>> Steve Langjahr: Today we're going to look at blood pressure and its control. But not from a central, but a peripheral perspective. Today's date October 23. This is lecture 18. If you think back to last Wednesday, we discussed a location in your medulla called the cardiovascular center. This receives input from peripheral receptors that give it information about prevailing blood pressure, prevailing oxygen levels, and the movement of the body. All of these mechanisms we called central mechanisms that control blood pressure and flow. Now, we're going to step outside the brain and look at peripheral mechanisms which control BP and BF. What's BF? Blood flow. So, the first of many, is a mechanism that is intuitively expected but not instantly necessarily understood. Here's the scenario, you're on a stationary bicycle in a gym. And your feet are going crazy turning the wheel. You expect and hope that blood would be directed to what muscles? Those of the leg. At the same time, you wouldn't expect much blood to be diverted to the arms. It makes sense that a tissue which is more active should receive more blood flow. And that's of course true, but that's not an explanation. It's more of a prediction, or an observation. But what I just described is something called auto regulation. Essentially, self-regulation. Also known as active hyperemia. Hyper means to improve, emia means blood flow. Active hyperemia is increasing blood flow to those areas that are experiencing a greater metabolic demand, a greater metabolic rate. So essentially, it's this. It's a local dilatation of arterioles, which improves blood flow to those areas which are active, or otherwise demonstrating a high metabolic demand. The beauty of this process is that it's not dependent on the central nervous system, it's not dependent on nerves at all, nor is it dependent on any chemical factor. So, it is not caused by, not dependent on, nerves or hormones. So, how then does it work? Imagine some cells which are, let's assume muscle cells. And if they're contracting they're obviously consuming what gas? And producing what gas? So, that changes the environment in and around these now contracting muscles. Wo, we begin with this premise that any increase in tissue metabolism is going to lower or deplete the extracellular 02 level at the same time add what gas? And CO_2, as it turns out, reacts with water to form acid byproducts and of course, as you know, if there's a shortage of oxygen what kind of metabolism is therefore enforced or otherwise required? And therefore, lactic acid is an expected by product. So, let's start again. the muscles are contracting. They're using more what? And with a shortage of oxygen they may be producing more? Lactic acid. They're also producing and accumulating high quantities of CO_2. Okay, fine. What does this do? The buildup of carbon dioxide and/or the decrease in local pH, causes smooth muscle to relax. And remember what are these vessels that are providing or delivering blood to this area anyway? These blood vessels are called arterioles, and their walls are made of smooth muscle. So, if the local environment causes a buildup of CO_2 and/or metabolic acid such as lactic acid, that causes arterial fatigue. That means the blood vessels relax. Or in other words, they dilate. Now, that's perfect because if they dilate what does that due to resistance, friction, which would otherwise impede blood flow into those areas. Friction goes down. Therefore, blood flow goes up. And why is that a perfect solution for this problem? Well, it increases blood flow and therefore

delivers more and takes away more? So, this is a perfect response indeed it's called autoregulation, because it's a local response to, in this case, increased metabolic activity, which therefore promotes fatigue or dilation of the arterioles and that brings in more 02. And takes away more CO2. So back to that stationary bike. Your feet are going around. where his blood flow directed? To your legs. Not because they need oxygen, but because of this mechanism which simply is a reflection of the increased tissue metabolism. Which builds up what gas? CO2. And leads to a deficiency of what gas? And leads to the buildup of what products? Perhaps lactic acid. That causes smooth muscle to what? And that in turn brings in more blood flow. So, naturally, this is a beautiful response and its significance is simply that it improves blood flow to those areas which are experiencing a high metabolic rate. And therefore, a high metabolic demand for more oxygen in the removal of CO2. The process is called, autoregulation. It's also known as active hyperemia. The benefit is that it works quickly, it works locally, doesn't involve the brain. doesn't involve any neural reflex of any kind. Nor does it depend on any hormones. It is, after all, auto regulation. A form of self-regulation. Part B here, these are a number of so-called chemical factors which can also adjust, regulate BP and BF. And the first one is CO2, carbon dioxide. Is there carbon dioxide naturally, normally in the blood? Yes, and we think of it as bad. But as it turns out, a little bit of carbon dioxide is actually necessary, and always found in the bloodstream. As we've already implied, CO2 has a direct effect on smooth muscle. What does CO2 due to the smooth muscle of arterioles? They what? Dilates them. We've already discussed that as part of auto regulation. But as it turns out, a little bit of CO2 is always necessary, and supportive in the sense that it maintains the normal activity of the neurons. The neurons where? In the cardiovascular center. So, let's take that fact and sort of speculate about how this could be injurious, or at least problematic. What we're saying is a certain amount of carbon dioxide is necessary to maintain the activity of the cardiovascular center. What would happen if CO2 levels were low? If CO2 levels were abnormally low, then these neurons could not perform. And therefore, the CVC would be i-word? Inhibited, and that would release, that would result in lower heart rate and therefore lower blood flow. With that said, what would cause CO2 levels in the blood to go down? You don't care that much. Certainly, it's easier to expect that CO2 levels would rise as they do with respiratory disease. But a strange thing happens when you hyperventilate, for whatever reason. What does that mean to hyperventilate? [Breathing heavy] To breathe rapidly and deeply. Now most of us don't do that deliberately, unless were just trying to demonstrate what that even means. But occasionally, a person will hyperventilate because they're upset, because they're