



ALZHEIMER'S

THE SCIENCE OF PREVENTION

Episode 7: The Gut-Brain Connection



- David Perlmutter, MD: When you hear the word bacteria, you might immediately associate it with a negative connotation.
- David Perlmutter, MD: After all, bacteria are the reason Mom tells you to wash your hands before dinner,
- David Perlmutter, MD: But, what if I told you that there are organisms living inside of you that are healthy bacteria, the kind of bacteria you can benefit from, the kind of bacteria that make you, well, you. The microbiome is just that. So, what exactly is the microbiome and how does it connect to Alzheimer's disease?
- David Perlmutter, MD: This episode focuses on the truly amazing understanding that our gut bacteria are playing an important role in our brain health. I can absolutely understand that for many of you, this relationship may seem at the very least, challenging. But, I can absolutely assure you that science has now shown that the microbiome, the collection of gut bacteria that we all have within us, as well as the chemicals they produce, play an important role in determining the health, the functionality, and even the destiny of the human brain.
- David Perlmutter, MD: We will explore exactly what is meant by the term microbiome and more importantly, how nourishing our gut bacteria may be a powerful strategy as it relates to Alzheimer's prevention. I'm Dr. David Perlmutter and this is Alzheimer's - The Science of Prevention.
- David Perlmutter, MD: In previous episodes of this series. We've learned that not only is Alzheimer's on the rise, but it is in fact a disease for which there is no meaningful treatment whatsoever.
- David Perlmutter, MD: More importantly, what we've revealed thus far is empowering information that shows us how we are not at the mercy of our genetics in terms of our health destiny
- David Perlmutter, MD: And, this applies in the context of Alzheimer's disease as well.
- David Perlmutter, MD: We've already reviewed some of the important tools available to you to help reduce your risk for Alzheimer's, including dietary strategies, exercise, avoiding various toxins in the environment, optimizing sleep, and avoiding and managing type two diabetes. We've also shown how these goals focus on reducing inflammation. Recent science has revealed the human

microbiome also plays a pivotal role in determining levels of inflammation within the body.

David Perlmutter, MD:

But, before we move any further, let's take a moment to learn exactly what the microbiome is all about.

Emeran Mayer, MD:

A microbe is a tiny organism that is invisible to the eye. On the other hand, microbes are the most abundant life form on Earth, and there's several what we call domains. Bacteria, viruses, archaea and fungi.

Leo Galland, MD:

Microbes are organisms that can only be seen under a microscope. They're tiny. Most of them have only one cell. The majority of microbes in your body are bacteria but there are some other microbes as well.

Leo Galland, MD:

There are viruses. There are yeast and fungi. There are organisms, which you'll loosely term parasites but not necessarily parasitic and they're all there. They're all living in your body interacting with the other organisms, interacting with the cells of your body and their presence helps to make you you.

Emeran Mayer, MD:

What we know most about those microorganisms in terms of the gut microbiome, is really for the bacteria. We're just beginning to learn about the viruses and fungi. Microbiota is an ecological community of microorganisms, primarily bacteria, that basically inhabit most living creatures on Earth. They are living on different surfaces outside our body. They live in the lungs and the gastrointestinal tract. The number in terms of the microbiome is staggering because we have several million genes in the microbiome, as opposed to the 20,000 human genes.

Emeran Mayer, MD:

There's been an explosion of research driven initially largely by studies in mice and animal models that has indicated that the microbes don't just live in the gut and break down fiber, but that the breakdown products, the metabolites, have vast effects throughout the body, pretty much in every organ, so including the immune system, particularly important target, metabolism, another big target, hormonal system. Also, the brain is an important target, and the mean time there's really not a part of the body including the skin, the liver, the lungs, that is not in some ways in communication with the gut microbiome. They have their own microbiomes, but in some ways there's this connection that there's a communication between those

organisms that live in the gut and produce molecules, actually can communicate with all these distant organs.

