

WED JUNE 21	LIVE BETTER LONGER: Five Breakthroughs Changing Aging FREE WEBINAR / 3pm ET (12pm PT)	
		
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TRANSCRIPT

Sarah Smith: Hello, and thank you for joining us today for 'Live Better Longer: Five Breakthroughs Changing Aging,' a webinar brought to you by the American Federation for Aging Research, Prevention, and Age of Majority.

I'm Sarah Smith, the Editor-in-Chief of *Prevention*, a Health and Wellness magazine that is doing great for its age, which is 73, because I and everyone who works here gets to learn something new every day. That's why I love partnering with AFAR on our Live Better Longer series, because I get to chat with leading experts to learn about what's going on in the field of aging.

Please know, though, that of course, these conversations are educational. We are not your doctor. so please, you can talk to them about anything that you might want to change about your health care. We're able to be here today because of some important partnerships afar, is a leader in supporting research into healthy aging.

Prevention, as I mentioned, has a long history of bringing the latest health advice and thinking to a broad audience and age of majority is a company doing great work to debunk myths and stereotypes around aging.

I'm so pleased today to be talking with Steve Austad, AFAR's senior scientific director, who holds prestigious positions with the University of Alabama at Birmingham and the Nathan Shock Centers of Excellence. He's also the author of the terrific book, *Methuselah's Zoo*, which we spoke about on another webinar, and I highly recommend. So, Steve, welcome. I'm so glad to be here with you today.

So, Steve, before we get started, really talking about the specific breakthroughs I would love for you to give us some context. As I was reading about the things that we're gonna go through today. I was thinking, you know, like, Wow, I mean, maybe I'll live to be 100. Maybe my son is gonna live to be under and 20. It's really amazing. But do you think we're at a particular turning point in aging research, you know, or we had a more study progression? Is it both? Give us some.

Steve Austad: I think we're at a tipping point, as they say. The tipping point is that in the last 10 or 15 years we've come up with literally dozens of ways to make experimental animals stay healthy longer and live longer. And what with the tipping point that we're at is we're starting to now try out these things in humans to see which of them actually work in humans as they work in animals. And you know, we've had some of these things like dietary restriction. We've done this as made experimental animals stay healthy longer for 70 years.

But we've never actually well, we try. We've tried to extend it to humans. But the one thing we found out is that humans can't do what mice can do. You know, mice are rats in a cage if you want to feed them, 30 or 40% less. Then they want to eat. Yeah, you can do that. It's no problem because they have no choice. You just give them this much food.

Humans, even if we pay them a great deal of money and make them, you know—give them counseling and everything—they can't quite keep that kind of long-term diet. But now we're in a new point. We're at a new point where we have some things that we are pretty sure are gonna work. And we're ready to try about humans. And in fact, some of those early trials are already under way.

Sarah Smith: That's really exciting. Okay, so let's dive in and talk more and talk specifically about some of these things that are, you know, really starting to change the field. So, the first one for us to talk about is our understanding of senescent cells. And you can tell me if I said it wrong, because I have a wide vocabulary from reading, but not always from talking. So, tell us first what these are, and how do they affect our health in a general way.

Steve Austad: Sure, these senescent cells are those that used to replicate because tissues need to be repaired and renewed. But they've run out of the amount of division that they can do, and so that they don't, they're no longer capable of dividing. And initially, when these cells were discovered, and they were discovered in dishes, they assume that they would die at that point.

But they don't, and that's the problem, because they just sit there, and they start oozing these very damaging chemicals.

And so, from being well behaved cells that help rejuvenate our tissues and all, suddenly they've become damaging cells. And that's why they're called senescent cells. "Senescence" is just another word for aging, really.

Sarah Smith: So, what do we know then, about repairing them?

Steve Austad: So, for the longest time it was a mystery. We know that even in the oldest people senescent cells form a very small fraction of all the cells in their body, and the mystery was always, what could these really be having any, you know, detrimental impact on our health if they're so rare.

And what was discovered was that yes, these things, that they use actually damage the surrounding tissue, and in fact, it can even convert some of the surrounding cells to senescent cells themselves. So they have a far greater impact than you would expect if you only knew the raw numbers. The other thing that we've discovered is that cells that don't really divide ever like the cells that make your brain, your heart muscle.

They can also show the same characteristics of senescence, that is, they can reach a stage where they no longer perform their function well, but they start to ooze these damaging chemicals. So we found out that yeah, that they're more, far more widespread than we thought.

Sarah Smith: So, can you talk a little about how we know this now?

