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Independent Research & further reading

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Contents

What is a Heart Attack?

> *"Most people don't understand what a heart attack is (...) When you have a plaque, a plaque is a buildup of a little fibrous material inside the artery, and that doesn't cause a heart attack. A heart attack is caused when one of those plaques cracks (...) patient may complain of chest discomfort or he may not complain of chest discomfort because remember, when you have a blockage like this, only 20% of the patients actually get chest pain (...) the plaque that come that cracks off and when it cracks open the blood that's going past it sees the crack and wants to repair it and forms a blood clot on it. So the final thing that shuts down that artery is a blood clot."*

Plaque rupture is widely recognized as the main cause of heart attacks, responsible for the majority of acute coronary syndromes. When the fibrous cap of an atherosclerotic plaque breaks, the lipid-rich core is exposed to the bloodstream, triggering the rapid formation of a blood clot that can block a coronary artery and cut off blood supply to the heart muscle. Ruptured plaques typically have a thin, inflamed cap and a large necrotic core, often infiltrated by immune cells, making them highly unstable. Studies estimate that around three-quarters of acute coronary events arise from this process, while others result from plaque erosion or alternative mechanisms. Risk factors such as high cholesterol, hypertension, and systemic inflammation increase the likelihood of rupture.

Prevalence of Chest Pain

Chest pain is the predominant symptom of heart attacks, reported in approximately 85–93% of patients. Large-scale studies consistently show it as the most common presenting complaint, although its absence is more likely among women, older adults, and people with diabetes. Patients with type 2 myocardial infarction also present less frequently with chest pain compared to those with type 1. Importantly, the minority who do not experience chest pain—around 7–13% of cases—often face delayed diagnosis and poorer outcomes.

References 1-4.

Blood Clotting Disorders

> *"We have more coagulation issues today than we ever did before, which means our blood, because of inflammation, is more ready to clot more easily."*

There is no strong evidence that coagulation disorders or clotting-related events are becoming more common in the general population. The prevalence of inherited conditions such as hemophilia and von Willebrand disease remains stable, though advances in diagnostic methods may increase reported cases. Increases in clotting complications have been observed in specific contexts, such as among patients with severe COVID-19, where thrombotic events contributed to a large proportion of deaths, and in rare instances following certain vaccinations or cancer immunotherapies. Higher rates of clotting are also seen in special populations, including individuals with thalassemia or liver disease. These trends, however, reflect particular circumstances rather than a broad population-wide rise in coagulation disorders.

Inflammation as a Key Driver

Systemic inflammation is a well-established driver of increased blood clotting. Inflammatory cytokines such as IL-1β and IL-6 activate platelets and change red blood cell structure, producing denser and more abnormal clots. Inflammation also induces tissue factor on immune and endothelial cells, which triggers the coagulation cascade, while simultaneously suppressing natural anticoagulant pathways and impairing the body's ability to break down clots. This prothrombotic state, often termed thromboinflammation, has been demonstrated in both experimental models and clinical settings, contributing to conditions such as sepsis, cardiovascular disease, and disseminated intravascular coagulation. Chronic inflammatory diseases, including diabetes and atherosclerosis, likewise sustain a hypercoagulable state and heighten thrombotic risk.

References 5-8.

Metabolic Dysregulation and Vascular Risk

“He was not a diabetic, but he was a pre-diabetic. That means he had a lot of insulin (...) Now insulin is a very atherogenic molecule. It causes smooth muscle proliferation. Smooth muscle is in the walls of the arteries. It causes vasoconstriction, it makes your blood more clotty, and it causes inflammation (...)

When you consume sugar or glucose, the body has to get rid of that glucose very quickly from the bloodstream because glucose actually is toxic inside the bloodstream (...) It glycates all the blood vessels and the walls and the components in blood and the hemoglobin as well. Glycates it, that means a glucose attaches itself to that molecule. So now that molecule can't work properly. That is why the higher your blood glucose, all your chemicals don't work well. Your enzymes don't work well, your hormones don't work well, nothing works well and your age prematurely because you're getting glycation (...)”

Hyperinsulinemia (high insulin) is widely recognized as atherogenic, with strong epidemiological and experimental evidence linking elevated insulin levels to the development and progression of atherosclerosis (a condition in which fatty deposits, cholesterol, and other substances build up inside the arteries, causing them to harden and narrow, restricting blood flow). High insulin impairs endothelial function by reducing nitric oxide signaling, increasing oxidative stress, and upregulating adhesion molecules that drive vascular inflammation. It also promotes the migration and proliferation of vascular smooth muscle cells, a key factor in plaque growth and arterial wall thickening. Additional mechanisms include stimulation of pro-inflammatory cytokines, alteration of lipid metabolism toward a more atherogenic profile, and reduced fibrinolysis, which favors clot persistence.