distraught, because they're angry and what is that due to CO2 levels? If you hyperventilate, if you exhale frequently you're throwing out, you're eliminating more what? And that's going to remove this normal supportive action on the CVC. In other words, the cardiovascular center will be i-word? Inhibited. Heart rate will what? And with the lower heart rate, so will blood pressure fall. So, you've heard this perhaps. Oh, she's hyperventilating. She might what? Faint. And so, at least from a first-aid standpoint, how to you intervene in an appropriate way? If they're hyperventilating, they're blowing off too much what? So, how can you compensate, or correct, or reverse that? Into a paper bag, yeah. Because if you exhale and inhale into a paper bag, therefore, you're inhaling back what? And therefore, preventing this embarrassing consequence. What's the consequence? Fainting, because if you remove this source of what? CO2, that will cause or remove the normal stimulation to the CVC. That will decrease heart rate and with it blood pressure. So, carbon dioxide is a bit interesting. Because excesses of carbon dioxide cause vasodilation but decreases in carbon dioxide inhibit the cardiovascular center. Therefore, cause embarrassing declines in heart rate and blood pressure. CO2. Next, a compound, which is definitely a chemical and naturally occurring hormone from the adrenal medulla. And of course, you know it as epinephrine. Epinephrine is circulated as hormones are, through the bloodstream. And what are the receptors that are acted upon by epinephrine? What kind of receptor response epinephrine or norepinephrine? Adrenergic, yes. And there are a number of kinds. In the heart we have beta 1, beta 1 adrenergic receptors. And epinephrine depolarizes these. Therefore, does what to the resting potential? Does what to the HR? Raises the heart rate. This is common knowledge. Epinephrine stimulates or increases heart rate and with it what? What follows from an increased heart rate is increased blood pressure. Especially systolic. Now, this hormone also acts elsewhere. It acts on beta-2 adrenergic receptors, which are particularly abundant in skeletal muscle and in coronary arterioles. And in case you forgot, that is, it's pretty easy to anticipate what would or should happen. When epinephrine is released, would you want blood flow to improve to skeletal muscles? Yes. Would you want it to improve through coronary arterioles? Yes. And how do you improve blood flow into any tissue you have to dilate. And so, we find that these kinds of arterioles have an abundance of beta 2 adrenergic receptors. So, they actually undergo fatigue or relaxation, which is vasodilation. That reduces PR in those locations. What's PR, and therefore improves what? Blood flow. Again, this is logical. It's easy to remember. But it's all hinging on the action here, at beta-2 adrenergic receptors. Remember though, we can't vasodilate all vessels without some penalty. We discussed this Wednesday. If we vasodilation all vessels we will lower resistance, but we will diminish returning blood back to the heart. And that has catastrophic effects on venous return. And therefore, stroke volume and so forth. So even though some vessels may, and do, dilate in response to epinephrine, others will have the opposite change. And those are cutaneous, renal and GI arterioles. Why do they react differently? Because they have different receptors. They have not beta-2 but alpha adrenergic receptors. These are actually going to be depolarized and so the muscle will not relax. It will constrict. Which will raise resistance or friction through these vessels? And therefore, do what to flow there? Decrease. So, we discussed this as a necessary response to ensure that blood flow returns to the heart. Because if we vasodilation uniformly and completely, we diminish venous return and therefore cardiac output. It's pretty clear that epinephrine is released when? What is the catchphrase that everyone knows applying to the release of epinephrine? Fight or flight. And does the heart rate increase? And does blood flow into skeletal muscle and coronary vessels improve? And is it also reduced elsewhere, such as through the skin and through the GI tract, and the kidneys? Yes. So, this is all essentially a chemical response, namely a response to epinephrine. The hormone from the adrenal medulla. There's another chemical, which you know of and indeed we've already discussed. It's called histamine. Our last mention of that was in response to injury, to cellular injury. Remember that? In fact, there were three compounds which are released as a result of tissue damage. They were? Histamine, bradykinin and prostaglandins. These, remember, serve to stimulate the chemo sensitive nociceptors. But histamine has other effects, perhaps more familiar to you. Histamine is indeed released from tissues in response to injury, or in response to an allergic reaction to some offending antigen. And therefore, it's associated with allergic responses. Yes, it does stimulate those receptors. What were those the? Chemo, sensitive nociceptors. But it also has these effects, which we've yet to mention. On blood vessels, it causes widespread general vaso what? Dilation. Not selective, but essentially universal vasodilation. And to make matters worse, it improves capillary permeability. Now what does that mean? Capillaries are normally permeable. But if you make them more permeable, what's going to leave in greater quantity is water. And if we take water out of the bloodstream, then we reduce blood volume and therefore drastically reduce venous return. Is this sounding good? It's not. Read on. Histamine in excess can also cause bronchial constriction. What are bronchioles? Airways into the lungs. This is going to make getting air in much more difficult. And getting air out much more difficult. You're going to have wheezing and certainly labored, maybe panicked sort of breathing. And so, these are pretty serious consequences. Basically, the result of too much what? Too much histamine, usually in response to an offending allergen. So, this boils down to a familiar syndrome called anaphylactic shock. It's tempting to think that it has something to do with lactic acid, because the words in there. But in fact, it has nothing to do with lactic acid. It comes from two words that are put together. Ana and phylaxis. Ana means excessive. Phylaxis actually means protection. So, roughly translated, anaphylaxis means excessive protection, or overprotection. In other words, it's an inappropriate and counterproductive response. In most cases, due to some offending