# Steven N. Austad, Ph.D.

Professor of Cellular and Structural Biology
The University of Texas Health Science Center at San Antonio
Interview transcript for *State of Tomorrow*™: Episode 9, *Aging with Dignity*

**What is gerontology?**

Gerontology is the study of the process of aging that can be studied at many levels. You can study it at the level of psychology. I happen to study the biology of aging.

**Why is it important to study aging?**

What's important [about the study of aging] is that it has enormous health implications. You can think of disease as the number one health problem in the U. S. Basically, all other diseases that we commonly die from, and get disabled by, are due to aging, but people usually don't think of it that way.

From a biological standpoint, it's also the neatest "big question" that we still don't have the answer to. If you think about the big questions in biology, [the question] "Why does virtually everything age?" strikes me as probably the most interesting.

**What have you discovered in your research on aging?**

The biggest thing that's surprising to me is that we discovered that by changing single genes in a whole bunch of different animals, we've been able to have major effects on how long they live — up to a six-fold increase in how long they live with the change of just one gene. Ten years ago if you had told me that was going to be the case, I would have said, 'No way. Impossible!'

I can explain it in layman's terms, but the point is "We really don't understand it." One of the genes that is changed in animals has to do with the way insulin is used in your body. How that translates into aging is still something that we're working on, but it seems to be a fairly general pattern. If you alter the insulin sensitivity that people have, it alters aging. But, it's a mystery exactly how that works.

**Tell me about the animals used in your research studies.**

I've got an unusual kind of research for the medical field. It's unusual in that I don't use traditional models. Traditionally, there are about three animals that get used for 93 percent of medical research — mice, fruit flies and rats. The animals typically are used in medical research don't age very well. They're very short-lived. They fall apart in a hurry. People study them because you can do a whole lifespan study in a short time.

My idea is that nature is smarter than we are. Nature has produced some ways to live long and stay healthy longer that we probably haven't thought of and we're not likely to discover by studying short-lived animals.

So, I look at animals that are exceptionally successful at aging: birds, bats, naked mole rats, things that people know little about except that they live a really long time.

Let's take a bat, for instance. Bats can live thirty or forty years in the wild. Now, a mouse in the laboratory just has to be able to crawl over the food dish. That's all it has to do to be able to stay alive. In the wild, a bat has to avoid predators. It has to find its prey. It has to go out and hunt, find its way back home. It has to be preserved in all kinds of functions. So there's an animal that's really successful at aging. It can teach us something that we're not going to learn from a mouse or a fly or a worm.

Hopefully we'll learn some novel mechanisms for how you keep animals from falling apart. We [humans] already do a pretty good job of aging. We live decades and decades and decades. So the idea is — Can we learn something to make us live even longer or stay healthier longer? I'm hoping we can learn by [looking at] something like a bat or a bird. If you calculate it the right way, they actually live longer than we do.

A lot of people think that oxygen is involved in aging. It produces these things called free radicals, which are really damaging to our cells. If you actually look at how much oxygen a bird or a bat processes in its lifetime, it's more than humans do. If there are novel mechanisms for preventing this kind of damage, or fixing it, that's a place we might be able to find that; so that's the rationale for what I do.

We're in the study's early stages. It used to be really difficult to do these studies because nobody knew the first thing about bats. But now, with this whole revolution in genome sequencing, pretty soon we're going to have a complete genome of a bat, which gives us many, many new tools to investigate how they operate. [It's] the same for marmosets, another animal that I work on. The genome sequence is almost done. Again, that opens up the whole sort of medical toolbox that we can use to investigate.

If we have a genome sequence — that's the sequence of every gene in the body, the order in which the DNA letters are arrayed — that gives us tools to fool with those genes, to manipulate them, like we can do in mice right now. It gives us tools for shutting down the action of a gene, maybe discovering novel forms of genes that we just don't see in humans or mice or the other animals. So that's the kind of tool having a complete genome sequence will give us.