Glucose Toxicity and Systemic Organ Damage

High concentrations of glucose in the bloodstream are toxic, leading to widespread cellular and organ damage. Chronic hyperglycemia increases oxidative stress, disrupts metabolic pathways, and activates processes that generate advanced glycation end-products, all of which impair normal cellular function. Sustained exposure damages tissues such as the heart, kidneys, eyes, and nerves, and also weakens immune defenses, raising susceptibility to infection. At the same time, high glucose impairs pancreatic β-cell function and worsens insulin resistance, reinforcing the metabolic imbalance. These mechanisms explain why both acute spikes and prolonged elevations in blood

glucose are associated with life-threatening complications and chronic diseases, underscoring the importance of tight glycemic control.

Glycation and Protein Dysfunction

Glycation is a non-enzymatic process in which glucose and other reducing sugars bind to proteins, lipids, or nucleic acids, forming advanced glycation end products over time. Unlike normal enzymatic glycosylation, glycation is damaging, as it alters the structure of proteins and diminishes their function. This modification can impair enzymatic activity, reduce the effectiveness of hormones, and disrupt essential molecular interactions. For example, glycation of insulin decreases its ability to bind to receptors and activate signaling, contributing to insulin resistance, while glycation of other proteins promotes misfolding, aggregation, and cellular toxicity.

References 9-15.

Insulin Resistance and Its Complications

> *"If I'm eating every three hours and I'm consuming glucose (...) I'm stimulating my pancreas. I'm stimulating my insulin. My insulin goes up, it comes down. But before it even gets a chance to come down, it goes up again. So the repeated consumption of and frequent consumption of glucose, it's causing my insulin to stay up (...) Now what happens is that, you continue this lifestyle for a few years, now the body, because these are hormones, will say, well, you know, I'm gonna need to make more insulin. Now you become insulin resistant. Any hormone that stays in your body for a long time, the body becomes immune to it. So the next time I eat the sugar, I'm gonna have to make more insulin to produce the same effect that is called insulin resistance (...)"*

Frequent consumption of glucose-rich foods keeps insulin levels repeatedly elevated, which over time contributes to insulin resistance. Persistently high glucose triggers oxidative stress, disrupts key metabolic pathways, and impairs insulin secretion, creating a cycle that drives further dysfunction. Insulin resistance arises when cells become less responsive to the hormone after prolonged exposure, requiring higher levels of insulin to achieve the same effect. This state is central to the development of type 2 diabetes and is linked to complications including cardiovascular

disease, kidney damage, neuropathy, and retinopathy. Chronic hyperglycemia also damages pancreatic β-cells, reducing their ability to produce insulin and worsening the condition.

References 16-19.

Insulin, Fat Storage, and Metabolic Disease

> *"insulin pushes glucose into the liver and you develop a fatty liver. It pushes the calories into production of new fats around your viscera. The viscera means in your belly, around your pancreas. You get visceral fat (...)*
>
> *Today, at least 25% of the population now have a fatty liver (...)*
>
> *That is why fasting benefits you so much, 'cause it gets rid of that worst [visceral] fat."*

Insulin and Fatty Liver Development

Insulin plays a central role in the development of fatty liver by promoting the conversion of glucose into fat within the liver. When glycogen stores are full, insulin drives de novo lipogenesis, converting excess glucose into fatty acids that are assembled into triglycerides and stored in liver tissue. Persistent high insulin levels and excessive carbohydrate intake amplify this process, particularly in the context of insulin resistance. In non-alcoholic fatty liver disease, insulin's fat-promoting action remains active or exaggerated, while its ability to suppress glucose production is impaired, leading to both hepatic fat accumulation and elevated blood sugar. This selective resistance helps explain why NAFLD is highly prevalent among individuals with type 2 diabetes and other insulin-resistant states.

Visceral Fat as a Preferred Storage Depot

Insulin actively promotes fat storage in visceral adipose tissue, including around abdominal organs such as the pancreas. By stimulating glucose uptake into adipocytes and driving its conversion into fatty acids, insulin encourages triglyceride accumulation within these depots. Visceral fat is particularly sensitive to insulin, with studies showing stronger and faster activation of insulin signaling compared to subcutaneous fat, making it a preferred site for storage. Insulin also supports the formation of new fat cells in visceral regions, further expanding capacity. Accumulation of

visceral fat is closely tied to metabolic disturbances, including insulin resistance, type 2 diabetes, and cardiovascular disease, highlighting the clinical importance of insulin's depot-specific effects.

Global Prevalence of Fatty Liver Disease

Fatty liver disease affects roughly one in three adults worldwide, with current prevalence estimates around 30–32%. Rates are higher in men than in women and are rising globally, having increased from about 22% in the early 1990s to over 37% by 2019. Prevalence also varies by region, exceeding 40% in the Americas and South-East Asia but remaining lower in Africa. The condition is especially common in high-risk groups, affecting more than half of individuals with obesity and nearly two-thirds of those with type 2 diabetes.

