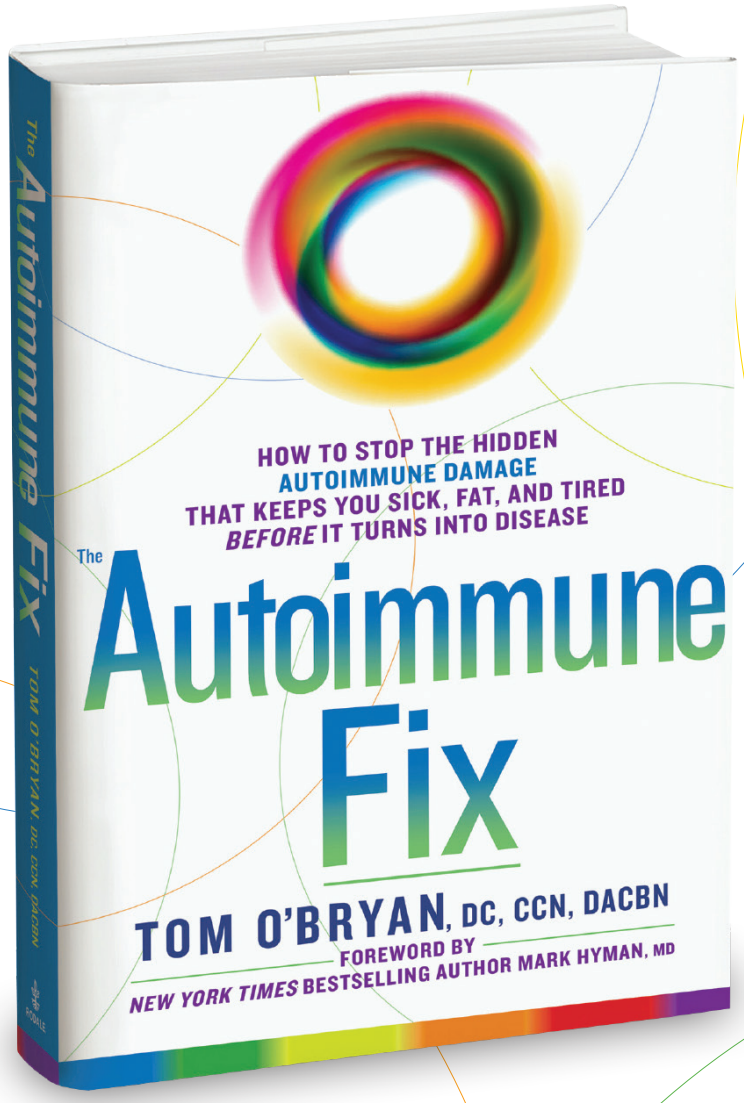


DR. O'BRYAN'S TIPS TO REBALANCE YOUR MICROBIOME

SNEAK PEAK FROM CHAPTER 3

THE ABSOLUTE NECESSITY OF A HEALTHY MICROBIOME

Imagine for a moment that you are a well-respected family physician. You've been practicing medicine long enough to have seen many of the youngsters you've stewarded through life grow up to be adults, and you have watched their parents age. You think you know all the ins and outs of the human body because you've treated every illness. Yet one day you attend a seminar for postgraduate education credits, and all of a sudden you're presented with startling new information: Researchers have just discovered a new organ in the human body, and it controls every aspect of your health.

This exact revelation is happening in medical offices across the country as scientists come to know more about the microbiome. The microbiome is the community of bacteria, yeasts, and viruses that live in the gut. In the last 10 years, it has begun to be recognized as an essential factor in overall health. Thanks to advances in science and technology, researchers have found that the microbiome is critical for more than digesting food: It is the control center for the entire body. As unbelievable as this statement sounds, that's the fact, Jack!

The microbiome is linked to manufacturing vitamins, regulating metabolism and blood sugar, and influencing both genetic expression and brain chemistry. For every message from the brain to the gut there are nine messages from the gut to the brain. These messages control the brain's response to stress, brain hormone production, the activation of the brain's own immune system, the growth of new brain cells (neurogenesis) and the adaptability of these new cells to learn (neuroplasticity), plus other functions.

The microbiome is the hottest topic in medical research today. In 2007, 396 new research papers were published on the subject. In 2015, that number was 5,512. That's 5,512 teams of researchers who spent months and months studying this topic, writing papers, submitting them for publication, and then being published. If you Google "microbiome" today, you'll see a listing of more than 19,000 recent studies, and each year brings new discoveries. For instance, we now know that we each are hosting a completely unique microbiome that comprises trillions of bacteria of several hundred species. The vast majority of microbes harbored in our intestinal tracts are thought to have beneficial effects, and while there are many different types of bacteria, they primarily fall into two big groups. The Bacteroidetes are supposed to be the dominant group that we host. The second group is the Firmicutes, and we're not as happy to have these as dominant houseguests. Individually, these Firmicutes bacteria aren't dangerous, but in high concentrations, they overwhelm the Bacteroidetes and take over, and the imbalance they create causes health problems—such as being a primary contributor to resistant obesity.

Your microbiome can weigh up to 5 pounds—nearly twice as much as the brain—and each bacterium it hosts is a living organism made up of cells and genes. Get this: There are between 100 to 150 times more genes found in your microbiome than the 23,000 genes found in your human DNA. Because of this, many experts have come to think of the microbiome as less like an

additional organ in the body and more like a whole other organism with a life of its own. It's a conversation that I often have with my colleagues after we've been teaching about autoimmunity. We start wondering, "Are we humans hosting a whole lot of bacteria, or are we bacteria having a human experience?" We appreciate that we are living with a parallel civilization inside of us, each assisting the other.

There are also 10 times more cells of bacteria in our gut than all the cells in the rest of the body put together. We know this because of the shape of our intestines. Remember, the intestines are a tube 20 to 25 feet long lined with microvilli, the shag carpeting that aids in digestion. If you could flatten out the microvilli, the surface of our intestines would be the size of a tennis court. We need that much surface in the gut because there's so much activity going on. And covering every inch of that surface are bacteria, packed in between each of the shags.

If you were born via natural childbirth, you inherited your microbiome from your mother. In the last month of pregnancy, the mother's body starts colonizing the vaginal tract with high concentrations of *Prevotella* bacteria, which covers the baby during childbirth. These bacteria carry a message down to the baby's gut, preparing it to create the digestive enzymes that break down breast milk and use it efficiently.

If you were born via a cesarean section, all bets are off. Instead of Mom's good *Prevotella* bacteria, you were instantly exposed to a plethora of foreign bacteria resting on Mom's skin and in the air of the delivery room, and you consequently have a higher risk of disease over the course of your life, and possibly a lower IQ.[1] In the most recent and largest study to date reviewing the birth information of 750,569 children born by C-section, children delivered by both acute (meaning "necessary for the baby and/or mother's health") and elective C-section had an increased risk of asthma, laryngitis, and gastroenteritis (inflammation of the intestines). Children delivered by acute C-section had an increased risk of ulcerative colitis and celiac disease, whereas children delivered by elective C-section had an increased risk of lower respiratory tract infection and juvenile idiopathic arthritis. The effect of elective cesareans was higher than the effect of acute cesareans on the risk of asthma.[2] I have met a number of ob-gyns who tell me that when they have to do a C-section, they will swab the mother's vaginal canal with something similar to a Q-tip and then rub the swab inside the newborn baby's mouth. They're trying to get some of the protective, instructional microbiota (like *Prevotella*) into the baby at birth any way they can.

