Introducing Episode Two: What to Eat & When to Eat for Longevity

0:00
[sci-fi music] - Welcome, to the Lifespan Podcast, where we discuss the science of aging and how to be healthier at any stage of life.
0:09
I'm David Sinclair. I'm a professor at Harvard medical school who researches the biology of aging
0:16
and I'm co-director of the center for the biology of aging. And I'm joined by my co-host and co author,
0:22
Matthew LaPlante. - Hey, we're back. - Hey, welcome. Good to see you again. - Good to see you again too.
0:28
- This is episode two. We're going to be covering when to eat and also what to eat within 24 hour periods,
0:36
as well as over a year, not just to maximize your wellness and how you feel and look,
0:41
but how to maximize your overall longevity. I'm going to talk about some of my protocols as well,
0:46
that I've developed over the last 20 years, being a researcher in this area and what works for me
0:52
and what might work for you, as well. If you missed episode one, don't worry, we're going to cover the basics here,
0:58
but you might want to go back and listen to episode one, because we cover some of the fundamental biology that may help you understand what we're going to talk
1:04
about today, even in more detail. So Matt, how've you been, man? - I'm good.

Thanking the Sponsors

1:10
Before we get started, we got got to thank the sponsors. - We do, let's go straight into that. - Yeah. - It's important that we thank
1:17
the sponsors because this podcast comes to you free. And we also get a chance to highlight some of the products
1:22
that we love and have been using, now for many years. Our first sponsor is "Levels".
1:27
Levels is an app that syncs with a continuous glucose monitor, which they provide and interprets your glucose data for you.
1:34
I've been so impressed by Levels that I've recently joined the company as an advisor, by monitoring your blood glucose,
1:40

Levels allows you to see how different foods impact you. I've had fun running tests of my own,
1:45
seeing how different foods impact my blood sugar levels. For example, I've learned that white rice and grapes really spike my blood sugar,
1:52
whereas potatoes don't, as we've discussed on this podcast, having stable blood glucose is really important,
1:58
not only for your daily mental and physical energy but also for long-term health. If you would like to try Levels,
2:05
you can skip the 150,000 people on the wait list and join them today. By going to levels.link/sinclair
2:13
that's levels.link/sinclair today's podcast is also brought to us by "Athletic Greens".
2:20
Athletic greens is an all in one daily green strength that supports better health and peak performance.
2:26
It's developed from a complex blend of 75 vitamins, minerals and whole food sourced ingredients.
2:31
It's filled with adaptogens for recovery, probiotics, prebiotics and digestive enzymes for gut health.
2:38
They also have vitamin C and zinc citrate for immune support. I've been drinking Athletic Greens
2:44
for a number of years now, as a way to cover all my nutritional bases. I'm often traveling
2:49
and sometimes my diet just isn't the best. So by drinking Athletic Greens every morning, I know I'm getting all the vitamins minerals
2:56
that I need to stay healthy. If you'd like to try Athletic Greens, you should go to athleticgreens.com/sinclair
3:03
and you can claim a special offer. They're giving five free travel packs plus a year's supply
3:08
of vitamin D3 and K2 . Vitamin D3 is important for the immune system and vitamin K2 is really important
3:14
for keeping the calcium out of your arteries and putting it into your bones where it belongs. So again, go to athleticgreens.com/sinclair
3:22
and claim this special offer. Today's podcast is also brought to us by "Inside Tracker".
3:28
Inside tracker is a personalized nutrition platform that analyzes data from your blood and your DNA
3:34
to help you better understand your body and to reach your health goals. I've been using Inside Tracker for over a decade now
3:41
and I'm the chair of their scientific advisory board. The reason I've long used Inside Tracker is
3:46

because they provide the best blood and DNA analysis that I'm aware of. They make it easy to get your blood drawn.
3:52
You can either go to a local clinic or like I do have someone come to your home it only takes 10 or 15 minutes.
3:59
It's really easy. And from their Inside Tracker presents your blood analysis in an easy to understand way.
4:04
There are graphs and they give you diet and lifestyle recommendations that help you improve your blood biomarkers.
4:10
Another feature that Inside Tracker has is their inner age test, which I helped develop.
4:15
The test shows you what your biological age is, how it compares to your chronological age
4:20
and what you can do to improve that number. So, if you'd like to try Inside Tracker, you should visit them at insidetracker.com/sinclair
4:29
and you'll get 25% off any Inside Tracker plan. Use the code Sinclair, my last name, at the checkout.

A Starting Place for Longevity: Eat Less Often

4:36
- Okay, so, David, when we sat down together,
4:42
three, four years ago, we started mapping out this book and I said, look, I need you to give me one starting place,
4:49
when we're talking about health advice. Like, there's so much health information out there. I need you to give me one starting place.
4:55
And you said immediately, [murmurs], I know, the one thing. So, let's start there, today - Right.
5:01
- because it relates to this episode. The one starting place. - Is, wait for it, drum roll.
5:07
- Drum roll, for longevity, the one starting place is? - Eat less often.
5:12
Those three words, eat less often. That is the one thing that will have the biggest impact on your longevity based on all the science we'll talk
5:18
about today. - Okay, and this doesn't mean eat fewer calories,
5:24
- It can. - necessarily. [overlapped chatter] - that's good. But a lot of people struggle to do that
5:31
to if you were calorie. - Well, it comes naturally. If you're down to one meal a day, which I am now,
5:36
you shed weight and then you get your 20 year old body back. That's a nice bonus.
5:41

But then you maintain that weight. You have a larger dinner, which is what I do to make sure I'm not
5:47
becoming malnourished. Clearly, we're not talking about malnutrition or starvation here.
5:52
It's about packing your calories into a shorter period of time. - That's because packing your meals into a shorter period,
6:00
almost inevitably means less calories, but that's not really what's happening here, right?
6:06
It's not just about less calories. It's about, what eating less
6:12
often does inside of our bodies. - Right, and we'll get to that. But really, it's not just about the period of eating.
6:18
It's the period of not eating that's so important for boosting the body's defenses against aging to maximize longevity and we'll talk about
6:25
how that actually works in a minute, but you can still have a large body
6:30
and fast and get the benefits. In my lab, we've looked at mice that are obese and trick them into thinking
6:36
that they're fasted and they live just as long as a skinny mouse. So really, it's about getting your body
6:42
into this state of defense at any weight, though, I would say that, there are certain optimal body weights that,
6:48
it's clear that if you're carrying excess weight, you're going to accelerate your aging clock. - What we don't want people to do is get the idea
6:55
though that, oh, good, this works even if you're overweight
7:00
and so I can stay overweight and then as long as I fast a little, it's going to be fine.
7:06
That's not what you're saying also. - Right, there are certain body weights,
7:12
waist to height ratio's are optimal, for humans is about 0.5. But yeah, losing weight is helpful,
7:18
we're not fat shaming, anybody, but we're going through the science. This podcast is about what the science says
7:23
not what's socially acceptable. And it is true that if you're leaner, you will live longer. That is a fact.
7:29
It's not necessary to get benefits by doing what we're going to say.
7:34
But also interestingly, as a side effect of eating less often, you will lose weight. I did, I've shed about 15 pounds
7:41
since the beginning of the pandemic and I look better, I feel better. And it's a nice side effect,

7:46
but ultimately what we're going to do here is, we're going to say, these are the kind of things you should consider in your lifestyle.
7:52
We're going to help you get there. We're going to ease you into it. There are some tricks that make it easier.
7:57
And ultimately you're going to end up with a lifestyle and hopefully a body that allows you to live decades longer.

