PART I

KNOWLEDGE IS POWER

The Engine that Drives Human Health Isn't Even Human

You've got friends in low places—trillions of them!

When I graduated medical school in 2006, we knew next to nothing about the gut microbiota. At that time 60 percent of gut microbes did not grow on a traditional culture plate, so we really didn't have a way to study them. We knew they existed but didn't have a way to extract any intel on them. And honestly, we weren't losing any sleep over it. I mean, we're talking about the bacteria in our poop! Butt bugs! From our perspective, those scalawags were just along for the ride and not necessarily playing an important role in our health.

But things changed dramatically with a laboratory breakthrough in 2006 that moved us past the culture plate and allowed us to peel apart the complex layers of our gut microbiome and study them. Up to this point we only knew of about two hundred species of bacteria that inhabited the human gut. Very quickly, we identified fifteen thousand species and there are estimates now that there may be as many as thirty-six thousand. Our barrier to research had been removed and the floodgates opened. Since then there's been an absolute *explosion* of science, with 12,900 papers on the topic in the last five years alone. To put that number into perspective, this represents a full 80 percent of the papers on the topic in the last forty years.

Maybe you've heard something about the importance of the gut microbiome, but trust me, whatever you've read is just scratching the surface. All of this science is coming at us incredibly fast, and admittedly it is a challenge for our

health care system to manage. It takes an average of seventeen years for new findings to go from publication to being in the clinic or in the consciousness of doctors, so most doctors are still functioning in the culture plate era. All have heard of the microbiome, but for most they haven't figured out how to include this information in their clinical practice. But why wait? I've monitored the emerging research with wide eyes and a gaping jaw and I'm ready to share it with you right now. No seventeen-year wait.

What we discovered when we learned to study gut bacteria is a shockingly broad, expansive community of microorganisms that live inside us in harmony, in balance, and with a purpose. We call this community the "gut microbiota." If we're referring specifically to the genetic code of this community, then we use the expression "microbiome." There are five types of microorganisms residing within you. They include bacteria, yeasts, parasites, viruses, and archaea.

Bacteria are living single-celled organisms that most of us grew up fearing. Believe it or not, our fears are strongly misplaced. Yes, there are some like *E. coli* or *Pseudomonas* that are bad and create issues for us. But most are actually good and are trying to help us. They're like dogs. Most are man's best friend, but some you'd rather not reach out to pet. For those, you need a dog whisperer. But if we're talking about the gut microbiota, then you need someone like me, the Poop Whisperer.

Fungi are multicellular organisms that, similar to animals and plants, have a nucleus and other organelles. They're more sophisticated than bacteria but, similar to bacteria, they are often thought to be bad even though many are trying to help us. They also compete with bacteria, which means that there's a zero-sum game: if one is flourishing, then the other is withering.

Viruses are tiny particles made up of DNA (or RNA) that don't have a cell at all and aren't even considered to be living, even though they share some qualities with us animate folk. Illnesses like influenza, HIV, and hepatitis B are often the first to come to mind when we think of viruses, but not all viruses are trying to hurt humans. In fact, most are an important part of the balanced gut microbial community and are necessary to keep our bacteria in harmony.

Parasites are nature's thieves. They steal energy from the host and try to remain undetected without offering any benefit. There are many types, ranging from giardia to the "trich" (pronounced "trick," a sexually transmitted infection) to the terrifying worms that can be up to eighty feet long and give me the heebiejeebies. Thankfully, most parasites (such as those worms) are rare in the Western world, although there are some that are more common than you'd expect. For example, sixty million Americans are chronically infected with *Toxoplasma gondii* and don't know it because they are asymptomatic.

And then there's archaea, my personal favorite. These ancient organisms were on our planet before oxygen even existed four billion years ago, and you'll find them miles deep in the ocean in rift vents or inside a volcano. You'll also find them chilling in the friendly comforts of your colon. The point here is that these are *resilient* organisms. We're just starting to learn about them, but, for what it's worth, they don't seem to compete with the bacteria and fungi for energy so they don't appear to be manipulated by diet quite as easily as the other parts of our microbiota.

The depth of the gut microbiota is hard to fathom. It's like trying to wrap your mind around the Battle of Stalingrad in World War II where there were nearly two million casualties in a single battle. The numbers are so astronomical that you're forced to ignore that each one was an individual, a real person. In this case, we carry thirty-nine trillion microorganisms in our colons. Thirty-nine trillion! Most of them bacteria.

But don't feel ashamed or grossed out by that—I mean, okay, it is kind of gross, but I'm here to tell you that the bacteria in your gut and, as you'll soon see, in your bowel movements, too, are a wondrous, magical community with amazing healing power. After all, even Ryan Gosling has bacteria in his colon. How bad could they possibly be?

So how many microbes is thirty-nine trillion? Imagine you are up in the northern parts of Canada on a very clear night, and you can look up and see literally every single star in the Milky Way. Take that number of stars and multiply it by a hundred and that's how many microorganisms are in your colon. That number clearly outpaces the number of human cells in your body. Depending on how you look at it, some would say you are only 10 percent human—and 90 percent bacteria! You're not just human, you're a superorganism that serves as an ecosystem for four of the six kingdoms of life: Eubacteria, Fungi, Archaebacteria, and Protista. The other two are Animalia (us) and plantae (what we eat). We are more than *just* human. We are the circle of life.

The human gut is all interconnected in a way that draws direct comparisons to planet Earth. Your gut microbiome is just as much of an ecosystem as the Amazon rain forest. It thrives on balance and harmony. In the jungle, all animals, plants, and microbes exist with a purpose, even the mosquitoes and snakes. They all bring something to that harmonious balance, and as much as I hate mosquitoes and snakes, their loss would have unintended consequences and diminish the health of that ecosystem. This is why biodiversity is critically important to any ecosystem.

The human gut microbiome is no exception. Diversity of species is critically

important to balance. Inside us are anywhere from three hundred to over a thousand species of bacteria (out of the fifteen thousand to thirty-six thousand in existence). When things are working the way they're supposed to, we have a diverse, abundant community of microbes living in harmony in our colon. The colon itself is healthy and strong with an intact barrier of cells to keep everything in its rightful place, and our microbiota plays its natural role as the workhorses of human health.

As residents of the intestines, it comes as no surprise that they are critically involved in digestive function. They work in teams to unpack your food, allowing you to extract the nutrients you need. There's not a meal that goes by that your microbes aren't busy at work helping you to break down your food and get the most out of it. It's hard to fathom, but in many cases these single-celled organisms are better at digesting our food than we are. As a result, we have evolved to rely on them for that.

Every single bite, all three pounds of food per day, flows downstream to your gut microbes. They are not passive observers. Our food is also their food. Yes, even invisible unicellular organisms need an energy source to fuel them. But not every microbe eats the same food. Each dietary choice you make will empower a specific group of microbes, while others will languish. If you permanently remove a food group, the microbes that thrive on that food will starve into extinction. They are procreating so quickly that the food choices you make in twenty-four hours will alter the evolution of fifty generations of microbes. It doesn't take days or even weeks to change your microbes; it only takes one bite. But you control what it is you bite into, and therefore you control the makeup of your microbiome.

The end result is a unique mix of microbes, as unique as a fingerprint. Those microbes go to work on your food and things don't end the way they started. Microbial metabolism leads to biochemical transformation of the food. In many cases, the healthy bacteria (let's call them probiotic) will reward us by molding our food into something that reduces inflammation and promotes health and balance. We call the health-promoting compounds created by our microbes postbiotics. But the opposite can also be true. Unhealthy food feeds unhealthy microbes, and they punish us by creating compounds that inflame our body. We'll be talking about a few of these, such as TMAO (trimethylamine N-oxide), in this book.

Anything that you put into your mouth will be processed by these microbes, including drugs. Which helps to explain why the same drugs can have a lifesaving effect in one person and a life-threatening effect in another. For example, the chemotherapy drug cyclophosphamide actually depends on gut

microbes to activate it. The healthier the gut, the better the chance at fighting off cancer with this drug, according to a 2013 study published in *Science*.

That's not the only thing we rely on them for. What's cool is that the health effects extend far beyond the walls of the colon. If I were to boldly define the entirety of human health, there would be five essential elements: immunity, metabolism, hormonal balance, cognition, and gene expression. That would cover our bases for everything we need to thrive as humans, and what's amazing is that the microbiota is intertwined with all five axes of human health. We're going to dive deeper into this, but let's start by acknowledging the gut microbiota as a command center of sorts for human health. Things happening throughout the body, the heart and brain included, often have their origins in the work of the gut microbes. They work as teams, but often with specialization.

Imagine the gut as a factory staffed by workers with many different roles. Each individual contributes his or her expertise toward the greater cause. And yes, there will be overlap in terms of expertise. If you lose Sally the engineer, but you replace her with Mark the engineer, you may find some differences in how they work but that their similar skill set allows them both to accomplish the required task. But if you lose an engineer and ask the conveyor belt operator to fill in, what's going to happen? Or what happens if instead of a range of specialties like engineers, conveyor belt operators, woodworkers, welders, and technicians, you just had every position staffed by sales reps? That's when the factory stops functioning well, signals get crossed, and things break down. In the same way, when you lack diversity in your gut microbiome, mistakes happen in those five major areas: immunity, metabolism, hormones, cognition, and gene expression. It's all interconnected, but at the heart of it is your gut microbiota.

We use the term "dysbiosis" to refer to the loss of harmony and balance within the gut. Damage or microbial disruption causes you to lose diversity and, in the process, see a higher proportion of inflammatory microbes emerge. In other words, the good stuff falls to the wayside, making more room for the not-so-good stuff to flood your gut. This is problematic because now the colon wall is no longer protected by a healthy community of anti-inflammatory bugs, and the result is damage to the tight junctions holding the colon wall together and an increase in intestinal permeability—some call this "leaky gut"—that leads to the spillage of something called bacterial endotoxin into the bloodstream. This bacterial endotoxin jumps on the vascular superhighway throughout the body, and wherever it goes, it sets a fire (better known as inflammation). It's bad news!

Bacterial endotoxin is produced by evildoer bacteria like *E. coli* and *Salmonella* and promotes inflammation that can range from smoldering and low-grade all the way up to life-threatening sepsis, shock, and multi-organ failure.

Bacterial endotoxemia has been linked to a myriad of diseases including autoimmunity, obesity, coronary artery disease, congestive heart failure, type 2 diabetes, Alzheimer's, alcoholic hepatitis, nonalcoholic fatty liver, osteoarthritis...I could keep going.

Sounds terrifying, but don't be scared. The light always drowns out the darkness. Let me give you an example. There's a bacteria known as *Clostridiodes difficile*, formerly known as *Clostridium difficile* (yes, like Prince and Puff Daddy, apparently bacteria change their names, too), and often called *C. diff* for short. *C. diff* is a pathogenic bacteria that can exist in the colon, even in those who are healthy and living their best lives. In this setting, the healthy gut bacteria outnumber the troublesome *C. diff* and are able to suppress it. Light outshines the darkness.

But if the gut is damaged and there aren't enough good guys, *C. diff* multiplies, becomes stronger, and causes colitis (severe inflammation of the colon) with abdominal pain, fever, and explosive blood-drenched diarrhea. It's not pretty. This can progress to sepsis, a life-threatening response to infection that can rapidly take even the healthiest of lives. When this is the case, emergency surgery to remove the entire colon may be needed as a last-ditch effort to get the infection out and save the person's life.

When I was in medical school in the early 2000s, we *only* saw *C. diff* in hospitalized patients who were taking antibiotics. In retrospect we understand that napalming the gut with antibiotics decimates the good bacteria, allowing the antibiotic-resistant *C. diff* to rise up and dominate. Back then we didn't fully understand this, so we tried to treat the *C. diff* infection with, you guessed it, another antibiotic. This worked for a while, but by around 2010 we were seeing more and more cases of antibiotic failures. We also were seeing *C. diff* pop up in a new group—young people who had never been on antibiotics and had never been in the hospital. Things were changing so quickly that most of what I was taught in medical school was outdated just a few years later. As antibiotic effectiveness dwindled, we became increasingly desperate as a medical community. Some people were requiring long-term treatment with antibiotics, while the less fortunate were losing their colon or their life.

