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Food Sensitivity Solutions: Restore Oral Tolerance So You Can Eat More Foods

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CHAPTER 1

Are you sensitive to multiple foods and not getting better? Here’s why

If you’re managing your autoimmune disease, chronic health disorder, or brain health, then you’re probably familiar with the autoimmune paleo (AIP) diet, also known as the leaky gut diet or autoimmune paleo protocol. Prior to its rebranding online, functional medicine practitioners called it the “elimination/provocation diet,” which I introduced in 2010 in my thyroid book as one tool to better manage Hashimoto’s hypothyroidism.

The diet has helped many people understand which foods trigger inflammatory or autoimmune reactions in them. Many people follow a customized version of the diet to successfully manage their condition. Some people, however, follow it religiously and do not experience sustainable improvement. In fact, they may develop sensitivities to new foods and even see their symptoms worsen.

This can be caused by loss of oral tolerance, the term researchers use to explain the immune system’s ability to appropriately tolerate foods while protecting the body from bacteria and other harmful compounds.

There are other types of tolerance. Chemical tolerance is the ability to appropriately tolerate the many chemicals in our environment without an immune reaction. Loss of chemical tolerance means a person reacts to a chemical or heavy metal the way they might react to gluten or dairy.

Self-tolerance is the immune system’s ability to respond appropriately to the body. Loss of self-tolerance leads to autoimmune disease, in which the immune system erroneously attacks and destroys healthy body tissue. A popular example of this is Hashimoto’s hypothyroidism.

When you lose one type of tolerance you’re likely to lose other types of tolerance as they have similar underlying mechanisms. Loss of tolerance is an exploding problem affecting an increasing number of people.

Does this mean you should abandon the AIP diet if you are just starting out on your health journey? No, identifying inflammatory triggers is still a vital introduction to managing autoimmunity.

The AIP diet was always meant as one of many functional medicine tools, not as a solitary approach to a complex health condition. If your health is not improving after removing inflammatory foods from your diet, that means you need to look for other factors.

Also, it is common in our busy lives to eat the same foods over and over, which can promote loss of oral tolerance. To maximize the potential of the AIP diet, it’s important to regularly vary the foods you eat and focus primarily on fresh produce.

In this article and in my online oral tolerance course, I will explain current understanding of what causes loss of oral tolerance and how to improve it.
Leaky gut repair as part of a larger oral tolerance protocol

One of my primary goals with the oral tolerance protocol is to show you how a one-size-fits-all approach to leaky gut doesn’t consider why a person gets leaky gut. This is why many people who follow the AIP diet for long periods of time either do not get better or may even get worse. The AIP diet is designed as an anti-inflammatory short-term introduction so you can determine which areas of your diet need adjusting.

This article does not get into the specifics of leaky gut — please refer to my books Why Do I Still Have Thyroid Symptoms? and Why Isn’t My Brain Working? and articles on DrKNews.com for more information on diet, lab tests, and protocols for addressing leaky gut.

A reminder about cross-reactive foods, such as gluten and dairy

It’s often necessary to eliminate certain foods from your diet, particularly gluten and dairy, that cross-react with tissue in the body. The proteins in these foods not only trigger an immune reaction to the food, but also to a specific tissue in the body. For instance, gluten cross reacts with neurological tissue in some people, thyroid tissue in others, and so on. Eating gluten will cause the body to attack those tissues in the body. Cross-reactivity also applies to other types of food proteins, such as dairy.

You can learn more about cross reactivity here or in my brain book, Why Isn’t My Brain Working?

However, with loss of oral tolerance you may develop food sensitivities to foods that are not cross-reactive. Improving your oral tolerance may help you reintroduce these foods to your diet.

Don’t forget about gut autoimmunity

Another thing important to consider is whether you have gut autoimmunity — an autoimmune condition attacking tissue in your digestive tract. Gut autoimmunity can produce a wide variety of symptoms and digestive disorders that may be beyond the scope of leaky gut or oral tolerance protocols alone. When symptoms are very stubborn or irresolvable, gut autoimmunity is something to consider.
Understanding what causes loss of oral tolerance and what to do about it

Understanding the immune system mechanisms behind loss of oral tolerance and multiple food sensitivities will help alleviate the mystery and frustration many people experience. Please keep in mind that functional medicine is about translating new research into evolving clinical protocols but does not offer cures, magic supplements, or guarantees. Human physiology is complex, highly individualized, and affected by many factors, some of which we are still learning about or don’t even know yet.

Dendritic cells: Key players in loss of oral tolerance

Dendritic cells are immune cells that roam the small intestine. They have long arms that sample different proteins and determine whether the immune system should react to them.

A key component of loss of oral tolerance and multiple food sensitivities is over reactive dendritic cells. They think practically everything they encounter needs to be attacked.

What causes dendritic cells to become overly reactive? Proteins that aren’t thoroughly digested due to deficiencies in stomach acid and pancreatic enzymes is one cause. Low SIgA cells, antibodies that are a first line of defense in the gut, are another. We can address hyper reactive dendritic cells by improving breakdown of proteins and increasing SIgA levels.

