ALZHEIMER'S
THE SCIENCE OF PREVENTION

Episode 3: The Alzheimer's Prevention Toolkit

David Perlmutter, MD: We've all been gifted with an amazing ability to heal and regenerate. This is made possible by systems in place in our bodies that help us resist infection, fight off disease, and stay healthy throughout our lives.

David Perlmutter, MD: What may not be common knowledge is that our brains have this ability, as well. Our brains have the ability to regenerate.

David Perlmutter, MD: In this episode, we will be learning about these mechanisms, their role in Alzheimer's disease, and how we can wield them to reduce our risk for developing this devastating condition.

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

David Perlmutter, MD: In previous episodes, we learned that not only is Alzheimer's on the rise, but that it is a disease for which we have no meaningful treatment whatsoever. This notion makes prevention absolutely paramount, but how exactly is prevention made possible? Let's explore some of the tools we have in our Alzheimer's prevention toolkit:

- We have the ability to change the expression of our genes through a process called epigenetics.
- We can grow new neurons in our brains through a process called neurogenesis, and this occurs throughout our lifetimes.
- We can rewire our brains through a process called neuroplasticity.
- We can prevent diabetes by maintaining healthy blood sugar levels, based upon the foods that we eat. We can choose a diet that preserves, nourishes, and optimizes our brains.
- We can nurture our gut microbiomes, the collection of microbes that live in our gut and play a pivotal role in our health and in our brain health.
- We can reduce stress, and thereby reduce inflammation in the brain.
- We can exercise to create healthier brains, and we can get good sleep, which is incredibly relevant for rejuvenating the brain.
- We can avoid environmental exposures that may threaten the brain and increase the risk for Alzheimer's disease.
- Lastly, we can support our bodies through smart supplementation.

David Perlmutter, MD: All of these empowering tools are available to us today, and as we progress further in this series, you will learn how to take advantage of all of them.

David Perlmutter, MD: We are all made up of DNA, our life code, and our DNA makes up our genes. These genes influence the story of our lives. However, our genes do not necessarily determine our future. We now know that we all actually have a say, in terms of which genes are expressed, and this is especially relevant when it comes to our health.

David Perlmutter, MD: The idea that we can influence our gene expression is called epigenetics, and it's incredibly empowering information. Let this sink in. Each of our decisions, with reference to lifestyle, changes the way our genes are expressed.

Dean Sherzai, MD, PhD: Every little step you take is a positive step. Eating an apple instead of the donut affects the epigenetics and walking to your work instead of driving adds to your epigenetics, meditation, and mindfulness reduce the stress which affects the hormones, which affects the genes. A good night's sleep significantly reduces the toxins that affect the genes. So all of those factors can push your genetic risk way back past your 90s and beyond. That's what epigenetics are. Epigenetics determine how you work with those genes, how you play with those genes and you have plenty of leeway to push it back.

David Perlmutter, MD: What an empowering notion it is that our genes do not determine our destiny. We influence our gene expression with every bite of food and every bit of exercise.

David Perlmutter, MD: Another amazing tool we possess is the ability to grow new brain cells. This is called neurogenesis, “neuro” as in neurons, which is the cells living within your brain, and “genesis” as in: new beginning. Incredible, isn't it? Research has shown that we can actually grow new brain cells, and this occurs throughout our entire lifetimes.

David Perlmutter, MD: Back when I was in medical school, we were told that we had a finite number of brain cells, and that with every beer we drank, we would lose 30 to 40 thousand brain cells.

David Perlmutter, MD: Well, we now recognize that we maintain the ability to grow new brain cells throughout our lifetimes, yes, well into our 90s.

Dominic D'Agostino, PhD: Neurogenesis is the formation of new neurons in the brain, and different areas of the brain have more robust neurogenesis rates happening. And as we age, or maybe taking a step back, years ago it was thought that we have the neurons that we have and they die off with age. And as we lose neurons, that can contribute to age-related cognitive decline. Science that emerged in the late '80s and the early '90s suggested that a process called neurogenesis was happening. And through dietary implementation and exercise we can actually stimulate this neurogenesis process, which is the formation of new neurons, which can contribute, potentially, to preserving and potentially even enhancing brain function and brain energy metabolism, too.

David Perlmutter, MD: Yes, we are grateful for the ability to grow new brain cells, but it also turns out that we can rewire and reshape our brains through a process called neuroplasticity, neuro as in neurons and plasticity as in plastic or pliable, movable, changeable.