Amy Berger, MS, CNS:

The microbiome is the bacteria that live inside us. We used to kind of think it was only in the gut. You'll always hear about the gut microbiome. We've learned in recent years that there's a skin microbiome, there's oral microbiome, obviously there's microbiome in the female genital tract. For the most part, these are the beneficial bugs that we want to have living inside us. We live in symbiosis. They help us, they help us stay healthy.

Leo Galland, MD:

Microbiome is the collection of all the microbes in your body and specifically it really refers to the DNA of those microbes.

Leo Galland, MD:

Here's a fascinating fact, there is 1,000 times more types of DNA from bacteria in your body than there is DNA that belongs to you.

Leo Galland, MD:

Bacteria growing in your gut affect every other aspect of your body. Your body does not exist without these bacteria. They've been present since birth, maybe even before birth and they especially affect the function of the brain.

Leo Galland, MD:

Over 90% of those substances, the chemicals circulating in your blood are not produced by your own cells. They are produced by the microbes most of whom are in your gut.

David Perlmutter, MD:

This is really important information. Now we can see why keeping our gut bacteria healthy is really important. First and foremost in the health of our gut bacteria is the food that we eat.

David Perlmutter, MD:

Food nurtures our gut bacteria, allowing them to do what they do best and that is keeping our bodies and our brains healthy. However, things like a poor diet, taking antibiotics or other medications directly threaten the health of our gut bacteria. We need to understand not only how to avoid these harms to the microbiome, but also how to improve its health.

David Perlmutter, MD:

This is also the reason why dietary fiber is so important, especially prebiotic fiber, since that is what our gut bacteria like to eat.

David Perlmutter, MD:

We will discuss the dangers of genetically modified foods that paved the way for a toxin called glyphosate to enter our food chain.



- David Perlmutter, MD: In addition, we will explore the impact sleep has on the microbiome and how exercise might increase the diversity of the bacterial species living within us.
- David Perlmutter, MD: All of these actions are focused on the microbiome and its role in inflammation, the pivotal mechanism underlying Alzheimer's disease.
- Amy Berger, MS, CNS: The biome can get out of balance, out of whack, and there is overgrowth of pathogenic bugs, insufficiencies of the beneficial ones, and they can cause all different kinds of health problems that manifest in various ways. There's some interesting research linking gut biome disruption to, not just Alzheimer's disease, but Parkinson's disease and some other neurological disorders as well.
- David Perlmutter, MD: You mentioned the importance of healthy gut bacteria. What do we do that threatens that health?
- Dale Bredesen, MD: So many things.
- Dale Bredesen, MD: Part of the problem with 21st century medicine here now is that we have made assumptions over the years. It's just as good to have a soda, if we put in something that's not sugar, then everything is going to be okay. Well, that turns out to be wrong. We can use Roundup and we can grow these great crops. Well, that turns out to be a disaster for your microbiome. This, of course, alters your microbiome. It alters metal binding. It does all the things that affect bacteria and plants, and therefore affect you.
- Dale Bredesen, MD: We've made assumptions over the years that have simply turned out to be wrong. As we now begin to understand this, we begin to understand, "Wait a minute. Glyphosate is not good for you. Wait a minute. Your gut microbiome is huge. Wait a minute. Eating things that cause leaky gut are huge. We need to correct these."
- Dale Bredesen, MD: The approach of many has been to close your eyes and stick your head in the sand and say, "This can't be, because we always did it this way and it's got to be fine". Well guess what? Obesity is on the rise. Type 2 diabetes on the rise. Alzheimer's is on the rise. Let's look at why that is.

David Perlmutter:

Can we visit the GMO discussion, the GMO argument as it relates to Alzheimer's?

Mark Hyman, MD:

Well, GMO is a very big topic. There's lots of controversy about it. There's back and forth evidence whether GMO foods are harmful or helpful. What may be more relevant is what we put on GMO plants. Glyphosate for example, is also known as roundup and there are many plants that are roundup resistant, meaning you can grow soybeans, and the soybeans are resistant to the roundup and it will kill all the rest of the weeds on the farm. Sounds like a good thing, but it turns out that glyphosate is being used in massive quantities because they're not working as well as they used to. And the amount of glyphosate in our food and our food system is driving changes that we hadn't expected. It increases the risk of cancer, according to the World Health Organization. It alters our gut microbiome, which is the bacteria in there that may drive change that lead to inflammation and toxicity.

