>> Human Physiology Steve Langjahr: Alright, in physiology. I guess this is lecture 5. We're going to talking about the complete story; we've given you up to now only the partial story of carbohydrate metabolism. In fact, we're going to expand and consider briefly how fats and proteins might also be involved in metabolic survival, metabolic reactions. So, here we go. We start with a reminder that the most productive form of catabolism utilized carbohydrates, because carbohydrates are the most abundant, the most available and the easiest to derive energy from. And speaking of carbohydrates, what's the most plentiful and therefore most useful of the carbohydrates?

>> Glucose.

>> Human Physiology Steve Langjahr: Glucose, C6H12O6. So, we've mentioned this sort of sweeping formula here which is a summary of what's going on. We know that for every glucose molecule we produce 6 carbon dioxide; 12 water molecules which we'll describe in detail tonight, and we also give off a lot of heat, wasted that is cast back into the environment. To do this, of course, oxygens involved and waters involved, but the real payoff, the benefit, the importance, the purpose is to produce this energy currency called ATP. And the number that we gave you, a maximum of 38 ATPs and you read other books or videos or whatever, that number seems to be hovering less than that, 36 seems to be the agreed upon number, but okay. We're not too concerned with that. Rather, tonight we want to at least explain how these ATPs are made and we already know there are two methods of phosphorylating ADP, right? One was called?

>> Substrate.

>> Human Physiology Steve Langjahr: Substrate. The other more productive was called?

>> Oxidative.

>> Human Physiology Steve Langjahr: Oxidative, so we're going to weave those facts into tonight's conversation. So, to begin then this is the grand scheme of things. We said that there are 19 reactions here and we're going to take you by the hand through each of those more or less. So, we're going to start with a scenario which is not very common, but yet occasionally resorted to and this is a situation where there's a shortage of oxygen. Even in a healthy person, are there moments, are there periods where you're selves are short of oxygen? The most common scenario is extreme or strenuous "E" word.

>> Exercise.

>> Human Physiology Steve Langjahr: Exercise. And that doesn't even consider other things like altitude or diseases of the lungs and so forth. So, for most of us that are healthy, we sometimes drift into anaerobic scenes, because of the inability to deliver oxygen down to the cellular level. The word "anaerobic" means literally without air; without oxygen. And so let's begin with that unlikely, but nevertheless, possible situation. The breakdown of glucose in the

absence of oxygen is called “glycolysis”, literally two words; glyco-lysis which means breaking glucose and the process occurs only when there’s an absence of oxygen. So, it’s not like the body decides, it doesn’t say “Well, I don’t feel like oxidative today. Let’s just go anaerobic.” No, it’s always aerobic unless there’s a shortage of oxygen. This occurs then in the absence or the relative absence of oxygen. It does not require any of the chemistry of the mitochondria. It certainly doesn’t involve the ETC; what’s that?

>> Electron transport chain.

>> Human Physiology Steve Langjahr: Electron transport chain, and we know that because it doesn’t involve the electron transport chain, it can only produce ATP by this meager method called “substrate phosphorylation.” So, these are facts associated with anaerobic glycolysis. It is important, not in the big picture, but in those rare sort of in a bind situation; in a bind meaning yourselves are temporarily running low on oxygen. So, it provides a backup, a kind of reserve at least a better than nothing source of ATP. Now as we go down these reactions which are basically unfolded on the page that you’re about to turn to, we’re going to essentially develop a kind of scoreboard here; a kind of tally and this will give us a numeric impression of where these ATPs are coming from and, of course, the grand total and some of the products along the way. So, we’ll call it our ATP Tally. And we’re going to begin, of course, at the beginning. We said that we start with this molecule of glucose which incidentally has how many carbons?

>> Six.

>> Human Physiology Steve Langjahr: Six. Incidentally, chemists like to number carbons just for fun; they’re a funny group. So, this is C1, this is C2, C3, C4, C5 and there’s C6. So, just a reminder, glucose is a 6 carbon monosaccharide. It comes from our diet and it can also come from the liver when we breakdown a polysaccharide; a polysaccharide is stored there known to you as?

>> Glycogen.

>> Human Physiology Steve Langjahr: Glycogen. So, we really don’t care where this glucose comes from, at least not in this discussion. We just want to begin with how many glucose molecules?

>> Six.

>> One.

>> Human Physiology Steve Langjahr: How many glucose molecules?

>> One.

>> Human Physiology Steve Langjahr: One. And this molecule has 6 carbons. The first reaction is shown here, and the product, the intermediate product is glucose 6 phosphate. That’s the name. And if you hear that description, glucose 6 phosphate you might think, oh well, glucose has been treated to 6

phosphates, but no, a single phosphate has been transferred from ATP onto the 6th carbon and where's the 6th carbon? Right there. So, at least in terms of what we're describing, this glucose molecule has now been changed and a phosphate is added at that location. So, it's no longer glucose. It's called what?

>> Glucose 6.

>> Human Physiology Steve Langjahr: Glucose 6 phosphate. Where did this phosphate come from? Well, actually it came off an existing A what? A?

>> TP.

>> Human Physiology Steve Langjahr: TP. And so if we are tallying up ATPs have we produced any so far?

>> No.

>> Human Physiology Steve Langjahr: No. Have we used any?

>> Yes.

>> Human Physiology Steve Langjahr: Yes. So, our scoreboard here shows a negative 1. Now this might seem awful or odd, but you've heard the expression I'm sure, you have to sometimes spend money to what?

>> Make money.

>> Human Physiology Steve Langjahr: Make money. So, this is an investment and we'll get it back, but we had to add this phosphate to this 6th carbon and basically it was donated or transferred from the ATP to this 6th carbon on the glucose molecule. All good? First reaction then, glucose converted to glucose 6 phosphate. The next reaction is basically adding yet another phosphate to the G-6-P, and also that phosphate comes from an available ATP. And that second phosphate is added here to the first carbon and now this molecule is temporarily equipped with not 1 phosphate, but 2. That molecule is shown right here and we have not given it a name, because as quickly as it forms, it immediately cleaves; that means it divides in half right along this axis, so now instead of 1 6th carbon molecule, we've generated 2 what?

>> Three.

>> Human Physiology Steve Langjahr: Three carbon molecules. Each of which has a phosphate, and that's the implication of this symbol we have 1, 2, 3 carbons and the yellow circle there a phosphate; the name of these intermediates, glyceraldehyde 3 phosphate. One again, that doesn't mean there are 3 phosphates. It just means the phosphate is on the 3rd carbon and notice that we have 2 G-3-Ps. To get to this point, we had to expend, we had to use yet another ATP. So, as we reach this level, have we generated any ATP?

>> No.

>> Human Physiology Steve Langjahr: No. Have we used some?

>> Yes.

>> Human Physiology Steve Langjahr: How many?

>> Two.

>> Human Physiology Steve Langjahr: Two. So, our tally shows at this point 2, a negative 2 actually and here we are at this intermediate G-3-P. In case we lost you we'll go back. We started with a 6 carbon molecule. We tacked on a phosphate. Where'd that come from?