Steve Austad: Well, we know we started knowing everything from looking at cells in a dish, and for the longest time there was a question: Do these things even exist in living animals? And then, about 15 years ago, people found some markers, some ways to do it. So then they could. They could look at those markers in mice, for instance, and say, Aha, yeah, we see that this blue marker, one of the markers, is a bright blue dye, right?

We can see these organs gradually turning bluer as they get older. And then some people started looking at skin biopsies from humans at all. And found,

yeah, those cells are actually in there and then we found some other ways to identify them besides this blue marker as well.

Sarah Smith: So, what's the significance, then, of identifying them? And then what are we? What do we think we can do to them? Are we trying to not have them? Are we trying to keep?

Steve Austad: We can't really prevent them from accumulating, they accumulate with age, but once we were able to identify them, it became possible to ask, Well, can we find drugs or chemicals that will kill them, because one of the things that happens when they reach this stage is that a lot of your cells in your body are killed all the time. It's a normal process that cells at a certain point will commit suicide.

These cells are very resistant to all of the signals that say, kill yourself, kill yourself. So, what we once we could identify them, though we could start to try to find chemicals that preferentially kill those cells, but not the healthy cells around them. And we've now discovered the handful of chemicals that do that very effectively in mice. And when we do that, we've discovered that, in fact, it improves the mouse health in, in, in multiple ways. So that's why it's so exciting.

Sarah Smith: What are some of the ways it? Does it make them younger? Does it slow down their aging? What is it?

Steve Austad: It kills them, kill them. And so then they're replaced by healthy cells, the cells around them will make. So the nice thing about these chemicals to the extent that they're that they also work in people.

And there are a whole bunch of early stage human trials underway is that it takes these cells a while to accumulate. Which means that let's imagine that we have this therapy that we say, Okay, you take this pill and it kills 70 of your senescent cells. Well, you don't have to keep taking that pill every day because you can wait. You can wait for them to begin accumulating again. And so this might be something where you're getting in your, your, your youth prolonging therapy once every few weeks or every few months.

Sarah Smith: Do you think that that's something that's really coming soon-ish for people, to be able to kill these cells?

Steve Austad: Yes. there are. Last time I checked. There were more than 40 early stage clinical trials of the of these drugs that kill these cells. Now, those clinical trials are not for prolonging aging. They're for fighting diseases, because that's the first place that we're going to see. Some of these anti-aging

therapies come, people are, gonna say, can they prevent this disease, or can they slow the progression of these diseases? So it'll probably be quite some time before we actually know if they can keep a healthy person healthy. But what we'll know far beyond that before that is, whether they can slow down or even possibly reverse the course of some very serious diseases?

Sarah Smith: Did they up? Are they directly associated with specific diseases? Or is it that they're present when there are.

Steve Austad: Yeah, yeah, no, they seem to be quite general. But there are specific diseases that we know are due to senescent cells. And so those are the first diseases that we want to address.

Sarah Smith: That is, that's very that's fascinating. And it that you were going, we we'd be going in to kill a certain kind of cell. But leaving the others in a safe way.

Steve Austad: Right? And with the right kind of drug delivery, we might be able to deliver this drug just to the part of the body that you want it to, maybe just through your lung, just to your liver, just to your brain.

So, you know, there's also a lot of progress going on and sophisticated drug delivery, which is not, you know. It's one thing to have the drug. It's another thing to get it to the right place at the right time. Right? So a lot of things have to happen and come together. But you're really seeing that starting to happen.

Sarah Smith: Yes, that's really exciting. Okay, so I want to talk about cells in another context. now. So I think there's some research showing the possibility of reprogramming cells. Can you tell us what that means and how it's different from the senescent cell situation?

Steve Austad: You know, we all started off life as this little bundle of cells of embryonic stem cells. And it was those cells that eventually transformed into all of the cells of our body. So in, you know, when we were very small of several hundred cells, some of those were these embryonic stem cells, and from those cells everything in our body arose. And for the longest time people were interested in what could those cells be used to help us fight off aging?

Well, it turns out in in about 15 years ago. Now it was discovered that we could turn any cell in our bodies into an embryonic stem cell like, so by giving it a certain cocktail of chemicals, the same cocktail that made them embryonic stem cells in the first place. And what that means is that we could take a skin cell or a blood cell, you know, or a kidney cell and reduce this age back to 0. If you think about it. That's pretty remarkable, and there are all

kinds of therapies that are likely to come out of that. But what we've discovered in the meantime is that if we give, let's say, a mouse, a certain dose of these cocktails. and we do it periodically. What it does is it partially turns some of the cells: back into a more embryonic or youthful state.

