Independent research & further reading

Guest: Dr Benjamin Bikman

Disclaimer 1: The literature presented here, directly (or as closely as possible), looks at statements made by the guest. In order to fully understand each topic mentioned, an extensive literature review (beyond the scope of this document) would be required.

Disclaimer 2: The information provided in this podcast and any associated materials is not intended to replace professional medical advice. For any medical concerns, it is essential to consult a qualified health professional.

Contents

Insulin resistance and health problems

"from things like Alzheimer's disease to heart disease to type two diabetes to liver failure, fatty liver disease, all of them are. Share a common metabolic core. That's my mission. And what is that common metabolic core? Yeah, it's a little known problem called insulin resistance"

Alzheimer's disease

The role of insulin resistance in how Alzheimer's disease develops is becoming more widely acknowledged. The main reason for this link is how insulin affects brain activity and its importance in brain physiology and cognition. Targeting brain insulin resistance has been shown to be a potential treatment for Alzheimer's disease.

References 1-6.

Type 2 diabetes

Insulin resistance is a major cause of type 2 diabetes, a condition marked by high blood glucose levels due to impaired insulin function and secretion (7).

Cardiovascular disease

Insulin resistance is associated with a cluster of metabolic and cardiovascular disorders, each an independent risk factor for cardiovascular disease (8, 9).

Adipose tissue and risk of type 2 diabetes

"stumbled on one paper that documented how when fat tissue is growing, it increases the risk of type two diabetes."

"It was so fascinating where when fat tissue is growing, it starts releasing pro inflammatory proteins"

- Fat tissue, especially visceral fat (VAT), plays a key role in the onset of insulin resistance, which can lead to type 2 diabetes (10).
- Inflammation in adipose tissue is a major contributor to insulin resistance and type 2 diabetes in obesity, along with potential factors such as inflammation and fat buildup in other tissues (11).

Fat tissue, inflammation and insulin resistance

"fat tissue secretes hormones, some of which promote inflammation"

"inflammation caused a problem called insulin resistance"

"So the most relevant feature with fat tissue contributing to insulin resistance is the size of each fat cell"

