Understanding Plasmalogens and Their Role in Alzheimer's Reversal

Heather Sandison, N.D. interviewing **Dayan Goodenowe, PhD**

Heather Sandison, N.D.
Welcome back to the Reverse Alzheimer's Summit. I'm your host, Dr. Heather Sandison. And I'm so pleased to introduce you to Dr. Dayan Goodenowe. His research into the biochemical mechanisms of disease started in 1990. His curiosity about the biochemistry of life is as insatiable today as it was then 30 years ago. In those 30 years, Dr. Goodenowe invented and developed advanced diagnostic and bioinformatic technologies. Designed and manufactured novel biochemical precursors and identified biochemical prodromes of numerous diseases including Alzheimer's. He also has studied Parkinson's, multiple sclerosis, stroke, autism, ALS, schizophrenia, bipolar disorder, depression, cancers like colon cancer, pancreatic, ovarian, breast, lung, kidney, liver and stomach. He is just getting warmed up and you can see why I'm so excited to have him here today. He's now going beyond disease. His new focus is to defeat the entropy of aging by creating strategic biochemical reserve capacity, such that the human body can maintain the physical and biological functions of life indefinitely and without disease. That is a tall order, but one that I know everyone here is excited to hear more about. Dr. Goodenowe, welcome.

Dayan Goodenowe, PhD
Thank you very much, Dr. Sandison and yeah, sounds like a tall order, but like all big projects, they start one brick at a time. And as you break things apart into their individual components, the complexity becomes less and less, and aging, Alzheimer's, neurodegeneration, most of these things seem so insurmountable because we look at the whole picture, all at once. It's like having

a messy house and don't know where to start. And then if you say, "You know what, I'm gonna start in one room and I'll get," and then by the time you're done, it doesn't look like the same as it did when you start, I think aging and these complex diseases, they overwhelm us because we think of them once they're here. And we don't really understand how we got here. And we don't look at how do we get to this level of neurodegeneration and the human body's designed to work. And I think people throw out all the basic logic that they use in their everyday life when it comes to their health. Because health feels like a black box. How does my heart work? How does my brain work? How does this? It's all so foreign and the words that scientists use and the technology, people just shut off. They can't think about it. It just feels so far beyond them. And they just kind of wait for something to happen.

And then they wait for someone to tell them what next. And so my background is in science and my PhD is in psychiatric medicine, looking at the biochemical mechanisms of disease and build a lot of technology looking at what causes disease. And you don't walk down the street and get hit by lightning and have colon cancer the next day. There's a prodrome, there's a period where you become at risk for a disorder. And then that risk eventually translates into clinical manifestation. And so the question really becomes is where does this all begin? And then to do that, you have to understand how the systems are designed to work in the first place and then work from there. And so Alzheimer's is an interesting story. It's one of the benchmark or beach heads, if you will, of this preventative medicine, regeneration restorative model, because it affects so many people and its such a emotional disease. You get cancer, yes, obviously it's bad, you die. But when you die of cancer, at least you die yourself of cancer.

When you die of Alzheimer's, you don't even die as yourself. It's a very, very tragic disease, in terms of not obviously for the person suffering from the disease, but all the caregivers around them. And so understanding this disease is very, very important and reams and reams of data have been generated over the years. So my contribution to the field really is looking at those biochemical mechanisms and understanding, is this just a one-way street to death? Or can these systems be rebuilt, regenerated, restored? And then obviously can we prevent them from degenerating, from the first place? And Alzheimer's, people think about the brain and they have a lot of misconceptions about how the brain is organized and how the brain works. And they think in a sense of complexity that it's not, people think the brain is like a computer, but the brain really isn't like a computer. It's more like the wiring harness of your car. It's a bundle of wires that connect different pieces. And just like the wiring in your house, where you have the copper

wire in your walls that are protected by a protective sheath and then you have a light switch on your wall that connects these wires. And so your brain is like that. And your brain is like a beach ball in the outer part of the brain, the surface area is the largest surface area. And that's where all the connections typically take place. And then in between those, you have these fiber like the wiring harness of a car. And that's typically when people talk about white matter and gray matter. The white matter is a connectivity for autism and multiple sclerosis type diseases. And then in diseases like Alzheimer's, where we're dealing with typically synaptic function, but it's not that cut and dry, it's a little bit of both. And so neurons and Alzheimer's deal with a very specific part of the brain, but all neurogenerations are not isolated. People who have Alzheimer's have other neurodegenerative disease issues as well. People with Parkinson's will have Alzheimer's like issues and so on and so forth. So generalized brain health is still generalized brain health, but the key of the human brain are those two components.

One, is the wiring, the complexity of the wiring goes from A to B and then there's the connective part. In the scientics, we call the white matter, the fiber bundles, if you will, the wiring bundle, that's like the corpus collasum, it's what connects the two sides of the brain. And then the switching is your synapse where the two neurons connect with each other and that's biological. Those are living cells that do that. It's not like copper and metal that's in your car. These are living things. These are things that we regenerate even all the time. So they require a supply of materials. They require the supply and diffusion. And so Alzheimer's cognition is fundamentally a disease of one class of neurotransmitter. And that's called the acetylcholine. And the brain has a bunch of these different types of wires for different purposes. Just like you have wires for your taillights, you have wires for your car engine.

And one type of wire, which is these cholinergic wires, are the ones that are more involved with our cognitive ability or executive function, memory, and so on. And these neurons require a certain type of electricity, what goes through these wires is a molecule called acetylcholine. And so people take acetylcholine drugs like Aricept, for example, that extends the activity of that neurotransmitter in the switching plate, the synapse. But that acetylcholine is what connects the two parts. So when you flip a switch on your wall, you're physically connecting two wires with that switch. It's either disconnected or it's connected, but of course your brain is biological and your brain moves neurotransmitters across this little gap called the synaptic cleft. And it's like having a shower head, when you have a shower head that has a multiple little outlets. And if you just turn your shower head off and on, off and on, off and on, off and on, that's kind of how a

synapse work. It just pulses these pieces of things and they connect across. And that's how the biochemicals go across. And the biochemical that goes across for Alzheimer's is this called acetylcholine.

Heather Sandison, N.D.
So I have a question there, because so many people have been prescribed Aricept, an acetylcholine esterase inhibitor. So it keeps, maintains more acetylcholine in that synapse, but this doesn't help. So if that's the explanation for what's going on, then why don't those medications help more?