Caloric Restriction is an Evolutionarily Conserved Anti-Aging Strategy

8:04
- We made the promise on this program to really stick to the science, to let people know when the science is coming
8:10
from studies involving animals. When the science is coming from studies involving human beings, the caveat here is really important.
8:17
Most fasting research has been conducted so far on model organisms,
8:24
but what we're seeing in those model organisms is fairly universal.
8:29
- Well, it is and the most reliable way to extend lifespan of any animal
8:34
or even a yeast cell is to restrict its calories. - Well, let's start there. 'Cause you started your career in yeast,
8:40
you still study yeast. And one of the really big breakthroughs
8:46
in understanding, how to extend the yeasts lifespan came
8:54
in your lab when you were studying, what happens when yeast are calorie restricted.
8:59
- Right, and that was the goal. The reason I went into aging research in part and why I was so optimistic about being able
9:05
to have a big impact is that we know that restricting calories works on everything from a yeast to a spider, a fish,
9:12
a worm, pet Labradors, and it was 2002, there was a great study
9:17
that showed you could lengthen lifespan of the Labradors from, what was it, 12 years to 14. - [indistinct] 1.8 Years.
9:24
And the only difference really was a 25% reduction in calories, in that study. - That's remarkable. So I went to MIT in the 90s saying,
9:31

I want to figure out how the heck this stuff works. How does this diet work? Because then we can bottle it. And we're basically at that point now,
9:38
but to your point, just taking a pill, isn't sufficient. If you add the pills, plus the diet, you get an additive, doubling effect.
9:46
So, we're going to go through supplements in another episode. Today, it's all about how to maximize when
9:51
to eat and what to eat. - And that's really important because not everybody can take supplements,

Dietary Longevity Strategies are Accessible (and Save Money)

9:56
not everybody can access the supplement. What, we're going to talk about a lot of things,
10:02
including things that you can do with $10 in your pocket and things you can do in a $100 in your pocket.
10:07
But this is something you could do with whatever you're paying right now, for food. - Well,
10:12
it saves money actually, - You can do it. It doesn't say [mumbling] spend less on food. - Right, and the kinds of food we're going to recommend
10:18
are fairly cheap foods. But getting back to yeast, I went to MIT to study this little fungus. It's a yeast cell you use to make bread and beer.
10:26
It's microscopic, put 10 of them together, you might see them as a little dot. That's a small they are, but I used to love yeast.
10:32
Literally, I would name them. there were little pets under the microscope. I'd follow them through their lifespan. - That's adorable [chuckles].
10:39
Yeah, I would get really sad when they would die after about a week 'cause I got to know them. [Matthew laughing] I would spend 14,
10:45
actually more, probably 16 hours a day, helping them along in their life, taking away their daughters, which is how we count.
10:52
- You know, David, if you love something, you really shouldn't take its children away. - Yeah. - That's pretty messed up.
10:57
- That's true, if you leave the daughters, unfortunately there's about 5 million
11:02
of them by the end of the experiment. And you can't find the original mother, that's- - So, these things, they divide and they expand and they expand.
11:09
- Exponentially, right? So, you've got to get rid of those daughters. You don't kill the daughters, you just move them away. But what we found was that when you reduce the amount

11:15
of sugar in the plate, so they eat glucose. This is what we gave them. 2% glucose makes them live about 25 divisions, daughters.
11:24
If you restrict that down to 0.5 glucose, So, you are down to 25% of that concentration,
11:29
they will live over 30. And, that's really cool, right? That you can, just by changing the glucose levels,
11:35
and we'll get to how that works in humans, very similar, you can extend life span. And what we showed was that there's a set of genes

A Low Energy State Triggers a Genetic Pathway Involving Sirtuin Activation

11:41
that controls that process. This isn't just glucose hurting the cell. There's a genetic pathway that gets triggered by low energy.
11:50
And these genes, we talked about in last episode, they called "sirtuins" and there are five of these genes
11:56
in yeast and seven in our bodies. And they respond to low energy. They're respond to other stresses as well,
12:02
such as high heat, low amino acids, high salt.
12:07
The sirtuins will get activated by these, what we call hormetic effects.
12:12
What doesn't kill them, makes them stronger. And in this case, low energy led to the activation
12:17
of these enzymes called sirtuins. And then they took care of the DNA repair
12:23
and also stabilization of the epigenome. Now- - There's a lot there,
12:28
let's slow this down and pace this out. Let's start with sirtuins. What's actually happening when,
12:35
in the case of yeast or any organism in this case, because it's very similar mechanisms, right? What's actually happening with sirtuins,
12:41
when yeast or any other model organism is calorie restricted, is fasted.
12:47
- Yeah, well their role is to extend the lifespan. So, what they're doing down at the very minute part of the cell,
12:53
is they're protecting DNA and making sure genes stay "on" when they should be "on", but what's happening to boost their activity
13:01
during caloric restriction, this low glucose level. We managed to figure out in the first couple of years,
13:06

when I moved my lab to Harvard Medical School, well, started my lab at Harvard Medical School. We found that low energy activates a certain gene.

NAD+ is Elevated by a Low Energy State

13:16
It has a name, it's called PNC-1. We have an equivalent gene in our bodies called NAMPT
13:21
and turning on that PNC-1 gene in yeast was able to activate the sirtuins because that gene makes a fuel
13:29
for the sirtuins called NAD. And so in our bodies as well, when we're hungry,
13:35
these genes come on that make more NAD, this very small molecule that the sirtuins need for fuel.
13:41
And then they do the protection. They repair DNA and they stabilize the epigenome.
13:47
- And this is the beginning plays that led to NAD boosters,
13:52
where we started going, oh, well, if we can boost NAD in other ways, and that's not, we'll talk about boosters in another episode,
14:00
but just to put that in the chronology of how this revelation came about
14:05
and why so many people are now taking the NR and NMN. - Yeah, that came out of our lab. We found two ways to activate the sirtuins synthetically.
14:12
One was to use the red wine molecule, resveratrol plus some other plant molecules that are now used in supplement market.
14:19
And that was a big craze in the 2000s from our lab. And then the second one, which is now, probably an even bigger craze is the NAD booster.
14:26
And a lot of people are shooting themselves up with NAD or taking NAD, precursor supplements.
14:32
You mentioned NR and NMN, we'll get to those in another episode. But you can mimic low glucose
14:37
in these yeast cells by giving them these NAD boosters. Or you can turn on this PNC-1 gene artificially,
14:43
and they live longer in all cases. And we found that if we deleted that sirtuin gene in the yeast,
14:50
either one of them or multiple ones, then caloric restriction in the yeast didn't work anymore,
14:57
which showed us, told us that this wasn't just glucose being bad for you. Glucose doesn't hurt you, it's that the low glucose
15:04
is activating the natural defense state of that cell, which we have inherited over the billions
15:10

of years, since we separated. - People who are just going to cut out that little part where you just say, glucose, isn't bad for you. And they're just going to play that on a loop
15:17
and it's going to be great [chuckles]. - All right, well, glucose is bad for you but not for the reason that you might think.
15:22
- So, we have a little better understanding now of how sirtuins are turned on by fasting.

Fasting, mTOR, and AMPK

15:29
We talked about two other classes of longevity genes in the first episode,
15:34
mTOR and AMPK, do you want to go really briefly through how these genes are impacted
15:41
when we restrict calories, when we fast? - The first one is mTOR, which stands for mammalian target of rapamycin,
15:48
the drug rapamycin. We talked a little bit about it in the last episode, but let's refresh everybody's memory.
15:54
This is protein complex in the cell that registers amino acids. When you have a lot of protein, you eat a big steak.
16:01
It's going to activate this mTOR protein complex that allows the cell, causes the cell to build things.
16:07
It's one of the reasons eating steak allows you to build more muscle, but that's not a recipe for longevity.
16:13
What we know from many animal studies, even in yeast, if you downregulate the activity of this mTOR protein complex, you get longer life.
16:21
Why? Because it's activating a process called autophagy, which recycles proteins. So when you're hungry,
16:27
this autophagy will get all the old proteins, put them in the recycling bin and then bring them out as fresh proteins.
16:34
And that seems to be really important for longevity. In fact, even if you just inhibit mTOR and stimulate autophagy, that's sufficient
16:41
to extend the lifespan of flies and even mice by dramatic amounts, even 30%.
16:46
- So, [indistinct] mTOR, we start with fasting, we get longevity and sirtuins. We start with fascinating, we get longevity in AMPK,
16:54
- Same thing. - Same thing. - But in this- - But in a different process. - Exactly, it's doing something else. Right. - And in this case,
17:00

when you're hungry, AMPK will go up. AMPK, if you're wondering, it stands for AMP-activated kinase,
17:06
and that's just an enzyme that responds to low energy. So when you're hungry, you'll make more of it. And one of the main things that it does is
17:12
it makes more mitochondria. We lose mitochondria as we get older. And when we exercise, we get more,
17:19
and this is a way of artificially stimulating that production. Why do we need more mitochondria?
17:24
Well, they're important for metabolizing things that you eat but one of the main things that they are used for is to make energy, chemical energy.
17:32
So, when you activate AMPK, you'll feel better. You'll have more energy and you also fight aging.