And now they've done that such that they've done some remarkable things. In one case they rejuvenated a nerve that usually in adulthood, there's all that certain nerves will not regenerate. So they did this. So in a regeneration of mouse, with a nerve, optic or nerve of a of a mouse.

Normally you cut that nerve, and the mouse is blind forever after. But we've given it this cocktail of cells that nerve actually regenerated itself and restores some of the vision. They've also given this to some mice, just to see if they live longer. One of the more recent papers, they did this to mice that were at the equivalent of about 70 human years, which is, you know, 20 to 23 months for a mouse, and the ones that got this partial reprogram. He'd live twice as long as the animals that didn't get that. So that's pretty remarkable.

Sarah Smith: That's really interesting that they lived twice as long. So in one example, you were talking about fixing eyesight, or something that we would have thought couldn't be fixed, and another. They just lived long. There wasn't necessarily a one obvious thing that they were fixing.

Steve Austad: Well with mice, mice almost all die of cancer. So what they were doing was that they were. They were, they were preventing the development of cancer. Now, I have to say, this is in. This is in a very early stage. This is not as advanced as the senescent cell therapies. There are some, you know, because anytime you start making a cell a more generalist. So you're pointing with the possibility that you could turn that cell into a cancer cell, which is that kind of general cell. So this is, this is not ready for prime time, not even close to prime time, but it's very provocative that if we can come up with the right cocktail, the right timing that this could be, even a more rejuvenating kind of therapy than with the senescent cells. But it's in very early stages, but there's a tremendous amount of work going on in in this area, because, this would be this would be huge if it were extended to humans.

Sarah Smith: Right, it sounds so. I wonder if, knowing that it's very early, do we have any sense yet—I mean, is this kind of reprogramming something you can do indefinitely to a cell or is it always going to carry that risk of turning it into a cancer cell or something dangerous? Or can they... can it just not take it at a certain point, I mean, are we going to live forever?

Steve Austad: Well, I mean, there's more to our bodies than just our cells. There's our bones, there's our, those are attachment. There's our ligaments. but it certainly has the possibility of keeping us healthy substantially longer. We don't know the how many times you could do this to, so we have no reason to think that you can't do this numerous times. We don't know that yet, and we also have to figure out well, how can we do this without increasing the danger that we're going to have these side effects like increasing the cancer rate. That that would be really awful, and that's why this research is probably going to go a little slower than the work on the senescent cells, because the drugs that they've that they're using for the senescent cells. And I don't want to really mention them, because I don't want people to run out. Start trying them out. Those are drugs that we know don't have much in the way of side effects a number of them. These, you have to be very, very careful with. So we have a lot of work to do. But, on the other hand. If this pans out it could be, it could be quite literally earth-shaking.

Sarah Smith: Right? So a lot of careful work coming. But for a very potentially huge breakthrough. Amazing. Okay? So our next breakthrough, I'm not gonna lie, reminded me maybe a little bit of vampires because it's about how young blood can rejuvenate damaged organs in older adults, animals. In the case of the research again. So you are here to reassure me that of course, nobody is drinking anybody's blood. so tell me, what's actually going on here with this research on, you know. Blood.

Steve Austad: Yeah, this is. This is probably the one that I think has the most promise in the near future. And so what the way that they discovered this is, they basically hooked the circulation of a young mouse to the circulation of an old mouse, so that their blood was mixing.

And what they found when they did that is, that the old mouse suddenly looked much younger. Its organs look much younger. Its brain and its muscles look much younger.

The downside of that was the young mouse suddenly looked like older now, and they've subsequently done it where they just did a transfusion. The transfusion of plasma, let's say, from an old mouse to a young mouse, making a young mouse older, and the vice of making the old mouse younger. So we do transfusions all the time. I mean, this is, you know, we're doing that. For years I've been trying to convince my students that you know how much people will be willing to pay for blood for people that are 20 years old.. The interesting thing is right now we we're not entirely sure if there's some magic chemical or group of chemicals in the young blood that's responsible for the rejuvenation, or where there is some damaging chemicals in the old blood. And what we're doing is, we're simply diluting those out. And there's some evidence for both.

And as we figure this, the thing is, even before we figure it out, there's the possibility and getting these transfusions. And I'm thinking, yes, it sounds kind of vampiric. But, on the other hand, it wouldn't surprise me if, 10 years from now, every time people donate blood, they don't just put their blood type on it, but they put their age on it. And it could be, I mean if we can identify the chemicals, and if it's chemicals and young blood, and then we could just dispense with the whole trans fusion business.