Dayan Goodenowe, PhD
Well, they help symptomatically. So the acetylcholine esterase inhibitors have been very reproducably shown to improve cognition short term, but they don't change the fact that your brain is degenerating. And so then the question's what's the neural process? So basically what you're doing there is you're just juicing up these synapse with the acetylcholine esterase inhibitors. You're not changing the biology of it. And so I know again am getting this, so what happens in the biological brain is that we get synapse release of neurons. So neurotransmitters are held in this little sphere called the vesicle. And it's trapped in there. And there's a signal called a action potential that signals the body to release these neurotransmitters. And that's a physical, it's like a soap bubble. And it has to hit the membrane and the bubble bursts and when it bursts, it opens up and it lets all these neurotransmitters go into the cab. Now, the scale at which the human brain does this is massive.

If you take a look at it, if you think of each one of those vessicles was a grain of sand, you have the same amount of vesicles in your brain as there are grains of sand in the Hoover Dam. That's how many vesicles you have in the human brain. It's an enormous number. And more importantly, those vesicles burst and reform at a hertz rate of around a hundred, which is a hundred times per second. So that means the Hoover Dam in your brain, with all the sand is bursting and reforming, bursting and reforming a hundred times a second, as you're listening to me speak right now, that's the massive scale of the human brain computing power. It's still from a hertz rate like you get a gaming computer, the human brain still operates at a capacity, almost larger than all computers combined sold in a year. And it allows a human brain to basically reach quantum mechanical capabilities. So when we create a thought, when you think, you are creating a new thing from nothing, it's almost like a quantum mechanical process. And what

allows you to do that is this large network of these vesicles bursting, neurotransmitters releasing. And then they combine into thoughts and we direct our thoughts. So this is why we can decide whether to have a chicken salad or a steak for lunch. There somehow we're able to move our consciousness using this power and it's tuned and we get better and better as we get older. Then we reach a point where we can't perform all these functions. So when we get into those issues, so the ability to actually form vesicles and release vesicles is a biophysical process. And it takes actual biological molecules to do it. And these molecules are lipids called phospholipids, kinda like soap in your, and there's a special type of phospholipid called plasmalogens that are particularly important in releasing these neurotransmitters and these molecules that you decrease as you get older. And the other thing people think about, so Alzheimer's, people think of Alzheimer's, there's usually three things that people think about.

They think about neurofibrillary tangles, these little protein tangles that deformed in the brain, you get amyloid plaques, which is this extracellular formation of protein. And you get brain shrinkage. Now, the brain shrinks like a, when you take a grape and a grape shrinks into a raisin, it becomes dehydrated because what keeps a grape plump on the outside is the fullness of water inside that grape. Now, your brain is made of fat. Our brain is lipids and fats and membranes and membranes are what gives us the compartmentalization. So when your brain shrinks, what you're doing is you're losing the fat of your brain. That's what you're losing, like a grape loses water to become a raisin, the brain loses fat membranes to become a shrunken brain. And so that's a physical loss. You're actually physically losing matter of the brain and that's a shrinkage process.

So the question is why are you losing these molecules? Are you not making enough of them? Are you consuming too many of them? Are they being broken down too fast? And so that's the critical component. And the other part people forget about, is there's basic operational fundamentals. The human body is made of membranes. And so when we talk about compartmentalization, you wanna be able to do certain things in certain areas, just like in your house, you have things that you do in the kitchen, things you do in your bedroom, things you do in your bathroom, and you compartmentalize those activities and you compartmentalize those activities with walls, we even compartmentalize greater. We compartment things that we do in our house that we don't do at work. And we have buildings. And so our world has compartmentalization in it. The human body has the equal level of compartmentalization, but again, it's biological. So all these wooden walls and steel walls that we build around us, our body

makes those things, but it makes them with biological material. And the material of the body makes uses is called phospholipids. And phospholipids are this fat, basically, they're like soap. And they have a polar head group on one end and a non-polar side chain. And they organize into what's called a phosphoipid bilayer. 'Cause basically, it's a wall, it's a biological lipid wall. And that's what gives your body the ability to compartmentalize why your heart is separated from your brain. And then even inside, when I talk about that wire in your wall, that coating is separated from the axon and the inside. And what separates those two things are these biological membranes. These biological membranes are made of phospholipids. Plasmalogens are one of these phospholipids. Some of these phospholipids we get from our diet, like our phosphocholine, choline is a big thing. We get from eggs. We get it from sunflower lecithin or soy lecithin. Choline is a critical nutritional molecule, technically-

Heather Sandison, N.D.
Talked about acetylcholine. And then now this is phosphocholine.

Dayan Goodenowe, PhD
Phosphocholine.

Heather Sandison, N.D.
Phosphocholine which is in the membranes. And so are those related to each other?. So if I'm eating more eggs, that choline is really important for multiple reasons.

Dayan Goodenowe, PhD
Yes, and so this is a fact that most people don't realize. All of the neurofibrillary tangles of the human brain, that form in Alzheimer's are caused by inhibitions of a biochemical system called methyltransferase. And this is a system that your body uses to make choline. So choline technically is not an essential nutrient. In the list of, from whatever organization gives you the list to essential nutrients, cause your body can technically make choline. But it's energetically demanding to do it. And if you don't make enough of it, your body starts scavenging other things for it. And so when people-

Heather Sandison, N.D.
Methyl donors, it sounds like as well, 'cause this is a methyltransferase. So if you don't have enough of those carbon and three hydrogens, then it's also going to be a struggle-

Dayan Goodenowe, PhD
Absolutely, and this is why high levels of homocysteine. If your doctor talks about homocysteine levels, you wanna keep your homocysteine levels low, not artificially, you don't want to fake it by a lot of the blood testing. There's supplements that you can take that will arbitrarily lower homocysteine. But homocysteine is a very valuable biomarker because it indicates how much your body needs or is efficient in it. And so phosphocholine from egg lecithin, soy lecithin, the other one that's important is creatine. Good old fashioned creatine is another thing we use for muscles. Our brain use a lot of it, but that's also big drive for methyltransferease. So choline is in your membranes and choline is also used for Alzheimer's and the neurotransmitter and acetylcholine.