Data in Humans vs. Model Organisms

17:37
- And you're using the words "you'll" a lot here. You're talking about like, presumably the people watching and listening
17:43
to this are human beings, but we should note that,
17:49
again, much of this research got done in model organisms. Human studies are a lot tougher.
17:58
- But we have them for humans. - We do have them for human, but there are fewer of them. And there's like, most of the sample sizes are much smaller.
18:05
- Yeah, but there's enough known about both mTOR and MPK to make pretty strong conclusions
18:11
that these are beneficial to human health as well. - For example- - But this is, I guess what I'm getting at here though,
18:16
is the reason why, I think a lot of people that would hear, well, there's all these animals studies,
18:23
we're making all these conclusions on animal studies and you don't have that many human studies,
18:28
but human studies are, they take a really long time. They're really expensive.
18:34
- Well, sure, and until this is a 100% proven, many of us will be dead. So the point is, we're going to give people the information
18:41
in this podcast, in the notes, we're going to provide references. They can read more to make informed decisions about whether they're going to try certain diets,
18:48
lifestyles and even medicines and supplements. - So, what we know from studies of mTOR and AMPK,
18:57
sirtuins is, tells our cells that times are tough. This triggers this metabolic shift

19:03
into a different form of energy, and all of that, not all of that,
19:09
but much of that we know from animal studies that we mentioned before. The majority of the research
19:14
on lifespan extension comes from model organisms, comes from animals that aren't us.
19:21
But we're not just entering, we're in a world right now, where we're doing this research on human beings as well.
19:29
- We are, it's a fascinating time because we've got two worlds and I walk in both worlds.
19:34
One is, there's clinical studies being done, some of which I'm involved in with NAD boosters at Harvard,
19:40
we've been testing two years of those in humans, placebo controlled, double blind trial.
19:45
- Like the gold standard stuff. - Right, and those go to scientific publications. But, because people can read the literature
19:51
and hear about things, there's this self experimentation world as well. A lot of it on the west coast of the USA
19:57
[Matthew laughs] and you hear stuff, and these are anecdotal but they also are interesting anecdotes that guide the clinical trials.
20:05
And it's this very interesting time where we're in, where there are parts of the population, let's call it 1% of the US that is not waiting
20:12
for the proof that this works. But I do want to say before we move on that there is pretty good evidence
20:18
that modulating these defenses in the body in humans also works
20:24
and should extend longevity. We're not just blind [stammers], I'm not crazy experimenting on myself and my father.
20:31
What we know, actually is that drugs that inhibit mTOR, rapamycin
20:37
in low dose, intermittent does mimic fasting and does boost immunity and does give biochemical changes
20:44
that mimic fasting and predict longevity. And there are people that are taking rapamycin.
20:50
Again, we'll talk about that in episode five. But there's also metformin, which is a diabetes drug and that activates AMPK.
20:58
And that's also by looking at tens of thousands of people, who take metformin for type two diabetes, been shown to slow down the occurrence,
21:05

not just of diabetes, but other diseases of aging. Together, just those facts
21:11
that I've told you make me convinced that fasting and the drugs
21:17
that mimic fasting are going to be important for long-term health but also wellness in your body today.

Evidence that Fasting is a Pro-longevity Intervention in Humans

21:24
- There's this other way of knowing, this other form of evidence for this that we haven't talked about yet, that I think is important to bring up here.
21:31
There's the double blind, placebo controlled studies that are ongoing right now that are showing
21:37
an impact in fasting on longevity. There's like you say, experimental, really interesting, like, wow,
21:43
that guy is looking really good and he's been fasting, sort of thing, right? - Yeah. - But then there's these,
21:48
large populations and subgroups of populations, all across the world
21:53
who have fasted as a part of tradition and culture for hundreds, thousands of years.
22:01
And there's pretty good evidence from these groups as well. - Right, well, let's name some of them.
22:07
- The genes in India. - In India. They're probably the most well-studied group.
22:12
And there's scientific evidence that they have the most number of people over 70 in good health than any other religion.
22:18
- Than any other group in India. - Fair enough. - And a lot of people [indistinct] go, oh, well, the genes are often are also vegetarian,
22:24
but lots of people in India are vegetarian and the genes are even doing better than them. - Yes, and we'll get to the vegetarian diet
22:31
and what the science says about that, versus a meat based diet. But there are other religions of, Christians fast, there's the Ramadan for Muslims.
22:39
These are not just coincidences, these aren't just religious practices. It's clear that humanity has figured out
22:45
that you feel better. You look better, you ultimately are disease resistant. It might even help cure diseases by going
22:51
through these periods of being hungry or at least not having food in your tummy. Why?
22:57
Because it activates these three longevity defenses that we just mentioned.
23:02

- Now, let's get into these really interesting, sort of gold standard studies.
23:07
There is one out of the Baylor College of Medicine. It was run by [indistinct].
23:14
This was published just last year. And it showed that fasting from Dawn to sunset
23:20
for four weeks improved blood pressure, reduced BMI, decreased weight circumference and,
23:27
and this is the important part. I mean, it's all important, but it upregulated DNA repair proteins.
23:33
This is what we saw on all these model organisms as well. - Yeah, there are dozens of studies showing
23:39
that periods of fasting is beneficial to people who are obese,
23:45
not just because they lose weight, but they turn on their body's defenses. They become more insulin sensitive. And their glucose levels come down.
23:51
Also showing that people of regular weight, like me, can benefit from fasting, there's a number of studies there.
23:57
And these were all in the show notes. If somebody wants to go and check them out, but what's really interesting is that certain diseases, type one diabetes,

Evidence that Fasting can Attenuate Human Disease

24:05
multiple sclerosis even cancer, those diseases seem to also benefit from fasting,
24:11
including when you combine chemotherapy with fasting, you get this double benefit for many types of cancers.
24:17
And then the final point that I think is really interesting is you can mimic fasting, say metformin, a number of doctors prescribe metformin
24:24
to patients with prostate cancer, because more studies are showing that these mimicry,
24:30
these molecules that mimic fasting or fasting or combinations of both will help you beat cancer.
24:36
- And to you, when you see a bunch of different disease states being affected.
24:43
You don't think that what's happening is that each of these individual diseases is being played upon. You think that the thing upstream,
24:49
the aging is being affected, right? - Yeah, well, most specifically those three defense
24:55
components in the cell, they take care of the body, not just for aging but to fight diseases in young people, middle-aged,
25:02

genetic diseases, even something you might not think of, like macular degeneration has been shown to be slowed down and even reversed by fasting.

