Today's November 6, 2017. This is lecture 22 in Phys, and we're arriving at this topic which we previewed or mentioned a while ago. Namely, gas exchange and gas transport. This might seem like the same thing, but these are very different things. Exchange and gas transport. It's really kind of like what you do at a grocery store. You exchange money for groceries. Then you put your groceries in your car, and you t-word. You what? You transport them home. So, these processes are separate, but yet they're related. One effects the other. So, first, let's talk about gas exchange which involves the acquisition of oxygen and the elimination of carbon dioxide. We're going to find out that this process is really predicated on passive diffusion. And, what are the principles or stipulations in passive diffusion? Molecules move from a? High concentration to a low concentration. However, when it comes to a gas, we're dealing not just with concentration, but rather something called gas pressure which is actually a function of two things. Gas pressure is a function of the density of the molecules, the concentration of the molecules. But, it also depends upon how rapidly the molecules are moving which is a function of temperature. So, to make this clear, what do you think about the air pressure in your tires of your car in the winter versus the summer? In which condition are the pressures higher? Summer. Because the temperature is warmer. So, it's not because the concentration is any different. Rather, the movement of the molecules. So, from now on, we're not going to talk about concentration. We're going to substitute the p-word, pressure. Pressure is a function of concentration, but also a function of the temperature of the molecules in question. And, of course, the air that we breathe is not a singular gas. We talk about it as if it were. We talk about the air we breathe, but is the air in this room a singular gas? No. Is it mixture of many? So, we have to speak, then, something called the partial pressure which is a look at the individual pressures of the gasses that are present in a mixture. So, by definition, partial pressure is the individual pressure that a given gas contributes to the total. And, what is the total air pressure of air at sea level? What is the total, normal pressure of air at sea level? It's 760. And, what do we know about pressure as we climb on this planet? As we get to, say, Mount Everest? Is the total air pressure there more or less than that? Much less. This is the highest peak on the planet. About 29,000 feet, and the pressure there, the total pressure there is just a fraction of what it is at sea level. Only 200 millimeters of mercury. But, the interesting thing is, the air up here has the same composition as the air down here. That is, it's still a mixture. And, what are the gasses that we know are found in air? Oxygen, carbon dioxide, and nitrogen. In fact, most of what we breathe is nitrogen. So, let's now look at the partial pressures of each of these gases starting with O2. The partial pressure of oxygen is a function of its concentration. That is the percentage that it contributes to the total air pressure. And, you may know this from other courses, but the air that we breathe is about 20% oxygen. So, if the total pressure is 760, what would be the partial pressure that oxygen contributes toward that total? It would be 20% of 760, and what is 20% of 760? It's about 150. So, that's an easy calculation. We just multiply .2 times the total pressure which is 760, and the partial pressure is, then, 150. Would that be true at Mount Everest? Well,

the oxygen content is still 20%, but it's 20% of a much smaller number. So, instead of 20% of 760, it's 20% of only 200. Therefore, the partial pressure at this altitude, quite a bit less than at sea level. What are the other gasses? Well, there are many, but the other gas that we care about is CO2. And, of course, the concentration of carbon dioxide on this planet is increasing, you may know, because of all the CO2 that we're generating. But, even so, the partial pressure of CO2 is really rather minimum. In fact, only what? .3 millimeters of mercury. Again, that's at sea level. And, the rest of the pressure that adds up to a total of 760 is nitrogen, N2. And, you don't hear much about nitrogen, even though it makes up 80% of the air that we breathe. You don't hear much about it because it's not biologically important. Do we inhale nitrogen? Yes. Do we exhale nitrogen? Yes. Is it toxic or otherwise significant biologically? No. So, it's there, and we have to account for its presence, but from a biological standpoint, it doesn't have much bearing on human physiology. So, the two important gasses, obviously oxygen and CO2. And, naturally, at sea level, all of the gasses would contribute to the total pressure at sea level. That's 760 millimeters of mercury. So, to repeat. How do you determine the partial pressure of any gas in a mixture? You multiply its percentage times the prevailing total pressure, and therefore, generate a number which is the partial pressure. Now, with that said, we have to get back down to this topic of gas exchange, and it's predicated on demonstrating and taking advantage of pressure gradients. In other words, the exchange of gasses is based upon passive diffusion of a gas from an area of high, high partial pressure to low partial pressure. And, by passive diffusion, we mean just that. There's no active transport. There's no energy involved. It's down, not a concentration gradient. Down a pressure gradient. Always from a high partial pressure to a low partial pressure. So, what we're about to demonstrate and put into a diagrammatic expression is these pressure gradients. So, here's a simplified diagram of the areas of concern. This circle represents the lungs. So, it represents an alveolus, and this race course represents the circulatory system, the vessels that carry blood out to the systemic cells. These are called arteries. And, the vessels that return blood to the heart, eventually to the lungs, these are called veins. Certainly, at the microscopic level, we have a network of permeable vessels called capillaries. And so, when it comes to gas exchange, there are two, two sites. This site which is between the alveoli and the pulmonary capillaries, and this site which is between the systemic capillaries and the tissues throughout the body whether they be muscles or organs or whatever. So, call this site one. Call this site two. Gas exchange here. Gas exchange here. And, before getting numerical or quantitative here, obviously, what gas are we expecting to acquire from the lungs? And, what gas to we expect to move into the lungs? And, what gas do we expect to leave the capillaries and therefore enter the tissues throughout the body? Oxygen. What gas do we expect to pick up and return to the lungs? Obviously, carbon dioxide. So, this process of gas exchange, again, depends upon