Fasting as a Strategy to Reduce Visceral Fat

Fasting has been shown to effectively reduce visceral fat, with evidence from both human and animal studies. Intermittent fasting and time-restricted eating protocols consistently lower visceral fat area in overweight and obese individuals, often alongside improvements in metabolic health markers. Prolonged fasting under medical supervision also leads to disproportionately greater reductions in visceral fat compared to total body fat. Mechanistic studies indicate that fasting preferentially mobilizes energy from visceral fat depots, a process that becomes more pronounced with longer fasting periods and when combined with exercise. These findings support fasting as a targeted approach for reducing metabolically harmful fat stores.

References 20-31.

Coronary Artery Disease Preceding Diabetes Diagnosis

> *"By the time you are diagnosed as having diabetes, you already have coronary artery disease."*

Coronary artery disease often develops before diabetes is formally diagnosed. Imaging studies show that adults with newly detected diabetes have roughly double the prevalence of coronary disease compared to non-diabetic individuals, even when no symptoms are present. Many patients exhibit silent or subclinical atherosclerosis that becomes apparent only once diabetes is identified. This reflects the underlying pathophysiology: insulin resistance and metabolic syndrome,

which precede type 2 diabetes, accelerate the development of atherosclerosis and coronary stenosis. As a result, significant coronary artery disease is frequently present by the time diabetes is first diagnosed, underscoring the importance of early cardiovascular risk assessment in at-risk populations.

References 32-35.

Ketones as an Alternative Energy Source

> *"ketones are an energy molecule produced by the liver (...) So because of fasting, your insulin levels are really low now, okay, 'cause you've been fasting, right? So now the fats start dissolving. So you get free fatty acids. The free fatty acids float into the bloodstream. Free fatty acids are fat products. They float into the bloodstream, they go to your liver. Your liver converts those into ketones. Now ketones are an energy source of the body, an alternative source to glucose (...)*
>
> *ketones are actually a cleaner fuel for the body. And in terms of producing reactive oxygen species in the metabolism, the way your mitochondria work, you actually produce less reactive oxygen species, which is damaging to your physiology when you're in ketones. And ketones are signaling molecules that also change your physiology in a number of ways. Number one, it causes the production of brain derived neurotropic factor."*

Ketones are energy molecules produced by the liver from fatty acids during fasting and act as an essential alternative to glucose. When insulin levels fall and glucagon rises, fat stores are mobilized, releasing free fatty acids into the bloodstream. In the liver, these fatty acids are broken down into acetyl-CoA, which is then converted into ketone bodies—acetoacetate, β-hydroxybutyrate, and acetone. These ketones circulate to organs such as the brain, heart, and muscles, supplying energy when carbohydrate availability is low. During prolonged fasting, they can provide more than half of the brain's energy needs, underscoring their central role in maintaining energy balance under low-glucose conditions.

Evidence suggests that ketones may act as a cleaner fuel than glucose by reducing the production of reactive oxygen species (ROS) during mitochondrial energy generation. While glucose metabolism can drive higher electron flow into the respiratory chain and favor ROS formation at key

sites, ketone bodies such as β-hydroxybutyrate enter the metabolic pathway in ways that may bypass these major ROS-generating steps. This difference can lessen electron leakage and reduce oxidative stress, offering a potential advantage for cellular health. Although more direct comparative studies are needed, current findings support the view that ketone metabolism is associated with lower ROS output than glucose oxidation.

References 36-42.

Stem Cells

> *So stem cells are, we all have stem cells and we all still make stem cells and they're produced by the bone marrow. These are pluripotent cells, cells made that will then go out and become whatever they need to become. So they can go out into your circulation, become a muscle cell, they can become a retinal cell, a skin cell. They can transform into anything (...)*
>
> *I'm particularly interested in the stem cells because of a thing called (...) Endothelial progenitor cells. Progenitor cells are, you see, you are always hurting your blood vessels. The lining of the blood vessels and the lining of your blood vessels have to be constantly repaired and they are repaired by the progenitor cells. When you do intermittent fasting and time-restricted feeding, you will produce more."*

Pluripotent vs. Multipotent Stem Cells

Pluripotent stem cells can become any cell type in the body, while multipotent stem cells are limited to specific lineages. Pluripotent stem cells can differentiate into cells from all three embryonic germ layers—ectoderm, mesoderm, and endoderm—meaning they can give rise to any cell type in the body except extraembryonic tissues (like the placenta). Multipotent stem cells can differentiate into multiple, but limited, cell types—usually restricted to a particular tissue, organ, or germ layer. For example, hematopoietic stem cells (HSCs) can become various blood cells, and mesenchymal stem cells (MSCs) can become bone, cartilage, or fat cells, but not neurons or liver cells.