But again, we know a lot about transfusing blood. There are very serious scientists doing very serious clinical trials for a number of again, of diseases from this right now, but I think it because it's something that we do all the time, anyway. that, this shows just a great deal upon it also doesn't violate any aspect of biology that I know. I could imagine that older organs are producing toxic some kind of toxic, you know, waste products that accumulate in the blood, and then our kidneys don't filter out, but that if we diluted those things out, they would be healthier for everything.

On the other hand, if there are some magical chemicals in in in young blood, and we and that would be. That would be... I guess that would be plausible as well that there are some things in young blood to help keep organs young until bad things start accumulating in the blood later in life. So the logic of this is one that makes so much biological sense to me that I have some great hopes for it.

Sarah Smith: That's so interesting. You're saying if the researchers can identify that it's the chemicals, that they could then create just those chemicals and dispense with the whole blood part of it.

Steve Austad: Right, and early on there was a thought that they'd identified one chemical but it hasn't really panned out so well, so they're still working on that. My thought is, if it is the young blood and not the lack of old blood that that it's likely to be a cocktail, and I simply say that because I think if it were something simple we would have found it already, because people been looking very intensely for it.

Sarah Smith: Right? And we're so comfortable with drug blood transfusions in general— in our culture it happens all the time—that you would think if it were, you know, super straightforward, we might know even more. I mean, of course, it's never been done as a trial until now, you know. We don't know the age of the blood that people getting.

Steve Austad: Yeah. I mean, when I was in graduate school I gave plasma, and I think I got every time I did it, or something. But now people are paying thousands of

dollars because there are people in these clinical trials that are getting these kinds of transfusions all the time.

Sarah Smith: That is fascinating. And I can I see a future with all kinds of interesting things happening in that. But this is we're talking. The mice are improving in overall health, or we're targeting specific areas of the body?

Steve Austad: It seems like every organ that's been looked at has been improved by this kind of mixing of young and old blood in the old animals.

Sarah Smith: So what is still the barrier, then to treatment to just people trying to do this themselves. That sounds horrifying. But you know, like, why isn't this a treatment? Now

Steve Austad: There was a company already that started doing this commercially, and the FDA got on them. And I think they're out of business now. But it's just it's just it's too preliminary and getting a transfusion when you need one. For some, you know. For instance, you had surgery, and you need to tread. That's one thing, but getting regular transfusions of blood, you know, every time you get a transfusion there's a small chance of something untoward happening. So I think we have to be a lot more certain of this. But I think this is something that's going to come fairly quickly. Very interesting. Yeah. Often seeing, you know, when there's a blood drive that there's, you know, a critical need, and I can't imagine, you know, taking from the critical need.

Sarah Smith: Very interesting. Yeah. Often seeing, you know, when there's a blood drive that there's, you know, a critical need, and I can't imagine, you know, taking from the critical need, for... You know, uh... So I suppose there's that issue, too.

Steve Austad: That is. Of course that would not be a problem if college students were getting paid several thousand dollars.

Sarah Smith: Yeah, if everyone under 25 were getting paid to do it. Yeah, we really, we wouldn't really have a shortage. Okay, let's talk about rapamycin now. So can you first give us a background on what the drug is. And also, if you could tell us where met formen fits in here, since I know that's often a buzzword in aging.

Steve Austad: Sure, sure. So there are a variety of 6 or 8 drugs that have been shown to increase longevity and prolong health, and most the one that's had the most robust effects. It's been studied the most is a drug called rapamycin. And rapamycin is already used in the clinic under fairly limited circumstances. It's if anybody has a stent in their coronary artery. That's stent is these days is

typically embedded with this because one of the things that rapamycin does is very good at preventing cell division. One of the problems with stents is that cells grow over the stents and they close off the artery again.

It's also used as part of an immunosuppressive cocktail. When people get a kidney transplant because a lot of the chemotherapeutic agents pretty toxic to the kidneys, and it's not, and it's also used in some chemotherapy cocktails as well. But it's never but what we found in mice. It's it has remark, I mean. You know, I told several journals of all the things that we know very well it doesn't mice, and they said, "That sounds like science fiction." So it makes them live longer.

There've been more than a dozen studies, and they all find the same thing. It actually prevents mouse versions of Alzheimer's disease. Well, you can give mice a caricature of Alzheimer's disease, and it's it slows down the progression and delays the onset of Alzheimer's disease. It also does the same for progeria, this disease that people get that's accelerated aging disease.

