>> Steve Langjahr: Today is May 9th, 2016. We're starting our final unit of investigation. And we're going to spend two lectures on the kidneys and their importance for homeostasis. So today we're going to begin, obviously, with a little review of the anatomy, then a description of the fundamental processes which occur in the kidneys. And we're really not going to pay much attention to the rest of the plumbing. That is, we're not going to go into the performance of the bladder, or the rest because it is, of course, the nephron which does the bulk of the work here. So this is very much like the lungs. So what was the working functional unit in the lungs, those tiny air sacks called alveoli. The microscopic units of functionality here are called nephrons. Each of your kidneys has about a million of these. It's not quite true, but I'll go ahead and say it, seen one nephron, seen them all because they are all anatomically very similar. So let's review the microanatomy of a typical nephron based on your recollection of the anatomy. Essentially, the nephron can be divided into two interconnected elements, the vascular components, which bring blood to and carry blood from the nephron. The vascular components that are important are the incoming arterial, incoming to the glomerulus. And that's known as the "afferent arteriole". The word "afferent" means "to travel into". Within the glomerulus, there is a bunch of capillaries simply called the "glomerular capillaries", or simply, the "glomerulus". The word "glomerulus" means a "ball", B A L L. This is a tiny microscopic ball of capillaries. And leaving the glomerulus is a smaller arteriole, which gets the name "efferent arteriole". Important to make that distinction that the afferent has a larger diameter than the efferent, which, as a result, tends to raise pressure in the glomerular capillaries higher than it would otherwise be. Not shown here, but certainly familiar I hope, is that the efferent arteriole connects to capillaries, which embrace and surround the rest of the nephron. And those are called "peritubular capillaries", which eventually connect to outgoing veins, eventually back to the renal vein, dumping blood naturally into the inferior vena cava. So much of the vascular elements have been removed here for simplicity. The important parts are the afferent arteriole, the glomerular capillaries themselves, and the outgoing vessel called the "efferent arteriole". Everything in yellow represents the so-called tubular components. These are parts of the nephron itself. And they begin with this little fish bowl, this enclosure, which was first described by Abraham Bowman, a scientist in the late 19th Century. And so in his honor, it's sometimes called, "Bowman's capsule," but today, it's more commonly simply called "the glomerular capsule". It's made of simple squamous epithelium, which makes it permeable. That means the molecules can enter this capsule easily after they've left the capillary network of the glomerulus itself. Bowman's capsule connects to a vessel, actually, a tubular component, which is kind of twisted and short. You know, this is called the "proximal convoluted tubule". That tapers down into a hairpin loop, which dives very deeply into the kidney. This dotted line demarks the surface of the kidney. Perhaps you recall the cortex and the deeper interior of the kidney, which is called the "medulla". So the loop, also known as the "loop of Henle", goes down deep into the medulla. Then it comes back up toward the surface, where it widens out again and changes names, this time now called the "distal convoluted tubule", which eventually joins up with others like it into a common area, a common larger tube called the "collecting duct", or "collecting tubule". This carries urine into the medulla again, and actually drips it constantly into the renal pelvis, which you might recall from gross anatomy. So these, then, are the basic features of a single nephron.

[Silence]

With that said, we want to now start our discussion of the actual physiology that occurs across and within a nephron. And essentially, these renal processes are three, all of which are collectively part of urination. When you hear the word "urinate," you think something you do in a restroom into some porcelain receptacle. But actually, that's not urination, that's micturition. All of you are urinating all the time, or you're in urinal failure. So urination as a word means simply to make urine. And you never stop making urine in healthy settings. So what are the processes that produce urine? First, a process called "glomerular filtration", indicated here at number one. Basically, this is a passage of water and solutes out of the glomerular capillaries into Bowman's capsule. This is not gravity-based, it's pressure-based. But it does produce what's called a "filtrate", which is the beginning of urine formation. But the important thing is that filtration alone does not conclude the process. Notice item two, "Is it possible for molecules, which were filtered, to be put back into the blood and, therefore, escape excretion through the urine?" The answer is yes. And what familiar abundant solute in the blood is easily filtered, but yet fully-recovered or returned into the peritubular capillaries, "G" word, glucose. Is there plenty of glucose in the blood? Is it small enough to be filtered? Yes. But does normal urine contain glucose? No. So by what process is that glucose normally returned; item two, tubular reabsorption. Essentially, molecules are selectively removed by various processes, and returned back to the peritubular capillaries, where they are returned to circulation. Is it possible for molecules in the blood to actually end up in the urine, even though they were too large to be filtered as a result of glomerular filtration; the answer is yes. And that process, item three, is the opposite, or reverse, of process two.