Over reactive dendritic cells: Improve breakdown of proteins

Many people digest foods poorly for a variety of reasons, including aging, poor brain function, poor diet, and more. You need sufficient hydrochloric acid and enzyme activity to break down the proteins as soon as possible so they don’t provide target sites for antibodies.

Supplement with hydrochloric acid. Hydrochloric acid (HCl) is the stomach acid vital for digestion of proteins. People with low HCl typically complain of not feeling well after eating meats. Supplementing with HCl when you eat meats will help break down the proteins better.

Supplement with digestive enzymes. Proteins are made up of chains of amino acids, the building blocks of protein. Enzymes are necessary to break apart these chains of amino acids so the dendritic cells don’t become overwhelmed by proteins that are not completely digested. Effective digestive enzymes include pepsin, bromelain, proteases, and more. Look for a high-quality, broad-spectrum digestive enzyme supplement.

Supplement with DPP-IV enzymes: Gluten and dairy intolerance is common among those with loss of oral tolerance. DPP-IV enzymes will help break down gluten and dairy proteins should your food be contaminated (they are not, however, able to neutralize the effects of purposely eating gluten and dairy).

Supplement with flavonoids. Certain flavonoids, which are beneficial plant compounds, have been shown to help block the immune response from dendritic cells. They include quercetin, luteolin, apigenin, and lycopene.

Avoid artificial food colorings. Artificial food colorings have been shown to bind to proteins, thus preventing their breakdown. Avoid artificial food coloring for this reason.

Over reactive dendritic cells: Boost SIgA levels

SIgA are antibodies in the lining of the small intestine that attach to a protein to tag it as a hostile invader, which alerts other cells in the immune system to remove it. They can prevent an immune response by surrounding immune reactive proteins before the dendritic cells attach to them.

This keeps the dendritic cells from becoming over active due to constant bombardment.

Low SIgA levels are common with adrenal fatigue, chronic infection, hydrocortisone or other steroid medications, or vitamin A deficiency.

Ways to boost low SIgA include addressing the underlying cause. This is not a quick and easy fix but it’s important. Do you have adrenal fatigue? Are you battling a chronic viral, bacterial, or fungal infection? Are you taking hydrocortisone or other steroid medication? Look for factors that may be chronically taxing your immune system.

Another strategy is to take Vitamin A. Vitamin A helps boost SIgA levels. Recommended dose is 5000 IU a day. Please note, this is retinol vitamin A and not beta carotene.
Regulatory T cells — key players in oral tolerance

Regulatory T cells (T reg cells) decide whether the immune system needs to mount an inflammatory response to a protein the dendritic cells have transported to the lymphatic system. Because the lymphatic system travels throughout the body, this inflammatory immune response can cause inflammation anywhere in the body.

Fortunately, we can profoundly influence T reg cell function to prevent inflammation include:

- **Glutathione**: Glutathione recycling; s-acetylglutathione; reduced glutathione; oral and topical liposomal glutathione; and glutathione nebulizer, IV, or suppository.
- **Vitamin D**
- **Omega-3 fatty acids**: A healthy balance of omega-3 and omega-6 essential fatty acids is necessary for healthy T reg cell function. Most people get too much omega 6 oils through processed foods. A healthy dietary intake of omega-3 is 3500 mg for a person eating 2,000 calories per day. In addition to dietary sources, fish, emu, and algae oil are supplement sources of omega-3.
- **Short chain fatty acids (SCFA)**: SCFA supplementation is good for those whose produce consumption is limited due to SIBO or other digestive factors. You may also want to supplement for additional benefit.
- **Endorphins** (from exercise, laughter, positive relationships, volunteering, etc.) are a way to dampen inflammation and modulate the immune system.

Liver function plays a key role in oral tolerance

The dendritic cells also carry proteins to the liver. There, “Kupffer cells” can trigger inflammation if the liver is toxic or has poor detoxification function. For some people, managing loss of oral tolerance depends on supporting liver function and detoxification. Supporting liver detoxification pathways may help reduce inflammation. I talk more about how to do this in my brain book and thyroid book, or you can read more here.

Diversity of gut flora essential to healthy oral tolerance

One of the pitfalls of going on a very limited diet is you lose your diversity of gut bacteria. Research has shown a rich diversity of gut bacteria is essential to maintaining oral tolerance. Eat a diet that consists primarily of vegetables and vary the vegetables you eat; just don’t eat vegetables you noticeably react to. A diverse array of fruit is important, too, but be careful you don’t spike your blood sugar with too much fruit or overly sweet fruits.

An ample amount of diverse produce daily increases the diversity and amount of gut bacteria, which in turn produce short chain fatty acids (SCFA). SCFAs help regulate T cells (T reg cells) to dampen inflammation.
Lesser known inflammatory triggers to watch out for

In addition to an anti-inflammatory diet, it’s important to also be aware of lesser known sources of inflammation.

For instance, excess salt has been found to be an inflammatory trigger in those with autoimmunity. Westerners eat about twice the recommended amount of sodium of 2300 mg, the equivalent to one teaspoon.

Those who have **low blood pressure** may consume extra salt in order to raise blood pressure. In this case, trial and error may be necessary to see what works. Glycyrrhiza, a compound in licorice root, may also be effective in raising blood pressure.