allergen. Now, what's a common allergen that you hear about, and know about and otherwise think as a significant life-threatening possible allergen? Peanuts. And some people have peanut allergies which can be actually what? Lethal. Through what? Anaphylactic shock. Now if it's not peanuts, it could be beestings, and remember the vast majority of people do not have much to fear. That is, anaphylaxis is not that common. But in people who are sensitive and have peanut allergies or allergies to beestings this can be, or course, life-threatening. What's the problem? Well, it's massive what? Generalized vasodilation, which reduces VR. What's that? Venous return which reduces EDV, what's that? End diastolic volume, which reduces SV, which is? Stroke volume. Which reduces systolic pressure. Which therefore reduces blood pressure. Which therefore reduces BF. What's that? And therefore, you're dead. And as if that weren't bad enough, it also causes bronchial what? Constriction. So, anaphylaxis is a serious, although not that common of a response. An over response. And people who are sensitive or otherwise aware of this potential in their own history would obviously be advised to protect themselves. Meaning avoid what? Avoid peanuts or avoid bees. Or whatever. But then also protecting in what way? Carry around something like this, which is not a Sharpie. This is a what? An EpiPen. Which contains what, let's guess. Epinephrine. Sells for 300 bucks, which is quite a controversy. You may be aware of. But nevertheless, this is a preloaded syringe containing epinephrine. Which can be shot into your muscles at any location. And therefore, compensate, protect you from what? Anaphylaxis a.k.a. anaphylactic shock. Now, incidentally, this contains what? And don't you have your own epinephrine? Yeah. Why then do you need this. Well, because your own epinephrine is usually too little and too late. And so, this can be protective for those folks who have a tendency a known anaphylactic tendency. Anaphylaxis. Too much what? Histamine. Finally, on this list, another repeat, pH. Which is not a chemical, but a measurement of hydrogen ion concentration, as you know. Just to be clear, pH is measured on a scale from 0 to 14 and the low numbers are acidic numbers. pH, that is an increase in acidity, which is synonymous with an increase in hydrogen ion concentration. Basically, contributes to arterial dilation. And this is not a new fact. because where on this page have we already said that? Well, it was right up here with an increase in CO2 and an increase in acidity. So, anything that generates acid will cause vaso, d-word. Dilation, which is actually useful. Again, why? Why would this response to acidity, be appropriate or otherwise welcome? If that area is producing acid why would dilating the vessels into that area be helpful? It would bring in more what? And take away CO2 and acid products, and therefore correct that problem simply through vasodilation. So, there you have it; 1, 2, 3, 4. These are all chemicals which can influence either vasomotor tone and/or heart rate. And therefore, serve to regulate heart rate, blood pressure and therefore blood flow. So, couple these with the ones we spoke of Wednesday. They were central mechanisms. These are what? Peripheral mechanisms. These work outside the brain, the others we dealt with Wednesday were reactions detected by receptors such as mechanoreceptors and such. Which acted on the cardiovascular center. So, let's leave that behind. And let's abruptly switch gears here, focusing on obviously important solution which is moving through the circulatory system. Namely blood. It's easy to dismiss blood as just that red stuff, or you know something that contains red blood cells. But it is a tissue and it determines a lot, indeed, it determines a lot about your health and well-being. So, let's define blood on an anatomical, a physiological, and a functional level. You know this fact already. Our very first lab we spun in a centrifuge a sample of blood. And we separated what from what? The plasma from the cells. And that measurement you might recall is something called the hematocrit. The ratio of cells to plasma. And what is that percentage ratio? Normally it's about 45% cells, 55% plasma. Does this matter? And if so why? If the hematocrit were to rise, that would suggest either a loss of water or gain of cells. And what would that do to the thickness of blood? What is the name for the thickness of blood? So, let's back up. If we have a high concentration of cells, then we're going to have a high? And that's going to raise resistance, and therefore reduce actually, blood flow. So, the hematocrit is hugely important as it affects viscosity, therefore resistance, therefore flow. And remember the hematocrit is not just a function of cells, but a function of water. What would dehydration in and of itself do? Dehydration by itself wouldn't change the number of red blood cells, but it would change the hematocrit making blood more the v-word, and therefore, reducing in the end blood flow. So, this ratio cells to plasma is pretty important even though it doesn't tend to change that much, that quickly most of the day. So, let's leave that behind for now. Let's look at cells. The cells are interesting and quite diverse. And they include three basic groups. The most abundant of which are erythrocytes. Indeed, erythrocytes are called that because the word erythro means red. So, what's the acronym for these cells? RBCs, red blood cells. Now, to be truthful, they're not red at all. Red blood cells are not red. But they contain something inside which is red. And that's what? And we'll get to that in a minute. Red blood cells are far and away the most numerous. That is the makeup most of the hematocrit. And as you already know, they're responsible for transporting oxygen and incidentally also CO2. What's the second most numerous type? Actually, it's the? Thrombocytes. They're also known as platelets because the resemble, well broken dishes. And so, the name platelet. the proper term though thrombocytes. Which comes from a word thrombus, which comes from the notion of a clot. So, these cells are involved in what process you think? Coagulation. And then, the white blood cells, which are actually the least numerous. But certainly not the least important. What's their acronym? Leukocytes, WBCs, white blood cells. Their numbers are nowhere near the other two, but their importance can't be dismissed. Because you know intuitively and basically these provide defense from infection. So, let's go on and talk more about leukocytes, which are the most diverse of the