It's called "tubular secretion". This is taking molecules selectively from the blood and putting them directly into the nephron, basically bypassing tubular -- or I should say, glomerular filtration. So to put this in perspective and make it rather simple, glomerular filtration adds things to the urine. Tubular reabsorption removes things from the urine, and tubular secretion adds things back also into the urine. So in summary, what happens -- that is, what the urine contains is a function of one, two, and three. Naturally now, then, we need to discuss each of these processes separately because they do operate somewhat independently. The first, then, glomerular filtration. When something is filtered through a filter, what you get is something called the filtrate. And the filtrate is mostly water, but it does contain small molecular weight solutes. That means something other than protein. Protein cannot be filtered because proteins are molecularly too what, too big; so small molecular weight plasma solutes. With that said, there's no protein normally filtered, nor are there any cells normally filtered. Remember, these membranes are semi-permeable, and they discriminate on the basis of molecular size. The forces that bring about and make possible glomerular filtration are summarized and enumerated here. And we need to understand their value and their definition, I suppose. First, shown here in green, is the driving force which pushes fluids into Bowman's capsule in the first place, and that's called "GCP", an acronym for "glomerular capillary pressure". In other words, it's the blood pressure in these capillaries. And how is blood pressure measured? What's the units of expression, millimeters of mercury. So the prevailing capillary pressure in the glomeruli is about 55 millimeters of mercury, which, incidentally, is fairly high. You know, that is, this capillary pressure is higher than most capillaries. But the thing is are we putting fluid into an empty space, or is this Bowman's capsule already filled with fluid? Well, it is. So this pressure is not unopposed. And the second pressure is the pressure of the fluid that's already in Bowman's capsule, and therefore, it's called "Bowman's capsule pressure". We show it working against the green arrow. That is, it opposes filtration. And even though it's a positive pressure, it's working against GCP. What is BCP normally about? 15 millimeters of mercury. There's one other pressure which works against filtration, and that's the osmotic pressure. Let's think about that. Remember, filtration produced a filtrate, which has no, what, no protein. So where is the higher water concentration, in the yellow, or in the red? Higher water concentration here. Will water have an osmotic tendency to go this way? Yes. Would that oppose filtration? Yes. What do we call that pressure? "GOP", which stands for, in this case, "glomerular osmotic pressure", which is a substantial number, 30 millimeters of mercury. So these are the pressures. Glomerular capsule pressure is working against glomerular capillary pressure. And so in summary, these last two pressures are in opposition to the first one. So let's do the math; 30 plus 15, 45. Subtract that from 55. What is the overall pressure, then, which is responsible for filtration, ten; ten millimeters of mercury. Why is that important to, well, calculate or even understand? If anything were to raise Bowman's capsule pressure, or glomerular osmotic pressure, what if this 15 went up five points? What if GOP went up five points? What, then, would net filtration pressure be; zero. And that would be renal failure, or renal shutdown. So what I'm trying to emphasize is that this net filtration pressure is not very high. And it doesn't take much to neutralize, or cancel it. And that would effectively shut down the kidneys. What would cause Bowman's capsule pressure, let's say, to be high? Well, anything that would obstruct the flow of urine. And never mind where. If we obstruct the flow of urine in the renal pelvis or elsewhere, would that pressure back up, increase that number and, therefore, decrease that, yes. And certainly, one familiar obstruction that you've heard of is a renal stone, a kidney stone. So to repeat, slight increases in either of these two can effectively cancel GCP, and therefore, shut down a kidney with disastrous consequences. Now, it's one thing to calculate these pressures and speak of glomerular filtration. And normally, it goes quite smoothly and wonderfully for healthy people. And how do we express filtration, that is, what unit do we use to measure its efficiency? We've talked about efficiency before. What unit of efficiency have we discussed for the heart; cardiac output. For the lungs, it was minute volume. In this context, it's called "GFR", "glomerular filtration rate". And it's expressed in -- well it's expressed in liters per day; in liters per day. And I remember when I first read this in a textbook they said the normal healthy GFR is 180 liters a day. And I was struck by that. I thought it was a misprint because that means what, 180 liters go through the kidneys, what, every day? That just didn't compute because certainly, you don't urinate 180 liters. But it turned out to be correct. It's just a testimony to how much is filtered, but yet at the same time, how much is reabsorbed. So it's an astounding number. But returning to the concept, GFR is really a function of many things. First of all, MAP. What's "MAP", "mean arteriole pressure". And it's a simple relationship. If MAP is low for some reason, what would that do to glomerular capillary pressure? That would lower it. What would that do to net filtration pressure? Lower it. What would that do to GFR? Lower it. On the other hand, if MAP is high, what would that do to glomerular capillary pressure? And therefore, net filtration pressure, therefore, urine output would soar. So in short, if you have low blood pressure, urine output will suffer, or decline. And if you have high blood pressure, you're going to be pushing more fluid into and through the glomerulus, and that will tend to raise urine output. And this is certainly within your experience. So let's just put into everyday examples; in fact, something we'll do next week in lab. What if you drank a liter of water right now? What would that do to your plasma volume? What would that do to MAP? And what would that do to GFR and your