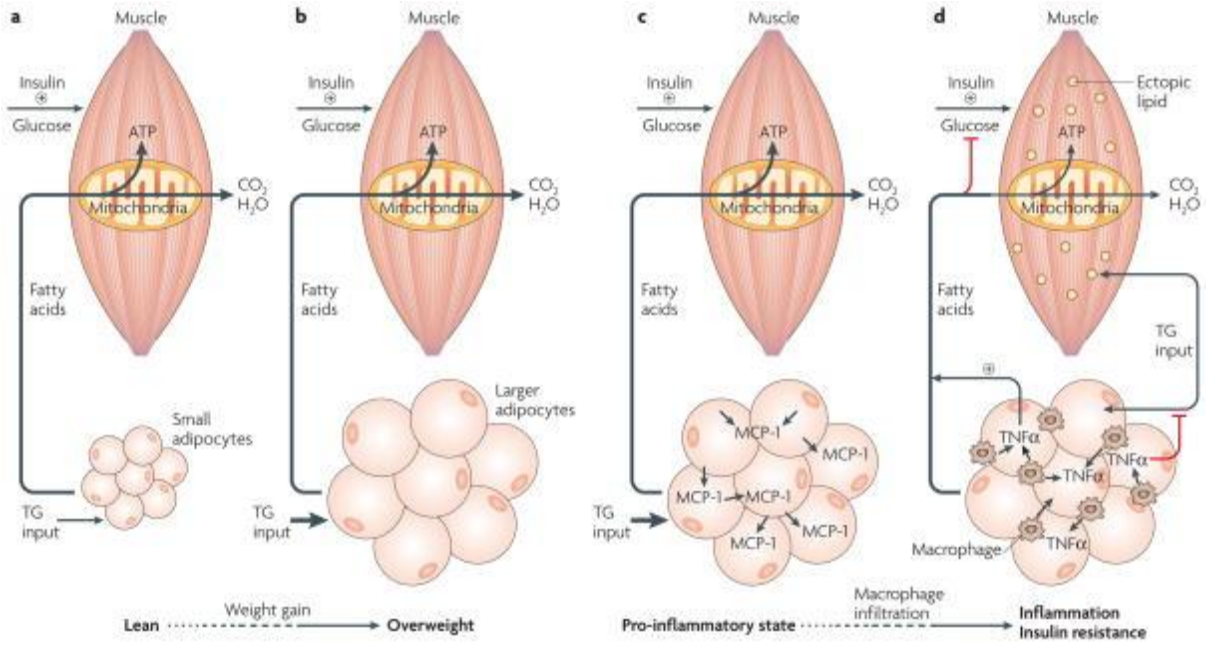

Figure from Guilherme et al. 2008 (12).

a. In a lean state, small fat cells store energy efficiently, and muscles use fat for energy when needed. Insulin works normally;
b. excess caloric intake causes fat cells to grow, but in overweight non-diabetic individuals, fat storage and muscle energy use can still function well;
c. with further fat overload, fat cells enlarge and release signals that attract macrophages, a type of white blood cell;
d. these macrophages cause inflammation, disrupting fat storage and muscle function, leading to insulin resistance.

Insulin resistance and hypertension

"Insulin resistance is the main cause of hypertension"

Research indicates that hypertension results from a complex interplay of genetic, environmental, and physiological factors, including oxidative stress, inflammation, endothelial

dysfunction, kidney function, and nervous system activity. Rather than having a single cause, high blood pressure develops due to multiple interacting influences. Insulin resistance has been shown to be associated with hypertension, though this relationship may be noncausal, with hypertension potentially causing insulin resistance or vice versa.

References 13, 14.

Insulin resistance, erectile dysfunction and PCOS

"Even the most common forms of infertility in men, it's erectile dysfunction. Well, that's because of insulin resistance of the blood vessels in women, the most common form of infertility is polycystic ovary syndrome, or PCOS. That's because of the insulin resistance affecting her ovaries and the ability to produce the proper sex hormones."

Erectile dysfunction

Insulin resistance has been associated with erectile dysfunction, as shown by a recent systematic review and meta-analysis (15).

"In fact, its connection to insulin resistance is so strong that just a few years ago, I was so struck by a title of a paper that had just been published which stated something like, is erectile dysfunction the earliest manifestation of insulin resistance in otherwise young healthy men."

Reference 16.

PCOS

Research suggests that PCOS results from a mix of genetic, hormonal, and environmental factors, including high androgen levels, insulin resistance, and prenatal androgen exposure, along with chronic inflammation and oxidative stress. Insulin resistance plays a role in PCOS by disrupting insulin signalling, which leads to hyperandrogenemia and causes metabolic imbalances. These effects worsen PCOS symptoms, creating a cycle of ongoing hormonal and metabolic disruptions.

References 17-19.

Ethnic differences in fat storage

"East Asians or Southeast Asians, have a very low capacity for fat storage"

"It's saying that Africans have better fat distribution, lower visceral fat, yep, and less metabolic risk because of that."

- East and Southeast Asians are genetically predisposed to accumulate visceral fat and face a higher risk of metabolic disorders at lower BMIs (30-32).
- Africans generally having less visceral adipose tissue (VAT) compared to Europeans and Asians (33, 34).

Insulin and ketones

"The relevance of ketones to the insulin is that insulin, in its absolute dictatorial powers over metabolism, will determine whether the body is making ketones at all. Now I don't want to get us onto that topic necessarily. Ketone metabolism is its own topic, but suffice it to say, even studying ketones is an indirect study of insulin because insulin controls whether the body's even making ketones or not."

Ketone production depends mainly on the liver's fatty acid availability and metabolism, which are influenced by fasting, low-carb intake, hormonal signals (insulin, glucagon, epinephrine, thyroid hormones), and the balance between fat breakdown and triglyceride formation. Insulin specifically regulates ketone levels by promoting their use and limiting production.

References 35-37.

<u>Insulin</u>

References 38-42.

Fast insulin resistance: stress, inflammation and too much insulin

"Stress is is a primary cause of fast insulin resistance. So too is inflammation. And then lastly, and this is going to sound somewhat paradoxical, too much insulin is also a cause"

<u>Stress</u>

Psychological stress can lead to insulin resistance by increasing cortisol levels, triggering oxidative stress and inflammation, and disrupting insulin signalling (43-45).

