The Anti-Viral Gut

Tackling Pathogens from the Inside Out

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Introduction

It is more important to know what sort of person has a disease than to know what sort of disease a person has.

—Hippocrates

On January 20, 2020, the British-registered *Diamond Princess* departed Yokohama, Japan. Five days after leaving port, an eighty-year-old man on board disembarked to seek medical attention for a fever and cough. One week later, Hong Kong officials announced that the passenger, Mr. A, had pneumonia as a result of infection with SARS-CoV-2, the virus that causes COVID. The *Diamond Princess* outbreak represents the kind of experiment we can't do in real life: put a variety of people together in close quarters, expose them to a novel and highly contagious virus, and see what happens next. Ultimately, one in five people on board would become infected, with a fatality rate of about 2 percent. Those numbers, particularly the small but significant percent who died, and the larger unknown number who survived but continued to have symptoms lead us to one of the most important questions of this and future pandemics: Why them?

Why do some people suffer from severe and even fatal forms of viral illnesses like COVID, while others experience only mild symptoms or none at all? Why, despite repeated exposure, do some people never get infected? What determines who makes a complete recovery

and who ends up plagued with post-viral "long-haul" symptoms? Is all of this just random luck, or are there important clues that could have predicted who would walk off the *Diamond Princess* and who would leave horizontally?

Those outcomes might seem random, but I assure you, they rarely are. Being on the winning team when battling viruses isn't because of good luck, or coincidence, or variations in viral virulence. It's due to differences in us, the hosts, and our defenses, and those differences are what determine your outcome. Put another way: it's less about the potency of the pathogen and more about the health of the host.

The idea that host health matters as much as or even more than the virulence of the pathogen is validated every day by people who get up close and personal with viruses and never get sick. Even dangerous viruses like Ebola are only able to successfully attack about one in every three adults they come into contact with, and just a tiny percentage of children. In 0.5 percent of people poliovirus crosses their gut lining, infects their nervous system, and causes crippling paralysis, while in the vast majority who are infected, it causes no symptoms at all. Even today with our arsenal of antiretroviral drugs, HIV can be a death sentence for some, while others live with the virus for years and never develop AIDS. Even more incredibly, about one in ten people are completely immune to HIV and will never become infected, even with repeated exposure.

It may seem like an outlandish idea that you, not the virus, are in the driver's seat, but it's really just common sense when you think about it. Healthy people avoid or recover from life-threatening conditions all the time, while the less hardy and infirm succumb to minor ones. That's true for cancer, heart attacks, viral infections, and virtually every other illness. Increased susceptibility and poor outcomes are, in fact, almost always predictable and preventable, or at the very least, forecastable, and reducible. Simple risk factors assessed in an

annual physical, such as blood pressure, cholesterol levels, blood sugar, weight, and smoking status, are extraordinarily accurate in predicting risk for coronary artery disease and heart attacks. And counseling and strategizing about that risk and how to reduce it are much more effective than any drug or medical intervention. It boils down to addressing vulnerabilities and optimizing your body's defensive capabilities. Unfortunately, we're so alienated from our own innate host defenses that we've become dependent on pharmaceuticals as the only solution. Medications are critically important for those who need them, but for the majority of us, our body's own ability to resist, heal, and recover from viruses is vastly superior.

This pandemic has opened our eyes wide to the importance of knowing how to fortify ourselves. COVID-19 has been the deadliest viral outbreak the world has seen in more than a century, but events like it aren't as statistically rare as you may think. A 2021 study from Duke University used records from past outbreaks to estimate the likelihood of them happening again and found the probability of a pandemic like COVID-19 recurring is about 2 percent in any year. That means someone born in 2000 would have about a 40 percent chance of experiencing one by now. The data also shows that the risk of these extreme outbreaks is growing rapidly. Based on the rate at which pathogens like SARS-CoV-2 have erupted in human populations in the past fifty years, the study estimates that novel disease outbreaks will likely grow threefold in the next few decades. At least thirty previously unknown viruses for which no cures are available have been identified in the last half century, including HIV, Ebola, hepatitis C, and now SARS-CoV-2. The reasons for these outbreaks are varied and complex, but most scientists agree that modifications to our food system, climate change, population growth, and more frequent contact between humans and disease-harboring animals are at least partly to blame. Now more than ever, it's critically important for

us to understand the direct link between gut health and vulnerability to viruses.

As viruses become more common, exposure to them is inevitable, but illness is not. It all depends on your terrain—your internal ecosystem, or "soil," that nourishes everything in your body, including your immune system—and on having a clear and accurate understanding of what "healthy" really means. The composition and overall health of that soil are more strongly predictive of outcome when you encounter a virus than any other characteristic, including age or the presence of comorbidities like heart disease or obesity. That soil is your microbiome—the trillions of bacteria and other microorganisms that live in your gut and serve as copilots for pretty much every one of your important bodily functions: digestion, synthesis of hormones and vitamins, metabolism of drugs, removal of toxins, communication with your central nervous system, gene activation, and, most importantly, training your immune system to mount just the right balanced response that can effectively clear a virus while avoiding an exaggerated reaction that can damage tissues.

