Health Effects of the Carnivore Diet

By Dr. Joseph Mercola | mercola.com

STORY AT-A-GLANCE

- Dr. Paul Saladino, a functional medicine practitioner, advocates the use of a nose-to-tail carnivore diet to heal many autoimmune conditions, and points to evidence suggesting the notion that all plants are beneficial may need to be revisited and revised
- Plant lectins can have harmful effects by binding to specific receptor sites on your intestinal mucosal cells and interfering with the absorption of nutrients across your intestinal wall. Lectins act as antinutrients and can have a detrimental effect on your gut microbiome by shifting the balance of your bacterial flora
- In studies where rodents were given very high amounts of methionine, an amino acid found in animal protein, a shortening of lifespan was observed, leading to the oft-repeated claim that animal protein shortens the lifespan
- Follow-up studies revealed it was not the methionine that caused this effect, but rather an imbalance of methionine to glycine in the rodents' diet. A nose-to-tail carnivore diet has a well-balanced methionine to glycine ratio and appears to provide all the nutrients your body needs
- A nose-to-tail carnivore diet may be optimized by combining it with intermittent fasting or another periodic fasting regimen

Dr. Paul Saladino[1] trained at the University of Arizona with a focus on integrative medicine. He completed his residency in

psychiatry at the University of Washington in 2019 and is a certified functional medicine practitioner through the Institute for Functional Medicine. In this interview, Saladino discusses the surprising benefits of the carnivore diet, especially for those struggling with autoimmune disease.

Initially, I was skeptical of the carnivore diet, but once I listened to Saladino's detailed analysis and justification for this approach, I changed my position and believe it is appropriate for a large number of individuals.

While at the time of this interview, Saladino was still a resident-in-training, he's developed profound expertise in this area by attending medical school twice, and diving deep into the medical literature.

"I graduated from college in 1999. I went to the College of William and Mary, studied chemistry and biology and did a whole bunch of molecular biology research there. My dad's a doctor, so I [was] steeped in medicine throughout my pre-career years and throughout my childhood …

I've always been interested in the way that health and disease affecting the quality of life and the way that food affected the way that I felt like a human being," Saladino says.

"I've been an athlete for most of my life, running and backcountry skiing and climbing mountains and so on. I was always kind of tuned into connections between food and health and disease. But when I got out of college … I took six years off and just spent the time in the mountains, exploring and adventuring.

Perhaps I already had this sort of seed within me of just questioning norms and asking interesting questions or being very curious. But that time certainly fed that. I hiked the Pacific Crest Trail … 2,700 miles. I climbed mountains throughout the Pacific Northwest, the Rockies in Colorado. I got into mountaineering and backcountry skiing.

Eventually, I realized that I really loved biology. I was really curious about some of these health questions. I wanted to go back to school. My dad is … an internist, an incredible man who spent so much of his life caring for patients. But I also saw him spend a lot of time working and not a lot of time being able to achieve balance and real self-work …

I went to physician assistant (PA) school at the George Washington University and then started working in cardiology with a group of cardiologists in Bend, Oregon. Cardiology originally was a good fit for me because I thought I was a runner at the time … This is what maybe is unique about my training … I went to medical school twice."

Looking for the root of disease

A PA can be likened to an accelerated shortcut to being a physician. They have nearly identical practicing privileges, although a PA works under the authority of a supervising physician.

So, Saladino went through two years of basic clinical science twice, which helps explain his deep understanding and appreciation of the biological sciences. He admits that while his initial interest was primarily determining the benefits and drawbacks of various drug treatments, he quickly developed an interest in understanding the actual root of the disease.

"I wanted to know how to change the course of a disease, how to get to the root cause of the disease. I know this is what you're fascinated by too. It unites a lot of us in these fields. It's, 'What is causing a disease?' This is the most interesting question to me and medicine.

That birthed my second career in medicine … Because I realized very quickly into my career as a PA that I was going to want to go back to medical school to get an M.D., to get a doctoral degree, to continue my training, to have the ability to

practice as a physician, and to do that practice from a perspective of someone looking for root causes of diseases.