urine output?

>> Increases.

>> Steve Langjahr: It would raise both, right? Have you ever done that, drank a lot of water and notice you have to go to the bathroom? I mean, it's kind of intuitive, but it's strictly a function of raising MAP. But MAP, even though it has this influence, is not usually something that changes or, even when it does, it's not mainly designed to change. That is, it doesn't have the primary influence on GFR. What does is this afferent arteriole diameter; this guy right here. Think about it. If this vessel is widened, would that move more blood into the glomerulus? Would that raise the pressure there? And would that then filter more stuff, and would that translate to more urine output? Yes. So simply put, anything that enlarges or dilates the afferent arteriole will raise glomerular capillary pressure, and therefore, raise urine output, UO. So that leads us to the next question, what exactly could do that? What factors will change the afferent arteriole diameter? First of all, as you know, arterioles are innervated by -- not parasympathetic, but just sympathetic. So sympathetic action here is already known to you. Remember, we're talking about the kidneys. And what sort of adrenergic receptors do renal vessels have?

>> Alpha?

>> Steve Langjahr: Alpha. And how are they going to respond to an increase in sympathetic action? Well, basically, they're going to vasoconstrict, right? And that will reduce glomerular capillary pressure. And that will reduce GFR. And that will reduce, what, what should you add or conclude -- anytime you raise GFR, what will that do UO? What's UO?

[Inaudible Comment]

Steve Langjahr: Urinary output. So if you reduce GFR, then you'll reduce urine output. And what's the opposite. Well, parasympathetic don't play this game because there are not parasympathetic receptors here. But if you decrease sympathetic action, that will tend to bring about some level of vasodilation. That will increase glomerular capillary pressure, that will increase GFR, and do what to UO?

>> Increase?

>> Steve Langjahr: Increase urine output. So these are the normal sympathetic influences on GFR, and therefore, urine output.

[Inaudible Comment]

Secondarily, anything that would constrict the afferent arteriole would, as we've already said, reduce GFR. And one of those that you already know and expect would be epinephrine. Does epinephrine have action on arterioles? Yes. What is epinephrine?

>> Hormone?

>> Steve Langjahr: Hormone from the adrenal medulla. What's it going to do? If we vasoconstrict, it's going to reduce GFR, therefore, reduce urine output. Then there's a compound that you've yet to hear, but we're introducing it tonight. It's called "renin". Renin is a locally-acting -- it's an enzyme, actually, secreted by cells of the juxtaglomerular complex, which is found within the kidneys specifically already labeled, actually, in the illustration that you have. For now, let's just accept the fact that it, too, is a vaso what?

[Inaudible Comment]

And what would that do to urine output? What would that do to GFR, constrict, decrease GFR, and therefore, decrease UO. What's UO?

>> Urine output.