Different Fasting Regimens

25:11
- Okay, so far we've been really broadly talking about fasting, calorie restriction
25:19
but we haven't talked about what that actually means.
25:25
Let's talk about, because there's a lot, I mean, if somebody goes online right now, they're going to say like, how should I fast?
25:31
They're going to get a thousand different recommendations. - It's confusing for sure. - It's really confusing. Do you want to just talk about what some
25:37
of these fasting regimens are? - For sure, let's do that. And we talk about them in our books
25:43
so that that's also our resource. I get questions every day from people. How should I fast?
25:49
And my first answer is, well, you're an individual, you've got a different lifestyle,
25:54
different tolerance for pain and hunger. You're a female or a male.
25:59
You've got different microbiome. These are really important things to take into consideration.
26:06
When we recommend things, what we're saying is, you can try this,
26:12
if it doesn't work for you, try something else. But also just to talk about one of our sponsors, Inside Tracker.
26:18
I use inside tracker because it's not just, oh, I feel better today. We actually have to measure things,
26:24
get a dashboard on your body, to know if what you're doing, whether it's exercise or in this case,
26:30
your diet and when you eat is working for you. And that's why I've been able to optimize my diet
26:35
over the last 20 in fact, 30 years. I'm not just guessing, I'm actually measuring, - You're measuring.
26:41
- Yeah. - It's a little insane that the way that we went about testing out
26:47
whether or not these different eating regimens were working for us, is like, do I feel better,
26:53
do I not feel better? It's so vague, it's really nebulous. - Well, you wouldn't drive a car without a dashboard.
26:59
So, why do we do that for our bodies, which are even more important. - Yeah, bad habits [chuckles]. - Yeah. That's what we do, right. That's what we've always done.
27:04

I feel [mumbles]. - Yeah, well, this is why I have auto pilot. I drive a little crazy.
27:11
I do that with my body as well. It's all an experiment. But let's go through the diets. Okay, so there's a fasting mimicking diet,
27:19
Valter Longo, colleague of mine from UCLA is a proponent of that.
27:24
That's his diet that lowers mTOR activity. It's low in these branched chain amino acids that I've mentioned. - Okay.
27:30
[stammers] a diet that mimics fasting or does that include periods of actually not taking
27:38
in any calories? - It's both but you don't have to be as rigorous about the period.
27:43
The food itself will- - So the food itself is being processed by your body
27:49
in such a way that the body is like, I could really use a little bit more, I could really like a little bit more.
27:54
- Yeah, you want them, to the body to be in a state of perceived adversity. Oh my goodness, I'm running out of food.
27:59
I'm not eating meat anymore because plants have less of these amino acids. So it responds to that low amino acid input.
28:08
Valter's done some great work, over the last few years, he and his group have shown that on this fasting mimicking diet,
28:15
which they can send you at home, that actually helps cancer patients survive
28:20
and get over chemotherapy quicker. Again, more evidence that fasting is good,
28:26
not just for longevity but for diseases. So that's one, the next one let's talk about which a lot of people call intermittent fasting.
28:33
We'll just call it fasting. This is a period, if you go longer than a day, some people do three days, some people go for a week.
28:41
I wouldn't go longer than that 'cause then you'll start chewing up your muscle, which you don't want to do. But these long extended periods
28:46
are doing a real deep cleanse on the body and turning on that autophagy, that process of recycling proteins very deeply.
28:53
Especially, once you get beyond the three-day mark, when your metabolism switches into what's called
28:58
chaperone-mediated autophagy, the deep cleanse. So that's fasting and then there's time restricted feeding,
29:04

which is what I do, 'cause I'm not very good at going beyond 24 hours. - Well, [mumbles] think most people would really struggle
29:10
to get there. - Yeah, time restricted feeding, which is what I do, which is, try not to eat till dinner.
29:16
That's hard enough, my hats off to people like Peter [indistinct], the [indistinct] podcast,
29:21
[indistinct] many of our audience will have heard of, he can go for a week and he's got a lot of willpower.
29:28
If you've ever met the guy, he's different than me. I'm more of a hedonist, but he - Is he grumpier
29:33
at the end of the week, do you think than he is at the beginning of the week though? I mean, like after all of that time. - He's always serious.
29:39
That's what I can tell you, but brilliant. But let get back to this time-restricted feeding.

Focus on Time-restricted Feeding (≥ 16 Hours of Fasting)

29:46
You want to have at least 16 hours of not eating or not eating very much.
29:52
And then you can have eight hours. So typically that means having a late lunch, if you skip breakfast or if you prefer to skip dinner, I'd skip that.
29:59
- Because we [mumbles] remember here is that there's a period of sleep in which you are not eating. And so, - That's the easy part.
30:04
what you're really doing is tacking on hours to the front of that and tacking on hours to the back of that.
30:09
- That's right, so when people say I'm skipping lunch, that's not as helpful. And so what I've done in my life,
30:15
let's just use me as an example of an average human being. 'Cause I'm pretty lazy and I'm not that driven.
30:24
I prefer to take a pill, which is not the right thing. What I started out in my life was not to eat breakfast.
30:31
And pretty much been doing that since I was a teenager. And that for me works because I'm not really hungry
30:36
in the morning, I have a cup of tea or a cup of coffee, and I still do that, a little bit of yogurt to mix my supplements with,
30:42
to dissolve them. - And you're not taking, you're not doing the yogurt. And I've actually seen you do this. The amount of yogurt that you put
30:47
into your little bowl is really minimal. It's basically just to mix up your- - a couple of spoons.
30:52

- Yeah. - That's it. And that's burnt off in 15 minutes. So it's not going to be a big deal for the rest of the day.
30:59
And I try not to eat at all until dinner. And then I have a really enjoyable, largish dinner,
31:05
but it's certain types of food. We'll talk about the types of food later, but that gives my body this long window,
31:11
more than 20 hours of not having glucose circulating from the external world.
31:17
Now what happens when you do that? And it takes a few weeks for your body to adapt, is that your liver will learn how to compensate
31:24
for lack of food. It's called gluconeogenesis, the generation of glucose from your liver.
31:30
And it actually overcomes the feeling of hunger. When you first skip breakfast and lunch,
31:36
you're going to be hungry. You're going to be nervous, you're going to say, I can't do this, Sinclair is an idiot. - Well, this is why people fail at this,
31:41
is because they run into that and they think, this is how life is going to be for the rest of the time that I'm on this diet.
31:47
I can't do this diet. - Right, but do it for at least two weeks. Because after the two week, especially by the three week mark,
31:52
your liver has now learned that you're not going to breakfast or lunch, and it will start making glucose at a steady level.
31:59
That's really important because it's known that if you have these spikes of glucose,
32:04
it leads to hunger when it crashes after a big meal, but also that when you get hungry, you eat.
32:10
So you're in this wave of hungry, eating- - Do you think people should ramp up, I mean, you said like,
32:16
do no breakfast and lunch for two weeks but should they ramp up by like breakfast first and let their liver get used to compensating
32:25
for no breakfast and then add lunch? - Well, I would skip one meal and then go for two. - Yeah.
32:30
- You can't do the whole thing. Most people will fail, but you're trying to avoid this thing I was just talking
32:36
about called reactive hypoglycemia, is that if you eat a piece of toast for breakfast or heaven forbid, a giant glass of orange juice,
32:44
you'll have this spike in sugar and you'll feel great, but then your body will put out too much insulin
32:49

and suck that glucose out of your bloodstream and put you into a glucose deficit and that's hypoglycemia.
32:55
And then you're hungry, you've got ghrelin coming out into your body and you feel hungry and you need eat something.
33:01
I'm at a state though, now, where I don't get those rises and crashes. My liver is putting out glucose from when I wake up till dinner.
33:08
And I've never been so focused. I've never been so brain fog free
33:15
because these crashes, what they do is they make you feel shaky or tired and brain fog.
33:20
And I wish I'd done this in my 20s and done it my whole life, because I've really never felt better, because of it.

