Dr. Lightfoot: [music] So I'm very pleased to welcome to the stage a long-time colleague of ours from right down the road in San Antonio, Dr. Tony Comuzzie.

Dr. Comuzzie: Thanks, Tim. Well, just to start out, I spent a lot of time as a student in this room, but never from this perspective, so howdy, everybody. So to give you a little background, I'm a genetic epidemiologist by training, but I'm not going to talk about genetics today. I want to talk about more the environmental influences on contributors to cardiometabolic health, and particularly from the perspective of the work we've been involved with utilizing nonhuman primates. So it kind of started out with the idea of monkey see, monkey do. So several decades back, investigators working, studying behavior of Japanese snow macaques would provision these animals. They would provide them with sweet potatoes. And one of the things they noticed, there was one female in the group that very early on would take those potatoes, would go over to the river, and wash them off. The idea being that perhaps, a clean potato tasted better than a dirty potato, without the grit and stuff on it. And what they didn't notice going forward is how the other animals in the group started mimicking her. And then they all started washing their potatoes. They later noticed, and that's what this picture is, the same female when they got access to the salt water, to the coastline, she would now take her potatoes and dip them in salt water, and eat them. And that spread to the rest of the population, so the idea is, I think as primates, and certainly as humans as you'll see, we've taken extraordinary measures to make our food taste good. And I think we can't underestimate that when we think about designing our experiments.

When you look at the anthropological record, the evolution of humans and such, from almost the earliest advent of the use of fire, one of those aspects besides keeping warm, and light, and keeping things away at night was the utilization of cooking. We started doing things to make our food taste better. And I point out to people these days, think about it. We have two 24-hour television stations devoted to nothing else than how to make your food taste better. So I mean, we made chefs celebrities. I mean, these are household names. So I think the thing that's important, again, is the fact that we focus so much on that, and this is not because it improves nutritional quality. It just improves the pleasure. So with Thanksgiving coming up next week, I think this is important thing to remind and to think about is the fact there's multiple studies that have shown, when we are faced with the opportunity for a wide variety of foods and the palatability is high, we tend to overindulge. And really not too surprising, yeah, we like things that taste good. And so you think about today's modern world. The fact that you walk down the street here and you can sample the cuisine from basically any culture you can think of. It's readily accessible, and it all tastes good. And we've done things to make it even taste better.

So what I want to talk about is some of the work we've done for a long time with our baboon colony, and won't go through all of the specifics, but I think there's one characteristic of the baboon in particular that's worth noting, and why I think it's made such a great model for these types of studies. And that is, baboons are highly omnivorous. That is, they will eat anything they come across, in effect. And if you think about it from a biological standpoint, most of the definitions of at least mammalian species are based on the dietary adaptation of the species. Wild cats don't eat grasses. They don't eat fruits. They're strictly carnivores. Cows, on the other hand, aren't out there eating a cheeseburger, right? I mean, things are adapted to exploit a particular type of food, and they do it very well. Humans, on the other hand, and the baboon is an example by extension, will eat anything. And like I said, you walk down the street, you find cuisines of the world. And in reality, you can travel around

the world and you will find people literally eating anything that is edible. Now, any one of us may not partake of that particular thing, but somewhere, someplace, somebody is, if it can be eaten, they are eating it. And I think what's important from the standpoint of this omnivore, particularly with the baboon as a model, that that's an important adaptation that you're able to exploit all these different food sources, get relevant energy out them, convert them to the things you need. And so relevant to the studies we did, we had about a 35-40-year study looking at the impact of a high-fat diet, a high-saturated-fat diet, on cardiovascular function, specifically on cholesterol metabolism. So these baboons were raised. They were fed a normal-- I say in quotes, normal monkey chow diet, very low in saturated fats at all, high in fiber, and such. And then we would challenge these animals for various periods of time with a diet that was basically still the monkey chow formula, but they would add raw lard to it. So that's how we put the saturated fat in it. You feed these animals for 7 weeks on that kind of a diet, typically. And what you would see is yeah, a subset of those animals would show a fairly significant response in their bad cholesterol levels. And so again, not too surprising, but we were able to tease out some of the underlying genetics from that.