>> Steve Langjahr: Urine output. What about a vasodilator? Wouldn't that have the opposite effect? A vasodilator would increase GFR, therefore, increase urine output. And some, but not all, diuretics work in this way. A familiar diuretic that you know by name is caffeine. I know you don't take caffeine as a diuretic, but in your experience, does caffeine intake affect urine output? Yes. How does it work? Caffeine vasodilates, vasodilates the afferent arteriole, therefore increases GFR, therefore increases urine output. So some diuretics, caffeine, for example, have a vasodilating action on the afferent arteriole. So quick look back. We've just talked about -- excuse me, glomerular filtration. We described three pressures that control and determine net filtration pressure. But basically, what controls filtration rate is the diameter of the afferent arteriole, which can either be constricted or dilated by drugs or the sympathetic nervous system.

[Silence]

Let's build a case for -- let's define now tubular reabsorption. We've already kind of made that case. Earlier, we said on a daily basis, how much water is filtered by your nephrons. Whoa, a hundred and what?

[Inaudible Comment]

A hundred eighty liters. How much of that actually enters the toilet? Hmm, 1.8 liters on a good day. And so what does that mean? That means 99% of this water was somehow, "R" word, reabsorbed. Another easy-to-understand example is glucose. Is there glucose in the blood? Yes. Is glucose filtered? Yes; 180 what, grams everyday. How much glucose ends up in the toilet?

[Inaudible Comment]

None. So how much of that glucose got returned; 100%. Again, this is in a healthy individual. So tubular reabsorption powerfully illustrated in those two cases. What about sodium, is there sodium in the blood? Yes. Is it filtered? Yes. Is it excreted? Yes. But still, what, 99.5% of the sodium in plasma is returned normally on a given day. And finally, something that you would expect is surplus, or otherwise toxic, urea. Urea is a nitrogenous compound derived from the breakdown of amino acids. Is it found in the blood? Yes. Is it filtered? Yes. But is some of that also reabsorbed? Yes; only, what, only 44 is reabsorbed. That means what, 56 is excreted; 56%. So these are four examples which testify to the importance, or at least the magnitude of tubular reabsorption. So now the question is, "How is tubular reabsorption accomplished?" There's really two ways, active or passive. Active transport involves carrier molecules, which move a given molecule, not down, but what, up a concentration gradient. So what are some of the molecules which are reabsorbed by active transport in the kidneys; first, glucose, amino acids, sodium, potassium, what's this, calcium, and this one is bicarbonate. And also water, soluble vitamins. They each have their own transport mechanism, which moves them not down, but what, up a concentration gradient. This reminds me of the work we did early in the semester when we evaluated the level of cell respiration for various tissues. Remember that? And what two organs were one and two, that is, the highest consumers of ATP? It was the liver and the kidney. And why is the kidney so ATP hungry? Well, it operates massive examples of active transport. And so, as we've already said, is there any glucose normally found in the urine. No; it's 100% reabsorbed thanks to what, active transport. Now, what do we know about active transport? Again, thinking back, active transport is an example of carrier-mediated transport. It demonstrates specificity; remember that idea? So does the carrier, which moves glucose, also move amino acids? No. There's a dedicated carrier for each of these that are on the list. And we also said that carrier-mediated transport was subject to a limitation, the "S" word, remember that?

>> Yes.

>> Steve Langjahr: Saturation. And so the rate, the ability to actively transport these things is ultimately limited by the number of available carriers. Now, why does this matter? The limit, the rate-limiting dependency on carrier molecules is defined as and known as "transport maximum". So here's the scenario. You just had lunch, and your lunch was -- well let's say, a candy bar and a liter of Coke. What happens to your blood sugar?

>> Spikes?

>> Steve Langjahr: And is more glucose going to be filtered? Yes. Will glucose be reabsorbed by active transport? The answer is yes. But can all of that glucose by returned knowing that that process is limited by the what, number of carriers. And when that limit is exceeded, when the carriers are "S" word, saturated, now what's going to happen? Will you have glucose in the urine now? Yes; because glucose has overwhelmed the ability to return that glucose. And never mind the candy bar and Coke analogy, are there people with high blood sugars due to an insulin deficiency? And do they then have sugar in their urine, which is a reflection of this concept? Yes. So this is just an example of how this ability to return a molecule can be limited by the number of available carriers.

[Silence]

It's also influenced by -- that is, reabsorption can be controlled by certain hormones, which is a vague statement, and what, some drugs. I know that's just a general remark, but simply put, if we interfere with active transport by various hormones or drugs, would that decrease the rate of reabsorption; yes. Would that increase the excretion; yes. So it turns out that controlling active transport is a very precise and specific way of regulating the excretion or the conservation of many of the things on this list.

