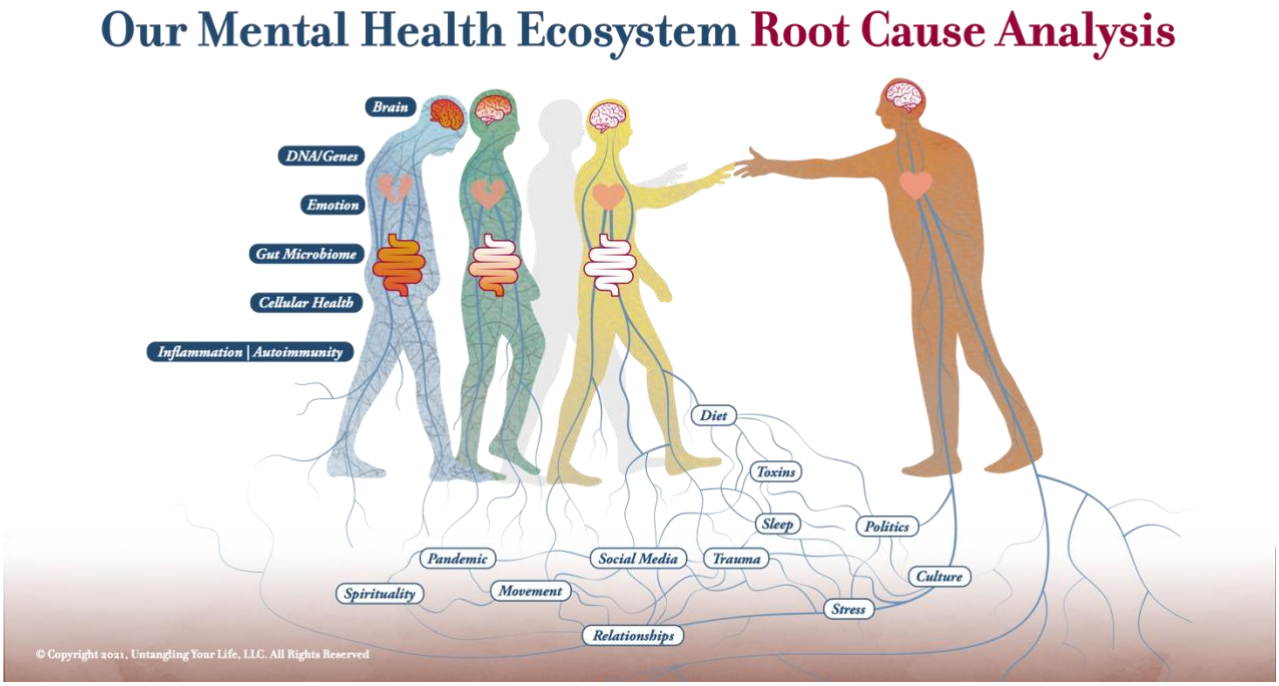
Bad Bugs and Mental Health

How Infections and Your Gut Microbiome Can Trigger and Perpetuate Psychiatric Conditions



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Are Infectious Diseases the Root Cause of Psychiatric Illness?

What you will learn in this blog:

> *Viral or bacterial infections are well known for causing physical distress, both in the short- and long-term. But could they also be the cause of you or a loved one's mental distress? Exciting new research suggests the answer to this question may be "yes"—and the conclusions could usher in a new era of psychiatric treatment. What makes a person more vulnerable to infectious disease-induced psychiatric illness… and is there any hope for a cure? Read on to find out!*

The Link Between Psychiatric Illness and Infectious Diseases

Dear Reader: have you ever wondered why a psychiatric illness develops, and what turns it into a chronic condition rather than an acute illness? Answers to these questions are crucial to alleviating the suffering of patients with chronic emotional illness, yet have remained elusive, until recent scientific breakthroughs. I believe these discoveries will revolutionize the practice of psychiatry and improve the lives of millions of patients. Exciting research is demonstrating that many chronic psychiatric conditions are triggered by common infectious diseases such as Lyme Disease, strep, mono, COVID, and Herpes. What would it mean to you or a loved one suffering from a chronic mental illness to learn that a virus or strain of bacteria may be the ultimate culprit—and that an antibiotic or antiviral medication may be the key to successful treatment?