The majority of your immune system is also located in your gut, so it's no surprise that the microbes on one side of your gut lining and the complex immune responses happening on the other are interdependent. If you want to have an immune system that can protect you, even in the face of persistent viral exposure, you must pay attention to what's going on in your gut because without a healthy and balanced microbiome, your immune system can't do its job properly.

Having an anti-viral gut isn't super complicated. It doesn't involve restricting multiple food groups or taking a bunch of different supplements. It's mostly about being aware and staying clear of the things that interfere with your virus-slaying machinery. That means discontinuing practices that are damaging to your gut microbes; preventing "leaks" in your gut lining that can allow viruses to penetrate and gain

access to your internal organs; maintaining adequate amounts of stomach acid that can inactivate viral proteins; making sure the mucus that's produced in your gut is healthy enough to trap and expel viral invaders; understanding the role of fever in halting viral replication; avoiding unnecessary antimicrobials that wipe out your bacterial foot soldiers; not sabotaging your immune system with too much stress and not enough sleep; and, of course, feeding your army of microbes the right stuff so they can do their job of keeping you safe from viruses. It all starts and ends with your gut. In the second half of the book I'll take you through the specific steps to ensure yours is optimized and ready to protect you.

It's disheartening to realize that a hundred years after the last global pandemic, there's so little focus on what the individual can do to increase their resilience to infection, despite the mountain of scientific evidence validating these simple methods for improving host defenses. Our individual and collective health relies on taking action because the reality is that most of us are eventually going to encounter SARS-CoV-2—and other viruses. Public health measures like vaccines and social distancing remain critically important, but strengthening your immune system by optimizing your gut microbiome is arguably *the* most effective strategy for safeguarding yourself and provides an additional layer of protection that ensures that if you are infected, you have the very best outcome.

There's a direct link between the medications you take, your diet and lifestyle, your microbiome, and your immune system, and understanding those relationships is an essential part of building a strong shield against viruses. The good news is that unlike your genes, which are more static, your microbiome is constantly changing, responding dramatically to shifts in your diet within as little as thirty hours of the food hitting your gut. And dietary changes don't just alter the composition of your gut bacteria—they also affect which of your disease-fighting

genes get turned on or off by those bacteria, influencing your susceptibility to infection via genetic mechanisms. Simple changes in environment can have a profound anti-viral effect, too: recuperating outside in the fresh air during the Spanish flu epidemic of 1918 reduced death rates from 40 percent to 13 percent, as a direct result of the germicidal properties of what we now refer to as the open-air factor.

I love animals, but I'm not one of those crazy people who thinks she can go into the lion's den at the zoo, make friends with the lion, and walk out unharmed. I'm not a magical thinker; I'm a doctor who believes in science. And science has shown us what our vulnerabilities are when it comes to infections like COVID. Despite the virus being novel, that science is not new. It's the science of gut health, immunity, and the microbiome. I've used that science in my medical practice to improve the lives of thousands of patients who suffer from immune-based gut disorders, and I know how to make it work for you. You can improve your resistance to viruses, even if you're elderly, sickly, or have multiple chronic medical problems. You may not be able to make yourself completely invincible, but by strengthening your gut-based defenses, you can dramatically improve your chances of surviving this—and the next pandemic—intact and in even better health. Hippocrates famously said that all disease begins in the gut. Whether you're trying to prevent infection, recovering from a recent viral illness, or dealing with chronic post-viral symptoms, some of the most important solutions are to be found there, too.

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PART 1

HOW IT WORKS

1

The Gut-Immune Connection

By creating an artificial environment, we're not stimulating our immune system enough. Germs are immune stimulants. They challenge you to be prepared.

—Deepak Chopra

Our gut microbes have been evolving with us for a long time—we can trace their origins to a common ancestor more than fifteen million years ago, but our formal understanding of these tiny creatures dates to the 1600s, when the Dutch scientist Antoni van Leeuwenhoek first looked at his own dental plaque under the microscope and saw "little living animalcules." A few centuries later, in the 1800s, the French chemist Louis Pasteur proposed his "germ theory" that certain diseases are caused by the invasion of the body by microorganisms and avoiding contact with them is the way to stay healthy. (It's hard to believe that prior to these groundbreaking findings, people thought foul odors or "evil spirits" were the cause of illness.)

This concept of avoiding germs like the plague has become foundational to modern Western medicine and is the driving force behind our efforts to find new and more effective ways to assault dangerous bugs, like the development of antibiotics and vaccines—discoveries that save countless lives every day. We've formulated medications like monoclonal antibodies that can help us combat viruses and illness if

our bodies aren't strong enough to fight them naturally and instituted widespread precautions to keep ourselves protected from pathogens. And simple yet important innovations in sanitation and hygiene, like Florence Nightingale's introduction of handwashing into British Army hospitals during the Crimean War, combined with social distancing and quarantining, have also become effective ways of limiting infectious outbreaks.