**How did you get interested in the study of aging?**

I got into this [research] from a strange perspective. I was a field biologist and I was interested in social behavior. And, for completely unrelated reasons, I was studying opossums in South America. For that study, I had to recapture my opossums every month. I suddenly realized that they were aging at this phenomenal rate. I'd catch them; they'd look great. They were healthy adults. I'd catch them three months later and they looked horrible. They had parasites. They had arthritis. They had cataracts. They were falling apart.

I thought, "That's a really interesting question. Why would opossums age so fast relative to other things, like a housecat, which ages much, much more slowly?" And the more I dug into it, the more it struck me as one of the fundamental unanswered questions of biology. I think it's the "big enchilada." If you have to [ask] the big biological questions, this is the one that would change the way we think about biology and certainly dramatically change the way we think about human life.

**Is it possible to stop or slow down aging?**

I think stopping aging entirely is a pipedream. But, the Fountain of Youth? Slowing it dramatically? I don't think that's impossible or a pipedream at all. In fact, I think it's virtually a certainty that we'll discover, within the next few decades, ways to substantially slow down aging. And I say that because we've been successful already at doing it in so many different animals and in so many different ways.

We can do it by changing the diet, by changing genes, by using certain drugs. We don't know if any of this will translate to humans, but some of it is likely to. So I'm really confident that this is just over the horizon.

**What is caloric restriction and what role does it play in your research?**

Caloric restriction [is] cutting down on the amount of food that you eat, that's part of it. Now that's been shown to slow aging just about every way we can measure it: mental aging, muscle aging, immune aging. That's been shown to work really well in rats and mice and several other animals. We don't know if it's going to work in humans yet. If it does, then we have a whole approach.

People obviously are not going to eat 60 percent of what they want to eat. That's how we do this in animals. But this is going to show what's going on inside our bodies [and what] you need to change to slow aging. Then, hopefully, we can design pharmaceuticals to do the same thing. So you'll take your little caloric restriction pill every day that'll make you age more slowly. That's the hope.

If it's not caloric restriction, then there are ways to manipulate the insulin, which is involved in how we use energy. There are so many things that we're finding in animals, that some of that is going to turn out to be relevant to humans. We just don't know which of them so far.

**Is there any truth to stories of people living 120 years or more?**

One of the interesting things about human longevity is that, for years and years, there have been these stories of "lost tribes" — people from remote mountainous regions that live a very long time, up to 170 years.

There was a big article in *Life* magazine in the 1960s about this area of the Soviet Union where everybody lived to be 120, 130 years old. It turns out, when people really investigated that, it was all bogus. It was all fraudulent.

These people all had three things. They all had very, very Spartan diets, they worked very hard, and they had no birth records that were reliable at all. That was the key. If you don't know when you were born, the odds are you're going to be a 150 years old by the time you die.

Now, among things that we've really authenticated, one of the most interesting studies is going on in Okinawa. Now this island is in Japan. That island has the longest-lived group of people in the world. Japan is the longest-lived country in the world. On this island there are the longest-lived groups of Japanese. So, there are active studies going on trying to figure out what is it about them. Was it their diet? Have they got some special gene variants that we don't know about? What is it?

Right now, one of the ideas is that they were sort of self-restricting their diets because they weren't very successful at getting food. Now that some of the big fast food chains have moved into Okinawa, the younger generation seems to be not living as long as the older generation.

**Should we be using science to extend life?**

Some people are actually a little bit uneasy about this. They think, maybe, that we're tampering with something that we shouldn't be tampering with. The practical applications are enormous. Let's just imagine that we've increased our life expectancy by twenty or thirty years. So life expectancy is 100 and people occasionally live to a 150. That would change everything you can think of: the way we live, the way we interact and family structures.

You might live with five or six generations of your family. It would change our career choices. You might have a career for forty or fifty years and say, “Ah, now I’m going to go do something I really want to do.” [You] have another career and another career after that. I can’t imagine anything that would change human life more dramatically.

Now about this ethical unease. If you think about it, what we’re really trying to do is extend human health. That’s what all medical research is doing. Medical research is sort of tampering with nature right at its base because it’s trying to keep you from dying from infections, keep you from dying of a heart attack, keep you from getting cancer. So, aging research is just doing this in really a more efficient way. Because if you can cure aging or if you can slow it, then you can really delay or prevent a whole host of disabilities and diseases.