>> ATP.

>> Human Physiology Steve Langjahr: ATP. Then we tacked on another phosphate, again donated by yet another ATP. Then we split this 3 carbon molecule into 2, excuse me, this 6 carbon molecule into 2, 3 carbon molecules and the name of each of these is glyceraldehyde 3 phosphate. This then is the intermediate where we're at and the next reaction is interesting because it happens, of course, twice in so far as we have 2 of these G3P and this reaction adds yet another phosphate to this intermediate. And notice that for the first time this coenzyme is involved, one that we've known and discussed; what is it NA?

>> D.

>> Human Physiology Steve Langjahr: D? And remember NAD is a coenzyme that works with what enzymes?

>> D.

>> Human Physiology Steve Langjahr: D?

>> Hydrogen.

>> Human Physiology Steve Langjahr: Hydrogenase. So, this is the first of many D hydrogenation reactions. So, if you're following this, notice the intermediate is called diphosphoglycerate and notice of course, we have 2 of those molecules. So tell me, how is diphosphoglycerate different from G-3-P? Two ways that it's different. Well, it's got 1 more what?

>> Phosphate.

>> Human Physiology Steve Langjahr: Phosphate. And it's got 2 less what?

>> Hydrogen.

>> Human Physiology Steve Langjahr: Two less hydrogens. So that's it. Where'd the hydrogens come from? They came off the glyceraldehyde 3 phosphate. What picked them up? NAD. And so NAD is said to be "R" word; reduced. Now, what do we know is the hoped for destination for these hydrogen atoms which have been picked up temporarily by the coenzyme NAD? What's the hoped for destination?

>> Mitochondria.

>> Human Physiology Steve Langjahr: Mitochondria. Because then those electrons can be carried through the ETC, but that's off the table here. Why are the mitochondria off the table in this scenario we're discussing?

>> Because of a loss.

>> Human Physiology Steve Langjahr: This is anaerobic and although there might be mitochondria there is nothing at the end of the ETC, there's no?

>> Oxygen.

>> Human Physiology Steve Langjahr: Oxygen. So, these hydrogens apparently have nowhere to go. They're kind of orphaned here for a while. Don't panic we'll find a home. But, as we review this reaction, to repeat, how is this intermediate diphosphoglycerate different from G-3-P? Two ways. It has what?

[Inaudible Response]

One more phosphate and 2 less?

>> Hydrogens.

>> Human Physiology Steve Langjahr: Hydrogens. But where'd that phosphate come from? We show it just as Pi, inorganic phosphate. So, strangely, but yet importantly, it doesn't come from ATP as these others have. And so this reaction, to summarize, does it produce any ATP?

>> No.

>> Human Physiology Steve Langjahr: No. Does it use any ATP?

>> No.

>> Human Physiology Steve Langjahr: No, but nevertheless, we've added another phosphate to this carbon and the molecule as described is diphosphoglycerate; a phosphate at either end. So, what are we going to; what are we going to put at the scoreboard here? To repeat, did we use any ATP at this stage?

>> No.

>> Human Physiology Steve Langjahr: Nope. Did we produce any ATP?

>> No.

>> Human Physiology Steve Langjahr: Nope. So it's a big fat what?

>> Zero.

>> Human Physiology Steve Langjahr: Zero. We did generate hydrogen and remember, those hydrogens normally go to what organelle? But the mitochondria is not in business because there's no what?

>> Calcium.

>> Human Physiology Steve Langjahr: So, for the moment we have no place, that is, this reduced NAD is going to remain reduced. That means loaded with hydrogen. Alright, so what's next? The next reactions we'll skip rather quickly. Reaction 1, 2, 3, 4 we'll not give them names because they're unimportant. The next intermediate that we're going to call out by name is important and worthy

of knowing, it's called pyruvic acid. How many carbons in pyruvic acid? Hum, let's count them; 1, 2, 3. How many carbons were in diphosphoglycerate?

>> Three.

>> Human Physiology Steve Langjahr: One, 2, 3. So, we haven't changed the carbon number, but how many phosphates are found in pyruvic acid?

>> None.

>> Human Physiology Steve Langjahr: None. How many were found in diphosphoglycerate?

>> Two.

>> Human Physiology Steve Langjahr: Two. So, clearly in the reactions that are left undescribed here, those phosphates had to come off and they're not just cut loose in space, those phosphates were added to available A?

>> DP.

>> Human Physiology Steve Langjahr: DP to make available A?

>> TP.

>> Human Physiology Steve Langjahr: TP. And what do you call that when we take a phosphate group off a substrate and put it directly onto an ADP molecule?

>> Sub.

>> Human Physiology Steve Langjahr: Substrate phosphorylation. So, if we look at this reaction, which incidentally occurs twice, we see that an ATP is made and made, so as we rundown to this level, what are we're going to put in our tally; have we generated any ATPs?

>> Yes.

>> Human Physiology Steve Langjahr: Yes. How many? One?

>> Two.

>> Human Physiology Steve Langjahr: Two. So, bingo. Right now we're breaking even, right? And as we follow this reaction sequence down to pyruvic acid, we see that the reaction that leads to pyruvic acid takes that second phosphate off and adds it to an available A?

>> DP.

>> Human Physiology Steve Langjahr: DP to make a A?

>> TP.

>> Human Physiology Steve Langjahr: TP, yet another example of substrate phosphorylation. Why does it happen twice? Well, because we had as you

saw, created 2 molecules from 1 and so it happens twice. As we then enter our scoreboard, what number would be expected next?

>> Two.

>> Human Physiology Steve Langjahr: Another 2. And so we've reached this intermediate by the name of pyruvic acid. And as we'll soon see, pyruvic acid has 2 ways to go chemically speaking. It can be converted to acetic acid or it can be converted to lactic acid. As you'll soon see, it can't go to acetic acid, because that's going to require the coenzyme NAD. And you might say, well isn't there any NAD? Well, probably not, because all of the NAD is going to be "R" word.

>> Reduced.

>> Human Physiology Steve Langjahr: Reduced and therefore unavailable. The good news is that pyruvic acid can be converted to lactic acid, and notice that that doesn't require NAD, but rather will take these hydrogens from the reduced NAD, and therefore, regenerate or oxidize fresh NAD as shown. That's complicated, so let's backup. Lactic acid is shown, pyruvic acid is shown, you don't need to memorize, but just look at the formula; how is lactic acid different from pyruvic acid. It has 2 more what?

>> Hydrogens.

>> Human Physiology Steve Langjahr: Where'd it get those hydrogens?

>> The NAD.

>> Human Physiology Steve Langjahr: Those hydrogens right there had no home, remember that? Don't say that on the exam, but they couldn't go to the mitochondria, after all there's no?

>> Oxygen.

>> Human Physiology Steve Langjahr: Oxygen. If we add these hydrogens to pyruvic acid that makes what?

>> Lactic.