Although there have been no long-term studies on this technique that I am aware of, it's rational to assume it does reduce the cesarean babies' future risk of numerous diseases, including autoimmune diseases. Of course, if a C-section is medically necessary, it is much more important to protect the baby's and the mother's lives than to worry about potential future health risks.

The microbiome is a primary component of the immune system in the gut. Seventy percent of our entire immune system resides in the gut, and the microbiome comprises the majority of that immune system. It's the modulator, or controller, of how the immune system in the gut operates. Just like a national guard is part of a police force yet works in its own unique way, the microbiome is a part of the immune system yet works in its own unique way.

Like the immune system, the microbiome is a collection of cells that function in unison with the gut immune cells that are designed to promote health, but when it becomes unbalanced, this can initiate disease.[3] We know that each of us has a unique microbiome that is influenced by genetics, our environment, and our dietary selections. There is a close relationship and an exchange of information between the gut bacteria and your immune cells sitting on that same gut wall. It is the initial part of your arsenal to control offending invaders.

Your antecedents—how you've lived your life so far—have a profound effect on the composition and diversity of your microbiome, much like it affects the immune system.[4] While others may tell you that aging is correlated with poor function and disease, this doesn't have to be the case. Addressing the microbiome is one important way for you to see reversals in many of the diseases related to deterioration, including atherosclerosis, colorectal cancers, organ atrophies, and serious infections.

WHEN BACTERIAL IMBALANCE OCCURS

Hippocrates made the statement thousands of years ago, "All diseases begin in the gut." We are just now able to confirm how right he was. The composition of the microbiome can shape a healthy immune response or predispose you to disease.[5] When your microbiome is poorly fed and cared for, harmful bacteria and fungi take over, making you more susceptible to chronic illnesses. When blood tests identify that you are on the autoimmune spectrum, it indicates a catastrophic failure of the microbiome allowing too many pathogenic bacteria (bad guys), which activate genes for inflammation and intestinal permeability.

Alessio Fasano, MD, believes, as I do, that a primary source of offending invaders that set off the autoimmune response is the imbalance of bacteria that live within us, increasing our risk for heart disease, cancer, stroke, Alzheimer's, diabetes, and other life-threatening autoimmune diseases. Hosting an unbalanced microbiome can also lead to depression, anxiety, memory loss, brain fog, and mood swings.

As we learned in the last chapter, genes don't predict disease. Instead, they identify the weak links in your chain where disease may develop (depending on how hard you pull on the chain). The bacterial genes of the microbiome influence our own genetic expression through epigenetics, which we discussed in the last chapter. For example, the bacteria in the microbiome help digest amino acids from foods and convert them into different brain hormones, called *neurotransmitters*. These neurotransmitters control everything from brain speed to mood to metabolism, which is how we can link the health of the microbiome to obesity: The availability of specific types of bacteria is one of the primary criteria to examine when people are unable to lose weight, even on calorie-restricted diets. If you've sincerely tried to count calories or diligently followed specific weight-loss programs and didn't get the results you wanted, it's very likely that the bad bacteria in your microbiome are acting as an emergency brake, holding your body back from losing weight.

An imbalanced microbiome pulls on our chain, so wherever your weak link is, that's where the link will break and leave you vulnerable to developing health problems. That's what's meant by a genetic vulnerability—not that you are destined to get such-and-such disease, but rather that if increased inflammation pulls at the chain too hard, then your genetic weak link will manifest. What's more, an imbalanced microbiome creates an inflammatory environment that will eventually be the last straw, creating intestinal permeability (the leaky gut), which allows food macromolecules (such as gluten) to sneak through the leaky gut into the bloodstream, which triggers an immune response to that food molecule. An abnormal microbiome will create inflammation and can cause intestinal permeability all by itself, even with a squeaky-clean diet. This is a major reason why some people who avoid the foods they are sensitive to may not feel better right away—they still have an ongoing inflammatory cascade in the intestines created by the imbalanced microbiome. The imbalanced microbiome is the environmental trigger pulling on your chain. However, your microbiome can begin to change in as few as 3 days when you change what you eat.

We learned in Chapter 2 that epigenetics controls how our genes express themselves. The major driver of epigenetic expression is the microbiome. It is the largest environment we deal with every day. It's interesting to me that humans are the dominant species on the planet, yet our genetic structure is so simple. For example, humans are made of about 23,000 genes. Compare us to a worm, which has 90,000 genes. So they're much more complicated than we are. Yet I believe that we don't have to argue too much that worms and human beings have different levels of sophistication in terms of what they're capable of doing.

So where does our sophistication come from? It comes from the fact that we really are made of two genomes. The human genome is fixed and rudimentary. You cannot change it. Then we have the microbiome, which contains 100 to 150 times more genes than the human genome. Genes control function. That means that the microbiome has 100 to 150 times more influence on our daily function than the human genome.

MEET THE PIMA INDIANS

The Pima Indians, Native Americans who have historically lived in the American Southwest near Mexico, pose an interesting question about microbiome and its impact on health. These indigenous people have lived in this arid part of the country for hundreds and hundreds of years. Driving through the area today, you can still see that there is nothing growing in the desert to eat, yet these people survived. One explanation for their survival is known as the *thrifty gene theory*: The Pima evolved to be very efficient with their food intake and were able to optimize their calories. The Pima used every calorie of food they took in or stored it for later use. When there isn't much to eat, you either adapt and get the most bang for your buck out of your efforts to harvest food, or you're malnourished and weakened, and you have a tougher time surviving. The

ones who survived had offspring who had their parents' strong genes. Those who weren't very good at utilizing calories couldn't acclimate to their harsh environment.

The major difference between the successful Pima and those who didn't survive was their microbiome. Their survival was dependent on developing a microbiome high in Firmicutes, the group of bacteria that hoard calories. Over time, these Firmicutes influenced the Pima DNA, so that their offspring also carried high levels of Firmicutes. In this example, the term "thrifty gene" doesn't apply to the Pima people's DNA but to the DNA of the bacteria.

Now fast-forward to today, where the Pima are no longer eating their ancestral diet and instead eat the standard American diet: They live on convenience food and junk food, not many vegetables, way too much sugar and bad fat, etc. The result is that the Pima are still hoarding their calories, and by the age of 35, 50 percent of Pima adults have diabetes, and 95 percent of those with diabetes are overweight and are at a higher risk of cardiovascular disease, high blood pressure, and dementia. Even though food is no longer scarce, their thrifty genes in their microbiome still send the message to hoard calories more efficiently that the rest of us can. This is why their rate of diabetes is far higher than the average in the United States. This time, their "thrifty gene" and microbiome are working against them.

The Origins of Dysbiosis

When the intestines contain the right balance of good and bad bacteria, they are described as being in a state of *symbiosis*. An imbalance in the microbiome is referred to as *dysbiosis* and is a primary source of inflammation in the gut and throughout your body. Dysbiosis can result from a deficiency of good bacteria or an overgrowth of harmful organisms, including unfriendly bacteria, yeast (candida), and protozoa. The composition of the microbiome is highly influenced by our environment. First and foremost, it is affected by dietary choices, because these bacteria eat our leftovers.