I think people in my field have been sort of responsible for this unease because they’ve tended to focus on extending life. But everybody, if you ask them, [will say] that’s not really what they’re after. It’s extending health. And it turns out, from a lot of animal research that we know, if you extend health, then you automatically extend life. But that’s not really the goal of the research. The goal of the research is extending healthy life.

Nobody wants to keep people around longer who are in semi-vegetative states. That’s really not a goal that we would be interested in pursuing.

**What do researchers hope to gain by studying aging?**

There is hope for specific disease like Alzheimer’s disease from looking at aging, generally. In fact, if you only look at diseases one at a time, you’re really asking for a catastrophe, because up to 50 percent of people over the age of 85 have Alzheimer’s disease now. If we just create more and more people of that age and we don’t do anything about a really serious disease like Alzheimer’s disease, that’s a huge public health problem and a huge problem, of course, to many people on a personal level.

Here’s the thing: Alzheimer’s is a disease of aging. If we can slow down aging, we can prevent the onset of Alzheimer’s disease for longer and longer and longer. There’s going to be some advances for people who are looking very specifically at Alzheimer’s disease. But there are also going to be advantages in preventing Alzheimer’s disease that just come about because we’ve been able to slow aging generally.

**What are some of the main ideas in your book *Why We Age*?**

Some of the main ideas in my book? There are animals of great interest to aging research that nobody’s investigating. Now I’ve begun doing that. Humans should be skeptical about products that are out there right now that claim to slow aging because none of them have been shown to do that, despite what they might say. But the future looks extremely bright for being able to slow aging in the future. And that’s really what the message of my book was. Don’t get too giddy about things that are around right now, but be very hopeful about things that’ll be around in the next few decades.

**Tell me about the Barshop Institute for Aging and Longevity Studies.**

The Barshop Institute — where you bring together a whole bunch of researchers who are focused on a field like aging — is really something that is ahead of its time. It’s a unique Institution. It’s the reason that I came here.

The idea is [that] aging is a complex field and involves every organ in your body. It involves genetics. It involves diet. You really need a big group of people to attack it from a bunch of different angles. To do that, you need an Institution that really has different investigators that focus on the same thing. The Barshop is the kind of Institute that’s ultimately going to be critical to solving this problem.

**What are these researchers studying?**

People are looking at mutant kinds of mice that live longer. They're looking at the chemicals in their body. They're looking at their cells to see if they can understand how they live longer. They're trying to discover new genes that might be involved in aging.

And here's an important point that I think also makes people uneasy. When we talk about changing a gene and changing aging, people automatically think, "Well, are these mad scientists planning on tinkering with our genes to make us live longer?" The answer is "No. No. That's just a tool."

What we want to do is find [information]. Genes just produce chemicals. What we want to do is use those genes to find the key chemicals that we need to address with drugs [in order] to slow the aging rate. So there are people doing that. There are people looking at how your body gets damaged as you get old and how to change that.

**How does the body get damaged and is there a way to stop or slow that damage?**

One of the big kinds of damage is damage due to these oxygen radicals. "Are there antioxidants that are particularly effective, for instance, at preventing or curing that kind of damage?" That's what all the people that you see walking around this building [are asking]. They're all struggling with some small piece of a puzzle that ultimately is going to be put together by the collection of researchers.

We take our food and our oxygen. We combine it and we get energy. But a byproduct of that is oxygen radicals, which are very damaging. So oxygen is both a source of life to us. But it's also a poison.

Many antioxidants have evolved in our bodies, and there are others in our diet that are preventive for these things. The idea is — "How do you prevent this damage?" Now, I have to tell you that just gobbling great amounts of antioxidants has been studied a lot now, and those do not seem to have any effect on how long people live. It's been quite disappointing. But those aren't the only kinds of antioxidants. There are also the ones that are produced inside our cells by our bodies. And, there are some — that some animals have — that work more effectively than those other animals have. So the idea is, ultimately, to discover which ones are the most effective. How do you target them to the most effective places?.Can you produce some sort of supplement, antioxidant that really works?.The stuff we have now — there's no evidence that it really does anything except make the people very rich who produce them.