Mark Hyman, MD:

If you have gut bacteria that are healthy from not consuming glyphosate, your brain's going to be healthier.

Leo Galland, MD:

The relationship between stress and the microbiome is bi-directional. The microbiome impacts on the way your body responds to stress but stress impacts the microbiome and may even select out for certain kinds of microbes depending on the nature of the stress.

Leo Galland, MD:

What does stress do to your gut? Well, it does a few things. First of all it alters the movement in the gut, the motility. Motility is one of the factors that keeps the microbiome well organized. Stress also may deplete certain bacteria.

Emeran Mayer, MD:

I think there's enough evidence now that negative effects on the microbiome, on the diversity, on the relative abundances of good and bad microbes, that we're seeing resilience of a diet that's high in refined carbohydrates and I think that's really what sugars are. I think other carbohydrates are actually very healthy. That plays a major role in the compromise microbiome that many people in Western societies, that has been linked to many of the diseases that we see. So, many diseases, or if you look at the health of the microbiome over the last 50 years, has clearly been deteriorating. If you use diversity as the main criteria for microbiome health, and many factors that contributed to this, certainly one aspect of it is the diet, the high

sugar, low fiber and high fat diet of Western diets. If somebody gets most of their calories from refined carbohydrates, automatically they're devoid of intake of fiber that comes with complex carbohydrates.

Emeran Mayer, MD:

So, what we have done as a society, we've taken all the fiber out of complex carbohydrates. We prefer white rice. We prefer potato strains that might have as little fiber as possible. We have liked white bread, taking out all the fiber. So, I think our food supply has shown an increase in these refined carbohydrates and a decrease in the healthy fiber containing carbohydrates. So, I personally think that that's one of the main problems that has happened.

Leo Galland, MD:

Sleep and the microbiome have a fascinating relationship. First of all, the normal pattern of sleep depends upon the microbiome and this may really be ... It surprised me when I first read it.

Leo Galland, MD:

It's the interaction between the microbiome, the immune system and the adrenal glands that creates this architecture to sleep where early sleep, so called beauty sleep, is really deep and very restful, and late sleep is full of dreaming.

Leo Galland, MD:

Now, if you're not sleeping, lack of sleep begins to impact immune function and it throws the whole architecture of sleep off. That begins to create a stress response in your body, which then starts to alter the composition of the microbiome.

David Perlmutter, MD:

Understanding the relationship between our food choices and other lifestyle issues to the health of our gut bacteria and how that translates into reducing risk for Alzheimer's disease is fundamental. A diet, for example, that's high in refined carbohydrates or things like chronic stress and exposure to antibiotics ultimately manifests as changes in the gut bacteria that may well be linked not only to Alzheimer's, but to other issues like coronary artery disease, diabetes, depression, and even cancer. Moving forward, we're going to take a deeper look at how imbalances in our gut bacteria present a powerful threat to the brain.

David Perlmutter, MD:

Without question, one of the most important roles of our gut bacteria is their role in metabolism.