>> Human Physiology Steve Langjahr: Lactic acid. And we really don't care. We're not trying to make lactic acid, but what benefit is that reaction? What is the importance of converting pyruvic acid to lactic acid? Not that we make lactic acid, but that we oxidize this coenzyme and, therefore, return and make available.

>> NAD.

>> Human Physiology Steve Langjahr: NAD. That's the importance of that reaction. And so these reactions on the screen are the sum total of this process called glycolysis. What kind of glycolysis?

>> Anaerobic.

>> Human Physiology Steve Langjahr: Anaerobic. Because what isn't involved or otherwise available?

>> Oxygen.

>> Human Physiology Steve Langjahr: Oxygen. In summary then, how many ATPs are made in anaerobic glycolysis? You could say 4 are made, but what's the net, what's the net production? We made 4, but we invested 2, so the bottom line is 2 ATPs per glucose molecule. And the end product is not pyruvic acid, but rather a lactic acid, not just 1 but how many lactic acid molecules?

>> Two.

>> Human Physiology Steve Langjahr: Two. You say wait a minute, I don't see 2. Well, I'm just trying to simplify this. How many pyruvic acids did we have?

>> Two.

>> Human Physiology Steve Langjahr: Two, so it stands to reason, yes, there'll be 2 lactic acids. To summarize again, what's the importance of this reaction sequence is that produces at least some ATP, not a huge amount, and all of the ATP that is produced is produced not by oxidative, but by?

>> Substrate.

>> Human Physiology Steve Langjahr: Substrate phosphorylation. Do we have an end product? Yes, its name is? Lactic acid. Notice incidentally, that the production of lactic acid that is converting pyruvic acid to lactic acid is reversible. So, it possible to make lactic acid back into pyruvic acid?

>> Yes.

>> Human Physiology Steve Langjahr: The answer is yes, but to do that, we'd have to takeoff these hydrogens and that would require the availability of a coenzyme called what?

>> NAD.

>> Human Physiology Steve Langjahr: Which is probably going to be in short supply. I don't mean the NAD is in short supply, but remember it's very apt to be "R" word?

>> Reduced.

>> Human Physiology Steve Langjahr: Reduced and there's just not a plentiful supply until, until what becomes available? That story is completely changed when what becomes available?

>> Oxygen.

>> Human Physiology Steve Langjahr: Oxygen. But at least for now, there is no oxygen. So, can lactic acid be converted back to pyruvic acid?

>> No.

>> Human Physiology Steve Langjahr: No. Not now, because there's no what?

>> Oxygen.

>> Human Physiology Steve Langjahr: No oxygen. When and if oxygen is available, lactic acid can be converted back. And this is, of course, is interesting because to most people if they hear the word lactic acid, they think of something evil or poisonous or nasty, but actually it's just a stupid acid not much different from pyruvic acid so there's nothing really poisonous about it. In fact, if oxygen is available, it will be quickly converted from lactic acid back to what?

>> Pyruvic.

>> Human Physiology Steve Langjahr: Alright, so it's only a temporary but yet terminal product only when we have no what? What's the scenario again?

>> Oxygen.

>> Human Physiology Steve Langjahr: And the name of this is anaerobic "G" word?

>> Glycolysis.

>> Human Physiology Steve Langjahr: Glycolysis. Rare? Yeah, rare because rarely do we have this dire situation where there's no oxygen. But, at least it's backup and 2 is better than 1; 2 is better than?

>> Zero.

>> Human Physiology Steve Langjahr: Zero. Anaerobic glycolysis. Now let's start the story again with a more lovely scenario, that is the way you're operating right now. I don't see anybody in lactic acidosis at the moment. So, plentiful oxygen, the room seems to be fresh and wonderful. So, actually it turns out that the reactions we just stepped through are going to happen just as before, but they are going to be some notable improvements and notable progression in this process. Yes it's going to start with and involve the reactions of glycolysis, but it's going to press past pyruvic acid, and it's going into a famous circle of reactions known either as the citric acid cycle for reasons that will be clear, or in honor of Hans Krebs; aA German self-physiologist who won the Nobel Prize for this. That's K-r-e-b-s. I say that because sometimes on exams people spell it crab cycle which is, which has to do with crustaceans I think. Anyway, it's an insult to Hans, rest in peace. Alright, so here we go. This is glycolysis, but not anaerobic it's what?

>> Aerobic.

>> Human Physiology Steve Langjahr: Aerobic. So, a much rosier picture and much improved in terms of ATP. Obviously for these reactions to happen, oxygen is going to be necessary and presumed to be available. And the role of oxygen is as we've said, basically just the final hydrogen that is electron acceptor. It doesn't get involved in the reactions until the end of the ETC; what's that?

>> Electron transport chain.

>> Human Physiology Steve Langjahr: Electron transport chain. Naturally then, at least the reactions that are part of the citric acid cycle depend on oxygen and the cytochromes, and therefore, they occur mostly inside that organelle called the?

>> Mitochondria.

>> Human Physiology Steve Langjahr: Mitochondria. This is, of course, the paradox of the red blood cell, which I always like to refer to. What's the red blood cell loaded with?

>> Oxygen.

>> Human Physiology Steve Langjahr: Oxygen. But it has no "M" word; it has no what?

>> Mitochondria.

>> Human Physiology Steve Langjahr: So, can you use any of that oxygen?

>> No.

>> Human Physiology Steve Langjahr: No. So even though it's loaded with oxygen, it's obliged to operate by anaerobic glycolysis. And you say, oh poor red blood cell. Well, actually that's okay, because what the red blood cell does doesn't really demand that much oxygen so it gets by just fine, but I digress. So, here we are back with this sequence of events which essentially concludes in the mitochondria, and produces ATP obviously and most abundantly by oxidative phosphorylation, but still incorporates and gets some profit from what? Substrate phosphorylation. So, it's not just oxidative, but also some contribution from substrate phosphorylation. Needless to say, this is the most important day in, day out provider of ATP. And needless to say, without this you're dead. That is, very shortly anyway. So, let's start again right from the beginning and let's tally up ATPs just as we did before. So, let's begin with what molecule?

>> Glucose.

>> Human Physiology Steve Langjahr: Glucose. It can come from the food we eat. It can come from glycogen, that is the breakdown of this polysaccharide. To remind you, how many carbons here?

>> Six.

>> Human Physiology Steve Langjahr: Six. So, we're starting with 1 6 carbon molecule. The first reaction is no different than before. We're going to have to take a phosphate off a what?

>> ATP.

>> Human Physiology Steve Langjahr: Off and ATP and add it here to the 6th carbon and, therefore, create this intermediate, just as before, called glucose 6 phosphate. Okay great. Any ATP made?

>> No.

>> Human Physiology Steve Langjahr: Nope. Any ATP used?

>> One.

>> Human Physiology Steve Langjahr: Yes. So, negative 1 just as before. Then, just as before, we're going to add another phosphate to the first carbon of this intermediate called glucose 6 phosphate. And as before, that phosphate comes at the expense of what?