And this is what makes Alzheimer's so unique versus other diseases because it uses a neurotransmitter called acetylcholine, but choline, the molecule part of it, it's an all of our cells. So when you talk about Parkinson's and we talk about the dopamine system, well, dopamine is a unique molecule. It's only found in the dopaminergic neurons and it has very specific proteins, it only recognize dopamine. So when you take L-Dopa for Parkinson's, it's only affecting these neurons related to Parkinson's. Alzheimer's, the choline system is all your neurons have choline in. But they have a selective... So you have this strangeness with Alzheimer's and that the neurons, they don't take up their neurotransmitter when a Parkinson's neuron for a dopamine neuron, when it releases dopamine, it takes dopamine back up. When it recycles, when it recharges itself, dopamine leaves, dopamine comes back. Alzheimer's that doesn't happen. What happens in Alzheimer's is see the choline leaves does its work.

It gets broken down and then choline comes back. So it actually and then it remakes, it actually resynthesizes the neurotransmitter in that neuron, which is very different from depression or anxiety, people are dealing with serotonergic system or people hear about the neurogenic system. The cholinergic system is a very unique system and it is unique because it has a special protein called the choline high affinity transporter. I know I'm getting in the weeds, but this is what brings up that neurotransmitter. What's weird about Alzheimer's is when I mentioned that process where the vesicles form and released the neurotransmitters is that membrane fusion process, the protein that brings the choline back in, that allows that neuron to recharge itself for the next pulse, that protein is actually on the vesicles that gets formed. All other neurons that the reuptake protein is just sitting there. And Alzheimer's the reuptake protein is on the vesicle. So anything that disrupts the circular formation, starves the neuron of choline and we get what's

called autocannibalism and shell shrinkage. So membrane fusion is one of their most critical components. And it's for all neurons, but the Alzheimer's neuron is most sensitive to that. And plasmalogens are the molecule that are used for membrane infusion. And so it's to obligate. Membranes can't fuse together without plasmalogens in them. And we lose plasmalogens as we get older, because we can't get them dietarily. And you have lots of 'em, 20, 30% of your enitre brain lipids are these plasmalogens. And you make all of them. 'Cause if you eat nice and healthy, say, "Oh, wow, I've got lots of these plasmalogens. So if I'm eating animal products, I'm eating fish, I'm eating this, I should be eating plasmalogens." But that's not true because a weirdness of their structure, they're designed to be sacrificed. So they have like a little fuse in them called the vinyl-ether bond and it blows up. The body makes these plasmalogens so that it will get consumed and protect other types of molecules. So you make lots of 'em and you use a lot of 'em. Problem is that when you eat them, they're acid sensitive.

So soon as they hit the stomach acid, acid in your stomach, they burst up. So when you eat a plasmalogen from a fish or from an animal, or from whatever, very little of that actually gets into your blood supply. So there's very little nutritional availability of plasmalogens so your body must make them all. And the body can make it from anything. It can make it completely from scratch, not dependent on any dietary, selective molecule to make your plasmalogens. But problem is, you are now dependent upon your own biochemical synthesis and it's made in a very special organelle called peroxisome. So some of you may have heard about peroxisome.. People take fibrates for people that when high triglycerides rise and they're trying to get their triglycerides lower. So again for Alzheimer's, you wanna make sure you keep your triglycerides right, your fast triglycerides under a hundred. That means your peroxisome function is working. So people that have low triglycerides and high HDL usually have good plasmalogens. those three things kind of go together in your blood testing results.

Heather Sandison, N.D.
What I notice is that people who have eat a lot of sugar, tend to have higher triglycerides as they reduce their sugar intake, those triglycerides come down and signficantly. Have you seen the same thing? And is there a correlation between sugar intake and plasmalogen synthesis?

Dayan Goodenowe, PhD
Yeah, so what happens is, so when we measure first in triglycerides, when your doctor says, " Hey, let's get a blood test and look at first in triglycerides. They're not measuring the triglycerides you

eat. They're not measuring the olive oil in your cupboard, or whether you're eating bacon fat or not. What you're actually measuring is what your body is making. You're actually measuring your body's synthesis of triglycerides. 'Cause that's what your body makes to store for later. So when you have a meal, your body has two gears. You have the fed state and the fasting state. In the fed state, I've just eaten a big meal. My stomach, my intestines, you're full of food. They're digesting proteins and fat and carbohydrates. And they're sending all this energy into my blood supply. And it's far, far more than what I can use at this point in time. Cause in my liver says, "Whoa, I cannot possibly use all this stuff. So I'm gonna store this stuff for later." And so what they'll do, what your liver does then is it packages the extra energy on triglycerides. Good old oil, exactly the same chemical structure as the oil sitting in your cupboard.

That's what your body makes, exactly the same stuff. And it sends it to your fat cells for later. So after a meal, your triglycerides could be like a thousand. Your blood could be white with fat, that's normal. Well, not gonna be normal, normal, but it's possible and it happens all the time. But then after a period of time, you're intestines, all that food that you've eaten, gets digested and burnt up. And at some point you've run out of that energy that you've obtained from your meal. And now, your body has a switch from this fed state to the fasting state. When it shifts to the fasting state, your fat cells become your stomach and your intestines. And so your body starts digesting that stored triglyceride in your fats. And it sends this energy again to your cells, your body, your liver, and this and that. When it gets to those cells and those cells can't process it, they're weakened or they you're diabetic because you have your sugar issues. Then your body say," Hey, I can't even process the energy that I'm sending from my fat cells." And so your body starts remaking triglycerides and sending 'em back.