But as we've decreased the amount of germs on our bodies and in our environment, something else has increased at an alarming rate—and that's our susceptibility to viruses. The increased risk of viral infection includes completely new ones like human immunodeficiency virus (HIV), as well as reemerging oldies like measles, and more transmissible and deadlier versions of some we were already familiar with, like coronavirus. And with COVID-19, we have seen how a global pandemic can impact our daily existence. This paradox of increased infection as we get rid of germs isn't really a paradox at all—it's confirmation of the critical role our microbes play in protecting us from viruses.

THE HIDDEN WORLD INSIDE YOU

Since the days of Leeuwenhoek and Pasteur, we've also made another incredibly important discovery: not all germs are bad! In fact, the trillions of microbes that call our body home are primarily helping rather than hindering us, with a specific purpose that's very much aligned with our own survival. Without these microscopic critters, your immune system wouldn't be able to protect you from infections or cancer; your heart, lungs, and liver wouldn't function properly; and you wouldn't be able to digest food, assimilate nutrients, or synthesize essential vitamins and growth factors that your body can't make on its own. Even your mental health would take a major hit because of the

lack of neurotransmitters that microbes produce and the close and necessary interaction between bacteria in your gut and your brain health and development. Why is understanding the relationship we have with our microbes so important? Because these organisms are, in fact, intimately involved in every aspect of our health—and they're especially critical for protecting us from viruses. Viruses can't survive on their own. They rely on their host's cellular machinery to allow them to live, reproduce, and go on to infect other hosts—a process known as replication. How easily they're able to hijack that machinery is what determines your outcome when infected with a virus, and that is in turn dependent on the trillions of microbes that inhabit your body. To understand how it all works, let's take a closer look at this hidden world inside you.

MULTIPLE MICROBIAL PARTS

The microbiome refers to all the organisms that live in or on your body—from your scalp to your toenails and everywhere in between, but mostly in your gut. This diverse universe includes bacteria, viruses, fungi, protozoa, helminths (worms, for those of us who have them), as well as all their genes. A staggering hundred trillion microbes that include thousands of different species inhabit your body—with more than a billion bacteria in just one drop of fluid in your colon alone. We are single individuals, but we're composed of multiple living, breathing, moving microbial parts.

To appreciate the role and function of your microbes, it's helpful to think of your body as a factory. Organs like your lungs, heart, and liver represent the machinery that keeps production moving: extracting oxygen, pumping blood, removing toxins, synthesizing hormones, and performing all of the other complicated tasks that keep us alive. Some of these tasks are automated, but most of the assembly lines

require constant monitoring, maintenance, and adjustment. We house the machinery, but who operates it? How does a complex process like, for example, digestion, actually happen? How does the food get broken down into its basic constituents and carried across the gut lining into the bloodstream where it can be transported to cells that utilize it as an energy source? Who helps produce the substances your body requires but can't make on its own, like B complex vitamins B_{12}, thiamine, and riboflavin, and vitamin K? How does your body distinguish between serious infection with a dangerous virus and colonization with a harmless one? How does your immune system know when to rally the troops to defend you, and when to ignore benign intruders that don't pose a threat? Your microbes are the ones carrying out all of these tasks—and more! They even turn your genes on and off, activating those you need and dismantling those you don't.

Like David Vetter, the famous "boy in the bubble" who had a disease that weakened his immune system, you'd have to live in a sterile and isolated environment with no contact with the outside world in order to survive without your multitude of microbes, and even that wouldn't be enough to keep you alive because of all the other necessary functions your microbes perform. Since you're their host and they rely on you for their survival, most of your microbes are very much invested in your well-being. If you die, they die, too, and when you prosper, so do they. It is the ultimate symbiotic relationship, and when it's healthy and well maintained, both you and your microbes thrive.

We can categorize your microscopic roommates into three main groups:

1. Commensal bacteria that cohabit peacefully with you, like *Streptococcus salivarius* in your mouth that are simply part of your normal bacterial ecosystem.

2. Symbiotic organisms (sometimes called mutualists) that play an active role in keeping you healthy, like certain strains of *Escherichia coli* in the gut that synthesize vitamin K, which is required for your blood to be able to clot properly.
3. Pathogens (including opportunistic flora) that can do you harm, like *Pseudomonas aeruginosa,* which can cause ear infections.

In a balanced healthy microbiome, groups 1 and 2, the quintessential "good" bacteria, far outnumber the pathogens or "bad" bacteria. There's no requirement for a microbiome composed entirely of good bacteria, but without sufficient commensals and symbiotic species, your microbiome can't function properly—and neither can the rest of your body, particularly your immune system.