David Perlmutter, MD: The neurons in our brains gather and transmit signals through a complex network. There are more than 100 billion neurons communicating through trillions and trillions of connections in the human brain. This vast network is modifiable. It can grow new connections throughout our lifetimes and, in fact, does so

Michael Merzenich, PhD: No matter what happens to you, your brain is plastic. No matter what your genetic burden is, your brain is plastic. We know that there are people who have a very bad genetic disposition that never develop Alzheimer's disease and live a grand old life. I strongly suggest that you use the plasticity of your brain to ensure that you're one of those. I mean, a vicissitude should be a challenge to you that you're going to really do something about it now and are really pay attention to your brain health and you're going to do that by living your life to the advantage of your brain.

David Perlmutter, MD: The complexity and beauty of our brains is absolutely stunning. I've been studying the brain for most of my adult life, and I'm still in awe of its capabilities.

David Perlmutter, MD: We want to protect our brains throughout our lifetimes. One of the key ways to prevent the development of cognitive decline and full-blown Alzheimer's is not becoming diabetic. We know that becoming a type 2 diabetic is associated with more than doubling the risk for developing Alzheimer's disease. In fact,

some have actually called Alzheimer's disease type 3 diabetes, because these two diseases share so many similarities. Some of the metabolic impairments we see in type 2 diabetes are actually found to be operating in Alzheimer's disease as well.

Suzanne De La Monte, MD, MPH: So how can Alzheimer's be thought of as a Type 3 diabetes? Basically, insulin is needed to keep neurons and cells in the brain working. And it's not just the neurons, the thinking cells, all kinds of support cells, the blood vessels, everything, they all need insulin, it's the master hormone of the brain. That turns out to be true in much of the body, you need insulin. So if the problem is only in the brain, then you could call it a diabetes of the brain and very selectively. And so insulin resistance means that no matter how much insulin you have, the brain is not obeying. That's like knocking at a door and nobody responds to it, they can't hear it. So the brain cells can't hear the insulin knocking away, let's get some work done, and they ignore it. So that's equivalent of insulin resistance so that's why if it's only in the brain or predominantly the brain, that's how you could make of Alzheimer's is a Type 3 diabetes.

David Perlmutter, MD: Type 2 diabetes is largely a disease based upon lifestyle choices. The most important of these choices is diet, but a healthy diet can do much more than just prevent and even treat type 2 diabetes. It can supply the fuel to your brain that your brain needs to function optimally.

David Perlmutter, MD: A brain-smart diet provides all of the life-supporting nutrients your brain needs

David Perlmutter, MD: It's a diet that's low in sugar, refined carbohydrates, and high in fiber and containing plenty of healthy fat.

Anna Cabeca, DO, FACOG: For people that are concerned about cognitive function and memory, I recommend that you have a diet that has a strong plant base, and a keto, I call it keto green, type of plan, so healthy fats for neurologic function, such as avocados, salmon, nuts, seeds. Those are all incredibly beneficial, as well as the microgreens, the cruciferous vegetables that are nutrient-dense, such as broccoli sprouts, alfalfa sprouts and crucifers like broccoli, cabbage, cauliflower and healthy amounts of those on a regular basis.

David Lugwig, MD: We have to address that metabolic problem at its source. Yes, weight loss is helpful, but the quality of the foods we eat, reducing insulin levels, calming chronic inflammation, the right

balance of protein, fat, and carbohydrates, can turn the situation around, even in rather advanced stages of chronic disease.

David Perlmutter, MD: Eating to support cognitive function and brain health is something we can all do every day.

David Perlmutter, MD: This has far-reaching effects. When we eat, we are actually also feeding our gut bacteria, collectively called the microbiome. The microbiome is the community of life-supporting microbes that live in your gut and play a pivotal role in your health and in your brain health.

David Perlmutter, MD: In addition to the food we eat, chronic stress, our levels of exercise, the restorative nature of our sleep, exposure to toxins, and even the supplements we take all have an impact on the health of our internal microbes. The ability to live in a way that nurtures our gut microbiomes is one of the most powerful tools we have for helping prevent Alzheimer's disease.

Leo Galland, MD: There's a lot of research emerging in the area of Parkinson's disease and to some extent Alzheimer's disease as well, which is finding that toxins start in the gut and then travel through the vagus nerve up to the brain and that these degenerative diseases are actually diseases that start in the gut and travel to the brain because the toxins follow the route of the nervous system and they are able to do this because inflammation creates excessive permeability of the barrier.

Leo Galland, MD: That's what a leaky gut is and the term is actually used in very austere major medical journals now.

Leo Galland, MD: The microbiome plays a role in maintaining healthy permeability, a healthy function of that barrier. There are a number of species of bacteria that are normally found in the gut that help to maintain the integrity of the gut lining.