Another potential inflammatory trigger is **BPA**, or **bisphenol A**, a chemical most commonly found in plastics, fire retardants in furniture and sleepwear, store receipts, and many other products. BPA has been shown to cause loss of tolerance in infants and have a huge impact in general on immune tolerance. Minimize your exposure as much as possible.

Tame histamine reactions to improve oral tolerance

It’s not uncommon for people who have lost oral tolerance to dietary proteins to experience **histamine reactions**.

Symptoms of a histamine reaction can vary but some of the more common include:

- Sinus issues and congestion
- Seasonal allergies
- Asthma
- Redness and inflammation of the skin
- Hives
- Migraines
- Joint pain
- Emotional instability
- Anxiety
- Irritability

Histamine reactions occur when antibodies that tag a protein as immune reactive also activate mast cells, the immune cells that release histamine.

Foods that commonly trigger a histamine response include aged and fermented foods, smoked foods, fish, and seafood (especially canned). Natural compounds that calm a histamine reaction include quercetin, butterbur, stinging nettle, and mangosteen.
CHAPTER 3  
Lab testing for loss of oral tolerance

Food sensitivity testing can help you in your quest to restore oral tolerance.

I use food immune reactivity testing from Cyrex Labs as these tests are extremely sensitive and consistent. They also test foods in the state they are normally consumed, such as raw versus cooked. This is because proteins change from raw to cooked state and you may react to a food in its cooked state but not its raw state. For instance, sensitivity to bacon increases ten times when it is cooked versus raw.

Also, some people react to foods when they are eaten together but not individually. The Cyrex Labs Array 10 Multiple Food Immune Reactivity Screen tests for a few of these.

Cyrex Array 10 also tests things such as thickening gums and artificial food colorings.

I use this testing to determine which foods may need to be eliminated. I also retest to determine whether your oral tolerance protocol is working.

For example, if you tested positive to 120 out of 180 foods tested on the Cyrex Labs Array 10, this is a strong indication of loss of oral tolerance. However, I do not tell patients to remove all those foods from their diet.

Instead, remove the foods to which you clearly react and begin a protocol to restore oral tolerance. Then test again. If you see fewer foods come back positive for immune reactivity you know you’re on the right path with the protocol.

I usually don’t see patients entirely resolve their food sensitivities. Instead, we look for a trend toward improvement.

Please note: If you clearly have loss of oral tolerance but your test comes back with few to no positive markers for food sensitivities, you likely have a depressed immune system. In this case, you need to follow strategies to boost SIgA levels.

You can screen for low SIgA prior to your Cyrex test by ordering a total immunoglobulin (IgG, IgA, and IgM) test.
Other factors that contribute to loss of oral tolerance

Hormone imbalances and loss of oral tolerance

If a person follows the oral tolerance protocol and does everything right but still isn’t improving, one avenue to investigate is hormone function. Hormones impact inflammation and every step of the oral tolerance pathway. This includes not only the sex hormones, but also thyroid and stress hormones.

Good hormone function is necessary for the gut lining to regenerate, to keep inflammation in check, and to ensure the brain communicates properly with the gut.

Stress and loss of oral tolerance

Chronic stress is one of the most common causes of hormone imbalances. Increased production of the adrenal hormones cortisol and catecholamines suppresses SlgA cells and intestinal immunity, thus creating an environment for bacterial overgrowth and loss of oral tolerance.

When gut immunity is weak, yeast and bacteria flourish and gastric ulcers can develop. In addition to addressing the root causes of your stress, whether it’s unstable blood sugar or a toxic relationship, adrenal adaptogens and phosphatidylserine can help support you through stress.

Blood sugar imbalances and oral tolerance

Every time blood sugar goes too low or high, this causes a stress response that suppresses SlgA cells and promotes inflammation and leaky gut. For most Americans, this response happens throughout each day. Blood sugar instability is also a major cause of hormonal imbalances and myriad metabolic disorders.

If you ignore your blood sugar it will be difficult to restore oral tolerance. Blood sugar is a deal breaker.

For more advice on supporting low blood sugar through diet and lifestyle, see the blood sugar sections in my thyroid and brain books or on my site.

Thyroid hormones and oral tolerance

If you suffer from thyroid hormone deficiency, many health problems may arise, including loss of intestinal integrity, immune function, and oral tolerance.

Thyroid hormone consists of two primary components, T3 and T4. T3 the active portion of thyroid hormone and is vital for intestinal integrity and repair, and thus oral tolerance.

Unfortunately, many patients take medication that is T4 only because that is the health insurance model. It is believed the body converts enough T4 to T3.

However, chronic inflammation hinders conversion of T4 to T3. As a result, many thyroid patients end up deficient in T3 and suffer from continued inflammation, leaky gut, and loss of oral tolerance.

This explains why many people feel better on thyroid hormone replacement that includes T3.

A variety of nutritional compounds have been shown to help in the conversion of T4 to T3.

It can also be helpful to rub topical liposomal glutathione over the thyroid gland to reduce inflammation.