Now, as part of that research team, I wasn't as much involved in the cardiovascular component as I was in the obesity component, but one of the things that struck me very early on is while exposure to a diet high in saturated fat, which we've all been told you need to lower your saturated fat intake, what we didn't see were really changes in body composition. That is, these animals did not really show any increase in weight during that time. They also didn't show any of the other changes we typically associate with metabolic syndrome, so we didn't say changes in triglycerides. We didn't see changes in glucose. And that always bothered me. And not that you can read this, but much like Steve said, it's a reminder to me. So we actually took here recently, a group of these animals, and fed them for 2 years on high-saturated-fat diet. And what we were able to find at the end, again, no real, clear pattern to any kind of weight gain or changes in these other metabolic parameters. And what we did is compare a group of animals who were the age and sex match - these are adult animals - who had been maintained on chow diet for a 2-year period against these animals who had been on the high-saturated-fat diet for a 2-year period. And what we found is almost equal numbers of some animals on both diets gained weight. Some animals on both diets lost weight. And the bulk of the animals really showed no significant changes. So even after 2-year exposure to a high-fat diet, a diet that is absolutely calorically more dense, they didn't show any significant changes in weight gain. And I think there's some important things that come into that, and I think this is what beginning to open our eyes has to do with the palatability and the variability of the diet, because again, like I said, they took raw lard, stuck it in the diet, and fed them to the animals. And if you've ever tried to eat a spoonful of Crisco, you realized it's not an easy thing to do. It just doesn't really taste all that great.

So what we came up with was our fast food diet. It's a high-fat, high-carbohydrate diet, and we wanted to see that if we added that, what kind of effects did we get? This was shortly after the AHA come out with their white paper on the potential impact of refined sugars in the diet, and how that might be contributing as well. But one of the things we did with this as well, we added fruit flavoring, which we varied randomly, and we baked it for 10 minutes. When you bake fat and sugar together, even for a short period of time, magic happens. You caramelize those, and it all tastes good. So if we looked at the basic consumption of diet of these animals on just the regular chow, we're feeding about 500 or so grams a day per animal. When we switched them to the high-saturated-fat diet, the one that wasn't baked, just the traditional one, that actually dropped down to about 300 to 350 grams a day. Now, some of my colleagues said, "Oh, they eat less because it's more calorically dense.

They don't need it." And that's when I'm saying, "No, I don't think so," because with our diet, when we switched them to it, they went from the 500 grams a day of chow to eating 800 to 1,000 grams a day, and they stayed at that level throughout the study. And so one of the things-- I can say it was clear this was triggering something else with these animals, and more importantly, what we were being able to show, particularly when we added a sweetened drink ad lib to them, that we got the kinds of changes that we would anticipate with exposure to an unhealthy diet. And I think particularly, the one that struck us was while we did see an increase in body weight, it wasn't as much as we thought it might be. We saw a really significant difference in body composition. And it wasn't just the fact that they were gaining more fat mass, but they were actually losing lean mass on that diet. And I think that begins to play into some of the secondary, sort of anecdotal observations of some changes in decrease in spontaneous physical activity. They were losing muscle mass in all of this.

So to begin the next phase of studies, we started talking about okay, now the fact is, I don't know what baseline consumption really is because obviously, the challenge diet we had always used, they eat less of that than they did of chow, and when we feed them this kind of diet, they're just completely blowing away what they consume on chow. Does that mean that they're not eating as much as they would like to on chow, again, because maybe it doesn't taste as good? So it makes it hard to compare. But we wanted to do a study where we could compare our fast food diet with a more prudent diet. And so we actually formulated one that instead of being saturated fat was monounsaturates. It wasn't simple carbs, had more complex carbs in it. But we added the flavoring, we baked it, did much the same thing. And the thing that's surprising-- and this is the aggregate data for the whole group that was looked at. That solid black line is sort of the calculated caloric need of the animals in the group. That little dashed black and white line in there is the consumption, the daily consumption average, on the week run-up until each of the diets were changed. That's just the normal chow. And then you see these other lines. So that pink line is the high-fat, high-sugar diet. So obviously, they're quite a bit above what they had been doing, and they stayed at that. But that green line that's in there, that's the prudent diet. That's actually the very healthy diet, and they're even eating a lot more of it than they are of the junk food diet. And the only one that gets above that is that dashed one at the top, and that's the junk food diet with ad lib access to water sweetened-- or Kool-Aid sweetened to about the same consistency with sugars of a soda.