That's really been my focus. I ended up working as a PA in cardiology for four years. At that point, I went back to medical school at the University of Arizona in Tucson, which has a pretty strong history of integrative medicine … They have the Center for Integrative Medicine there …

As I looked at medicine differently, food seemed to be such a huge part. The things that we are putting into our body really seem to be a big part of what created health and disease …

Right now, I'm in the last month of my four years of residency at the University of Washington. I've got one month left to finish residency. But it was really the first seven years of my medical training after being a PA that kind of set the stage for this next sort of exploration, curiosity, realization for me …

I had this incredible privilege to see medicine through the eyes of someone who had been in the trenches. I thought, 'OK. Now I'm learning medicine again. What is going on here?' Every time I learned something, I thought, 'What is the root cause here? What is going on?'

What happened for me was this constant kind of disappointment, this constant sort of struggle realizing, 'The pharmaceuticals are incredible, but they're not treating the root cause. People don't often get better' … I was looking for tools that worked … I had the suspicion that it was diet. What I'm learning is that there may be an ideal diet for everyone, or it might be individualized. It might be some of both in there."

The carnivore diet

When Saladino discovered the carnivore diet, he'd already been

contemplating ancestral norms and evolutionary ideas, asking questions such as: "Where have humans come from? How do we eat? What is the most congruent way of eating for humans that are going to give us optimal health?"

He admits the idea of the carnivore diet is "super radical." He first heard of the carnivore diet from Jordan Peterson on a Joe Rogan podcast.[2] He talked about his daughter Mikhaila, who had a bad case of juvenile rheumatoid arthritis (JRA), which is an autoimmune inflammatory disease.

She had multiple joint replacements at a young age, which crippled her. "She discovered this way of eating only animal meat," Saladino says, and over time, her symptoms improved.

"In medicine, we talk about case reports. I love case reports because I want to see how things actually work at a real level," Saladino says. *"It was so striking to me that someone like Mikhaila could essentially reverse and completely heal from JRA and then the depression that was connected with it, probably because of the concomitant immunologic and inflammatory mechanisms with this radical dietary change.*

I thought, 'That is really striking. I want to study that.' Then Jordan Peterson talks about the fact that he had anxiety and sleep apnea and other issues himself. They improved when he started eating an animal-based diet."

Might plant diets trigger autoimmune problems in some people?

Now, why would an animal-only diet be more effective than a plant-only diet? Everyone "knows" plant foods are good for you and a crucial part of a healthy diet. Saladino continues:

"I love that this notion just turned it all on its head. It just tipped everything over and I thought, 'Wait a minute. It

kind of makes sense. Maybe plants don't want to get eaten. Maybe plants aren't good for humans?' In the beginning, I was very skeptical and I thought, 'I really need to dig into this,' and so I did …

This fundamental premise, this idea that plants and humans, plants and herbivores or plants and animals have coevolved, and every life form really have one goal. That's to push its DNA into the next species and to continue the lineage of that species.

A mustard plant wants the mustard plant to continue. An oak tree wants the oak tree to continue. Life and ecology is this beautiful intermingling of all these species working together but fighting and eating each other and trying to kill each other, but sometimes being symbiotic.

This concept that 'Maybe plants don't want to get eaten after all,' maybe this unconditional narrative that all plants are good for you all the time, maybe we should question that. That's a pretty radical concept because I think even within the functional medicine sphere, there's this notion that all plants are good for you and the more plants you eat, the better.

But this counterculture, disruptive concept that for some people — perhaps for all of us, perhaps just for some people — plants can trigger autoimmunity through a variety of mechanisms is really intriguing."

The plant paradox

I've previously highlighted the work of Dr. Steven Gundry, who wrote the book "The Plant Paradox." In it, he succinctly explains why and how plants, which are allegedly beneficial for us, can be harmful at times. Gundry's premise is based on the harmful effects of lectins, plant proteins, sometimes called sticky proteins or glycan-binding proteins, because

they seek out and bind to certain sugar molecules on the surface of cells.