[Silence]

We'll come back to that idea before we're done tonight. But thinking just, again, in general terms, what's the opposite of active transport?

>> Passive?

>> Steve Langjahr: Passive. What's the difference? Passive doesn't involve or require the use of a TP. And usually, it occurs not up, but --

>> Down.

>> Steve Langjahr: Down a concentration gradient. Best example here is water. Water is passively transported always from a high water to a low water concentration. And the name of that process you know is "osmosis". So we make this statement, which in fact is what we've already said occurs in the intestine. Think back to last week's look at the large intestine. What gets reabsorbed in the colon; water. By what means; osmosis. Why is most of the water being absorbed at that point and not earlier on? What was missing earlier on is that there wasn't a sufficiently-high water concentration. So we said then that water follows the return of various solutes. And so it does here too. With that said, let's go back to the earlier remark. In diabetes, is there sugar in the urine? Yes. And would that sugar in the urine inhibit the osmotic return of water? Yes. So diabetics not only have sugar in their urine, they have a lot of what, water in their urine. Because water can only be reabsorbed after the active reabsorption of other solutes, including, for example, glucose. And whether or not water is reabsorbed is also fundamentally dependent on the permeability of this piece of the nephron. This piece of the nephron is called the "collecting ducts". Normally, it's permeable to water, therefore water does leave, that is, is reabsorbed. But this permeability is subject to change. And when the permeability is tighter, or less, then there will be correspondingly less water reabsorbed. So we're going to find out that the absorption of water is not just dependent on osmosis, but also the permeability of the collecting ducts, which it turns out is influenced by hormones, one of which we'll get to Wednesday. And then aside from osmosis, there is the case of simple diffusion. And that includes molecules such as urea and others, which tend to follow, what?

>> Water?

>> Steve Langjahr: Water reabsorption. That's easy enough to memorize, but what does that mean? Let's use dots. Let's say these dots represent urea, okay? As we move through the nephron, is urea going to be reabsorbed? Yes. And so as we get over here, will there be less urea? Yes; because much of it has been what, reabsorbed. What then can happen is that now water will be reabsorbed. And that does what to the urea concentration now that water's left?

[Knocking Sounds]

Now its concentration is back up. And that would favor the reabsorption of even more what, urea. So simply put, if water doesn't get reabsorbed, then the urea concentration does not increase. That would compromise or lower the ability of urea to be returned, hence the expression, what's it say? Urea is reabsorbed following water reabsorption. So if water reabsorption is less, so then will urea reabsorption.

[Silence]

Finally, there's tubular secretion. Let's try to be clear on what that even means; and maybe we should back up. This process here that occurs in the nephron at the very beginning pushes things into Bowman's capsule. That was called what?

>> Filtration.

>> Steve Langjahr: Filtration. What do we call when things leave the nephron and return to the blood?

>> Reabsorption.

>> Steve Langjahr: Reabsorption. What do we call it when things are taken out of the blood and put directly into the nephron? That's secretion. What are some examples of this process and by what means does secretion occur? First, as you'd expect, active transport can be involved. And this is especially true for H plus, hydrogen ions, and also K plus, potassium. These are actively transported. That means, not down, but up a concentration gradient, which tends to raise their concentration in the urine; certainly necessary at times. Does the body have an excess of hydrogen ions that would benefit from the active tubular secretion of it? And the same could be said for potassium. So this helps to control the loss of at least these two commodities, hydrogen ions and potassium ions. Also some foreign chemicals, for instance, drugs, in this case, antibiotics and penicillin, and certain waste products, creatinine, are actively transported. Therefore, they appear at higher-than-expected levels in the final urine. What is the other process aside from active transport? It must be --

>> Passive.

>> Steve Langjahr: Passive. And this applies to molecules, such as ammonia, NH3, always moving down a concentration gradient. That means from a high concentration in the blood to a lower concentration in the filtrate, or in the nephron. So before we press ahead, let's just summarize real quick. The process of making urine is a three-step, or three-stage process. First, the "F" word, what, glomerular filtration. The return of solutes and or the return of water, that's called "tubular reabsorption". And the deliberate movement of molecules from the blood into the nephron, that, finally, was called "tubular secretion". So to say it again, filtration adds things to the urine, reabsorption takes things out of the urine, secretion adds them back in. So the composition of the urine at any given time is a function of those three processes. In the time we have left tonight, we want to look at what regulates the reabsorption; that means, the conservation or elimination of electrolytes. And the electrolytes that the body monitors, or otherwise looks carefully at, are classified as cations or anions. And cations are those that have what charge?