the establishment, the exploitation, of these pressure gradients. In other words, we have to show the gradients numerically speaking so that we can actually expect or otherwise show passive diffusion. So, let's add some numbers? What have we already said about the prevailing PO2 and the prevailing PCO2 in the air that we breathe at sea level. What's the partial pressure of oxygen? It's right up here. It's what? One fifty. And, what's the partial pressure of CO2? .3, .3 millimeters of mercury. And, it would be tempting to assume that when we inhale this air that those values, then, would be reflected or otherwise generated here in the lungs. And, that would be true if these containers were empty. But, based on what we've said before, are the lungs, are the alveoli, ever really empty? No. So, we're not putting air into an empty vessel. Rather, we're putting air into a space which already has air. And so, we're, at best, going to be diluting this residual air with fresh air from the outside. So, I'm bracing you for this fact. The numbers we're about to put in here are not going to match the atmospheric level because this air is residual air which is somewhat stale. And, therefore, we can't expect the pressure which we have on the outside to immediately or completely transform the lungs with respect to their pressures. In sense, then, we're diluting this fresh air with stale air which occupies these alveoli. And so, quite interestingly, the PO2 in the alveoli is never as good as it is outside and is somewhat diminished by the quality of air which remains always in the lungs. So, outside, 150. Inside the alveoli, best case scenario around 100. What we find in much greater partial pressure is the PCO2 which tends to hover or stay around 40 millimeters of mercury. Quite a bit more than we find externally. And so, those are the facts. These are the partial pressures which prevail, and of course, there are some gasses which are not mentioned here. Is there nitrogen in here? You bet. Is there water vapor in here? Yes. So, just to be clear, there are other gasses, but our focus is on the partial pressure of these important physiological gasses. And so, now, with that said, let's see what happens in order to bring about the proper exchange of these gasses here in the lungs. And, rather than jump off into the arterial system, let's start at the end. That is, let's look at venous blood which is coming back to the lungs through the body that is from various locations in the body. And, incidentally, what's the usual word which is used to describe blood coming back through veins? Deoxygenated. And, that's a fair enough word, but it's really an oversimplification. Because the blood coming back is not totally, not totally deoxygenated at all. It's just relatively deoxygenated compared to the arterial blood, as we'll see. And, those numbers are bore out in these figures. Notice the PO2 is not zero, but actually a pretty healthy 40 millimeters of mercury. And, the CO2 is certainly high. And, as an average, about 46 millimeters of mercury. So, as this blood moves, now, toward the lungs, do we see, do we have pressure gradients which would favor the expected exchange that we've talked about? What gas to we expect to leave the blood and move into the lungs? Carbon dioxide. Is there a pressure gradient that favors that diffusion? Yes, it's 46 versus what? So, which way is CO2 going to go? It's going to go from the blood into the alveoli. And, from there, of course, it will be expelled or exhaled to the outside. Do we have a gradient that favors the entry of oxygen into the blood? And, what is that gradient? It's 100 versus what? One hundred versus 40. So, which way is oxygen going to move? It's going to move from the lungs into the capillaries. The name of that process is? Passive diffusion occurring from a high partial pressure to a low partial pressure. Nothing fancy. Passive diffusion from a high partial pressure to a low partial pressure. And, if that's true, and if it's efficient and complete, what's the best we could hope for in the PO2 and PCO2 in the blood that's leaving the lungs, otherwise known as arterial blood? First, could this number ever be greater than 100? No. Because if this is 100, there's no way this could be more than 100 because we're relying on what process? It's passive diffusion. If this were 600, obviously, it would involve some kind of active transport which simply doesn't exist. So, with all that said, what's the best this number could be knowing that this is usually around 100 millimeters of mercury. Best that could be would be 100, and you might even argue with that because you might say, well, wait a minute. As oxygen leaves the alveoli, that number would get lower. And so, sooner or later, these would sort of maybe average out. And, this might be 70, and that might be 70. But, whoa. Let's remember. As oxygen leaves the alveoli, does this number get smaller? Actually not. How can oxygen leave the alveoli and that number remain 100? Well, what are we doing? We're bringing in new air all the time. So, even as oxygen leaves the alveoli, that number remains rock solid at about 100. And so, the very best we could expect over here in arterial blood would be a perfect match, and indeed, that's the case. Also, in a similar way, could the CO2 ever be less than what we find here? No. And so, as a practical matter, the arterial gasses pretty much reflect the alveolar gasses. And, the only caveat to that statement is this. These numbers in the arterial blood will always match these numbers in the alveoli in the healthy individual. And, what would be an unhealthy individual in this context? Are there people who have lung disorders like emphysema or maybe pneumonia or something that diminishes the ability of gasses to diffuse? And, if the barriers to diffusion are somehow great, would this number, then, match that in the alveoli? No. And so, in lung disease, what might be the expectation here? It's not going to be this pretty picture. That is, these numbers are not going to match the alveolar numbers. In an unhealthy lung, this number would be much, much, and that number would be much, much higher. So, this normal arterial blood gas would be true only in what? Only in the healthy individual. So, to back up and repeat, we have this blood coming into the lungs which is returning there from the body's venous network. And, what's the usual name given to this kind of blood? But, it's not really deoxygenated. It still has a healthy 40 millimeters of mercury of O2. It does have a relatively high PCO2, but naturally, that's expected. And, are these pressures conducive to the proper gas exchange that we expect should occur here? What gas do we expect to leave the blood? CO2. Why will it do so? Because it's moving from a high partial pressure to a low partial pressure. Why does oxygen leave the lungs and go into the blood? Once again, passive diffusion from a high to a