



# ALZHEIMER'S

## THE SCIENCE OF PREVENTION

### **Episode 1: The Alzheimer's Epidemic**



David Perlmutter, MD:

Our brains play such a fundamental role in our being. They're responsible for our mood, our memory, our ability to think, and strategize, imagine, and even communicate with others. And the list goes on. So it's easy to understand why having a brain that is healthy and working optimally is so important to living a life that is meaningful and enjoyable.

Max Lugavere:

Our brains are who we are. Our brains enable us to think, to forge relationships, to be creative, to get things done. These are all aspects of a cognitive domain known as executive function. Our brains are really important in terms of being successful, being able to be altruistic and to delay gratification and to be more focused and to remember things better.

Ayesha Sherzai, MD:

We are our brains. The personality that we have is our brain. The emotions that we show and depict comes from the brain. We all know that the decisions and the emotions, whether sadness or happiness, and the decisions we make about each and everything in life comes from your brain. So why wouldn't we worry about it? Why wouldn't we care for it?

David Perlmutter, MD:

We can all appreciate that having an optimally functioning brain is critical to enjoy life, in order for us to experience life with happiness, health, and purpose. But the unfortunate truth is that brain disease keeps far too many of us from enjoying these aspects of our lives. And of these diseases, Alzheimer's is clearly the most important. It is a disease for which we have no meaningful treatment whatsoever.

David Perlmutter, MD:

In the United States alone, some 5.5 million people have been diagnosed with Alzheimer's disease, significantly detracting from their ability to enjoy life, and certainly impacting their loved ones as well. We now know more than ever about actually preventing this disease. And this series is dedicated to exploring exactly how and why this information really matters in changing the destiny of your brain.

David Perlmutter, MD:

I'm Dr. David Perlmutter, and this is Alzheimer's - The Science of Prevention.



David Perlmutter, MD:

Alzheimer's disease has now reached epidemic proportions. Currently, there are 40 million people diagnosed with Alzheimer's around the world. 5.5 million of those are in America. It's been estimated that about every three seconds, someone is diagnosed with dementia globally and certainly, of those diagnoses, the most common form is Alzheimer's disease. We are right now spending about \$250 billion in caring for Alzheimer's patients right here in America, and this number exceeds \$1 trillion today globally. Experts agree that these numbers are going to increase quite dramatically as we move forward. All in the context that this is by and large a preventable disease. And keep in mind that if you live to be age 85 years, your risk of Alzheimer's, again a disease for which there is no treatment, is 50/50. That's the flip of a coin.

Dean Sherzai, MD, PhD:

Alzheimer's is the fastest growing epidemic in the west. It's by definition when your cognitive capacity, be it a visual, spatial attention, memory or any of those domains, is affected to the extent where you can't do some of your activities of daily living. That's called dementia. Alzheimer's is a subtype of dementia, dementia being the umbrella category...and has certain specific pathways and specific ways that it manifests. As the third leading cause of mortality and morbidity in the US, it's questionable. Some people say fourth or sixth, but we know that it's underestimated and underreported.

Dean Sherzai, MD, PhD:

It's number one in the UK and number one in Japan, and it's growing rapidly. In fact, mortality and all the other chronic diseases has been in the decline. Diabetes, heart disease, cancers. Yet in the last 15 years, prevalence and mortality from Alzheimer's has grown by 123%. And that number is only increasing exponentially. So every family will be affected by this disease in the next few years.

Dale Bredesen, MD:

This is a global problem that is a trillion dollar problem that will bankrupt Medicare, that will literally change healthcare throughout the world, because it reaches so many people. Currently in the United States, about 15% of people, lifelong, will develop Alzheimer's. It has become the third leading cause of death in the United States.

Lisa Mosconi, PhD:

Alzheimer's disease is the most common form of dementia all over the world, it currently affects 5.8 million people in the United States alone. And the prevalence is expected to triple by



the year 2050 with an anticipated or estimated 14 million Alzheimer's patients in the United States alone.

Suzanne De La Monte, MD, MPH:

So economically, what happens with Alzheimer's? First of all the patients who are becoming disabled, if you will, due to cognitive impairment, they can't take care of themselves, right? They can't shop, they can't walk around, they can't do much for themselves.