"those two hormones (cortisol and epinephrine) have in common is that they both want blood glucose levels to climb."

"If both of those signals are too incessant, or they continue to be present and climb, then insulin has to work harder and harder, and then we have insulin resistance. So stress is a cause of insulin resistance."

References 46, 47.

Sleep

"Just one bad night of sleep was sufficient to increase our stress hormones, which in turn is sufficient to cause insulin resistance that quickly. Now, thankfully, one good night of sleep resolves it all. And so as much as stress was a quick cause, it's also a quick solution."

Reference 48.

<u>Inflammation</u>

"Even then, if a person were wearing a continuous glucose monitor on the back of their arm measuring their glucose levels, they would see their glucose levels are much, much higher, like significantly higher during the time that they're struggling with this infection. That is a reflection of insulin resistance. Insulin is having a harder time keeping the blood glucose levels in check. Anytime inflammation is up, insulin resistance will be up as well."

Infections often raise glucose levels, worsening insulin resistance and increasing the risk of hyperglycemia, which can make recovery more difficult. Interestingly, strict blood glucose control with intensive insulin therapy has been shown to reduce infection-related complications and lower mortality in critically ill patients (52).

References 49-52

Too much insulin

Elevated insulin levels, known as hyperinsulinemia, can both result from and contribute to insulin resistance, creating a cycle that worsens metabolic dysfunction (53).

Carbohydrates consumption and meal frequency

"where 70% of all calories. These globally, are carbohydrates, and now, perhaps with the best of intentions, our experts are telling us that we should be eating six times a day"

Americans have generally followed dietary guidelines to reduce fat intake and increase carbohydrate consumption over the past 50 years, with carbohydrate intake rising from 39% to 51% of total caloric intake between 1965 and 2011 (54).

Research on meal frequency and health outcomes is mixed, and there is no consensus about the ideal number of meals per day. While some studies support fewer meals a day, especially for weight management, others support more frequent meals, which may lead to reductions in total and LDL cholesterol. However, more research is needed.

References 55-60.

Insulin's return to normal levels after breakfast

"So depending on how much carbohydrate we ate for breakfast, it could take our insulin levels three or even four hours to come back down to normal."

After consuming a 60g carbohydrate meal, blood glucose usually returns to baseline within 3-4 hours, with larger meals extending this by roughly an hour (61).

The size of fat tissue

"Steve has 10 kilos of fat on your entire body. That's probably too much for you. Ben has 20 kilos. And yet it's possible that I'm healthier metabolically than you, and that's because it's not the mass of fat that matters most. It's the size of the fat cell that matters."

References 62, 63.

Women

"This is why women, despite universally being fatter than her male counterparts, are healthier with regards to insulin resistance in every single metabolic problem. It's because women, as a result of her particular sex hormones, have more fat cells, but they're smaller, so she has more fat but smaller fat cells and small fat cells are healthy, insulin sensitive, anti inflammatory fat cells, but the bigger the fat cell gets, the more it initiates a cascade of events, or a series of events, that creates insulin resistance."

Research suggests women store more subcutaneous fat in the gluteal-femoral region, while men have more visceral fat in the visceral depot. However, mean fat cell size doesn't seem to differ between the two genders (64). In fact, some studies mention women having larger subcutaneous adipose (fat) tissue (68, 69).

References 64-69.

Lifespan of fat cells

"Fat cells will live about 10 years and so typically, by the time if you think, if you look at a newborn, during infancy, childhood and puberty, the number of fat cells is going up once they finish puberty, so mid to late teens for a young woman, late teens or even early 20s for a young man, usually, at that point, the number of fat cells they have is going to be very static."

Fat cells have an average lifespan of about 10 years, with approximately 10% of cells replaced annually (70, 71).