low partial pressure. So, this is strictly and only due to passive diffusion. So, now, we have this gas which is moving out into the body. And, it encounters the second capillary network which is basically at any level between capillaries and tissues, be it muscles or organs and so forth. And, what do you think? What do we expect to happen? What gas do we expect to leave the blood and move into the tissues? And, we'd have to show what? A pressure gradient. And so, what would you imagine the PO2 to be on average in tissues throughout the body? Would it be more than 100? Probably what? Less. Could it be much less? Whatever number we put in here, obviously is a function of what these tissues are doing. And, if these tissues are active, metabolically active, they're using more what? So, the number we're about to put in there is not a fixed number but subject to change depending upon the activity, the metabolism of these tissues. But, let's put some numbers in there. As a general rule, the PO2 in most tissues probably around or less than 40 millimeters of mercury. And, in a similar way, we'd expect the CO2 to be a reflection of metabolism. It might be, usually is around 46 or even more. So, before discussing what happens, what determines these numbers is a function of the metabolic rate of these tissues. Let's say these are muscles. Let's say they're contracting. Would the O2 be lower than 40? Yes. Would the CO2 be more than 46? Yes. So, the activity of the tissues really dictates what these actual numbers might be. But, even in a relatively inactive tissue, they are usually a PO2 of less than 40 and a PCO2 around or greater than 46. And so, are there pressure gradients that favor the proper exchange? What gas did we hope and expect would leave the blood and go into the tissues? And, is there a gradient that favors that movement? What is it? It's 100 versus what? A hundred versus 40. What gas is going to leave the tissues and move into the capillaries? Carbon dioxide. Is there a gradient that favors that? Yeah. Forty-six versus 40. So, naturally and according to these numbers, gas exchange will occur from a high partial pressure to a low partial pressure. In other words, oxygen will leave the capillaries. Carbon dioxide will enter the capillaries. And, notice, as a result of this, that the venous blood coming back is a perfect match. That is, it tends to reflect the partial pressure of these gasses in the tissues. And, with that said, could these venous numbers be different from what we've got here? Could the PO2 ever be lower than 40? Yes, especially if that's lower than 40. And, could the PCO2 be higher than 46? Yes. If the PCO2 in the tissues is greater than 46. And, what would cause the O2 to be lower and the CO2 to be higher? Metabolic activity of the tissues. So, again, if these are muscles, and they're contracting, you would expect these numbers to change accordingly. The O2 would be much lower. The CO2 would be much higher. In short, these values pretty much reflect the values that are going on at the tissue level. So, there you have it. This was all about, what is it? Gas exchange. Exchange occurring here. Exchange occurring here. In both cases, it's just a matter of? Passive diffusion from a high partial pressure to a lower partial pressure. Of course, this is predicated not just on the activity of the tissues, but also the efficiency of circulation and the condition, the health, of the lungs. To say it again, if the lungs are unhealthy, would we expect normal gas exchange to occur there? No. Would these gasses suffer? Yes. Would the tissues suffer accordingly? Yes. So, all of this is based upon the assumption that everything is healthy and working as it should. But, that's not always the case, especially if you consider emphysema or infections of the lungs which would interfere with gas exchange. So, this is all about gas exchange, and it obviously means the movement of gasses through semipermeable membranes. Again, on the basis of passive diffusion. These gasses are dissolved in the liquid portion of the blood, and what is the liquid portion of the blood called? Plasma.

But, you probably know that plasma is mostly water, yes? And, water cannot and does not have the capacity to really move, that means transport, as much gas as really needs to be transported to provide for the health of these tissues. And, one notable apparent omission from all this discussion so far is the red blood cell. And, what does the red blood cell contain which is not so much involved in gas exchange, but certainly involved in gas transport? What's that molecule? Hemoglobin. So, this discussion doesn't even consider the RBC or the hemoglobin that it contains, but yet we know that's important, not for a gas exchange but for gas what? Transport. So, let's go there now. Because without hemoglobin, simply put, plasma could not transport enough oxygen or CO2 to really get the job done. Hemoglobin is the key to making this work as it should. So, oxygen transport, the first of two considerations. First. Is it possible for the plasma to transport at least some oxygen? The answer's yes. What is plasma mostly made of? And, can water dissolve oxygen? Yes. Fish use that. I mean, after all, how do fish get oxygen? It's not from the air. It's form the water they're swimming around in. So, to say it again, is water a solvent for oxygen? Can you dissolve oxygen in water? Yes. But, as it turns out, that's okay for fish, but not for us because how much of the oxygen which is actually transported in the human body is transported in plasma? Less than what? Less than 2%. What that statement is saying is that water is not a very good solvent for what? Not a very good solvent for oxygen. Notice that this equation or expression features two arrows. So, just to be clear, where does oxygen enter the plasma? Where in the body is oxygen moving into the plasma? At the lungs. Where is it leaving the plasma? At the, at the tissue level. So, to say it again. Where is it entering the plasma? At the lungs. Where's it leaving the plasma? At the tissue level. So, with this expression, you would say that oxygen is entering the plasma in the lungs and leaving the plasma and entering the tissues at the capillary level throughout the body. But, still, 2% is just 2%. And, certainly, could we live, could we transport enough oxygen in plasma alone? No. So, how is 98% of the oxygen transported in the circulatory system? Not in the plasma. But, actually attached to a molecule found only in red blood cells. What's that? Hemoglobin, abbreviated of course Hgb. Now, hemoglobin is an iron containing protein which is actually made of two molecules, heme, H-E-M-E and the protein part which is called globin. As it turns out, based on what you see here, hemoglobin, the molecule hemoglobin, can carry up to how many oxygen molecules? Up to four, and when it is loaded with those four, it's said to be saturated. It's carrying as