David Perlmutter, MD: Now I mentioned earlier that stress can harm the gut bacteria, but stress has many additional detrimental effects.

David Perlmutter, MD: Levels of our hormones, levels of inflammation, and even blood sugar are also negatively influenced by chronic stress. All of these are connected to brain health. Reducing chronic stress is, therefore, critical when it comes to helping prevent Alzheimer's disease.

Max Lugavere: Your body's stress response is so attuned to things that might be anxiety provoking. And what happens when we're chronically stressed out is that ... well, we have the same physiological response to psychological stress that we would to physical stressors like that lion running towards us. And this is fine in an acute sense, but when it's a chronically activated system, it causes stress hormones to remain chronically elevated. And they've actually shown that chronically elevated cortisol relates to smaller memory centers in our brains. It's also a great way of reducing BDNF, which is that powerful growth factor that the brain uses to stay plastic. And it's just bad in other ways as well. It's a catabolic thing, meaning it breaks down your muscle tissue, which is not good because we know that having stronger muscles relates to better brain health over time.

Anna Cabeca, DO, FACOG: It's estimated that 90% of all physician appointments are due to stress-related complaints. So stress we're talking about as the 21st century epidemic, right? Everyone has it. We're exposed to it in so many ways. It's really going out of control, from perceived stress to real stress through physical challenges, emotional and relational stressors. Those are all having a significant effect on our body.

Anna Cabeca, DO, FACOG: The link to how that affects our brain health is really substantial.

David Perlmutter, MD: One of the best ways we can reduce stress is through exercise, but exercise impacts far more than our levels of stress. It affects virtually every organ and system in the human body.

David Perlmutter, MD: Exercise confers a laundry list of benefits which, in addition to stress reduction, includes improved insulin sensitivity, increased neurogenesis and neuroplasticity, increased blood flow to the brain, and more. All of these are very relevant, when it comes to Alzheimer's prevention.

Kirk Erickson, PhD: What we've found in our research was that 12 months of brisk walking was capable of actually increasing the size of this really important region involved in memory formation. What this indicates to us is that this brain area, the hippocampus that is so closely linked to memory formation and Alzheimer's disease, remains really plastic, it's malleable even in older adulthood.

Kirk Erickson, PhD: What's really remarkable is that only 12 months of brisk walking was capable of actually reversing the decay that we found in this brain structure.

David Perlmutter, MD: Exercise also helps you get a better night's sleep, which is really a very important thing because, while we sleep, our brains are restored and rejuvenated. Sleep is the period during which our brains literally flush out all of the waste that builds up during the day. Getting enough quality sleep is critical for optimal brain function and helping reduce your risk for Alzheimer's disease.

Michael Merzenich, PhD: Sleep is controlled by a brain. If the brain is healthy, sleep will be healthy. It's a rule. And if the sleep is healthy, it will contribute to keeping the brain healthy. It's a circle. You want to be in the circle in which the brain is advantaging the sleep and the sleep is advantaging the brain.

Michael J. Breus, PhD DABSM: So this is a question that I get on a very regular basis, why is sleep important? And so, first of all, I like to tell people that sleep is just as important as diet and exercise. In today's world, people are oftentimes talking about wellness, talking about becoming healthier and things of that nature. Yet, historically, we really haven't seen a lot of emphasis on sleep. Well, I'm here to tell you, sleep turns out to be one of the most critical factors in your overall health for many different reasons. I oftentimes am telling people sleep affects every organ system and every disease state. Everything you do, you do better with a good night's sleep.

David Perlmutter, MD: Though our detoxification systems are especially active during sleep, they're also basically running 24/7. Although we have an innate ability to detoxify, certain compounds can still be harmful. Toxic environmental exposures are very common. If we learn what they are and where they are found, we can better avoid them.

Anna Cabeca, DO, FACOG: Toxins are any substance that interfere or negatively affect our body. For example, we can have toxins from chemicals that we're exposed to, whether it's in our skin products, our skincare products, our makeup, et cetera. If it disrupts our normal physiologic functions, it is toxic to our body. And we are exposed to so many types of toxins on a daily basis, whether it's in the air we're breathing, off-gassing from furniture or carpets, paint, chemicals that we've used to clean, we're absorbing toxins from that. Let alone, what's really interesting is that it's estimated that by the time a woman leaves the house in the morning, we've put on over 160 chemicals. While we look and

the CDC studies toxins, it's the cumulative effect of toxins that is really the problem. It's the rub.

David Perlmutter, MD: We'll be going into significant detail about how to identify and avoid toxic environmental exposures, in episode 11, learning how to protect your body from the harms caused by these chemicals.