Some — including wheat germ agglutinin (WGA), found in wheat and other grass-family seeds — bind to specific receptor sites on your intestinal mucosal cells and interfere with the absorption of nutrients across your intestinal wall. As such, they act as "antinutrients," and can have a detrimental effect on your gut microbiome by shifting the balance of your bacterial flora. Saladino had already investigated lectins as a means to improve his own eczema.

"I think one of the ways that I differ greatly from mainstream medicine in my conceptualization … is I don't believe in 76,000 diseases. I believe in like five diseases. Everybody manifests them a little differently. I kind of knew that my autoimmune disease was probably the same as almost everybody else's autoimmune disease.

If I could understand what was triggering my autoimmune disease, maybe that will be the first start of this journey, this first thread that I could pull on to understand what was causing other people's autoimmune diseases, because autoimmunity, inflammation, these are almost synonyms. If we can understand that, we can help a lot of people.

I was just going through this process. Gundry's work was a part of it. I think that now I would disagree with him on many issues … [He] has some great ideas about lectins …

I think … he's tried to create the lowest lectin, plant-based diet that he can with a small amount of meat … But I think that he and many others are misunderstanding a series of studies done in the '60s and '70s with rodents and methionine overfeeding that suggested excess levels of methionine would shorten the lives of these rodents.

Gundry and some other people have said, 'Animal protein shortens lives of humans' … I was actually a vegan 13 or 14

years ago. I explored that … My impression is that most of the plant-based physicians when they're saying the animal protein shortens lives, they're referring to these methionine studies."

Imbalance of methionine-glycine ratio is the problem

As noted by Saladino, in studies where rodents are given very high amounts of methionine, a sulfur-containing amino acid found in animal protein, a shortening of lifespan is observed. However, rodent diets are quite different from human diets. Mice and rats are not eating salad and steak. They're given chow to which certain nutrient ratios have been added or subtracted.

When the amount of methionine in the rat or mouse diet is increased by about 2%, lifespan starts to dwindle. The original conclusion was that excess methionine might shorten human lives as well, and some human biochemistry research suggests that might be the case. However, if you look at subsequent studies, you find there's more to the story.

"[W]hen they did the next study, they took the methionine out of the diet a little bit. They did methionine restriction. What did they see? They saw lengthening of the life of the rats … That was further strengthening their first hypothesis. But then the magical thing happened.

They gave them a large amount of methionine or the same amount of methionine, 2% of the diet with more glycine. What did they see? They saw an extension of the lifespan. Then they realized — and this is what I think everybody's leaving out — that it's not about the excess methionine. It's about the imbalance and the methionine-glycine ratio.

We know this from human biochemistry. If you look at the

folate cycle, if you look at methylation, if you look at the way we handle methyl groups, methionine is a methyl-containing amino acid. We know that homocysteine is converted to methionine by a series of enzymes. This involves the methylenetetrahydrofolate (MTHFR) gene, which makes L-5-methylfolate.

Your body uses L-5-methylfolate with homocysteine and the enzymes methionine synthase (MTR) and methionine synthase reductase (MTRR) … to add a methyl group to homocysteine to make methionine. Methionine is the precursor for S-adenosyl methionine (SAM-e). SAM-e does all these methylation reactions in the body.

But what we know is that excess methionine is buffered by glycine. Our body will use glycine to buffer methionine. If we get too many methyl groups and we don't have the corresponding amino acids to buffer them, the biochemistry can get kind of messed up.

Then the hypothesis, which I think is fairly compelling, is that too many sulfur-containing amino acids can create oxidative stress. Homocysteine is a sulfur-containing amino acid. I think there's good evidence that too much homocysteine probably causes oxidative stress by the same mechanism.

What we're looking at is a balance between sulfur- and nonsulfur-containing amino acids. We need the glycine, which doesn't have any sulfur, to sort of balance and buffer the methionine. There is this interesting concept that if we eat too much methionine, we will imbalance glycine.

Glycine is such crucial amino acid. If we use up all of our glycines to buffer methionine, we won't have enough glycine to make two very critical proteins: collagen and glutathione."

Can a carnivore diet provide all the nutrients you need?

Glycine is the smallest and simplest of the amino acids. Methionine and glycine are found in muscle meat at a ratio of about 2% methionine and about 7% to 8% glycine. In connective tissue, you find about 0.9% methionine and about 23% to 24% glycine, which isn't surprising because connective tissue consists mostly of collagen.