>> ATP.

>> Human Physiology Steve Langjahr: At the expense of ATP. So at least temporarily we have a 6 carbon molecule with 2 phosphates and so our scoreboard would show, once again, a negative 1 to reflect the use of ATP to get to this point. This 6 carbon molecule doesn't remain as such for long. It's split right down there and so instead of 1 6 carbon, we now have 2?

>> Three.

>> Human Physiology Steve Langjahr: Three carbons. Each with a single phosphate; each entitled G-3-P which stands for glyceraldehyde 3 phosphate just as before. Alright. When do things start to change? Well, the next reaction is just as before, that is it produces diphosphoglycerate and the extra phosphate comes not from ATP, remember Pi stands for?

>> Inorganic.

>> Human Physiology Steve Langjahr: Inorganic phosphate and that's added to this first carbon of these 3 carbon intermediates and so there's no loss, there's no expenditure of ATP. As before, this is a dehydrogenation reaction. How do we know it's a dehydrogenation reaction?

>> Because of NAD.

>> Human Physiology Steve Langjahr: NAD. Now the enzyme is not shown there, but at least you should mentally assume that the enzyme called dehydrogenase, actually it's called G-3-P dehydrogenase is there. What we're focusing on is rather the coenzyme, because it's picked up 2 what, from what? Picked up 2 hydrogens from the G-3-P, and therefore, produced this intermediate called diphosphoglycerate. But now the picture is very different, because previously we said the mitochondria was closed, but now it's available. What makes it available now? What's different?

>> Oxygen.

>> Human Physiology Steve Langjahr: We have oxygen. So, these hydrogens will be escorted to what organelle?

>> Mitochondria.

>> Human Physiology Steve Langjahr: And they'll be processed as electrons and protons shown at the bottom of the page you're probably looking at, and

therefore, for these 2 hydrogens, once they move through the ETC we can expect how many ATPs to be produced?

>> Three.

>> Human Physiology Steve Langjahr: Three. Let's make sure everybody's with me. These hydrogens are going to go into the "M" word?

>> Mitochondria.

>> Human Physiology Steve Langjahr: Mitochondria. They're going to be passed as electrons; they're going to go through the cytochrome system, otherwise known as the ETC. And from our work last Wednesday you know that if they come in, if they come in carried there by NAD, there's opportunity to produce 1, 2 and what?

>> Three.

>> Human Physiology Steve Langjahr: Three ATPs. Then what picks up these electrons ultimately at the end?

>> Oxygen.

>> Human Physiology Steve Langjahr: To make what?

>> Water.

>> Human Physiology Steve Langjahr: Water. Okay, great. So, back to this. Whereas before there was no ATP generated here, we know these hydrogens will be processed through the ETC and we can expect how many ATPs as a result? Right here.

>> Three.

>> Human Physiology Steve Langjahr: Three, and from that? Three, so 3 plus 3 is?

>> Six.

>> Human Physiology Steve Langjahr: Six. So, that's the number which is much better than the previous number; what was there before?

>> Zero.

>> Human Physiology Steve Langjahr: Zero. Six is better. And these have been made not by substrate phosphorylation, in fact, they haven't even been made here. They've been made inside the mito?

>> Chondria.

>> Human Physiology Steve Langjahr: Chondria, by the process of oxidative phosphorylation. But, we're going ahead and we're going to say we expect 3 here and we expect 3 here, so 3 plus 3 is?

>> Six.

>> Human Physiology Steve Langjahr: Six. Okay, great. The next reactions are the same as before and lead us down once again to pyruvic acid. Remember, the intermediate that we've left was diphosphoglycerate. How many phosphates on diphosphoglycerate?

>> Two.

>> Human Physiology Steve Langjahr: Two. How many phosphates on pyruvic acid?

>> None.

>> Human Physiology Steve Langjahr: None. So, obviously those 2 have been taken off 1 at a time and they've been added to available ADP to make what?

>> ATP.

>> Human Physiology Steve Langjahr: And what do you call it when you take phosphates off a substrate and put them directly onto ADP?

>> Substrate.

>> Human Physiology Steve Langjahr: Substrate phosphorylation. So, there's 1 times 2 is what? Two. There's 1 times 2 is? Two. And so as before, 2 and 2 leading us down to pyruvic acid, which as you can see has no phosphates and is a 3 carbon molecule. How many pyruvic acids have been made? Two, because it stemmed earlier from these intermediate G-3-P. Now what happened to pyruvic acid before? Pyruvic acid was converted to?

>> Lactic.

>> Human Physiology Steve Langjahr: Lactic acid. That's not going to happen now, and it's not because the cell doesn't want to or doesn't need to, it's nothing like that. It's just that now it has plenty of something it didn't have before, it has plenty of NA?

>> D.

>> Human Physiology Steve Langjahr: D, and therefore, the reaction to lactic acid would simply not occur. Instead, pyruvic acid would go straight away to the next intermediate which is called acetic acid and that's going to, of course, take us away from these reactions which are called aerobic glycolysis and essentially introduce us to this cycle which we said is called the citric acid cycle. So this, which is on the screen, is the end of glycolysis. What kind?

>> Aerobic.

>> Human Physiology Steve Langjahr: Aerobic. Is it an improvement over anaerobic?

>> Yes.

>> Human Physiology Steve Langjahr: Yes, because instead of, instead of just 2 we can do the math and see that more ATPs have been made. So, let's now

carry on from pyruvic acid and explain or go through the infamous citric acid cycle. Here we are back with pyruvic acid. How many did we generate from a single glucose molecule?

>> Two.

>> Human Physiology Steve Langjahr: Two. So, naturally we're showing 2 pyruvic acids. The next reaction produces acetic acid as promised. Acidic acid incidentally is known to you, it's simply vinegar and it has, well I'll ask you; how many carbons in acetic acid? You might say, how am I supposed to know? It's not even shown. But let's look, pyruvic acid undergoes, well 2 things, notice that NAD is involved and takes off 2 hydrogens from what?

>> Pyruvic acid.

>> Human Physiology Steve Langjahr: Pyruvic acid. And notice that CO2 has come off of this reaction. So, with that said, how is acetic acid different from pyruvic acid? Tell me 2 ways that acetic acid is different from pyruvic acid.

>> One less carbon.

>> Human Physiology Steve Langjahr: It has 1 less carbon.

>> Two less oxygen.

>> Human Physiology Steve Langjahr: Two less oxygen and also 2 less?

>> Hydrogen.

>> Human Physiology Steve Langjahr: Hydrogens. Okay. Now we don't much care about the carbon dioxide, that's just going to go away and end up in your breath, but we do care about these hydrogens. We keep our eyes on those hydrogens because right now they have been accepted by this coenzyme called NAD. And we know they're going to be escorted into this organelle called the?

>> Mitochondria.