Stem Cell Populations in Bone Marrow

Stem cells produced by adult bone marrow are predominantly multipotent rather than pluripotent. The main populations are hematopoietic stem cells, which generate all blood cell types,

and mesenchymal stem cells, which give rise to tissues such as bone, cartilage, and fat. While several rare populations of pluripotent-like cells have been identified in bone marrow—such as very small embryonic-like cells, multipotent adult progenitor cells, and MUSE cells—these are uncommon, and their true pluripotency and physiological relevance remain debated.

Role of Endothelial Progenitor Cells in Vascular Repair

Endothelial progenitor cells (EPCs) are stem-like cells found in bone marrow, blood, and vessel walls that play an important role in repairing damaged blood vessels. They can differentiate into endothelial cells, the lining of blood vessels, and directly incorporate into injured areas to support re-endothelialization. In addition, EPCs release growth factors, cytokines, and other signaling molecules that stimulate local endothelial repair and new vessel formation. Through both direct and paracrine mechanisms, EPCs help maintain vascular integrity, and their abundance and functional state are considered markers of vascular health.

Fasting and Endothelial Progenitor Cells

Fasting has been shown to increase both the number and functional capacity of endothelial progenitor cells. Human studies report that intermittent fasting raises circulating stem and progenitor cells with EPC markers, while short-term fasting interventions in overweight and obese adults improve endothelial function and EPC activity. These benefits appear to be mediated by enhanced autophagy, a cellular repair process, and by improvements in glucose metabolism, both of which support vascular regeneration.

References 43-48.

Benefits of Fasting on Immune Function

> *"we know that fasting also boosts your immunity. People who fast get less infections get less sore throats and coughs and colds, and the viruses that are going around the immunity is better."*

Fasting can enhance aspects of immune function, particularly within the innate immune system. Short-term fasting increases neutrophil and natural killer cell activity, boosts autophagy, and

reduces inflammatory cytokines such as IL-6 and TNF-α. These effects contribute to lower systemic inflammation and improved cellular repair. At the same time, fasting alters adaptive immunity by reducing circulating T cells and shifting lymphocyte populations, which may represent a temporary redistribution of immune resources. While this can prime cells for rapid activation upon refeeding, it may also transiently suppress certain adaptive responses. Overall, intermittent and short-term fasting regimens tend to strengthen innate immunity and reduce inflammation, though effects vary with fasting type, duration, and individual health.

References 49-53.

Fasting and Growth Hormone

> *"You make more growth hormone in fasting (...) the best way to actually increase your growth hormone production is to do intermittent fasting."*

Intermittent fasting reliably increases growth hormone production, with marked effects even after short fasting periods. A single 24-hour fast can raise circulating growth hormone levels by five- to fourteen-fold, independent of weight loss, and prolonged fasting further amplifies secretion by increasing both pulse frequency and overall concentrations. These hormonal shifts help preserve lean mass, stimulate protein synthesis, and promote fat breakdown, supporting the body's adaptation to food scarcity. While the magnitude of the effect varies by baseline hormone status and fasting length, evidence from both human and animal studies confirms fasting as a potent stimulus for growth hormone release.

References 54-57.

Sugar Addiction

> *"addiction is a real thing. So when you consume carbs and you consume sugar, you will go through withdrawal and this withdrawal will only last for a week or so. And then after that, it's gonna get better."*

Animal studies consistently show that sugar can induce addiction-like behaviors, including bingeing, craving, tolerance, and withdrawal, with neurochemical changes similar to those seen in drug dependence. In humans, however, the evidence is more limited and inconsistent. Some studies report withdrawal-like symptoms—such as headaches, cravings, and reduced well-being—during sugar reduction or cessation, particularly in adolescents and in certain clinical groups, but these findings are not universal. More often, addictive-like eating in humans is linked to highly processed foods that combine both sugar and fat rather than sugar alone. Overall, while sugar may produce dependence-like effects in specific contexts, the concept of sugar addiction in humans remains debated and requires further study.

References 58-62.

Gut Microbes as a Source of Essential Micronutrients

> *"There's a symbiotic relationship between the gut and you. They produce micronutrients which get absorbed into your bloodstream (...)*

Gut microbes play a symbiotic role in human health by producing essential micronutrients that the body can absorb. Bacterial species in the large intestine synthesize vitamins such as B1, B2, B6, folate, B12, and vitamin K, which enter the bloodstream through specialized transporters in the colon. These microbial contributions can provide a substantial share of daily vitamin requirements and support key processes including DNA synthesis, energy metabolism, immune regulation, and blood clotting. The extent of this benefit depends on microbiome composition and diet, and disruptions in the gut community can impair micronutrient availability with consequences for metabolic, neurological, and cardiovascular health.

References 63-68.