So when triglycerides are over a hundred, that means that your energy of your cells, your cellular energy capacity is impaired. And it's usually either peroxisomal or mitochondrial. So to your question of sugar and diabetes and high blood sugar, these are systems of reduced glycolytic capacity of your cells. Means your cells can no longer process glucose properly. And so glucose builds up and since the glucose builds up in your blood, your body says, "Oh, I can't have that." And so your body starts pumping more and more insulin says, "Well, I'm gonna part, pushing this glucose down." And that's what insulin resistance is. Insulin resistance is simply caused by your cells being unable to process glucose. And so your glycolytic capacity is low. So it could be peroxisomal, could be mitochondrial, but your energy is bad. And so fasting, exercise, all these things, better diet that that reduces your glycolytic food supply. So all those things, they reduce

the glycolytic load of your cells. And if your cells can now process the glucose that's there, then all of a sudden, there's less glucose in your blood. There's less requirement for insulin and insulin resistance disappears because you don't need insulin, you no longer insulin resistant because you are actually digesting, you're processing the glucose that's coming in. So all that goes hand in hand. So people that are on ketogenic diets, or more importantly, the intermittent fasting is very, very important because that allows the body to build. And peroxisomes are your building prop cells, organelles, mitochondria are your burning cells. So your body works like your iPhone cell, like during the day you're out running around. your phone's unplugged and it's busy, the light's bright, and it's doing this and it's doing that. It's checking this and checking that is on whatever you're doing on your phone. And it's burning up energy. It's not doing background checks and making sure everything's ready.

Then the day ends and you plug it on your charger, the light goes off and it starts recharging. that's your fasting state. The human body is designed to work during light hours. And then at nighttime, when we're not supposed to be eating and we're not supposed to be, we have this caloric restriction, this natural caloric restriction that occurs during our day and your body switches to the fasting state. And when you're in the fasting state, you're running on fat energy triglycerides. And that's when you build your hormones, all your hormones are built, your membranes are built, your plasmalogens are built. So your fasting state is really critically important. So this intermittent fasting, or at least having only one insulin pulse per day. So if you have to snack, have non-insulin sensitized, sensitizing snacks. And I always tell people to skip breakfast breakfast. If you can wait and have your first meal at two o'clock in the afternoon, that's the best way to getting intermittent fasting.

Skipping breakfast is the best way to get that. If you can get all your calories in a six to eight hour window, it's one of the most healthy things that you can possibly do to your human body. And it does it, because it actually helps make these plasmalogens. And get these plasmalogens into the brain. The other thing that people miscalculate is cholesterol. Cholesterol got a really bad name. The other really critical fat for all your memories is cholesterol. `People with APOE get really freaked out about this, the APOE genotype. But when people get cholesterol levels is below, total cholesterol below 200, really increases your all-cause mortality, increases your Alzheimer's issues. We talked about HDL and LDL, but these are the fats that are part of our membranes and our ability to keep all these membranes. So plasmalogens the-

Heather Sandison, N.D.
The bat and it's such a breath of fresh air to hear you say this. Cause this is also the backbone of our stress hormones and our sex hormones and all of that signaling going to our brain. And when we're told over and over again, it's getting flagged at 200, even though the American Heart Association and the American Diabetes Association say that you do not need to have that under 200, your total cholesterol under 200, unless you have active heart disease or active diabetes. So there's a whole chunk of people who are being told by their primary care providers that they need to take statins because their total cholesterol is over 200, no one is really suggesting that's a good idea if you look into it but it's getting flagged anyways.

Dayan Goodenowe, PhD
The lowest rate of all-cause mortality in humans is cholesterol between 220 and 260, period. That's 162 countries, probably 30 million subjects. As soon as your blood cholesterol, your total cholesterol levels gets under 200, your all-cause mortality doubles, having-

Heather Sandison, N.D.
Depression, your background is in psychiatry. Depression anxiety, when I see somebody's cholesterol at 140, 130, I just go, "Oh my gosh, you're not producing sex hormones, you're not producing any of the things that are gonna be necessary for you to maintain a healthy mood or HDL."

Dayan Goodenowe, PhD
Exactly, and your HDL levels are really critically important. Getting your HDL above 50, it certainly should be about 60. When HDL starts dropping below 50, if you're choline deficient, your body can't share cholesterol. You have two cholesterol systems. You have your LDL system, which is mostly kind of total cholesterol's kind of proxy for that. But that's a cholesterol system that distributes cholesterol. It's like an energy grid. Where have a main power plant, and then all the houses have their own little solar panels. So you have LDL system is the main power plant. It's sending cholesterol to all the cells of the body. It doesn't push cholesterol. With the cholesterol on your blood, is not being pushed on your cells, that your will take the cholesterol that they want. When you take the electricity, the power company doesn't push electricity into your house, you draw electricity from the grid as you need it. And your cells draw cholesterol from the blood supply as they need it. And so that's what the LDL system, and it actually pulls it in, the LDL particles, 'cause cholesterol is fat, think about it, you can't take bacon fat and pour it down your

sink. Because it's gonna just clog up things. So what body does is it puts all this fat on these proteins, which are highly water soluble. And so they stick on these proteins and that allows the body to distribute these fat molecules 'cause your is basically water. You have all this aqueous water systems. So we use these proteins. One of these is LDL protein, LDL cholesterol. So LDL cholesterol is a big piece of water soluble protein with a bunch of cholesterol stuck on it. And it gets distributed and your cells say, "Hey, I need cholesterol, I'm gonna pull cholesterol in," that's your LDL system. Now, your HDL system is when you make your own, you have your solar panels, and you're saying, "Hey, I'm generating energy in my house, but hey, I'm making more energy than I'm using. 'Cause I'm not home today. My solar panels are still working, but I got no nothing, no TVs on, nothing's on. So I'm gonna donate some of my energy back to the grid." And so the HDL system is you're donating it back in.

It's saying, "Hey, I am so healthy. I am so energy efficient in my cells. I can actually share my energy with the rest." In the brain, that's really important because your cells wanna share their cholesterol with each other and they share their cholesterol using the HDL system. And so HDL is how you get cholesterol outta your cells and distributed and so that's your export. And the combination of those two things, allows your body to tune. It says, "Okay, I can get higher or lower." 'Cause all your cells are different and you're different. Even the three-dimension of the sphere of the cell, there'll be parts of the cell that will need more cholesterol than other parts. So it needs to be able to move that cholesterol around and share it around and that's how it does it.

Heather Sandison, N.D.
Take us back to APOE because of APOE 4, 4 status. We know people have a one in two chance of developing dementia. APOE 3, 4 is a one in three chance of developing dementia, way more than the average in the population, which I think is like a 14% chance. So there's a lot of confusion about what we know and what we don't know about APOE 4, 4 status or 3, 4 status having one of those APOE 4 alleles and what happens as it relates to fat synthesis. So we know that it puts us at risk for dementia, but fats, plasmalogens are kind of these phospholipids. So they're half fat, half water soluble. Tell us how plasmaogens are related to this APOE and then fat metabolism in general.