Continuous Glucose Monitors

33:26
- We can actually measure this now with continuous glucose monitors. - Right, and this is a shameless plug
33:33
to one of our sponsors. - I did not [stammers] I was not intentionally, creating this moment for a shameless plug, but we can.
33:39
- Yeah, well, let's mention them 'cause it makes this podcast free. So, Levels provides glucose monitors that you stick them
33:45
on your arm and they measure the glucose levels and I've used one of them. And what I found was that there were certain foods
33:50
that spike my sugar really high and then I get the crash. And it's very clear that when I'm feeling jittery and hungry,
33:56
I am in that hypoglycemic state that comes after a big meal or even a piece of toast for me or a bagel.
34:02
That's really important 'cause then you'll learn what your microbiome and your body responds to well and not.
34:09
For me, I was surprised that white rice, toast, grapes were really bad and potatoes weren't that bad.
34:17
And so, now I've optimized my diet to not have these periods even after dinner where I feel crappy.

Genetics Influence How an Intervention Affects Aging

34:24
- And not everybody is going to respond the same way. Like you said earlier, we all have different lifestyles.
34:29

We've got different genes. Jim Nelson's work's been informative in this.
34:35
- Yeah, so Jim did a important study in mice, again, not humans, but it tells us that genetics is important
34:41
'cause he took very similar mouse strains, strains of, some are called black 6
34:47
and then some white ones. And he crossed them together to make of genetic diversity, a colony of about a hundred different types of mice
34:54
and put them on the standard caloric restriction protocol, which by recollection, it was close to 35% of what a mouse would eat,
35:01
given food all the time, ad libitum, we call it. And about half the strains of mice lived longer.
35:07
And then about a third of what the remaining ones lived shorter. And that was a shock because we thought caloric restriction always works.
35:14
That's not true, it can depend on your genetics. And we've now learned that some strains of mice
35:19
and probably humans as well are much more sensitive to this diet, these types of diets. And you probably want to do it a little less
35:26
than someone else. And you only know that if you try it on yourself and measure things.
35:32
- I like this idea that we're you're all just, sort of lab rats running around, trying things out right now.
35:39
- Well, I get criticized by some doctors advocating that, you're not supposed to be experimenting on yourself.
35:46
Even people say, you shouldn't be allowed to have continuous glucose monitors. How dare you measure your body?
35:51
And my view on that is, well, we should ban bathroom scales, if we're not allowed to measure our body. - Well, I love the fact that you're doing this
35:57
because I'm going to let you do it, ahead of me. And then I'm just going to wait and see what really works and what doesn't really work.
36:05
And that becomes a starting point. But that is sort of what you've been doing. I mean, what you've been doing for a really long time and you've been pretty open with people about,
36:12
like, here's what I'm doing and here's what I'm doing right now. And it hasn't been consistent for 20 or 30 years.
36:18
Sometimes you start and stop things too, because it's working and it stops working or it feels like it might be a good idea and it doesn't,
36:24
that's what we're all doing. - Well, I've made plenty of mistakes, I don't talk about my mistakes as much as I should probably, but I've had times where I ate the wrong things

36:31
and ate too much and gained weight. And my Inside Tracker results were horrendous.
36:37
- Did you ever make any mistakes in fast- like when it comes to fasting itself? 'Cause you've tried different kinds of fasts,
36:43
which one really didn't work for you? - Well, they were all beneficial.
36:49
Skipping your breakfast was good. I think, what got me into trouble was when I tried

A Trick for Fasting: Filling your Body with Fluids

36:54
to do it without preparation. So I said, okay, I'm going to just skip lunch and go to dinner
37:00
without knowing how to do that or being in the right mindset. And I had to quit multiple times.
37:05
I spent years trying to do this. I could never get rid of my love handles. And this final time that worked for me,
37:12
worked because I found a trick, and that trick, I'm not going to tell you,
37:17
I'll tell you. - No you have to [laughs]- - The trick is that you want to fill your body with fluids. For me, constant coffee, tea, hot water,
37:25
all the way through the day. Being hydrated and filled with liquid takes away any feeling of hunger.
37:32
Also nuts, if you really, you need to eat something. A bit of protein is known to take away the feeling
37:37
of hunger rapidly. - Yeah, this is what my buddy, the cardiologist, John Day, tells his patients
37:42
when he's working with them is, like, look, if you got to eat, just start with a handful of nuts
37:48
and just give me 20 minutes after that. You're not going to be hungry - Right. - After 20 minutes.
37:54
- So, there's an interesting story about the role of protein and hunger. And it was first discovered by a friend of mine,
38:00
Stephen Simpson in Australia, and he was studying locusts. And he found out that what turns a locust
38:05
into a swarm was a lack of protein. And when they get too low in protein, they go crazy on.
38:11
- Locusts get hangry. - And they start eating each other, it's that bad. - Yeah, and everything else in their sight.
38:17
- Yeah, and we even see this in the mice that we have on low protein diets, they get super mad and they even attack each other.
38:24

So you don't want to be too low in anything. You don't want to be hangry. But getting back to what really works for me is,
38:31
I've trained my liver to produce enough sugar that I don't feel hungry anymore. And if I do, I'll keep drinking liquids.
38:37
And if I get really hungry, I'll nibble on some nuts. And that for me has worked really well. I've got my 20 year old body back
38:43
for the first time in my life. - And I'm never going to go back. - But you are going to be hungry. Anybody who starts this, they're going to be hungry at first.

Intermittent Fasting with Adequate Nutrition (IFAN)

38:48
- Of course, - they're going to be a hungry- - It's not easy, I'm not saying that it's going to be easy, - Yeah. - but it's worth it.
38:53
- And there is an important point to make here. And we sort of touched on it at the beginning,
38:59
but I think, we need to circle back to it 'cause it's so important because we're not talking about starvation, we're talking about intermittent fasting
39:08
with adequate nutrition, that adequate part's really important. - Yeah, so the acronym would be, IFAN
39:15
all right, trademark that one. IFAN, let's call it the new type of dieting,
39:21
by the way, intimate and fasting I learned about a month ago. is the most popular diet in the US.
39:26
We talk about it in the book, that might be part of it. But it's important that we add the "AN" at the end because we need the adequate nutrition
39:34
and there's one sponsor, we haven't mentioned, which is "Athletic Greens". [both laughs]. But this is true, the reason that I take a drink,
39:41
Athletic Greens- - You're really good at work in these in. - Well, they're important to us. But the important part is that,
39:47
the adequate nutrition is important is necessary. Otherwise you're going to be causing more harm than good.
39:54
So when I take Athletic Greens, I drink it in the morning, I know I'm getting all those nutrients that I might not get during the day.

Things to Avoid: Excess Sugar and Protein

40:00
- So, now that we sort of set the stage for,
40:05

when we eat, which is really important, when we eat, we still have to acknowledge,
40:12
we have to eat sometimes. Sometimes you're going to, if you intermittently fast, if you're going 20 hours without food,
40:19
you're going to have breakfast or you're going to have dinner. So yeah, there's going to be something on your plate.
40:26
It's really important, also, what's actually on your plate. And that's what this next half of this episode is about,
40:31
is what we should eat when we are eating.
40:37
And maybe the best way to start this really though, is to talk about what definitely shouldn't be, or not definitely shouldn't.
40:43
There should be a lot less of on that plate. - Right, well, the big killer is sugar.
40:49
- Yeah. - Glucose, particularly fructose is also pernicious. And if you give animals lots of glucose
40:56
and especially fructose, they will get fatty liver disease. They'll get diabetes, it's really bad. - And this one is absolutely not controversial, right?
41:03
Like, we're going to talk about meat later and people are going to be like really up in arms. But if you say like the big killer is sugar,
41:08
there's not like a group of people that's going to come hunt us down. Sugar is bad.
41:14
- It is and- and why? - Well, why? Well, there are two reasons that glucose is bad when it spikes,
41:20
three, if you include the brain fog but let's just talk about physiology here. One is, that you're going to have glucose attached
41:26
to proteins that makes them glom up. Think of it like caramelized body parts. This'll ultimately lower your longevity.
41:33
Reduce your longevity, give you type two diabetes and probably cardiovascular disease on top of that.
41:39
So that's one, keep those glucose levels down. But also, what glucose is going to be doing to you at high levels, is shutting off those protective mechanisms.
41:47
Remember, particularly AMPK and the sirtuins. They get switched off by sugar.
41:52
So, by having that up for most of the day, if you're eating three meals plus snacks, your defenses against disease
41:58
and aging are going to be working at a minimum. So instead, keep those glucose levels low and consistent.
42:04