three. They break down into two families right away. Those cells that have granules, visible granules in the cytoplasm, and those that don't. Those that have granules are called granulocytes. And those that don't are called agranular, or nongranular leukocytes. From anatomy, you might recall that the granular white blood cells are further divisible according to how they stain, how they change color in laboratory testing. And so, they break out into three subtypes; neutrophils, basophils and eosinophils. Not all of these are phagocytotic, we'll get to their specific functions in a minute. But the names that you hear are based on how they respond to dyes or stains which are actually rendered or applied in a hospital or scientific lab. The agranulocytes, don't have visible granules in the cytoplasm. And they break out right away into two subtypes; lymphocytes and monocytes. Lymphocytes implies cells that come from the lymphatic tissues, from lymphoid organs. And they break out into two, may be familiar subtypes, B cells and T cells. These are important in body defense. B cells, especially important in the production of antibodies. Monocytes and macrophages are similar in that they are essentially both phagocytotic, except that monocytes live and work inside the circulatory system. Macrophages squeeze out of capillaries and therefore go to work in to the areas outside capillaries, in the interstitial spaces. So, these are essentially the same cell. They're just named according to where they work. Cells that work inside the circulatory system are called monocytes. Those that squeeze out of capillaries and work in the interstitial space, those are called macrophages. So, this is our roadmap, a basic, well chart, which shows the relationship, the names of these cells and also the plasma. Let's go into each of these more in-depth starting with plasma. What's mostly plasma made of? Water, 90%. And it's easy to dismiss that and say okay it's just water. But remember not too long ago we said that water influences the V word, what's that? And it also includes the other V word, volume. In other words, what does dehydration due to blood volume? What does it do to viscosity? So, obviously it has effects on venous return and on blood flow. So, we can't just say oh, water great. Water's very important as it dictates or has an influence on viscosity and also blood volume. And incidentally, also on electrolyte concentration. I mean let's take an electrolyte, sodium. Should there be a certain concentration of sodium in the blood? Yes. But remember concentration's not just the amount of sodium but the, C word. And does the amount of water determine the concentration of this electrolyte and that electrolyte? Of course. So, three things impact, that is three things are impacted by volume changes. That is, water changes. You can affect the volume, the viscosity and electrolyte concentrations. All of which have repercussions that are pretty significant. Aside from the water, what else is there? I mean it's not just water. What is plasma made of? Cell nutrients. What are some nutrients by name? What are some organic molecules which provide nutrition for cells? Glucose, amino acids, and FA, what's that? These are all was that these are all prevalent, important organic substrates for metabolism. Is there always sugar in the blood? Yes. Is there always a supply of amino acids? Yes. Are there also fatty acids in the blood? Yes. And these are intended for and used as cell nutrients. And remember metabolism doesn't just use organic molecules, it also produces organic molecules as a byproduct of metabolism. So, these would be called cellular waste products. Including, mostly urea, which is a nitrogenous compound. What's that mean? Nitrogenous, containing nitrogen. Urea is mainly derived from the breakdown of protein. And even though in small concentrations it's not toxic, it can be in high concentrations. So, what would you expect? What organ would you assume would deal with metabolic waste products and help eliminate them or escort them out of the body? The urinary system. So, urea is handled naturally by the kidneys. And the same is true for this. Be sure you read it carefully, because it's not creatine it's creatinine, which incidentally is derived from creatine. Another nitrogenous waste product. And so, as we've already said, these are essentially eliminated from the body, but they are unavoidable daily products of metabolism. Then also in the blood and making up a sizable concentration of solutes, are those called blood proteins. Also called plasma proteins. These are confined to the bloodstream. That means they don't leave the bloodstream unlike nutrients. Why can't these proteins escape capillaries. The simple reason is they are what? And they're way too big. Their molecular size is too big. They do not, they cannot diffuse across capillaries. So, they are confined to the bloodstream. But what then do they do? They are certainly not nutrients. What are the types of plasma proteins that have importance in plasma? Most of blood proteins are albumin. Albumin is essentially there to provide osmotic balance. That is prevent the excessive loss of water. Think about this. If we didn't have albumin in the blood than the concentration of solutes there would be low. Therefore, the concentration of water there would be high. And water would have a great tendency to leave capillaries. And so, the function of albumin is to retain, to hold, to prevent the diffusion, to prevent the osmosis of water outside of capillaries. And therefore, it preserves blood volume and it also contributes therefore to blood viscosity. Albumin is made by the liver and any shortage of albumin would lead to water loss from the capillaries and the consequence on viscosity and venous return that you can imagine. Thirty-five percent of the blood proteins that are here, are of a different kind, these are globulins. Globulins break down into at least three. So, here we go. The first category of the globulin group are those called alpha, alpha globulins. These consists of a number of lipoproteins, especially high-density lipoproteins. High density is not so important. But what is a lipoprotein. That's intuitive. A lipoprotein is a protein that has a lipid. High density lipoproteins are known by this acronym HDL. And these are part of a normal assessment, that is a normal blood test. High density lipoproteins actually remove lipids, especially cholesterol from the bloodstream. And return them back to the liver, so they can be eliminated in the bile. Is that useful? Do you want to scavenger up, cholesterol, remove it from the