Dayan Goodenowe, PhD
Yeah, so APOE is a big pet peeve of mine. And it's in my book, I'll go through in great detail for APOE carriers, 'cause there's a lot of work and scientists love complexity, It's like how many

angels can we put on ahead of a pin? That's what we do all day long. We dig deeper and deeper and deeper and if you dig deep enough, there's always something interesting to find. But for all of you APOE 4 carriers, let me just describe in very simple form. 'Cause for Alzheimer's related issue, there's only one thing related to APOE and that is reverse cholesterol transport, that's it, a hundred percent. So I just talked to you a little bit about these proteins, that move cholesterol around. So the LDL, the main cholesterol distribution is called apolipoprotein B, ApoB and the main HDL protein is called ApoA. And so over last 50, however many years we've studied these proteins, we've labeled them. Now, apolipoprotein B, your LDL particle, that particle actually gets absorbed by LDL receptors. It gets pulled in. So when you take a statin, what statins do is they block your body's, build your cells. What statins do, is they turn off your solar panels. Makes your solar panels don't work, so they turn 'em off.

So the only way you can get energy or cholesterol in your cells is by pulling it from the grid. So by shutting off your solar panels, we force the cells to pull all the cholesterol from the LDL system. And by sucking all the LDL out, we bring LDL levels down. That's how fats work. Now, HDL particles, they don't enter your cells. They stay on the outside of your cells. They're the FedEx truck, they're waiting for the cholesterol come out. When the cholesterol comes out, it'll take it out. So HDL particles cannot go in. Apolipoprotein E is very unique, it's ambidextrous. It can enter the cell, it has both LDL activity and HDL activity. It does both things. Now, in your brain, what makes APOE important is your brain uses APOE for both LDL and HDL functions. So you do not have apolipoprotein B. There's no LDL in your brain. And there's very, very little A, your brain basically uses apolipoprotein E, it uses it for both the LDL mechanisms and the HDL mechanisms. So uses this for both things.

So because your rest of your body is like an interstate highway system. I'm shipping things from Chicago to New York. The brain is Chinatown. The brain is a whole bunch of little streets connected by little, and so everything's local. And so you don't have these very big arteries, moving things back and forth. And so brain uses apolipoprotein E because it can use it for both things and how it separates the different functions is that there's different proteins. Some proteins will bring in and some below, so long story short. So we know have these alleles, so when you get APOE in the brain, we have these different genetic mutations. So you have the E2 variant and E3 variant and E4 variant. And it's all related to this disulfide bridges, like this cystine bonds. So proteins connect to each other, kind of like two magnets on a screen door, if you will, And a sulfur in one and a sulfur another, they'll connect. And the mutation that makes the

difference between the APOE genotypes is the ability to form these disulfide bonds. And it affects only one protein in the brain, just one, is a critical one. And it's one of the proteins related to cholesterol transport, reverse cholesterol transport. So what happens for APOE 4 carriers is that they have, so the difference between the APOE genotypes is your ability to export cholesterol. So E4 carriers are cholesterol savers. They not leaky, their cells do not leak out cholesterol. And that's protective for other things like viral infections, bacterial infections. The reason why we still contain E in a genome is that it actually is a protective genotype. But as you get older, your compensation mechanisms for the cholesterol clearance, becomes less and less and less. So what was healthy earlier becomes unhealthy later. So a natural E4 carrier should have cholesterol higher, 'cause of your LDL levels because an E4 carrier, it saves more cholesterol than the other ones. So an E2 carrier can't hold cholesterol for the life of them so they're always leaking cholesterol. It's like a teenage kid with an allowance.

They're just spending it every week. So your E2 carriers are just, they're making cholesterol and they're getting rid of it, making it, getting rid of it. And so they can't hold onto cholesterol. So that's why LDL levels in E2 carriers are always lower and LDL levels in E3 carriers are kind of in the middle and LDL levels in E4 carriers are a bit higher and that's natural and that's how it should be for them. Now, the yin and the yang of cholesterol export are these HDL protein or these protein export and plasmalogens. So the other thing that drives cholesterol export called reverse cholesterol transport, HDL export is plasmalogens levels in your membranes. So what happens to what we published in a large population in Chicago was that plasmalogens levels neutralize the APOE genotype affect on Alzheimer's. So an E4 carrier with high plasmalogens does not have an increased risk of Alzheimer's disease. It completely neutralizes that.

And as important, genes don't do anything. Genes have mechanisms. Genes, give us, I call it the genetic adaptability. People think that genes are deterministic and they're not, there is no such thing as a gene for disease. It looks like it, it feels like, it sounds like it, it sounds like it sounds so normal, sounds so logical. But it's actually not the case. We're born with adaptability to our environment. Your genes have no idea what you're gonna do tomorrow or the next 10, are you gonna eat a pint of ice cream, or you need a steak? It has no idea what you're going to do. And so they have to sit back behind their little nucleus and they have little sensors saying, "What the heck are you doing to me today?" And then they're gonna adapt to whatever they experience. So we have certain genetic adaptabilities. And if your environment gets out of your adaptable windows, you get diseases, you can't... And so it's our responsibility to live within our genetic

windows. Our genes can change to a certain degree. We can adapt, if you exercise, you're gonna increase your oxidative capacity and your body's going to adapt to your changing environment. So you can do healthy things to increase your genetic window that you can say, "You know what, I have more options available to myself now. My body can handle better adverse circumstances because I've trained it to do so." it's like having a basketball player that only shoots hoops. All he does is go every day, he goes to the free throw line and all he does is shoot free throws. And you go, "Wow, look at this awesome guy, man, he can just shoot hoops all day long." When you put him in a basketball game and he's crap because he can't play anything, he can't do anything, but shoot hoops. He can't dribble, he can't move around. He can't pass, he can't block. And so we train ourselves out of these things. And so this is what bad diets will do. And so these is where health style things do make your events, but what they do is they keep you from becoming more and more narrow in your function.

Heather Sandison, N.D.
For a medic effect, basically where we create a little bit of stress on the system, whether it's through calories or through temperature, like hot and cold or even with oxygen, we can do this a little bit with contrast oxygen therapy. And as we ask the body to do more, it's capable of more. And we wanna make sure that as we age, we continue to do this so that ourselves have that, like you're describing this dynamic ability to respond to the environment.