For more information about how to support your thyroid health, please refer to my book Why Do I Still Have Thyroid Symptoms?
Female hormones and oral tolerance

Hormones affect inflammation and oral tolerance because immune cells have receptors for hormones. This is why hormone fluctuations in women (PMS, perimenopause) can cause inflammation. Also women need sufficient estrogen to regenerate the gut lining, keep inflammation in check, and help the brain communicate with the gut.

It’s common to see women who struggle with hormone fluctuations also struggle with an inability to manage their immune function, tame inflammation, or improve oral tolerance. Estradiol, the most active form of estrogen, is vital to brain function in women, which is in turn necessary for good oral tolerance. Estradiol is also necessary for the lining of the small intestine to stay healthy and be able to regenerate and to keep inflammation in check.

The ability to break down and clear estrogens from the body is also important to oral tolerance. Estrogen not properly metabolized by the liver can turn into a more toxic and inflammatory form. You can read more about metabolizing estrogen here.

In fact, most women we see clinically do not have an estrogen deficiency but rather an excess of estrogen. Symptoms of excess estrogen include bloating, swelling, depression, weight gain, and mood changes. At the same time, phytoestrogens can impact the uptake of estrogen at estrogen receptor sites. Phytoestrogens are compounds that enhance or modulate estrogen receptors. A variety of botanical compounds can help sensitive receptor sites to estrogen, including black cohosh, dong quai, indole d-carbinol, genistein, and daidzein. (Note: Synthetic estrogens, such as in birth control pills, do not show up on lab tests. However, synthetic estrogens can bind to estrogen receptor sites so that a woman has symptoms of estrogen deficiency but a lab does not reflect true estrogen levels.)

Excess testosterone in women

The most common hormone imbalance in women is high testosterone. In fact, it is the number one reason for female hair loss. Excess testosterone is a result of insulin surges caused by eating too much sugar, too many carbohydrates, or overeating. These insulin surges up regulate an enzyme in the ovaries called 17‘20 lyase, which triggers testosterone production. The excess testosterone then promotes insulin resistance in a vicious cycle. This can play a significant role in loss of oral tolerance. To lower testosterone, you must support blood sugar stability by eating a diet that does not spike blood sugar and exercising regularly to make insulin receptors more sensitive.

Stress and hormonal imbalances in women

In menstruating women, the most common cause of hormonal imbalance is chronic stress. Chronic stress in women leads to pregnenolone steal. Pregnenolone is a hormone used to make several hormones, including estrogen, progesterone, and the stress hormone cortisol.

The body can make only so much pregnenolone. If stress is chronically high, it “steals” pregnenolone from the sex hormones to make enough cortisol to meet the ongoing stress demands. High cortisol degenerates the intestinal lining and suppresses immune SIgA cells, both of which contribute to the development of oral tolerance.

To balance hormones, address chronic mental and physiological stress (blood sugar and inflammation are the most common causes) and support stress handling through diet and lifestyle and with adrenal adaptogens and phosphatidylserine. However, if balanced hormone function does not return in perimenopausal or menopausal women, you may want to consider bioidentical hormone therapy with a qualified and experienced practitioner.
Male hormones and oral tolerance

When it comes to male hormone imbalances, the biggest battle is inflammation.

Testosterone is made by Leydig cells in the testes. Leydig cells are extremely sensitive to and destroyed by inflammation. The testes cannot grow new Leydig cells in an environment of chronic inflammation. Thus testosterone production gradually declines.

If a man receives testosterone hormone therapy while in an inflamed state, Leydig cell population goes down even more — the body does not make new cells if it senses there is plenty of testosterone in circulation. A man may feel better for a few weeks initially after hormone therapy begins, but as Leydig cell numbers continually decrease symptoms return.

Inflammation also increases estrogen in men by upregulating the aromatase enzyme. This not only gives men female characteristics of estrogen (male breasts, crying, hips), but it also further drives down testosterone. Men who use testosterone therapy may see their estrogen levels go up on blood tests due to this mechanism.

Aromatase is in body fat so overweight men may struggle with excess estrogen. Weight loss can release stored estrogen into the bloodstream, worsening symptoms of excess estrogen for a while. Fortunately, the botanical chrysin, delivered in a liposomal cream, can help dampen aromatase activity in men.

An aggressive anti-inflammatory diet and lifestyle approach is necessary for men struggling with inflammation-induced hormonal imbalances. High doses (several thousand milligrams) of emulsified turmeric and emulsified resveratrol can help combat this inflammation. Dose according to inflammation, not body weight, raising the dose gradually until you notice improvement.

Stress and male hormones

As with women, chronic stress from blood sugar imbalances, inflammation, and lifestyle can impact hormone balance in men. Diet, lifestyle, and nutritional therapy protocols can help manage this mechanism.

However, sometimes when the stress response is removed and the pathways are supported, balanced hormone function does not return and bioidentical hormone therapy may be warranted in older men.

Part I Conclusion

The beauty and the curse of functional medicine is that everything is intertwined with something else. The hard part is knowing where to begin. The good part is you can start feeling better across multiple fronts once you understand your underlying mechanisms.

The immune system is delicately balanced and impacted by everything the body encounters. Virtually all systems in our body play a major role in how well our gut, brain, and immune system function. Maybe you are one of the lucky ones who is constitutionally strong and notices significant relief from chronic sensitivities with a few basic changes.