But remember, the light drowns out the darkness. So in our time of desperation, modern medicine turned to the most bizarre and humbling of places —human stool. That's not a typo, folks! Yes, we used poop as our treatment. It's called a fecal transplant, and it's not as novel as it may seem. The earliest reports are from ancient China more than fifteen hundred years ago. Turns out, when you transfer the fecal microbiota of a heathy person into the colon of an extremely sick person—or, in this specific example, when you douse the *C. diff*

with healthy poop—this vicious, drug-resistant infection reacts like the Wicked Witch of the West after Dorothy threw the bucket of water on her. The *C. diff* cries, "I'm melting, I'm melting," and the person is cured—not just better, but *cured*—in one or two days. I told you, the light drowns out the darkness. I'd call it a miracle, except miracles aren't supposed to be reproducible.

So what is it about a fecal transplant that makes it so special? It's actually pretty simple: You are restoring balance to the gut microbiota. You're putting the right bacteria back to work in the factory. When you do that, they do their job and immediately dominate and suppress the pathogenic *C. diff*, just like we previously described happens in someone who is colonized but doesn't have the infection.

"But isn't my stool just waste from food digestion?" you may be asking. Nope. Sixty percent of the weight of your stool is actually bacteria, both good and bad. Sixty percent! It's a snapshot of what your gut microbiota looks like. Not a perfect snapshot, but it's essentially a blend of bacteria from throughout the colon. Even if you fast, you'd still produce stool because your gut microbiota is constantly replicating and turning over.

We all love a feel-good story, right? The comeback of the century, the millennium even, is our stool. What was the least valuable thing on the planet ten years ago has become the savior of modern medicine. People say, "Food is medicine." It's true, but "Poop is medicine, too!" For generation after generation we disparaged it with poop jokes when we should have been celebrating it, or at least giving it a respectful tip of the cap. We didn't realize that our stool was the chariot carrying our celebrated gladiator, the gut microbiota. I'm not exaggerating; I sincerely believe our bowel movements should be the sixth vital sign. Body temperature, pulse, respiratory rate, blood pressure, oxygen saturation, and last (but not least) bowel movement quality. It really is a powerful window into our health.

My point here is that balance is absolutely critical to the gut flora and to every part of your body that operates in communication with it. All those years that we were trying to destroy the bad guys, all we needed to do was empower the good guys. When that balance is in place, your gut microbiota is really, really good at taking care of you. So powerful are the organisms in your gut that even in their "waste" form they can heal someone who's deathly ill.

There's no need to live in fear of the darkness when this book will help you create the light. Rather than trying to destroy the bad guys, let's work together to empower the good guys, restore balance to our command center, and allow the thirty-nine trillion workhorses to naturally enhance our immune system, metabolism, hormonal balance, cognition, and gene expression.

The awesome power of our gut microbiota for total body health

A healthy, diverse gut microbiome does so much more than just suppress pathogenic bacteria, process our drugs, and help us to process our food. It operates as the command center for all five axes of human health. It's bordering on science fiction, but it's absolutely true. I totally believe that all health and disease starts in the gut. The awe-inspiring power in our microbiota makes me reconsider my place on this planet. We, too, are a part of nature's balance, and inside us is this community that we need just as much as it needs us—we're better together! And when we take care of them, they take care of us.

SYMPTOMS ASSOCIATED WITH DAMAGE TO THE GUT MICROBIOTA (DYSBIOSIS)	
INTESTINAL	EXTRAINTESTINAL
Abdominal pain or cramping	Weight gain
Gas	Fatigue
Bloating/abdominal distension	Brain fog
Food sensitivities	Difficulty concentrating
Food allergies	Mood imbalance
Diarrhea	Anxiousness
Constipation	Skin breakouts
Mucus in stool	Joint pains or muscle aches
Nausea	Weakness
Indigestion	Bad breath
Heartburn/reflux	Sinus congestion
Belching	Shortness of breath/wheezing

Insights into the immune system from a toddler's diaper

While most of us are stunned by the emergence of human waste as actual medicine, someone who would probably not be so surprised by this revelation is Professor David Strachan, an epidemiologist at the London School of Hygiene and Tropical Medicine. In 1989 Strachan proposed the hygiene hypothesis upon observing that infants born into a household with more siblings were less susceptible to eczema and allergic rhinitis. You may have heard of his hypothesis—it's the theory that excessive cleanliness is behind the explosion of allergic and autoimmune disease. It's why some families encourage their kids to play in the dirt to benefit their immunity!

Professor Strachan's observations were a good start. But modern science is now showing us that we need to take it a step further. The true problem is not so much excessive cleanliness as it is damage and disruption of the healthy gut microbiota. As I mentioned, a full 70 percent of the immune system lives in the gut, separated from our microbiota by a single layer of cells that is a fraction of the diameter of a hair and undetectable by the human eye. That single layer of cells acts like a three-foot rickety wooden fence between two house parties—with the immune system at one house and the microbiota at the other. The parties may be separate, but they're not *really* separated. They're deeply intertwined, feeding off each other's energy, sharing drinks and laughs, in constant communication with one another. Evidence has shown us that the microbiota helps foster proper development of immune cells, identify invaders, get immune cells to the needed location, and then enhance their infection-fighting power. A healthy gut microbiota translates into an empowered, strong immune system that optimally functions to identify a threat when it exists—infectious or even malignant—and eradicate it. You can't separate the gut microbiota from the immune system. If you hurt one, you will hurt the other.

Evidence for the gut-immune relationship comes from the autoimmune and allergic epidemic. These conditions are indeed exploding around the world. Asthma, allergic rhinitis, and eczema are examples of allergic diseases, where the immune system aggressively attacks a benign outside stimulus. From 1960 to 2000 the incidence of asthma increased at least tenfold in the Western world. A similar, disturbing rise in autoimmune diseases has occurred in parallel. Type 1 diabetes, multiple sclerosis, and Crohn's disease are autoimmune diseases, where the immune system decides our own body is the enemy and goes on the attack. Since the 1950s, the rates of type 1 diabetes, multiple sclerosis, and Crohn's disease have each risen 300 percent or more.

Allergic and autoimmune conditions are much more common in industrialized nations than in agricultural ones. For example, the number of new cases of type 1 diabetes in Finland per year is 62.3 per every 100,000 children, compared with just 6.2 in Mexico and 0.5 in Pakistan. You could argue that that's due to genetic differences, but they also appear to increase in prevalence within countries as they become more industrialized. Croatia, for example, has seen an increase in Crohn's disease from 0.7 per 100,000 (in 1989) to 6.5 (in 2004), coinciding with modernization, and Brazil saw Crohn's disease and ulcerative colitis increase by 11 and 15 percent *every year* from 1988 to 2012, respectively. Doctors from these countries have to come to the United States to learn about these conditions because the problems didn't exist in their countries until recently, so they don't know how to care for their patients.

Evidence suggests that our gut microbiome not only changes with allergic and autoimmune disease, but it may predict or even cause these immune system conditions. For example, researchers analyzed the dirty diapers of three hundred

toddlers at three months of age. They discovered that specific changes in the gut bacteria this early in life already predicted which children would subsequently develop asthma years later. But to prove that the gut microbes were actually causing the asthma, they transferred the stool from the diapers into special germfree mice. Yes, they did a fecal transplant from a human into a mouse. And to be clear, the human stool wasn't from a person with asthma. Instead, it was from a three-month-old's poopy diaper who was felt to be at risk for developing asthma. So what happened? Well, the mice all developed inflamed lungs, indicative of asthma.

We evolved to have an immu ne system to protect us from infection, the leading cause of death up until just a century ago. Our gut microbes have been a part of that evolution from the very beginning, and as a result they play a critical role in immune function. Yes, this can mean that damage to the microbiota puts us at risk for immune dysregulation, manifesting with autoimmune and allergic illness. But on the flip side, a strong microbiome empowers the 70 percent of neighboring immune cells for optimal function to protect us from infection and malignancy. When we take care of our microbes, they take care of us.

IMMUNE-MEDIATED CONDITIONS ASSOCIATED WITH DYSBIOSIS

Type 1 diabetes mellitus

Celiac disease

Multiple sclerosis

Asthma

Food allergies

Eczema

Seasonal allergies

Eosinophilic esophagitis

Dermatitis herpetiformis

Psoriasis/psoriatic arthritis

Scleroderma

Chronic fatigue syndrome

Antiphospholipid syndrome

Restless leg syndrome

Sjögren's syndrome

Rheumatoid arthritis

Ulcerative colitis

Crohn's disease

Microscopic colitis

Ankylosing spondylitis

Lupus

Interstitial cystitis

Autoimmune hepatitis

Primary biliary cholangitis

Primary sclerosing cholangitis

Sarcoidosis

Fibromvalgia

Guillain-Barré syndrome

Behcet's disease

Kawasaki disease

ANCA-associated vasculitis

The Microbiome Code for personalized food processing

The diet industry has for a very long time told us that weight gain is within our control if we could only have the self-control to do enough

CrossFit/Zumba/yoga in combination with the right diet, whether that's Paleo, SlimFast, Weight Watchers, Keto, or juice cleanses. But what if it all comes down to the bacteria in our guts? That's what researchers recently set out to discover when a report emerged of a young woman, just thirty-two years old, who underwent a fecal transplant for a chronic *C. diff* infection. What ensued got both scientists and the press into a tizzy. In the sixteen months after her fecal transplant she had dramatic, unintentional weight gain—going from 136 pounds up to 170 pounds. Her body mass index increased from very nearly a normal, healthy weight (BMI of 26) up to overt obesity (BMI of 33). Nothing else in her life had changed: not her diet, not her stress level, not her level of physical activity. Just the fecal transplant.

Normally weight gain of this kind wouldn't be such a big deal except that for the first time in humans we had illustrated an idea that has been shown repeatedly, time after time, in animals: that our gut microbiota has extreme control over the way that we process our food and our metabolism. So much control, in fact, that the same food can yield totally different effects depending on the gut microbiota involved.

One study took identical human twins who were genetically the same but one was obese and the other thin. Researchers took stool from the twins and transferred it into germ-free mice, and the mouse that got the lean twin's stool stayed lean and the one who got the obese twin's became obese. Despite the fact that both mice were fed the exact same diet and exact same calories, they found that the body type transferred.

So many of us have spent years working really hard to lose weight—exercising, eating well, doing all the things experts (and the not-so-expert) are telling us to do—and now we understand why that might not be working. We need a little help from our friends. You can give the exact same food to two different people and the differences in their microbiota will determine what they ultimately get out of that food. Mind blowing, isn't it?

But it doesn't stop there. Our microbiota doesn't just regulate our metabolism in a calories-in, calories-out sense. It is also deeply intertwined with our endocrine system, affecting our response to insulin. After a meal your blood sugar level rises and the cells in your pancreas respond by releasing insulin into your bloodstream to lower your blood sugar. If you have diabetes, you have an inadequate supply of insulin to control your blood sugar, so it stays elevated. Type 1 diabetics have an autoimmune disease that destroys the part of their pancreas that produces insulin. As we discussed before, autoimmune type 1 diabetes connects back to gut health. On the flip side, type 2 diabetics have a fully functioning pancreas running on overdrive but they are unable to produce

enough insulin to keep up with the body's demands. This is a result of insulin resistance, meaning more insulin has to be produced to achieve the same effect. Insulin is a growth factor. What do you think happens when you promote increased growth in the body? Type 2 diabetes has been linked to esophageal, colorectal, pancreatic, hepatocellular, renal, breast, endometrial, and urinary cancer.

Cancer stinks. Literally.

Did you know that dogs can actually smell colorectal cancer? They were 98 percent accurate in detecting colon cancer from a series of stool specimens. And you thought they were just sniffing backsides for fun? Give man's best friend some credit! Colorectal cancer is the number two cause of cancer death in America, and emerging studies are showing that specific bacteria in the colon play a role in its development, which may explain how they're able to do this. Alterations in gut bacteria have been associated with a number of emerging cancers: breast, gastric, esophageal, pancreatic, laryngeal, liver, and gallbladder carcinomas. Ongoing research is being performed to determine the degree for which the bacteria are actually causative.

We've already shown that your gut bacteria differentially regulate your response to food and can affect weight gain. How about your body's response to insulin? In an absolutely fascinating study, adult men with metabolic syndrome and insulin resistance received a fecal transplant from a lean donor. This led to a change in their gut microbiota associated with improvements in insulin sensitivity and a lowering of their blood sugar. Unfortunately, the effect only lasted a few weeks because they didn't change their diet, so the new microbiome couldn't be sustained.