Table 1.1 • Predominant Bacteria Present in Humans

LOCATION	BACTERIA
Skin	*Staphylococci, Corynebacteria*
Mouth	*Streptococci, Lactobacilli*
Nose	*Staphylococci, Corynebacteria*
Throat	*Streptococci, Neisseria*
Stomach	*Helicobacter pylori*
Small intestine	*Bifidobacteria, Enterococci*
Colon	*Bacteroides, Enterococci, Clostridia*
Urinary tract	*Corynebacteria*
Vagina	*Lactic acid bacteria*

What Do Your Gut Bacteria Do?

Symbiotic organisms—the quintessential "good" bacteria—perform lots of important functions. They help you digest food, maintain the integrity of your gut lining (the barrier that keeps bowel contents—and

viruses—separate from the rest of your body), crowd out harmful pathogens, and train your immune system to distinguish between friend and foe. They also convert carbohydrates into critical metabolites like short-chain fatty acids (SCFAs) that help guide your immune response, and they synthesize many of the enzymes, vitamins, and hormones that you can't make on your own. Food can't be properly broken down and its constituent parts can't be fully absorbed without these essential gut bacteria, which means that even if you're eating a super-nutritious diet, if you don't have a healthy microbiome, you may not be able to absorb and assimilate all of the vitamins and nutrients in your food.

ROLE OF GUT MICROBES

- Digest food
- Produce digestive enzymes
- Convert carbohydrates to short-chain fatty acids (SCFAs)
- Help your body absorb nutrients such as calcium and iron
- Synthesize B-complex vitamins like thiamine and folate
- Synthesize fat-soluble vitamins like vitamin K
- Synthesize hormones and neurotransmitters
- Maintain the integrity of the gut lining
- Keep the pH in your gut balanced
- Metabolize drugs
- Neutralize cancer-causing compounds
- Promote angiogenesis (growth of new blood vessels)
- Crowd out pathogens
- Train the immune system to distinguish friend from foe
- Activate anti-viral efforts
- Modulate genes

You're Only as Healthy as Your Gut Bacteria

Ever notice how some people never get sick when everyone else has the flu or a cold? They're exposed to the same virus as everyone else, but because of their healthy microbiome populated with lots of essential "good" microbes, they're able to defeat the virus and stay healthy. The very young, whose microbiome is still developing and who therefore lack the microbial diversity necessary for a strong immune system, and the very old, who also have fewer microbial species and less diversity, tend to be the most vulnerable, but there are lots of external factors at play, too, in which we have a key role. The medications we take, the food we choose to put on our plates every day, and the environments we expose ourselves to are some of the major influences that we have control over. Overzealous use of antibiotics can put you at risk for viral infection by killing off good microbes along with the bad ones; a low-fiber diet literally starves many of the bacterial species that are essential for proper immune function; and a super-sanitized environment can also put us at risk by exposing us to pesticides and other microbe-depleting chemicals and limiting our contact with soil microbes that can enhance our own internal bacterial communities (I'll get much more into the nitty-gritty of these enemies of the microbiome in Chapter 11).

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Now that you have a better sense of your microbiome and the many important functions it performs throughout your body, let's focus on the connection between your gut microbes and your immune system and how that relationship, when it's healthy, protects you from viruses.

HAND AND GLOVE

Your body is in constant contact with external and internal threats that pose a direct danger to your health: harmful viruses and other

pathogens in the environment, plus internal waste and toxins that can build up in your body and lead to chronic inflammation and disease. Your immune system protects you from all of it—cancer, infection, and more—and helps you recover after injury. It's your first and best line of defense, and it's especially important now, with the reality of global pandemics, plus all the chemicals and carcinogens we're exposed to on a daily basis. But how does this internal surveillance system actually work to protect you from viruses? It turns out that your gut microbiome and your immune system have an extremely close interdependent relationship, and that hand and glove interaction is critical to a properly functioning immune system that can keep you safe and healthy.

Your immune system tolerates an enormous and constantly changing mass of harmless microbes, while at the same time recognizing and responding to dangerous viruses that it's able to spot amid a pool of trillions of other organisms. How is it able to distinguish friend from foe so precisely and then launch an attack that destroys one while preserving the other? The fact that more than 70 percent of your immune system is located in your gut provides an important clue. The thin lining of your intestinal wall, known as your epithelial barrier, has immune cells on one side and bacteria on the other, and both sides interact continuously with each other. Immune cells in your gut lining pump out substances to help defend against invaders, while microbes help guide and modulate those cells, ensuring a balanced immune response. Let's go over some immunology basics to better understand the relationship.

Immunology 101

Your immune system is made up of two armies: an innate system that you're born with and an adaptive one that develops over time. Your innate system is your body's first line of defense, responding quickly but in a general and nonspecific way to invading pathogens. For instance,

if you get a cut in your skin, your innate immune system activates cells and proteins that kill any bacteria that may have entered through the wound.