Calcium, Vitamins, and Cardiovascular Health

> *“calcium supplements actually increase the risk of cardiovascular events (...) I stop all calcium supplements on all my cardiac patients and I tell them, you should take vitamin D3 so you'll absorb calcium better into your gut and you take vitamin K2 because vitamin K2 is gonna make sure that you don't get the calcium buildup in the wrong places in your vasculature (...)*
>
> *If your coronary calcium score is zero, you have no calcium, then you are in a good place. If you have coronary calcium, you need to go see a good cardiologist that's gonna do a prevention program because it means you already have atherosclerosis.”*

Calcium Supplements and Cardiovascular Risk

Calcium supplements have been linked to a modestly increased risk of cardiovascular events, particularly myocardial infarction, in several large randomized trials and meta-analyses. Reported risk increases range from about 15–30%, with the effect most consistently observed in older adults and postmenopausal women. By contrast, calcium obtained through diet does not show this association and may even be protective, suggesting an important distinction between supplemental and dietary sources. While some studies report no significant risk, the overall evidence indicates that calcium supplementation, unlike dietary calcium, may carry cardiovascular hazards and should be used with caution.

Vitamin D and Enhanced Calcium Absorption

Vitamin D plays a crucial role in enhancing calcium absorption in the gut. Its active form, calcitriol, activates vitamin D receptors in intestinal cells and increases the production of calcium transport proteins such as TRPV6 and calbindin, which shuttle calcium across the intestinal lining. Human and animal studies show that without sufficient vitamin D, calcium absorption falls sharply, leading to bone disorders such as rickets and osteomalacia, while supplementation restores uptake and supports bone health. Clinical trials confirm that maintaining adequate vitamin D status significantly improves intestinal calcium absorption, particularly in older adults and postmenopausal women.

Vitamin K2 and Vascular Calcification

Vitamin K2 has well-established biological mechanisms that could reduce vascular calcification by activating proteins such as matrix Gla protein (MGP, a vitamin K–dependent protein that inhibits vascular calcification, preventing calcium deposition in blood vessel walls). Animal and cell studies consistently support this protective role, showing that vitamin K2 supplementation can limit calcification. In humans, however, clinical trial evidence is less clear. While supplementation lowers biomarkers of calcification risk, most randomized trials have not shown a significant reduction in vascular calcification progression over one to two years. Some subgroup findings and meta-analyses suggest a possible slowing effect, but results remain inconsistent and modest. Overall, vitamin K2 may support bone and vascular health, yet its capacity to redirect calcium from arteries to bone in clinical practice has not been conclusively demonstrated.

Coronary Artery Calcium Score as a Risk Marker

A coronary artery calcium (CAC) score is a powerful marker of cardiovascular risk. A score of zero indicates no detectable calcified atherosclerosis and is associated with very low risk of heart attack or related events in the short to medium term, a finding often described as the “power of zero.” By contrast, any CAC score above zero signals the presence of coronary atherosclerosis, even if still subclinical. Individuals with detectable calcium face a several-fold higher risk of future cardiovascular events, and risk rises progressively with higher scores. For this reason, a positive CAC score typically warrants preventive strategies and ongoing cardiovascular monitoring.

References 69-79.

Warfarin (Coumadin) Use and Coronary Artery Calcification

> *“If you're taking Coumadin, Coumadin is a type of blood thinner that lowers your vitamin K1 levels and it'll also lower K2 (...) So you will get increased coronary calcification (...) So patients who are taking warfarin for example, or Coumadin, have been shown to have increased coronary calcification…”*

Warfarin (Coumadin) use is strongly associated with increased coronary artery calcification, supported by both imaging studies in humans and mechanistic evidence. Observational research shows that patients on warfarin experience greater progression of coronary calcium compared to non-users, with some studies suggesting a dose- and duration-dependent effect. The mechanism is

well established: warfarin inhibits vitamin K–dependent proteins such as matrix Gla protein, which normally prevents calcium from depositing in arterial walls. Animal studies confirm this pro-calcific effect, and comparisons with direct oral anticoagulants show that the association is specific to vitamin K antagonism. While a few cross-sectional human studies report no significant link, the bulk of evidence indicates that long-term warfarin therapy increases vascular calcification risk.

References 80-81.

Dietary Fiber and the Growth of Beneficial Gut Bacteria

> *"Lots of fiber because the fiber is gonna be eaten by your bacteria and you're gonna get a wide variety of good bacteria eating fiber"*

Dietary fiber serves as a key substrate for gut microbes and reliably promotes the growth of beneficial bacterial groups such as Bifidobacterium and Lactobacillus. This effect is most pronounced with soluble and prebiotic fibers like inulin, fructo-oligosaccharides, and galacto-oligosaccharides, which are efficiently fermented in the colon. The resulting increase in these bacteria supports gut health not only directly but also through the production of short-chain fatty acids such as butyrate, which have systemic anti-inflammatory and metabolic benefits. While responses vary depending on individual microbiome composition and habitual fiber intake, the overall evidence strongly supports fiber's role in fostering beneficial bacteria.

References 82-85.