blood and return it to the liver so that it can be lost in the feces? Does that sound like a good thing? And so, at least from a clinical standpoint, would you want your HDL value to be high or low? Remember what's it do? It scoops up, it attracts and removes cholesterol. Returns it back to the liver so that it can be eliminated in the bile. Does that sound like a good thing? What if we don't? Then the cholesterol is going to build up in the blood and it's going to plaque out. That means coat the inside lining of the small vessel called arterioles, and we gave that a name the other day. When you have too much fatty streaks in your arterioles, that's called atherosclerosis, which obviously reduces blood flow and therefore has an adverse effect in all tissue. So, what was the question? Will you get a measurement of HDL in any clinical examination of your blood? And would you want that number to be high or low? High. This is sometimes called good cholesterol, which is a misnomer because it is not cholesterol. But again, sometimes we have to simplify things for patients. HDL, high density lipoproteins. Alpha globulins also contain some clotting factors. And we're leaving that vague. But certainly, what would that suggest? What's a clotting factor? Something that helps promote coagulation. Is that a good thing? Is coagulation sometimes, usually helpful and indeed important. So, all in all that's a good profile of alpha globulins. Beta globulins contain low density lipoproteins, LDL. And these are the lipoproteins, which actually move cholesterol from the liver out to and throughout the blood system. Now, remember is cholesterol useful? Is cholesterol a steroid valuable for cells? See we have this negative feeling about cholesterol. But is cholesterol a good thing? Yeah. Because cell membranes are made, at least in some sense by what? So, there's a need for LDL, but at least in terms of your profile, your clinical measurement would you want your LDL to be a low number or high number? Low. This is sometimes called the bad cholesterol. And again it's a misnomer because not cholesterol all but to remind you, HDL and LDL are simply lipo what? lipo proteins that are moving cholesterol either toward or away from the liver. And therefore, have that job of lipid transportation. Finally, in this category are gamma globulins. Probably you've heard of those. Gamma globulins are sometimes given in hospital settings because they comprise and make up a family of proteins called antibodies. So, someone is suffering from an infection, very often they may be given a shot of what. Gamma globulins which will boost, temporarily, their immunity. Gamma globulins then have that therapeutic or clinical significance. Now outside the globulin group, we also have still other blood proteins, 4% of which are called fibrinogen. Fibrinogen is a clotting factor produced by the liver. And we'll discuss this certainly Wednesday, maybe next Monday. But clearly follow this. If it's a clotting factor and if this compound were low in concentration, what would you fear, or otherwise worry about? You don't have a clotting factor, therefore, you'd have a tendency to what? Bleed. And so, the importance of fibrinogen is that it prevents inappropriate bleeding or hemorrhage, it's important in normal coagulation. Incidentally, sometimes you hear the word serum used. And it sounds like they're talking about plasma. And in fact, serums is the same thing as plasm, except it's missing one thing. Serum is plasma without? And this is useful in laboratory or research settings, because serum, unlike plasma will not c-word, clot. And that's the difference between serum and fibrinogen. Still not done with plasma. Because plasma is a aqueous solution containing a number of inorganic ions, including all of these. What's this, Na, K, Ca, Mg and that? What's Na, sodium. Okay, cheap joke. Potassium, calcium, magnesium. And that's bicarbonate. All of these, well at least the first four are extremely important in resting potentials. And therefore, excitability of nerve and muscle. So, we don't need to belabor these. And therefore, upsets in these would obviously disturb resting potentials. Therefore, neuromuscular excitability. Bicarbonate, we'll learn later is important as a buffer. It helps to ameliorate, that means modified pH. And therefore, maintain a proper pH balance in the circulatory system. So, remember we're talking about electrolyte, c-word. Electrolyte concentration. Which is not just a function of the amount. Remember, concentration is the amount per volume. So never mind sodium, what can affect its concentration is not just sodium but the presence or absence of water. So, what would dehydration do to the concentration of any of these electrolytes? If you're dehydrated, you have less? Therefore, the concentration of all of these go up accordingly. So, we don't want to think of these numbers as solely dependent on the ion itself. But, remember, based heavily on the presence or absence of water. Finally, plasma's going to contain hormones. And those would be quite different depending on the source. That is, plasma from me would contain different hormones than plasma from you. And what hormones are we talking about? Well, any hormone. Could be thyroid, could be testosterone, could be estrogen, could be epinephrine. And so, all we're saying is that plasma is the vehicle, the solvent in which hormones are circulated as well. And we're were still not done. Because are there chemicals in the blood, which are actually gases? Does plasma contain oxygen? Does it contain carbon dioxide? And are they important? Sure. So, I hope we've made the case, that plasma is not just water with some goodies in here, but rather it's quite a sophistic recipe, a recipe consisting of nutrients, waste products, hormones, plasma proteins, electrolytes and even gases, the two most important oxygen and CO2, plasma. But let's leave them. Let's talk about the cells, which we only introduced. And here's a kind of relative size and approximate appearance for many of these. And in fact, not tomorrow, but a week from tomorrow you're going to be sampling your own blood. And you're going to be examining and actually counting certain numbers of these cells. And those numbers are important clinically to establish whether your blood is normal in composition. So, for no good reason, let's start with thrombocytes? What's the other name? There it is right there, platelets. These have no nucleus so they don't reproduce in circulation. And blood cells in general are reported as a concentration, that is numbers of cells per; per what? What is that