>> Human Physiology Steve Langjahr: Mitochondria. In fact, all the reactions that were about to occur already are in the mitochondria because the enzymes that we're referring to are only there. So, it's not like these have to be taken to the mitochondria, these reactions occur and only occur in the mitochondria, but nevertheless, what happens to these hydrogens? To repeat, those hydrogens are going to be introduced to the electron transport chain and, therefore, there will be 1, 2, 3 opportunities to make what A?

>> TP.

>> Human Physiology Steve Langjahr: TP. So, how many would we calculate; that is, how many ATPs can we expect here and there? Three plus 3 is?

>> Six.

>> Human Physiology Steve Langjahr: Six. So, our tally is, well 6 more. And the name of this intermediate is acetic acid. How many carbons in acetic acid just to keep that mentally?

>> Two.

>> Human Physiology Steve Langjahr: Yeah, 2. How do we know it has 2? Pyruvic acid had 3.

>> We lost one.

>> Human Physiology Steve Langjahr: But we lost a carbon and, of course, and a couple of oxygens too. At this point, acetic acid picks up an available coenzyme which is simply called coenzyme A and we're not going to really make much about that; we're not going to make a big deal of it. We're not going to get into where it came from, but like many coenzymes, we said coenzymes are made from available water, soluble, vitamins and so on. So, let's assume coenzyme A is there and move on. The next reaction which is actually the gateway to the citric acid cycle, takes an intermediate product from the end of that cycle called oxaloacetic acid. You heard that word for the first time yesterday. It turns out that oxaloacetic acid has 4 carbons, just FYI, and acetic acid we've already said has how many?

>> Two.

>> Human Physiology Steve Langjahr: Two. So, if these react together, citric acid would have how many carbons if it makes any sense at all, 4 plus 2 is?

>> Six.

>> Human Physiology Steve Langjahr: Six. And notice that water doesn't come off this reaction, but actually is necessary, but other than that, is there anything remarkable? Does the production of citric acid by these reactants acetic acid and oxaloacetic acid; does that apparently produce any ATP?

>> No.

>> Human Physiology Steve Langjahr: No. Does it use any ATP? No. So, what would we enter in this location? Nothing. Basically it's, well a wash. But it does produce this molecule citric acid which should be known to you, if for no other reason, why is it called citric acid? It's found in citrus like lemons and oranges and limes, okay. How many carbons?

>> Six.

>> Human Physiology Steve Langjahr: Six. Now, the rest of the cycle is loaded with fancy compounds with complex names and if you want to know that, it's in your book. But, that's not our focus. Our focus is on hydrogens and on reactions that we said are so important namely dehydrogenation reactions. So, as it turns out, citric acid is converted to something you can find out what it's called, but we'll call it just A, and then A is converted to B. Without giving those intermediates any dignity or any name, what's going on here at this reaction? How is B different from A from what you can tell?

>> Two less hydrogens.

>> Human Physiology Steve Langjahr: It has 2 less hydrogens and it has 1 less?

>> Carbon.

>> Human Physiology Steve Langjahr: And it has 2 less?

>> Oxygen.

>> Human Physiology Steve Langjahr: Oxygen. So, this reaction is another dehydrogenation reaction. In fact, it's also called a decarboxylation reaction because we get rid of the CO2. So, even though it may not be that important, to repeat, how many less carbons does B have than A?

>> One.

>> Human Physiology Steve Langjahr: One. And how many less hydrogens does it have?

>> Two.

>> Human Physiology Steve Langjahr: Two. What is the usual fate for these hydrogens?

>> Mitochondria.

>> Human Physiology Steve Langjahr: Well, we're already in the mitochondria but okay. They're going to go through the electron transport chain. And how many ATPs can we expect here?

>> Three.

>> Human Physiology Steve Langjahr: Three. And how many over here?

>> Three.

>> Human Physiology Steve Langjahr: Three. So, if we're doing the math that would be 3 plus 3 or if you wish, 3 times 2 which is 6. I like to call this the 3 O'clock position for no good reason other than it's the 3 O'clock position. And what's next? The next reaction takes B and converts it to C. If you want to know the names, go for it. But, how is C different from B from what you can tell?

>> One less carbon.

>> Human Physiology Steve Langjahr: It's 1 less carbon, yeah, and it has 2 less?

>> Hydrogen.

>> Human Physiology Steve Langjahr: Hydrogens and of course, 2 less?

>> Oxygen.

>> Human Physiology Steve Langjahr: Oxygen. In fact, this reaction is the same as the one before, and so obviously C has 2 less carbons than A. But,

we don't really care, again, our eye is on the hydrogens, and once again, what coenzyme is involved?

>> NAD.

>> Human Physiology Steve Langjahr: NAD. This is a dehydrogenation reaction which takes these 2 hydrogens and processes them through the electron transport chain. With that said, how many ATPs can we expect by way of oxidative phosphorylation?

>> Three.

>> Human Physiology Steve Langjahr: Three plus what?

>> Three.

>> Human Physiology Steve Langjahr: Three. So, by any means of calculation 3 times 2 is?

>> Six.

>> Human Physiology Steve Langjahr: Six. Okay, great moving on. Down here at the 6 O'clock position, after C is converted to something we're just going to call D and notice that reaction is unremarkable in the sense that it doesn't produce anything that we really care about. But, down here at this final so-called 6 O'clock position, D is converted to E hum? And an interesting thing happens because there's enough energy released in this reaction to take a Pi; what's that?

>> Inorganic.

>> Human Physiology Steve Langjahr: And tack it on to an existing ADP to make what?

>> ATP.

>> Human Physiology Steve Langjahr: So, this is obviously not oxidative phosphorylation, but rather the direct transfer of phosphate on to ADP which is, of course, called?

>> Substrate.

>> Human Physiology Steve Langjahr: Substrate phosphorylation. How many ATPs are made at this spot, this single reaction?

>> One.

>> Human Physiology Steve Langjahr: One. But we do it how many times?

>> Two.

>> Human Physiology Steve Langjahr: So, 1 times 2 is?

>> Two.

>> Human Physiology Steve Langjahr: Two. And so our energy tally shows a plus 2 at this point. Remember, all of these reactions that we're not describing are occurring and can only occur inside mitochondria. The next reaction, all it the 7 O'clock position, takes E and converts it to an intermediate called F. You can find out the name if you're curious. But once again, we can tell right off that this is a dehydrogenation reaction. How do we know it's a dehydrogenation reaction? We're losing hydrogens, but the curious thing here is our friend NAD is not involved, instead its cousin FAD is involved. FAD, Flavin adenine dinucleotide. So, what. These hydrogens are still going to be processed through the ETC, but we said earlier that if FAD is the carrier rather than 3 only what?

>> Two.

>> Human Physiology Steve Langjahr: Two. So, we can't expect and don't get 3 ATPs, but rather 2; 2 times what?

>> Two.

>> Human Physiology Steve Langjahr: Two times 2 is 4. So, we'll plug in a 4 at that location. Now as we run around and complete the cycle, there are intermediates that are left unknown or I should say unnamed, they're certainly known, but the final reaction that's worthy of attention converts H which is actually malic acid to oxaloacetic acid where we entered this circle. And as you can see, this is another one of those dehydrogenation reactions requiring obviously a dehydrogenase enzyme and what coenzyme seems to be playing here?