Fermented Foods as Sources of Probiotics and Postbiotics

> *"fermented foods will give you not only the bacteria themselves (...) but they also have the postbiotics."*

Fermented foods can provide both live microbes and microbial byproducts, though the balance depends on the product and how it is processed. Foods like yogurt, kefir, kimchi, and sauerkraut often contain live bacteria and yeasts that may function as probiotics when present in

sufficient amounts, but pasteurization or heat treatment can eliminate these organisms. Regardless of viability, all fermented foods contain postbiotics—bioactive compounds generated during fermentation such as short-chain fatty acids, enzymes, and cell wall fragments—that can contribute to health. Thus, while not every fermented food guarantees live probiotics, all deliver postbiotic products of microbial activity.

References 86-88.

Sleep Deprivation, Gut Dysbiosis, and Metabolic Dysfunction

> *"lack of sleep causes a change in your gut microbiome (...)*
>
> *One night of bad sleep, you become insulin resistant the next day."*

Disruption of the Gut Microbiome

Sleep deprivation disrupts the gut microbiome, though the extent differs between animal and human studies. In animal models, both acute and chronic sleep loss consistently reduce microbial diversity and shift the balance toward pro-inflammatory bacterial families, changes that are linked to increased gut permeability, inflammation, and metabolic dysfunction. Human studies show subtler effects, such as increases in the Firmicutes-to-Bacteroidetes ratio (two dominant bacterial phyla in the gut) and shifts in bacteria associated with metabolic health, though findings are sometimes inconsistent and vary by individual. Overall, the evidence supports that poor sleep promotes dysbiosis (an imbalance or disruption in the composition and function of the body's microbial communities, often in the gut, which can impair health and contribute to disease), which may in turn contribute to inflammation, impaired metabolism, and neuropsychiatric vulnerability through gut–brain axis pathways.

Acute Effects on Insulin Sensitivity

Even a single night of sleep deprivation is enough to impair insulin sensitivity in healthy individuals. Controlled studies show that one night of total or partial sleep loss reduces glucose disposal and increases endogenous glucose production, indicating both peripheral and hepatic insulin resistance. The effect is substantial, with insulin sensitivity dropping by 16–25%—a degree of

impairment comparable to several nights of restricted sleep or even to metabolic effects seen after high-fat diets. Mechanistically, sleep loss elevates plasma free fatty acids and other metabolites that interfere with insulin signaling.

References 89-96.

Mold Toxicity

> *"almost 70% of homes these days have some form of mold toxicity in them (...)*
>
> *we know that it [mold] causes a systemic inflammatory reaction in the body (...)*
>
> *There's a condition called fungal sinusitis. Again, it comes down to mold (...)"*

Mould and dampness are common issues in residential housing worldwide, with prevalence estimates ranging from 10–50% in affluent countries. In Australia, one in three houses are affected, while international figures report 35% of homes in New Zealand, 16.5% with dampness indicators across Europe, and up to 47% in the United States. A large survey in the UK found damp in 23.3% of households and visible mould growth in 45.9%, with clear associations between mould exposure and adverse health symptoms, particularly in children.

Household Mold Exposure and Inflammation

Household mold exposure is a well-recognized driver of inflammation in humans, particularly through effects on the respiratory system and immune activation. Mold spores and fragments can trigger the release of inflammatory cytokines such as IL-6 and TNF-α (signaling proteins that drive immune responses), while certain species also produce mycotoxins that contribute to immune dysregulation. Human studies show that individuals living in mold-contaminated homes often display elevated inflammatory markers in blood, alongside respiratory symptoms and impaired lung function. Early-life exposure can shape immune responsiveness into later childhood, and genetic susceptibility may heighten risk. Overall, evidence from both experimental and clinical studies confirms that household mold promotes inflammation and can exacerbate conditions such as asthma and hypersensitivity pneumonitis.

Fungal Sinusitis

Fungal sinusitis refers to a group of sinus disorders caused by fungi, ranging from relatively mild allergic reactions to severe, invasive infections. It is broadly divided into **invasive forms**, where fungi penetrate sinus tissues (seen especially in immunocompromised patients, such as those with uncontrolled diabetes or undergoing cancer treatment), and **noninvasive forms**, where fungi remain in the sinus cavity without tissue invasion. Noninvasive types include fungus balls (dense clumps of fungal growth) and allergic fungal sinusitis, which involves an exaggerated immune reaction often linked to asthma or allergies. The most common culprits are environmental molds such as Aspergillus. Symptoms can vary widely, from nasal congestion and sinus pressure to life-threatening complications like bone destruction or spread to the brain in invasive disease. Diagnosis typically relies on imaging, tissue examination, and fungal cultures.

References 97-106.

Soaking Rice Reduces Arsenic Levels

> *"first and foremost soak your rice in water and then discard the water after an overnight soak because it contains arsenic in it…"*

Soaking rice in water before cooking can reduce its arsenic content, though the degree of reduction depends on conditions such as soaking time, temperature, and rice type. Standard overnight soaking typically lowers arsenic by 20–40%, with greater reductions—sometimes up to 80%—achieved when soaking is done at higher temperatures or with additives like citric acid or salt. Both white and brown rice benefit, though brown rice retains more arsenic overall. Importantly, the soaking water should be arsenic-free, since contaminated water can raise rather than lower levels. While soaking improves safety by reducing arsenic, it can also leach out some beneficial nutrients, including potassium, selenium, and B vitamins.