Most of us have abnormal microbiomes from adhering to the standard American diet of low-nutrient foods and living a sedentary lifestyle. The foods you eat profoundly influence the types of intestinal flora you carry and their behavior. This in turn affects how you burn and store calories and produce energy, and it determines the number and amount of neurotransmitters (brain hormones) you make, which in turn controls your moods and behaviors as well as your risk for disease. For example, foods containing gluten, casein (a protein found in dairy), and corn are thought to have endotoxin-like effects that can contribute to dysbiosis. What's more, about 75 percent of the food in the average Western diet is of limited or no benefit to the microbiome, especially for the bacteria found in the lower gut. Most of it, composed specifically of refined carbohydrates, is already absorbed in the upper GI tract, and what eventually reaches the large intestine is of limited value, as it contains only small amounts of the minerals, vitamins, and other nutrients necessary for maintenance of the microbiota.[6]

Every cell in your body reproduces itself. As we've already learned, we have an entire new body every 7 years. Some cells reproduce rapidly, some are quite slow. The fastest-growing cells in your body are found in the lining of your intestines. You have a completely new lining every 3 to 7 days. It's like a snake shedding its skin—new cells replace the old ones quickly. The fuel for those cells to reproduce is called *butyrate* or *butyric acid*.

Butyrate is a by-product of digestion involving good bacteria feeding on vegetable fiber. If you're not eating enough vegetables or if you don't have the right microbiome, you won't make enough butyrate. This is one of the more important reasons to eat a variety of vegetables—to supply the starches needed for our "good bacteria" to feed off of and make butyrate.

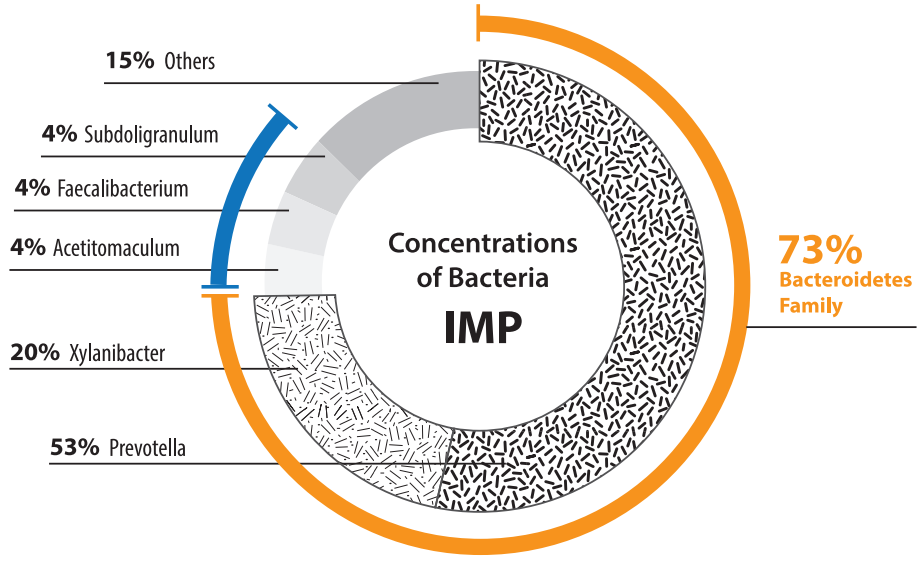
If you do not have enough butyric acid, your cells are still going to reproduce, but you are building your house out of straw instead of brick. You're still going to make new cells every day, but if you don't have enough of the right raw material, your cells will be weak. However, the right amounts of butyrate can (1) build strong, healthy colon cells that have a much better chance of functioning normally, (2) allow both the intestinal wall cells as well as intestinal immune cells to calm down and rest in a state of "ready to protect when needed," and (3) reduce the inflammation that is a primary trigger in developing obesity.[7] Many studies site a correlation with building your house out of straw instead of brick to a vulnerability in developing colon cancer. Having the right amount of butyrate is protective against the development of this type of cancer.

Remember the triad of development for autoimmune disease, which includes intestinal permeability? Here's exactly where food selection becomes important. The foods you eat play a major role in determining if you have enough butyrate. If you have enough butyrate, you help heal intestinal permeability, the gateway in the development of autoimmune disease.

Autoimmune disease is particularly prevalent in the Western world because our diet has so significantly damaged our microbiomes. In a 2010 Italian study, researchers compared stool samples of African tribal children to children living in Europe, and they found dramatic differences. The children in the African tribes who still eat the way their ancestors ate don't end up with many of our most common autoimmune conditions (like allergies, asthma, eczema, acne, rheumatoid arthritis, psoriasis, or multiple sclerosis). The difference is the microbiome. The African children have a much higher rate of good bacteria and a limited amount of bad bacteria, as well as a unique abundance of good bacteria that were completely lacking in the European children. The researchers hypothesized that the African children's microbiome allowed them to maximize energy intake from fibrous plant foods (producing higher butyrate levels) while protecting them from inflammation.[8]

In the diagram on page 7, the European children have a four-fold increase in the calorie-hoarding Firmicutes family of bacteria. The African children have higher concentrations of the Bacteroidetes family, which is a critical component of a healthy microbiome with low vulnerability to developing autoimmune disease. So while we in the Western world may have advanced in our knowledge of the comforts and safety of life, we are just learning that the balance of the microbiome is the key to a disease resistant, slim, and healthy body.

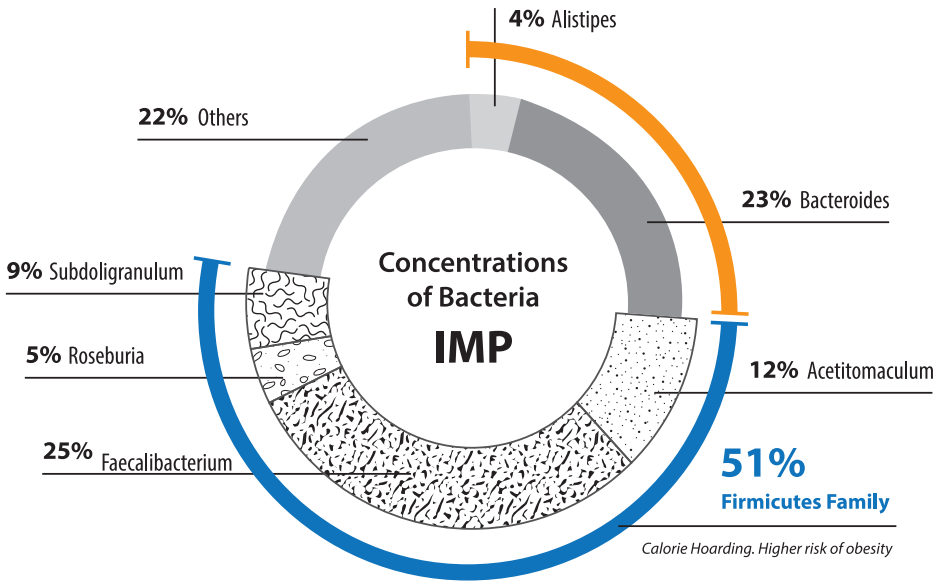
African Village Children



BF

Prevotella, Xylanibacter	Bacteroidetes Family	73%
Acetitomaculum, Faecalibacterium, Subdoligranulum	Firmicutes Family	12%