>> NAD.

>> Human Physiology Steve Langjahr: NAD; picking up 2 what?

>> Hyrogens.

>> Human Physiology Steve Langjahr: From what? H which is malic acid. So to say it another way, oxaloacetic acid is different from this because it has 2 less?

>> Hydrogens.

>> Human Physiology Steve Langjahr: Hydrogens. And of course, where do those hydrogens go, they go through the ETC and so we can expect how many ATP?

>> Six.

>> Human Physiology Steve Langjahr: Three times 2 is 6. And so, that's it. That is, we're back. We're back to where we started because we're generating oxaloacetic acid which is a 4 carbon molecule. Yep.

>> Where did those 4 come from?

>> Human Physiology Steve Langjahr: Where did the 4 come from? These 4? Okay, FAD is a coenzyme similar to NAD. It picks up how many hydrogens?

Two, but it comes into the electron transport chain, as you can see at the bottom of the page, not at the beginning but kind of at the middle. And so instead of 1, 2, 3 it only produces?

>> Two.

>> Human Physiology Steve Langjahr: Two. So, 2 plus 2 is?

>> Four.

>> Human Physiology Steve Langjahr: Four. Good question. Now, we're at the end but yet we don't call oxaloacetic acid an end product; why is not a terminal product? Because it picks up incoming?

>> Acetic.

>> Human Physiology Steve Langjahr: Acetic acid and, therefore, goes around again. But at least we're at the end of the story here, because if we were to continue, that is if we go around again, we would have to expect the input of acetic acid which would require, of course, the earlier reactions that brought us to that point. So, it's the end of our tally anyway and if you do the math you'll find that it's 38 more or less' 38 by our count. If you go to current textbooks or other arguments they'll explain why it's probably not 38, but let's go with that. And of course, oxaloacetic acid is not an end product so what is? The end products which we said all along are CO2 and what? Water. So, where is the carbon dioxide? Let's count them. How many are there supposed to be?

>> Six.

>> Human Physiology Steve Langjahr: Six. So, there's 1 got it? Where's the next 1? There. Where's the next 1? There. How many is that? One, 2, 3 but why do we count 6?

>> Happens twice.

>> Human Physiology Steve Langjahr: Happened twice. Where's the water? You might say, well there's water, there's water but actually this is not water coming off this is water going in. So, you might say well I don't see any water coming off, but what you're not noticing of course is that at the end of the electron transport chain, oxygen picks up these protons and makes what?

>> Water.

>> Human Physiology Steve Langjahr: Water. Twelve times actually. So, the 12 waters are the result of combining oxygen with the protons and electrons and both of these are described as terminal products; end products, because nothing happens to them. That is, nothing changes them. What happens, in fact, to CO2 and water? They go away and where do they sometimes end up? The air that we exhale. Do we exhale water? Do we exhale CO2? So, we don't really care except that we're at least saying, yeah those are terminal or end products. What we do care about and always have, is the ATP. How many?

>> Thirty-eight.

>> Human Physiology Steve Langjahr: Thirty-eight. Were they all made by oxidative phosphorylation?

>> No.

>> Human Physiology Steve Langjahr: No. How many were? Well, you can figure that out. It might be a good exercise. Can we say that the Krebs cycle is synonymous with oxidative phosphorylation? No it's not, because the Krebs cycle makes what? ATP by?

>> Substrate phosphorylation.

>> Human Physiology Steve Langjahr: Substrate phosphorylation. In fact, how about this question; deliberately a trick question. How many ATPs are made with 1 turn, 1 turn of the citric acid cycle? I'm going to play the Jeopardy theme here.

[Singing]

How many ATPs?

>> One.

>> Human Physiology Steve Langjahr: One, yes just 1. You say, well wait a minute 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 these are not made by the citric acid cycle. These are made through the electron transport chain. So, I said it was deliberately tricky and not that I want to trick you, but I want to make it clear that these are not actually ATPs being made; ATP is made through the electron transport chain. So, literally to repeat the question, 1 turn of the citric acid cycle really only produces 1 ATP, and by what means? By what means? Substrate phosphorylation. That makes the citric acid cycle seem kind of wimpy, but it's really it's this cycle that supports oxidative phosphorylation. What do I mean? It supports, it provides what 4 oxidative phosphorylation?

>> Hydrogen.

>> Human Physiology Steve Langjahr: Hydrogens and so naturally it's valuable not because it makes ATP by oxidative phosphorylation, but rather that it generates hydrogen, protons and electrons that move, of course, through the ETC. All this depends upon what? What molecule that we said is available and actually the ultimate electron acceptor? Oxygen and if oxygen is not there, the ETC what?

>> Will shut down.

>> Human Physiology Steve Langjahr: Shuts down, and therefore, we're generating all these hydrogens that have nowhere to go and that forces this system to revert back to anaerobic glycolysis which is bad for a couple of reasons; one, it generates only what?

>> Two ATP.

>> Human Physiology Steve Langjahr: Two ATPs and the other reason it produces a lot of lactic?

>> Acid.

>> Human Physiology Steve Langjahr: Acid. Now I made it sound like lactic acid is, you know, nothing, a big deal. But when lactic acid builds up, and builds up, and builds up it becomes a?

>> Big deal.

>> Human Physiology Steve Langjahr: Big deal. Because it causes something that can be lethal called?

>> Acidosis.

>> Human Physiology Steve Langjahr: Lactic acidosis, yeah. Every time I say that I think of Tom Cruise in the movie "A Few Good Men." You should rent that [inaudible]. Anyway, here's the scenario; it's down in Cuba. Jack Nicholson, you know, "You can't handle the truth!" Are you with me on that movie? Okay. Anyway, these recruits haze this recruit and they shove a rag down his mouth and they kill him, alright? And his cause of death was lactic acidosis; lactic acidosis. Anyway, sorry to digress but just keep flashing on that. So anyway, it's a cause of death and so even though we painted lactic acid as being not that bad, it's not that bad because very often it can be converted back to what?

[Multiple Speakers]

Provided what's available.

>> Oxygen.

>> Human Physiology Steve Langjahr: But if not, it's going to stay what?

>> Lactic acid.

>> Human Physiology Steve Langjahr: And you'll be dead. So lactic acid is, in some instances, the cause of death. Now at this point, you're saying OMG. What am I supposed to do with this? Do you want me to memorize this page, this stupid what is it, 20; page 22 yeah I can do that. It would be a waste of your time. I'm not going to ask you to write these reactions down on an 8 1/2 by 11 sheet of paper. Actually instead, we're going to put you in a scenario and say, how many ATPs would be calculated? And you'll be able to use information, if it makes sense, to answer such questions. So, clearly it's important not just to memorize, but to understand this information. And you might say, well I understand it. You've made it understandable thank you. But, the test is what? If you're sitting here and nodding your head you got to understand it; the real test is to be able to turn to somebody else and what?