>> Positive.

>> Steve Langjahr: Positive. Anions have a negative charge. The most important -- the most abundant cation in the plasma is sodium. Is sodium an ion that can be filtered? Yes. Is it capable of being reabsorbed by one means or another? Yes. Can it be secreted? Apparently not. So the only two ways to control sodium is to adjust filtration, and/or adjusting TR. What's that, tubular reabsorption. When it comes to potassium, is potassium found in the blood? Yes. Can it be filtered? Yes. Can it be reabsorbed by one means or another? Yes. Can it also be secreted? Yes. So three ways the kidney might influence the concentration of this electrolyte. Chloride, found in the blood? Yes. Small enough to be filtered? Yes. And is also reabsorbed to one degree or another by TR, what's that, tubular reabsorption. And the same can be said for bicarbonate. So these are just facts. What we want to do now is talk about how each of these potential influences can bring about a change in the concentration of these electrolytes in the urine. And it turns out that sodium and potassium are somewhat linked. That is, what happens to one influences the others in ways that we're about to

mention. So starting over. Sodium can be adjusted by changing what?

[Inaudible Comment]

Filtration and also changing tubular reabsorption. What influences filtration rate? Well, that goes back to a previous part of this lecture. Filtration rate is a function of changing the diameter of the afferent arteriole. And if you widen this up, will that filter more? And would that lead to the loss of more? Yes. It's very much like what you might do at a sink. Imagine this is a sink. I open the faucet. Does water spill into the basin? Yes. If I close the faucet, is there less? Yes. Is there sodium in that water? Sure. So when I increased the water flow, will we be losing sodium, too? Yes. But is that a very precise way of controlling sodium? No; because changing the flow of water changes the loss of everything in the water. So what I'm saying is yes increasing or decreasing the filtration rate will influence the loss or conservation of sodium, but it's not a very precise or specific way to get a handle on that. So here's what I mean. If anything raises the GFR, will that move fluid through here faster? Yes. And that will allow less time for what, less opportunity to reabsorb the sodium. Will the urine, therefore, have more sodium anytime the GFR is up? Yes. And is the opposite true? That is, will low GFR slow the flow of urine, and will that allow more time for reabsorption? And if so, what does that do? More ion reabsorption opportunity means less ion excretion, which otherwise means conservation. So I know this is a lot of information, but let's just try to simplify it. If you raise GFR, will that move stuff through here quicker? What will that do to the ability to reabsorb? If things are moving through faster, there's less time for, what's the word, reabsorption. Therefore, there'll be more ion excretion, which is equivalent to saying sodium would be lost. And the opposite it true, if you slow down GFR, there's more time for reabsorption, therefore there will be less ion excretion, which is, of course, going to increase conservation. So as true as this is, it's not very specific, because changes in GFR are just that, changes in GFR, and don't single out any particular solute that might be in the filtrate. So what is the other mechanism? Let's go back. Sodium can be adjusted by changing what, the GF, glomerular filtration, or adjusting the what?

[Inaudible Comment]