**Let's talk about some of the animals in your research studies.**

One of the animals that we work on here is called the naked mole rate, one of the ugliest critters in creation. And just like my opossums, people started studying them because they have this unusual feature of their life, which is that they live in big social colonies like honeybees. Most of them are sterile workers. There's just a queen and a king and they make all the babies of the colony.

People were interested in them because of their social life, but they found out, by accident, that they live a really long time. They live until their mid to late twenties, maybe even longer. They're about the same size, but ten times as ugly, as a mouse. They also live about ten times as long as a mouse. And they seem to be extremely adaptable to the laboratory. So that's going to be one of the key animals that we investigate — to try to figure out how you take something that lives this amount of time and make it live ten times that amount of time. I don't really anticipate we'll be able to make humans live ten times as long as we do now, but you never know.

**Does body size affect longevity?**

There's a complicated relationship between body size and longevity. If you look across animals, generally the smaller you are, the shorter-lived you are. And that's one of the reasons that the mole rats and the bats are so interesting. They're really tiny. They have a really high metabolism, meaning they are burning lots of oxygen, but they live a really long time. Larger animals, on the whole, live longer than smaller animals.

Humans, though, are kind of exceptional because they live much longer than they should for their body size. So what this means is, if you calculate how long things live by how big they are, something like a naked mole rat or a bat is actually, substantially, longer-lived than a human.

Now, the other interesting thing is that within a species there is some evidence that smaller animals live longer. And this is a great hope in humans, [especially] for those of us who are not too big to begin with. We don't know if that's true with humans. The data are a mess. But in mice, if you make them smaller by restricting their diet or by altering them genetically, they live longer. [It's] the same with dogs. Your little Pekinese is going to live longer than somebody's Great Dane, and it ages more slowly as well. This is one of the amazing things. Something like a dog, that we know so much about and people care about, yet we still don't have the faintest clue as to why little ones age more slowly than big ones. It's something that I hope we can get going here at some point.

Rats. Smaller rats live longer than larger rats. Even horses. There are some breeds of horses that are tiny that live much longer than your regular horse. So the whole body size, longevity thing is complicated.

**What is the difference between "health-span" and "lifespan"?**

A health-span would be the number of years that you live where you're healthy, where you can do all of the things that you need to do to lead a normal life, as opposed to lifespan, which could include a long period of disease and disability. What we would like to do, of course, is shorten that part of the life and lengthen the healthy part of the life. It's not clear that you can get rid of that time of disease and disability at the end, but it is quite clear, at least in animals, that you can extend the healthy part of the life dramatically.

**Which has the greater influence on how we age — genetics or environment?**

Genetics versus environment is pretty interesting. We know a lot about that. You hear this cliché: "To live a long life is to have long-lived parents." And that's true within limits. About a quarter of the differences in how long we live is due to genes, is due to who your parents and your grandparents were. But that means three-quarters of it is due to something else.

Environment — now, some of it might be environment that we can't do much about, like the environment when you were in your mother's uterus. But clearly, we can do a lot about our environment after we're born. So that's where there's really great hope for just changing lifestyles, changing dietary habits, maybe developing pharmaceuticals and living healthier lives.

One of the interesting things is exercise. You know, exercise has a very marginal effect on how long people live. It's only about as long as you spend exercising. That is, the optimal amount of exercise, if you calculate it over your lifetime, will give you about an extra two years of life, which is about how much you have to spend exercising. So that's not so encouraging.

But what exercise does is, it keeps you functional longer. So if you want to be healthy when you're 70 and 80 years old, you want to be able to play with your grandkids, carry them up the stairs, then exercise is the key to that. It's not the key to living to be a hundred years old. You know, 100-year-old people are not those people who are running marathons their whole life.

So how can you do the best with the genetic endowment that you've got right now?.Right now the best thing we can tell you is the familiar, old, boring stuff that your mother probably told you. Don't eat too much. Get plenty of exercise. Don't smoke. Drink moderately. That kind of stuff is the best advice we have today. Come back to me ten or twenty years from now and I'm likely to say something completely different.