>> Explain.

>> Human Physiology Steve Langjahr: Explain it to them. And if you can't do that, then you really don't understand it or you've got gaps in your understandings, so that's what you have to do. That's why you need to get into a dialogue with other students. That's why you need to go to SI. That's why you need to have a study group of your own. Sir?

>> Can you go again from B to the [inaudible] acid; can you go again?

>> Human Physiology Steve Langjahr: Here?

>> Yeah, from D, from D in the circle.

>> Human Physiology Steve Langjahr: Okay. We'll call this the 9 O'clock position. This reaction produces H which we're not going to give a name to; actually it is malic acid. And then we go to what oxaloacetic acid. This is the final reaction in the? What is this called the? There's the word, not crab please!

>> Krebs cycle.

>> Human Physiology Steve Langjahr: Hans Krebs is turning over in his grave. He won the Nobel Prize for this and he should, because this is not just you and me, it's every living organism that has a ma-ma-ma-ma mitochondria. It's anyway, pretty damn important. Alright, sorry I digressed. Here we are. This is the final reaction of the?

>> Krebs cycle.

>> Human Physiology Steve Langjahr: And it's a final dehydrogenation reaction. How do we know it's a dehydrogenation reaction? Well?

>> NAD.

>> Human Physiology Steve Langjahr: NAD. NAD picks up hydrogen. So how is oxaloacetic acid different from H?

>> Two less.

>> Human Physiology Steve Langjahr: Two less hydrogens. What's going to happen to these hydrogens? They're going to go through the?

>> ETC.

>> Human Physiology Steve Langjahr: And as many as what?

>> Three.

>> Human Physiology Steve Langjahr: Three ATPs have been made. How many times has that reaction happen? It happens twice. Why does it happen twice? Because we ended this cycle not with 1 but 2 pyruvic acids. So, expect how many? Three plus what?

>> Three.

>> Human Physiology Steve Langjahr: Three and that's why we have what?

>> Six.

>> Human Physiology Steve Langjahr: Six. And that rounds out our tabulation. So, okay we said we were going to go beyond the glucose catabolism, because you might argue, well I never eat glucose so it doesn't apply to me. Well, that's another story. You eat plenty of carbohydrates and it's all almost entirely converted to glucose. But are there times when you're short of glucose? When your blood sugar is low? Certainly in famine situations or even in voluntary starvation. So, are other substrates able to access, to exploit, to enter in some of these reactions? And the short answer is yes. So, here in summary very simplified summary, we show glucose which is in the center of glycolysis, later the citric acid cycle. But let's just say you're short of glucose; what does the body stored; what is the kind of organic molecule which is deliberately stored for situations where there is a carbohydrate shortage?

>> Sugars.

>> Human Physiology Steve Langjahr: Fat. We got lots of it most of us. And so, well we all do because that is what it's for and neutral fats are triglycerides made of how many 3?

>> Fatty acids.

>> Human Physiology Steve Langjahr: Fatty acids and 1.

>> Glycerol.

>> Human Physiology Steve Langjahr: Glycerol. Without getting into the intimate chemistry here, glycerol can be converted to G-3-P and where does it go from there? Well, down and around sure. And of course, not 1 fatty acid, but how many?

>> Three.

>> Human Physiology Steve Langjahr: Three. Those can be oxidized, that is the hydrogens can come off and the fatty acids can be converted to acetic acid, also known as acetyl-CoA which picks up the CoA. If we come in here we're going to go what? Around not once, but what?

>> Twice.

>> Human Physiology Steve Langjahr: Not twice.

>> Three times.

>> Human Physiology Steve Langjahr: Three times. Why 3 times?

>> Three fatty acids.

>> Human Physiology Steve Langjahr: Three fatty acids for every TG. So, without doing the math, although you should, how many ATPs can be made with 1 fatty acid? Well, do that math and then do it 3 times for fatty acids. In short, will a fatty acid, excuse me, will a fat produce more ATP than a single glucose?

>> Yes.

>> Human Physiology Steve Langjahr: Yes. You say well what if I run out of fat? Heaven forbid, but you might, that is there are scenarios and so can protein be called upon? Yeah. But protein has a higher calling. What are some of the important functions of protein that you'd rather not compromise by breaking it down to burn it. Alright, enzymes and antibodies and muscles and so forth, but in dire situations proteins can be reduced to the building blocks. What are the building blocks of proteins? Amino acids. You can deaminate those. That means takeoff the amine group and that will generate either pyruvic acid and/or acetic, excuse me, oxaloacetic acid and can those be entered into and provide energy throughout early or latter stages of glycolysis and the citric acid cycle? Yes. And so in short, can protein provide for energy? Yes. But that's not desirable why?

>> Because the proteins are.

>> Human Physiology Steve Langjahr: The proteins are important for enzymes and antibodies and muscle proteins and so forth. So, I always resort to this stupid analogy, but it's kind of fun. You know, you're up in a mountain cabin and how you heating the place? It's a remote cabin, so you don't have you know cable. So, you're heating the place because you're putting wood in the fire, right? Plenty of wood, that's glucose. Suddenly you're out of glucose what now? Suddenly there's no more firewood, what now?

>> Furniture.

>> Human Physiology Steve Langjahr: Furniture. Furniture is soft and cushy, so that represents what?

>> Fat.

>> Human Physiology Steve Langjahr: Fat. Now the furniture is gone. What now?

>> The structure.

>> Human Physiology Steve Langjahr: Now we start pulling the studs out of the thing and why is that obviously not a good thing to do? Pulling the studs out of this house? Pretty soon the house is gone, same analogy here. So, is protein breakdown desirable? No. Is it sometimes resorted to? Yes. But, clearly glucose is the preferred and obvious, obvious source for energy; fat comes in when there's a shortage and proteins only in dire emergencies; prolonged starvation. So, that's a lot, but yet we've got to at least open the door to our final topic for this unit which we'll complete next week actually, and that is the flipside, the opposite of catabolism. Remember we said catabolism works with the opposite process called anabolism. And to refresh your memory, what does catabolism provide for anabolic reactions?

>> ATP.

>> Human Physiology Steve Langjahr: ATP. What do anabolic reactions provide for catabolic reactions?

>> Enzymes.

>> Human Physiology Steve Langjahr: Enzymes. So, when it comes to anabolic reactions, the most important are those that produce protein. And proteins are produced endlessly, endlessly in all cells, again to remind you, what are proteins produced for? What are some of the things that are made of protein? Enzymes, antibodies, muscle proteins, actin, myosin, cell structure so the cell has a voracious appetite for ATP mainly to provide the energy to make what?

>> Protein.

>> Human Physiology Steve Langjahr: Protein. In fact, protein synthesis determines the physical and functional properties of any cell. What makes this cell different from that cell is the kinds of proteins that it has or doesn't have, right? So, how is a muscle cell different from a skin cell? It has different p-p.