MM3, cubic millimeter. A cubic millimeter, you should appreciate is 1 millimeter tall, 1 millimeter wide, and 1 millimeter deep. It's about as much blood as you can put on the head of a pin, p-i-n. It's just a do, but yet in that small volume how many thrombocytes would be normal? A quarter of a million. So, that should be pretty impressive. Remember, thrombocytes are those associated with clotting. They're derived from, they're produced by mega karyocytes which are found in bone marrow. What kind of bone marrow? It doesn't say, but you should know. What are the two types of bone marrow, we've got yellow and? So, guess what? These come from red bone marrow. And as we've already said, these are fragments of larger cells called mega karyocytes. And they are non-nucleated. What they do do their function is to contain and release a compound called serotonin. Which, I'm sure is a shock here, because the last time, the first time you heard the word serotonin was in unit two. We mentioned it's an important neural transmitter. And this serotonin has nothing to do with that serotonin. But the name, incidentally, is based on what it does here. In fact, serotonin was discovered in the blood way before it was discovered in the brain. And the word serotonin is useful. Sero, meaning serum, and tonin, meaning to tighten. So, it's a rough reference to it's effect on vessels. What does serotonin do to arterioles? It's right here, it's a local what? Vasoconstrictor. And how does that affect bleeding? If a vessel is leaking, or damaged, or cut serotonin is released as a result of platelet adhesion to that wound. And therefore, what happens to the vessel accordingly, the vessel what? Constricts. Does that help control blood loss? Yes. And also, these thrombocytes contain so-called clotting factors, which promote coagulation. A topic we'll get to soon enough. So, the take-home message is simply this, if you read a laboratory report and it says the patient has a thrombocyte concentration of 100,000 does that sound healthy? No, that's way low. And what would be the danger or concern? Hemorrhaging, because this is important in coagulation. Indeed, for that reason, someone who is hemorrhaging, would benefit from the transfusion of what? What kind of cell would you want to give somebody who is bleeding from unknown sites? You'd want to give them a lot of platelets. And in fact, that's called a packed platelet transfusion. Meaning lots of thrombocytes. So, they're important. Next, by far, the most abundant are erythrocytes. What's the abbreviation? Red blood cells. And their numbers are, well imposing. Again, we talk about numbers, but we're really talking about concentration. Sometimes you'll hear somebody say what's your blood cell count? Well, that's not really correct. It's not a count, it's a concentration. Cells are always expressed not just as a number, but as a concentration. Cells per what? Millimeter cubed. And in a single cubic millimeter you have at least in a male, what five million. In fact, you make the cells at the rate of 1 million every second. One million every second. And where do they come from? They're produced in red bone marrow. As you know, their shape is very characteristic. They don't have a nucleus. So, we say they're not on nucleated. In fact, red blood cells are unique in another way. They not only don't have a nucleus, they don't have mitochondria, they don't have nothing. I know that's bad language. They don't have nothing, it's a double negative. What do they have? They're basically just stupid bags of what? Stupid bags of hemoglobin. That's all they are. Now, that doesn't diminish their importance. And we'll get to hemoglobin in a moment. But before we do this number, what is it? Five million, applies to what? So, what's the implication? Females more or less? And why less? Two reasons. The number of red blood cells is really a reflection of muscle mass. And which gender has, as a rule, more muscle mass. And what does muscle mass have to do with erythrocytes? In a moment we're going to see that it is after all erythrocytes that transport that gas what? So, you see and appreciate the correlation. The other reason that females have a low or lower RBC concentration is that they lose blood on a monthly basis. At least during their reproductive years. And that's called menstruation right. So, that accounts for a number, maybe 4.5 million, not 5 million. Now, the production of red blood cells, incidentally, even though it is prodigious, meaning impressive, is not without regulation. So, let's take this scenario which is easy to predict. You change your address from Lancaster to Big Bear. I'd like to do that. But anyway, now you're at 7000 feet or whatever it is up there. What's the concentration of oxygen at that level? And so, what happens do you think to your red blood cell count and why would you think that? Red blood cell will go up. It's easy to say, well that's because you need more oxygen. But that's not an explanation, that's teleology. The explanation is this, when you're in rarefied air, rarefied air, meaning air with less concentrated oxygen, your kidney will detect that and produce a hormone called EPO. EPO is erythropoietin, which stimulates bone marrow to make more what? Red blood cells. This strategy is not lost in athletes. What do I mean? If you're a long-distance runner, you might train or run in Big Bear. Why? Because if you live in that location, your kidneys will make more what? Erythropoietin. Therefore, your number will go beyond 5 million to maybe 5.5 or maybe 6 million. Would that be useful if you're an athlete, an Olympic contender? Because it would provide the delivery of more oxygen. But hold on, even though your RBC value is up. What does that do to the hematocrit therefore, and what does that due to the viscosity, and what does that due to the resistance, and therefore the flow. So, this notion of raising your RBC has a certain validity, but in excess it can be counterproductive. That means, diminish blood flow because it raises viscosity. That said, erythropoietin is available. You can get a prescription for it. A doctor can write you a prescription for that hormone. And never mind athletes who would justify or otherwise qualify for this kind of prescription? Let's go back to cancer. What are the cells that are often adversely targeted by chemotherapy? Red bone marrow. What happens to RBC values in cancer therapy, therefore? And would this hormone be useful to restore their RBC value? And so, maybe this is a little political and off-topic, but this is how Lance Armstrong got away with what he was doing for a while. You