European Union Children



EU

Alistipes, Bacteroides	Bacteroidetes Family	27%
Acetitomaculum, Faecalibacterium, Roseburia, Subdoligranulum	Firmicutes Family	51%

Symptoms of Dysbiosis

When the digestive system is out of balance, the following symptoms may occur:

- A sense of fullness after eating
- Amenorrhea (absence of menstruation)
- Bloating, belching, burning, flatulence after meals
- Chronic intestinal infections, parasites, yeast, unfriendly bacteria
- Chronic vaginitis (vaginal irritation)
- Dilated capillaries in the cheeks and nose in the nonalcoholic
- Fatigue
- Greasy stools
- Indigestion, diarrhea, constipation
- Iron deficiency
- Nausea or diarrhea after taking supplements
- Postadolescent acne or skin irritations (including rosacea)
- Rectal itching
- Skin that bruises easily
- Systemic reactions after eating
- Undigested food in the stool
- Weak or cracked fingernails

Dysbiosis and Antibiotics

Dysbiosis can also be caused by medications, primarily the use and abuse of antibiotics. Interestingly, the epidemic of autoimmune disease coincides with the introduction of antibiotics. Taking an antibiotic is like dropping a bomb on your microbiome: The drug damages or destroys everything in its path, including both good and bad bacteria. Over time, the bad bacteria become resistant to the antibiotics, prosper, and create an imbalance in our intestines, triggering inflammation that goes systemic. In a meta-analysis of 4,373 papers, researchers concluded that individuals prescribed an antibiotic for a respiratory or urinary infection develop bacterial resistance to that antibiotic. The effect is greatest in the month immediately after treatment but may persist for up to 12 months.[9] So if you're experiencing recurring ear, sinus, or lung infections, it may be caused by the fact that your body is no longer responding to the medication your doctor is prescribing.

Antibiotics definitely have their place in medicine. They effectively treat bacterial infections. But when they are overused, or if your immune system is busy fighting off other offending invaders,

they can cause more problems because they kill all bacteria, good and bad.

Unfortunately, the last 3 decades have seen the overuse of antibiotics in both the medical community as well as conventional farming. This has resulted in a systematic depletion of the good bacteria in our intestines. Seventy percent of our immune system is found in the intestines, and our primary protection from colds, flus, viruses, cancer cells, and more is supposed to come from the beneficial bacteria naturally occurring in our gut. When the good bacteria are further reduced from a dose of antibiotics, inflammation increases, intestinal permeability increases, and we are at a higher risk of infection and disease.

Often, antibiotics are prescribed to treat illness they are not created to address. Antibiotics can't treat a cold or a yeast infection. In fact, the reason why so many children do not resolve their ear infections with antibiotics is because 14 to 28 percent of ear infections are caused by fungus or yeast, not bacteria.[10]

All of us are exposed to antibiotics, whether by prescription or not. Farmers spray their vegetables with antibiotics, and animals like cows and chickens are given antibiotics to make them stronger. Antibiotic residue is in meat and poultry products, vegetables, and our water supply. It is so very challenging to understand how governmental agencies that are supposed to be protecting us allow the indiscriminate use of these powerful drugs in so many situations where they are not necessary. There is no reason on earth why we should be spraying our vegetable crops with antibiotics and thus dripping gasoline on the inflammation fire every time we eat them. This is another reason why supposedly healthy foods have become unhealthy for us. Any part of our food chain that is treated with antibiotics results in an inflammatory food.

Another problem with antibiotics is that they stimulate the production of biofilms, a type of polymer (hard plastic) that bacteria produce to protect themselves. It's like a force field created to protect bacteria. Biofilms prevent antibiotics from reaching bacteria. According to a CDC 2013 report, antibiotic-resistant bacteria cause more than 23,000 deaths per year in the United States alone. This is one of the ways that super-bugs, or bacteria that are resistant to antibiotics, are created (the second way being a lack of competition for resources in the gut). The National Institutes of Health says that it can now take up to 100 times the standard dose of antibiotic to kill a bacterium if it has a strong biofilm. This is why you may be taking more antibiotics than before to fight off an infection. The longer we have low levels of bacteria in our bodies that shouldn't be there, the more likely the biofilms will develop.

Dysbiosis and Stress

Last, dysbiosis can be caused by stress, ranging from environmental exposures such as pollution, chemicals, radiation, and low-quality, nutrient-poor foods to the stresses of our everyday lives, including dealing with not feeling well. Stress has become such an ingrained part of our day that it's no wonder our microbiomes are a mess.

Our understanding of stress and how it affects the body was first noted by Hans Selye, MD, PhD, a Hungarian physician who also earned a doctorate in organic chemistry. In the 1950s and 1960s, Dr. Selye first explored the critical concept of the adrenal glands as our first line of defense against stress. Whether we face chemical, emotional, or physical stress, our adrenal glands allow us to respond in a healthy way. They are in charge of determining when to activate the famous "fight, flight, or fright" response.

Dr. Selye and other scientists at the time already knew that there are two different nervous systems in our body: the parasympathetic nervous system and the sympathetic nervous system. When you are in a stress mode, the fight, flight, or fright response kicks in, and your sympathetic nervous system is activated. Dr. Selye pointed out that our bodies are designed just like those of our ancestors, going back tens of thousands of years ago when we lived on the savannas of Africa, which means that we respond to the stresses of life just like our ancestors did. Here's an example: One of the physiological manifestations of fight, flight, or fright is a reduction of bloodflow to the skin. When our ancestors were in a stressful situation (hunting, fighting an animal) and the sympathetic nervous system was the dominant

MEET PAUL

After dental surgery, my friend Paul was given a prescription for antibiotics to ward off potential infections. Soon afterward, Paul noticed some unpleasant changes in his health. He started feeling bloated most of the time, and he felt like a cold was coming on every 4 to 6 weeks. The fatigue that followed was taking longer and longer to lift.

Paul's deteriorating health took away his motivation to exercise, and he gained a little more than 10 pounds. When the joints in his body began to feel achy all the time, he assumed it was from the lack of activity. What he mostly wanted to do every day was to stay home and watch TV. When he couldn't get off the couch for 2 days in a row, his wife sent him into my office.

Paul told me what was going on, and I realized that his achiness was stemming from inflammation in his joints caused by LPS infiltration from intestinal permeability that was caused by the antibiotics. Paul didn't realize that the antibiotics he had taken had triggered an internal crisis in his body (dysbiosis), and his microbiome was sending a crisis message. It signaled the immune system to create inflammation, causing intestinal permeability, allowing LPS to get into his bloodstream, which deposited in his weak link—his joints.

Upon testing, we confirmed that Paul's LPS levels were quite elevated. Even though Paul didn't think he was sensitive to dairy or gluten, I asked him to take a 3-week break from both, just to see. To his surprise, even before the 3 weeks were over, his joint pain decreased and he went back to exercising while he followed my gluten-free, dairy-free, sugar-free diet. Within 6 weeks, he had lost the added weight. He told me, "Dr. O'Bryan, I finally feel like myself again. I understand what you were saying when you told me to listen to my body."

functioning system at that moment, there would be a reduction in bloodflow to the skin. Why? So that we wouldn't bleed excessively when we were fighting for our lives. Fast-forward to our everyday, stressful lives. When we are in a sympathetic dominant state, which we are most of the time, we have a reduction in bloodflow to our skin. How might that manifest? Acne, psoriasis, or vitiligo (loss of pigment causing white patches in the skin). We could go through every system in the body and demonstrate similar lifesaving, protective responses that occur in a sympathetic dominant state. But we're not supposed to live like this 24/7.