Collagen is typically constructed from three amino acids: glycine, proline, and hydroxyproline, at a 1-to-1-to-1 ratio. So, there's a significant difference between collagenous tissue and muscle meat.

"When we are thinking about eating a carnivorous diet, I am a strong advocate for this concept of nose-to-tail eating, this idea that evolutionarily, our ancestors were certainly eating the whole animal, both from a spiritual perspective or a respective perspective for the animal and from a functional pragmatic perspective. They wanted all the calories and all the nutrients," Saladino says.

"If you look at an animal, there are unique nutrients in muscle meat. There's a whole unique set of nutrients in the liver, and … unique amino acid composition in the connective tissue. There are unique nutrients in the bones. There are unique nutrients in the bone marrow and the fatty tissues. You can see this animal as this sort of fascinating partitioning of nutrients.

The idea of a carnivore diet or a whole-foods, animal-based diet became much more viable for me when I realized … studying anthropology that our ancestors were, in fact, eating the whole animal. Every indigenous culture that I'm aware of on the planet that's living now eats the whole animal.

Then you think, 'Now it makes sense.' It's not just about

eating steak. You're really getting this incredibly diverse array of nutrients in the whole animal … You can get every single thing that we need. It's really interesting to kind of break it down and says, 'You're getting calcium in the bones. You're getting copper to balance the zinc in the liver. You're getting this B vitamin in the liver. You're getting this B vitamin in the muscle meat.'

But what we find is that we have to eat the whole animal. If we just eat the muscle meat, we're really going to be missing out on nutrients. But that's such an incredible postulate to say, 'Wait a minute. I can get all the nutrients that I need as a human by eating an animal nose-to-tail?' That's incredible. It's like the best multivitamin ever.

I would argue further that animal-based nutrients are much more bioavailable than plant-based nutrients. They're in the right ratio, which is incredible if you look at zinc, copper, calcium, and magnesium. Then it kind of makes sense when you think about it from an evolutionary perspective. A deer or an elephant is a mammal. They're much more similar to a human operating system, to human physiology, than a plant is.

We can get some nutrients from plants, but an animal looks so much more like us, that it's so much more compatible with our biochemistry when we take it in. The last part of the equation is that we can do all that, eating animals nose-to-tail without any of the antinutrients … that might be present in plants.

It appears that some people may be uniquely sensitive to those anti-nutrients. My hypothesis … is that may be the root cause for a lot of autoimmunities."

Organ meats in a pill

If you struggle with the idea of eating organ meats, you could consider a whole food supplement. There are now a few

companies that provide desiccated organ tablets. Some of the better ones are sourcing grass-fed animals from New Zealand, allowing you to get desiccated brain, liver, pancreas, and spleen.

"A lot of people are finding improvements in histamine issues with the kidney," Saladino says. *"The best thing would be to eat kidney because it has diamine oxidase (DAO) …*

But a lot of people are taking the desiccated organ complex with kidney from Ancestral Supplements or another manufacturer and getting improvements in histamine issues because of the DAO that's in that."

What about mTOR activation?

One of my initial concerns and one of the reasons why I seriously doubted the carnivore diet would be a good idea is the chronic activation of mammalian target of rapamycin (mTOR), a protein-sensing pathway involved in aging. When mTOR is activated then autophagy is inhibited, and that is the last thing you want to do on a long-term basis, as it is a prescription for metabolic disaster.

However, as I listened to Saladino's presentations, it became clear that it was a no-carb diet and would clearly put people into ketosis. And if they further restricted their eating window to six hours and did a one-day-a-week fast, there should be more than enough time to inhibit mTOR and activate autophagy.

For quite some time I was overly fearful of eating too much protein and over activating mTOR activation as it can speed aging and decreases life span. Some people are even taking rapamycin supplements to continually suppress it. But you do need to activate mTOR now and then, especially if you want to have any hope of ever increasing your muscle mass.