METABOLIC CONDITIONS ASSOCIATED WITH DYSBIOSIS

Obesity
Nonalcoholic fatty liver disease
Type 2 diabetes
Coronary artery disease
Hyperlipidemia
Chronic kidney disease
Gout
Nonalcoholic fatty liver disease
Alcoholic steatohepatitis
Acute alcoholic hepatitis
Alcoholic cirrhosis
Chronic pancreatitis
Chronic pancreatitis

But you don't need to have diabetes to show an influence from your gut microbiota! In another study, researchers discovered that foods had a very different blood sugar response in each person. The gut microbiome was responsible for this unique response. Using solely an individual's gut microbial profile, they were able to predict which foods would cause less of a blood sugar spike. It was different for every person. In other words, you have a unique, completely personal response to the food you eat that is a reflection of the makeup of your gut microbiota. Good ole bio-individuality, my friends!

Discard all (or most) of what you've ever learned about metabolism, diabetes, and weight loss. It's a loss of diversity in the gut microbiota, increase in pathogenic bacteria, and low-grade inflammation from bacterial endotoxin that is associated with diabetes, weight gain, and obesity. There is also evidence to suggest that our gut microbes control the release of hormones that regulate appetite and energy balance, such as leptin, ghrelin, GLP-1 (glucagon-like peptide-1), and peptide YY. Increased microbial diversity in your gut equals improved metabolic health and insulin sensitivity.

So when we properly nourish our gut microbiota, we are rewarded with microbes that extract everything that we need from our food and nothing that we don't, signal us when to stop eating so we don't overdo it, and promote a natural metabolic balance that doesn't require us to count calories in order to maintain a healthy weight. A healthy microbiome makes it happen effortlessly.

It's not your fault you're hormonal!

The influence of the gut microbiota on the endocrine, or hormonal, system extends far beyond diabetes. The gut is literally the largest endocrine organ in the body, deeply involved in securing hormonal balance. Take estrogen, for example. Gut microbes secrete the enzyme β-glucuronidase, which activates estrogen so it can do what it's supposed to do throughout the body. Imagine the flow of estrogen as a dammed river, and the microbes have their hand on a lever that controls the floodgates. When working just right, estrogen levels are delicately flowing in that sweet spot—not too much, not too little—to give the good stuff: stronger bones, lower cholesterol, clear skin, fertile ovaries, and a voracious sexual appetite. A healthy gut microbiota does that for you.

But what happens if you're loose on the floodgate? The body gets flooded with excess estrogen, which has been associated with endometriosis, endometrial hyperplasia, and breast and endometrial cancer. No surprise, we find damage to the gut microbiome in association with each of these conditions.

Alternatively, if the microbiota are too restrictive on the floodgates, you get an estrogen drought. Polycystic ovary syndrome (PCOS), which is characterized by menstrual irregularity, abnormal hair growth, weight gain, acne, and insulin resistance, is a condition that is characterized by estrogen dysregulation. But

PCOS is a true loss of hormonal balance where there is an increase in androgens (or testosterone) in addition to altered estrogen. As it turns out, androgen production is also mediated in part by the gut microbiome. *Clostridium scindens* is a gut bacteria known to convert glucocorticoids (think cortisol) into androgens in the gut. So if you have too much *C. scindens* you'll have androgen excess. A healthy gut microbiome keeps our estrogens and androgens in balance, while dysbiosis has been found in association with PCOS.

It's quite clear that there's a gut-hormone axis, but let's take it a step further. It appears that there may be a gut-testicle axis, too. Fellas, listen up! Remember the model for dysbiosis? Damage to the gut microbiota causes increased intestinal permeability (leaky gut) and allows release of bacterial endotoxin into our system. Well, bacterial endotoxin leaves the gut and travels through the blood to the testicles, where it wreaks havoc. Science says it causes loss of testosterone and sperm production. It's kind of like gut health—induced "shrinkage." (Sorry for that mental image.) Not to mention the impact on mental health, which often includes loss of self-esteem and confidence.

But the link between gut health and hormones doesn't stop there. Have you ever been on a date and found yourself either super attracted to or turned off by your date based upon their smell? It's been demonstrated in animal studies that bacteria control the release of guaiacol and other phenolic compounds that produce our odor profile. These are actually pheromones that play a role in sexual attraction and mating behavior. In other words, our microbes are actually our matchmakers in waiting. What's interesting is that different microbes release different smells. The healthy microbes produce a fragrance worthy of Aphrodite, while the pathogenic bacteria drop a stench bomb that keeps people at their distance. Not every microbe makes a great wingman!

And while we're on the topic, have you ever wondered why we kiss? It's actually an expression of love to share your microbiome with another person. Every time we kiss we exchange eighty million microbes with our partner, and vice versa. There is speculation that kissing may have evolved as a way of sampling a potential lover's microbiome for compatibility. Yes, we are human. But everything that we do as humans involves our microbiota one way or another, even the way we love one another.

ENDOCRINE AND HORMONAL CONDITIONS ASSOCIATED WITH DYSBIOSIS

Endometriosis Polycystic ovary syndrome (PCOS) Endometrial hyperplasia Hypothyroid Breast cancer Endometrial cancer

The second brain's power over the first brain

Upstairs is your brain. Downstairs is your gut. Most would think of these organs as two very separate entities, with the brain operating as central command and the gut as what, well, makes you poop. In the hierarchy of things, clearly the brain would come out on top. But recently that line of division has become a bit blurred because we've discovered that the gut is a separate nervous system known as the "second brain" or the "enteric nervous system."

This might be the first time you're making this connection, but brain health actually starts in the gut—and that's because they are in constant communication with each other. Literally right this second, there are over five hundred million nerves in your intestines sending feedback to your brain through the vagus nerve. That's five times more nerves than you'll find in your spinal cord. That is a lot of information!

That's only the beginning. Gut microbes are able to communicate with our brain using the immune system and through the release of neurotransmitters, hormones, and signaling molecules. Neurotransmitters like serotonin and dopamine play a powerful role in our mood, energy levels, motivation, and sense of reward. Gut microbes both produce and respond to neurohormones like serotonin, dopamine, GABA (γ-aminobutyric acid), and norepinephrine. In fact, 90 percent of serotonin and 50 percent of dopamine are actually produced in the gut. Precursors of serotonin and dopamine are able to cross the blood–brain barrier and alter our mood or behavior. Taken in sum, intestinal serotonin is able to influence gut motility, mood, appetite, sleep, and brain function.

That's just serotonin. Your gut produces more than thirty neurotransmitters. In Chapter 3 we will discuss one of the major ways that your gut can improve brain health—through short-chain fatty acids. A healthy gut microbiome is able to extend its influence across the blood—brain barrier to keep our mind sharp, our energy level high, and our mood relaxed. But on the flip side, damage to the gut microbiome has been associated with Alzheimer's, Parkinson's, migraine headaches, chronic fatigue, autism, and ADHD.

With the gut acting as home base for these neurotransmitters, you can see how mental health conditions like depression and anxiety emerge when there's a problem in the gut. I see it every day in my clinic. For instance, there is tremendous overlap between irritable bowel syndrome (IBS) and depressed

mood and anxiety. And for the longest time, we mislabeled these patients. We did not understand that at the root of their anxiety or vicious mood swings could be a gastrointestinal issue. It's now clear that when you have alteration or damage to the gut bacteria, you alter serotonin balance, and thereby alter both mood and gut motility. The end result is an IBS patient with anxiety. One of my mentors, Dr. Douglas Drossman, has for decades been at the center of the research to clarify this important connection.

We've also learned that IBS patients have altered function of the five hundred million gut nerves. It's what we call "visceral hypersensitivity," meaning that they will have intestinal distress, nausea, or abdominal pain in response to triggers that most people don't even notice. For example, IBS patients often *think* they produce more gas, but they actually don't. Instead, they produce the same amount of gas but they just react to it differently—due to increased visceral hypersensitivity.

Even our behavior is influenced by our gut. There is evidence to suggest that gut microbes control our cravings. Have you ever gone away on vacation for a few days and can't wait to get home and have one of your old stalwart meals? That's your microbiome speaking to you. In fact, gut microbes may put their well-being over ours by manipulating our eating behavior—some of them want us to eat sugar and fat, which are bad for us but good for them! They can promote their fitness at the expense of ours. You know how some people love chocolate (slowly raises hand) and others can take it or leave it? Well, we've found that "chocolate-desiring" people actually have different microbial metabolites in their urine than do "chocolate-indifferent" individuals, despite eating identical diets. Those microbial metabolites may be the signal that drives you to crave chocolate, which begs the question: Are we merely zombies, doing the will of our bacterial overlords? Are we pseudo-possessed by the bacterial demons in our gut? MUAAAHAAHAAA!

Okay, now that I've got you all bug-eyed and freaked out, let's keep in mind that you are a creature of free will. Remember, you get to choose what you put in your mouth and swallow, and those choices are what will ultimately determine health in our microbiome and throughout our body. More important, your cravings and taste buds can change and you can train your gut to fall in love with things that are actually good for you. Following the plan in this book will allow you to break free once and for all—it's as though we're performing an exorcism from your gremlin-gut microbes and replacing them with guardian-gut angels.

Alzheimer's disease
Parkinson's disease
Schizophrenia
ADHD
Amyotrophic lateral sclerosis
Chronic fatigue syndrome
Restless legs syndrome

Anxiety
Depression
Autism spectrum disorders
Bipolar disorder
Migraine headaches
Fibromyalgia
Hepatic encephalopathy

How the genetic game was turned on its head by microbes

Since 1953 when Professors James Watson and Francis Crick described the structure of DNA, it seemed that genetics held the keys to understanding human health and disease. Nearly fifty years later and after a massive coordinated international effort among one thousand scientists across twenty institutions, the Human Genome Project culminated in 2000 when the human genetic code was unlocked for the first time. This was as big as it gets from a scientific perspective.

Sadly, for all the hype, the returns on this breakthrough have been incredibly disappointing. You've no doubt noticed that we have not resolved all medical problems since the year 2000. Why did genetics alone not heal us? Well, we have since discovered by studying identical twins that less than 20 percent of disease is based on genetics. Yes, there are some, such as cystic fibrosis and Down syndrome, where if you have the genes then you get the disease. But taking all chronic disease across the board, more than 80 percent of your disease risk is determined by your environment and exposures during your lifetime. There's a silver lining here. You are not the victim of the genes you were born with. You may have certain predispositions—we all do. But you ultimately control your health destiny, in large part through the effects of your diet and lifestyle on your microbiome.

In a letter to *Science* magazine in 2001, Professor Julian Davies warned that decoding the human genome was not enough to understand human biology because there are more than a thousand bacterial species living in and on the human body and they are critically affecting human life. We previously noted that there are more bacteria than cells in the body, but let's take it a step further and talk genetics. More than 99 percent of your DNA comes from microbes. Yes, your genes are less than 1 percent human! Further, our human genomes are virtually identical—up to 99.9 percent the same. But our microbiomes may be as much as 90 percent *different* from one person to the next.

Beyond holding the cards on a genetic monopoly, our gut microbes also exert

tremendous power over the expression of your genes through something called epigenetics. Imagine your gut microbiota as controlling a light switch and the wiring behind the wall is your genetic code. The gut microbiota is not changing the wiring behind the wall, but it can turn the lights on or off. You can't change your genetic code, but you can effect which genes get turned on or off. That is insanely powerful, if you think about it.

An example of this concept of epigenetics is celiac disease. Celiac disease is a condition in which the immune system decides that gluten is the enemy. Gluten is a protein found in wheat, barley, and rye. Every time someone with celiac disease consumes gluten, the immune system lashes out and attacks their intestine, causing inflammation that shows up as diarrhea, weight loss, and abdominal pain. This is incredibly dangerous because people with celiac disease who continue to consume gluten can develop small intestine lymphoma, which is nearly universally fatal.

Celiac is a genetically motivated disease. This means that you must carry the gene for celiac to get it. If you don't have the gene, you can't have the disease. About 35 percent of Americans carry the gene for celiac but only 1 percent manifest the disease. In the last fifty years we've seen a 500 percent increase in celiac disease. So what explains the rapid increase? Clearly not a shift in genetics during that brief period. So what is it that determines who ultimately expresses the gene? Dr. Elena Verdú from McMaster University in Canada showed us through a series of eloquent studies that there are three criteria that must be met to develop celiac disease: 1) presence of the gene, 2) exposure to gluten, and—you guessed it, 3) alteration or damage to the gut microbiota.

We thought that cracking the human genome would produce major breakthroughs in medicine because we thought that human health was primarily determined by genetic makeup. Nope. We are a superorganism with a genetic makeup dominated by the invisible microbes within us. And this is actually a good thing! Rather than worrying about the 0.5 percent of your DNA that you simply cannot control, let's optimize our microbiome through diet and lifestyle and enjoy the positive effects it has on 99.5 percent of our DNA plus our epigenetic expression.