- David Perlmutter, MD: Changes in the gut bacteria translate to a significantly increased risk for elevation of blood sugar.
- David Perlmutter, MD: And as we've explored, elevation of blood sugar represents one of the most powerful risk factors for the development of Alzheimer's disease.
- David Perlmutter, MD: The other important consideration as it relates to the microbiome, circles back to the important role of our gut bacteria in keeping inflammation in check, simply stated, damage to the bacteria can cause increased inflammation and that is hugely important since Alzheimer's disease is an inflammatory disorder.
- David Perlmutter: We're hearing a lot these days about leaky gut. We know that leaky gut can pave the way for inflammation. How might that play a role in Alzheimer's?
- Mark Hyman, MD: Well, we can't even imagine. Most of us, how our gut, which is this tube, it's literally outside of us, can cause damage to our brain, which is supposed to be locked in our skulls across that impermeable barrier called the blood brain barrier. Well, it turns out not only can you have leaky gut, but you can have leaky brain and that is causing so many of the inflammatory processes to be active. So when your gut is out of balance, when you have a microbiome that is dysregulated, it's like a garden with too many weeds or with toxic plants in them or when you have an injury from bad foods or from various things that we're having our environment like glyphosate or gluten, it's causing leaky gut. The things that are inside that tube, which is outside of you, leak inside of you across this barrier and end up causing inflammation because 60% of your immune system is underneath that lining.
- Mark Hyman, MD: And when that lining breaks down the poop and the food particles leak across into your immune system and your immune system says, "Hey, this is not me. Let's fight this battle." And creates a massive inflammatory response and it's affecting every part of your body, including your brain.
- Leo Galland, MD: There is a very definite relationship between the gut microbiome and Alzheimer's disease...there are a handful of mechanisms by which the microbiome may contribute to Alzheimer's.



- Leo Galland, MD: First of all, there is the effect on glycemic response. Alzheimer's is associated with elevations of blood sugar. The glycemic response, blood sugar response that you show to a meal is very strongly influenced by the microbes living in your gut.
- Leo Galland, MD: Second, there are certain bacteria that produce enzymes or fragments of proteins called peptides that contribute to the kind of pathology that is seen in the brains of people with Alzheimer's.
- Leo Galland, MD: These enzymes and these peptides travel through the nervous system to the brain to do their damage but they come not from your body. They originate with these organisms either in your mouth or in your intestine.
- Leo Galland, MD: Those are the ways in which the microbiome is important for Alzheimer's disease.
- David Perlmutter, MD: We're hearing so much about the important role that our gut bacteria are playing, in general health and now even in brain health, how might that be reflected in risk for Alzheimer's?
- Jeffrey Bland, PhD: So the microbiome as we now call it, which is this complex ecology of all these interesting species of organisms that live in our gut is an extraordinary and now kind of re-found chapter in medical history because we have to go back at least a hundred years to kind of understand that this is not totally a new concept that it's been around, but it's just kind of been modernized.
- Jeffrey Bland, PhD: The gut has this extraordinarily robust immune system called the gastrointestinal associated lymphoid tissue, where more than 50% of our antibodies on our body are produced in our gut immune system. So actually the center of our immune system is in the gut.
- Jeffrey Bland, PhD: We know that the brain's immune system is intimately connected to the gut's immune system, which is intimately connected to the microbiome, which is then influenced by our lifestyle. Through how we eat, how we think, what we drink, drugs and alcohol that we're exposed to. All these things modulate the effect on the microbiome, what I call the camping ground. This is a big camp out.

Jeffrey Bland, PhD:

The surface area of our gastrointestinal tract is about that of a doubles tennis court and that a doubles tennis court is occupied as a campground for literally hundreds if not thousands of different types of microorganisms that all have their own camp region. And when you disturb that, that's called dysbiosis. And those bacteria can be of three families. They can be, we call a symbiotic that actually induce a positive immune function. They produce vitamins and amino acids, and then there's the commensals. Those are the bacteria that are there that kind of don't do harm, but they don't do good. They just take up space.

Jeffrey Bland, PhD:

And then there's the small percentage that we call parasitic, that can actually induce injury to our immune system. And in fact, in a gram of stool, there are more bacteria than there are stars in the known universe of which in a healthy microbiome, you have a 99% of them being either the friendly or the commensals with only very small, less than 1% being the parasitic. As however you get dysbiosis, you get rebalancing and you get more of these, clostridia another organism that can produce toxic secondary byproducts, which have effects not only in the immune system, but can be direct neurotoxins.

Jeffrey Bland, PhD:

This is a huge new breakthrough to understand why it is that people that have gluten problems have dementia. You know, people said, well, hold on, isn't gluten a problem with the gut where you get inflammatory bowel disease? No, you can get appraised in whose responsive, adverse to gluten, whose major effect is on brain immune function and that connects to dementia. So now it's a whole new revolutionary, breakthrough, and understanding of the microbiomes connection to neuronal function.