Adaptive immunity takes longer to develop because it evolves from learned experiences. It keeps a record of every potential pathogen you've encountered, so that it can recognize and destroy it when it enters your body again, utilizing more precise weaponry that targets the specific germ you're trying to fend off. While it may take a few days for adaptive immunity to kick in the first time you encounter a virus, the next exposure will generally result in a much faster response, and for some viruses, like measles, no illness at all with subsequent encounters because you have become "immune." Vaccines rely on adaptive immunity: when a small, harmless amount of protein from a virus is introduced into your body, your adaptive immune system will remember it if and when it encounters it again. Adaptive immunity is also known as acquired immunity and involves two different types of white blood cells: B lymphocytes, which make antibodies that destroy the pathogen itself, and T lymphocytes, which act as air traffic control for your immune system—removing any cells that have been infected and damaged by the pathogen, activating other immune cells, and regulating the immune response.

For some infections, like the flu, adaptive immunity doesn't reliably protect you because there are lots of different viruses or strains, and catching a cold or flu from one doesn't usually provide specific immunity against others. As we've seen with SARS-CoV-2, viruses can also mutate, and the new variant may not be recognizable to your adaptive immune system. Sometimes there can be overlap, though, and an infection with one virus can give you some protection against another. That's what researchers in Boston found when they identified people who had previously been infected with harmless coronavirus variants. When those same people got infected with SARS-CoV-2

years later, they weren't as sick. They had lower rates of needing a ventilator, fewer ICU admissions, and fewer deaths. Those Boston patients were a classic example of how prior exposure to germs can actually prime your immune system so that it can protect you from more dangerous pathogens down the road.

Another example of protective adaptive immunity was seen with the 2009 H1N1 influenza strain. When it emerged, it caused more severe illness in younger people. Globally, four out of five H1N1 deaths occurred in people under sixty-five. That's very atypical for flu deaths, which usually occur in older adults. It turned out that many of the older people had been exposed to a relative of the strain decades ago—and that previous exposure created a memory within their immune system that was able to protect them from H1N1.

Too Much

Having good adaptive immunity is one thing, but a stronger than normal immune response can actually lead to problems. Too much or too prolonged of an immune response can create overreaction to common exposures and cause food allergies, reactions to medications, allergies to bee or wasp stings, asthma, hay fever (allergic rhinitis), hives (urticaria), and dermatitis. These are all conditions that have become commonplace in the last half century and directly correlate with abnormalities in our microbiome that have also occurred during this time period. One example is the startling increase in the incidence and severity of food allergies that coincides with an increasingly processed food supply and high antibiotic use.

Autoimmune diseases, a family of chronic, often debilitating, and in some cases life-threatening illnesses that affect almost one in five Americans, are another classic example of an overactive immune system. Their mechanism, regardless of what organ they affect, is that they prompt your immune system to wage war against your body's

own healthy tissues, overreacting to normal stimuli with an exaggerated inflammatory response. Autoimmune diseases represent a new breed of illness that emerged mostly in the last century and include conditions like Hashimoto's thyroiditis, type 1 diabetes, lupus, multiple sclerosis (MS), rheumatoid arthritis, inflammatory bowel disease (Crohn's and ulcerative colitis), eczema, and psoriasis. There are more than a hundred different types of autoimmune diseases, and chances are you or someone in your family suffers from one (or more) since they affect about fifty million people in the United States alone. Different autoimmune diseases frequently affect the same person, suggesting a common root cause with varied manifestations rather than multiple distinct illnesses. In addition to genetic predisposition, depletion of good bacteria from antibiotics and other medications, and a diet that's lacking in the fiber needed to support the growth of essential species is at the root of many autoimmune diseases.

Not Enough

An underactive immune system (immunodeficiency) means your immune system's ability to fight infections as well as most types of cancer is compromised or entirely absent. Most cases are acquired ("secondary") due to illnesses like HIV infection or environmental factors like malnutrition. Immunodeficiency can also be due to genetic diseases that you're born with ("primary"), like severe combined immunodeficiency (SCID). Another common cause of immunodeficiency is medications that weaken your immune system, like biologics, steroids, or chemotherapy. Not only do these drugs dramatically increase your risk of infection—especially infections from viruses as well as "opportunistic" organisms that in immunocompetent people are usually benign and harmless—but they also interfere with your immune system's ability to detect and remove malignant cells, putting you at increased risk for cancer, too.

Just Right

Successfully fighting viral infections relies on what I like to call the Goldilocks principle: an immune response that's strong enough to clear the virus and keep you safe, but not so powerful that it damages parts of your body and harms you in the process—a condition known as cytokine storm. And this is where having a healthy gut comes in, since your gut bacteria are intimately involved in guiding your immune system to create that immune equilibrium. How exactly does it do that?

ANTI-VIRAL STRATEGIES

Mice raised experimentally without a microbiome can't survive in the real world outside of a sterile environment—and neither can germ-free humans. Bacteria in your gut are involved in every step of your immune response and employ specific strategies to protect you from viral infections.