It's time to transform your health from the inside out!

What once was dismissed as poop is now the star quarterback for human health. Yes, it can be intimidating that most modern diseases have been connected to damage to the gut microbiome. But remember, we are not helpless victims

stricken with disease. We have the power of science on our side, and for the first time in human history we actually know enough about the gut microbiota to understand it and start to use it to our advantage. In this book I will use diet and lifestyle to rebalance your gut microbes. You'll see your digestion, immune system, metabolism, hormones, cognition, and gene expression become optimally aligned, and you'll transform into the microbe-empowered superhuman that you are.

To view the 55⁺ scientific references cited in this chapter, please visit me online at www.theplantfedgut.com/research/.

Twenty-First-Century Life: Overfed, Undernourished, and Hyper-medicated

Our modern lifestyle is destroying our gut AND our health

When I first met Kristen she sat with her shoulders slumped and her brow creased with worry. She came in to see me, hoping I'd address the chronic abdominal pain and diarrhea she'd been struggling with for years, but when I asked her to tell me more about what was going on, she launched into a litany of other concerns: "I feel sick all the time, Dr. B. I'm overweight, anxious, and depressed. I've got migraines and seasonal allergies so bad that I sometimes take antibiotics three or four times a year for sinus infections. I was also recently diagnosed with polycystic ovary syndrome." She took a deep breath. "And that really scares me." She told me about the slew of medications her various doctors had her on, and that she thought she may have sensitivity to gluten and beans and has eliminated them as part of doing the Paleo diet. Unfortunately, she wasn't feeling better so she was thinking about trying the Keto diet because she had several friends doing it and they were losing weight.

Kristen needs a plan that actually works. She knows she wants to fix her gut, but the approach of "eliminate symptoms by eliminating the foods that cause symptoms" hasn't worked for her. After multiple experts villainizing their poisons du jour—gluten, grains, phytates, lectins, carbs—Kristen misses the feeling of simply enjoying a meal. She wants to eat food that she loves, eat it in abundance and without restrictions, and not be constantly running away from food monsters. The good news for Kristen and everyone reading this is that I

know exactly what you need to heal your gut.

Patients like Kristen are incredibly common in my gastroenterology clinic. Every day I meet people with stories like hers: people with complex medical problems, even at a very young age, coming to my clinic with digestive issues like irritable bowel syndrome (IBS), acid reflux, chronic diarrhea, abdominal pain, gas and bloating, or constipation. Often several at once. And what's shocking is how many *also* have immune-mediated disorders like type 1 diabetes, celiac, multiple sclerosis, Crohn's disease, ulcerative colitis, or rheumatoid arthritis, and are often coping with depression and anxiety, hormone imbalances, and weight gain, too.

It's not just in my clinic—nationwide, the statistics back this up. As a country we are fatter, sicker, and more heavily medicated than at any other time in human history. More than 72 percent of Americans are overweight—that's essentially three in four people—and 40 percent of us are carrying thirty or more pounds of extra baggage around our waist and hips. For the first time in over a hundred years, the U.S. life expectancy just dropped for the third year in a row. The last time this happened was from 1915 to 1918—when U.S. involvement in World War I and literally the worst influenza pandemic in modern history combined to kill nearly one million Americans. Last I checked we weren't conscripting an army for global battle or ravaged by a plague, so what's our excuse?

Despite advances in medicine and our spending more money on health care than any country in the world by far, our life expectancy is actually contracting. And now 60 percent of Americans age twenty or older are using prescription drugs. In fact, the percentage of us using five or more medications has doubled in the last twelve years. Yes, modern medicine has given us some wonderful treatment options—believe me, if I get sick, I want one of my esteemed colleagues caring for me—but we can't ignore the downsides of our love for quick-fix pills and overreliance on medications. Consider that in 2014 alone, nearly 1.3 million Americans sought emergency room treatment for adverse drug effects, and about 124,000 people died from them.

For me, and I'm guessing for you, too, since you picked up this book, these aren't just numbers on a page. Behind the numbers are real people—people like Kristen, who need more than another diagnosis, an additional script to fill, or yet another fad diet to follow based on bad science. If you're struggling with digestive issues, autoimmune illnesses, mental health, heart health, hormonal imbalance, weight gain, diabetes, or any related concerns, including side effects from taking several medications, I hear you and I see you. Many, many people sit across from me day after day in my clinic, often with tears in their eyes, who

are struggling, too, and who need real help now. I have a fire in my heart to find the solution for these ailments that goes beyond a patch on the hole. We need to get at the root cause to reverse these diseases and prevent new ones.

The trend in our life expectancy isn't bad luck or a mere coincidence. Did you know that at least seven of the top ten causes of death—the things that are lowering our life expectancy—are caused by lifestyle? In order, they are: heart disease, cancer, chronic obstructive pulmonary disease (COPD), stroke, Alzheimer's, diabetes, and kidney disease. The problem is caused by lifestyle and yet we completely (and inexplicably) ignore lifestyle as a therapeutic option, choosing medications as our primary treatment option. By ignoring the cause we will never get to the root of the problem.

Sadly, the pharmaceutical industry has hijacked our health care system. Big Pharma runs the studies, they control the research, and here we are with three in five U.S. adults taking prescription drugs, 269 million prescriptions for antibiotics per year, 115 million proton pump inhibitor prescriptions, and 30 billion doses of nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and naproxen. Meanwhile, obesity, and all the health issues that stem from it, seems to be becoming the new normal. On so many levels—our health, our food, even how often we poop—we are normalizing abnormal.

A medication treats symptoms. It artificially props up something that's broken. It doesn't prevent and it certainly doesn't treat root causes. It's time for us to stop waiting for the bomb to drop when our health deteriorates and we desperately need "sick care," and instead embrace true "health care" by preventing our problems with lifestyle medicine.

So when patients like Kristen come to me with a long list of symptoms, asking, "Doctor, why is this happening to me?" I don't just see the digestive issues they've come to me for; I see a web of interconnected symptoms. I see digestive concerns intertwined among multiple systems within the body: gynecologic, endocrine, neurologic, the immune system, even mood. And I know that the answer isn't cutting out gluten or beans or simply adding an additional medication for IBS—those are just covering up symptoms. The answer is at the root of it all—the place where it's all connected is in the gut.

Modernization and the origins of modern epidemics

In the late nineteenth century the average life expectancy was just forty-seven years and the top causes of death were infections. Infectious diseases such as smallpox, cholera, diphtheria, pneumonia, typhoid fever, tuberculosis, typhus,

and syphilis were rampant. Heart disease and cancer were there, but a small problem compared to infections. Thanks to Louis Pasteur's discovery of what we now call modern germ theory, we finally understood that behind the top causes of death is a germ. In response, bacteria became public enemy numbers one, two, and three. So what are you going to do about it? Well, we did what humans have always done at every stage of human history—we innovated to find a solution to the problem in front of us. As we entered the twentieth century we started adding chlorine to our drinking water, developed vaccines, improved sanitation, and began metal canning and early preservatives. Good news, it was working: polio was on the brink of extinction, and many other infectious diseases, including smallpox, were on the decline. Then penicillin was discovered by Sir Alexander Fleming in 1928 and it became commercially available in 1945. Our life expectancy rapidly jumped over the coming years, and in 1969, U.S. Surgeon General William Stewart confidently declared to Congress that it was time to "close the books on infectious diseases."

Anything that good is going to get overutilized. We doubled down on this approach. In 1928 women were encouraged to "disinfect" with Lysol douche—yes, the same Lysol that today is used to scour toilets and floors. After World War II, we developed synthetic herbicides, fungicides, and insecticides. We added fluoride to the water. We discovered that antibiotics and synthetic hormones accelerated livestock growth, so we started pumping our livestock with both. We created antibacterial soaps and astringents and industrial cleaning products. If bacteria were the enemy, we were basically nuking the crap out of them. There's no question: We were winning this war.

And then heart disease and cancer emerged en masse.

Meanwhile, technology was developing on all fronts, for better or for worse. The number of food additives skyrocketed to more than ten thousand, the vast majority of which had never had human testing because they got approved under a loophole called GRAS (Generally Recognized As Safe, pronounced *GEE rass*). Remember this acronym—GRAS—because I'm coming back to it in a minute. Additionally, the pharmaceutical industry exploded and now more than fifteen hundred drugs were approved by the FDA, which explains why there was no nutrition training in medical school—we were spending all of our time learning about these drugs, their uses, and their side effects. Plastics, which contain bisphenol A (BPA), known to have estrogen-like effects, were invented and began to be used abundantly—in everything from food storage to floss and from clothing to baby toys. We developed planes, trains, automobiles, and motorized scooters to reduce our mobility. Advances in television, computers, smartphones, and video games made it easy to forgo exercise and hijack our

brains and our daily sleep-wake cycles. Why read a book when watching the movie only takes ninety minutes? Why build a fort and imagine a game when a video game will do all the creative heavy lifting for you? Why go to sleep when the sun goes down when you can read Twitter all night long?

In 1994, genetically modified organisms (GMOs) first arrived in our stores. Today more than 80 percent of all genetically modified crops grown worldwide have been engineered to be herbicide tolerant. What this means is that the genetically modified plant survives being sprayed with herbicides while the surrounding plants (and potentially other life) all die. For example, Monsanto, the leading developer of GMOs, created a range of crops with a genetic trait that makes them impervious to the herbicide glyphosate, specifically soy beans and corn. We need massive amounts of soy beans and corn to support animal agriculture in the United States. This is a boon for genetically engineered farming as yields of corn, cotton, and soybeans are said to have risen by 20 to 30 percent through the use of genetic engineering. Meanwhile, the use of toxic herbicides, such as glyphosate in Roundup, has increased fifteenfold since GMOs were first introduced. That's good for business if the bottom line is enhancing your bottom line. In March 2015, the World Health Organization determined that the herbicide glyphosate is "probably carcinogenic to humans." A more recent study found a 41 percent increase in non-Hodgkin's lymphoma in those with high exposure to glyphosate. Adding credence to this association, in a prospective cohort study of more than sixty-eight thousand French volunteers, those who primarily ate organic foods were less likely to develop non-Hodgkin's lymphoma and postmenopausal breast cancer compared to those who rarely or never ate organic foods.

Why I buy organic whenever possible

By definition, if a food is certified organic it is not genetically modified and was not sprayed by glyphosate. I don't think this is the only reason to buy organic produce, however. I view it as an investment in my health, our family's health, and the health of our planet. The chemicals being used in modern agriculture aren't affecting only us; they're affecting the health of our soil. If you don't have healthy soil, you can't have nutritious food. Human health starts in the dirt. We need to protect this precious commodity. When you spend your money, you are placing your vote in a way. You are empowering an industry. I, for one, choose to empower our organic farmers and regenerative agriculture. They are healers just as our doctors are. Only with them can we enrich our soil, increase biodiversity, and heal ecosystems large (our planet) and small (your gut). Let's rally behind them and give them the support they deserve.

Let's take a step back for a moment and consider our modern life in the

broader context of human evolution. Since the very first human, the microbes have been a part of our story. Every single human life has been a buddy tale about our relationship with our microbes. We rose and fell together. We coevolved. For most of the three million years we lived in a famished, violent world, exposed to the elements. Life was about survival, and most of us succumbed at a young age to infection, starvation, or bodily injury. We needed to live long enough to procreate and continue our species. If not, we'd go extinct. So our microbes helped us to develop an immune system to fight infection, clotting factors to stop bleeding, and efficient ways to harvest and store energy from our food. For example, the insulin resistance seen in type 2 diabetes is actually a protective mechanism to maintain fuel for the brain in times of starvation. As part of species preservation we evolved a taste for salt, sugar, and fat because in famine those promote survival. We became wired to crave those things.

Now consider the American college kid, lying on the couch all day playing video games, drinking soda, and having pizza delivered. The human experience is radically different in just the last hundred years. We've moved indoors, become sedentary, obsess over electronics, spray everything (including ourselves) with chemicals, and have a limitless food supply that exploits our taste for salt, sugar, and fat. And now the inflammation, clotting, and energy preservation that we needed to keep our species alive is the very thing causing cancer, cardiovascular disease, obesity, and diabetes. What once helped preserve our species has become our fatal flaw.*

And right now, as we speak, our microbes are evolving to adapt to the new environment. Given their central role in human health, we can either passively let them spin out of control with our destructive lifestyle, or we can embrace them as our "secret sauce" for longevity and healthy aging. My goal with this book is to help you shake off the detriments of a twenty-first-century life by engineering your microbiome for health and longevity. In order to do this, we need to pay attention to anything that disrupts the gut microbiota. Let's take a deeper dive into how the things we put into our mouth and swallow—medications and food—affect your gut health.