David Perlmutter, MD:

So with elevation of blood sugar and increasing inflammation, we have two powerful mechanisms that are well described as being related to increased risk for Alzheimer's.

David Perlmutter, MD:

But, here's the good news, the empowering news. Both blood sugar and inflammation can be improved when we take steps to improve the health of our gut bacteria.

David Perlmutter, MD:

And, this is important information for sure as it relates to the health of your brain.

- David Perlmutter, MD: You've learned a lot so far about how the trillions of bacteria living within your intestines play such an important role in determining your brain's destiny.
- David Perlmutter, MD: We absolutely need to prioritize diet and other lifestyle choices to cultivate a robust and healthy microbiome and that will lead to optimizing brain function as well as a brain that is resistant to disease. This is how we resist inflammation and this is how we reduce our risk for diseases like Alzheimer's.
- David Perlmutter, MD: In a very real sense, you determine the fate of your gut bacteria, these trillions of organisms living within you basically eat what you choose to eat. When they've been nurtured, your health is optimized and you are more resistant to disease. A healthy microbiome is vital in an Alzheimer's disease prevention plan. Let's find out what you can do to nurture a healthy microbiome
- Emeran Mayer, MD: A probiotic is any life organism that has a demonstrated beneficial effect on the health of the organism of humans. A prebiotic is basically the food for the microbes. It's whatever microbes can metabolize and use for their own energy requirements is a prebiotic. And there's wide range of substances. We talked about the plant-based fiber as a major one. There's other substances that you can use. There's polyphenols or any large molecule that's too large to be absorbed in our small intestine, and gets into the colon, and has a beneficial effect on the health, and the growth, diversity, of the microbes is considered a prebiotic.
- Amy Berger, MS, CNS: Prebiotics are a type of fiber that feed the probiotics. They sort of feed the good bacteria in the gut. These beneficial bugs will feed on that fiber that we find in things like Jerusalem artichokes and inulin and things like that.
- David Perlmutter, MD: So with this important relationship then between the microbiome and the brain, what advice might you give people in terms of lifestyle choices that can be good for the gut?
- Jeffrey Bland, PhD: Ancient diets that people ate but which were built on indigenous foods, had some really important role to play in the community of bacteria that live in our guts. And so unrefined foods of multiple plants sources. Foods that have what we called prebiotics are the food for bacteria, for friendly bacteria, all have very important roles to play.

Jeffrey Bland, PhD:

Indigenous diets where people had stable and very healthy microbiomes were people who ate a lot of these foods that actually contribute these prebiotics to keep their microbiome healthy. So I think we're starting to take all that information from indigenous cultural diets from what we've done from dietary analysis, looking at the microbiome, looking at the effect of microbiome on immune function and start to say, hey, we have a lot more control over this.

Jeffrey Bland, PhD:

If we eat the right things and eating a lot of refined, processed snacks and garbage foods are absolutely the wrong way to go, it's gonna definitely disturb your microbiome in a way that's going to increase your inflammation and increase your dysbiosis and increase the potential for neurological adverse immune response.

Leo Galland, MD:

The one factor that is most associated with a healthy gut is microbial diversity. Your gut is like a rainforest and biodiversity is the key to health.

Leo Galland, MD:

The best way to nurture a healthy microbiome is to avoid those foods that provoke inflammation in your gut. We know what they are.

Leo Galland, MD:

We know that a Western standard American kind of diet that's high in both fat and sugar that has a lot of added fat that's depleted of fiber...that kind of inflammation provoking-diet causes leaky gut, it causes inflammation in the gut, it disrupts the microbiome and sometimes in very drastic ways.

Leo Galland, MD

I mean, it really diminishes the diversity of bacterial species that are growing there and remember that biodiversity is important for health. Then you need to feed your gut well.