Suzanne De La Monte, MD, MPH:

So that means somebody else has to do it and that person is usually a relative or a close friend serving as a caretaker, which means that whatever they were going to be doing, they do less of, or they become double or triple workers, so they're doing their regular job and they're doing this. The second thing is you have to hire someone maybe, so now it's an economic drain, a choice between sending your child to college A or B or taking care of your parent or relative. So that's a big economic burden. They spend several hundred billion dollars a year just in this country for taking care of people who become disabled... the person who is demented is not functioning well and doesn't enjoy what they're doing, the person taking care of them doesn't enjoy taking care of them, and they get frustrated and depressed and there's a huge emotional burden on them besides the finances. And then the people who they're supposed to be taking care of, say their offspring, are also getting a bad deal because now they're being neglected due to the fact that more attention has to be paid to the person who is chronically ill.

Suzanne De La Monte, MD, MPH:

So it has a huge impact up and down the family at all levels, and then if you multiply that by a nation, it's even worse.

Amy Berger, MS, CNS:

Alzheimer's disease is emotionally and physically and financially devastating to families. The hardest job in Alzheimer's disease is the caregiver. The person who is afflicted, obviously it's terrible. It's horrible what happens, but the loved ones and caregivers that have to watch that, that have to watch their mother, their spouse, their friend literally become somebody unrecognizable, the caregivers themselves actually incur increased medical costs because of the stress. And they often neglect their own care and their own health. It's absolutely devastating to the families and the loved ones.

Michael Merzenich, PhD:

I don't believe that, in a sense, Alzheimer's is a disease. I think it's a catastrophic end stage of a progression of change that is probably in most individuals preventable. I think that basically



everything about the process that leads to ultimate collapse is natural. The body is responding, the brain is responding in a sense, in a natural way in progression that ultimately is self-destructive.

David Perlmutter, MD:

Now that we understand the devastating impact that Alzheimer's has on patients, their loved ones, and their communities, let's have a look at why the incidence of Alzheimer's is increasing so dramatically.

Dean Sherzai, MD, PhD:

Alzheimer's is increasing because of several reasons. One is because we are an aging society. And before we go on to explain that, I have to say that just because you're aging, it doesn't mean you have to develop Alzheimer's

Dean Sherzai, MD, PhD:

And the other factor is the environmental changes that we've seen in the last 50 years. There's a lot that's been added to our water, to our foods, to our environment that we're not accounting for. And I'm sure that that has a component as well.

David Perlmutter, MD:

We are indeed, an aging society. Medical technology had advanced such that we are living longer and longer. However, this does not fully explain the exponential increase in Alzheimer's diagnosis.

David Perlmutter, MD:

Rather, the evidence suggests that the biggest drivers of this explosion are actually changes in our environment and the way in which we live our lives. And almost all of these changes are driving a process that is at the heart of Alzheimer's and virtually every other chronic degenerative condition you can think of. And that is inflammation. Inflammation comes from the Latin word *inflammare* which quite literally means to set on fire. Inflammation it turns out, is present in the brains of nearly all Alzheimer's patients. And it's important to understand that this is different from the healthy type of inflammation that helps you heal from wounds. Instead, this is a chronic, smoldering process that is tremendously damaging to the body, and especially the brain. This chronic inflammation is linked to all manner of diseases, but most important to this conversation, it is a core part of our discussion of Alzheimer's.

David Perlmutter, MD:

What is the main mechanism that's involved with damaging the brain in Alzheimer's?

Mark Hyman, MD:

The main thing that causes damage to the brain also causes damage to every other age related disease, whether it's

diabetes, heart disease, cancer, obesity, hypertension, and it's inflammation. And it's not the kind of inflammation where you get a sore throat or a swollen finger. It's hidden inflammation and it's inflammation in the brain and your brain has only so many ways of saying ouch. And one of the major ways is getting demented and losing your memory. So treating inflammation is critical and they've done big studies giving people Advil for example, doesn't do anything. You can't give people drugs that shut off inflammation because you're not dealing with the cause of the inflammation and dealing with the causes of inflammation are critical.