David Perlmutter, MD: Another great way to support your body is through supplements. Supplements help with various deficiencies, and some of them even bolster brain health. We are lucky to have access to these supplements, which give our bodies and brains the extra support they need.

David Perlmutter, MD: We can change our gene expression through our lifestyle choices. We can grow new brain cells and form new brain connections throughout our lifetimes. We can prevent and potentially reverse the brain toxic effects of diabetes and insulin resistance. We can improve our diets, lower our stress, enhance our sleep, get more exercise, avoid toxins, and take supplements to help lower our inflammatory load and protect our brains. We have the tools we need to take meaningful action towards preventing Alzheimer's disease today.

Ayesha Sherzai, MD: The thing that excites me the most about Alzheimer's prevention is the fact that every small thing that you do on a daily basis makes a big difference. When it comes to brain health and health in general, there's always a lag effect. When you do something, you don't necessarily see the benefit right away. Unlike other things like where you put on something on your skin or you get hurt on your skin is quite visible. You see it there. You get hit on your arm or your leg and you see a bruise. You get burned, you see the inflammation, you see the blisters. But what happens inside our bodies is we actually don't see it. So people can't really connect lifestyle with brain disease.

Ayesha Sherzai, MD: But when you're a scientist and when you're a physician, when you get to see hundreds and hundreds of MRIs and CT scans of the brain, and when you're in the midst of it and you see how cholesterol change, how blood sugar change, how insulin resistance is reversed. It's such an exciting field. And so that excites me. With the neurodiagnostic, with the fact that people understand the concept of prevention, they're coming forth to the clinic to get themselves tested. To get an MRI, to get a neuropsychological test score, to get a blood test and then see

how they change, it actually motivates them. I'm glad that this conversation is going on. I'm glad that we're doing this because this is the most important public health service to tell people that whatever you do every day makes a difference and you actually prevent Alzheimer's disease.

Max Lugavere: Exercise, diet, critically important. Stress mitigation, sleep is very important. Getting good sleep. These are all parts of the Pie. Incremental improvements in any one area, go for it. I think at the end of the day to really make a noticeable dent on the way that our brains work, I think it's good to look at every area of our lives and see where we can make those brain healthy tweaks.

Mark Hyman, MD: The good news is that every little bit counts and what we understand about the brain is that it's resilient, that it can repair, so making changes in your diet can be profound. Just cutting out added sugars, just adding a little more vegetables, doing walking. You don't have to be a marathon runner, but just walking a little bit every day can have a profound effect on Alzheimer's. Doing five minutes in meditation, doing a little bit of sleep hygiene so you sleep better, simple things, taking a multivitamin, taking some fish oil, vitamin D, it doesn't have to be all or nothing. Little things make a big difference.

Amy Berger, MS, CNS: Alzheimer's disease is a multifactorial disease. There's not just one single thing going wrong, so in order to address it, you can't really just use one single intervention. There's not going to be one single magic bullet. If this is a multi-factorial complex illness, you need multiple different strategies addressing it from different angles. Dale Bredesen uses his roof analogy. If you have a roof with 36 holes in it, you can patch five holes and you still have a roof with 31 holes. You may not have to address every single thing, but you have to address as many of them as you can.

Dale Bredesen, MD: I think that things are changing. Looking from the other end at the biochemistry of the neurodegenerative process, we start to see these beautiful links between what's actually happening in the test tube, and what's happening in your brain, and what's happening with nutrition, and what's happening with sleep, and what's happening with exercise, and what's happening with detoxification, and what's happening with stress. Now we're starting to be able to see how these link up directly.

David Perlmutter, MD: We are so grateful to our guest experts for telling us about these tools to help prevent Alzheimer's disease.

David Perlmutter, MD: Here are some of the actionable steps you can take today, that we will be covering in much more detail in further episodes.

- We can prevent, manage, or even reverse type 2 diabetes by optimizing blood sugar through dietary change.
- Eat a brain-smart diet that is low in sugar and refined carbohydrates, processed foods, and prioritizes whole foods, vegetables, and healthy fats.
- Nurture your microbiome.
- Reduce chronic stress.
- Exercise regularly.
- Get a good, high quality night's sleep.
- Reduce toxic exposures.
- Support your body through the use of important supplements.
- All of these lifestyle changes will go a long way towards helping prevent Alzheimer's disease.

Amy Berger, MS, CNS: I think at this point in time, we have a lot more tools than most people realize, because going by what the scientific literature indicates is causing this disease or what precisely is going wrong in the Alzheimer's brain, there are very much interventions that we can take that are diet and lifestyle in nature that should be able to potentially prevent this.