Modern health care, drugs, and your microbiota

It comes as no surprise that antibiotics absolutely decimate the gut microbiota. Just five days of ciprofloxacin wipes out about a third of gut bacteria and your gut microbiota are never quite the same. Most species recover within four weeks, but some are still absent after six months. In the case of clarithromycin and

metronidazole, the effects are still evident four years after treatment. And just four days of three broad-spectrum antibiotics can permanently destroy nine beneficial species of bacteria. The result of all these antibiotics is a "new normal" microbiome with more antibiotic-resistant microbes that leaves us vulnerable to infection, allergic conditions, osteoporosis, and obesity. I'm sure you recall all the problems we had with antibiotics and *C. diff* infection up until we started using fecal transplant. Pretty disturbing stuff when you consider that there are 269 million antibiotic prescriptions in the United States each year and a recent study suggested that 23 percent of antibiotic prescriptions are flat-out inappropriate while another 36 percent were questionable.

Antibiotics aren't the only medicines causing trouble. In one study, 24 percent of tested drugs altered gut bacteria. For example, proton pump inhibitors increase the risk of small intestine bacterial overgrowth and *C. diff.* Nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and naproxen alter the gut microbiota, destroy the intestinal lining to create ulcers, and predispose to inflammatory bowel disease and microscopic colitis. Oral contraceptives have been associated with the development of both Crohn's disease and ulcerative colitis. Frankly, these are just the tip of the iceberg. There are so many other medicines that I have concerns about, but the studies haven't been done yet.

The SAD diet is literally killing your gut

While medications are huge, let's not ignore the most important change over the last hundred years—our diet.

According to U.S. Department of Agriculture estimates, 32 percent of our calories come from animal foods, 57 percent from processed plant foods, and only 11 percent from whole grains, beans, fruits, vegetables, and nuts. The average American eats twenty-three pounds of pizza, twenty-four pounds of artificial sweeteners, twenty-nine pounds of french fries, and thirty-one pounds of cheese per year. The United States also has the highest meat consumption in the world—about 220 pounds of meat per person per year. We eat meat thirty-two times for every single time a person in India sits down to have it in their meal. Yet there are fad diets out there trying to convince you to double down on this trend. That it's not enough; we need more.

The Standard American Diet (SAD) stands in stark contrast to the people who live in the Blue Zones as described by Dan Buettner. These are the regions of the world where people are living much longer compared to the rest of us. There are five Blue Zones: Okinawa, Japan; Sardinia, Italy; Nicoya, Costa Rica; Icaria, Greece; and . . . *drumroll* . . . Loma Linda, California.

Wait, what? Cali? Yes, right here in our own country lives a group of people who use the same health care and the same food systems and they live ten years longer than most Americans on average. They are also ten times more likely to live to a hundred! Who are these mystery people? They are the Seventh-day Adventists, whose theology teaches them that they will come back to re-inhabit their bodies and therefore they emphasize health and self-care. They have proven that it's entirely possible to be a healthy American.

So here are these five geographic regions scattered around the world, completely culturally distinct, yet there are common themes in the food that they eat. All five are at least 90 percent plant-based. There's an emphasis on seasonal fruits and vegetables, legumes, whole grains, and nuts. Cow's milk is not a part of their diet, and meat is consumed sparingly, using it as a celebratory food, a small side, or a way to flavor dishes. In contrast, the Standard American Diet relies heavily on processed food, meat, and dairy pounded on our poor gut microbes three times a day with snacks and desserts to boot. What's it doing to us? Let's break down the science behind the elements:

Sugars and highly refined carbohydrates

The average American crushes 152 pounds of sugar *and* 120 pounds of grains per year, most of which are highly refined to strip away the fiber, causing them to be rapidly absorbed in the small intestine rather than slowly digested. Think white bread/rice/pasta and sugary cereals. These are not healthy carbohydrates! The result is a dramatic loss of gut microbial diversity and the rise of inflammatory bacteria that love simple carbohydrates. And then we wonder where our sugar cravings come from.

Salt

Processed foods are loaded to the gills with salt. The average American consumes nearly three pounds of salt per year. Three pounds! We only need a few ounces. Anything more has consequences, including in the gut microbiome, where it drives autoimmunity by inducing helper T cells, which can contribute to hypertension.

Chemical preservatives, additives, and colorants

Does it come as a surprise that the ten thousand food additives in our food supply may be destroying our microbiota? Numerous food additives have already been shown to damage the gut microbiota, while more than 99 percent of them haven't been studied. For example, two commonly used emulsifiers—carboxymethylcellulose and polysorbate 80—reduce microbial diversity, induce inflammation, and promote obesity and colitis in mice. Titanium dioxide (TiO)

nanoparticles, found in more than nine hundred food products, worsen intestinal inflammation.

Additives such as these were snuck into our diet through the "Generally Recognized As Safe" loophole. They were GRASed into our diet. Yes, GRAS needs to be used as a verb because that's the only way to adequately describe the careless acceptance of chemicals into our food supply by our regulatory agencies.

Some would argue that if these chemicals are consumed in limited doses they are safe based on animal model studies. I strongly disagree. To GRAS is to assume safety until proven otherwise. That's a huge assumption given that animal models often don't translate to humans. We have no human studies for most of these ten thousand additives, and we definitely don't have long-term studies. Anyone who would claim confidence that these additives truly are safe for long-term human consumption would be doing so without human research to say so. There are ten thousand chances for us to be wrong in our assumption of safety, and it only takes us being wrong once to cause harm. Rather than GRASing things into our food supply and hoping for the best, I believe it best to be skeptical until actually proven otherwise.

Artificial sweeteners

"These artificial sweeteners are awesome! All the flavor, no calories!" —Dr. B, 2013

"Keep that crap away from me!"—Dr. B, today

How about artificial sweeteners, ubiquitous in diet soda beverages and loads of other places? When they came to market we thought, "Zero calories, that *has* to be better than sugar, right?" It's intuitive! Turns out they're actually worse because they induce changes in the microbiome that promote inflammation, insulin resistance, and liver injury. You will actually be *less* tolerant of sugar by using artificial sweeteners.

And then there's the downright scary stuff . . . Remember from Chapter 1 the explosion of *Clostridioides difficile* that's occurred in the last twenty years? *C. diff* infection was fairly rare and only seen in hospitalized patients on antibiotics in the early 2000s. Just ten years later we're seeing five hundred thousand infections per year and thirty thousand deaths including in college kids who have never stepped foot in a hospital or had recent antibiotic use. Our antibiotics stopped working so we desperately reach for human feces, used as medicine, to save our butts. Literally. There has to be an explanation, right? Turns out that a

dietary additive that you've probably never heard of called trehalose was GRASed into the American, European, and Canadian food supply in 2000, 2001, and 2005, respectively. Trehalose is a sweetener that the food industry loves because it improves the stability and texture of foods. It's used in pasta, ice cream, even beef. You can buy it by the kilogram on Amazon and throw it in your coffee. But a 2018 publication in *Nature* showed that: 1) trehalose promotes the growth of nasty, virulent strains of *C. diff* infection in an animal model; and 2) the timing of implementation of trehalose into our food supply coincides with the emergence of the *C. diff* epidemic with these exact strains worldwide. It took eighteen years for us to identify the problem. So has trehalose been taken off the market due to safety concerns? Unfortunately, no. "All you've shown is an association, without proof of harm in humans." See how that works? It will be very difficult to roll back the ten thousand food additives we've GRASed into existence.

Closing the book on processed foods

The thing about processed foods is that you're starting with something that's healthy in its natural state, and you are modifying it. As you progressively change that food, it becomes less and less nutritionally valuable. At some point, the food that started healthy becomes poison.

If you go back one hundred years, this simply wasn't a part of our diet. Take a moment to think about that: the sheer volume of man-made chemicals we're putting into our bodies, and the unrealistic expectation that our microbiota will be able to process and eliminate them without any damage. It's a shock that we don't drop dead from this stuff and a total testament to the adaptability of our microbiome, even if this is likely contributing to mass bacterial extinction.

It comes as no surprise that every 10 percent increase in consumption of ultra-processed foods is associated with *more* than a 10 percent increased risk of developing cancer and a 14 percent risk of early death. So what happens when you hit American levels of consumption—50 or 60 percent?

I don't think that every food additive is harmful in the long term, but we don't know and likely will never know. There's only one foolproof way to protect yourself from the potential poisons in our diet—get rid of them!

Unhealthy fats

Not all fats are unhealthy, but most of the fat in the American diet is of the unhealthy variety unfortunately. Study after study in an animal model has shown that a high-fat diet causes an unhealthy balance in the microbiota, impairs intestinal barrier function, and leads to the release of bacterial endotoxin. As you recall from Chapter 1, this is the model of dysbiosis, and bacterial endotoxin has

been linked to autoimmunity, obesity, coronary artery disease, congestive heart failure, type 2 diabetes, Alzheimer's, alcoholic hepatitis, nonalcoholic fatty liver, osteoarthritis, and even "low T" in men.

Do the animal model findings translate to humans? Yes. A recent study in humans held dietary fiber constant and varied the amount of fat in the diet—20, 30, or 40 percent of calories. After six months they saw the microbiome shift to a progressively more inflammatory profile when fat was higher, confirmed with higher systemic inflammation. More fat, more problems.

So which fats are good and which are bad? The above study was done with vegetable oil, which can often be partially hydrogenated and high in trans fats. Other sources of trans fats are baked goods, chips, fried food, canned biscuits, nondairy creamer, and margarine. There is universal agreement that trans fats are unhealthy. Check the label for trans fats and don't buy it!

On the flip side, there is universal agreement that monounsaturated fats (MUFA) and omega-3 polyunsaturated fats (PUFA) found predominantly in plant foods are healthy! We see this validated in microbiome studies that show oleic acid—a monounsaturated fat found in olive oil—and omega-3 PUFAs promote the growth of beneficial microbes, correct dysbiosis, and reduce bacterial endotoxin release. They even enhance microbial diversity. These fats actually protect the microbiome.

And then there's saturated fat, predominantly found in animal foods as well as in tropical oils like coconut oil and palm oil. Cardiologists are screaming and shouting that it causes obesity, heart disease, and diabetes. Low-carb dieters disagree, and *Time* magazine says "Butter is back." But what does the microbiome say? The results in the microbiome have been consistent. Saturated fat encourages the growth of inflammatory microbes like *Bilophila wadsworthia*, alters intestinal permeability, and leads to the release of bacteria endotoxin. Translation: saturated fat causes dysbiosis. It even disrupts our normal biological rhythm in a way that promotes obesity. If you care about the health of your microbiome, then "Butter is not back" and we should probably rethink this ghee-and coconut-oil-in-the coffee fad.

Animal protein

"So where do you get your protein from?" That's the question that patients always ask when I discuss a plant-based diet with them. I get it. We've been taught that protein is the be-all and end-all of nutrition. Our obsession with protein fuels the heaviest meat consumption on the entire planet. But what's interesting is that "where you get your protein from" is incredibly important to gut health.

The source of the protein, whether from plants or animals, can have very different effects on the microbiome. For example, plant protein increases the growth of anti-inflammatory species like *Bifidobacterium* and *Lactobacillus* while suppressing the destructive ones like *Bacteroides fragilis* and *Clostridium perfringens*. The result is correction of leaky gut.

On the flip side, diets high in animal protein have consistently been associated with increased growth of inflammatory microbes like *Bilophila wadsworthia*, *Alistipes*, and *Bacteroides*. These bacteria produce toxins like amines, sulfides, and secondary bile salts. Amines cause food sensitivity at baseline, and then when you char meat it turns them into carcinogenic heterocyclic amines. Hydrogen sulfide has been associated with ulcerative colitis. Secondary bile salts have been associated with cancer of the colon, esophagus, stomach, small intestine, liver, pancreas, and biliary tract. No surprise, this consumption of animal protein results in increased intestinal permeability and inflammation.

And then there's the association between animal protein and TMAO, which has redefined our understanding of America's number one killer—cardiovascular disease. When people ingest L-carnitine (abundant in red meat and some energy drinks and supplements) or certain choline (found in red meat, liver, egg yolk, and dairy products), the gut bacteria produce trimethylamine Noxide, or TMAO. Increased TMAO means increased risk of heart disease, stroke, Alzheimer's, type 2 diabetes, chronic kidney disease, peripheral artery disease, congestive heart failure, and atrial fibrillation—to name a few. Unhealthy food feeds unhealthy microbes that produce unhealthy compounds. It's a vicious cycle that's only broken by replacing unhealthy food with healthy food.