"as an adult, have the same amount of fat cells really, regardless of what we eat"

Fat cell number and size change throughout life, shaping overall fat mass and distribution. During infancy and adolescence, fat tissue expands mainly by increasing fat cell numbers, while in adulthood, the total number remains stable despite a 10% annual turnover. Research shows that dietary interventions can alter fat cell numbers, as seen in rats where food restriction reduced fat cell counts in various fat depots (Bertrand et al. 1984). Fat mass tends to peak in middle age before declining and redistributing later in life, which can contribute to health issues like type 2 diabetes and atherosclerosis. Additionally, fat cell turnover and lipid content play key roles in metabolic health, with low turnover linked to insulin resistance and dyslipidaemia.

References 72-74.

Fat cells and ethnicity

"Understand why different ethnicities were getting diabetes, type two diabetes, so differently, and it is entirely a function of how big are your fat cells"

"On one end, you'd have Caucasians, kind of Northern European Caucasians on the other end, and you'd have East Asians, like Chinese, Japanese, Korean East Asians. And then if you look at that same spectrum of people making fat cells through their life, an East Asian will be making fat cells. And then stop right about here, about sort of so very few fat cells. Relatively speaking, across all the ethnicities, they have very few fat cells. A Caucasian. On the other end of the spectrum, they went way higher."

- South Asians have an increased adipocyte area compared to white Caucasians, which contributes to ethnic differences in insulin, HDL cholesterol, adiponectin, and ectopic fat deposition in the liver (75).
- Asians have lower BMI but higher percent body fat than whites, with greater differences in upper-body subcutaneous fat in females (76).
- Healthy Asian Indians exhibit insulin resistance, dyslipidemia, and increased cardiovascular risk compared to Caucasians, with increased visceral fat contributing to these abnormalities (77)
- Asian populations have a higher body fat percentage at lower BMI compared to Caucasians, with differences in body build, slenderness, and muscularity contributing to the different relationship (78).
- Asians have higher body fat and abdominal obesity compared to Caucasians, potentially predisposing them to insulin resistance at a lesser degree of obesity (79).

Type 1 diabetes and weight loss through skipping insulin injection

"It is, it is literally impossible for the type one diabetic to get fat if they are skipping their insulin injections."

"It works so well that it's actually a formal eating disorder called diabulimia."

Type 1 diabetes is linked to a higher risk of eating disorders, especially bulimia nervosa and binge eating, and an increased likelihood of insulin misuse or omission, particularly in females. This behaviour is related to weight concerns, body dissatisfaction, and mental health issues, including anxiety and depression. Studies have found that up to 31% of youth and women with type 1 diabetes intentionally omit insulin to lose weight and up to 60% of individuals with type 1 diabetes admit to misusing insulin. It is important to note that insulin omission and disordered eating are associated with poor blood sugar control and a higher risk of diabetes-related complications.

References 80-85.

Insulin response and meal composition

"But there are studies in humans to show that if you give humans isocaloric meals, so the exact same number of calories, but they in the same amount of protein, but you differ those meals based on the amount of carbs to the amount of fat. ... This lower carb, higher fat version will have a lower insulin response"

Reference 86.

Metabolic rate and carbohydrate consumption

"if you have someone going a full day eating the same number of calories, but lower carb calories, their metabolic rate will be almost 300 calories higher in that day"

In a systematic review, the "mean difference in energy expenditure was 26 kcal/d greater with lower fat diets", when compared to a low-carbohydrate isocaloric diet (87, 88).

Premature infants

"born premature will be more likely to have learning disorders later in life is because premature baby didn't have time to get very fat. And fat baby is healthy. Baby and fat baby gets into ketosis."

References 89-91.

Ketones versus glucose as a source of fuel for the brain

"And if you and I were to fast for 24 or so hours, we may get up to about one millimolar of ketones. And yet, even then, the brain has already switched to get the majority of its energy from the ketone."

References 92, 93.

Vegetarians

"Maybe one final point on this, although it is a bit of a barbed comment, people may find this somewhat amusing or disappointing or frustrating the title of a book just published, which is that vegetarians have smaller brains. This is seen in humans, that the less a human eats meat, then the smaller the brain becomes."