Lisa Mosconi, PhDi: As a scientist and a clinician, I think we have faced a lot of resistance towards the notion that Alzheimer's prevention is visible and just in recent years, I think more and more doctors and scientists are actually embracing the notion that we can prevent Alzheimer's disease in many cases. A notion that was considered unthinkable even just five, maybe 10 years ago. There's definitely hope, we're learning that the health of our brains is largely in our control, which is also very empowering because we now know what kinds of things affect the brain that we have control over and also makes us accountable. For many years, Alzheimer's was seen as a blameless disease. Like it just happens to people, you have in your genes or it's just that you're older and now instead, we really need to take responsibility for a good part of what happens inside their brains. It takes discipline, it takes commitment, but the benefits are for life.

Sarah Gottfried, MD: I loved my grandmother so much. I grew up just three miles from her. She used to pick me up from the bus stop every day and drive me home. She loved martinis. In fact, she had two to three pretty much every night. She did not have a career and she was frustrated about that. She loves soap operas, and she watched them all day long. She also loved sugar. So I grew up baking chocolate chip cookies with her. Now, when I was seven years old, my beloved grandmother would pick me up at the bus stop and start to get lost driving the five miles to her house. Within about five years, she was diagnosed with Alzheimer's disease. She languished in a nursing home for 18 more years, unable to recognize any of us, unable to connect. It was heartbreaking. It drove me to go to medical school.

Sarah Gottfried, MD: Second model, my great-grandmother, this is my mother's father's mother. Her name was mud because my grandfather couldn't say the German word for mother. So we called her mud and the name stuck. She was a bit of a radical. She only ate Whole foods. She thought packaged foods were horrendous. She didn't think that you found the answer to health in the bottom of a pill bottle. She believed that you find the answer to health in the way that you architect your day and architect your life, full of purpose and meaning and intention.

Sarah Gottfried, MD: She would show up at our house in Maryland with suitcases full of kale and wheat berries, and had a way of eating that was way ahead of her time. She slept on a board because she felt like sleep in an erect spine was incredibly important. She practiced yoga starting in the 1950s. When she came to my wedding at age 96, she flirted mercilessly with every man who was there and danced with them. She outlived four husbands. She died in her sleep peacefully at age 97 at home living independently with zero chronic disease.

Sarah Gottfried, MD: So I have these two very different models of health. I want to be like my great-grandmother. She did all the things that we know can help prevent Alzheimer's disease. She did not eat sugar. She was very careful about alcohol. She used to say, I love wine, but it doesn't love me. She was known as the squeaky wheel. She had no chronic disease. That's what I want. So when I think about Alzheimer's disease, especially the family history that I have, 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

David Perlmutter, MD: As we continue on in this series, we're going to learn about how blood sugar is related to Alzheimer's disease and how to prevent and manage, and even reverse type 2 diabetes.

David Perlmutter, MD: We will learn what a brain-smart diet looks like and cover dietary approaches shown to be helpful for the brain, including ketogenic diets, fasting, and whole food, plant-based diets, as well.

David Perlmutter, MD: Then we will gain a deeper understanding of the microbiome and the far-reaching effects of our gut bacteria on every part of the body, including the brain.

David Perlmutter, MD: We will see why exercise is so very important for the brain and describe practical steps for incorporating exercise into our daily lives.

David Perlmutter, MD: We will also learn much more about what happens in the brain while we sleep and exactly how much sleep is needed for healthy brain function.

David Perlmutter, MD: We will explore some very valuable supplements for the brain, including the omega-3 DHA, whole coffee fruit concentrate, and prebiotic fiber.

David Perlmutter, MD: We have all of this to look forward to in this series, as we cover all of these topics in great detail, helping you to build a lifelong Alzheimer's prevention plan.

David Perlmutter, MD: To be clear, your health destiny is in your hands. It's really great that you're watching this series, but that is obviously not enough. The purpose of this series is to evoke change. It's to evoke changes in your behavior and to have those changes start immediately.

David Perlmutter, MD: In our next episode, we will gain a better understanding of genetics and to what extent genetics influences the risk of Alzheimer's disease. Is there a gene for Alzheimer's? If so, what

does it mean to have this gene? We'll also learn more about epigenetics, neurogenesis, and neuroplasticity, and how to use this information to promote the growth of new brain cells and strong networks in your brain.

David Perlmutter, MD: All of this information fundamentally relates to the notion of preventing Alzheimer's disease, and I can't wait to share it with you. I will see you in our next episode, How to Change Your Brain for the Better.