Or perhaps you are one of the many for whom loss of oral tolerance is a red flag asking you to begin making some major shifts.

Addressing the root causes of our health disorders is never easy. Luckily, plenty of other people are on the same journey and there is amazing support online these days.

Though it’s a journey that requires more work and discipline than taking a prescription drug (and I’m not knocking prescription drugs, there are times they are necessary), many people are exponentially rewarded for their efforts in the way of more energy, better mood, and less suffering.
Oral tolerance Section II
The microbiome and short-chain fatty acids
CHAPTER 5
The Microbiome

In the first section I talked about why many people develop an increasing number of food sensitivities on restrictive healing diets and what to do about it. The primary cause is called loss of oral tolerance, and it essentially means your immune system has lost the ability to appropriately manage the food you eat. As a result, it starts reacting to everything.

In this section, I delve more deeply into some finer details of these concepts, giving you more information on the history and importance of the gut microbiome and the incredibly important role of short-chain fatty acids, or SCFAs. SCFAs are the most overlooked and under-utilized compounds in functional medicine today, and have profound impacts on your gut, immune, and brain health.

Penicillin’s discovery shoves gut microbiome research into the shadows

In 2005, the National Health Institute (NIH) created the $150 million Human Microbiome Project to better research the microbiome. It has been a boon to our discoveries about human health and how to better treat disease. However, as groundbreaking as this science has been, it is actually well behind the curve; the first major study on the human microbiome was conducted more than 100 years ago in the early 1900s. Back then, Russian microbiologist and deputy director of the Pasteur Institute Elie Metchnikoff showed that friendly gut bacteria and fermented foods were vital to good health. Although he received a Nobel Prize for his work, his microbiome work faded into obscurity and was completely eclipsed 20 years later by the discovery of penicillin. Anyone who has seen antibiotics knock out a dangerous infection knows penicillin was a revolutionary discovery. However, it also created a “kill everything” mentality in medicine without incorporating Metchnikoff’s vitally important findings about the influence of gut bacteria on health and immunity (Metchnikoff continued to drink sour milk daily and is now known as the “father of natural immunity”).

Although he received a Nobel Prize for his work, his microbiome work faded into obscurity and was completely eclipsed 20 years later by the discovery of penicillin. Anyone who has seen antibiotics knock out a dangerous infection knows penicillin was a revolutionary discovery. However, it also created a “kill everything” mentality in medicine without incorporating Metchnikoff’s vitally important findings about the influence of gut bacteria on health and immunity (Metchnikoff continued to drink sour milk daily and is now known as the “father of natural immunity”).

Now, thanks in part to antibiotic-resistant bacteria, we have come full circle to the gut microbiome and ground-breaking findings, such as the use of fecal transplants. Researchers have found fecal transplants from healthy donors can alter the gut bacteria in an infected person to eradicate antibiotic-resistant infection. That’s right — they take poop from a healthy person and use it to inoculate the gut of an infected person. It’s working so well the FDA has approved the procedure for certain strains of resistant bacteria. Imagine if we had just continued to follow Metchnikoff’s path in the first place.

Microbiome researchers are also learning what supplement marketers don’t want you to know, that there is no perfect probiotic. Several thousand species of bacteria have been identified so far, and it’s no longer appropriate to designate some as good and some as bad. It’s more complex than that and involves their relationship to one another, the person they inhabit, and the outside environment. The environment plays such an important role in the microbiome that scientists can tell a lot about a person simply by analyzing their gut bacteria, such as whether they were born by C-section or vaginally or where they live on the planet. In fact, researchers discovered people living in the United States have the least diverse gut bacteria of the populations studied, with microbiome diversity falling well below the second least diverse population.

Although we can alter our gut microbiome to affect our health, researchers theorize about one-third of the microbiome has a genetic link and is set for life. This may help explain why some people do everything right but constantly struggle with chronic health conditions, obesity, allergies, and immune imbalances. The good news is we can still have some influence on our gut microbiome health by making it more diverse. One of the key discoveries from the gut microbiome project is that lack of gut bacteria diversity is a primary factor in what makes people unhealthy. Poor diversity makes you more prone to chronic disease, while the more diverse your gut bacteria are the healthier you are. It impacts every facet of health.

As such, every field in medicine is researching the gut microbiome to improve health and reverse disease, with major studies being published on topics that have long since been understood in functional medicine, such as the concept of leaky gut and the importance of gut health to immune and brain health.
The gut microbiome is a dynamic organ that can change within three days

What are some factors that cause poor gut diversity? They include:

- Eating meat and dairy from animals raised on antibiotics
- Not eating enough produce
- Eating the same foods over and over, even if they are healthy foods
- Taking antibiotics
- Excessive alcohol consumption
- Pesticides and herbicides

The key to a healthy gut microbiome is to consume a diversity of produce and other whole plant products in your diet (eating a wide variety of animal products is not going to diversify the microbiome).

Researchers are beginning to refer to the microbiome as a dynamic organ that can change within three days and is more complex than the liver.