Anna Cabeca, DO, FACOG:

When we see cognitive decline, we have to start asking, "Well, what's causing it?" Inflammation in the body, impaired cell to cell communication, and let's address those underlying root causes that are creating the problem to begin with versus labeling another diagnosis on them or writing them off because you're over 70.

Max Lugavere:

Inflammation can produce feelings of depression, feelings of anxiety and ultimately, inflammation in midlife is related to reduced brain volume later in life. It's definitely something that is closely tethered to conditions like Alzheimer's disease and other forms of dementia, and heart disease, and type two diabetes and obesity.

Dean Sherzai, MD, PhD:

So the mechanism of how Alzheimer's first manifests or starts in the brain is a little different than we previously thought. It's multidimensional, multipronged. Some people first develop... insulin resistance, whether it be diabetes or prediabetes, that process starts the inflammatory per cascade, which leads to increased inflammation in the brain to the point that at some point, the system of reserve in the brain is actually overwhelmed. And that leads to amyloid and Tau and then neuronal damage. But more importantly axonal damage. The connections between neurons are damaged. And one of the first areas is actually affected is, actually the area for focus and short term memory in the hippocampus. And then the cascade just starts rolling from there, going then to greater brain and then...Alzheimer's.

David Perlmutter, MD:

Therefore, we shouldn't expect a single magic bullet approach to its prevention. Instead we need a multi-pronged approach that addresses each of the insults linked to the development of Alzheimer's.



- David Perlmutter, MD: Insulin resistance in diabetes, poor sleep, lack of exercise, all of these can combine to worsen inflammation and therefore increase the risk of Alzheimer's. So we need to address all of them in combination.
- David Perlmutter, MD: We have to look at the big picture of what's going wrong, at how everything ties together. Let's learn what is actually happening in the Alzheimer's brain.
- Kirk Erickson, PhD: In an Alzheimer's disease patient, there's profound changes in many different aspects of the brain. There's changes in the very core cellular components of the brain that disrupt its functioning, disrupt how one cell communicates with any other cell in the brain. There's disruptions in the communication, there's disruptions in gene expression patterns.
- Kirk Erickson, PhD: How neurotransmitters and different chemicals are created and released by the brain. All of this results in a general deterioration of some brain structures and the increase of pathology. There's what's referred to as amyloid plaques. There's neurofibrillary tangles or a protein called Tau that ends up disrupting the communication systems.
- Kirk Erickson, PhD: All of this results in deterioration, atrophy, dysfunctioning of the brain. That can ultimately lead to many more changes in the brain and its emergent properties in not only memory function, but also in aspects of personality and mood. I think in terms of our hope for new treatments on the near horizon for treating or preventing Alzheimer's disease, I think that we have to start looking more at the prevention aspects.
- Ayesha Sherzai, MD: I review MRIs on a daily basis at the hospital and the clinic. When the disease has progressed in a patient with Alzheimer's disease, you see that the brain has shrunk.
- Ayesha Sherzai, MD: Hippocampus, which are two areas of the brain size of my thumb that are responsible for encoding memory, getting information from your environment and putting it to the right folders, files and cabinets in your brain or changing short-term memory to long-term memory, that's usually shrunk. You get to see a lot of what we call white matter disease. So what white matter disease is what it sounds like. These are these white spots in the subcortical areas of the brain or in the central part of the brain, which are the fibers coming out from the neurons. These white spots signify inflammation at the vascular level.





Ayesha Sherzai, MD:

Remember, we have about 400 miles of small blood vessels in our brain. It's an incredibly vascular organ. So unhealthy lifestyle, whether it's not eating the right foods or not exercising or not sleeping, causes inflammation in the inner lining of these arteries and capillaries. So you see vascular damage in particular areas of the brain, and it looks pretty scary. On the other hand, for a healthy person, you see a really nice plump brain. It's not shrunken at all. You don't get to see these white spots.

Ayesha Sherzai, MD:

For people who have aged successfully, you get to see a bigger size brain because activities like exercise, by keeping your mind active and providing the right environment for your brain to grow with the right kind of nutrition and stress management creates more connections. So you see that the size of the brain is quite different in a person who has aged successfully compared to the brain of somebody who is just riddled with the pathology of Alzheimer's disease.