much as it can. In that form, it's called oxyhemoglobin, and it is, therefore, carrying its maximum load of oxygen. Notice here, too, that this expression is a two-way street. So, just to be clear, where is oxygen acquired and attached to hemoglobin? Where does it go onto the hemoglobin? Where does it go onto the hemoglobin? Where is oxygen plentiful and otherwise loading onto hemoglobin? Lungs. Where's it coming off the hemoglobin? At the tissue level. So, the arrow to the right occurs at the lungs. The arrow to the left occurs at the tissue level. And, this is, of course, a reversible reaction based upon pressure gradients. So, with that said, what is the relationship between the loading and unloading of the hemoglobin molecule? And, this might seem like an obscure question, but we're asking this. Here's hemoglobin. I've now picked up four molecules of oxygen. Can I carry anymore? No. What would you want me to do? I mean, if want or need were even part of the process, would you want me just to take this oxygen and dump it off and come back totally empty? Or would you rather the molecule more or less handed out according to the conditions that the RBCs encounter? Would it make more sense to get it and dump it, or would it make more sense to get it and then sort of unload as it encounters different levels of PO2? Well, the latter. So, that relationship is important and expressed in this basic curve which is called the HgbO2 Dissociation Curve. And, it's, of course, going to require some explanation. So, on the vertical axis, we see percent Hb, Hgb saturation. And, that means just that. Notice its percentage from zero to what? So, if a hemoglobin is carrying four molecules of oxygen, it's said to be s-word. It's said to be 100% what? So, what are the ranges? Obviously, from zero to 100. And so, as it turns out, hemoglobin starts out its mission fully saturated, and that's revealed in this horizontal axis and the numbers that are there. The numbers are PO2. From zero up to what? A hundred. Now, before we go on, you might wonder why that doesn't go beyond 100. Why not 200? Why not 300? Why not whatever? What is the maximum PO2 under normal conditions at sea level in the alveoli? A while ago, we said it's 20% of that which was what? But, yet, in the alveoli, it's already only 100. So, as you go back to the previous page, you'll see the PO2 in the alveoli is at most, at best, what? And so, we don't really need to go any more for that reason. Plus, obviously, from this graph, how saturated is the hemoglobin at a PO2 of 100? It's what? It's 100%. So, what if we went out to 150? It'd still be what? Hundred percent saturated. If we went to whatever. It'd still be 100% saturated. And so, this chart doesn't need to go beyond here for two reasons. One, the PO2 in the lungs is never more than 100, and even if it were, it couldn't bring about any greater saturation than 100%. This is interesting in a number of ways because is it possible to get the PO2 in your lungs to be more than 100? It is if you're not breathing room air. Could you breathe pure oxygen? And, would that change that 20% figure to 100%? And, would the PO2 in the lungs be much higher accordingly? Yes. But, would that result in any greater saturation of the hemoglobin? No. So, that's the interesting thing, and certainly almost comical. Because are there places you can go in Las Vegas or down in LA where you can sit down and give $20 and breathe what? [inhale] pure what? [inhale] Oh, and people say, oh, this is so great. This is so wonderful. Well, that's pure BS. It's pure placebo because if you're breathing pure oxygen, are you saturating any more of your hemoglobin? No. Are you really getting any more oxygen into your blood? No. Because the plasma can only carry what? And the hemoglobin can only carry that. So, inhaling pure oxygen, have fun. Spend your money. But, it's a waste of money. You say, "Well, wow. I've seen football games where the players are breathing oxygen. What's going on there?" I don't know. It's pure BS. But, hey, if it makes you feel better, do it. Now, you may say, "Well, wait a minute. Why, then, do they have oxygen in hospitals?" Well, that's a different story. Because usually in hospitals, we don't have healthy people. We have what? And so, they have respiratory problems. Is there a time and a place for breathing pure oxygen? Sure. But, you and I, save your money. So, interesting but sort of off topic. So, here's the hemoglobin. It's leaving the lungs. It's leaving the pulmonary circulation. How loaded? How much saturated is it? Hundred percent. And, notice that it remains highly saturated until it starts to encounter tissues with progressively less PO2. And, why did we single out 40? Where did we last mention 40 millimeters of mercury for oxygen? It was at the tissues. So, this is the average prevailing PO2 at the tissues. And, what's interesting about this curve is the degree to which the hemoglobin remains saturated or otherwise becomes unsaturated. And, you can interpret this graph pretty easily by just extending this line until it intersects the red. And then, carrying it over. So, even though there are no numbers here, what are they? This is 20, 40, 60. Wait a minute. 10, 20, 30, 40, 50, yeah. Okay. You can do it faster than I. So, cutting to the chase. As hemoglobin moves through the tissues, how much of it remains saturated? How much of it has lost or otherwise become desaturated? What's this number right there? Eighty. That means that what percentage remains saturated? Eighty percent. Eighty percent. How much of oxygen is actually given up? Only 20%. This further, this further sort of invalidates that remark we made earlier. What did we say about venous blood? What's the usual description of it? Venous blood is what? De-, well, it's not. Because the hemoglobin is still what? Eight percent saturated. It only lost what? It only lost 20%, provided, provided it went through an area with only 40 millimeters of mercury. But, we said before, can that number of 40 be much less? Can it be 30, 20, even less? And, what would make those partial pressure in the tissues less than that? Exercise. So, in exercise, certainly, there's more oxygen to be given up, but at least in the healthy and normal state, 20% of that oxygen comes off. Eight percent remains in place. So, hardly is the blood in veins deoxygenated. It's still 80% saturated with oxygen. So, only 20% is released. 80% is retained. Now, this is true in a typical trip around the circulatory system. But, naturally, there are circumstances which would or should influence this so-called dissociation curve. And, the first one that we've already mentioned is simply the PO2. And, the relationship is this. The lower the PO2, the hemoglobin has less a-word. Now, what does that mean to have affinity? Affinity is what? Attraction. So, when there's lower PO2, the hemoglobin doesn't have more affinity. It has what? And, if I have less affinity, that means I'm giving up, giving up more what? More oxygen. So, lesser affinity means the greater release of oxygen which is perfectly appropriate, perfectly expected for this situation. What do I mean? I'm hemoglobin. I start out fully saturated. I'm not moving into an area with 40 millimeters of mercury of oxygen. How much desaturated do I become? 