References 107-112.

Overcooking, Advanced Glycation End Products, and Health Risks

> *"when you're blackening your food and over blackening your food, it's called advanced glycation end products. So when you over burn your food, when you overcook your food, you're creating these molecules, now you're consuming these molecules and they've been shown to cause a radical increase in the inflammation in your body"*

Overcooking food, particularly through high-temperature dry-heat methods such as frying, grilling, roasting, or baking, substantially increases the formation of advanced glycation end products (AGEs). These molecules are produced through the Maillard reaction, in which proteins and sugars react under heat, and their levels rise markedly with prolonged or intense cooking, especially in foods rich in protein and fat. Comparative analyses show that fried, grilled, and baked foods contain the highest concentrations of AGEs, whereas gentler methods such as boiling or steaming result in significantly lower levels. Diets dominated by heavily processed or overcooked foods therefore contribute to greater AGE exposure, which is associated with adverse metabolic and inflammatory effects. Selecting cooking methods that use lower temperatures or shorter durations can reduce AGE formation and its potential health risks.

References 113-118.

Fruit Consumption and Cardiometabolic Health

> *"So our overconsumption of fruit is another factor that is contributing to coronary artery disease and diabetes and fatty liver (...)"*

High fruit consumption is not associated with an increased risk of cardiometabolic diseases; instead, it is consistently linked to protective effects. Large cohort studies and meta-analyses show that higher fruit intake lowers the risk of cardiovascular disease, improves blood glucose control, and supports healthier lipid profiles. Regular consumption is also associated with reductions in waist circumference, fasting glucose, LDL cholesterol, and triglycerides, with some evidence of modest blood pressure benefits. These effects are observed across diverse populations, including individuals with obesity and metabolic syndrome. The quality and diversity of fruit intake appear especially important, with studies finding the greatest protection when a wide variety of fruits are consumed.

While 100% fruit juice and dried fruits can be included in moderation, excessive intake may diminish benefits due to higher sugar and lower fiber content. Overall, evidence strongly indicates that high fruit consumption reduces, rather than increases, the risk of cardiometabolic disease..

References 119-122.

Dental Hygiene and Cardiovascular Health

> *"These unequivocal data to show that if you have bad teeth, bad dental, hygiene, bad bacteria in your mouth, you're gonna get valvular disease such as aortic stenosis, premature calcification of your aortic valve, and you're gonna get coronary calcification. That's been proven unequivocally."*

Poor dental hygiene is strongly associated with an increased risk of cardiovascular and valvular diseases, including atherosclerosis, heart failure, and stroke. Large cohort studies and systematic reviews demonstrate that conditions such as periodontal disease, tooth loss, and infrequent tooth brushing significantly elevate the likelihood of major cardiovascular events, even when controlling for other risk factors. The mechanisms are well understood: chronic oral inflammation and transient bacteremia (the presence of bacteria in the blood) promote systemic inflammation, endothelial dysfunction, and arterial plaque formation, while oral pathogens can also contribute directly to valvular injury and endocarditis. Importantly, interventional evidence indicates that regular tooth brushing, dental visits, and periodontal therapy reduce cardiovascular risk markers and event rates, underscoring the causal relevance of oral health in systemic disease.

References 123-127.

The Vagus Nerve, Gut–Brain Communication, and Inflammation

> *"Your gut health is so important that the body has dedicated a huge nerve called the vagus nerve just to take care of your gut (...) When you fix the gut, your vagus nerve will be able to work more efficiently…"*

The vagus nerve plays a central role in maintaining gut health, serving as the primary neural pathway in the gut–brain axis. Around 80% of its fibers transmit signals from the gut to the brain (afferent), while the remaining 20% carry signals from the brain to the gut (efferent). Through this bidirectional communication, the vagus nerve regulates gut motility, secretion, and nutrient absorption, while also exerting powerful anti-inflammatory effects via the cholinergic anti-inflammatory pathway, which suppresses the release of pro-inflammatory cytokines such as TNF-α (tumor necrosis factor-alpha). It also interacts with the gut microbiota by sensing microbial metabolites and gut hormones, thereby influencing microbiota composition, intestinal permeability, and systemic homeostasis. Clinically, low vagal tone has been linked to worse outcomes in inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS), and vagus nerve stimulation (VNS) is being investigated as a therapeutic strategy to reduce gut inflammation. Stress can impair vagal activity, worsening both gut function and inflammation, while a healthy vagal response supports not only digestive health but also metabolic balance, appetite regulation, and even mood.

References 128-130.