The good news is that a plant-based diet promotes a gut microbiota that just doesn't know how to make TMAO. Studies show that about four weeks after giving up red meat, people's TMAO levels drop dramatically. This explains why in *The Lifestyle Heart Trial*, Dr. Dean Ornish showed that through a low-fat vegetarian diet, smoking cessation, stress management, and moderate exercise, patients actually *reversed* coronary artery disease. Meanwhile the control group got worse and worse.

What's interesting is that increased animal protein can produce weight loss in the short term but causes a shift in the microbiome that's bad for our gut health in the long term. I suppose now would be a good time to have a little chat about the fad diets that offer weight loss in exchange for heavy meat consumption . . .

Fad Diets

Let me make this clear . . . I don't look down on people who do fad diets. In fact,

I applaud them for having the courage to change their diet in an effort to be healthier. But the million-dollar question is, "Are these diets good for your microbes?"

Let's start with the Paleo diet, our most popular and most often recommended dietary approach today. The idea is that we should eat the way our ancestors ate because modern agriculture is at odds with our ancestral biology. That means meat, eggs, vegetables, fruit, nuts, and roots are on the menu while dairy, sugars, grains, legumes, processed oils, salt, alcohol, and coffee are not. Some of this I love; some of this I don't.

But who cares what I think? Let's look at the science. In a recent study, consumption of a long-term Paleolithic diet was associated with dramatically higher TMAO levels, reduced *Roseburia* (protects against inflammatory bowel disease), reduced *Bifidobacterium* (protects against irritable bowel and obesity), and increased *Hungatella* (produces TMAO). In other words, the Paleo diet shifted the microbiome away from health and toward disease. Even though all of the groups in the study ate a similar amount of meat, they saw dramatic differences in the amount of TMAO produced, with the highest level being in those who were most strict in following the Paleo diet. Elimination of whole grains was the main factor responsible for increased *Hungatella* and TMAO levels, demonstrating that categorical eliminations can have unintended, potentially serious consequences.

Anyone want to guess what an even more restrictive Keto/Carnivore diet does to the microbiome? In a groundbreaking study by Drs. Lawrence David and Peter Turnbaugh, a group of people cycled between a completely "plant-based diet," which was rich in grains, legumes, fruits, and vegetables, and an "animal-based diet," which was composed of meats, eggs, and cheeses. This "animal-based diet" could also be called the "Keto diet"—extremely low carb, very high fat. It could also be called the "Carnivore diet"—100 percent animal products, no plants.

So what happened? There were dramatic changes of the study's participants in the microbiome in less than twenty-four hours. It didn't take long. The animal-based diet saw the disturbing emergence of inflammatory bacteria like *Bilophila wadsworthia*, *Alistipes putredinis*, and *Bacteroides*. This was expected with high levels of saturated fat and animal protein. Remember, these are the bacteria that produce toxins like amines, sulfides, and secondary bile salts. Meanwhile, there was starvation and recession of the healing microbes like *Roseburia*, *Eubacterium rectale*, and *Faecalibacterium prausnitzii*. Similar to the Paleo diet, this is a shift away from health and toward disease. Perhaps the most disturbing part is the rapid emergence of *Bilophila wadsworthia*, known to produce

hydrogen sulfide, which promotes inflammatory bowel disease. It's alarming to consider that in less than five days the foundation is being laid for the development of Crohn's disease or ulcerative colitis with this diet.

But these low-carb, high-fat diets are helping people to lose weight, right? Folks, we have to learn that you can lose weight, look great on the outside, and be absolutely rotting on the inside. It's short-term gain and long-term pain. Do you know the average life expectancy of a professional body builder? It's just forty-seven years. Weight loss doesn't always translate into better health.

To view the 55⁺ scientific references cited in this chapter, please visit me online at www.theplantfedgut.com/research/.

The Fiber Solution: Short-Chain Fatty Acids and Postbiotics for the Win

Our guts are STARVING to be Fiber Fueled

So what can we do to restore order and bring out the best in our 'biota? Where do we begin if we want to heal our guts to reverse or prevent illness? Is it probiotics? Bone broth?

Well, if you were sitting across from me in my office, I'd be going straight for my secret weapon—fiber. I know what you're thinking. "Fiber? Really? Fiber is, like, the most boring thing on the entire planet, Dr. B," or "You mean that gross white powder my grandma mixes into a glass of water every morning so she can poop?"

And to that I'd say: Fair enough. Fiber has gotten a bad rap, and those tasteless fiber supplements are only partly to blame. It's also the fact that until very recently we had absolutely no idea just how amazing fiber is for your gut microbiota. You most likely have preconceived notions about it that make it hard for me to make fiber cool or sexy. For a while now, the diet conversation has been all about protein and, more recently, fat. Nobody has been talking about boring old fiber. I'm here to tell you that fiber is the first, and potentially the most powerful, solution to restoring health to your gut microbiota, and from there your overall health.

But for this to work I need you to unlearn what you think you already know. I'm not talking about fiber as you know it. It's time for a reboot. A renaissance. A rebranding. It's time to stop thinking about fiber as being vanilla and boring

and get to know it in a whole new light. Fiber is so much more than you once thought it was. Yes, fiber is the real deal, folks. If by the end of this chapter you want to intentionally mispronounce it as "FIRE," I don't blame you. I'm going to resist that urge for this book, but if we ever meet in person I hope you'll shake my hand and tell me the secret code, "Fiber is FIRE."

Did you know that 97 percent of us consume an excess of protein, yet we still constantly ask, "Where am I going to get my protein from?" We live in a country with a pathologic protein obsession. Meanwhile, we are figuratively and literally starving for fiber. "Starving?" you say. "In this country? Where nearly three in four are overweight?" Absolutely. Your gut is completely FIBER STARVED. Imagine your gut as a dried-out, postapocalyptic wasteland, with a lone tumbleweed rolling through. That solitary tumbleweed represents your fiber! Less than 3 percent of Americans get even the recommended *minimum* daily intake. That means 97 percent of Americans are not receiving the *minimal* daily recommended amount of fiber, let alone what I would characterize as optimal. Of all of the essential nutrients, this may be our greatest, most prevalent deficiency. Yet, we're not talking about it and no one seems to be concerned. Enough with the protein obsession; it's time we turn our attention to the vital question: "Where am I going to get my fiber from?"

Fiber, the phoenix: Let's burn it down and watch it come back stronger!

Okay, taking it from the top: What is fiber? In nature, fiber is a part of the plant cellular structure. Plants have a total monopoly on this nutrient. So if you want it, there's only one way to naturally get it: from plants!

From a nutritional perspective, fiber is a carb—it's what we would refer to as a complex carbohydrate. If you take multiple sugar molecules and link them together, you'd get fiber. That doesn't mean it behaves like sugar by any means. It doesn't. Digestion of refined sugar starts in the mouth and in about twenty minutes it's already been absorbed in the small intestine. Meanwhile, fiber remains unblemished as it passes through your mouth, stomach, and even fifteen to twenty feet of small intestine so that by the time it reaches your colon, it's the same molecule that went in your mouth.

Two of the biggest myths about fiber are that all fiber is the same and that it does nothing more than go in one end and shoot out the other like a torpedo. Let's dig deeper.

Have you turned into a carbophobic?

If just seeing the word "carb" gets your heart racing and your face flushing, then it's happened. But don't worry; it's not your fault. There's been so much negative press for carbs. They're not very "in" and they haven't been for quite some time. You've been taught that carbs are bad for you; they spike your blood sugar, increase your food cravings, and you need to avoid them if you want to lose weight. Is it true? Sometimes. But not in whole food form.

Yes, refined, processed carbs like table sugar or high-fructose corn syrup, white bread or white flour will spike your blood sugar, leading to a vicious cycle of food addiction, weight gain, and constant hunger. That's because they've been stripped of their fiber. As you're about to learn, fiber is directly responsible for balancing our blood sugar and triggering our satiety hormones so that we know when to say, "That's enough, thank you."

Complex, unrefined carbs found in whole plant foods are chock-full of fiber, vitamins, and minerals. In contrast to that vicious cycle above, complex carbs actually lower blood sugar—even prevent diabetes—and decrease weight and body mass. The point is that we shouldn't make assumptions about our food based upon macro- or micronutrients. We need to look at whole foods. The fear surrounding carbs is appropriately placed with the refined carbs in processed foods, but completely misplaced with the unrefined carbs found in whole plant foods. Seriously, fruit is *actually* the low-hanging fruit!

Myth #1: All fiber is the same, and all you have to do is count grams.

You've been taught that all fiber is created equal—that whether it's in your breakfast cereal, the milky powder your grandma drinks, or in a granola bar, all forms of fiber are interchangeable. All you need to do is count the number of grams and you're good to go. What you've been told is dead wrong.

The source of the fiber you eat is critically important. The fiber in your cereal or breakfast biscuit is not the same as the fiber in your quinoa. This is conceptually similar to how the source of our fats and our protein determines the impact on our microbiome. It's an oversimplification to reduce fiber to a number of grams and pretend that all grams are created equal. As you're going to learn in Chapter 4, I have a much better way to source your fiber.

We've been taught to count grams of fiber for two reasons. One, it's easy, and we like easy. And two, we have no clue how many types of fiber actually exist in nature. It's incredibly difficult to analyze the chemical structure of dietary fiber, and there are four hundred thousand plants on our planet, three hundred thousand of them being edible. So there must be hundreds of thousands—if not millions—of types of fiber in nature. But we haven't gotten around to figuring them all out yet.

Given the complexities in analyzing dietary fiber, we've simplified it by saying there are two basic forms of dietary fiber: soluble and insoluble. You can

tell which is which by submerging the fiber in water. If it dissolves, it's soluble. If it doesn't, it's insoluble. While I will occasionally make references to the difference between soluble and insoluble fiber, just know that in both cases we are talking about huge categories of fiber and that most plants contain some mix of both.

Myth #2: That fiber just passes through us.

If you do a quick Google search on fiber, you'll find the general health benefits of fiber: It contributes to fantastic bowel movements by correcting diarrhea and constipation and increasing the weight and size of your bowel movement, lowers cholesterol, and controls blood sugar. These are all great things, and we should be celebrating these health benefits of fiber, for sure! But at the same time we have been doing the undersell of the century here, folks.

We've all been taught that fiber pretty much goes in the mouth and out your . . . well, you know, and along the way it sweeps some stuff out. And while there may be some truth to these statements, we're being excessively simple about an incredibly complicated nutrient. So let's take a closer look.

We humans lack the ability to process fiber by ourselves. Sure, we've got some enzymes called glycoside hydrolases that help us break down complex carbs, but we only have seventeen of them—just seventeen!—and none of them are designed for breaking down the larger molecules like fiber. In other words, we big strong humans are literally incapable of processing fiber on our own.

Now, if we lived encapsulated in a sterile bubble free from bacteria, we would never know the true power of fiber. But we get by with a little help from our friends. Because guess where you can find lots and lots of fiber and complex carbohydrate-processing enzymes? Yes, in our gut microbiota. Compared to the shockingly inadequate seventeen that belong to us, our gut microbiota may contain upward of sixty thousand of these helpful enzymes.

The fact that our microbiomes contain this insane number of digestive enzymes makes sense when you remember that there are three hundred thousand edible plants and potentially millions of types of fiber in our diet. By outsourcing fiber digestion to our microbes, we are taking advantage of their adaptability. Every single plant, every single type of fiber requires a unique team of microbes working in concert to get the job done. It's demanding work, but what follows is magic. The breakdown of fiber by gut bacteria unleashes what I believe is the most healing nutrient in all of nature: (*Drumroll, please!*) short-chain fatty acids (SCFAs).

Short-chain fatty acids (SCFAs) to the rescue

We've learned about our "good bacteria." But how do these powerful microbes actually do their incredible work? Good bacteria have the ability to transform certain types of fiber into electric, organic power manna—they're called SCFAs.

There are three main types of SCFAs: acetate, propionate, and butyrate. These are literally as they are described: short-chain, meaning made up of two, three, or four carbon atoms connected together in acetate, propionate, and butyrate chemical compounds, respectively. The three SCFAs work in the body as a complementary group. In the interest of understanding them better we generally study them in isolation, but always keep in mind that there are studies and then there's real life. In real life, these molecules are meant to work together, in the proper balance, for the good of your health.