20%. I'm still holding on what? But then, I keep going, and I find, ooh, here's an area with only ten. Now, I'm going to become what? So, again, the lower the PO2, the lesser the O2 a-word. And, therefore, the greater release. And, that is expected, appropriate, and useful. The second of three factors or influences on this dissociation curve is pH. And, before we go there, let's just think about what would be logical or seemingly appropriate. I'm hemoglobin. I'm now going into an area, and this area is acidic for whatever reason. But, what would cause this area to be more acidic than, say, other areas? Why is this area more acidic, you think? Maybe it's producing lactic acid. And, why would it be doing that? Because of anaerobic circumstances. What would be appropriate for hemoglobin to do? Hold onto more oxygen, just run right through, or get rid of more? So, it makes sense that hemoglobin would be sensitive to pH. That is, it would become less saturated. That is, less affinity, and therefore, do what with respect to the release? So, that's the relationship. Any area of high acidity tends to make the hemoglobin not more but less attracted to oxygen. Therefore, releasing more oxygen which would obviously correct or at least be beneficial to an area of high acidity. Let's say it again. Why would an area have high acidity? Lactic acid. Why does it have lactic acid? Because it's short of? Would this help? Would this provide or release more oxygen to those areas? Yep. So, it makes logical sense. And, by the same token, areas of lower acidity cause the hemoglobin to have a higher affinity which means it's less likely to r-word, less likely to release oxygen. So, that is the pH story. And, if this is understood, you now can look at this graph. One shows the typical red curve which is the normal dissociation curve. The other shows a blue one and a black one. Both of these are the same shape. They have the same curvature, but this blue one is said to be a right shift because we've taken that red line and move it what way? We move that red line what? To the right. The black line is the same as the red, but we've moved it not to the right but to the left. Black is called a left shift. Blue is called a right shift. Now, which of these, right or left, demonstrates or shows lesser affinity for oxygen? How can you figure that out? Here's our 40, and to remember, what is the level of desaturation that occurs at a PO2 of 40. It was just what? Just that up there. What is that? That's 20. And, now, in the blue, what's this? You see, that's somewhere over here, 45 or 50. So, now, the same partial pressure will release, release what? More oxygen. So, putting this to a question, this response to pH is demonstrated in the blue of the black? Blue. Because at a pH, I should say at a PO2 of 40, there's much more oxygen given off, and that's because hemoglobin has not a more, but a lesser oxygen affinity and greater oxygen release. And, interestingly, the same behavior is reflected in temperature. And, easy enough to predict or at least logically presume. If I'm hemoglobin, am I going through an area which is warmer, what would you think would be the appropriate thing to do? Hold on to oxygen, or get rid of some there? Why would getting rid of oxygen in a warm tissue be expected or useful? Why is that tissue warm? More m-word. Metabolism. Using more what? And, would, therefore, that tissue which is warmer benefit with the delivery and release of more oxygen? Yes. So, when there's high temperature, hemoglobin once again has a lesser O2 affinity which translates to a greater release. In a similar way, low oxygen tends to transform hemoglobin and have it a higher affinity. So, this curve can shift in accordance to different pHs and different temperatures. And, which shift is demonstrated by high acidity and high temperature? Is it the right shift or the left shift? It's the right shift. Because much more oxygen is given up which is appropriate to correct or remedy these problems. High acidity, the result of low oxygen, and high temperature, probably certainly benefitting from more oxygen delivery as well. So, be sure that you make sense here. You don't want to accept or memorize what I've just said, but rather, make sure it is logical and fits with your expectation. If we want to deliver more oxygen, we have to have lesser what? Lesser oxygen affinity. And, that will be true in areas of high pH or areas of high temperature. Now, all of this page is based on what gas? But, is oxygen the only gas to consider? In fact, you could argue that oxygen is not even the most important gas, at least based upon our previous discussions. What gas is the human body more sensitive to, a decline in oxygen or a buildup of CO2. It's a buildup of CO2. So, even though we put a lot of emphasis, a lot of concern about oxygen, it's CO2 that deserves at least equal attention. And so, in a similar matter, how is CO2 transported? Can water dissolve carbon dioxide? Yes. In fact, based on this number, would you say water is a better, a better solvent than, I should say, a better solvent for CO2 than oxygen? What was the maximum quantity or percentage of oxygen that can be moved in the plasma? Two percent. Here, it's up to 10%. So, in short, water dissolves carbon dioxide better than it dissolves oxygen. But, still, that's only 10%, and can we transport all of the CO2, apparently in plasma alone? No. It turns out the hemoglobin, once again, is involved in the transport of this gas. It's all too simple to remember that oxygen is carried by hemoglobin, but is carbon dioxide as well? The answer's yes. Not on the same site, but at least on the same molecule. And, based on what you see here, how many carbon dioxide molecules can a single hemoglobin apparently transport? Only what? Only one. And, when it receives and binds to that single carbon dioxide, it's also said to be saturated. It can only carry one CO2 molecule. The name of that molecule is carbamaminohemoglobin, and like it to not, it's kind of a funny name, but that's what it is. How much carbon dioxide that is being transported is transported on hemoglobin? What percentage of 100% is carried in this manner? Only what? Thirty. How much is carried, dissolved in the plasma? What's 30 plus 10? So, obviously, we're missing or otherwise not yet aware of the other 60%. The other 60% is carried in the following manner. Remember, a while ago, we said carbon dioxide is always formed or produced along with a H2O, and especially inside the red blood cell, there's an enzyme called carbonic anhydrase. Which converts CO2 