David Perlmutter, MD:

You might think that you have no need to worry about Alzheimer's, but the truth is if you have a brain, then you are at risk for developing this disease. We now know that the changes that the brain undergoes that lead to Alzheimer's begin 20 to 30 years before the symptoms begin to show up, or even earlier. And that means that people in their 30s need to be taking precautions today. Waiting until symptoms show up may mean that it is too late to right the course. And this is something that we all need to be concerned about. We all need to take the necessary steps to prevent this disease today.

Georgia Ede, MD:

Most young people don't think they need to worry about things like Alzheimer's disease until they're much older, but nothing can be farther from the truth, I mean you really cannot start too early to worry about this, because whatever you're eating now is already damaging your brain. I know that sounds scary but it's true. So for example, they have found evidence, you can look at the brain, you can look for signs of insulin resistance on special imaging scans called PET scans, and you can see whether or not people have insulin resistance this way. And they've tested people as young as 24 years old and found evidence of insulin resistance of the brain. And to me, as a college psychiatrist, that's really chilling.

Sarah Gottfried, MD:

I believe Alzheimer's begins in your brain probably 30 to 40 years before a diagnosis. So we've got compelling data, looking



at brain scans, especially of women, showing that there's changes that predate the diagnosis by decades.

Michael J. Breus, PhD DABSM:

If you're really trying to nail down a period of time in your life when you need to start thinking about sleep for Alzheimer's, here's what I would tell you is young adulthood is probably where you want to go, starting in the 20s and 30s. And of course that's the time that everybody thinks they're bulletproof and they can go without sleep forever and stay up late on the weekends and work during the week.

Lisa Mosconi, PhD:

So for many years people would think about Alzheimer's, we used to think about Alzheimer's as a disease of old age. And mostly we associate Alzheimer's and dementia with old age because that's when the symptoms become really evident but in reality, the disease begins with negative changes in the brain in mid life. So when people are in their 40s and 50s and 60s.

Lisa Mosconi, PhD:

I think people should start making lifestyle changes in an Alzheimer's preventative way as soon as possible, it's never too late to start, but the sooner you begin the more benefits you really gain.

David Perlmutter, MD:

Typically, people first start thinking about Alzheimer's or becoming cognitively impaired when it starts happening. In other words, later in life. What's wrong with that strategy?

Mark Hyman, MD:

You can't wait until you're already suffering from memory loss to start thinking about this. This process occurs 20, 30 years, maybe even longer before you get your first symptom. This is documented through sophisticated PET scans, which look at the brain and development of amyloid. So we know we have to start early and you have to start basically in prenatal classes because what the mother eats affects the children's risk of disease.

Mark Hyman, MD:

You have to start with children and what they're eating, whether they're breastfeeding or not, affects the microbiome and the regulatory system around inflammation. Look at your exposure to toxins. Look at your biomarkers that relate to Alzheimer's, what's going on with your blood sugar and insulin? What's going on with your levels of B vitamins? What's going on with your gut? What's going on with your toxic load? What's going on with your level of exercise, sleep, stress, all of these play a huge role and unless you think about these things early and try to live a life that's managing these factors, you're going



to put yourself in increased risk. Yeah. What's frightening is that now one in four teenagers has prediabetes or type 2 diabetes. These people are at risk for Alzheimer's, so it's important if you're in your 20s or 30s to focus on this issue, to look at the fact that you may be slowly gaining a little bit of belly fat. Well, that is not a good thing if you have belly fat, that's brain damage.

David Perlmutter, MD:

With this new understanding, recognize that whether or not you are showing symptoms of cognitive decline, this series is for you.

David Perlmutter, MD:

The mentality of modern medicine in the western world is one that suggests that we can pretty well live our lives come what may, and then when we develop a problem, we suspect there is going to be a magic pill to take care of our illnesses. Well, while that may be true for some diseases, it certainly is not the case with respect to Alzheimer's disease. There is no meaningful treatment whatsoever. And yet we now recognize that preventive strategies are really effective.

David Perlmutter, MD:

So let's find out what we can be doing right now to help prevent Alzheimer's.

David Perlmutter, MD:

Dr. Bredesen, can you give us your five most important bullet points for an Alzheimer's prevention program?