How often were our ancestors exposed to extreme stress, requiring a fight, flight, or fright response? Not very often. We can imagine that occasionally their lives would be in danger or that they would need to be hyperalert. Yet they lived in tropical climates where nothing but organic food grew year-round. That's why we have a stress response to chemically laden and often genetically modified foods. Our forebears didn't need a coat to keep them warm in the winter. That's why when we feel cold, it puts stress on our system, activating an adrenal response.

We know that we're supposed to live a relatively mellow life and rarely activate our adrenal glands because they are in fact very small. In a healthy pair of adrenals, each gland is the size of a walnut. If we were supposed to be stressed all the time, wouldn't the organ be larger, like the heart?

Yet in the crazy lifestyle that we live today, we're under tremendous stress, operating almost constantly in a sympathetic dominant state, taxing our bodies, and creating a continual stress response. On autopsies of people who die of disease, it's been found that the adrenal glands were completely overused and had shrunk to the size of a peanut. Yet on autopsies of same-age people who died of trauma (like a car accident) but no disease, the adrenal glands were the size of a walnut. How in the world could peanut-size, shrunken glands support our crazy life? They can't. That's why we don't respond to stress well: We've worn out the stress response system, and the toll shows wherever we have a weak link in our chain.

As a medical student, Dr. Selye observed that patients suffering from different diseases often exhibited identical signs and symptoms. In his words, they were "stressed." The signs of severe adrenal stress include dizziness upon standing too quickly; having to wear sunglasses even on cloudy days; increased pulse rates; shorter, quicker breathing; and recurrent muscle tension.

He later discovered the general adaptation syndrome, a response of the body to demands placed upon it. Dr. Selye was the first to point out that stress induces hormonal autonomic responses. Over time, these hormonal changes, if excessive, can lead to physical manifestations. He was the first to identify that excess stress wears out the body and causes disease. His definition of stress was anything that activates a sympathetic nervous system response, whether it's chemical, physical, or emotional.

In a 1955 article in the medical journal *Science*, Dr. Selye showed how arthritis, stroke, and heart disease are all affected by stress-induced overworked adrenal glands. His research was conducted on mice, and he was able to demonstrate how changing their environment by adding recurring stress could alter them physically. One mouse was allowed to lead a normal mouse life in the

laboratory. The other was worked hard by constantly being placed on a hamster wheel or by being thrown into water above its head, swimming to exhaustion. The result was that the adult relaxed mouse was twice the size of the stressed mouse. It had a beautiful coat, whereas the stressed mouse was half the size and looked wiry. It developed disease and died earlier.

Dr. Selye identified the stages of adrenal function. Normal adrenal response is referred to as *sympathetic dominance.* When the fight, flight, and fright response occurs day in and day out, our adrenals go into a state of adrenal fatigue, and their response is less thorough. When the fight, flight, or fright response continues, we go from adrenal fatigue to adrenal exhaustion, and it becomes difficult to elicit an adequate response. When the fight, flight, or fright response continues further, we go into a state of adrenal depletion and we are unable to respond. Now the stress we are being exposed to cannot be addressed or diffused by our stress hormones, and it hits our body full force. This means that when you have a stressful life and you've worn out your adrenal glands, another organ has to deal with each particular stress. For some people, the thyroid takes over, but then you start taxing your thyroid, especially if it is the weak link in your health chain. If you can no longer make adequate amounts of the adrenal hormones that deal with sugar intake, known as glucocorticoids, the blood sugar regulating system that has to pick up the slack is the pancreas, which responds to the stress by making more insulin. Over time, you develop insulin resistance. Then here comes diabetes, and you are on the autoimmune spectrum.

We are supposed to live in a state of parasympathetic dominance. Because of our lifestyle today, we are living in sympathetic dominance all the time. We're constantly on alert in everyday life, so much so that most people, especially those who have been diagnosed with autoimmune disease, have gone from adrenal fatigue to adrenal exhaustion to adrenal depletion. The result is that stress hits you much harder and more often. If you're feeling burned out, it's because you are. And so is your body's ability to be resilient. Without the mechanism to return to a parasympathetic dominant state, you become extremely vulnerable to developing any disease, depending on your weak link.

What organ controls the entire relationship of how our bodies respond to the stress of life? You might think from this discussion that it was the adrenal glands. Doctors used to believe that until just 5 years ago. Now we know that the microbiome is the central computer directing the microbiota-gut-brain (MGB) axis.[11] The microbiota sends chemical messengers to the brain along the spinal cord and through the bloodstream. These messages instruct the hypothalamus how to respond to perceived stress. The hypothalamus tells the pituitary glands which stressors are the priorities, which then sends messages telling the organs what hormones to produce.

Here's an example. It's April 14. You haven't done your taxes, and you have a sinking feeling in your stomach. You wake up in a sweat. You might notice that your pulse is up as you try to figure out a strategy to get the work done. Inside your body, a healthy microbiota begins taking charge. It sends a message to the hypothalamus, which sends a message to the pituitary glands, who send a message to the adrenals to produce more glucocorticoids. You need these because an increase in glucocorticoids increases your alertness so you have more brainpower to stay up late and finish

filing your taxes. When you are in the midst of doing your taxes, you'll notice that sinking feeling is gone. Your microbiota is no longer sending a stress message because you are deep in the stress response and acting appropriately.

However, if your microbiota is out of balance, the anxiety you woke up with wouldn't go away and might even increase while you filled out the paperwork. You don't have the support in your gut needed to keep your brain calm. In fact, the severity of the stress response is 2.8-fold higher, producing stress hormones when you don't have the right microbiota.[12]

You can decrease intestinal permeability by lowering your stress levels. As we learned in Chapter 2, activation of the nervous system increases intestinal permeability.

Stress hormones weaken and damage the gut lining, leading to leaky gut. When you have intestinal permeability, the lipopolysaccharides from the gut breach the cell wall and get into general circulation, stimulating more immune cells, which in turn send a message back up to the brain, which creates more stress, activating the immune response and producing more inflammation. Intestinal permeability maintains the cycle, but the excessive stress in our lives will trigger intestinal permeability all by itself. Our bodies were designed to run as smoothly as a Rolls-Royce, but our lifestyle has them running like Ramblers.

Every doctor tells patients to reduce the stress in their lives. Realistically, we can't drop the stress in our lives overnight. We have kids, jobs, and a lifestyle that we're locked into. We can reduce the stress in our lives over time, if we have a plan to do it. However, how the body physically handles stress while we're in transition to a lower-stress life is where we can make an impact now. We can shore up the microbiome so that when stressful situations happen, we have more resilience to handle it better. If you can get your body healthier, your body will allow you to manage your stress more effectively.

For example, I've never been a great sleeper. On a typical night, I used to sleep about 5 hours. One of my primary concerns from a health perspective has been my sleep, because I know how critically important shut-eye is to cellular regeneration: You heal when you sleep, so if you don't sleep, you don't heal well. But once I balanced my microbiome, my sleep improved. I can now sleep 6 or 7 hours solidly, without making any other changes to my lifestyle. And because I'm better rested, my body heals quicker, and I can handle the daily stress of life much better.