and water to this. What is it? H2CO3. That's? carbonic acid. Now, carbonic acid is a weak acid, but nevertheless, it does ionize, and when it does, it produces hydrogen ions and this, which is HCO3 negative. That's bicarbonate. And so, where is the CO2? Now you see it, now you don't. The 60% that we are thinking about is not carried as carbon dioxide but actually represented in this molecule which is bicarbonate. So, to back up, what percentage of the CO2 which is transported is dissolved as carbon dioxide in the plasma? Ten percent. Which is, what percentage is being carried on the hemoglobin molecule? Thirty. What percent is actually being transported as bicarbonate? It's a full 60%. Now, that is true enough, but remember, we don't exhale carbon dioxide, I should say, we don't exhale bicarbonate. What do we exhale with every breath? Not only do we exhale carbon dioxide, we exhale water. Ever exhaled on some glass? Do you see water? So, where in the body is carbon dioxide being moved in this direction? Where is there a buildup of CO2 which would cause this reaction to move to the right? At the tissues. Where in the body is CO2 being eliminated and cause this reaction to go from right to left? In the lungs. So, be sure in your notes that you have this direction indicated as occurring at the tissue level, and the opposite direction occurs at the lungs. And, of course, this meshes well with what we eluded to the other day. What happens when you hold your breath? First, and obviously, what happens to the PO2 in your blood? But, what happens to the PCO2 in your blood? And, that PCO2 reacts with what? To form what? Which then acidifies what solution around your brain and spinal cord? And, what, remember, is the ultimate reason that you cannot hold your breath indefinitely? It's not a decline in oxygen. It's a buildup of? And, it's not even a buildup of CO2. It's a buildup of? Hydrogen ions. So, anything that interferes with the elimination, anything that blocks the exhalation of CO2 will cause a buildup of what? Hydrogen ions. Which, by any other name is called acidosis. In fact, when it's due to a failure of the respiratory system, it's called respiratory acidosis. And, what sort of conditions that you know of and can think of would lead to that dangerous condition of respiratory acidosis? Anything that would prevent the elimination of CO2. And, would asthma do that? Would bronchitis do that? Would emphysema do that? Would pulmonary edema do that? Yes. So, what we're trying to say here is that the relationship between CO2 and hydrogen ions is important because it influences the pH of the cerebral spinal fluid and therefore, the integrity and performance of the nervous system and the respiratory center as well. So, as we leave this page, we emphasize that what percentage of the CO2 is transported, dissolved in water? What percentage of the CO2 is transported by dissolving it in water? Ten percent. What percentage is carried on the hemoglobin molecule? And, what percentage is carried as bicarbonate? Sixty percent. This makes it sound like hemoglobin is not important, but it's accounting for what percentage? Thirty percent. So, just as a side note, what do we usually call, what's the single word that's used to describe low levels of hemoglobin? Low levels of hemoglobin, it's the a-word. Anemia. And, what do we fear or assume is the real issue or concern there, anemia? Not transporting enough what? But, is carbon dioxide also being impacted? Yes. So, anemia, even though we focus on the O2 problem, is also cutting into the ability to transport carbon dioxide, even though, of course, 60% is still carried, as it always is, by bicarbonate. So, that's our story of gas exchange, and what was the second? Gas exchange and t-word. Transport. Exchange occurs at two sites, in the lungs and then at the tissue level. Transport occurs, of course, as we move through the circulatory system. With what molecule playing a key role in both gasses? Hemoglobin. Does hemoglobin carry oxygen? Yes. Does it carry CO2? Yes. Which gas does it carry most of? Oxygen. And, a final reminder, can hemoglobin also carry carbon monoxide? Yes. In fact, it has a greater affinity for what? Greater affinity for carbon monoxide than it does oxygen. So, if you're breathing even small levels of carbon monoxide, hemoglobin will bind to that. And, that's not bad except that it now is not binding or cannot bind to what? So, again, carbon monoxide, per se, is not poisonous. It's just that that carbon monoxide is occupying a site normally reserved for what? And, therefore, you're going to die from asphyxia, also known as hypoxia. What's hypoxia? Low levels of oxygen. Anyway. Little side note. So, now, catch my breath. We're moving into a whole different territory, the next moments here and on Wednesday. We'll look at this system, the gastrointestinal system which, clearly, is concerned with and normally equated to the digestive system. But, we want to be clear from the outset that this system does more than just digest food. In fact, digestion is only the first of four very important processes which are accomplished along this very lengthy tube. So, the first of these four processes is simply digestion. Digestion, as a word, has two basic levels, that is a physical or gross level, and then a molecular level. So, things like chewing are mechanical, physical processes which reduce the size of the food and make it easy to swallow and move it along. But, ultimately, digestion involves and requires not just gross breakdown, but molecular breakdown to allow for the absorption of these organic molecules. And, in fact, at least the molecular aspect of digestion cannot and would not be achieved without secretion. Secretion from exocrine glands which are located strategically along the GI tract. The first are in and around the mouth. What are those glands that secrete? Salivary glands. And, elsewhere, not to forget the pancreas and the cells of the GI tract. And, we'll focus and itemize what they secrete, but for now, secretion means any additional products which are involved in enzymatic breakdown, emulsification, which means liquifying fat, and also changing or effecting the pH along the way. And, finally, mucus. We think of mucus as a negative thing, and it can be, especially in the respiratory tract, but mucus is your friend here. What system are we talking about? It's the gastrointestinal tract, and mucus forms a nice, protective coating which actually prevents the self-digestion that is the breakdown of your own tissue. So, mucus very valuable and welcome along the GI tract. Third process which is understood and never stops is motility. Motility means faithfully and continuously moving things along from mouth to anus. And, that's necessary to ensure efficiency and the complete execution of the process of digestion. Motility is a muscular event which requires the action of smooth muscle for the most part, which as