The most important way your gut bacteria protect you is by regulating your immune system to make sure you have the appropriate response when you encounter a virus. Since most of your immune system is in your digestive tract, it's not surprising that your immune response is heavily influenced by the number and diversity of your microbes. Gut bacteria train your immune system how and when to respond to threats, turning up the response to fight invading viruses, or turning it down in situations where overshooting the mark and recruiting too many immune cells could lead to excess inflammation and organ damage—the deadly cytokine storm we've become so familiar with during the COVID pandemic. An intact and healthy complement of gut bacteria is therefore not only beneficial but also necessary for that Goldilocks immune equilibrium: a response that's robust enough to clear viruses but not so active that it ends up doing more harm than good.

Another anti-viral strategy of gut bacteria is creating a physical barrier that blocks viruses from penetrating deeper into your body. Viruses literally have to wade through a dense army of bacteria—plus their surrounding web of mucus and the epithelial gut lining—to penetrate common entry points like your nose, mouth, gastrointestinal tract, and lungs. A compromised microbiome weakens that physical barrier, creating cracks that allow viruses to seep through, gain access to your internal organs, and run amok in your body.

Deploying chemical weapons against viruses is another way your microbes protect you. When confronted with a viral threat, gut bacteria trigger your immune cells to release virus-repelling substances called interferons (so named because they "interfere" with viruses and keep them from multiplying). Interferons are proteins that are part of your natural artillery against viruses. They notify your immune system when harmful germs or cancer cells are in your body, and they recruit killer immune cells to fight those invaders. Common gut bacteria like *Bacteroides fragilis* and other commensals in your digestive system are the ones that raise the alarm and stimulate immune cells in the walls of your intestines to release interferons and other chemical weapons.

Here's an example of how it works: The very contagious *Rotavirus* causes a diarrheal illness that kills half a million children each year. But when anti-viral proteins from specific gut bacteria are injected into mice suffering from *Rotavirus,* they successfully halt the infection. Not surprisingly, we see almost five times higher rates of *Rotavirus* and more severe infection in children who have recently been treated with antibiotics and are missing some of those crucial protective bacteria. The same mechanism of bacterial protection is also true for other viruses like influenza, with increased susceptibility and worse symptoms when antibiotics precede the viral illness.

In order for viruses to infect a cell, they need to attach to specific

receptor sites (also called binding sites) on the cell membrane. They accomplish this through special attachment proteins in their protective shell that surround the virus's genetic material. In the case of SARS-CoV-2, those now famous spike proteins bind to ACE-2 receptors that predominate in our lungs and gastrointestinal (GI) tract. The ability of a virus to attach to a specific receptor determines what cells it can infect, which is why we see so many respiratory and GI symptoms with COVID. Bacteria like *Lactobacillus* outsmart viruses like coronavirus by competing for the same binding sites, which interferes with the ability of the virus to bind to their receptors. Without that binding the virus can't enter cells in your body and cause illness. And that's why we need lots of helpful bacteria like *Lactobacillus* around.

Predictive Power

Infection with a virus prompts your immune system to produce substances (cytokines) that control the growth and activity of other immune cells and help manage the immune response. In some cases, this response can be excessive, causing widespread tissue damage, septic shock, and multiorgan failure. This so-called cytokine storm is a leading cause of death in people with severe cases of COVID. Analysis of these patients shows that underlying microbial imbalance is associated with elevated levels of inflammatory cytokines and tissue damage, confirming the influence of the microbiome on the immune system response.

People with severe viral infections often lack certain helpful bacterial species in their gut that are essential for regulating their immune response. The resulting immune disequilibrium as a result of those missing microbes is what puts you at risk for life-threatening inflammation, not just in your lungs but throughout your body. In a large study of patients with COVID, the composition of the microbiome

predicted development of severe respiratory symptoms and death with 92 percent accuracy, which is much more accurate than cardiovascular status, age, or other traditional assessments of outcome. Why is this so important? Because unlike your genes, which are fairly static, or your age, which you can't change, or heart disease, which you may not be able to reverse, you have a great deal of control over what's going on in your gut. The purpose of this book is to help you connect the dots between your gut health and your immune health and chart a course to make sure both are fully optimized to protect you.

If we take a closer look at the digestive system of COVID patients with poor outcomes, we see high levels of an undesirable gut bacteria called *Enterococcus faecalis* (*E. faecalis*). *E. faecalis* can penetrate your gut lining, enter your bloodstream, and cause life-threatening infection, and that's why overrepresentation of *E. faecalis* in your microbiome is so dangerous. High levels of this bacteria are the top predictor of COVID severity. But just as too much of an undesirable species like *E. faecalis* can be problematic, not enough helpful ones can be just as deadly. Disease severity in COVID is inversely correlated with the gut bacteria *Faecalibacterium prausnitzii* (*F. prausnitzii*)—an essential and highly beneficial species that's cultivated by eating a high fiber diet. The relationship between *F. prausnitzii* and viral infections is clear and direct: the more *F. prausnitzii* in your gut, the less sick you'll be if you get infected.