Viruses and Bacteria May Attack Your Mental Health Ecosystem

New scientific discoveries showing how viruses and bacteria can destructively interact with your "mental health ecosystem"—comprised of your immune system, gut microbiome, and personal genetics—are resulting in a huge paradigm shift in the field of psychiatry, neurology and immunology. These new discoveries may help explain the root causes of your psychiatric symptoms and their persistence over the years, and could open the door to adding immunotherapy to traditional psychiatric medications.

If you or someone you love has suffered from a chronic emotional illness that has been difficult to diagnose and treat, **there may be "non-psychiatric" answers related to your immune system and its response to infectious diseases to help you feel well for good.** Let's dig in!

Which Common Infectious Diseases are the Root Cause of Psychiatric Illness?

New evidence demonstrates that infectious diseases such as Epstein Barr Virus (the cause of mononucleosis) can trigger and perpetuate Bipolar Disorder, and that Lyme Disease can trigger and perpetuate many conditions, including developmental disorders, autism spectrum disorders, schizoaffective disorders, bipolar disorder, depression, anxiety disorders, eating disorders, decreased libido, sleep disorders, addiction, opioid addiction, cognitive impairments, dementia, seizure disorders, suicide, violence, anhedonia (lack of pleasure in life), depersonalization, dissociative episodes, derealization, and other impairments.

Long COVID has served as an impetus for bringing many of these new discoveries into the spotlight. Long COVID's psychiatric manifestations can include depression with anhedonia, anxiety, and cognitive impairment (brain fog), as well as disturbances such as psychosis, obsessive–compulsive disorder (OCD), post-traumatic stress disorder (PTSD) and sleep disturbances.

Many other infectious agents have also been implicated, including tick-borne illnesses such as Babesia and Bartonella, Coxsackie virus, Candida, Mycoplasma (a source of pneumonia), and others.

How Infectious Diseases Attack the Brain

Infectious diseases like the ones described above can trigger what is now known as "Infection-Induced Autoimmune Encephalopathy", an abnormal immune system response resulting in inflammation of brain tissues. This response can also lead our immune

system to create antibodies that attack our brain's own neurons in addition to the virus or bacteria itself, making symptoms worse.

Here's how that can happen: on their surface, invading bacteria or viruses can share many of the same proteins that lie on the surface of our brain cells, which is known as "molecular mimicry." Certain factors—such as genetics, problems in our gut microbiome, specific toxins, and others—can weaken our immune system functioning. In a weakened state, our immune system can get "confused" about what, exactly, it is supposed to attack. Antibodies and white blood cells mark the bacteria or virus as "invaders" to rid the body of them, but because of the similar protein signature, they go after our own neurons and synapses and attack them as well… leading to significant consequences for our psychiatric state.

Is the Root Cause an Active Infection, or a "Hit and Run?"

Sometimes the virus or bacteria hides out in the body in a dormant state, lurking and ready to activate once again under certain stressful conditions. At other times the infectious diseases cause a "hit and run" condition—even though our immune system gets rid of these "bad bugs", their damaging effects may persist for months or years and cause numerous emotional and cognitive problems

Are Antibiotics and Antiviral Medications the Future of Psychiatric Care?

Psychiatric medications can help stabilize and improve mood and anxiety and insomnia symptoms, and treat psychosis—and many also modulate the immune system by reducing inflammation. These medications play an important role in the lives of many patients. That said, **the future of psychiatric care may very well include immunologic medications as well.**

This "immunologic" approach to treating psychiatric illness first involves using sophisticated laboratory tests to diagnose brain inflammation and autoimmunity. I will be

discussing these tests in future blogs. Depending upon the test results, referral to an infectious disease specialist, immunologist, or integrative medicine doctor is often the next step. A psychiatrist will work collaboratively with these doctors to determine each of the root causes of the chronic psychiatric illness.