Dale Bredesen, MD:

Number one, diet. It turns out to be incredibly important to get yourself into mild ketosis, to have an anti-inflammatory diet, to improve your insulin sensitivity, to optimize your microbiome. These things are all a critical part of the diet. And of course, appropriate times of fasting as well.

Dale Bredesen, MD:

Then, secondly, exercise, both strength training and aerobic exercise. If you happen to like high intensity, great. Again, this helps you with a number of factors. Then sleep, try to get seven to eight hours of sleep, and make sure that it is good high quality sleep. You want to allow sleep to enhance your cognition.

Dale Bredesen, MD:

And then reducing stress levels. When I was training, the idea of telling someone that they should actually seek joy, and that they should go out and do meditation and things like that, I

thought that was a joke. But it turns out that I can't ignore the data. No question, these things help in a number of ways.

Dale Bredeesen, MD:

And then brain training turns out to be very helpful, and doing this a few times a week. If you want to learn a new language, something like that, challenging your brain to support. Basically, your brain is going to enjoy being in this better environment that you have provided it, and it will respond very nicely.

Dale Bredeesen, MD:

And then beyond that, if there's hormone balancing that needs to occur, if there are specific herbs, you can talk to your practitioner about that. If there are specific nutrients, all of these things are critical, but these are the basics that will make cognitive decline a rare condition.

Georgia Ede, MD:

So the changes I think are most worth making for brain health, are avoiding processed foods, refined carbohydrates and vegetable oils.

David Ludwig, MD:

Over time, this highly processed diet takes a toll, leads to, over time, rising insulin resistance, chronic inflammation, and then for too many people, development of type 2 diabetes, which we know about, and type 3 diabetes, which affect the brain, and sets the stage for Alzheimer's.

Dominic D'Agostino, PhD:

So I think optimizing brain function and optimizing general health really comes down to what I call the trinity of health. And that's sleep, optimize your sleep. And that's totally, extremely important for brain function. Optimize your nutrition with low carbohydrate. Nutrition can really optimize brain health for most people. And really just getting your body moving and doing some form of exercise that works for you. That could be walking the dogs. That could be lifting weights. That could be riding your bike, whatever. But sleep, low-carb nutrition and just getting your body moving a few times a week are really the three things that are needed, that are non-negotiable, I would say, for enhancing and preserving brain function.

Emeran Mayer, MD:

We have indirect evidence, that dietary interventions that we now know have an important effect on the microbes. They have a positive or slowing effect, for example, on the progression of Alzheimer's disease. By far, the most likely mediator of that is clearly the gut microbiome.

Valter Longo, PhD:

So, the answer is start at 20, if not earlier, if possible, but if the reality is that you haven't started at 20, and you're 55 or 65, it doesn't matter. I think, particularly, using ketogenic, and using Fasting Mimicking Diets, and revolutionizing brain metabolism I think has got a real potential, even when somebody is in mild cognitive impairment.

David Perlmutter, MD:

We are so grateful to our guest experts for sharing their incredible knowledge with us, in this very intriguing area of science. In this series, we're going to learn about the tools we all have in our tool kits that can be utilized to help prevent Alzheimer's disease.

David Perlmutter, MD:

In episode two, we will learn about the gaps in the current standard of care and why we have actually failed to develop therapies.

David Perlmutter, MD:

In episode three, we will learn about the many tools that we have at our disposal to help prevent Alzheimer's.

David Perlmutter, MD:

In episode four we will learn about how genetics relates to Alzheimer's and explore the new science of epigenetics, and also neuroplasticity, and even neurogenesis, the ability that we have to grow new brain cells.

David Perlmutter, MD:

In episode five, we will learn why preventing diabetes is critically important for brain health, and what we can do to help reduce our risk for becoming diabetic in the first place.

David Perlmutter, MD:

In episode six we will learn why what we eat is relevant for brain health, and how to eat to help prevent Alzheimer's disease.

David Perlmutter, MD:

In episode seven we will learn about the microbiome, the gut bacteria, and the role it plays in cognitive function, and also how we can nurture a healthy gut microbiome.

David Perlmutter, MD:

In episode eight, we will learn about the role of stress in Alzheimer's, and ways we can reduce stress.

David Perlmutter, MD:

In episode nine, we're going to learn about exercise, a powerful medicine for the brain and how to incorporate exercise into our lives.