If you're trying to predict who is going to do well and who is at serious risk during a viral outbreak, you need look no further than the gut. A small smear of stool obtained from your rectum will provide you with more valuable and accurate information than any other data points, including demographic information like age, ethnicity, or gender; clinical data like oxygen saturation, inflammatory markers, or levels of white blood cells; or medical history like whether you have heart disease, diabetes, or lung disease. Even when you combine all of

these factors, they still don't have the predictive power that assessing the health of your microbiome does, and that's true not just for COVID but for almost any viral infection. In the future, as we learn even more about which species help versus hinder, microbiome assessment may become a vital tool in identifying at-risk groups who need earlier intervention or closer monitoring when infected.

We know that compared to healthy people, people who get sick from viral infections tend to have preexisting conditions like obesity, cardiovascular disease, diabetes, or a weakened immune system, but all of these conditions are themselves strongly correlated with an unhealthy microbiome. Given what we know about the connection between the health of your microbiome and outcomes from viruses, it's not surprising that these patients are sicker. But why do so many people have an unhealthy microbiome in the first place? What is it about our current lifestyle that creates changes in our gut flora that put us at risk?

In Praise of Germs

Modern practices such as chlorinated drinking water, industrial agriculture, pesticides, and antibiotics have improved our lives in countless ways, but they've also brought health challenges by creating a super-sanitized environment that's associated with less microbial richness and diversity. Alcohol and the high-fat/high-sugar highly processed Western diet compound the problem because they don't nourish our essential gut flora. That leads to a decrease in important bacterial metabolites that are necessary for immune equilibrium and an increased risk of autoimmune diseases, allergies, and more severe viral infections.

You need interaction with germs to train your immune system how to respond appropriately to stimuli in your environment—what to react to and what to ignore. An immune system that doesn't get up close and personal with enough germs early on is like a child with

overprotective parents—ill-equipped to deal with problems when they inevitably happen. Not having enough exposure to microbes can lead to defects in your immune tolerance, which means a trigger-happy state of heightened activity where harmless encounters with normal gut bacteria, proteins in food, and even parts of your own body are treated like the enemy and attacked by your immune system.

Of course, during a pandemic a certain level of vigilance about exposure to germs is required. The trick is to employ tactics that rid your immediate surroundings of any viral threats while still maintaining exposure to health-promoting microbes. You also need to feed your gut bacteria an appropriate diet so they can churn out substances to help protect you, and avoid unnecessary antimicrobials that are ruinous to your bacterial foot soldiers. I'll provide all the details about how to do this in Part 3, "Strengthening from Within—the Anti-Viral Gut Plan." In the meantime, let me tell you about one of my patients who was fortunate to have lots of exposure to nature, microbes, and fibrous vegetables growing up, and what happened when that all changed.

THE MICROBIOME-LIFESTYLE CONNECTION

I diagnosed a patient of mine, Anjali (you may remember her if you read my second book, *The Microbiome Solution*), with Crohn's disease two years after she moved to the United States from India to attend college. She was raised in a vegetarian household in a village where every day, her mother or one of her relatives cooked lentils, chickpeas, mung beans, potatoes, okra, and other locally grown vegetables from scratch, made with plenty of anti-inflammatory spices like turmeric, and shared by multiple generations of her extended family living together in the same household. When she moved to the United States, Anjali continued to eat a vegetarian diet, but one that looked very different from what she grew up on: her daily fare was now pizza,

french fries, bagels, and the contents of the vending machines at school. She developed adult acne, acid reflux, and indigestion that eventually turned into bloody diarrhea and severe ulceration throughout most of her colon and small intestine.

Anjali had never heard of Crohn's disease and didn't know anyone who had it, but her case was one of the most severe I had ever diagnosed. We eventually got her into remission using a combination of conventional medication and dietary modification, reinstituting an unprocessed high-fiber diet similar to what she ate as a child in India. In her case, it seemed that the protective effect of growing up in a rural environment with lots of exposure to microbes and fibrous foods was no match for the detrimental effects of the Western diet and a super-sanitized lifestyle. Anjali's story illustrates the importance of a healthy microbiome in protecting you against disease, especially those that involve your immune system.

It's What's Inside That Really Counts

When I hear reports of people having severe COVID, or worse, even succumbing to the virus, in addition to feeling sad for their families and loved ones, I'm always immensely curious about their medical history—particularly what's going on in their gut. Someone may look perfectly fine on the outside, but do they have a healthy-functioning immune system? Are they dealing with an autoimmune disease that puts them at high risk for poor outcomes as a result of a disordered microbiome? Have they been on medication that may have significantly altered their gut flora? What does their diet look like? There are lots of additional determinants of health that play a role in outcome from viral infection—and we'll be discussing several of them throughout this book, but the gut-immune connection is fundamental to your ability to survive and thrive in a world full of viruses. To understand the significance of gut and immune health in the context of viral

threats, it's helpful to introduce another concept that is as consequential as germ theory, if not more so.