There is no significant evidence that vegetarians have smaller brains compared to non-vegetarians. A study that looked at brain volume as a function of self-reported vegetable intake

found an inverse association with grey matter volume change. However, another study found that a diet rich in vegetables, fruit, whole grains, nuts, dairy, and fish, combined with a low intake of sugary drinks, has been linked to larger brain volumes. Vegetarian diets have been associated with low levels of nutrients, namely vitamin B12. Consequently, vitamin B12 deficiency has been linked to increased brain volume loss in an elderly population. However, supplementation can be taken to overcome these low levels. There is not enough research to understand the effect of a plant-based diet on brain volume.

References 94-98.

"And why does depression go up so much when people stop eating animal source foods? It's because you are depriving the brain of what it needs."

Some studies suggest that vegetarian diets are associated with higher depression scores and increased risk of depressive symptoms, while other studies indicate no significant association.

References 99-101.

Insulin resistance in puberty and pregnancy

"increasing the risk of cancer"

A systematic review and meta-analysis of observational studies found increased risks for pancreas, liver, kidney, stomach, and respiratory cancers in insulin users compared to non-users (102).

"in pregnancy, insulin is playing a role in growing the placenta"

Reference 103.

"She also needs to become a little insulin resistant to give a little more glucose to her baby"

Insulin resistance in pregnancy helps transfer glucose from the mother to the fetus, supporting proper fetal development. However, excessive insulin resistance can result in gestational diabetes, increasing the risk of fetal overgrowth and other pregnancy complications.

References 104, 105.

"the offspring of mothers who have gestational diabetes are significantly more likely to gain weight and be chubbier or fatter than their counterparts and to later develop Type Two Diabetes (...) these infants have a 40% higher chance to be obese and have metabolic convocation in their teenage years and beyond"

Reference 106.

Breast cancer

"One, although people might not appreciate this, is that one of the best ways for a woman to reduce her risk of breast cancer is actually having babies. It's very well known, very well documented, that if a woman has a fan has babies and breastfeeds, her risk of breast cancer goes down"

Reference 107.

Birth control

"This is very well known that estrogens can drive breast cancer, so women who use birth control will also have a higher risk of cancer"

Reference 108.

"research says that birth control pills that contain both estrogen and progesterone have been linked to a small increase in breast cancer risk, though the absolute risk is still relatively low and typically falls back to average within a decade of stopping. One key study that was done in 2017 was a meta analysis in the New England Journal of Medicine, which found that women using hormonal contraception had a slightly higher risk of breast cancer compared to non users."

References 109-113.

Cancer, insulin and pregnancy

"you take a breast tissue that is tumor tissue and compare it to like if you take a breast tumor and compare it to the normal tissue right next to it like that, it would have shared its origins with the cancer from the breast. Will have seven times more insulin receptors than the normal breast tissue"

Reference 114.

"high insulin is promoting fat cells getting bigger, that high insulin is also accelerating the growth of the tumor cells (...) the main one of the main mutations in breast cancer is a seven fold, so a seven times increase in the number of insulin receptors, and insulin wants to tell things to grow."

References 115, 116.

"earlier pregnancies typically reduce lifetime breast cancer risk, whereas having a first child later can slightly increase it."

References 117, 118.

Alzheimer's disease

"people with Alzheimer's disease almost always have some detectable instance of insulin resistance, if not full on diabetes, type two diabetes"

Insulin resistance, a hallmark of type 2 diabetes, has been increasingly linked to Alzheimer's disease pathogenesis. Research suggests that over 80% of AD patients have diabetes or abnormal glucose levels, indicating overlapping mechanisms (119).

"Depression has a brain glucose hypo metabolism to it. Migraines have a brain glucose hypo metabolism. Epilepsy and Parkinson's disease. So all of these disorders of the brain, of the central nervous system, the one thing they all have in common is the brain isn't getting enough energy from glucose."

Glucose hypometabolism is a characteristic of various neurological conditions, including Alzheimer's disease, Parkinson's disease, epilepsy, traumatic brain injury, and schizophrenia (120).

"another way of saying that is the one thing all of those seemingly unrelated brain problems have in common is that they all have some degree of insulin resistance, but then it's no surprise that they all benefit when ketones can swoop in to save the day."

References 121-124.

Loneliness and mortality

"Loneliness is a greater contributor to death than cigarette smoking, and it's not even close."

Contrary to some media reports, a study comparing social isolation, loneliness, and smoking found that poor social integration was less strongly associated with total mortality than cigarette smoking (125).