THE MICROBIOME'S ROLE IN HARNESSING LPS

As we saw in Chapter 2, the microbiome protects us from lipopolysaccharides (LPS), which are detrimental to the health of the immune system. LPS are one of the most-studied and most-destructive aspects of an unhealthy microbiome. One of the main jobs of the microbiome is to keep LPS in check. Here's the problem with LPS and why they cause so much damage: When we lose the protective dominance of good bacteria in the microbiome (which almost all of us have lost), the amount of LPS produced is overwhelming to the body, and—as we learned in the last chapter—causes inflammation.

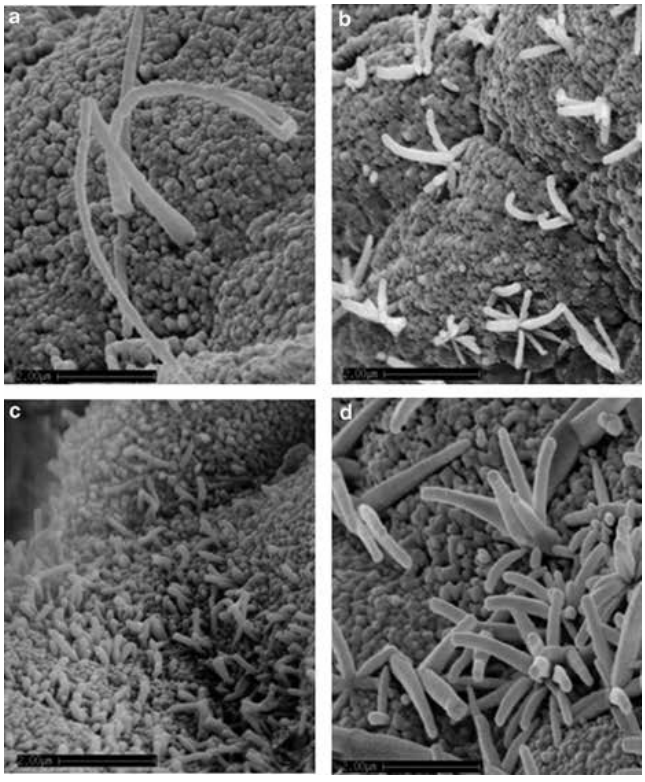
One of the essential features of a healthy microbiome is its production of *bacteriocidins*, enzymes that destroy unfriendly bacteria. With the development of an unhealthy microbiome due to unhealthy food choices or antibiotics, our protective capacity diminishes and LPS flourish. Now you have a mess in the gut, and the LPS penetrate the walls of the intestines, triggering the systemic inflammatory cascade. How can we prevent this? By reestablishing a healthy microbiome.

SUPPORTING A HEALTHY MICROBIOME

I was recently asked the following question during an interview: "What's the one thing you would do, more than anything else, if you were going to focus on being healthy?"

My recommendation is to focus on creating a healthier microbiome. All the little steps that are easy to implement will add up to having a robustly healthy microbiome. Nothing is more important to the function of your body. Nothing has more control. Nothing impacts more of your tissues and organs than the microbiota. It's the big kahuna.

Luckily, the microbiome can easily be rebalanced. In just a day or two of changing your diet, you can begin to change and reduce dysbiosis. First, avoid the foods you may be sensitive to. When you have food sensitivities, the immune system responds with an inflammatory cascade in the gut. Every forkful can have a detrimental effect on your microbiome, even if you don't feel bad as you eat it. The inflammatory cascade kills off the good bacteria, and pathogenic bacteria begin to prosper, creating an imbalanced environment in the gut. For example, in one study of celiac children, 39 percent had abnormal bacterial growth in their intestines, and many of these bacteria were never before identified in humans. When the offending gluten was removed for 2 years, the unknown bacteria disappeared for 81 percent of the children.[13] This shows that when you remove the foods you are reacting to—beginning with gluten, dairy, and sugar—you can positively affect your microbiome.



The rod-shaped bacteria in these photographs were previously unknown but often occur in more than one-third of children with celiac disease.

FIX #1: FOODS THAT SUPPORT A HEALTHY MICROBIOME

My Transition Protocol includes better food selection, probiotics, and prebiotics to help restore a healthy microbiome. The foods that support the microbiome are grouped into four categories.

1. **Choose foods high in polyphenols—colorful, high-fiber fruits and vegetables.** Polyphenols are micronutrients found in the bright colors in fruits and vegetables and have an incredibly beneficial effect on the microbiome.[14] You may have heard of resveratrol, found in red wine, and the benefits of dark chocolate or green tea. It's the polyphenols that provide much of these foods' health benefits. Polyphenols occur within a diverse class of plants and are associated with strong-colored fruits (like berries) and vegetables (like red tomatoes). Fruits and vegetables that are high in polyphenols have the same dark color throughout. While eggplants have a nice, dark skin, the flesh is white, so it isn't a high polyphenol choice. A better choice would be dark, leafy greens like spinach or kale.

   The most exciting information about polyphenols is that studies have shown the interaction between polyphenols and the microbiome is bidirectional: Gut microbes affect the absorption of polyphenols, which then affects the growth of bacteria, which then affects a 75 percent reduction in cardiovascular disease.[15] In 2003, the *British Medical Journal* published a paper titled "A Strategy to Reduce Cardiovascular Disease by More Than 80%." The authors of the paper did a meta-analysis in which they pooled together benefits of separate drugs. Using this logic, they concluded that a "polypill" made up of a statin to reduce cholesterol, three blood pressure medications, a baby aspirin, and folic acid would reduce the risk of cardiovascular disease by more than 80 percent. This was published on the front page of

GO AHEAD, EAT CHOCOLATE EVERY DAY

Eat a little dark chocolate every day to increase your intake of polyphenols and prebiotics. Take a square of the very best dark chocolate (at least 70 percent cacao) that you can get and put it on or under your tongue. Don't let it touch your teeth. Let it sit there without chewing, so that it slowly dissolves in your mouth. In this way, you saturate your taste buds to send the message "chocolate is here" to your brain via the oral thalamic tract that leads from the mouth right up to the brain. Chocolate stimulates the production of endorphins and enkephalins, which are 200 times more powerful than morphine in how they stimulate the feel-good sensors in your brain.