Dayan Goodenowe, PhD
And you have to give people enough time. What I notice a lot with the athletes that I've worked with and aging, they think, "Oh, more is better." But remember so I tell people, exercise is bad for you, recovering from exercise is good for you. It's recovering from the stress. So you gotta give your body enough time to actually recover from the stressor that you give it. So it's good to work out, work out to complete exhaustion to complete failure, but make sure you rest It is that rest period that allows your body to recover and train itself, get prepared for the next long term event. So anyways, we're getting off on all these things.

Heather Sandison, N.D.
There's something that I have to ask you because it's one of the questions that comes up most often with my patients. And we've seen APOE 4 carriers go on a ketogenic diet and have really great responses, cognitively. And also that their lipid profiles look better. However, there's a lot of, I would almost call it trepidation. As people learn more about APOE 4 status or 3, 4 status and

they think about eating more fats or getting on a ketogenic diet. And it particularly with MCT oils or coconut oils, there's a lot of confusion and questions around how these high fat diets might impact someone with positive APOE 4 status. And so what I hear you saying is, well, maybe we can just override that by using plasmalogens as supplementally, or do we understand enough about fat metabolism in the brain that maybe this isn't as much of an issue as we thought, or like, can bring-

Dayan Goodenowe, PhD
Well, it's quality of the fat. It's very, very important. And so the ketogenic diet, it's important to use it for its correct purpose. So what you're doing is you're extending the fasting state. You're preventing fed states from occurring and your body should have at least one fed state per day, for the most. You can go for fast, you can fast for a week, if you wanted to. Those things, caloric restrictions are good. Now, when you burn fat, you create a lot of acid. So the other thing with the ketogenic diet is people need to work on... they're not getting fruits as many fruits and vegetables in the diet. Those things reduce the acidity. And so you need to make sure you should be checking... People that are on a ketogenic diet, shouldn't just be checking their ketones status, they should be checking the pH of the urine and they should be taking bicarb. And they should make sure that their electrolyte balances are maintained, your sodium, potassium, magnesium balance. And those are very easy. There's lots of supplements out there. You can take like an Alka-Seltze gold, there's a pHAlo there's supplements out there that give you bicarb. 'Cause when you're burning pure fat, you're creating a lot of acid and that creates other issues for your body, makes it hard for your body. So you wanna make sure you neutralize all the acid that you're burning, creating from fat metabolism. So that's one thing when people get stuck on a huge ketogenic diet, they don't keep track of their acidity levels and keep their as-.

Heather Sandison, N.D.
Tons of veggies, but it's not just.

Dayan Goodenowe, PhD
And then bicarb, we live in a very acidic environment, good old fashioned baking soda, but you can get the potassium versions and it's important to keep your acidity levels low. It helps clear things outta your, your kidney function better, if you're on a ketogenic diet and you're exercising a lot, then you're creating lactate and that other addition acidic environment so you want to deal with that. And so yeah, exactly so fat diet is fine. There's nothing wrong with that at all. Like

anything in this world, you just need to deal with it. Quality fat, getting lecithinized, phosphocholine in your food supply. Add them to your meals is very, very important because just triglyceride is quite stressful. So you want good quality fat. It's just carbohydrates not bad. You want complex carbohydrates. Too much pure fat, it's just like too much pure sugar. You're just replacing one evil empire with another. But it is healthy. But you wanna be able to live. You wanna create a lifestyle that you can sustain. When you're talking about longevity, you're talking about mental health, it's not a diet that you can do for a month or two months. It's a diet you need to be able to do for 30 years. So you need to create a lifestyle that is sustainable. It has to fit within your own personal environment. And you can't deprive yourself so badly that you feel that life isn't worth living. And so you have to create programs that are sustainable and logical 'cause sometimes we get too fanatical about one thing and then we can't maintain it long enough to give us long term effect.

So but the bottom line though, is what you just mentioned is a hundred percent correct. When people get rid of the sugar intake, this is another part of people. You think science has everything figured out, we don't. And even if we did, you couldn't possibly measure it frequently enough in an individual to give them so much satisfaction. What happens when you've seeked to a kenogenic diet or a fat-based diet is that you are spreading your day out. And so your body isn't that smart. It relies on you to be smart. So when you have a meal, when you eat a major meal, your first part of your meal, you start digesting food and all of a sudden your body is experiencing all this glucose and things that it wasn't experiencing 20 minutes ago. I said, and it has no idea whether you ate a chocolate bar or a four-course meal. It has no idea at that point in time. So it starts pumping on some insulins, "I'm gonna get some insulin go on here, put this glucose out." And it's gotta somehow predict how much food you're eating at that point in time.

Now, if you just ate just enough sugar to elicit an insulin respond, then that insulin works and it's still there and there's no sugar left. And that's why when people drop, they get this post insulin shock, hypoglycemic shock. And even if you're measuring your blood glucose levels, that doesn't mean you're not getting hypoglycemia in certain parts of your body that aren't being measured. It's not perfect science. And if you feel headaching and bad and all that kind of stuff. So when you get to a ketogenic fat diet, that actually spreads that out. So one of the big benefits of that is it prevents this hypoglycemia aspect, 'cause once your body switches to fat metabolism, it is happy. People think about this. Most of the day, you're not eating. We don't eat 20 hours of 24-hour day. So your body mostly runs on stored energy. And what does your body prefer to

store? Your body doesn't store glucose. You store short term, it doesn't store complex carbohydrates, it stores fat. That's what your body chooses to store to eat later. It chooses fat, it likes fat. It likes saturated fat, actually. Palm oil is the cleanest burning energy source of the human body. That's what your body actually makes to store for later. Then it burns it later. So if you can think about what your body actually does, it stores fat for use later so it likes fat. So it likes to burn fat, it likes to run on fat. That's what it prefers over anything else. And so, yeah, so it's a good thing when people deal with these things, but all things in moderation. So anyways, so all these health lifestyle things are important but they only get you so far. Certain dietary supplements, vitamins, there's certain nutritional components in our food supply, but there's a difference between nutritional vitamins and therapeutic supplementation of vitamins.