We know that the genetics of that disease. So it's easy for us to do it in mice, and when we do that they might stay healthy longer when we do it. It delays several cancer types in mice. It prevents entirely prevents some types of cancers. It prevents atherosclerosis and later life heart failure. It improves vaccine response. And this is one of the things that's actually been found in people as well. There's been a small trial where they took all, so that in originally they took old mice, gave them a dose of rapamycin, and then gave them a flu vaccine, and found out that the older mice responded as well as young mice typically do.

And there was a similar study in humans where they gave people rapamycin. And they way to older people, people 65 and older, and then they gave them a flu injection and found out. They mounted a greater antibody response. Rapamycin has even been shown to prevent periodontal disease. Believe it or not, it mice? Yeah. So this is just remarkable. Yeah, very, almost like a little miracle. So for quite some time there. There are a few human. Been a real hesitancy by the medical community to adopt this because it's already used in the clinic, and it's used when people have cancer and transplants at all.

There are a lot. There are some known side effects, and that has put the medical community off. But those were in doses that were therapeutic, not doses that were necessarily for the prolongation of health. We don't know. We don't know if this would work at the same way in people that it works. I might may or may not. I think we ought to find out. Now. There's already an informal group of people who are who are dosing themselves with

rapamycin. They're getting their doctors who prescribe them rapamycin, and for some something or other. So. you know that's one of the things we don't know, but its effects in mice are absolutely Earth shaking.

Now metformin is interesting because it's another drug that attacks. So the process is that go on inside the cells. Unlike the senescent cells that you're trying to kill a cell. This, you're trying to change its internal chemistry, which is what's the most popular type 2 diabetes drug in the world.

It's not shown to have a really big effect in mice. But in humans, because millions of humans have taken metformin for 60 years. And there was one study that showed that the people taking met metformin because they were diet, but to control their diabetes. We're actually living longer than the people matched for age and socio-economic status and all that that we're not diabetic.

And so that was really quite earth-shaking. And because metformin and we know so much about it, safety is very, very safe. Drug. there's a lot of interest in doing a large clinical trial with metformin to see if it. You know, there's some observational epidemiology that is this group of people. We're taking that format in this group of people. We're not. That shows that it seems to prevent cancer and coronary heart diseases and dementia But again. These are observational studies. They're not experiments, and there's all kinds of reasons to interpret those with a great deal of caution. You know.

Observational studies were what made estrogen look like the wonder drug of the 1990's, and then is when we did a proper clinical experiment turned out. It was a lot more complicated to that. But Metformin is very, very interesting. The problem with getting a metformin trial has been that because it's off patent. It's as cheap as aspirin. nobody stands to make any money, so it's been hard to find the funding for that.

But there's about another half dozen drugs that it might have shown the promise of rapamycin, the interesting thing about them. And this may be the thing that aging biology contributes to medicine this brand new. So most of those only work in one sec. And that is something that's brand new. And it's shocked everybody, and to the extent that that turns out to translate to humans. It means that we may soon start personalizing medication by sex. And so far that pretty much hasn't happened. But it's something that really deserves some looking into

Sarah Smith: That sounds so unusual. That would be a whole other way of thinking about what people are taking right? Like a, person who's diabetic.

Steve Austad: Who's a woman versus or just or any people? Right? You're saying, Yeah, right? And you know, people are talking now about personalized medicine that you won't get this this kind of medication for your cancer. If you had this genetic make of it all, I think the first place, is going to come into medicine is right here differences between men and women. Biology.

Sarah Smith: I mean right when you say it like that. Of course it makes sense. I mean, there's been a lot of breakthroughs and understanding, and that women aren't just like smaller men. Right and right, it's a whole different biology.

Steve Austad: And men are just shorter lived women right? Right?

Sarah Smith: Well, you know. Before we actually go on to the next one, because there's already been some questions about this topic. And I thought, Let's just address a couple of them right now, and we can always come back audience to more questions about this. But you know the this, this, the safety issue of you said. Some people are already starting to take metformin in particular, people. A lot of people take metformin, right? But are there people taking rapamycin?

Steve Austad: Now, okay, so yeah, there's an informal study group. They have about at least 300 people that are interested.

Sarah Smith: So you know, as we said at the beginning, you know we're not. We are not giving medical advice, but what? When someone talks to their doctor about this. What is that conversation? What you know? Would you discourage it? What! You, as someone who's like looking at the research and the fact that there hasn't been a trial, but also that it's so promising, you know.

Steve Austad: I would discourage people from trying anything that hasn't had a proper clinical trial. But there are people who are so invested in their long life and health that they're willing to take risks that most of us would not be willing to take. And there certainly are risks. So I would say to people. Look, talk to your doctor. If your doctor doesn't recommend doing something. Don't do it. But again, you know, people have their own priority.