You won't get the brain fog, you'll get fewer proteins modified that'll lead to disease.
42:10
And thirdly, importantly, you'll actually stimulate your body's natural defenses against disease and aging.
42:16
- So, the first step, sugars, let's get rid of the sugar. - Yeah. On that note,
42:21
by the way, I gave up dessert at age 40, though, occasionally I steal it and it doesn't count if you steal it, right?
42:27
- No, I think there's like a special little pocket it goes into that doesn't count against- - It's invisible. - Right. Inside tracker doesn't pick it up.
42:34
- Right, here's the point, You can quit something but you don't have
42:39
to be draconian about it. I still like to steal a few scoops of ice cream
42:44
if I see it but I'm not going to eat a giant bowl of ice cream every night. That's a quick way to shorter life span.
42:50
- We're not trying to ruin everybody's joy. - No, not at all. Often when I give talks at dinners, people skip dessert after I've spoken.
42:56
I feel bad about that. - Well, you remember we were talking about doing an experiment where we would have a conversation around a table
43:03
with people and then have the servers come with like, a birthday cake or something and you just like, watch them.
43:09
- We still should do that. But yeah, so glucose is a bad one. Something else to avoid is super high protein
43:16
because mTOR, it can be activated but you don't want to activate it all the time. 'Cause it's not going to turn on the autophagy,
43:23
the defenses to recycle proteins. - And this one is going to a lot of people off. - Well, yeah, there's a lot of people
43:28
who believe that carnivore diets are the best for longevity. - And for some people, a lot of aminos are appropriate.
43:40
- Well, certainly if you're an athlete or you want to bulk up, there are short-term gains. You'll feel better if you eat meat,
43:45
you'll obviously have the protein to build up that muscle. But we can go through the evidence when you look
43:52
at populations at what they eat and how long they live, as well as the short-term effects when you eat
43:58

a high protein, carnivorous, red meat based diet, those changes will be good in the short run,
44:05
but long-term, there's no evidence, in fact, I would say there's counter evidence to that being beneficial for longevity, if that's your goal.
44:13
- And that's because of the inhibition of TOR - In large part, yes, the sirtuins will also get switched off by high protein as well.
44:20
- So, aminos are important. We have to have them, if we don't have them, we die.
44:25
But you can get aminos from plants as well as from animals. - Yeah, it's funny when I say
44:32
I've gone vegetarian recently, which is a fact- - Where are you going to get your protein? - Yeah, where do you get protein from but what do you think plants are made of?
44:38
It's also mostly protein. Now, they're not as bioavailable. So, you're getting like two thirds the amount
44:44
as you would from a steak- - Your body has to work a little harder for it. - Great, I want my body to work harder. It's good for it, it burns energy,
44:49
it's also activating these defenses as we mentioned. So I'm now trying out this, a full vegetarian diet.
44:55
I'm not yet vegan but that actually probably works even better for longevity as the science will tell.
45:01
- How's it working for you, you feeling? Do you miss meat?
45:06
- I do, I love meat. I think meat tastes great, but I'm more and more inclined to enjoy [indistinct]
45:15
as well. - So we're starting to go down and talk about vegetarian diet, plant-based diets here. We're going to talk about a lot of those different choices

Branched Amino Acids, Red Meat, and mTOR

45:22
in a minute here, but I do want to take us back for just a second
45:27
to what's happening. Like, really was actually happening in the inside of our bodies. When [stammers] and I still eat meat,
45:34
I haven't followed you down this path yet. I love the steak. When I put a steak on my plate and I eat it,
45:42
what's happening, what are those aminos doing? - Well, before you get aminos out of meat,
45:48
you need to digest it and so the first step is, acid in your stomach is going to break down that meat into amino acids,
45:54
and then your microbiomes can utilize a lot of them. And then those amino acids are also going to leach
45:59

into your bloodstream. So, now you've got these amino acids circling in your body, circulating, and there are three ones
46:06
that are particularly important to know about, it's leucine, ISO leucine and valine
46:11
also known as the branched-chain amino acids. And these are used by the body to sense protein intake.
46:18
And the sensor is this protein complex we talked about called mTOR. And when there's lots of these three
46:24
branched-chain amino acids, particularly leucine, it will be activated. And this mTOR, the role is to say,
46:30
wow, I got lots of amino acids, let's build muscle, let's repair cells, let's do all good stuff,
46:35
which is why you you feel good if you eat red meat and your microbiome can handle it.
46:40
- Yeah, I feel great, I feel like I can fight a lion. - Yeah, and you might have to fight a lion to get it.
46:46
But what actually is going on that's deleterious in the long run is that mTOR can do something even better
46:54
for your longevity than build new muscle. It actually can turn on this recycling program called autophagy.
47:01
And that is very clear. There's no debate as to whether autophagy is good for you or bad for you.
47:06
It's definitely good. So, what I think people could do is to, if they want to eat meat, go for it,
47:12
but try to focus on plant-based food more often so that there are periods during the week when there aren't
47:20
as many, leucine, isoleucine, valine molecules floating around in your body. So that you have a chance for your mTOR downregulation
47:27
to recycle proteins. Now, why do you want to recycle proteins? You might say, well, who cares about recycling proteins.
47:33
Well, Alzheimer's disease is a good example of proteins that get modified and accumulate in your brain.
47:39
And it happens not just in the brain, but in all tissues. We have these old proteins that linger, 'cause us to get old to malfunction,
47:45
but it's reversible and it's reversible, by fasting, it's reversible also by having lower levels
47:50
of these branched-chain amino acids, at least part of the week. - Let's talk about these primarily plant-based diets.

Plant-Based Diets Protect Against Aging

47:58
There's lots, I mean, there is vegan diets out there. You said like, for many people, that's probably going to be the gold standard
48:05
but a lot of these plant-based diets have a little bit of meat in them. There's the Mediterranean diet. There's the Okinawan diet.
48:12
- Lacto-ovo vegetarianism. - Right, lacto-ovo vegetarian diet. Is there anything you want to say about these
48:18
or can we talk about them as an umbrella group, don't you call 'em like blue zone diets?
48:26
- Yeah, well, let's talk about blue zones in a minute. I think, what's interesting is that, there was a really big study
48:31
by the Adventist Health Group, 2013. - Yeah. - Let's talk about that, because what they calculated was the chance
48:37
of dying based on various diets and these were thousands of people.
48:43
And what they found was that, what's called the hazard ratio, went down the more vegetarian and vegan you were.
48:49
What does that mean? Your chance of dying goes down. And the number goes from zero to one. Whereas, one is you're pretty likely to die tomorrow,
48:57
whereas a low number, which is around 80, means you've got 20% less chance of dying on any given day
49:04
with this hazard ratio. So, the numbers are the following, non-vegetarians are at one, if you call that one,
49:12
compared to that, the next best one was semi vegetarians at 0.92
49:18
and lacto-ovo vegetarians, 0.91. Okay, so almost a 10% reduction in mortality, death.
49:27
And then you get into vegans, with 0.85, so, that's 15% reduction in death,
49:34
and then the best one was Pesco vegetarian. So, getting a little bit of meat- - Little bit of fish, - Yeah, little bit of meat
49:39
from fish, probably the fish oils in there are beneficial. And then you're down to 0.81. So that's a 19% reduction
49:47
in your chance of death at any given day, late in life. - Okay, now, that's all cause mortality, but we can also now see this in biologic aging
49:55