When you take a B6 or you take a hundred milligrams of your B vitamins, you're getting a pulse and you're getting it into your cells and getting it to where it needs to go sometimes. So sometimes as we get older, we need these supplements. And so I like balanced approach back. But for Alzheimer's, it's this membrane choligenic system, plasmalogens, the methyltransferase system is critically important. Make sure that you have your homocystein levels low and you get good quality fat, the phosphocholine in your diet. And so I'm a big believer. We have a lots of data on MRI. The brain can be rebuilt. Alzheimer's is not only curable, it is reversible and it's preventable. It absolutely, 100% categorically with no caveats, that is the truth. I've seen it in my own eyes, I've seen it in my own family. I've done it personally. So it's doable, it's absolutely 100% doable.

Heather Sandison, N.D.
We see it here clinically every day.

Dayan Goodenowe, PhD
Yeah, but it doesn't come free. It's not magical, It's not magic It's actual systematic performance and understanding what you're trying to achieve and you need to restore that member structure and function, restore that cholinergic system. And then you have other things, you change the lifestyle that got you there, in the first place. And aging is aging.

Heather Sandison, N.D.
What have doctors seen in terms of improvements, when one of their patients gets on plasmalogens?

Dayan Goodenowe, PhD
Well, derotic, I get people that their lives are restored. We've published what was coming up. We presented at the Alzheimer's conference. We're publishing it now, it's coming up soon. But people with a late stage Alzheimer's CDR 3, clinical dementia rating at the maximum level, they're down MCI level. They're going from urinating in the closet to being violent and being on the wandering to having a normal life. Up in the morning, having breakfast. Mobility's a big deal. We get a lot of improvement in mobility. So what people see is first, first is a subtle cues. So as a scientist, when we're doing clinical trials, people have a hard time understanding when I put my scientist hat on you're all lab rats. It's very selfish, it's for me. When I run a clinical trial, I run a clinical trial for me. I say, "I'm gonna identify my inclusion criteria. What kind of people do I want in my trial?" They have to follow these criteria. And it's like high school,`` I'm saying, "Who has the nicest dress at prom?" So I'm gonna say, "Okay, this is my selection of people that I'm gonna test." And there's these standard tests that we have that are accurate, which is great for us. So we can compare upon ourselves, your memory, drawing and all these kind of things that we do these psychometric test that we do.

And then we use these as the common metrics for scientists to talk to other scientists about things. But for everyday people, it's all useless crap because it doesn't help you in your everyday life. So when people talk about their real life, but they normally notice is that the vision gets better. They get eye contact, they start seeing their loved one. Their eyes get a little brighter. They get a little more engaged in conversation. They start getting up and answering the phone that they didn't even get before. Or all of a sudden they're answering the door or they're engaging in their world, they're engaging. And then things come, they start remembering people. And I have dramatic stories, my aunt for example, she got to the point where she couldn't recognize her son. And now, she can recite everybody in her fiftieth wedding anniversary album right now. She's walking again. And so these are real, real things, they happen to people. And so plasmalogens are a critical component. And they are a big hammer. They're one of the biggest hammers we have in our, 'cause it really has a huge association with reduced cognition but also reduced mobility.

Heather Sandison, N.D.
This has been in a liquid form for a long time and I know there's a flavor kind of thing.

Dayan Goodenowe, PhD
Oh, yeah, so it's in a gel cap now, so.

Heather Sandison, N.D.
It's in a gel cap, okay, great. So these are available in a gel cap. And how is this different? Because I know there's a cost difference between a fish oil.

Dayan Goodenowe, PhD
So fish oil, so when you talk about your essential fatty acid, the things that your body, when talk about membranes before I'm building all these walls. And your body's very smart in a sense that it uses things for multiple purposes. Fat's one of those things it uses for multiple purposes. It uses it for energy. You burn it into carbon dioxide and water. Your body is essentially a hybrid electric car, you burn hydrocarbons to charge a battery, and it's a whole different conversation. But so the essential fatty acid, so there's certain fatty acid that your body can make. You're saturated in this omega-9 oleic acid, you can technically make that in the store. There are certain fatty acids that your body cannot make. That is your linoleic acid like your corn soy, can only get too much of that, as a general rule, but we it's very critical, still important. And then we have our omega-3. So omega-6 is your linoleic, your omega-3 is your linoleic flax oil and your body uses that to make a complex long chain fatty acid called DHA. And that DHA is your fish oil. But your body makes your own DHA. And what DHA is, it's a very long molecule with a bunch of double bonds, makes it kinky. And so when it fits in that membrane, when I talk about the biological membrane, it makes it fluid because it breaks up the structure a little bit and keeps-

Heather Sandison, N.D.
Yeah, and so a wall, you need a high integrity wall that can decide who comes in and who goes out and this makes it more, there's less of a decision there. So more coming in and going out without, without yeah.

Dayan Goodenowe, PhD
And you have different memories. So DHA, your fish make DHA and so do we. And so of all the animal species out there, fish oil has high concentrations of this DHA molecule. And so if you eat fish oil, you get this DHA and which is important because it's energetically demanding for you to make enough DHA. Plasmalogens are not DHA, plasmalogens are that backbone. They're what the DHA is attached to. DHA is attached to the plasmalogen backbone. And so we actually make

two types of plasmalogens. One is the DHA plasmalogen, that's for membranes, that's for that switching plate concept. The other one is you omega-9 and it's designed for multiple sclerosis and autism, very powerful for improving sleep at night. And it's an anti-inflammatory, it's designed for that white matter. It's for the protective coating, it's for the signal transactions. So people have to think about, when I talk about this wiring harness concept, I also tell people, you can think of your neurological system like a radio and an old radio, we have the dial and you're tuning the station and the fiber that contains the signal, that is like tuning it. So if you have like in multiple sclerosis and autism, when you have inflammation, you have static. It's like static, it's like the station is not tuned. The signal is not going clean, it's leaking out. And when you have a static, it's not moving properly.

If you turn the volume down, you can kind of hear the music behind the static. But if you turn the volume up, all you hear is static. So when you want your neurological system to work properly, once you get the signal tuned, then you then crank up the volume as high as you want, because now you've got the signal. So the white matter, these omega-9, your oleic acid, olive oil type molecules, those form as nice, tight, protective coating. And so that's what an omega-9 plasmalogen does. And that's what we designed for stroke and concussion and autism and serendipitously sleep improvement. So it's really powerful reducing neural inflammation. And then the DHA plasmaslogen is designed for function. It improves the neuromuscular junction in synapse dysfunction. So they're very, very different. They're very, very different.