For example, has a patient's Lyme Disease been reactivated after lying dormant? Has their mono infection come back? Is there an active strep infection? Are there antibodies to brain tissue? Depending upon what the tests show, treatment may involve antibiotics, antiviral medications, immune modulating medicines such as IVIG or Rituximab, or others such as maraviroc, aspirin, celecoxib, statins, and more.

Using Immunologic Medications to Fight Psychiatric Illness: An Expert's Perspective

My colleague and friend Dr. Gary Kaplan, an integrative medicine specialist and founder of the Kaplan Center for Integrative Medicine and the Foundation for Total Recovery, has pioneered the evaluation and treatment of infection-induced autoimmune conditions. Here is what he has to say about the present and future possibilities of this type of approach:

> *"We are at the beginning of a revolution in medicine. Immune dysregulation caused by an infection is in and of itself not a new concept in medicine. But the idea that immune dysregulation caused by an infection may be the underlying cause of diseases as varied as depression, obsessive compulsive disorder, chronic fatigue syndrome, fibromyalgia, chronic Lyme syndrome, post COVID syndrome and many others is not only revolutionary—it also presents us with an opportunity to not just treat symptoms but legitimately talk about a pathway to a cure. This approach also presents us with a number of challenges as it requires us to think completely differently about why people get sick.*
>
> *"What is unique about the people who develop chronic illness? Post-COVID syndrome affects somewhere between 10-30% of people who get sick. Chronic Lyme impacts about 20% of people who get Lyme disease. Everyone else gets sick and then fully recovers. Why? Genetics is unquestionably part of the answer. This is a rapidly developing area which is already guiding our therapies. The other issue is epigenetics. Literally meaning 'on top of the gene,' epigenetics is the study of how the environment can modify gene expression without actually changing the gene itself. Environmental factors that can 'set us up' for chronic illness include early childhood trauma, environmental toxins such as mold toxicity,*

and heavy metals such as mercury or lead toxicity. Pesticides and herbicides in our food, sleep disorders, even our diet can cause multiple problems. All of these things can cause damage to our 'second brain'—the gut microbiome—and can modify our gene expression to weaken our immune system. A weakened immune system is at risk of misfiring and over-reacting, making mistakes and becoming the problem itself.

"Treatment requires an individualized, whole-person approach: identifying and addressing all of the issues that 'set you up'; looking for, identifying, and treating any infections that may have been missed; and fixing the immune system that has become part of the problem. This is the path to recovery."

The Next Great Frontier of Root Cause Psychiatry

Reader, in prior blogs I have shared with you two of the great frontiers of psychiatry: genetics and the gut microbiome. The next great frontier is our immune system. If you or a loved one are suffering from a chronic mental illness, emerging scientific discoveries in the field of "psychoneuroimmunology" can bring you hope through the use of cutting-edge laboratory tests that uncover its root causes, and help guide treatment. These biotechnologies are advancing at a breathtaking pace, and I am incredibly excited about how they can pave the way to bring hope and alleviate the suffering for those who are struggling with chronic emotional problems.

Psychoneuroimmunology is so important that **I will be writing my next twelve blogs** about how it may finally bring you the answers that you (and your physicians) have long sought. I hope you'll join me as we explore this new frontier together.

Immunologic and Infectious Disease Testing

If You Think You May be a COVID Long-Hauler Let's Uncover the Root Causes

As we discussed in our blog about the root causes of Long-COVID, a principal underlying problem in many patients with Long-COVID is an immune system that is not functioning properly. Sometimes this immune system dysregulation also results in a reactivation of microbes that have caused prior infections such as Lyme spirochetes, Epstein Barr Virus, Herpes viruses, and others. Another blog discussed how Infectious diseases are known to cause some psychiatric illnesses

To determine what is wrong with the immune system, one or more of the following immunologic tests and/or infectious disease screening tests will be ordered by our physicians for patients treated in our Long-COVID treatment program. Specific tests are selected based upon the patient's personal history, family history, and presenting symptoms.