>> Proteins.

>> Human Physiology Steve Langjahr: Proteins, and is therefore, specialized, but it's no exaggeration to say that protein synthesis determines what a cell can do and what a cell can't do. And this process of producing proteins is not haphazard. It's very tightly orchestrated under the control of the molecules which you know represent the blueprints of life, the instructions for protein synthesis namely nucleic acids. What are the 2 nucleic acids by acronym that come to mind?

>> DNA.

>> Human Physiology Steve Langjahr: DNA and RNA. These are the players which really determine what proteins are made, when they're made, when they're not made and so nucleic acids are in charge. So, clearly we need to focus and reexamine DNA and RNA if only briefly, we'll get into the hairy details next week. But DNA is called deoxyribonucleic acid. It is, of course, made of subunits called nucleotides; deoxyribonucleotides. This molecule was first identified, first discovered in the nucleus of the cell; hence the name nucleic acid, and in fact, DNA is confined to the nucleus which sounds like a prison sentence, but that's true. It's confined to the nucleus because it's too big to leave the nucleus, but that's okay. It does its work inside the nucleus. It is a huge molecule made of billions of nucleotides, but as huge as it is, it normally too small to be photographed even with sophisticated instruments. The only time DNA becomes photographable is when this DNA is wound tightly onto proteins spools called histones; you might know that from biology, and therefore, it becomes thick enough and dense enough, condensed enough to actually be seen with microscopes. And in that form, the DNA assumes a different name, it's called chromosomes, and in fact, it's not just DNA, it's DNA with these protein spools. In fact, not; well yeah next week I'm just thinking. Next week you're going to extract DNA and take it home. That is show it off to the friends and family this is my DNA, because we're going to actually remove it from the cells of your cheek; I hope you don't mind. If you do, don't do it. But anyway, I

think you know from biology this is a basic simplistic statement that DNA contains the code, the information for the synthesis of 10s of thousands of different what?

>> Protein.

>> Human Physiology Steve Langjahr: Protein. And that code is represented in a bit of information that you also know by name is called a?

>> Gene.

>> Human Physiology Steve Langjahr: Gene. So, let's be clear, a gene is not a chromosome. Chromosomes contain thousands of genes, but by definition a gene contains just the information for what?

>> One.

>> Human Physiology Steve Langjahr: The synthesis of 1 protein. Now is that, when I was in your seat many years ago, nobody had a clue as to how many genes there were in the human genome. So, I remember being told, well it's probably I don't know, probably 50 million. That's a wild guess that turned out to be totally wrong. But, the amazing thing is that number every year seems to be revised down; revised down; revised down and now our best guess is that there are 25,000 different what? Genes. And that's kind of underwhelming because we'd like to think of ourselves as, you know, fancy machines but it is the best guess. And so even though DNA is a huge molecule, much of the sequence is garbage or otherwise not really functioning as a g-e-n-e. But beyond all these trivial facts, an interesting thing that you've heard and need to remember, we all share, everybody in this room shares 99.9% what the? Same genes. So, the only thing that makes me different from you is that 1/10th of what? One percent. The only 2 people in the world that have exactly the same genes are people who are called?

>> Twins.

>> Human Physiology Steve Langjahr: Identical twins. But, we're more alike than we're different and certainly that number alone is staggering. How does RNA relate? RNA is a different nucleic acid; ribonucleic acid. You could say it's the servant to DNA, but that's just an analogy. It really is a molecule which is manufactured, that is made from scratch using the DNA as a template. And the function of RNA and you know this already, so I'll throw out terms that you've heard; mRNA, tRNA, rRNA; these are the various sub-forms of RNA which diffuse that means leaks out of the nucleus, and go to work in the nucleus to conclude the process of protein synthesis, because RNA contains the information that has been what?

>> Copied.

>> Human Physiology Steve Langjahr: Copied not off the entire DNA but just a segment called a gene; hence the name messenger RNA which is the key player in this final step of protein synthesis. The important thing is this

sentence here; RNA assembles" that means puts together amino acids in a what specified sequence to produce a unique protein. And if you're going to highlight anything, there it is; specified what? Sequence. So, as an analogy what makes a word meaningful? Is it the number of letters? Is it the kind of letters? No it's the sequence of those letters. And so if this sequence is messed up the protein will be messed up and that is worse than useless. I'm getting a little too far into the game, but I guess I'll go there. Why is making a protein which is missed sequence worse than not making it all? Well, does it take a lot of effort and energy to make protein? Yes it does. And if it turns out that it's useless, making it is now worse than not making it at all, and so clearly the accuracy of this process is important and many of you guess that we're talking about a mistake which is really not usually not by definition a problem with RNA, but a problem with DNA. So, when DNA is mistake or messed up that's called the "M" word.

>> Mutation.

>> Human Physiology Steve Langjahr: Which leads to messed RNA, which leads to messed up proteins, which leads to a messed up cell maybe death or other horrible things. What's worse than death? Okay. Anyway, let' summarize as we wrap for today. This is just a cartoon, but it's the big picture and we began today with this story which was you recall, carbohydrate catabolism. So, glucose is used to make ATP and the byproducts of CO2 and water. This was the process to see where it was ca?

>> Catabolism.

>> Human Physiology Steve Langjahr: Tabolism and what does catabolism provide or otherwise give to the opposite reactions? It provides ATP. The opposite reactions are those that take raw materials like amino acids and hook them together at the expense of energy and where's that energy come from?

>> ATP.

>> Human Physiology Steve Langjahr: ATP to make proteins; proteins for what? Proteins for structure, proteins for antibodies, proteins for enzymes, proteins for muscle contraction. So, if you want to label and distinguish these, this, this represents catabolism, this represents anabolism and the sum total of all of them is the "M" word.

>> Metabolism.

>> Human Physiology Steve Langjahr: Metabolism. Metabolism is the co-operative, interdependent reactions that are catabolic versus anabolic. What orchestrates the anabolic reactions are clearly the nucleic acids and here's our famous DNA confined to the nucleus which generates as we'll talk about on Monday various forms of RNA which then are involved in the sequencing, the sequencing of what? What are we sequencing? Sequencing amino?

>> Acids.

>> Human Physiology Steve Langjahr: Acids to make certain proteins. Even though this doesn't show the details, it's worthy to reflect where does the cell get its glucose? Where does it get its amino acids? Well, that was earlier in our discussion. All of these things are had from the bloodstream, right? But how does glucose get into cells?

>> Facilitation.

>> Human Physiology Steve Langjahr: Facilitated diffusion. How does amino acid get in there?

>> Active.

>> Human Physiology Steve Langjahr: Active transport. So even though this is a simplistic and general diagram, it does remind us of where we've been and where we're going which is, of course, the last 2 lectures Monday and Wednesday devoted to this process called?

>> Protein.

>> Human Physiology Steve Langjahr: Protein synthesis. So that's it. I'm tired and I know you are too. So, have a great weekend and we'll see you back on Monday.

[Background Conversations]