Your Terrain

Around the same time Pasteur was popularizing his theory, another Frenchman, Antoine Béchamp, proposed an alternative view of how and why we get sick. Béchamp's "terrain theory" stated that disease isn't able to develop in a truly healthy environment and that germs only lead to disease in an unhealthy host. Put another way, terrain theory focuses on the soil rather than the seed and makes the case that the same pathogen ("seed") can pass harmlessly through your body rather than make you sick if your ecosystem ("soil") is healthy. Therefore, paying attention to the health of the host—elements like our microbiome and immune system that make up our "terrain"—and not just the potency of the pathogen we're confronted with—creates resilience to a wide range of infections and illnesses. Béchamp believed that the more unhealthy and out of balance you are, the more susceptible you are to illness and the sicker you'll get when you come into contact with a virus.

As physicians, we see germ theory at work every day when people become ill after exposure to specific pathogens. But it's also logical that our body's terrain is a powerful force in helping to protect us against those illnesses. Terrain theory suggests that if a person has a healthy and well-balanced microbiome and immune system, any organisms they encounter will be dealt with by their body without causing severe sickness. Both theories play an important role in understanding how exposure to viruses can lead to illness.

We wash our hands and avoid people who are sick because of germ theory, but we maintain a well-functioning ecosystem that's able to fight viruses through eating a healthy diet and minimizing exposure to immune-suppressing and microbe-depleting drugs because of

terrain theory. The realization that the health of the host, not just the potency of the pathogen, also determines outcome from viral exposure is a simple but essential concept. Once you understand that you, as the host, are in the driver's seat when it comes to battling viruses, the path forward for how to emerge victorious becomes clear.

Overkill

Treating an off-kilter terrain with heavy hitters like immune-suppressing drugs or broad-spectrum antibiotics is like using Roundup to get rid of a few weeds in your backyard. It will definitely destroy any problematic giant hogweed or poison ivy, but at great cost to the insects and soil microbes that are the foundation of any healthy garden. Adrian Higgins, *Washington Post* columnist and author of three garden books, thinks that if you are turning to herbicides regularly, there is something wrong with your approach to gardening. I think the same can be said of an entirely medicalized approach to restoring or maintaining health that doesn't take into account the important nutritional and lifestyle factors that are at the heart of gut and immune well-being. When you prescribe steroids for autoimmune disease, or doxycycline for acne, you are treating a symptom, not the problem. Of course medications aren't the only thing that mess up your terrain—as I'll explain in Part 2, the Standard American Diet, too much stress, not enough sleep, and a number of other factors also compromise the health of your soil.

Weeds fill empty spaces and thrive in disturbed soil. If you spray them without addressing the void, they return swiftly. So the most effective and sustainable way to control them is to crowd them out with beneficial plants. I'm not a gardener, but as an integrative gastroenterologist, my approach to illness is microbe-sparing whenever possible, for the simple reason that repopulation yields healthier crops—and guts—than eradication. For example, in my patients with bacterial

overgrowth, instead of antibiotics I recommend restoring their terrain with fermented foods, a high-fiber diet, select probiotics, and daily exposure to dirt. It takes a little longer to work but has a high rate of success, has a low likelihood of recurrence, doesn't remove large swaths of healthy bacteria along with whatever you're trying to eradicate, and avoids secondary problems like yeast overgrowth that antibiotics cause. These are the benefits of a terrain-restoring approach.

FORENSICS

We hear about "totally healthy" people succumbing to viral infections all the time. While that can and does happen, diseases, including viral ones, generally don't just fall out of the sky and flatten us. We can almost always, according to principles of science and logic, predictably follow the breadcrumbs backward to uncover the vulnerability in our terrain that allowed infection and illness to develop.

Understanding the importance of your own innate host defenses and appreciating how easily they can be dismantled provides an opportunity to think about prevention in new ways that's less scorched earth, more organic gardening, and ultimately—more successful.

GETTING SICK IS NOT INEVITABLE

Exposure to viruses on its own isn't what makes us sick; it's defects in our terrain—depletion of our healthy gut bacteria, an imbalanced immune response, our stressed-out modern lifestyle, and ultra-processed diet—that ultimately turn that exposure into an illness. Exposure to viruses is inevitable. Getting sick is not. Sometimes you're dealing with a really bad bug, and no matter what you do, you're screwed. But more often than not, a defect in your terrain is what turns that exposure into a winner for the virus and causes you to lose the battle.

The health of the host is as important as the potency of the pathogen—and maybe even more important. We need an intact and well-functioning microbiome and immune system in order to make sure that inevitable encounters with viruses don't lead to serious infection. But what if I told you that not all viruses pose a threat to your health and that, in fact, many of the astonishingly large number of them living inside you form part of your genetic makeup and play a role in keeping you—and the planet—alive? In the next chapter we'll explore the fascinating and only recently discovered world of the virome and its relationship to human health.

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