Jobs this microbiome “organ” performs include:

1. The gut microbiome makes nutrients. The gut microbiome makes 50 percent of vitamin K, as well as folate and most B vitamins. An unhealthy microbiome can explain why people take handfuls of supplements yet are still deficient in important vitamins. Our bodies are also very dependent on the fat-soluble forms of vitamin A, E, D, and K, all of which depend on a healthy gut microbiome.

2. The gut microbiome activates polyphenols, antioxidant plant compounds. These polyphenols depend on a healthy microbiome to be metabolized into a usable form. For instance, soy, gingens, and green tea extract all contain compounds that are active only when metabolized by the gut microbiome.

3. The gut microbiome regulates your metabolism and how you use calories and insulin. Researchers are finding obesity is linked to imbalanced gut microbiome profiles that may have started in infancy. Many obese research subjects have poor microbiome diversity while their lean counterparts show more diversity. This means the obese person’s gut will harvest more energy and store fat more easily from the same amount of calories a thin person eats. Microbiome research is going to profoundly impact how we treat diabetes and obesity in the future.

4. The gut microbiome influences immunity.

5. The gut microbiome influences brain health. Seniors that lack microbiome diversity are more susceptible to neurodegenerative diseases such as dementia and Alzheimer’s. The gut microbiome is also linked to mood and psychiatric disorders and other brain-based disorders.

Gut bacteria diversity starts before and during birth

It was once believed babies were born with a sterile gut that began to colonize with different bacteria in the vaginal canal during birth and then after from the environment. Now we know bacteria in the amniotic fluid begins to colonize the infant’s gut before it’s even born.

In fact, we can see this in premature infants, who show less gut bacteria diversity than full-term babies, and it’s possible survival rates are linked to this diversity. This also means that a woman’s microbiome will have a lifelong impact on the microbiome of her children. Whether a child is born vaginally or via C-section also creates lifelong microbiome signatures. A baby born vaginally will be inoculated with bacteria from the vaginal wall while a baby born via C-section gets its bacteria from skin.

This helps explain why babies born via C-section have microbiome signatures that predispose them to obesity. Some research also showed mice that were delivered via C-section and received their gut bacteria from skin contact were more depressed and anxious than mice delivered vaginally.

Additionally, breastfeeding makes a big difference in a baby’s gut microbiome health compared to formula feeding. You can see now why babies born via C-section and fed formula have a higher risk of obesity and other health issues. These children go on to be more susceptible to childhood illnesses such as chronic ear infections that require antibiotics, which only further reduce microbiome diversity and promotes obesity. In fact, research shows penicillin can induce obesity!

This isn’t to make you feel guilty if your child was delivered via C-section, but rather to give you information to better understand your health or your child and areas where extra support may be needed. It also will help you be realistic about your health outcomes. If you grew up with a severely compromised gut microbiome, your health journey may be about having more good days than bad days versus health perfection.

Also, it’s important to realize a microbiome issue doesn’t necessarily produce gut symptoms. Instead, symptoms could be chronic pain, fatigue, stubborn autoimmune symptoms, brain fog, mood disorders, memory loss, and more.
CHAPTER 6
The hidden treasure in microbiome diversity: Short-chain fatty acids (SCFAs)

Why is gut bacteria diversity so important? Because diverse and plentiful gut bacteria produce enzymes that in turn raise levels of short-chain fatty acids, powerful gut signaling compounds with far reaching effects on brain and other parts of the body. The three primary SCFAs critical to health are:

- Butyrate
- Propionate
- Acetate

Bacteria not only produce SCFAs, but also need SCFAs to produce more SCFAs in a mutually beneficial cycle. SCFAs also act as signaling molecules and bind to cell receptors, meaning they are critical for influencing many functions in the body.

In fact, SCFAs are the most under-utilized yet most effective way to deal with many gut, immune, and brain issues. I have been using them significantly more in my practice in the last two years and seeing improved results.

Low-calorie dieting paradigm woefully outdated — gut bacteria and SCFAs are key

SCFAs bind to receptors that control appetite and hunger, burn body fat more efficiently, and turn off insulin resistance. When microbiome diversity is poor and SCFAs are low, a person is likely to always have a large appetite, be prone to insulin resistance, and store fat better than they burn it. You can see why the “calories in, calories out” model is woefully outdated. If gut bacteria diversity is lost, the signaling properties of SCFAs are lost, and the result is an “obese microbiome.”

Scientists were able to demonstrate this in a study involving lean and obese subjects. Using fecal transplants, they inoculated the guts of obese men who had high blood pressure and high blood sugar with the gut bacteria from lean men. Within three weeks, 50 percent of the obese subjects experienced weight loss and improvement of the symptoms associated with high blood sugar.

The effects from a single treatment only lasted about three months, but it’s a breakthrough finding in the treatment of diabetes and obesity. It also provides additional insight into why the nation with the lowest diversity in the gut microbiome also has the highest rates of obesity.

This type of study was first performed in mice, in which obese mice were made lean and lean mice were made obese simply by inoculating them with each other’s gut bacteria.