Each type of fiber we consume produces a different mix of these SCFAs when processed by good bacteria. But don't worry about trying to get specific ones for specific problems—the key here, which you'll learn all about in Chapter 4, is to consume a diverse mix of fibers, meaning a diverse mix of plants, to get the benefits of *all of them*.

The different "-biotics" for gut health: pre, pro, and post

Before we go any further into the science of SCFAs I want to explain something. I'm sure you've heard of probiotics; we've all seen those yogurt commercials. Probiotics are all the rage and have been for some time. But have you ever heard of prebiotics or postbiotics? In short, probiotics are living bacteria that have been demonstrated to have beneficial qualities to us humans. Prebiotics induce the growth or beneficial qualities of the probiotics. They're essentially food for the good bugs. Postbiotics are the healthy compounds produced by bacterial metabolism.

In other words:

Prebiotics = Food for healthy gut microbesProbiotics = Microbes with beneficial qualitiesPostbiotics = Compounds produced by gut microbes

Taken a step further . . .

Prebiotics + Probiotics = Postbiotics

The word "prebiotic" literally did not exist until 1995, but it is increasingly becoming a part of the American vernacular. It is defined as "a substrate that is selectively utilized by host microorganisms conferring a health benefit." In other words, prebiotics (the substrate) are utilized by the microorganisms (probiotics) to confer a health benefit by producing postbiotics. Which is just the nerdy way of saying my formula: prebiotics + probiotics = postbiotics.

Not all fiber is prebiotic. Most soluble fiber is prebiotic, while most insoluble fiber is not. We often call insoluble fiber roughage. The roughage is the part that's untouched by our digestion or our microbes, and therefore launches out the bottom like a torpedo.

Fiber isn't the only prebiotic though! Resistant starch, found in foods like oats, rice, potatoes, and legumes, is technically not fiber but it behaves in a very similar way to soluble fiber. It passes through the small intestine unblemished and is fermented by our colon microbes. A mother's breast milk also contains something called human milk oligosaccharides, or HMOs, that function like soluble fiber and feed the baby's developing gut microbiota. So if we want postbiotic SCFAs, we should get prebiotic soluble fiber and resistant starch in our diet and we should breastfeed our young ones.

All roads point to SCFAs for human health. They are the dominant driver of gut health and they have benefits throughout the body.

Going beyond fiber for next-level prebiotics

While fiber is a strong and reliable source for prebiotics, healthy prebiotics exist in other plant compounds as well. The healing properties of numerous plants—including cocoa, green and black tea, pomegranate, apples, and blueberries—are at least partially attributable to phytochemical polyphenols, which are antioxidant compounds. Ninety to 95 percent of polyphenols make their way down to the colon, where they're magically transformed by our microbes and activated to their health-promoting form. Similarly, omega-3 polyunsaturated fatty acids found in walnuts have been shown to be prebiotic. Yay, healthy fats! So while polyphenols and omega-3's don't produce short-chain fatty acids like fiber, they do have an effect on our gut microbes and cause the release of health-promoting compounds, also known as postbiotics.

Nutritional karma and the power of positive momentum

Now let's come back to SCFAs, your good gut bacteria, and fiber. Healthy bacteria can't survive without fiber. In fact, studies have shown that fiber

consumption increases the growth of healthy bacteria species such as *Lactobacilli*, *Bifidobacteria*, and *Prevotella*. Eating fiber also increases the diversity of species within the gut. These beneficial effects are what qualify it as a prebiotic. The prebiotic effects of fiber feed and nourish the healthy microbes in our gut. Your gut bacteria goes from slumped over and worn out to energized, steadfast, and powerful.

Those reinvigorated microbes release SCFAs from fiber to heal the colon. First, the short-chain fatty acids do as their name suggests and make the colon more acidic. This change prevents the growth of inflammatory, pathogenic bacteria—the bad guys. Next, SCFAs take it a step further and directly suppress dangerous strains like *E. coli* and *Salmonella*. In Chapter 1 we learned that dysbiosis is characterized by a loss of balance between the healthy microbes and the inflammatory ones. By suppressing inflammatory microbes, SCFAs are helping to restore that balance.

Now we're building momentum toward a healthier gut. Fiber is feeding the healthy microbes, and they're multiplying. As they increase in number, they're producing more and more SCFAs for us even though you're consuming the same amount of fiber. You have trained your gut to produce SCFAs, and it's become increasingly efficient at doing that. These SCFAs are suppressing the inflammatory microbes, giving the healthy microbes an even more decisive advantage over the inflammatory ones. This is a form of positive health momentum, and it starts building on itself as we get more and more healthy microbes producing more and more SCFAs. But keep in mind, the linchpin here is fiber. Everything I've described is contingent on fueling your gut microbes with prebiotic fiber.

As you can see, regular consumption of fiber trains your gut microbiome not only to process fiber, but to actually get even more beneficial postbiotics out of it! In exercise we call it muscle memory. In life we call it practice. Either way, our microbes are no different. If you regularly expose them to fiber in your diet, they will adapt to that regular exposure and get really, really good at extracting SCFAs for you. With that comes a myriad of benefits that I'm just starting to tell you about.

But here's the problem—the flip side is also true: a diet lacking in fiber will drain your gut of its fiber-extracting capabilities and make it less capable of getting postbiotics from your food. When you don't practice, you lose your skill, right? Just two weeks on a low-fiber diet causes an altered gut microbiota that starts to literally eat away at the intestinal lining, causing breakdown of the protective barrier and susceptibility to disease. Not good. And remember how I said that 97 percent of us aren't even getting minimal fiber? And that six of the

top ten causes of death in the United States are caused by nutrition? And that most of those are linked with dysbiosis of the gut? You're starting to get the FIRE for fiber burning a little now, aren't you?

This is a really key point that I want to get across. You can call it nutritional karma—"do good and you will receive good." Or you could say that you're not what you eat but what your gut microbiota eats. The point is that your food choices leave an imprint in your microbiome and those choices will either train your gut bacteria to take care of and protect you or empower evildoers to hurt you. Your choice.

What else can SCFAs do? Well, they also fix up your colonocytes, which are the cells lining your colon. Maybe you've been led to believe that fiber provides no energy since it's not absorbed? Believe it or not, 10 percent of our daily caloric requirements are met with fiber-derived SCFAs as the energy source. In fact, the main source of energy for our colonocytes are SCFAs, providing up to 70 percent of their energy. Specifically, the colonocytes seem to love chowing down on the SCFA butyrate, so most of the butyrate is taken up by the gut lining where it contributes to a healthy colon. Like taking a beautiful historic home that's been run haggard and restoring it to its original glory, butyrate fixes up the lining of the gut.

"Doc, how do I fix leaky gut?" Here is your solution.

Back in Chapter 1 we talked about dysbiosis, which is when damage to the gut microbiota causes increased intestinal permeability, which leads to release of noxious bacterial endotoxin. Remember that the gut wall is meant to act like a physical barrier exerting control over what stuff gets access to your blood. After all, it's in the gut that your body is most exposed to the outside world. This blood—gut barrier is meant for protection, but holes can occur in the wall allowing bacteria, antigens, and toxic substances like bacterial endotoxin to get past the intestinal wall, activating the immune system. This increased intestinal permeability, which some refer to as "leaky gut," happens when tight junction proteins that are meant to keep cells connected to one another end up being broken, thereby creating gaps between the cells. Good news: SCFA butyrate actually *repairs* leaky gut by increasing the expression of tight junction proteins and has been shown to actually decrease endotoxin release.

And while we're on the topic, inflammation caused by increased intestinal permeability affects the function of the intestinal lining, including its nerves and muscles. This leads to diarrhea or constipation, bloating, and abdominal pain. Unfortunately, even just transient inflammation of the gut and intestinal

hyperpermeability can cause sensitization and altered motility that persists long after resolution of the inflammation. You may recall from Chapter 1 that the hallmarks of irritable bowel syndrome are altered gut motility and increased visceral hypersensitivity. SCFA butyrate has been shown to increase colonic motility and decrease visceral hypersensitivity. So if you suffer from IBS, then you want this.

Let's take a step back for a moment here, folks. What I'm telling you is that SCFAs are a *vital nutrient* for intestinal health. They are the dominant energy source for your colon, support a healthy gut microbiota, repair leaky gut, reduce release of bacterial endotoxin, promote intestinal motility, and decrease visceral hypersensitivity. Read that sentence again: Let it sink in. I just described the cure for dysbiosis. I believe that dysbiosis is at the root of most modern disease. SCFAs can correct dysbiosis, and that's only the beginning of the health benefits they offer.

If correcting dysbiosis, supporting a healthy gut microbiota, repairing your colon, and reversing leaky gut weren't enough, this superhero energy fans out throughout the body and works its healing magic. Let's take a look at some of the most impressive capabilities of SCFAs beyond the gut.

Immune system and inflammation

Just beyond the wall of your intestine sits 70 percent of your immune system. This is your little army. When infection or even cancerous cells arise, it is the responsibility of your immune system to clear it out. Sounds simple, but it's not. How do you separate friend from foe when there are thirty-nine trillion microbes in the gut, thirty trillion human cells in the body, and your "host" is scarfing down three pounds of food per day, most of which is some deviant form of real food? That's a ton of responsibility. The slightest bit of confusion by the immune system leads to failure. Overreact and you get allergic or autoimmune issues. Underreact and you get infections or even cancer. So how do we get it juuuusssssttttt right?

Well, SCFAs are the way that our gut microbiome connects to our immune system. It's how they communicate with each other. SCFAs act as a crisis negotiator, getting the immune system to cool off if it's too hot.

Dysbiosis and the release of bacterial endotoxin promote inflammation, which is a good thing when you have an infection or injury but isn't good when it's constant and unneeded. It's unrelenting low-grade stress on the body, including the immune system. Thankfully, SCFAs address both dysbiosis and bacterial endotoxin release, which makes them a great first step toward regulating the root cause of all inflammatory conditions.

Beyond that, SCFAs have been shown to inhibit three of the most powerful inflammatory signals in the body: NF-κB, IFN-y, and TNF-α. I've heard people say that "your genes load the gun and your lifestyle pulls the trigger." If that's the case, then SCFAs disarm the gun and take it out of your hand. SCFAs make immune cells more tolerant to gut bacteria and reduce gut inflammatory markers. Believe it or not, they even make immune cells more tolerant to your food, helping to prevent food allergy and sensitivity. SCFAs can even communicate directly to an important part of our immune system called regulatory T cells, which you can think of as "suppressor" cells that cool off the immune system, encourage tolerance to your own cells, and prevent autoimmune disease. More on that in a bit.

We've seen more evidence of the power of fiber fueled SCFAs against inflammation in studying patients with Crohn's disease, a form of inflammatory bowel disease (IBD). In Crohn's, the immune system attacks the intestine, causing inflammation. It can affect any part of the digestive tract, from your lips to your backside. The inflammation in Crohn's can be so severe that it can actually erode through the wall of the intestine and cause abscesses or a connection between two parts that isn't supposed to exist, which we call a fistula. Suffice it to say that Crohn's is a horrible, debilitating condition that is becoming increasingly common in the Western world.

So let's take a look at how Crohn's disease develops and you'll see how SCFAs could make a difference. In people with Crohn's, we see decreased diversity, loss of butyrate-producing organisms, bacterial specifically Faecalibacterium prausnitzii, and an overgrowth of pathogenic bacteria, specifically *E. coli*. But this isn't just any *E. coli*. . . . No, no, no. This is an extra-nasty variety called adherent-invasive *E. coli*. Gives me the chills typing it, that's how nasty it is. Anyway, this *E. coli* behaves like a sociopath just broken out of prison, and immediately starts unleashing pro-inflammatory proteins like a flamethrower as it proliferates, further enhancing dysbiosis and the rise of more E. coli. This loss of balance in the gut, decrease in good bacteria, and increase in E. coli affects the tight junctions and leads to increased intestinal permeability. There is a strong association between depletion of *F. prausnitzii* and the immune system no longer being tolerant of the intestinal microbiota, meaning the immune system starts going haywire. Meanwhile, the absent intestinal barrier allows *E. coli* to invade the intestinal wall, which activates the immune system to attack the *E. coli*. And there you have it—inflammatory bowel disease.

As you can see, just like in life, when bad things happen in the body it's a series of events that lead to the problem. If we were functioning in the business

world, we'd do a root cause analysis to figure out the source of the problem and address it. Could a *fiber-starved* gut be the root cause of Crohn's disease?