- David Perlmutter, MD: In episode 10, we're going to learn about the importance of restorative sleep for brain health and how we can optimize our sleep.
- David Perlmutter, MD: In episode 11, we're going to learn that environmental exposures may well increase your risk for Alzheimer's disease. Further, we're going to learn about what you can do to avoid exposing yourself to these risks.
- David Perlmutter, MD: In episode 12, we will learn about some of the very best supplements for the brain, and give you some very important recommendations. All of these empowering episodes will cover the most up-to-date and well-researched information available, and provide practical steps for taking advantage of this leading edge science.
- David Perlmutter, MD: What percentage of Alzheimer's do you believe could be prevented?
- Dale Bredeesen, MD: Well, if you look at the genetics, then you would say that 95% could be prevented, because it's only five percent, a little less than five percent actually, where the genetics seem to have a very high penetrance. Is it possible we could even prevent those? We don't know yet, so it may be better than 95%, but I believe that that 95%, where these are sporadic, could be prevented, virtually all of them.
- Sarah Gottfried, MD: When I think about Alzheimer's disease...I know that 99% of my risk of Alzheimer's is actually in my hands. Meaning that I can make choices each day to reduce my risk of Alzheimer's disease.
- Sarah Gottfried, MD: With my fork, with the exercise that I do, with the way that I rise above stress, with the way that I take care of my gut and reduce inflammation track and measure it. With the way that I connect with other people, with the way that I map my life onto a purpose and meaning and intention. So I want to give people that sense of hope that there is so much you can do.
- Jeffrey Bland, PhD: We are at a revolutionary stage as we're expecting to live longer and live healthy throughout those years. So we not only extend our lifespan, but our health span. The information that you are imparting to not only your patients, but the world at large through your communication efforts and your diligence, is



gonna make a real positive difference in sustaining what most people really want to have throughout the course of their years in the planet, which is cognitive function, the ability to enjoy life and to be the masters of their own destiny.

Amy Berger, MS, CNS:

Alzheimer's disease is very scary, it's very frightening, and it's very seemingly mysterious. I think we know enough about the connections between chronically high insulin and chronically high blood sugar and the abdominal obesity and the stress, and all of these things that affect metabolism and metabolic health, we know enough about that to take matters into our own hands. So we should feel encouraged. We shouldn't feel scared, we shouldn't feel disempowered. We should feel hopeful, we should feel powerful, because you can go to the supermarket and potentially reduce your risk for Alzheimer's today.

Leo Galland, MD:

Alzheimer's disease starts long before there are any symptoms of cognitive impairment, which means that everybody should be making lifestyle changes.

Leo Galland, MD:

I mean, if there's a condition that you don't want, it's Alzheimer's disease and you should start making the changes that prevent it as early in life as you can.

Leo Galland, MD:

Today is the day.

Anna Cabeca, DO, FACOG:

Whatever you're dealing with, you can have a better tomorrow, and you're worth it. You're worth the investment in yourself. You're worth in the energy it takes to do so. It will change your life. Not only that, what we look forward to as we're getting older are those healthy relationships, that we're surrounded by people we love, and they love us and we love them.

David Perlmutter, MD:

What's the reward for people these days in terms of brain health?

Michael Merzenich, PhD:

Well, first, David, it's called a better life. That's a reward. Remember that your brain is you. It's you. You want your brain to be vital, alive, vibrant, full of it. It's you. You want to be everyday in the operation when you get up, you want it to be lively and you want it to be alert to what's happening. You want it to be full of the wonders of the world. You want it to be joyful.

David Perlmutter, MD:

I hope you're as excited as I am to jump into this series.



David Perlmutter, MD:

As we've heard several times, it is never too early or too late to start caring for your brain. Once you start making the changes that we'll cover in this series, you might notice that you start thinking more clearly, forgetting less, and generally feeling better throughout the day. No matter where you are in life, you have the power to take control of your health destiny. In our next episode, we're going to take a closer look at the standard of care for Alzheimer's disease and why our current treatment strategies are falling short.

David Perlmutter, MD:

I can't wait to share this information with you. I will see you in our next episode, Untangling Alzheimer's Disease, What's Going Wrong?