A similar mechanism was also demonstrated in a study of healthy pregnant women. In the third trimester, the women were found to develop the microbiome of an obese person in order to harvest more energy for the pregnancy. Many female patients of mine have complained of being unable to lose the pregnancy weight after their second or later births and it’s worth exploring whether getting “stuck” in the pattern of an obese microbiome is a reason why.

With ample plant fiber and diversity of gut bacteria, insulin and appetite come under control and the body is able to burn calories more efficiently versus being more efficient at storing them. The possibilities of altering the gut microbiome as a treatment for diabetes and obesity has made diabetes researchers very excited these days.
Gut bacteria diversity and the brain

Another exciting area of research is the effect of gut bacteria on the brain, including on mood and personality. Researchers have been observing fascinating effects of gut bacteria on mice. For instance, researchers used brain scans to study brain development in normal mice and in germ-free mice with no gut bacteria. All the germ-free mice showed impaired brain development. Why? The gut microbiome acts as a signaling organ that influences cell migration, a necessary part of brain development, and brain derived neurotrophic factor (BDNF), which plays a role in learning and memory. In other words, a healthy and diverse microbiome is essential to brain development and health.

Given what we now know about the gut microbiome and the brain, it’s time to explore this connection in children, even starting in the womb. I look forward to research that may help us one day better treat children with autism, learning disorders, allergies, food and chemical sensitivities, asthma, skin disorders, and so on that have become so common today.

We also have to stop thinking of the brain and the gut as two separate entities because they are intimately connected. Anatomically, you can follow the path of the vagus nerve from the brainstem into the gut. The vagus nerve is the highway through which signals from hormones, neuropeptides, and bacteria travel back and forth between the gut and the brain. For instance, researchers have discovered that Parkinson’s may have its roots in unhealthy gut bacteria that trigger degeneration in the dopamine centers of the brain, thanks to communication via the vagus nerve. Just as we saw what happens to obese people and mice who received the gut bacteria from their lean counterparts, so can we see similar effects on mood and personality. A variety of studies have shown that gut bacteria can make timid mice courageous, aggressive mice calm, relaxed mice anxious and paranoid — and vice versa.

Imagine the implications for people struggling with anxiety because of their microbiome signature. This isn’t to say all cases of anxiety or other mood disorders are bacteria-based. After all, in the Dutch obesity study, only 50 percent of the obese, pre-diabetic subjects responded to inoculation with gut bacteria from lean subjects. We still need to learn why some subjects respond to bacterial inoculation and not others.

The three types of biotics

Most people are familiar with probiotics, the healthy bacteria we can take as supplements or have in our guts. Some may also be familiar with prebiotics, the plant fibers gut bacteria need as a fuel source.

A third type of biotic is postbiotics. These are the metabolites, or by products, created by bacteria when they digest prebiotics. Examples of postbiotics are SCFAs, perhaps the most influential postbiotic. Other postbiotics include lipopolysaccharides (LPS) — inflammatory compounds created by infectious bacteria. Postbiotics significantly influence brain function, both positively and negatively. Bacterial infection and inflammation in the gut causes inflammation in the brain, a leading cause of brain degeneration. In other words, fire in the gut means fire in the brain.

Unfortunately, we can’t feel inflammation in the brain as the brain doesn’t contain pain fibers. Instead, brain inflammation symptoms include brain fog, depression, anxiety, irritability, and memory loss. Although brain inflammation may cause loss of brain function, it won’t cause physical pain. (Headache pain is believed to happen when dilated blood vessels press on surrounding nerve fibers.)

Likewise, gut inflammation does not necessarily cause gut pain because the gut doesn’t have pain fibers. Abdominal pain happens when these nerve fibers on the outside of the gut walls are activated by distension. However, in most people gut inflammation and leaky gut don’t “hurt” in the gut, though they may cause many troubling symptoms or pain elsewhere in the body due to inflammatory compounds traveling from the gut into the bloodstream. Therefore, it’s important to be aware of symptoms of brain and gut inflammation since you won’t feel them the way you will feel inflammation in a joint. Inflammation makes its way into the brain not only through the vagus nerve but also through a leaky blood-brain barrier. The proteins that cause leaky gut also cause leaky brain, and if you have leaky gut you can be sure you also have leaky brain. You can measure LPS and protein antibodies that identify leaky gut and leaky blood-brain barrier through Cyrex Labs.

The microbiome and heart disease

When most people think of heart disease risk, they think of red meat and cholesterol. However, studies show your microbiome plays a role in heart disease risk. For instance, red meat promotes arterial plaque in some people but not others depending on their microbiome. For the high-risk groups, carnitine, an amino acid in meats, metabolizes into a compound that damages the vascular system. When researchers treated the at-risk group with antibiotics, they saw a drop in the carnitine metabolite that damaged blood vessels.

The same has been found with salt and high blood pressure. Some people’s microbiome makes them prone to high blood pressure from salt and, so far, researchers haven’t figured out a way to alter that. This kind of research gives us an idea of what a health checkup might look like in the future and how treatments and advice can be customized by assessing each person’s microbiome signature. It also will hopefully shift health care and popular culture away from shaming people for their health issues or weight.
CHAPTER 7
Improving your gut microbiome health and diversity

Although the science shows about one-third of our microbiome is set for life, the good news is we can still influence the other two-thirds with sometimes profound improvements in health and well being.