If you eat that one square of chocolate every day and let it melt in your mouth for about 2 minutes, you'll most likely feel very satisfied. If you want more, go ahead and have another piece. I've never ever, ever had a patient want more than two squares if they follow this method. This way, you can have dark chocolate every day and not gain weight or throw your blood sugar out of balance.

most newspapers in the country. Interestingly enough, the authors had filed a patent for this polypill. Eight months later, a second paper appeared in the *British Medical Journal* titled "The Polymeal: A More Natural, Safer, and Probably Tastier (Than the Polypill) Strategy to Reduce Cardiovascular Disease by More Than 75%." Using the same logistical analysis, the researchers demonstrated that eating cold-water fish four times per week, as well as eating foods high in polyphenols like dark chocolate, garlic, almonds, a pound of vegetables, and red wine every day, reduces the risk of cardiovascular disease by 75 percent. The estimated life expectancy free of cardiovascular disease increased by 9 years for men and 8.9 years for women.[16]

In Chapter 7, you'll receive complete instructions on how to add polyphenols into your diet every day, including salads filled with greens and crunchy, colorful cruciferous vegetables. It is the insoluble fiber in these vegetables that the bacteria thrive on that promote being lean and healthy. Other foods high in polyphenols can be eaten every day, but in moderation, including fresh garlic, fresh raw almonds, and 70 percent cacao or higher dark chocolate. Cocoa has been shown to influence the microbiome toward a more health-promoting profile by increasing the relative abundance of good bacteria.[17] What's more, chocolate is thought to modify intestinal immune status, lowering the expression of IgA antibodies.[18]

2. **Choose the right carbohydrates—avoid processed carbohydrates that feed bad bacteria:** chips, French fries, breads, white rice, cookies, crackers, desserts, and sugars. These foods put your body in a chronically hungry, metabolically damaged, fat-storing mode. Eating them can increase your risk of intestinal permeability and may alter the makeup of your microbiome, upsetting the balance between "friendly" and "unfriendly" bacteria.

However, eating good carbohydrates can actually reduce obesity by increasing beneficial bacteria. In 2006, microbiologist Liping Zhao, PhD, conducted an experiment on himself to replicate findings that showed a link between obesity and the microbiome in mice. At the time, Dr. Zhao was overweight and in poor health. He adopted a diet that included whole grains (brown rice) along with two traditional Chinese medicine foods: Chinese yams and bitter melon, both of which contain a particular type of indigestible carbohydrate (a prebiotic that encourages the development of one form of good bacteria, *Faecalibacterium prausnitzii)*. He monitored his weight loss as well as his microbiome. Two years later, he had lost a total of 44 pounds by restoring his good bacteria.[19] In a 2016 study from the Department of Twin Research and Genetic Epidemiology at King's College London, it was found that the bacteria produced by eating these same foods (*Faecalibacterium*) is significantly associated with reduced frailty.[20] This is important, because frailty is a useful indicator of overall health deficit, describing a physiological loss of reserve capacity and reduced resistance to stress.

Carbohydrates containing artificial sweeteners promote unhealthy gut bacteria that cause obesity. In one study, the sugar substitute saccharin was shown to alter the function of 115

different pathways in the gut because of the microbiome controlling glucose tolerance, leading to obesity. The bacteria that aid in the digestion of saccharin turn the switch on to store energy as body fat and alter the gut microbiome.[21]

3. **Eat grass-fed red meat and healthy fats.** When you eat healthy fats, including the fats found in avocados, olive oil, coconut oil, nuts, fish, free-range poultry, and grass-fed beef, there is no evidence of lipid raft transcytosis (discussed in Chapter 2), which is responsible for moving LPS into the bloodstream. In Chapter 7, you'll learn more about choosing the best fats for this program.

4. **Eat one forkful of fermented foods every day.** A hundred years ago, people thought yogurt was healthy for you but were not exactly sure why. We now know that it is because of the fermentation of the bacteria in milk: Every time you eat yogurt, you get a dose of good bacteria. However, because so many people have a dairy sensitivity, and because the quality of most pasteurized yogurts found at the grocer is so poor and low in beneficial bacteria by the time it reaches your table, we are going to focus on eating fermented vegetables and drinks like kefir (a cultured/fermented milk), KeVita (a cultured/fermented coconut water), and kombucha (a fermented tea) to encourage the growth of good bacteria in your gut.

   Fermented foods are those that grow bacteria in them or on them. They are some of the best detoxifying agents available. The beneficial bacteria in these foods are capable of drawing out a wide range of toxins and heavy metals. The ancient method of fermenting unlocks nutrients from food, breaks down some of the starches, and adds beneficial bacteria and enzymes to every bite. Fermented foods are a better choice than over-the-counter probiotic supplements. Not only do fermented foods provide a wider variety of beneficial bacteria, they also give you far more of them. For example, most probiotic supplements contain fewer than 10 billion colony-forming units (CFUs). But fermented vegetables can contain 10 trillion CFUs of bacteria. Literally, one serving of fermented foods is equal to an entire bottle of a high-potency probiotic. Every day, you need to eat just a little bit, such as one forkful of fermented foods like sauerkraut and kimchi, both made from cabbage. You can purchase fermented vegetables or follow the recipes in Chapter 10 to make your own. If you find that you have a little gas or bloating after eating fermented vegetables, it is a biomarker of dysbiosis (abnormal gut bacteria in high concentration). It doesn't mean the fermented foods are bad for you; it means your threshold for digesting them is very low. So reduce your dosage: Try a tablespoon of sauerkraut juice on your salad with your normal salad dressing so that the taste isn't so strong. Next week, try 2 tablespoons per day. This is an example of transitioning—you are taking an accurate evaluation of where your body is currently functioning and moving it in the direction of better functioning.

FIX #2: PROBIOTICS

Probiotics is the term for the good bacteria in your gut. For a healthy microbiome, probiotics need to be the majority of all your gut bacteria. There are thousands of different types of probiotics, and each is defined by its genus (for example, *Lactobacillus*), by its species (such as *rhamnosus*), and by its strain designation (often a combination of letters or numbers). The concept of a bacterial "strain" is similar to the breed of a dog—all dogs are the same genus and species, but different breeds of dogs have different attributes, and different breeds are good for different tasks. You don't bring a Chihuahua to your door if you need a Rottweiler.

The use of probiotic supplements is still in its infancy. We really don't know exactly how to use them to create a healthier microbiome. We do know that they work to balance immune function and decrease inflammation by helping you maintain a healthy environment in the gut. They are available as nutritional supplements that increase beneficial bacteria in the gut and crowd out bad bacteria. They can also heal intestinal permeability. Different strains of even the same species of probiotics can vary in their specific bacteria.

Probiotics are most effective when they are combined with a high- fiber diet that features lots of vegetables every day (remember the Polymeal). Vegetable fiber is critical for creating butyrate, which, as we discussed earlier, is the fuel for the fastest-growing cells in the body: the inside lining of the intestines. This is a critical concept and the reason why I don't encourage fiber supplements, because I have never found a study where fiber supplements increase butyrate levels. The right fiber acts as a fertilizer that helps the probiotic grow and proliferate good bacteria in your microbiome. And because probiotics interact with the digestive system, each strain performs differently depending on your gut's unique environment. This means that one type of probiotic doesn't work the same for everybody. To find the supplement that will work best for you, choose a broad-spectrum, high-potency probiotic. "Broad spectrum" means that it contains more than one strain of probiotics. You might try different formulations to find the one that works best for you. Your test results that we'll investigate in Chapter 5 will guide your selection based on your own deficits.

When purchasing probiotics, follow the guidance of the International Scientific Association for Probiotics and Prebiotics. They recommend that you look for supplements that list the following information on their packaging:

- **Strain**
- **CFUs** (colony forming units). How many live microorganisms are in each serving? When does the product expire? Packaging should ensure an effective level of live bacteria through the "best by" or expiration date.
- **Suggested serving size**
- **Health benefits**
- **Proper storage conditions**
- **Corporate contact information**

FIX #3: PREBIOTICS

Even the best of dietary intentions can cause problems. A gluten-free diet may actually contribute to dysbiosis. When you follow a gluten-free diet, you remove many of the carbohydrates necessary to feed good bacteria. Gluten-free foods are not known to contain healthy prebiotics. You are in effect starving your own bacteria unless you replace the gluten with prebiotics.