the function of moving and mixing materials along the system from beginning to end. And, usually, we hope, it's unidirectional. What's that mean? One way. Can it occasionally back up? Yeah. Not too much fun. But, motility is usually faithfully from mouth to anus. And, finally, and most importantly, the function that's performed by the GI tract is absorption. In fact, it ought to be called the absorptive system, not the what? Not the digestive system. Digestion's important, but what really matters is not digestion but the actual transfer of materials from the GI tract into the lymphatic system or into the circulatory system. And, if this fails, then obviously, your acquisition of nutrients is going to suffer. You're going to lose weight and have a number of other repercussions. So, in the time we have left today, we'll knock off or at least consider the first two, and we'll postpone or finish off the last two on Wednesday. So, let's do this. Let's start at the beginning, and where is food normally placed? Most people find it convenient to put it in their mouth. You can shove it up other areas, but it doesn't really work as well. Just being silly. So, what goes on in the mouth? As important as it seems, the answer is not much. What goes on in the mouth first is some degree of mastication. That's what? Physical chewing. Can you get by without mastication? Can you just ram food down there and skip mastication? No, you can't. But, at least for most us, we enjoy this part. It's kind of, well, why is it valuable or useful. First of all, it physically reduces the size of the food so that we can swallow these otherwise bulky commodities. But, it also liquifies food because we're adding, at this time, some degree of saliva. Saliva from three bilateral salivary glands that you may or may not remember. Three bilateral, so that's how many? Six. And, the saliva that they constantly produce is mostly water, 97% water, and what's the function of that water? Two-fold. It helps to moisten the food so that it's not as dry or gritty. And, it also liquifies, and therefore brings into solution many of the solutes that are in food. And, taste, taste is predicated on doing just this you cannot taste anything until it is in a water-soluble mode. So, saliva helps to liquify food which brings about its ability to be tasted. And, tasting is, of course, one of the more pleasurable aspects of what goes on here. Saliva is also not just water, but it contains this enzyme which we used and talked about previously. It's amylase. What's the substrate that amylase works on? The only substrate is? Carbohydrate. Meaning complex carbohydrates, starches, and polysaccharides. So, we say that salivary amylase begins the process of carbohydrate hydrolysis, but as true as that is, is the process completed? Are all carbohydrates totally and completely hydrolyzed by the action of salivary amylase? The answer is no. For obvious reason. First of all, food doesn't spend that much time, doesn't spend that much time in the mouth. And, you might say, well, wait a minute. Doesn't this amylase get swallowed along with the food? And, might it continue to work in the stomach? Well, the first part of that's true, but the last part's not. Does amylase get swallowed with the food? Yes. Does it continue to work in the stomach? No. Why not? Stomach is way too acidic and way outside the pH optimum of amylase. So, somewhat surprisingly, amylase has a brief opportunity to work. It only works for the time that you put or keep food in your mouth. But, don't worry about it. There are other amylases that are added later. Before leaving this topic, we want to mention that even though saliva is constantly being produced, is it produced more in certain settings or scenarios? The answer's yes. And, it's because it's a reflex. There are pressoreceptors in the mouth and also what? Which respond to the chemical composition of food and the sheer presence of food, the physical bulk of the food. And, this sets up a reflex by way of the medulla which brings about autonomic stimulation of the salivary glands, namely a reduction in sympathetic and an increase in parasympathetic which cause more saliva to be produced. And, this is mediated not only by pressoreceptors and chemoreceptors, it can also be augmented by other things such as sights, smells, and what? Even tastes and what? Sound. Now, this might seem odd, but yet it's familiar to you. If you see a billboard that shows a jumbo Jack, if you go into a theater where popcorn is being popped, do these encounters cause you to think about food and, indeed, start to drool a little bit? Yeah. So, that's a reflex. Even sound, what famous Russian physiologist is noted for that? Pavlov. He trained his dogs to come at the sound of a bell, and he found that sometimes the bell was just enough to stimulate anticipation of food. And so, it represented a reflex. So, all of these are contributors to salivation. It's not just a presence of food, but also sights, smells, tastes, and even sounds. Moving down into the stomach. We can skip the esophagus because it's essentially a 30 second trip down there. What does the stomach do or have which is involved in secretion or digestion? It does have pepsin. And, that's part of a complex mixture that is a solution called gastric juice which is produced by the cells of the stomach. Gastric juice contains HCL. What's that? Which has a number of functions. The most important, or at least one you're familiar with is that it changes the pH of the stomach and makes it very, very low, very acidic. And, this seems to be necessary, in fact, to activate what enzyme? What enzyme is part of this so called gastric juice? It's pepsin. Our very second lab it was, we demonstrated that pepsin works best not in a neutral but a very acidic climate. And, that is the stomach, and that is maintained by the HCL. But, still, you could wonder or certainly question why acidity is important other than that. It turns out that acidity by itself denatures food protein, therefore making it more easily hydrolyzed by pepsin. And, also here's the word, what is it kills what? It kills? Most bacteria. Of course, it's not all bacteria. It's what? Most. And, that's important because are bacteria contaminating our food all the time? Yes. If HCL killed all the bacteria, we wouldn't have these outbreaks of E. coli sickness and so forth. So, this is not all bacteria but must bacteria. And, surprisingly, there are bacteria that actually enjoy this acidity, that have actually evolved and adapted to this low acidity. If you've had microbiology, you know this H. pylori which was discovered in recent times quite to the amazement of the established medical community who simply agreed that bacteria couldn't live in the stomach. But, lo and behold, they can, and H. pylori are responsible for what? What condition that everybody knows of is caused by H. pylori? It's ulcers. Ulcers. Years ago, when I was taking