Tubular reabsorption. And how is sodium reabsorbed. Back a page or two, tubular reabsorption of sodium is only by active transport. So is that amenable to specific adjustment? Can we control just sodium reabsorption? The answer is yes. And it turns out that those carriers and that mechanism are controlled by hormones, too, which we'll care about. And the first one is abbreviated "ANP", which is an acronym for what, "atrial natriuretic peptide", which is actually a hormone produced from a strange source, produced from what, the heart. But like any hormone, it goes into the blood, and in this case has an effect on the kidney. What exactly does it do there? ANP decreases what, active sodium reabsorption. What does that mean? If we block reabsorption, is that going to increase or decrease excretion? We block reabsorption, therefore, more sodium will remain. And that will do what to excretion, increase it. So it leads to more sodium loss, or excretion. This hormone, you would guess, and you'd be right, basically responds to excessively high levels of sodium. And you can read more about this in your textbook. The other hormone, which is more familiar, more important, in fact, comes from the adrenal cortex. It's called "aldosterone". It's a steroid, and its action is to increase active sodium reabsorption. It actually ramps up the active transport of sodium. What does that do? Clearly, it's the opposite of this. So if we increase sodium reabsorption, then that's going to mean what, less sodium excretion, which is also known as simply, "conservation". With that said, certainly as an example, we can see the importance of aldosterone. Let's just step out of context for a minute. What if your adrenal cortex could not, or did not, produce enough aldosterone? What wouldn't happen? Well, sodium reabsorption would suffer, and there would be great loss of sodium. And could that be lethal by losing lots of sodium out the kidney? Yes. So clearly, this hormone, as well as ANP, dictate and control the amount of sodium which is either conserved, or lost, in a given 24-hour period. And interestingly, aldosterone not only responds to and affects sodium, it at the same time increases active potassium, what, secretion. So that takes a moment to process, because this hormone leads to sodium, what, conservation, but would lead to potassium loss. And that is logical because we know that these are linked to receptor potentials; that is, resting potentials and so forth. So the balance of these electrolytes and their connectivity here makes some sense. But still, we haven't answered -- we haven't even asked the question, "When and how is aldosterone released?" So here's our final topic for tonight. And it's called the "renin-angiotensin mechanism", which summarizes the factors that control the release of aldosterone. The control of aldosterone clearly is important in sodium and potassium homeostasis. So let's talk about a scenario to illustrate the steps or changes that occur. Let's take -- lets begin right here with sodium loss. What would cause there to be a loss of sodium from the body?

[Silence]

Well, there could be many things. Could diarrhea do that? Could sweating profusely do that? So never mind the cause, anything which would lead to a sodium loss has the following impact. When there's less sodium in the blood due to what, sodium loss, then that's going to obviously translate to low intra, what, intratubular sodium. That means sodium in here is going to be, what, low, okay? And that will actually stimulate cells in the vicinity, which are called the "JG cells", the "juxtaglomerular cells". They respond to, what, apparently, low intratubular sodium. These cells in the kidney produce this enzyme called "renin", R E N I N, which then enters the blood, and converts an existing compound there called "angiotensinogen", to another molecule called "angiotensin I", Roman Numeral I. Backing up, where does angiotensinogen come from, the liver. And by itself it has no effect whatsoever. That is, this is an inert compound. But in the presence of this enzyme, what, renin, it's converted to angiotensin I. Okay so far? Incidentally, what does "angiotensin" as a word even mean? What does the prefix "angio" mean, "artery". "Tensin" means "to press, or contract". So "angiotensin" is a word implying that this compound constricts arteries, or at least arterioles. Actually, though, angiotensin I by itself doesn't do much of anything. But it is converted immediately on the spot from an available and preexisting enzyme called "ACE", which everybody calls "ace" but it stands for "Angiotensin Converting Enzyme". So what is this?

[Silence]

Angiotensin converting enzyme converts angiotensin I into angiotensin II. Okay? Now things start to happen, because angiotensin I has two effects. First, it targets and stimulates what, the adrenal cortex, which as we just said, is the source of this hormone called "aldosterone". Aldosterone, in turn, targets the kidneys, and causes, as we've already said, an improvement in sodium reabsorption, and therefore, a conservation of sodium, meaning a decrease in sodium, what, excretion. At the same time, aldosterone improves potassium secretion, which leads to a greater potassium loss, that is, a greater potassium excretion. So we're not done with this, but let's at least look at the big picture. What was the stimulus which triggered these chain of events, sodium loss. Did the net result in the end help reverse that? Did we improve sodium conservation, and therefore minimize its loss? So does this help fix or reverse that; yes. At the same time that we're conserving sodium, we're also eliminating potassium, one of the consequences of this hormone. Moving backwards along this mechanism, we see the player here, angiotensin II, which we said stimulates the adrenal cortex. It also causes peripheral what, vasoconstriction. Now, there must be some sense, some logic, some benefit in all this. So let's look at more of what's up on the screen. Low intratubular sodium can be due to any loss of sodium. But it can also be the result of lower GFR. That is, if we decrease filtration, we will in turn decrease the concentration of sodium in the filtrate. And that can be due to what, low BP, which could be due to low plasma volume. And so what would cause low plasma volume? Well, it could be dehydration, it could be hemorrhage. And does this mechanism help that? Remember, when we improve sodium reabsorption, we're also going to improve chloride and water reabsorption. So will water be conserved as a result of this as well? Yes. And that would work against, or at least help correct this initial problem if it was a contributing factor.