Prebiotics are food components that cannot be digested by the body but are consumed by the beneficial bacteria to help them function. Chocolate or cocoa is considered a prebiotic that is also rich in polyphenols.[22]

NEXT STEPS

Now that you understand the different factors that push on your immune system, it's time to see what health issues you may be dealing with, even if they are on the very beginning of the autoimmune spectrum. The next chapter features two quizzes—but don't worry, they're fun. Our first goal is to identify what is currently occurring in your body, and the earlier we can do this, the better. Then you can learn to arrest the development of damage before you have a diagnosable dis ease. The tests in Chapter 4 are critical for understanding how you will manifest optimum healing.

SAMANTHA'S STORY: PHASE 3

My patient Samantha's microbiome was directly affected by the antibiotics and other drugs she was given to treat her acne as a teenager. Later, during her lupus treatments, the steroids and chemotherapy medications pushed her microbiome over the edge. By the time I met her, her stress levels were high, which contributed to the problem as well. Aside from the damage caused by her food sensitivities, she suffered from constant bloating, which was a direct result of the gut imbalance. Even though she wasn't really overweight, she told me that she always felt heavy, almost dense, but just assumed that feeling was normal.

I started Samantha on a simple plan of incorporating fermented foods into her diet. I explained that she doesn't need a whole lot of them, just a little bit every day. Everyone finds the right balance. With fermented foods, too much is too much, and too little is not helpful at all. I usually start adults at 1 tablespoon per day and have them rotate the fermented food choices: one day sauerkraut, one day kimchi, one day miso soup, etc.

Samantha was able to calibrate what she needed and responded to the fermented foods very positively. When I asked her how she felt, she told me, "I'm eating a half cup of sauerkraut every day with my lunch. It's been very helpful and nourishing, and it's caused a detox on some level. And it's allowed me to slowly add back foods into my diet that I used to avoid. Now that my gut is more balanced, I can eat certain fruits again without pain or gas. And I don't have bloating anymore. My friends have noticed that I've lost some of my curves, but I realize that was just bloat. I even feel lighter."

I also recommended that Samantha take prebiotics, which would work in concert with the fermented foods. Prebiotics and probiotics help to create an alkaline environment in the gut that reduces inflammation.

ENDNOTES

1 J. Simon-Areces, "UCP2 Induced by Natural Birth Regulates Neuronal Differentiation of the Hippocampus and Related Adult Behavior," *PLoS One* 7, no. 8 (2012): e42911.

2 K. Kristensen and L. Henriksen, "Cesarean Section and Disease Associated with Immune Function," *Journal of Allergy and Clinical Immunology* 137, no. 2 (Feb 2016): 587–90.

3 J. R. Marchesi et al., "The Gut Microbiota and Host Health: A New Clinical Frontier," *Gut* 65, no. 2 (Feb 2016): 330–39.

4 H. J. Zapata and V. J. Quagliarello, "The Microbiota and Microbiome in Aging: Potential Implications in Health and Age-Related Diseases," *Journal of the American Geriatrics Society* 63, no. 4 (Apr 2015): 776–81.

5 J. L. Round and S. K. Mazmanian, "The Gut Microbiota Shapes Intestinal Immune Responses during Health and Disease," *Nature Reviews: Immunology* 9, no. 5 (May 2009): 313–23.

6 S. Bengmark, "Nutrition of the Critically Ill—A 21st-Century Perspective," *Nutrients* 5, no. 1 (2013): 162–207.

7 G. D. Hermes, E. G. Zoetendal, and H. Smidt, "Molecular Ecological Tools to Decipher the Role of Our Microbial Mass in Obesity," *Beneficial Microbes* 6, no. 1 (Mar 2015): 61–81.

8 C. De Filippo et al., "Impact of Diet in Shaping Gut Microbiota Revealed by a Comparative Study in Children from Europe and Rural Africa," *Proceedings of the National Academy of Sciences of the United States of America* 107, no. 33 (Aug 17, 2010): 14691–96.

9 C. Costelloe et al., "Effect of Antibiotic Prescribing in Primary Care on Antimicrobial Resistance in Individual Patients: Systematic Review and Meta-Analysis," *BMJ* 340 (May 18, 2010): c2096. doi: 10.1136/bmj.c2096.

10 T. J. Martin, J. E. Kerschner, and V. A. Flanary, "Fungal Causes of Otitis Externa and Tympanostomy Tube Otorrhea," *International Journal of Pediatric Otorhinolaryngology* 69, no. 11 (Nov 2005): 1503–8.

11 A. I. Petra et al., "Gut-Microbiota-Brain Axis and Its Effect on Neuropsychiatric Disorders with Suspected Immune Dysregulation," *Clinical Therapeutics* 37, no. 5 (May 1, 2015): 984–95. doi: 10.1016/j.clinthera.2015.04.002.

12 N. Sudo, "Role of Microbiome in Regulating the HPA Axis and Its Relevance to Allergy," *Chemical Immunology and Allergy* 98 (2012): 163–75. doi: 10.1159/000336510.

13 G. Ou et al., "Proximal Small Intestinal Microbiota and Identification of Rod-Shaped Bacteria Associated with Childhood Celiac Disease," *American Journal of Gastroenterology* 104, no. 12 (Dec 2009): 3058–67. doi: 10.1038/ajg.2009.524.

14 N. Hayek, "Chocolate, Gut Microbiota, and Human Health," *Frontiers in Pharmacology* 4 (Feb 7, 2013): 11. doi:10.3389/fphar.2013.00011.

15 A. Duda-Chodak, "The Inhibitory Effect of Polyphenols on Human Gut Microbiota," *Journal of Physiology and Pharmacology* 63, no. 5 (Oct 2012): 497–503.

16 O. H. Franco et al. "The Polymeal" (see chap. 1, n. 8).

17 M. I. Queipo-Ortuno et al., "Influence of Red Wine Polyphenols and Ethanol on the Gut Microbiota Ecology and Biochemical Biomarkers," *American Journal of Clinical Nutrition* 95, no. 6 (Jun 2012): 1323–34. doi:10.3945/ajcn.111.027847.

18 M. Massot-Cladera et al., "Cocoa Modulatory Effect on Rat Faecal Microbiota and Colonic Crosstalk," *Archives of Biochemistry and Biophysics* 527, no. 2 (Nov 15, 2012): 105–12. doi: 10.1016/j.abb.2012.05.015.

19 Mara Hvistendahl, "My Microbiome and Me," *Science* 336, no. 6086 (Jun 8, 2012): 1248–50.

20 M. Jackson et al., "Signatures of Early Frailty in the Gut Microbiota," *Genome Medicine* 8, no. 1 (Jan 29, 2016): 8.

21 J. Suez et al., "Artificial Sweeteners Induce Glucose Intolerance by Altering the Gut Microbiota," *Nature* 514, no. 7521 (Oct 9, 2014): 181–86.

22 I. R. Redovnikovic et al., "Polyphenolic Content and Composition and Antioxidative Activity of Different Cocoa Liquors," *Czech Journal of Food Sciences* 27, no. 5 (2009): 330–37.