In my article on oral tolerance and in my oral tolerance program, I talk about the ways in which you can significantly improve your gut microbiome health. This will impact all facets of your health, including your ability to have fewer food sensitivities and tolerate more foods.

As I mentioned before, I also believe SCFAs are one of the most under-utilized nutritional compounds that can have a profound effect on your immune, brain, and gut health.

However, it’s not enough to simply take SCFA supplements. SCFAs need an environment rich in fiber from a diet that is predominantly plant-based. SCFAs help fuel the production of more SCFAs, so good health requires a symbiotic relationship between gut bacteria, a diet high in plant fiber, and SCFAs — this is an area where you can really influence your health on your own.

Also, while butyrate and the other SCFAs may be vital to a healthy gut microbiome, they do not fight off the bacterial and yeast infections in your gut, nor do they compensate for a diet high in sugars and junk foods that promotes an infectious environment. You will have to do the work toward that end yourself as well.

The importance of SCFAs for repairing leaky gut

SCFAs and butyrate in particular are vital to healthy gut function and repairing leaky gut:

**Sufficient butyrate and other SCFAs nourish the mucosal lining of the gut.** In fact, poor gut bacteria diversity is a factor in causing leaky gut in itself because your beneficial bacteria may feed on your mucosal lining to survive in the absence of sufficient plant fiber.

**Butyrate binds to proteins that promote blood flow to the gut.** In addition to oxygen, healthy blood flow to the gut also delivers nutrients and healing compounds and helps remove harmful compounds so the gut can function more efficiently.

**Butyrate helps dampen inflammation in the gut.** It does this by inhibiting inflammatory immune compounds and binding to regulatory T cells, activating them to dampen inflammation. In fact, SCFAs train T regulatory cells to fight autoimmunity in the brain and block the response that causes multiple sclerosis.

**Butyrate inhibits over active dendritic cells that lead to loss of oral tolerance.**

**Butyrate plays a role in the synthesis of tight junction proteins.** Tight junction proteins comprise the gut barrier, allowing in nutrients while keeping out undigested foods, bacteria, yeast, and other pathogens. Leaky gut happens when these tight junction proteins break down. In fact, butyrate is so essential to gut health that a butyrate deficiency is all that’s needed to acquire leaky gut absent of infections or inflammatory triggers. Research has shown the gut mucosa receding like a melting ice cap in the absence of sufficient butyrate.
SCFAs can mitigate the effects of antibiotics.

Supplementing with SCFAs

The best way to boost your supply of SCFAs is to eat an abundant and diverse array of produce. Switch it up regularly, explore the produce aisles, and shop in markets that carry produce you’re not accustomed to in order to surprise your gut with new plant fibers.

That said, you may benefit from supplementing with SCFAs as they will help your existing bacteria turn all that plant fiber into a bounty of SCFAs.

When you start taking a SCFA supplement, start with one capsule and work your way up. You can mix it in with food if you like; that’s an easy way to get it to children. If you are breastfeeding, your baby will get it from your breast milk. Some people even like to add them to an enema bag.

If you feel an energy boost from one capsule, that’s a sign your gut microbiome is in poor shape and your gut bacteria diversity and SCFAs need support. Work your way up to two capsules twice a day. Some people take more. It usually contains sodium, so make sure to drink plenty of water and not overdo it.

Another key nutrient to support boosting SCFA levels is glutathione. Glutathione is a master antioxidant and can dampen inflammation in the gut — gut inflammation is one of the primary factors inhibiting gut bacteria diversity so it’s important to dampen it.

I tell my patients to take their butyrate supplement with a mix of veggies (including a veggie smoothie you make in the blender — but watch your blood sugar and go easy on the fruit juice) and some high quality, absorbable glutathione, such as s-acetyl glutathione, oral liposomal glutathione, or a combination of the two.

You can also take glutathione precursors such as n-acetyl cysteine. Take glutathione or glutathione precursors several times a day and experiment with dosages to see what has an effect on dampening inflammation.

Conclusion

I realize the information surrounding the gut microbiome, SCFAs, and oral tolerance is vast, but hopefully it gives you new understanding into what the body desires for optimal gut, immune, and brain function.

What excites me most about this information is how far reaching the potential of these therapies is and the fact that the average person can make big changes on their own at home.

It’s important to remember many other factors can be at play in your health journey and that addressing gut microbiome and SCFAs isn’t meant as the single magic bullet. Chronic undiagnosed infections, inflammatory triggers, dietary issues, lifestyle or emotional stressors, anemia, autoimmunity, and brain function disorders are just a few of the issues that can play a role in your health.

However, I hope this information gives you another puzzle piece to fit into your overall health strategy.
Have autoimmunity? Reacting to multiple foods and chemicals?

Build a more resilient, less reactive immune system with Dr. Kharrazian’s 3D Immune Tolerance Program.

Videos Led by Dr. Datis Kharrazian

Workbooks

Microbiome Mashup Recipe Collection

Microbiome Diversity Diary

Oral Tolerance Recipe Guide

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Environmental Toxins Evaluation Guide

Oral Tolerance Supplement Recommendations

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