Worms longevity with restricted glucose intake

"What she found, I think it was worms. She found in worms that if they restricted the glucose that the worms were eating, they would live 50% longer, or some, some fantastic increase in the how long the animals lived."

The study found that adding glucose decreased life span by about 20% (126).

Autophagy and longevity

"autophagy equating to longevity? I don't disagree with that. I think that probably is a very valid view."

Autophagy seems to play a crucial role in promoting longevity by maintaining cellular homeostasis, reducing cellular damage, and supporting tissue health.

References 127-131.

Ketogenic diet and longevity

"They could let the animals eat as much as they wanted, but it was a ketogenic diet they lived significantly longer than their other litter mates that were eating the normal, high carb Chow, similar to what humans eat nowadays"

An unrestricted ketogenic diet may extend longevity and improve healthspan in mice (132, 133).

Cholesterol and longevity

"they found that they also the longest lived people had high cholesterol levels."

Higher cholesterol levels may be linked to greater longevity in older adults, though this relationship is complex and influenced by individual health factors and genetic predispositions.

References 134-137.

Cholesterol and sex hormones

"Mitochondria, for example, mitochondria have to have a cholesterol molecule in them in order to work like the very powerhouse of the cell, and the more you lower cholesterol through, say, drug interventions, the more you compromise the mitochondria, the sex hormones. All sex hormones are built on cholesterol. It's no surprise, if someone takes a cholesterol lowering medication, their sex hormones go down."

Mitochondria require cholesterol for functions such as steroid hormone synthesis and membrane maintenance, but excessive mitochondrial cholesterol can impair mitochondrial function and contribute to disease pathology.

References 138-140.

Cholesterol-lowering medications and libido

Cholesterol-lowering medications, particularly statins, may decrease libido by lowering testosterone levels, although some studies indicate that they can improve erectile function in men with hypercholesterolemia.

References 141, 142.

LDL and infections

"LDL actually helps the body fight infections, so it's also an unsung hero of immunity"

LDL may play a role in binding and neutralizing certain bacterial toxins and pathogens, potentially providing some protective effects against infections, although its role is less clear and less studied compared to HDL.

References 143, 144.

Smoking and insulin resistance

"so they found that if you took healthy, non smoking people and had them start smoking, they became insulin resistant."

Smoking, including exposure to environmental tobacco smoke, is associated with increased insulin resistance, which can be partially reversed by smoking cessation.

References 145, 146.

Exposure to diesel exhaust gas

"You published a study in 2024 which found that exposure to diesel exhaust gas. Yes, associated with increased fat mass."

"the animals that were exposed to the diesel exhaust particulates had fatter fat cells and more insulin resistance than the animals that had just been breathing normal room air"

Reference 147.

Air pollution and diabetes

"you look in areas where they have higher pollution levels, where the particulates are higher in the atmosphere, and those same areas are always fatter and more diabetic"

References 148, 149.

Liposuction

"And so it's no surprise that over the ensuing years after she's had liposuction, not only does she not experience any improvement in any health marker, nothing gets better with regards to her health."

Liposuction can lead to improvements in insulin sensitivity and reductions in fasting insulin levels, glucose, and triglycerides, while also being metabolically safe.

References 150-154.

Ketosis and Alzheimer's disease

Ketogenic diets and ketone supplementation may improve cognitive function and provide neuroprotective effects in Alzheimer's disease by offering an alternative energy source, enhancing mitochondrial function, and reducing neuroinflammation and oxidative stress.

References 155-158.

Ketosis and metabolic rate

"So ketones will increase metabolic rate of fat tissue."

Ketones enhance mitochondrial respiration in fat tissue without increasing ATP production, which may help explain the rise in metabolic rate (159).

Ketosis and muscle injury

"ketones actually make muscle more resistant to injury"

Ketones may improve exercise performance and recovery, but current research does not specifically conclude that they make muscles more resistant to injury.

References 160-163.

Ketone drinks

Reference 164.