because we now have clocks that we can use to measure our biological age.
50:02
And there are studies now also that are showing that these diets are effectively reducing biological aging as well.
50:10
- Right, and there were a couple of these, there's a one-year study looking at a diet of mostly vegetarian.
50:16
But the one that I think is really exciting is one that just came out a couple of months ago that looked at mostly women
50:23
on a Mediterranean diet plus exercise over two years. And they could now calculate what happens
50:29
to your biological age over those two years, having switched the diet and they had various recommendations.
50:34
It's very typical Mediterranean, limit alcohol, if you have red wine, that's fine.
50:39
A little bit of fish, only use olive oil as your fat and focus mostly on plants.
50:45
That was their lifestyle. And then exercise was walking and some other weightlifting. - That's the Fourier study.
50:51
- Yeah. - Okay, so the interesting thing about this study, at least to me, the thing that jumped out at me is it came out of Geovanna Masala's lab
50:59
at the Cancer Institute in Italy. And like, [mumbles] well, why do people
51:05
whose primary responsibility is to study cancer care about aging? And it comes back to this thing that you've been saying all along,
51:11
which is that if we can reduce people's biological aging, we can cut diseases off where they actually start.
51:18
- Well, that's exactly right. These diseases that we think are just diseases are mostly caused by aging itself.
51:24
And that slowing down that clock by fasting or eating the right foods, Mediterranean diet,
51:29
is now shown not just to slow down the ticking of the clock, but probably reverses your age as well.
51:35
And that's a mind blowing concept. You have to think about that for a minute, that it's possible by changing your diet
51:42
to reverse your biological age. - One of the diets that stands to do this well,

The Okinawa Diet and Blue Zones

51:49

likely, that I know you're a big fan of is the Okinawan diet.
51:55
You were on the Okinawan diet for quite some time, right? - Yeah, I was, the Wilcox brothers wrote a book
52:00
in the 2000s that I loved. And it's mostly carbohydrate, so there's a fair amount of rice
52:06
but probably could have done better with a bit of brown rice, white rice sends your glucose through the roof. - Right. - But mostly what I was eating were Chinese
52:13
and or Japanese vegetables that I could get at the local market, so they're organic, fresh,
52:19
green, full of vitamins and soy. Mostly it was that, it was a plant-based, soy-based diet
52:24
with a little bit of fish. And I looked great, I felt great. And then my kids came along
52:30
and we ate pizza for a few years, but it was great while it lasted. And if you look at the Okinawans, on the island of Japan,
52:38
they are arguably the longest lived people on the planet, but they have other things that are good for them. Things like, social structure and exercise,
52:45
they work until they're in their 90s or 100s- - None of these things happen in a void. - Right, but that lifestyle is probably the ultimate
52:51
for human longevity. And we know this because if Okinawans moved to say, Hawaii, which a lot of Japanese did.
52:58
Then they don't live long anymore. - Yeah. You talked about lifestyle, this is a really big part of,
53:04
you said you wanted to get back to the blue zones idea. You go across the world,
53:09
you look at these communities of long lived people. They have a lot of things in common,
53:18
and we've been talking about diet today. So, let's just jump into that. And there has been criticism of blue zones too.
53:25
- Yeah, so Dr. Harriet hall has said that those demographic data, people's ages weren't actually correct. But if you dig into it, they did a really good job.
53:32
So, Dan Buettner I think is right in saying that these people tend to live a long time, out of hundreds of people that they check the records of,
53:40
going back in the city records, there was one person that was misjudged. What was it?
53:46
- They thought they were like, 111 and they were actually 107 or something. - Yeah, big deal.
53:51
- Of course, all studies have caveats, but this I think is really clear that areas of the world that have the right combination of foods, exercise,

53:59
social structure, they do live longer. This is no surprise, even in yeast when
54:05
we don't give them social life but when we modify their diet or give them food in a time restricted fashion, they also live longer.
54:13
So, I don't understand, why it's controversial. - There's one more idea

Xenohormesis

54:19
about how we should eat that I know you're a big fan of, there's less research behind it,
54:27
but you believe pretty strongly I'd say and there is evidence, but I think it's still emerging
54:35
and there needs to be more research. But, this idea of xenohormesis, this idea of eating plants that have,
54:42
not just eating a plant-based diet, but specifically focusing on plants that have experienced stress.
54:50
Talk about that and why you are,
54:57
so focused on this idea. - Well, the xenohormesis concept,
55:03
Konrad Howitz and I, coined this term in the mid 2000s, trying to explain why
55:08
so many plant molecules are good for us? It just cannot be a coincidence. And we came up with this idea,
55:13
really prompted by a 2003 nature paper that we co published, that found that there were
55:19
at least 20 plant molecules called polyphenols that activate the sirtuin enzyme called Sirt1,
55:26
the number one out of the seven family members. And when I looked into it, these polyphenols do remarkable things to the body.
55:34
The one that got the most media attention, because it's in red wine is resveratrol, but there's piceatannol and there's fisetin and quercetin
55:42
these are supplements that people are getting excited about only now, but when you look into it, they activate and inhibit pathways or proteins in the body
55:51
that are known to be important for health and longevity. And in some cases, the same molecule will inhibit one protein and activate another one
55:58
in just the right way to promote health. That cannot be a coincidence. There's no way that that could just happen randomly.
56:06
So the idea is that we've evolved mechanisms to sense when our food supply,
56:11

the plants that we eat are stressed. - Because it's like an early warning system. - Right, we're humans, we can see
56:16
that the plants are wilting and we know that the crops are dehydrated. We can measure the soil.
56:22
Most organisms on the planet don't even have eyes. How would they know if their food supply is going to run out
56:28
unless they sensed the stress, the fear in those foodstuffs. And so when you stress a plant, you get more resveratrol,
56:36
you get more quercetin, piceatannol. And if you look at- - What kind of plants? we should say, I mean, it's not every plant
56:42
that we're going to get those things- - Of course, it's every plant. - Is it every plant that- - Well, plants have sirtuin genes and they need to survive just like we do.
56:49
And they make these polyphenols in order to survive when they run out of, or running out of water and nutrients-
56:56
- Okay, where are we going to get most, though? or even preyed upon by caterpillars,
57:01
but in our food supply a lot of plants have very few of these molecules.
57:07
Why? Because we think that the faster they grow and that the less stress that they have, the better.
57:12
It's actually more profitable for a farmer to grow plants that grow really quickly and have no stress, but are they better for us?
57:18
Absolutely not, so how do we know if a food has been stressed? Well, you can start with the generalization that if they're grown out in a field organically,
57:25
without pesticides, probably this most stressed, right? But also there are foods that are intentionally stressed.
57:31
Red wine is one, the best red wines are ones where the vines are dehydrated
57:37
or have fungus growing on them. There's a good reason for that. We know that they taste better.
57:43
Why? Because Xenohormetic molecules are made along with molecules that taste good
57:49
and are filled with color, it's the plant defenses. And so what I look for are plants that are organic,
57:56
local and colorful because those are the ones that are most likely to have those molecules.
58:02
In the case of red wine, choose grape varieties that are stress sensitive.
58:07
Pinot noir is one of the most sensitive, if not the most sensitive, grape variety. And that's why it has the most resveratrol

58:14
of any other type of wine. - Let's bring this all together now.