What I also came to realize is that activating mTOR and increasing muscle mass is even more important as you age. Sarcopenia or loss of muscle mass as you age can dramatically contribute to frailty. So, it is a fine balance.

Insulin is primary mTOR activator when in ketosis

As noted by Saladino, there's an important distinction to be made here, and that is that when you are in a ketogenic state, insulin is a far more profound activator of mTOR than leucine.

Needless to say, a carnivore diet is about as low-carb (ketogenic) as you get. There's virtually no carbohydrates. You're going to be generating massive amounts of ketones as a result, and you'll already be in ketosis.

The question is, can these two approaches — the carnivore diet and partial fasting to trigger autophagy — be successfully integrated? Based on Saladino's explanation of how the carnivore diet affects mTOR, it appears they might make for an excellent hybrid program.

"In a gross oversimplification, [mTOR] is kind of like the anabolic lever. It's the 'build your body up' side of your metabolism. It's balanced by 5' adenosine monophosphate-activated protein kinase (AMPK), which is the more catabolic. When we're eating … we're sort of activating mTOR … When we're not eating, we're generally triggering AMPK …

There has to be a balance … What's fascinating to me about the mTOR story is that when I really dug into this, the literature would suggest there are two ways to activate mTOR. There are different mechanisms, but they both do it. One of them is proteins, specifically leucine. One of them is insulin …

In terms of insulin and leucine, if we compare those … insulin had a much greater effect on mTOR, turning it on. The insulin

effect also acted much longer, on the order of three to four hours. Leucine certainly will turn mTOR on, but it has a lesser effect. I think, relatively speaking, at the risk of putting a number on it, it was about 30% less, and then it did it for only about 45 minutes to one hour.

What we're seeing here is we can activate mTOR with protein, specifically leucine load … But if we activate mTOR with leucine, it's kind of on and then off about an hour later. If we activate mTOR with insulin, then it's going to be on for three to four hours. People can leverage this in whatever direction they want.

But with regard to a carnivore diet, some of the interesting discussion is around the question, 'Will eating … nose to tail … over-activate mTOR?' I think what's interesting is it probably won't if we look at the molecular mechanisms because it will primarily be a leucine switch of mTOR that we're turning on. It'll be on-off, on-off, rather than the insulin switch of mTOR.

Relatively speaking here, I think there's an interesting possibility that if we're eating carbohydrates, we're going to trigger more mTOR through the actions of insulin and the insulin-glucagon ratio than we are with protein. The carnivore diet is kind of like a unique example because there's essentially no carbohydrate.

When we look at ketogenic diets, like a carnivore diet, we know that insulin is very low … When we eat food, insulin is going to rise. But in a ketogenic state, we know that insulin and glucagon are going to rise together. That ratio is not really going to change.

This comes up a lot in discussions with people. They say, 'Isn't eating a lot of protein going to spike my insulin? Isn't eating a lot of protein going to turn on gluconeogenesis? My blood sugar is going to spike.' That's not

what we see at all, especially on a carnivore diet, because the insulin and the glucagon are going to rise a little bit, and they rise concomitantly, so then the insulin-glucagon ratio doesn't change.

When the insulin-glucagon ratio stays consistent, you're not really activating mTOR through insulin. You're not getting a big insulin spike at all … If someone's not in ketosis, if they're not fat-adapted and you eat a bunch of protein, yes, you're going to get a big spike in your insulin. That insulin-glucagon ratio is going to change drastically. But this is in stark contradistinction to the way that insulin responds when you're in a ketogenic state."

Carnivore diet may work well with partial fasting regimen

In summary, Saladino believes there's little risk of overactivating mTOR with leucine on a nose-to-tail carnivore diet along with appropriate time-restricted eating and fasting.

So, the answer to the question "can these two approaches — the carnivore diet and partial fasting to trigger autophagy — be successfully integrated?" the answer seems to be yes. From an evolutionary perspective, it seems clear humans have hunted animals for meat (although not necessarily exclusively). Mankind also fasted for periods of time.