Sarah Smith: Could you explain why, from your perspective, clinical trials are so important for patient safety? Because I think we hear a lot about them. They sound very exciting, you know, but what is their function in terms of our safety?

Steve Austad: Particularly, first of all, to see what levels of drugs are toxic. Right? and the other thing is, they're long term effects. It may not be obvious early on. So it may be that you're taking this drug, and it's fine to take it for a year, but if you take it for year after year, if your clinical trials are really the best way

that we have to tell if a drug is safe and effective at whatever it's supposed to do.

There's really no shortcut, you know, just like men and women are different biologically, mice and people are different biologically. And just because something has a really robust benefit in a mouse does not mean that it's gonna have the same benefit in people.

You know, we're very much more successful at curing cancer in mice than we are at people more than 90% of the clinical trials of drugs that were effective in mice fail in people. And that's something they to keep in mind. Right?

Sarah Smith: Yeah, that's an important reminder. Right? This is all very exciting stuff. But I'm glad that you put that in perspective there for us. What's our last breakthrough, that we're gonna talk about before we take more questions, is something that's more accessible and safe for a lot of people which is intermittent fasting. Time-restricted eating. And I know that this is fascinating to a lot of people from a weight loss. Perspective. but there are some amazing breakthroughs related to health span, too. Right? So what do you think is most exciting about this research?

Steve Austad: I think the most exciting. So we've known for a long time that reducing calorie intake has all these benefits in in in many species. Not just mice. But we're not sure of at this point, even though we've been studying this for years, is whether the benefits are because of the effect on weight loss, or whether there's something else.

We used to think that it what you needed to do to get the benefits of this diet was to keep doing it day after day, month after month, year after year, and people can't do that. I think we've had several human trials now, and it doesn't matter. You could pay people \$100,000 a year. They cannot stay on a 30% less calorie diet. But for those of us who worked with animals for a long time. One of the things that I should have noticed earlier. I didn't. Somebody else did, I should. Is that when you're restricting these animals and you go in to feed them every day. They're hanging on the cage bars waiting for you, and they gobble up all their food and just right away. And so we weren't just feeding the animals. That last. What we were doing is we're also making them fast for about 23 h a day.

And someone finally thought, well, maybe it's not the calories themselves. Maybe it's the fasting. That's the important thing here and there is this whole fasting physiology that if you don't eat for 8 or 10 or 12 h your body starts to change the way it works. It starts to turn on a lot of protective processes, and

all so out of that, and out of some very promising work with mice came the idea that maybe the important thing was to have a period of fasting.

And now there, all these diets that have come about, that are various ways of enforcing a certain level of fasting. Some of them ask you to fast for a day or 2 each week someone will say, Well, eat all you want, but eat it in a restricted amount of time. And if you do that than the rest of the time you're fasting. Those are proving very effective for weight loss. And the most important thing is this is stuff that people can do. You know, people can eat from 10 in the morning to 6 at night, and that's it, and it may have dramatic benefits beyond weight loss.

One of the things that we don't know from the animal studies is the effect of this restriction because it's effective making mice less obese, or is it the extreme leanness? You know we really don't know. There were 2 primate studies, one of which sort of did the obese lose obesity, the healthy body weight, and those showed a big impact on survival.

Another one took healthy body, weight and restricted there, and there were some benefits, but there was no longer life. There was, you know, there were some health benefits. So it's not entirely clear what this is doing. But the fasting physiology. It's already been shown in mice, for instance, to help mice recover from major surgery faster and be less likely to die. And it's also been shown to help some people recover from the nausea and all the side effects of chemotherapy.

So yeah, there's a great deal of promise here. It's something that we can do is probably gonna be a while before we can identify what? Whether it has these massive general health benefits or not. But people can do it.

Sarah Smith: Yeah, right? Especially as you describe the 10am-6 pm eating. Because there's a lot of ways that people can try intermittent fasting. Is there one that you've seen in the research that seems the most either effective or effective plus doable?

Steve Austad: My daily routine. I don't eat breakfast, you know. I eat a kind of a brunch on a dinner, so it's very pleased. It's like if you'd been taking metformin for years, and then you heard about the metformin effects. How pleased you would be. But yeah, it was. Is that preferable to fasting entirely for 24 h a time or two a month. I don't. I don't know. We we'll find out, though. But the fact is that people could do it if all it does is wrote reduce obesity that will have an enormous health impact by itself. Right?