Main Takeaways

58:20
There's a lot of information here, but there's sort of a checklist.
58:25
And, so let's talk about like, if people are going to have like four takeaways here,
58:30
five takeaways. Eat less often.
58:36
You would say, start with eating less often by skipping one meal a day and moving from there.
58:42
- Yeah, and don't snack and don't snack. - And don't snack. - Yep. Avoid sugary drinks and foods. - Okay, eat less often when you do eat, kill the sugar.
58:50
- Yeah. - Yeah. - I focus on, I try to eat artificial sweeteners
58:56
and natural ones, so Stevia is a big one for me and there are some others that are out on the market
59:02
that are naturally occurring sweeteners. - Okay, start working toward reducing your meat intake.
59:09
If you're dieting, if your diet is aimed at longevity,
59:15
very likely, you're going to need to drop your meat intake. - Yeah, it causes a lot of concern
59:21
of people who are pro meat but the data is the data. And we've got these references in our show notes
59:27
that reducing the amount of red meat and in particular processed meats,
59:32
is beneficial for long-term health and even prevention of cancer. One of the things that's not appreciated about red meat.
59:38
And I'll just mention this is that it's not just that they have more
59:44
of these three branched-chain amino acids that prevents mTOR from doing its good stuff to the body.
59:50
There's also a molecule called TMA that is in the meat that goes into the bloodstream,
59:56
the liver turns it into a toxic molecule called T-M-A-O. And this TMAO is showing, at least in animals,
1:00:03
probably in people, to enhance, accelerate cardiovascular disease.
1:00:08
So I would say- - And cancer too, right? Yeah. - Yeah. - And so, what we want to do is to limit the nitrates, the preserved meats,
1:00:16
if you like a good steak by all means eat one, it's not going to kill you. But if you try to just push yourself

1:00:22
towards a more plant-based, plant focused diet and maybe have some red wine occasionally,
1:00:28
a lot of olive oil with oleic acid, which activates sirtuins as well. The Mediterranean diet is the one that I think is,
1:00:37
likely to be the easiest to do in the Western world and to have the biggest bang for the buck.
1:00:42
You can go a little bit further, like I have, don't eat meat and eventually maybe I'll give up everything,
1:00:48
that's dairy and eggs. But the Mediterranean diet is a very enjoyable diet. I lived on it for over a decade.
1:00:55
And one of the things that's not well known is that there are studies of Mediterranean diet
1:01:01
versus Western diet. And it's a massive difference. There's one here that was published in, just 2000.
1:01:09
There was a reduction in mortality- - In 2000 or? in 2000, the year 2000. - So, it's 20 Something years ago.
1:01:17
- It's 20 something years ago. But there are a lot of studies since, there's at least five studies that have backed this up.
1:01:22
If you switch to a Mediterranean diet, if you're under 80 and you do that,
1:01:29
you reduce your mortality, chances of death on any given day by 31%.
1:01:34
- [mumbles] like, if you're under 80, which means you can still take advantage of this, even if you're way deep into your life.
1:01:41
- Right, and I would say, probably in this study, they just didn't include it, people over 80.
1:01:46
So I don't know for a fact that it wouldn't work on 80 year olds, - Sure, right. - But yeah, that's the point that's really important,
1:01:52
often when I give talks to crowds, they are elderly. And often the question comes up, is it too late for me?
1:02:00
The answer is, it's never too late. Dietary changes in older people can have massive benefits.
1:02:07
Some people say, oh you need to have a carry a bit of fat, if you're over 80, you should have a little bit of body fat.
1:02:13
- There was a study that a lot of people latched on to that they got really excited about because it was like, oh, if you're older, you can be fat.
1:02:20
- Yeah, well, it turns out that's not true. When those studies have been redone,
1:02:25
being lean as an older person is also beneficial. If you look at, go to a nursing home,
1:02:30

I don't know how many people listening have been to a nursing home but when you go there, look around who's alive.
1:02:37
They're not giant men who are obese. They're little women who are skinny.
1:02:44
There's an experiment right there. It's obvious, right in plain sight. - Okay, so,
1:02:50
eat less. Start working toward fasting, cut the sugar,
1:02:56
cut the meat, eat the veggies. Don't cut the meat and respond with a bunch of carbohydrates, eat the veggies.
1:03:04
And if you are going to eat the veggies and you can find ones that have been stressed out
1:03:09
and are enjoying a little Xenohormetic, you may enjoy a little Xenohormetic effect from that.
1:03:15
- That's great and there's even an order, which you can eat your meals to reduce the blood sugar spike. You can put the sugar at the end of the meal.
1:03:24
So, dessert is fine if you, but put it at the end, don't start with sugar and don't start with the carbohydrate
1:03:29
because that will immediately spike your glucose. - So, if you are [mumbles] go back to that, like the second and third point, if you are going to eat sugar,
1:03:35
eat it at the end of a meal. - Right, what you ate during the meal and in which order also makes a difference.
1:03:42
[overlapped chatter] - that's just, - Oh my goodness, eating candy during the day is just going to
1:03:48
make you feel lethargic when that sugar goes away. - Well, we're doing this really horrible thing to children by telling them that their lives are,
1:03:55
like sugar is this really great thing that they should have all the time. They should be able to have snacks that are ladened with sugar and [murmurs] breakfast
1:04:01
that starts with sugar and- - Yeah, well, I blame the food industry for that. 'Cause they want to sell more food.
1:04:07
And we've been taught that children should never go hungry. Breakfast is the best meal of the day.

Obesity, Eating Habits, and Aging

1:04:12
And we've got an obesity epidemic in kids, no surprise. And what parent doesn't feel guilty
1:04:18
when their kid feels hunger, but for longterm health, even programming the epigenome
1:04:24
for long term health requires some hunger in individuals.

1:04:30
And what we do to kids is we say, big breakfast, here's a snack, here's your lunch, terrible lunch, typically at schools, public schools,
1:04:38
big dinner, go to bed full, wake up, eat some more. We're not just causing problems for these kids physiology
1:04:46
for the long run, 20, 30 years later, 'cause their epigenome is now set for feast not famine. - Right.
1:04:53
- But we're also setting them up for obesity, which shuts off their survival programs right now.
1:04:59
So, their bodies are aging quicker than they otherwise would. - I wonder if that's not a really important frame to put,
1:05:09
what we call the obesity epidemic into is, it's not just an epidemic of making people bigger.
1:05:15
It's an epidemic of making people age faster. - Absolutely and we're going to see the impact
1:05:21
of this in two or three decades from now with an increase of these diseases because the clock has been accelerated.
1:05:29
- So this is, most of our listeners, most of the people that are listening to this,
1:05:34
watching this are going to be adults who're going to be making decisions for themselves. But,
1:05:40
much of this, if not all of this is really translatable to what parents should be starting
1:05:45
to help their children develop the habits of eating in these patterns as well.
1:05:51
- Right, and it's okay to be hungry. - once in a while. - Exactly. - Yeah. - Yeah. And not just have food lying around

Metabolic Winter Hypothesis

1:05:58
that whenever they want to snack, they can. That is the way that we evolved.
1:06:04
We have this metabolic winter hypothesis that we've published. When we were,
1:06:09
going back probably a hundred thousand years ago, back to 6 million. What was our lifestyle? We were cold and hungry.
1:06:15
These days we live in air conditioned and heated houses with food always available, which goes against what we've evolved to be optimal.
1:06:23
And so we've got to go back to those days where, occasionally we were hungry, occasionally we were cold. We'll get to cold therapy later.
1:06:30

But basically the concept, if there's nothing else that you remember about this topic, just remember this that we need to put our bodies
1:06:37
in a state of want for them to fight diseases and have ultimate health in old age and give us longevity.

Preview for Episode 3: Beneficial Stress

1:06:44
- That's a really good place I think, to stop for now, because the next thing we're going to talk
1:06:50
about is other ways to put our bodies into states of stress.
1:06:55
That's episode three. Do you want to preview that, just a little bit? - Well, there's certain things you can do. We're going to talk about exercise
1:07:01
and cold therapy and so on. As these are ways of making the body feel like it's in a state of adversity.
1:07:06
- And do very much, what fasting and these diets do, which is activate these longevity genes.
1:07:13
- That's exactly it and the exciting part about the world we live in now, as we're learning, what is the best combo of those things?
1:07:20
And we'll talk about that in next week's episode. Thank you for joining us today. If you're enjoying this podcast