Well, yes: SCFAs are relevant in protection from Crohn's disease on a mechanistic level because they make immune cells more tolerant to gut bacteria, help suppress an overactive immune system, repair leaky gut, and create protective bacteria to keep the gut healthy. Additionally, in a recent study a semi-vegetarian high-fiber diet basically crushed an omnivorous diet in terms of keeping people with Crohn's disease free of disease activity and in remission. Those on a semi-vegetarian diet maintained a 92 percent remission rate compared to just 33 percent among omnivores in a prospective trial.

And in similar fashion, what if a high-fiber, plant-centered diet proved to be beneficial for other autoimmune, inflammatory conditions? Well, it does. In humans, a vegan diet has repeatedly been demonstrated to be beneficial for disease remission in rheumatoid arthritis. For example, in a randomized controlled trial 41 percent of patients on a vegan diet showed clinical improvement of their rheumatoid arthritis compared to just 4 percent on a "well-balanced" non-vegan diet.

So not only do SCFAs correct dysbiosis and heal leaky gut, but they also create a powerful link between the microbiome and immune system that serves to make the immune system work properly. Adequately fueled by SCFAs, the immune system does its job confidently and effectively. Without the SCFAs, the immune system becomes insecure, confused, paranoid, and weak. In other words, the immune system is dependent on gut microbes to support it with SCFAs. The gut microbes are dependent on you to offer fiber fuel that can be transformed into SCFAs. Again, these gut microbes aren't just passively along for the ride. They play an active, central role in our health.

Cancer

As we've learned, SCFAs correct dysbiosis, fix leaky gut, reverse bacterial endotoxemia, and optimize the immune system. Those effects create a good foundation for the prevention of cancer. We know from Chapter 1 that dysbiosis has been associated with several types of cancer: colorectal, gastric, esophageal, pancreatic, laryngeal, gallbladder, and even breast cancer. But is there anything special about SCFAs that can help us in the fight against cancer beyond just "healing the gut"?

Let's start with the basic premise that cancer development requires unchecked cell multiplication and growth. In order for this to happen, the DNA in the malignant cell needs to be able to copy itself before dividing into two cells. Histone deacetylases, or HDACs, are required to allow this process to occur. So

if you could shut down the DNA copy process by blocking the HDACs, you'd effectively be pulling the emergency brake on the runaway cancer train.

Since the 1970s we've known that butyrate inhibits HDACs, altering gene expression in malignant cells and, as a result, inhibiting the root of cancer formation—unchecked proliferation. But when you have dangerous cells that you're dealing with, it's not enough to just slow down their growth. You need to stop them in their tracks, and the way this is done is by causing apoptosis, or programmed cell death. Sounds violent, but it's actually a normal part of cellular regulation and is by no means rare. Every day between fifty and seventy billion cells fall on the sword in altruistic fashion to protect the greater good of the whole organism. SCFAs help us in the fight against cancer by specifically eliminating cells that could turn into cancer.

Once again, studies on people who consume a high-fiber, plant-centered diet and reduce their cancer risk offer proof that these principles really translate to our real life. Let's go straight to the source and start with the most powerful, most well-respected study on the topic by Dr. Andrew Reynolds in *The Lancet*. He pulled information together from 243 prospective studies. This is a scale that is rarely seen in clinical research, yet at the same time he restricted his data to high-quality studies: prospective cohorts and interventional randomized trials. In the end, fiber found in whole foods was shown to protect against colorectal, breast, and esophageal cancer. Further, high dietary fiber in the study was still pretty low—between 25 and 29 grams per day. In the Western world, our fiber consumption is so poor that even the high-fiber consumers are below goal. Nonetheless, the results suggested that as you extend your dietary fiber intake higher, the protection against colorectal and breast cancer only gets greater.

Colon cancer is the number two cause of cancer death in the United States right now. Number two! And that's despite billions of dollars spent on our colon cancer screening program. Dietary fiber has been *repeatedly* shown to protect us from colon cancer. For example, in a prospective study of 1,575 people with nonmetastatic colorectal cancer, consuming more dietary fiber helped people live longer. For every 5 grams of increased fiber consumption, there was an 18 percent lower risk of death from colorectal cancer and 14 percent lower risk of death from any cause during follow-up.

And just to put the cherry on top, three major studies—a large 2017 meta-analysis, the prospective EPIC-Oxford study, and the Adventist Health Study—all reached the same conclusion when it comes to diet and cancer risk. A plant-centered, fiber fueled diet lowers your risk of developing cancer. Mic drop.

So SCFAs and fiber offer protection from cancer, the number two cause of death in the United States. How about heart disease and stroke—the number one and number five causes of death? In the same mega meta-analysis on dietary fiber published in *The Lancet*, Dr. Reynolds and his science squad also found dietary fiber consumption to be associated with lower body weight, reduced incidence of type 2 diabetes, lower total cholesterol, and lower systolic blood pressure. These just so happen to be the risk factors for coronary artery disease and stroke.

SCFAs affect multiple tissues in a concerted action to improve blood sugar regulation. They help protect against glucose intolerance, improve insulin response in the pancreas, and suppress fatty acids in the liver and peripheral tissues. This isn't exactly a revolutionary concept. There are studies dating back to the 1980s suggesting that soluble fiber is protective against type 2 diabetes. But modern studies, such as the recent *Science* article by Dr. Liping Zhao, dug more deeply and have shown us that following a high-fiber diet promotes the growth of SCFA-producing microbes that improve blood sugar regulation.

It's not just what you eat but the effect it has on your microbiota that determines your diabetes risk. There's something that was originally called the "lentil effect," but now we call it the "second meal effect," that illustrates this idea. If you give two people an amount of bread or lentils for lunch that have the same number of calories, you will of course see less of a sugar spike with the lentils. No surprise. But then these two people both have white bread for dinner, you'll *still* see less of a sugar spike in the person who had lentils for lunch. Same meal at dinner, but different effects based upon what you ate for lunch. We now understand that this happens because the bacteria that we empowered at lunch are working their SCFA magic to protect us at dinner. Score one for legumes, if you're keeping track.

SCFAs also lower cholesterol by having direct control over the critical enzyme in cholesterol formation and by increasing excretion of cholesterol in bile. Further, SCFAs directly activate a receptor in fat cells that decreases fatty acid uptake, and therefore suppresses fat accumulation.

Each of these mechanisms protects you from obesity. Additionally, SCFAs promote the release of satiety hormones that tell you when you've had enough. This is a wildly underrated benefit that we are sacrificing with our current highly processed, low-fiber diet. It allows you to feel nice and adequately full without crossing the line to where you need a pair of sweatpants, a three-hour nap, and an energy drink to get your day back on track. (Not that there's anything wrong with sweatpants!) When you are eating real food, nature works the way it's supposed to and you simply stop eating at the right time without counting calories and without overeating. As proof of concept, a randomized crossover

study recently showed people experienced greater satiety and increased satiety hormones after eating a plant-based burger with tofu than after eating a pork and cheese burger, even though the two meals were matched for energy and macronutrients. Same number of calories, same macros, but better appetite control with the plants. Shocking, right?

Finally, patients with symptomatic coronary artery disease have been found to have depleted levels of butyrate-producing gut bacteria. In animal models SCFAs have been shown to protect against congestive heart failure and high blood pressure. More recently they've also been shown to prevent atherosclerosis by maintaining gut barrier function and limiting bacterial endotoxin release, which leads to less vascular inflammation. A recent study in humans with congestive heart failure found an absence of SCFA-producing microbes and an increase in TMAO-producing microbes. These patients had less butyrate and more TMAO coursing through their blood. And so we now understand at least in part why a plant-centered diet is good for the heart. SCFAs are the antithesis of TMAO.

Cognition

Like a Roman warrior throwing a spear, the superhero bacteria in our gut also unleash SCFAs all the way upstairs to the brain. What's interesting is that many molecules cannot travel to the brain due to a wall of protection called the bloodbrain barrier. Most molecules are stopped there at the wall, like being stopped at the VIP line at the most exclusive club in New York City. (I wouldn't know what that's like because I'm a nerd and have never been, but I watched enough *Entourage* to at least be able to pretend.) So imagine that when the SCFAs show up, the velvet rope is withdrawn and they're given free access to the hottest club, our most precious organ, the brain.

On the other side of that velvet rope, SCFAs continue to work their magic. The same chemical that reverses dysbiosis, heals leaky gut, strengthens the gut microbiota, optimizes the immune system, and regulates appetite and metabolism also connects the gut microbiome to cerebral function. The effects are once again broad and powerful.

You know how many people with leaky gut also complain of brain fog? And how we also discussed above that SCFAs can activate tight junction proteins to repair increased permeability in the gut? Well, it appears that SCFAs work similar magic on the blood–brain barrier.

SCFA butyrate has demonstrated a profound effect on improving learning and memory. This has been demonstrated in models of Alzheimer's, heavy metal toxicity, traumatic brain injury, and even neurologic infections (which sounds

terrifying). I will tell you firsthand that the mental clarity that I've had since changing my diet has been life changing for me. Being totally real, there's no way I could've written this book before. I didn't have the stamina, focus, or neural plasticity.

Speaking of Alzheimer's, one of the hallmarks of Alzheimer's disease is the accumulation of amyloid plaques between nerve cells in the brain. Researchers are currently working on treatments for Alzheimer's to block the production of amyloid. Millions if not billions of dollars are being spent on this. While they continue that quest, I want you to know that laboratory studies suggest that SCFAs interfere with the formation of this exact same amyloid.

Laboratory studies also show that butyrate protects the brain in models of Parkinson's disease. This is quite interesting when you consider that human studies have found that patients with Parkinson's disease have lower levels of the bacteria that produce SCFAs and, as expected, lower levels of SCFAs in their stool. For what it's worth, Parkinson's disease patients almost all have digestive issues, with constipation being the most common among them.

Finally, children on a high-fiber diet demonstrate better cognitive control (multitasking, working memory, and maintaining focus) than children who eat a lower-fiber diet. So SCFAs may help ADHD. I'd far rather kids eat a salad than take Ritalin.

Bringing back fiber

Dr. Justin Sonnenburg showed that Westernization has led to a loss of gut microbial diversity in his study that compares the Hadza of Tanzania to Americans. The Hadza are one of the last remaining hunter-gatherer societies on the planet and provide insights into what our life and our microbiome may have looked like in primitive times. They consume 100 or more grams of fiber a day in their food, and during a year will include around six hundred plants in their diet. The average American gets a pathetic 15 grams of fiber per day and has fifty or fewer species of plants in their diet. The differences in the microbiota are profound. The Hadza have about 40 percent more diversity than the average American and about 30 percent more diversity than the average Brit.

Consider that African Americans have sixty-five times more colon cancer than rural Africans. Sixty-five times! One interesting study involved switching the diets of a group of African Americans and native Africans for two weeks. The Africans did a high-fat, low-fiber diet while the African Americans did a high-fiber, low-fat diet. Do you want to guess what happened?

When the native Africans began eating our American diet, they saw their

SCFA butyrate levels decline and their TMAO levels increase. The reciprocal effect ended up being true for the African Americans. "Africanization" of the diet increased butyrate by 2.5-fold while "Westernization" cut butyrate quantities in half. Remember how secondary bile salts are known to cause colon cancer? A typical African diet reduced colonic secondary bile acids by 70 percent, while the Western diet increased them by 400 percent.

One last little mind-blowing nugget I want to leave you with: Dr. Sonnenburg also did a mouse study showing that the Western diet induced loss of microbial diversity that could be compounded over a series of generations. If your grandmother had twelve hundred species of microbes in her gut as a child, but by the time your mother was born she had nine hundred, that's what your mother got. Then if your mother loses three hundred species, now you start off at six hundred—half of what your grandmother had. Perhaps it comes as no surprise in this study, the main factor that protected against this generational loss of diversity was adequate prebiotic fiber consumption. Granted, this is just an animal study. But it's impossible to re-create in humans and it really makes sense.

If it seems too good to be true, it might just be that we've been ignoring it

The benefits of postbiotic SCFAs may seem a little too good to be true, but the science is real. SCFAs aren't just important, they're *absolutely vital* to gut health. They offer a solution to dysbiosis by correcting leaky gut and reducing bacterial endotoxemia. They feed and empower the healthy microbes in your gut so they can do their job! They also play a role in human health throughout the entire body. They offer protection from the most deadly diseases in the United States. That by itself should make it the talk of the town, the focus of our national conversation in our quest to better health. Yet this superstar languishes in anonymity. It's time to change that. I'm building a fiber bandwagon. Who's coming with me? Invite your friends. Grab your family. Let's be loud and proud so they can hear us. It's time for us all to be *Fiber Fueled*.