Heather Sandison, N.D.
And then phosphatidylcholine is the other one that we talked a lot about, which you can take as a supplement. And so how is that different from plasmalogens?

Dayan Goodenowe, PhD
So phosphatidylcholine is, so it's phosphatidyl. So it's still a regular glycerol backbone. So there's two types. So all your lipids in the body, you can think of your lipids, your fat, like a power strip, like a power strip with three plugins. You got a power strip with three plugs. And if you plug in a fatty acid on all three, if I put oleic acid, oleic acid, oleic acid, I have olive oil and that's olive oil in my cupboard and that's called a triacylglycerol. So triacyl, so there's three acyl bonds. And that's what a regular triglyceride is. And then if you replace one of those three with choline, a phosphocholine or phosphoethanol or another phosphate group, that's what creates a phospholipid. And so you have two fatty acids, so you still have two oleic acids. And then you

have this polar group called choline. That's what a phosphatidylcholine is. So again, phosphatidylcholine, that's what's the backbone is being attached to a classic glycerol backbone. Plasmalogens, it's a backbone that three carbon backbone, that's different. It's a plasmalogen backbone, it has an ether bond. And that's what your body has to make that you don't get from your diet. And so phosphocholine provides that choline molecule and lipids so that's why those phospholipids are different. So the plasmalogens that we manufacture are plasmalogen precursors. They're designed to enter the cells of your body, so your cells can make their own plasmalogens. So it goes into the cells of your brain, into the cells of your muscles and those cells then convert it to the final plasmalogen. So it's like, when people have experience with Parkinson's, when you take L-Dopa for Parkinson's, you're not taking dopamine, you're taking a precursor because the dopamine won't get where it's going and it has side effects, but L-Dopa will get into the cells. And then the dopaminergic cells can actually make the dopamine they want, as much as they want.

And so plasmalogen precursors have the same kind of design, they're called alky-acyl-glycerols. And they've been around for years and years and years and years. We've just make very pure forms of them, like old shark liver oil and those type of, so alky-acyl-glycerols have been around a long time. Lots of positive asp... But the problem is the supply of it in the environment. If I take shark liver oil, they're squealing, there's a bunch of other, and you can't get the actual type of plasmalogen you need. And so that's why we make pure Omega-3, the DHA plasmalogen, for performance for neurological function. That's a critical one for the APOE 4 carriers, you need the DHA 'cause that's the reverse cholesterol transport one, but for people with autism and MS and sleep issues and neuralinflammation, diabetic neuropathies, the omega-9, we call it ProdromeGlia is designed to calm those, it is a neurological calming, it improves the protective sheath of your neurons.

Heather Sandison, N.D.
So I know our summit attendees in here are gonna be really curious to learn more and also see how they can get the benefit. So where can they learn more about you? You have a book called "Breaking Alzheimer's" I have it here, excuse me. And then you also have a company. So tell everyone where they can find out more about you and about getting plasmalogens.

Dayan Goodenowe, PhD
So the company's called Prodrome Sciences. So prodrome.com is where products are available, blood testing, certain supplements and even just general stuff. Then educational is up my drgoodenowe.com. And I put a lecture series for Alzheimer's specifically. And I call it the definitive lecture series in Alzheimer's. There's like 12 videos, and it's a long. It's like an hour each. And it goes through each system, goes through neurofibrillary tangles in precise detail, over 50 years of research of different things. I'll give you the epidemiological information. You worried about amyloid plaques, which is the issue with Alzheimer's disease. So issue with APOE 4 carriers. So APOE 4 carriers have a higher propensity to get amyloid plaques and then that amyloid plaque is an association. So I go through that in great detail, what amyloid plaques are and why. Basically an APOE 4 carrier who doesn't get increased amyloid has no increase risk of Alzheimer's. So amyloid is a kind of a biomarker of that APOE 4 mechanism.

So I go through that, brain shrinkage, mitochondrial function so I'll go through each of these things in detail 'cause a lot of stuff we talk about seems fantastical, but it's not. Our level of knowledge of these diseases is very, very high. We know these diseases and we've known about them for many, many years. The problem is the implementation of this knowledge into the general community. And that's why I've moved from standing in a glass tower, watching humans get sick and die. And so what we're doing now, is we're getting more interventionists, how do we systematically intervene in a scientifically valid, precise way? And that's what we're doing now on many levels. But yeah, you can go through that in great detail. However deep down the rabbit hole you choose to go, I'm happy to go there with you, but-

Heather Sandison, N.D.
Yeah, its great to have that educational resource, it's amazing, thank you for creating that. Thank you for writing the book and then also making the plasmalogens available to people so they can start implementing relatively, effectively and efficiently.

Dayan Goodenowe, PhD
Yeah and you get a good doctor on your hand, you get a good a natural pathic doctor or a functional med doctor and don't discount conventional medicine, but you start dealing with these... People have to realize that human body's designed to work. And you have to get people to get this age-matching concept out of their head. It prevents the elderly people from demanding function of their body. You don't buy a 30-year-old car and say, "You know what, it's

okay, it doesn't need breaks. Old cars don't have breaks." No, doesn't matter how old, breaks are supposed to work. Whether it's a 30-year-old car or a brand new car, your brain is supposed to work. And you should ask yourself and you should look for function. And doesn't matter how old you are, things are supposed to work. And if you have the expectation of work, then you have to say, "What's wrong with my breaks." Same thing in your brain, the logical structure of our human body is logically organized the same way everything in your life is, it just uses weird names and words and things and drugs and so on, but don't throw your own logic. People who've gotten successful got through their lives by looking at things in a logical way. Don't throw that logic out the window when you start dealing with your health, thinking, "Oh, I can't handle this." No, expect it to work and then if you expect success, you will find your way through it.

Heather Sandison, N.D.
Yes, expect more, expect the body to heal, I love it. And there's a lot of hope out there with everything we know and everything that we're learning. Dr. Goodenowe, thank you so much for joining us. I've learned so much from you and I know our attendees have as well and I just couldn't be more grateful for your time and-

Dayan Goodenowe, PhD
Thank you, okay, welcome, cheers.