Ketones and cognition

"The animals that had the ketogenic diet were much faster at remembering which shape they'd gone to for whatever the treat or reward might have been. So there these are, it's easy to do. The nice thing about animals is that they're all genetically identical, which wipes out some of these confusing variables in humans. I'm unaware of any evidence that takes a human gives them a shot of ketone and measures their cognitive performance before and after. The only evidence at the moment is people with cognitive decline. Where you take someone who obviously is not thinking as well as they were, give them ketone, and now they are thinking better. That's that's published. So multiple case reports. So you take someone whose cognition is compromised, give them ketones, and then their cognition improves."

Ketones, particularly from medium-chain triglycerides and ketogenic diets, may improve cognitive function in individuals with mild cognitive impairment and Alzheimer's disease (166-168).

Ketones and oxidative stress

Research suggests that ketones can reduce oxidative stress by enhancing antioxidant defenses, modulating gene expression, and inhibiting oxidative stress pathways. However, there is also some evidence indicating ketones might increase oxidative stress.

References 169-172.

Ketogenic diet and microbiome

"There's no evidence to support that there's any harmful change in the microbiome"

Some studies suggest that a ketogenic diet affects the gut microbiome by decreasing beneficial bacteria like Bifidobacteria and increasing potentially harmful ones like Proteobacteria. However, other research indicates it may not significantly alter overall microbial diversity but can still influence specific bacterial populations and inflammation.

References 173-178.

Gut microbiome and overall health

"People, dieticians, will say, well, a diverse microbiome is a good microbiome. Well, prove it. How do we know that? How can you prove that?"

An imbalanced gut microbiome, or dysbiosis, is associated with various health issues, including metabolic and cardiovascular diseases, gastrointestinal disorders, immune dysfunction, inflammation, and neurodegenerative conditions.

References 179-183.

Ketogenic diet and diabetes

"if someone has type two diabetes, if they adopt a ketogenic diet, they will be off all of their diabetes medications in months, all of them"

Low-carb and ketogenic diets can support the management of type 2 diabetes and obesity, but their long-term effectiveness, safety, and sustainability remain uncertain.

References 184, 185.

Ketogenic diet and epilepsy

"same with epilepsy, that many forms of epilepsy, so depending on the person, they would benefit from being in ketosis forever"

The ketogenic diet has been shown to be an effective treatment for drug-resistant epilepsy, especially in children, by reducing seizure frequency. However, more research is needed to assess its effectiveness in adults.

References 186-188.

Sweeteners

"So like diet drinks, not the zero drinks, but the diet drinks will have aspartame as the sweetener. Is there a difference? There is a difference, and I'll get to that other one in a moment, because that should be having diet. Well, I personally go to diet rather than zero, but that's because aspartame is the soul sweetener in the zero in the diet, rather, and it has no effect on insulin. So too, erythritol, sorry, erythritol is a little right around aspartame is generally a good one, but monk fruit extract, stevia, and especially allulose, those are inert when it comes to insulin. You know, allulose stevia, monk fruit extract, aspartame, no effect. Erythritol, no effect. But erythritol, that ending O L is reflective of a class of sweetener called the sugar alcohol."

References 189-191.

Salt, insulin resistance and high blood pressure

"salt is not a key contributor to blood pressure. It's actually insulin resistance. Insulin resistance will force the body to hold on to salt. Insulin resistance will force the blood vessels to be very constricted, all of which play together to make for a very high blood pressure."

Research suggests that high salt intake is a key contributor to increased blood pressure and cardiovascular disease risk. Salt affects multiple organ systems beyond blood pressure, including the heart, kidneys, and brain.

References 192-195.

"the main contributor to high blood pressure is insulin resistance,"

Insulin resistance is linked to high blood pressure through mechanisms like sodium retention, increased sympathetic nervous system activity, and altered glucose metabolism (198, 199).

Cardiovascular aerobic fitness, muscle mass and longevity

"if you look at longevity and look at the markers of muscle strength versus the markers of cardiovascular aerobic fitness, the aerobic fitness markers are terrible predictors of longevity."

- Markers of cardiovascular aerobic fitness, such as VO2 max and cardiorespiratory fitness, are predictors of longevity and cardiovascular health, with higher levels associated with reduced risk of cardiovascular disease and mortality (200, 201).
- Greater muscle mass is associated with lower mortality and improved longevity (202)

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