know, Lance. I guess a lot of you never knew, or, anyway. Lance Armstrong was a huge cyclist. He won the Tour de France seven times or something. And then it was found out that he was using illegally what? And he said well hold on I have a doctor's prescription. Therefore, it's okay. Why did he have a doctor's prescription? He had testicular cancer. So, it was all legit. Until it was found out that well, he was you know, overdoing it on this. And therefore, had an unfair advantage, and they actually took away all those ribbons and metals. EPO. Now, back to hemoglobin which is abbreviated Hgb. Hemoglobin is the red iron containing pigment. And not terribly different from the M word. What's that similar pigment also containing iron which is found in red blood cells, I mean red muscle. Myoglobin. Now, let's be clear, myoglobin is not found in the blood, myoglobin is found only in muscle. And not even all kinds of muscle, only in the slow oxidative types. Hemoglobin is not found in muscle, hemoglobin is found in red blood cells. Hemoglobin carries oxygen. It also carries carbon dioxide. So, it carries these two important blood gases. Couldn't be, therefore, more important. Incidentally, and we'll get to this later, hemoglobin carries oxygen, but it equally enjoys carrying a different gas called CO. CO, not to be confused with CO2, it's what? And what is CO? Not carbon dioxide, it's carbon monoxide. Now, why does this matter? Hemoglobin normally carries oxygen. But in the presence of that gas, it will actually bind to carbon monoxide, therefore be less able to carry oxygen. So, is carbon monoxide deadly? Yes. Not because it is. What do I mean? Carbon monoxide is not a poison, it's not a poison. But it occupies the spot on hemoglobin normally reserved for? And so, in the presence of carbon monoxide, you're not going to be moving any oxygen. Therefore, you die from asphyxiation. Carbon monoxide is in cigarette smoke, but it's also a biproduct of internal combustion engines. Do people sometimes resort to that gas as a means of exiting the word? Do people commit suicide with carbon monoxide, I don't have to tell you how to do it. And oftentimes, this happens accidentally in homes or in institutions. Because after all, this gas is a byproduct of combustion, especially internal combustion engines. So, I always liked this story here, it was actually in the AV press years and years ago. It was about a pilot who was flying a private plane, solo, across the plains of Kansas. Now, any device that is any mechanized machine which emits this gas. What is this gas? Typically, there would be, and should be devices for detecting it. Because this gas is odorless, colorless, and tasteless. So, in the cabin of airplanes there's a detector called a CO detector. And you should have these in your home. In fact, it's a law. So, I'm going to come to your house one of these times and make sure you have one, no. It is a law. But back to the story. This guy had an airplane, and he's supposed to have what? A CO detector. But he decided it wasn't important, or it wasn't working. And so, carbon monoxide came into the cabin and therefore what gas is not being transported to his brain anymore? And therefore what happened to his level of consciousness. So, normally when someone blocks out in an airplane, the plane crashes and that's the end of the story. But no, he had it on autopilot. So, the plane just kept flying. Now, normally, two things happen here, you either run into something, like a mountain, in which case you're dead. Or you run out of gas, in which case you crash and you're dead. But no, this is Kansas. There is no mountains, and so he did run out of gas, and his plane normally would have crashed, but no, it just landed itself. Now, normally when you land, you hit power lines and barbwire and buildings and you're dead. But no, this is Kansas. There's none of that. And this is in winter time. So, there's a perfect blanket of what? All right. So, the plane lands itself. He wakes up hours later, and you know goes out and buys a lottery ticket, because that was the luckiest day of his life. Interesting story. And what makes the story even more impactful is that he's a doctor. He's a doctor. So, he had enough money to buy an airplane, but not enough to provide for a CO detector. Just thought that was funny. All right so, let's move on to what? Leukocytes. We hardly have to emphasize their importance. It's common knowledge that these provide defense against infection. Without these, you're dead. Of course, you could say that about any cell, that we just discussed. Their numbers are not that impressive, 4000 to maybe 10,000. If they get much below the 4000 mark, you're dead. If they get much over the 20,000 mark, you're dead for different reasons. But let's go into these. Remember they're granular and nongranular. The granular include eosinophils, basophils and neutrophils. You can read about them, you'll see pictures about them. That was mainly anatomy, so we're not going to bog down on that topic, except that they are for the most part developed and released from red bone marrow. So, this testifies to the importance of red bone marrow. If you lose red bone marrow, what are you not going to be making? Well, these, but you're also not going to be making reds. You're also not going to be making thrombocytes. So, you're dead on three counts there. And the importance of red bone marrow is beyond dispute. Now, the most abundant of these three are the neutrophils. Neutrophils make up 70%. You don't need to remember that. But 70% more or less of all these granular leukocytes. They're hugely phagocytic, they live for maybe 24 hours. And essentially, they give their life for you, that is they are involved in phagocytosis, which usually kills them. Neutrophils what do they phagocytize? They phagocytize bacteria which might be contaminating your bloodstream. They also help, that is the other variety here, the eosinophils are important in attacking, recognizing and removing multicellular parasites. And if you've had microbiology you know what we're talking about. So, these numbers, that is the number of eosinophils would be elaborated or increased as a result of exposure to a parasitic infection. And finally, the basophils are involved in in the inflammatory response. Now, we think at this point, maybe inflammation is bad, but we're going to prove to you that inflammation is good. And in that context, they also release, what? they release histamine, which is a primary mediator of inflammation. They also produce and release not coagulants, but what? Now, what's an anti-coagulant? Obviously, something