[Silence]

Back to this, ACE. What was that?

[Inaudible Comment]

Angiotensin-converting enzyme. It's found normally in the blood. So it's not released in any different quantity here. And so its job is to convert angiotensin I to angiotensin II. If you've heard of that compound, ACE, it's probably because friends or family are taking drugs, which are ACE inhibitors. So what would a drug which is an ACE inhibitor do? If we block this enzyme, then angiotensin I would not be converted to angiotensin II. Therefore, aldosterone would not be released. Therefore, sodium would not be reabsorbed. Therefore, water would not follow. And so what "D" word would seem to describe an ACE inhibitor? "D" word

[Inaudible Comments]

Hmm. What do you call a drug that causes you to pee more?

>> A diuretic.

>> Steve Langjahr: A diuretic. Would an ACE inhibitor be a diuretic? Let's follow this through. Block this enzyme. This won't be made, this won't be stimulated, this hormone won't be released, this won't happen, this won't be reabsorbed. Therefore, is water loss the net result?

[Silence]

And with all that said, who would need or benefit from an ACE inhibitor? Remember, ACE not only converts angiotensin I to angiotensin II. Angiotensin II also is a peripheral, what, vasoconstrictor, which by itself, would do what to blood pressure?

[Inaudible Comment]

So people who are taking an ACE inhibitor are basically helping to correct what problem that they face or otherwise have, high blood pressure, hypertension. And how does an ACE inhibitor help high blood pressure. Well, it does it two ways. It gets rid of sodium, it gets rid of water, and also prevents peripheral vasoconstriction. That's three ways, actually. So ACE inhibitors are useful, and indeed the most common medication for people with what condition, high blood pressure, also known as "hypertension"; hypertension. But this is, of course, the -- what is it, the renin angiotensin mechanism. Can it work in reverse? What does that mean? This basically is kicked off by any loss of what?

>> Sodium.

>> Steve Langjahr: But what if there was a gain in sodium? Let's just follow that through. You just ate a bag of pretzels. Gain of sodium? Therefore, there wouldn't be low intratubular sodium, there would be high intratubular sodium. Therefore, the JG cells would not release, what, renin. Therefore, angiotensinogen would not be converted to angiotensin I. Therefore, no angiotensin II. Therefore, no stimulation of the adrenal cortex. Therefore, no aldosterone. Therefore, no what, sodium reabsorption. Therefore, high sodium what, excretion. Would that be logical, appropriate and welcome when you have high sodium intake; sure. So this mechanism, which protects against, or otherwise helps correct low intratubular sodium, also shuts down and helps to conserve sodium -- or I should say leads to the loss of sodium when there's too much sodium. Not tomorrow, but a week from tomorrow, we're going to be doing an investigation of this mechanism and others. And I'd just mentioned pretzels kind of flippantly. But actually, we're going to have two groups. One group's going to consume a lot of water. And the other group's going to consume just pretzels, which are known to be high in what, sodium. And then we're going to monitor their urine output, that means their volume and their sodium in their urine, over the next two and the half hours. And just to give you a preview, if you drink -- I should say if you eat a lot of sodium, would this mechanism be shut down and would your urine therefore contain a lot of sodium; yes. So even though we're pointing to this hormone, what is it, aldosterone, it's part of a grander mechanism, and its level or lack of it will effectively control what? It'll effectively control sodium, chloride, and water, and also at the same time, potassium. One final remark, notice that high plasma potassium by itself stimulates the adrenal cortex directly. So it's not part of the renin angiotensin mechanism. What would cause high plasma potassium? Well, there are many things, but certainly, you probably know that bananas as an example have a lot of potassium. So if you ate a bushel of bananas, would that raise plasma potassium; yes. Would that stimulate the adrenal cortex to release more of this hormone, and would there be more potassium loss as result; yes. So just to note as we conclude that potassium factors into this, but it's not part of the what, not part of the renin angiotensin mechanism. That, by itself, controls just the release of renin and the activation of angiotensin. Quite a lot tonight. Probably overwhelming, especially since your mind is focused on tomorrow, as it should be. So there will be time to catch up and review this before going on. So I'll be by my phone all night.

[Background Sounds]

Operators are standing by.

[Background Sounds]