Sarah Smith: Of course, that that is correlated to so many other issues, right? So solving that would solve other some other issues. You know, we're talking about eating here. Could you also address exercising, even though it's maybe there's not like one big breakthrough here, because I just I feel like they often go hand in hand when people talk about just living a healthier lifestyle, is there? you know. What? What do we know about the benefits of exercise on aging?

Steve Austad: I think there has been something of a breakthrough here that the breakthrough is that we keep discovering more and more benefits of exercise and the things that we didn't realize 10 years ago is how good exercise is for preserving the brain, for staving off dementia, a normal cognitive decline.

There are even things now called myokines that are things your muscle produces that seem to be beneficial. So your muscles are in certain sense like a hormone organ. And I often call it physical activity instead of exercise. Just because people think of exercises, you know, you're dripping sweat, and you're exhausted, and all that is it kind of exercise, but just a good moderate walk is also exercise, and people tend to forget that. And I know there are people who hate to sweat, but they could still benefit from moderate exercise, but doing it regularly and like, I say, we're discovering more and more and more benefits of this. But the I think, the muscle-lung-brain connection. It's something that few of us suspected. But now there's just abundant evidence.

Sarah Smith: Well, that that's great, especially with the way that you, the way that you're meeting. And it's really not just about the, you know, that word exercise, because I mean, we find that. And prevention, too, that sometimes exercise feels like, okay, that's the thing you do for 30 min. And you sweat a lot. And maybe you have to go to the gym and forget it, right? But really, isn't it better to be moving more in general throughout the day? I mean, I don't know if there's specific aging brain related research on that. But that's what we tend to recommend information. Go for it, and then later go for another short one, you know, don't just sit all day after you went after you burned some calories. So after this, we're all going to get up and walk around. Okay, okay?

So before we get to questions, more questions from the audience. you know, you've mentioned clinical trials. We've talked about exciting things happening. And are there ways that any of us here today can get involved in that kind of thing to help this research and maybe benefit?

Steve Austad: Well, that's quite interesting. Yeah, there are places on the NIA's website that list the clinical trials. My thought is that the best thing? If you're interested in getting one of these clinical trials is to find out the researchers that are involved in them. See if you're eligible. And one of the things about clinical trials is that they all have eligibility criteria.

It might be that you need to be in a certain age range or not be taking these medications, or something. Certainly things like the TAME trial which is the metformin trial that that people are recruiting from. That's well known, you know AFAR has been very involved in in advocating for that trial, and certainly contacting afar would be one way to get connected with people that are running that trial. But for the others, I'd say the best thing to do would be to go online. Look for the trials and to find out who's running them, and then volunteer for them.

Sarah Smith: Well, that's great. I mean, I think that's a just such a good reminder that we can. We can be volunteering for it. We don't have to wait for people to necessarily sign to us. I'm gonna take some questions from our audience, and I have. There's an interesting one. That's sort of a big picture about the field. And the question is that sometimes ideas of longevity and health are intertwined.

So do you see the this field of aging research trying to help people live longer, shorten the time of ill health—is it both?

Steve Austad: Yeah, I think the we usually talk about living longer as a kind of shorthand for what we really mean, which is staying healthy longer. But it could. It's probably it's likely that if we come up with ways to keep people healthy longer they will live longer.

What we would really like to do is make people live longer, and when they eventually died, to die with virtually no period of ill health. And my thought is, if we could keep people healthy, closer to the end of their lives, that would be a tremendous help, even if they didn't live longer. so I think, in increasing health, prolonging health.

That's really what we're all about. It's just that. It's quite often easier to talk about longer life because it takes less explanation. But it's really longer health that the that the field is really pursuing.

Sarah Smith: Okay? And this is sort of related. That's helpful, you know. So are these potential therapeutics. Are they? Are they going to be targeting the biology of aging or the symptoms of aging.

Steve Austad: No, that's a key distinction. Thank you for that. So it's really targeting the biology of aging, and the good thing about that. The real benefit of this and this is a whole new style of thinking about health and medical intervention is, if you target the biology of aging, what you really are doing is potentially preventing or delaying all of the problems of aging at the same time. Whereas if you treat the symptoms of aging, because say, well, you know what if we can just delay people getting cancer? Well, that'd be great. But then that's going to be more. People will get heart disease.

You know, and if we, if we cured our disease well, that just means more. People get dimension and cancer, and all because you're only dealing with one thing at a time. If you target the biology aging which underlies all these things, plus many, many more, you know, muscle, weakness, osteoporosis, arthritis, all those things, then potentially, with a single approach, you can play these things as a group, and that would be the most massive health benefit that we that we could offer. Right?