LDL Cholesterol and Longevity: Age-Dependent and Contextual Effects

> *"The most recent data (...) shows that patients who have the highest LDLs actually make it into the nineties and live a healthier life. It's not the LDL, it's the damaged LDL that's the problem."*

Research on LDL cholesterol and longevity shows a complex, age-dependent relationship. In older adults, particularly those over 60, several large cohort studies have found that higher LDL cholesterol levels are often associated with lower all-cause mortality or no increase in mortality compared with lower LDL levels. This inverse association is especially notable among the "oldest old" (80+), where higher LDL has been linked to reduced risk of death. One possible explanation is LDL's role in immune defense, which may help protect against infections and other non-cardiovascular causes of death.

However, lifelong genetic evidence tells a different story: Mendelian randomization studies consistently show that individuals with genetically lower LDL cholesterol—through variants in genes such as LDLR or PCSK9—tend to live longer, primarily due to reduced cardiovascular disease risk. Importantly, very high LDL cholesterol (≥190 mg/dL) remains a strong predictor of cardiovascular events and mortality, even in elderly populations. Taken together, the evidence suggests that while

moderately higher LDL may not be harmful—and may even appear protective in older adults—maintaining an intermediate range is optimal for longevity, with both very high and very low levels linked to increased risk depending on cause of death.

References 131-135.

Statins: Potential Adverse Effects

> *"For the most part, [statins] are [safe], but at least 20 to 30% of patients will suffer from sarcopenia (…) many of them also do develop mental diseases (...) Also, they can cause liver dysfunction, so you need to watch that."*

Muscle Loss (Sarcopenia)

Research indicates that statins are not consistently associated with muscle loss, or sarcopenia (age-related loss of muscle mass and strength), in the general population. Large-scale, long-term studies in middle-aged and older adults have generally found no increased risk of sarcopenia, reduced muscle strength, or impaired physical performance among statin users. Genetic studies using Mendelian randomization (a method that uses genetic variants to test causal relationships) also show no evidence that statins cause muscle loss, pointing instead to age as the primary factor. However, findings in specific groups are more mixed. Some research has reported weaker grip strength and reduced muscle-related quality of life among older statin users, while other studies suggest potential benefits—such as a lower likelihood of sarcopenia in patients with heart failure, possibly due to improved vascular function. Importantly, risk may vary by statin type, dosage, and individual health status. Overall, most evidence does not support a direct link between statins and sarcopenia, though careful monitoring of muscle health remains advisable in vulnerable patients.

Psychiatric Illness

Current evidence indicates that statin use is not associated with an increased risk of psychiatric illness, and may in fact be linked to a reduced risk of depression in some populations. Large cohort studies and meta-analyses, including analyses of millions of participants, consistently show no significant association between statins and conditions such as depression, anxiety, or suicidality. Some findings even suggest that statin users experience lower rates of depression and

anxiety, particularly in those with cardiovascular disease. While rare adverse psychiatric reactions—such as insomnia, nightmares, or mood changes—have been reported, these events are uncommon and typically reversible. Overall, statins have a favorable psychiatric safety profile, with possible protective effects against certain mood disorders in specific groups.

Liver Dysfunction

Contrary to earlier concerns, statin use is not associated with liver dysfunction and is instead linked to improved liver outcomes in both the general population and those with chronic liver disease. Large-scale studies involving millions of participants demonstrate that regular statin use lowers the risk of developing new liver disease, reduces liver-related mortality, and decreases the incidence of hepatocellular carcinoma (HCC). In patients with chronic liver disease, statins are associated with slower fibrosis progression, reduced risk of hepatic decompensation, and greater likelihood of fibrosis regression. Among individuals with non-alcoholic fatty liver disease (NAFLD), statins are considered safe, do not raise liver enzyme levels, and may even reduce markers of liver inflammation such as ALT. Although rare cases of liver injury have been reported, these events are extremely uncommon and do not outweigh the clear protective benefits of statins for liver health.

References 136-145.

Depression and Inflammation

> *"Depression is not something psychological (...) that very symptom of depression is a symptom of your inflammation."*

Depression is not solely caused by inflammation, but inflammatory processes play a significant role in the development and persistence of the disorder for a subset of individuals. Elevated inflammatory markers such as CRP (C-reactive protein), IL-6 (interleukin-6), and TNF-α (tumor necrosis factor-alpha) are found in roughly 25–50% of patients with depression, and inflammation can predict the onset of depressive symptoms. The relationship is bidirectional: inflammation can increase depressive risk, while depression itself can promote inflammatory responses. Importantly, inflammation is most strongly linked to specific symptoms such as fatigue, sleep disturbances, appetite changes, and anhedonia. Experimental evidence shows that inducing inflammation, for example through cytokine therapy, can trigger depressive symptoms, and some

patients respond to anti-inflammatory treatments. These findings support the existence of an “inflammatory depression” subtype, but overall, depression remains a multifactorial condition influenced by diverse biological, psychological, and social pathways.

References 146-151.

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