Leo Galland, MD:

Feeding your microbiome involves eating high-fiber foods, fruits, vegetables, nuts, seeds, if you do eat grains, whole grains, not refined grains, legumes if you tolerate them.

Leo Galland, MD:

And also foods that are rich in ... anti-inflammatory nutrients that are found in plant foods and omega-3 fats, which are found in seeds like flaxseed and chia seed and are found in cold water oily fish like salmon.

- Leo Galland, MD: Those are all anti-inflammatory. They help to nourish a healthy microbiome. You also need to be really careful about exposure to substances that decimate the microbiome.
- Leo Galland, MD: Your food should be organic whenever possible because non-organic conventional food is...exposed to herbicides.
- Leo Galland, MD: The animals are given antibiotics and you ingest those antibiotics when you eat the meat or drink the milk of those animals.
- Leo Galland, MD: Exercise has a very beneficial effect on the microbiome and there have been numerous studies done on cardiorespiratory fitness and gut microbes.
- Leo Galland, MD: You take people who are controlled for all other variables, those with the highest level of cardiorespiratory fitness have the healthiest microbiomes and aerobic exercise has a positive impact on the gut microbiome and encourages the growth of bacteria that produce substances that not only enhance exercise performance but also nourish the lining of the gut.
- Leo Galland, MD: Good stress management has an impact on the microbiome because of the devastating effects of stress on the organisms that live in your body.
- David Perlmutter, MD: We are so grateful to our guest experts for sharing their incredible knowledge with us on this exciting new field of microbiome research. Even though this field of research is relatively new, let me assure you, it's getting a lot of attention. We have learned that it is absolutely essential to nurture a healthy microbiome. Here are some actionable steps you can take today to do just that.
- David Perlmutter, MD:
- Eat probiotic foods. Probiotic foods are fermented foods. Foods like yogurt, Kombucha, Sauerkraut, Kimchi, one of my favorites, and any kind of fermented vegetable. These are foods that have ample amounts of beneficial bacteria.
 - Eat prebiotic foods, prebiotic foods or fibrous foods that good bacteria love and these include things like asparagus, garlic, onions, leeks, Jerusalem artichokes, dandelion greens and Mexican yam or jicama. These foods serve as food for your healthy gut bacteria.

- Eat a diet that is low in refined sugar and processed carbohydrates and
- avoid consuming pesticides and herbicides by choosing non-GMO organic foods whenever possible.
- Exercise regularly.
- Get seven to nine hours of high quality sleep each night.
- Practice reducing stress. We'll be learning more about great stress reduction techniques in episode eight.
- If you choose to eat meat, make sure it's organic and grass fed so that it was raised without the use of antibiotics.

These are simple but powerfully effective steps that will absolutely help you nourish your microbiome immediately.

David Perlmutter, MD:

If you think this is overwhelming, don't be discouraged. First, consider how important this is for you in the broad scheme of things. Second, choose one part of the program that you can implement today. Maybe it's just increasing your prebiotic fiber by eating more asparagus or dandelion greens, or you decide to reduce your sugar consumption.

David Perlmutter, MD:

Every bit counts. Whatever we can do to optimize the health of the microbiome will go a long way toward having a healthier body and a more disease resistant brain. The health of the microbiome is paramount in Alzheimer's prevention, a disease for which again, we have no meaningful treatment.

David Perlmutter, MD:

The health and balance of your microbiome is in your hands and the benefits of a healthy microbiome are profound. You have the power to drastically improve your health through nourishing your gut bacteria. Start implementing these changes in your life right away and your brain and your body will thank you.

David Perlmutter, MD:

Remember, the ability to nurture a healthy, robust microbiome is a critical tool you have in your Alzheimer's prevention toolkit.

David Perlmutter, MD:

In our next episode, we're going to look closely at the effects of stress on brain health and explore ways to avoid and manage stress.

David Perlmutter, MD:

Chronic stress is one of the most important factors when it comes to the health of our brains and preventing Alzheimer's disease. And, I can't wait to share with you why.



David Perlmutter, MD:

I'll see you in our next episode. Stress and Alzheimer's, How to Regain Balance.