And so now, I'm really confused because what's my good comparator, because I don't think we've ever really thought about this. So obviously, the chow diet isn't really normal patterns of consumption. They certainly eat more of the bad diet, but they also eat more of the good diet. So now you have to try to disentangle this impact, but I think all of this is driven by that palatability component. And so this is just comparing some of those changes, and we got some interesting things because again, even on the very healthy diet, they were consuming more of it, more calories, so we did see changes increase in body weight. We saw some other changes with some of the other markers, and some of that's just what we would expect to see as you increase body weight. So again, what is the healthy component to this? But I think from a research standpoint, there's a couple of things that are important to take home, and part of that is that from the primates, I think that these are a really underutilized resource in that if you want to talk about good comparators for humans, particularly when you look at the long-term evolutionary adaptations, that they offer some real insight, particularly in terms of their dietary adaptations, how they feed, what they typically feed on, and such. But I think the under-represented part is the concept of palatability in designing any type of animal-based research study because I think we fall into a bad idea with the thinking that okay, the animals in the research center, they will eat whatever I feed them. Which they will because they really have no choice, but are

they really eating, or feeding, in the same behavioral pattern they would if things tasted better? And I think that we certainly saw that with our primates, and I know several colleagues at other primate centers now are particularly beginning to look more at this and considering the actual palatability of the diet.

And like I said, it doesn't take that much work to actually increase or improve the palatability. That simple thing of baking, which kind of goes back to the advent of human use of fire. You start cooking things, you really increase that. So we certainly see that with a little effort, we can increase that part of it. But I think the other thing that was important from all of this is that while we had a reason to focus so strongly on saturated fats, that you really have to consider the whole diet. People don't eat nutrients in isolation. We eat foods. And typically, if you're eating a high-fat diet consistently, you're probably also consuming a lot of simple carbohydrates. So to really develop and balance our model required the fact that you've got to consider how people feed, and that is both high-fat and high-simple-carbs, unfortunately. So I'm right at 12 seconds. Thanks.

Dr. Lightfoot: Thank you, Dr. Comuzzie. We've got several questions for you. We have Mike from [inaudible]. Have you looked into the effect of gut bacteria based on these types of diets?

Dr. Comuzzie: No, we haven't, but it is one we want to look at because obviously, changes in carbohydrate sources would have a big impact on how the gut microbiome functions, and also then the feedback to the rest of the system.

Dr. Lightfoot: So we have someone with sharp eyes that said your table on body weight gain in baboons fed extra lard showed significant gains in females, but not in males. Is there evidence for this sex difference in humans? This is from Susan.

Dr. Comuzzie: Yes, so actually, that is a good eye because it's not a huge increase, but it is statistically significant. And it was females and not males. And frankly, we don't have a good idea. There's a number of speculations, and working with a group of graduate students at the University of Texas right now to follow up on that data, and yeah. We're thinking about it, but yeah. Like I said, it wasn't huge pounds, but it is a significant increase in females over males.

Dr. Lightfoot: Excellent. This is Matt from Western University. What happens to body composition of the chimps when they are on a complex carb diet?

Dr. Comuzzie: So I don't know about chimps. These are baboons, but I would assume they would be somewhat similar. But yeah, so again, when we added that drink, I think it becomes another confounder because one, you've got the simple carbs and the fat in the solid diet, and they definitely consume more of that, and I think we begin to see some of those body composition changes. But when they're given access to a sweetened drink, it just seems to trump everything else. I mean, these were normal, healthy, adult males that only had ever had access to water, and during the course of the experiment, still had access to water, but almost completely abandoned drinking water, and would drink on average, somewhere between a liter to 2 liters a day of that. So I think that some of those effects on the body composition may just be from as much the sugar-sweetened beverage exposure as it is the solid diet.

Dr. Lightfoot: And you told me it didn't just change how much they drank. It changed their drinking behavior--

Dr. Comuzzie: Exactly.

Dr. Lightfoot: --where they laid around and drank straight from the spigot.

Dr. Comuzzie: Yeah, no, [inaudible], we didn't-- I can only make comments anecdotally because the

way the experiment was designed, we weren't thinking about looking at behavioral shifts in them, but these were animals housed in large, outdoor enclosures, and the enclosures on both sides had animals on normal chow and water exposure, and when the experiment started, you could walk out there and all these animals are climbing up and down in the cages. All the movement looks pretty similar. Once we started giving them access to the drink and the high-fat, high-sugar diet, what you saw was that activity just started dropping, and like you said, the behavior. So you'd watch an animal, normally would walk up to the water source, take a drink, walk away, come back later. With access to the sweetened drink, they would walk up, sit down, drink--many of the males would not ever even turn loose of the nozzle. They would sit holding it, and drink more, and drink more.

Dr. Lightfoot: Their own beer hat, right?

Dr. Comuzzie: That's what I said. It looked like a bunch of guys sitting at the bar with their beers.

Dr. Lightfoot: So thank you so much, Tony, for the talk.