Sarah Smith: I'm going to go back to some specific questions about the specific breakthroughs we talked about. So the senescent cells. What are some of the common diseases that they cause? I think maybe you mentioned that there were some that were related and... Is cancer in this discussion?

Steve Austad: Cancer is in the discussion. So this is what's interesting is, there's been so much interest in this across the National Institute of Health. Not just the people study aging with peaceful study all these diseases that the NIH is just started a 130 million dollar enormous network of program to actually map for all of the senescent cells in the body. There are specific diseases like idiopathic pulmonary fibro that are very clearly associated with cells in essence. But, as far as we know, even things like dementia, cardiac disease, a whole bunch of things could be associated with cells. We're again now. We can identify them better and better.

We're actually working to identify better or better markers. Because there are some markers that work good on some cell types and not so well on other types. so yes, cancer is in the is in the conversation all the disease arthritis. One of the first trials is going to, no doubt be an arthritis trial. So anything? That's because one of the things that senescent cells do is they cause inflammation and inflammation is at the basis of so many of the maladies of aging.

Sarah Smith: Right? That's a powerful thing to try to balance right? The problematic chronic inflammation versus the helpful. Right? So yeah. When we were talking about rapamycin and you brought up personalized medicine, you know, starting now, maybe being more part of our future. Do you think that

how people take the medicine or take the treatment matters like, is it a pill? Is it an injection? Can you get it from food? You know? What is? Is? Is that going to be part of what is being studied?

Steve Austad: That's probably not. Yeah. That is, people will get the medication in the way that it's best delivered, and by that I mean the way that it can get best get to the tissue in in the least invasive way. You know nobody wants to get a shot every day if they can take a pill every day. However, what I think we are going to be looking into is there a best time of the day to take your medicine. You know. Most of our jeans are turned off and on a daily rhythm.

But yeah, we don't really think of getting your chemotherapy, let's say at 8am rather than at 2pm. It's whenever you can manage to get your appointment, but it may turn out if there's a best time of day to take virtually any medication. But we haven't really investigated that very well. Usually medications are: we want you to take it this many times a day. And okay, it's best to take them with a meal, but nobody's really thinking about, "Well, this should be taken after 11 pm." But it wouldn't be at all inconceivable if it turned out there's a real best time of day to take your medication. And I think this is something. These biological clocks, which every cell in our body has, are going to be very much more important than we are thinking about them at this point.

Sarah Smith: Okay, here's another one on thoughts, on combining interventions. The question is about targeting more than one small molecule at a time or concurrent therapies.

Steve Austad: Yeah, I mean, it's quite likely, quite likely, that multiple interventions, multiple therapies will be more effective because it may be that this therapy attacks this part of the biology of aging, but not this other part of the biology of aging.

I mean one of the things we don't study in in our animal models, but it may. It may be that this is good for you if you exercise, but not if you don't exercise, and this is good if you don't exercise. But if you do so, there's that kind of multiple therapeutics as well. What else do you do in your life in this? Does that matter? Because it very likely could. You know, if you want to get big muscles. You want to take this therapy, but stay away from that therapy.

Sarah Smith: Alright. I think we're just about time to wrap up here. But if you could just send us off with to something, I mean, we've talked about a lot of things, and you could repeat something that you said. But what? What are you most excited and optimistic about as we go forward?

Steve Austad: Well, what I'm most excited about the fact that we're finally starting to try all the things that we know work so well in animals, out in people. And I think that you know some of them are going to fail. But we can't be discouraged because we know that, you know, progress takes a lot of failure. You need a lot of failure to get a success. But once we get this success, it's going to change everything. Once we have an intervention that really targets the biology of aging. We're looking at least 10 to 20 health more healthy years that's going to affect social relations that can everything in life in a good way, I would say, and that's likely to happen, you know, within our lifetime. And that's a I think, something that nobody else in human history is likely to have thought about.

Sarah Smith: That is very exciting, and I look forward to talking to you more, Steve, as these things, you know, develop, and we can look back on this one and say, "Gosh, remember when that was a just a mouse trial?" And here we are, you know, with a we're talking about taking it ourselves. So...

Steve Austad: It's always a joy and talk to you, Sarah.

Sarah Smith: Thank you so much, and thank you to everyone who joined us today. for this really great session, please. you know this is a regular series that we do, 'Live Better Longer,' and you can follow AFAR and Prevention on social media to keep up to date, and as always, please check out afar.org because it's a terrific organization that's doing great work and can always use our support. So, thank you, everyone, and enjoy your afternoon.