this course, people said, "Well, ulcers are caused by stress." That was the end of the story. Now, we know it's not true at all. It's due to the presence of these bacteria. What are they? H. pylori. So, the treatment of stomach ulcers has gone from get rid of stress in your life to what? Get rid of these bacteria and antibiotic therapy. Now, moving from the stomach, only one final comment. Can you live without a stomach? Well, you say, well protein wouldn't be hydrolyzed, but protein's going to be hydrolyzed elsewhere. So, the truth is, the stomach is what I call a convenience organ. What do I mean? Convenient. You can stuff yourself and then go about your day. Can you live without the stomach? Yeah. But, then what? Then you got to what? Eat all the time. Which is not, you know, particularly convenient. So, it is something you can live without, but it is certainly great for the sake of carrying on ordinary daily activities. Small intestine, hardly small, that is a very lengthy tube approaching 20 feet in length. And, among the secretions that are produced here are those from the pancreas, located right at the proximal end of the small intestine. And, the pancreas secretes a number of things. First, sodium bicarbonate, NAHCO3. Now, from chemistry, you know or should know that sodium bicarbonate is used to n-word. Neutralize acidity. And, is the stomach loaded with HCL? And, will that hydrochloric acid overflow or move into the small intestine without exception? Yes. Is that hydrochloric acid welcome in the small intestine? No. What neutralizes and therefore restores a more normal pH is the presence of sodium bicarbonate. Without this, then the small intestine would remain very acidic, and the following enzymes would simply not perform. Because all of these enzymes we're about to list are from the pancreas, and all of them have and require a neutral pH optimum. Starting with trypsin. Trypsin is one of many proteolytic enzymes, meaning breaking down protein, breaking it down into poly, what? Polypeptides. You might say, "Well, wait a minute. We already did that. Pepsin already did that." No, well, pepsin started the process, but trypsin will complete the process. Pepsin alone cannot and does not hydrolyze all of the protein. The end result is that these polypeptides are finally reduced in size and become available as amino acids which are absorbed later in the small intestine. Lipase, another enzyme you've heard of, also produced here by the pancreas. Its substrate is what? Breaks down what? Triglyceride, also known as fat. And, that is, then, reduced in size to glycerol. That is, one glycerol and three fatty acids. Then, a return of this enzyme. It's not s amylase, but what? P. amylase. Actually, it's the same stuff. Why do we call it p., why did we call it s? Hmm. S was salivary amylase. P is pancreatic amylase. But, it's still the same. And, you might question why we need it. Remember how long was salivary amylase able to do its thing? Only during that brief period of time when the food is in the mouth. So, p. amylase basically finishes the process which hardly even started by virtue of salivary amylase. In other words, it takes complex carbohydrates and reduces them to simple sugars so that they can be absorbed elsewhere in the small intestine. And, finally, there are enzymes that are called nucleases, and these break down or hydrolyze nucleic acids. What are the two nucleic acids that we eat? DNA and RNA. And, you probably didn't think you were eating DNA, but are you all eating cells of one kind or another? Animal cells, plant cells. Do cells have nuclei? Do cells have DNA and RNA? Yes. Do we need nucleic acids? Yes and no. We don't need nucleic acids. We need what they will produce through their hydrolysis. We need the building blocks nucleotides. And, that means RNA nucleotides and DNA nucleotides. As we finish this page, and as we finish this lecture, a couple of interesting comments about what's going on here. As we mentioned a moment ago, the stomach produces and adds to its interior HCL. What's that? Hydrochloric acid. Now, where did that come from? Well, anything that an intestinal cell adds to the interior of the GI tract had to be, at some point, extracted from or obtained from the blood. So, as you can see from this drawing, apparently the stomach cells remove H2CO3. What's that? Carbonic acid. They also remove CL, chloride, and therefore, they have what they need to produce and secrete HCL. Okay. Great. Now, you might say, "Well, so what?" Think about it. If we're taking these things from the blood, are we upsetting the composition of electrolytes and even the pH of the blood? Never mind what we're about to say. If you take these things from the blood, how would the blood have been transformed? We're taking away what? And also, sodium which will follow. And, we're also removing what? This acid which is carbonic acid. So, would the blood be transformed accordingly? Yes. And, its pH, how would its pH be changed? We've taken an acid out. So, we're making it not more acid but less acid. Could the electrolyte change, and/or the pH change be detrimental or at least critical to the rest of the body? In other words, is this a good thing? Well, it seems like it's beneficial, even necessary, but the beauty of this system is that the things that it takes from the blood, what do you think? The things that it takes from the blood are eventually going to be returned to the blood. And, here's how that goes because the pancreas, as we just said up here, removes bicarbonate, sodium bicarbonate, for the sake of neutralizing this acid and, therefore, produces once again, this acid H2CO3. And, in the end, all of these commodities are reabsorbed at the distal most end of the small intestine. And so, check this out. Check that out. What things were taken early on? What things were returned? All good, right? Did we use these things for various functions here and there? Yes, but did we return them back to the bloodstream, and therefore protect the homeostasis of the blood? Absolutely. And, with that said, could that be jeopardized, especially if things move too quickly through the GI tract? What's that very unpleasant condition where things move too quickly through the GI tract? Diarrhea. And, therefore, little opportunity to r-word. Reabsorb. And, would there be upsets to electrolytes and pH accordingly? Is diarrhea, uncontrolled, long-term diarrhea lethal? It is lethal. Why? Because it upsets the pH and the electrolyte composition of the blood simply because you're moving things through too quickly and allowing no opportunity for the recycling or return of these things. So, even though we think of diarrhea as just unpleasant, it is, in some cases, lethal because of the disturbances to electrolytes and especially pH of the blood. That's as far as we can manage. It's a lot of information for one time. We'll see you tomorrow. Is there a quiz? Yeah. Should be fun.