that doesn't promote coagulation, but actually inhibits coagulation. You might thing that bad. But is there some justification for minimizing coagulation? Is all coagulation all the time a good thing? No. So, anticoagulation is also protective, because it prevents inappropriate clots from coming along. Those are the granular. The agranular are somewhat made in red bone marrow. But, at least the lymphocytes are manufactured by lymphoid tissue. In case you forgot, those are the lymph nodes, the spleen, and the tonsils. And therefore, those that are produced here are called lymphocytes. The lymphocytes come in two flavors, no, not really flavors. They come in two forms, T cells and B cells. We're going to get to this later, I just want to give you sort of a quick introduction. The reason these are called T cells is that they are derived from their ancestry, actually come from a gland which sits above your heart. Not to be confused with the gland in your neck, which is the thyroid, this one that sits in your chest above the heart, the thymus. Hence the name T cells. These are important because they're effective against microbes that live where? Let's read that, intra-cellular. Which means viruses. And therefore, they tend to recognize and destroy your own cells if they become infected with viruses. They also recognize tumors and they also recognize and destroy tissue transplants. Which is a bad thing, but they don't know it. I mean after all tissue transplant is a modern approach. But these cells see a tissue transplant as foreign and so they basically destroy tissue transplants. And therefore, raising the question how do people survive if they've had an organ transplant. Well, obviously you have to suppress what cells in order to tolerate, in order not to reject those tissues, you have to suppress T cells. Which is a tricky business, because you can suppress these, but if you suppress them too much then you're dead, because you no longer have any infection resistance. The other type is a type of agranular or nongranular are called B cells. The name comes from bone marrow. These are effective not against so much viruses, but extracellular microbes, mainly bacteria. And these are produced and are important in response to again, bacterial infections, because they mature, that is B cells become plasma cells. Which then produce a group of proteins that we mentioned earlier today, namely antibodies. So, I know this is sort of vague and simplistic for now, but simple, simple discussion here. If you were low on B cells then you wouldn't be able to make what? And therefore, you'd have less resistance to that, that, that, or that. And of course it's logical that making antibodies can be of course artificially induced by stimulating B cells. This is the basis of vaccination, which we'll talk about on Wednesday. And then also a type of non-granular leukocytes are the NK cells. I love that term, it's actually standing for natural killer. Somebody had a sense of humor. and these are those that bind to and chemically dissolve or eliminate viral infected cells; including also tumors that arise from mutation. If you read that sentence you say, well, that sounds a lot like T cells. And in ways that we'll discuss NK and T cells are part of the same effort, especially to eradicate viral infections. And then, we're still in the agranular category. There are monocytes which we said develop later in their life span into macrophages. Let's see if I've got a picture of that. Here we go. Inside the circulatory system, they're called monocytes. Once they leave, they're called macrophages. Same cell, different name. And these are important in phagocytosis. that is consuming microbes and cellular debris. They also help initiate, stimulate and promote the action of T cells in ways that we'll discuss on Wednesday. So, some of this information is very vague and general, but it will become more precise and defined after Wednesday when we discuss immunity and the involvement of lymphocytes and white blood cells in general. So, okay, let's finish with this. This is a simple list statement really of the functions that blood provide. First, obviously transporting gases. What two gases? CO2 and oxygen. Now what part of blood does that? Just to put a real fine point on it, do monocytes transport oxygen or co2? No. Do any of the whites? No. Do the reds? And what part of the red blood cell? What is the capacity, what is the content of a red blood cell that allows it to do that? Hemoglobin. Now, incidentally and we said it earlier, does plasma contain and transport some oxygen? Yes. So, if someone says what part of the blood does this, you say red blood cells. And also, don't forget the plasma. But of those two, obviously red blood cells do most of the work. What about transporting well, lipids, and wastes and nutrients? There's no cell that does this. No cells do this. So, this function is entirely in the hands of what? Plasma. Plasma transports nutrients, wastes, and also lipids, and hormones for that matter. Thermoregulation. Which deserves a definition. Thermoregulation means controlling body temperature. And you might think well, what does that have to do with the blood? Is the blood warm? How did it get warm? It moves through tissues that are producing, among other things heat. So, does blood pick up heat from living cells? And is that heat then moved and circulate by blood? And is that important? Well, sure it is. Sometimes we have too little heat. Sometimes we have too much heat. How does the blood adjust or factor into that? Remember through the skin we have blood vessels, yes? And if a blood vessel is constricted, that's called vasoconstriction. That's going to keep blood away from the surface. And if we keep blood away from the surface, then we're going to conserve what? On the other hand, if we dilate these vessels, then the heat it closer to the surface, where it can radiate away. And so, vasodilation leads to heat loss. So, thermal regulation is not really a property of blood so much as it is a property of vasoconstriction and vasodilation. Hormone transport. Naturally, a plasma function. And immune responses clearly under the functions of all of these sundry white blood cells. Including the granular and nongranular. And another function on there, which I thought was there but I guess it never was, is coagulation. I mean isn't coagulation an occasional function that is important and protective? And what cells are involved in coagulation? Thrombocytes. So, quite a number of functions in no particular order. But each one essentially the result of either specific cells and/or the plasma.