**What about the social consequences of aging? Is there any research being done in this area?**

The social, psychological, care-giving issues concerned with aging are a different field. Most scientists, most biologists at least, are very myopic. They really focus on their small problem. I've been forced to look a little bit more broadly because I was asked by the President's Council on Bioethics to come and justify to them why we should be working on slowing human aging. So I've probably given this a little more thought than most of my colleagues.

I think we should be interested in that. I think anybody working on this problem ought to be forced, once a year at least, to go out to a nursing home, a place where a whole bunch of people with Alzheimer's disease and their families are, because it reminds us of the kind of thing that we're trying to help people with. If you just see your laboratory animals all the time, it's easy to forget that.

**Are society's attitudes changing about aging?**

I've heard the saying that the sixties are the [new] forties, but I thought it was seventy that was the new fifty! I think it's true. Even without any dramatic breakthroughs, the way we think about aging, and the way people who are aging behave, have changed dramatically. And it's probably because of the Baby Boomer generation. This huge group of people that's had everything their way their whole lives is now reaching that age where we used to think of people as elderly.

It's now not unusual to hear of 65-year-olds running the Boston Marathon. Twenty years ago that would have been newsworthy, but now you have to be 85 years old to get in the newspaper because you ran in the Boston Marathon. You see people playing basketball and doing things that you never would have guessed twenty or thirty years ago. And in fact, the demographers who study the amount of disability have said, even in the last twenty years, a 60-, or 70- or 80-year-old is much healthier than they were twenty years ago.

So there's been dramatic changes in our ability to keep people healthy, and also attitudinal changes — what's appropriate for people that [once were considered] elderly, like the new 50 is 70. Those sorts of things are different now, and I think that's a great thing. [In terms of] my own personal experience with aging in my family, my parents both died in their early 80s, but, thankfully, they didn't have long periods of disability.

For the longest time, when I was studying aging, I never even thought about people. I just thought about this really intriguing biological puzzle. But the more I've been forced to confront what's going on in my own family, and people asking me about the social implications of what I do, it really has forced me to think more and more in personal terms. And then, of course, I'm getting older myself and that also makes you [more aware].

You like to think that you don't change with age, but suddenly you wake up, you look in the mirror, you go, "Wait a second!" You know, "Who is that person?"

I was in a pharmacy not long ago and the person ahead had to give her birth date to the pharmacist and I realized she was the same age as I was. I thought she was really much older. It was kind of a shock, you know. It's one of those things that happens, that you don't think about very often. But when you do, it's a shock. It makes me think, "I've got to hurry with my research before it's too late for me."

**If your animal research reveals important findings about aging, what's the next step?**

Let's imagine that we've discovered a compound that slows aging in a mouse. Now, are we going to be ready to suddenly recommend that people try that? Well, mice aren't people; they're really very different, although to some biologists mice are just people with fur and a tail. It's really more complicated.

So the idea is “What do you do next?” Well one of the things that we have decided to pursue is developing an animal for testing these kinds of compounds that’s a primate like we are. It’s related to us, but it’s small and it has a short life. This is a marmoset. They’re about the size of a rat but they’re a primate. The thing is, they only live ten to fifteen years. So if we started giving this compound that we hope slows aging to a marmoset when it was five, we ought to be able to tell if it’s having an effect by the time it’s ten.

So, studying these small, unusual primates is to have a stepping stone to develop things that work in mice. If it works in a primate, then you might be ready to suggest, “Okay. It’s time to try this out in humans.” Or, suggest that humans might want to start doing it themselves.

So that’s the big question: “Why does aging occur?” Is it somehow beneficial — biologically beneficial? And the answer is “No. It isn’t.” It’s a byproduct of things that are going on in our body that are beneficial: eating, breathing, reproducing — all of those things. But there’s no evidence that aging is a good thing for any animal.

**What does the future hold?**

We can perceive the future more than any animal can, and that, I think, is one of the reasons that we’ve focused on this problem. Animals, even if they have fairly sophisticated worlds, don’t think, I’m sure, about getting older. But we do, and we would really like to see if we could, at least, make it take longer for us to get older.