"I think there's absolutely a role for intermittent fasting, time-restricted eating, longer fasts — 24, 48, 72 hours — where you really shut everything off and you turn on AMPK," Saladino says. *"You shut mTOR down permanently for a little while, and then turn it back on with protein and meat …*

I would argue that the meat or the animal foods are a little bit more of a precise switch for mTOR. You can just be like,

'On, off, on, off.' Like I said, you can exercise, turn it on, get anabolic, work out, build muscle, regrow and then do other phases where you're breaking down, doing autophagy or apoptosis and totally recycling your cells."

I've previously written many articles detailing the ins and outs of intermittent fasting and cyclical partial fasting. This is also the topic of my latest book, "KetoFast." I've also written about the importance of eating your last meal at least three hours before bedtime.

Aside from preventing the deterioration of your mitochondria, avoiding late-night eating will also help inhibit fat accumulation. NADPH creates fatty acids. If you eat food before you go to bed, thereby providing your body with energy that you're not using, then something must be done with that energy. Since you're not moving, your body stores it away for later use.

To store the energy as fat, your body uses NADPH to make fatty acids. As a result of that creation, your NADPH levels plummet, thus reducing your body's ability to recharge your antioxidant structure. I think this may be one of the most important justifications for not eating three or four hours before bedtime.

Other topics covered in this interview

Saladino covers a lot of ground in this interview — more than can be included in this written summary, so I encourage you to listen to the interview in its entirety. In it, we also cover the following topics, and consider the following questions:

•The best use of polyphenols — Most polyphenols are plant-based and are beneficial for autophagy and the activation of various metabolic pathways.

Fisetin and quercetin are now used for senolytic therapy, leading-edge longevity strategies to remove senescent cells (cells that stop reproducing but are still active and create inflammatory molecules, typically cytokines that cause metabolic havoc). You don't need a large percentage of senescent cells to radically accelerate the aging process.

•Is there a dark side to sulforaphane (the anticancer compound found in broccoli)? According to Saladino, there might be, as sulforaphane is actually a plant toxin and the Brassica genus is a significant contributor to endemic goiter and cretinism (a prenatal condition caused by inadequate iodine).

•Alternative ways to increase glutathione besides plant-based sulforaphane, such as heat stress, cold stress, exercise, fasting, and nutritional ketosis.

•How green smoothie cleanses can backfire by overloading on oxalates, and how you can mediate against oxalate toxicity by adding calcium oxide (which binds to oxalate and allows it to pass unabsorbed through your digestive tract)

•What does Saladino's personal bloodwork look like after eight months on a nose-to-tail carnivore diet, and what does it say about its health effects?

More information

By the time this interview airs, Saladino will have completed his residency and opened his private practice focusing on functional medicine for the treatment of psychiatric and nonpsychiatric ailments. You can learn more about Saladino and his practice on Paulsaladinomd.com.

He plans on doing virtual consultations as well, so you may benefit from his experience even if you're in another state. To schedule a virtual or in-person consultation, email him at PaulSaladinoMD@gmail.com.

Saladino is also writing a book and is starting to speak at various conferences. He'll be at KetoCon in Austin, in June 2019. He also has a podcast called "Fundamental Health With Paul Saladino M.D.," which you can find on iTunes, Stitcher, Spotify, and YouTube. In closing, Saladino says:

"I think this is one of the conversations that I really like having … It's saying, 'Hey. This is a radical thing. We really need to examine this carefully and do blood testing and make sure it's safe for people because it seems to help people with autoimmune disease.'

I've seen people with Crohn's and ulcerative colitis and eczema and psoriasis resolve, which is just mind-boggling … But the flipside is you need to make sure [it's safe] … 'Are people going to get deficiencies?' I don't think so. I think there's an evolutionary basis for this. But how do we show this is safe and get some pilot studies going?

Because it's my strengthening suspicion that this is going to be a very useful tool for us in the medical world moving forward … What I've learned about functional medicine is that it all starts in the gut. Every functional medicine doctor has to be a gastroenterologist …

I'm going to be treating patients in my practice who are psychiatric and non-psychiatric because I really think it's all connected … I'll be treating people with all sorts of conditions, from GI to autoimmune … I really believe that a lot of psychiatric illness is autoimmune in nature and that a big part of improving that in the future is going to be treating people from that perspective, in a very holistic way."