Depending upon the results of the test, we may refer the patient out to prominent immunology, infectious disease, or neurology practices for further evaluation and treatment. We collaborate with our colleagues in these fields to combine their therapies with the psychiatric medications that we prescribe. These outside practices may prescribe medications such as immune-modulating therapies like IVIG or Rituximab, antibiotic or antiviral medications, or other possible medications that target the patient's immune system problems such as maraviroc, pravastatin, plasma exchange, and others.

Immunologic Tests Help Uncover Causes of Brain Fog, Depression, Fatigue and Anxiety

Vibrant America/ Vibrant Wellness Gut Zoomer ● Purpose: A unique opportunity to take a close look at the microbial world that exists in our gut, as 70% of our body's immune system resides in the gut, and 75% of the cells in the intestinal tract function as immune system cells. The gut can be a source of chronic inflammation, and also the gut

microbiome actively programs various immune system functions. To learn more about this test, please visit here.

IncellKine via IncellDX ● Purpose: IncellDx has developed a test for molecules that promote inflammation, such as cytokines, and chemokines that attract white blood cells into brain tissue. Using clinical research results combined with artificial intelligence, they provide our treating doctors a written consultation report with findings and treatment recommendations, and also offer a telehealth visit with one of their doctors for a live discussion of findings and recommendations. To learn more, please click here.

Cunningham Panel via Moleculera Labs ● Purpose: This panel consists of a series of high complexity blood tests that assist clinicians in diagnosing infection-triggered autoimmune neuropsychiatric syndromes that create antibodies that directly attack brain tissue. ○ To learn more about the panel, please click here.

KBMO FIT 176 ● This test analyzes your sensitivity and immune system response to 176 different foods, coloring, and additives, identifying dietary sources of systemic and brain inflammation that cause chronic emotional distress. Please review the KBMO webpage for more information.

Infectious Disease Testing Uncovers Causes of Long-Hauler Pandemic Fog and Chronic Fatigue

Vibrant America/ Vibrant Wellness Tickborne 2.0 ● Purpose: A test for detection of tickborne diseases, where some of the microorganisms that cause the disease can hide out in the body and be reactivated later when our immune system has been weakened, for example by COVID. To learn more about this test, please click here.

Quest or LabCorp blood studies ● Purpose: We can screen for a number of different infectious diseases that may have been reactivated including Epstein Barr Virus (mononucleoisis), Herpes Viruses, Strep, and others.

Long COVID: The Brain Fog Pandemic

Long COVID affects up to 30% of individuals who were previously infected. A variety of psychiatric symptoms can become chronic, including brain fog, depression, anxiety attacks, panic, and more. This blog will explain the root causes of long COVID symptoms, and how you can overcome them.

Long COVID Brain: What is Long COVID?

Dear Reader, we are coming up on three years since the onset of COVID. For some, those years may feel like an eternity, particularly those known as “Long Haulers.” If you are suffering from long COVID or know of a friend or loved one with persisting symptoms, you realize how debilitating this condition can be. The medical term for long COVID is “Post-Acute Sequelae of COVID” (or PASC for short), and it is estimated that between 10-30% of people who tested positive have lingering symptoms beyond three months. Some long COVID patients have had 20 or more symptoms that persist, as this scourge can affect multiple organs and systems throughout the body. When it affects the brain, many patients report brain fog, depression, anxiety, and panic attacks—“long COVID brain”, in

What Causes Long COVID?

Researchers are exploring a number of possible causes of long COVID, including persisting coronavirus infection, viral fragments that have not been cleared from cells, gut microbiome problems, chronic inflammation, mitochondrial malfunction (mitochondria are the cellular “power plants” that create energy to enable life itself), direct damage to tissue, blood clots in small arteries, autoimmunity (antibodies that attack both the virus and our own cells), immune system dysregulation, and reactivation of microbes “hiding out” in the body from prior infections (e.g. Lyme spirochetes, Epstein Barr virus, strep, etc.).

In a prior blog I discussed how these viruses and bacteria can trigger psychiatric symptoms such as cognitive problems (brain fog), post-traumatic stress disorder (PTSD), depression, anxiety including obsessive-compulsive disorder (OCD), mental fatigue, and

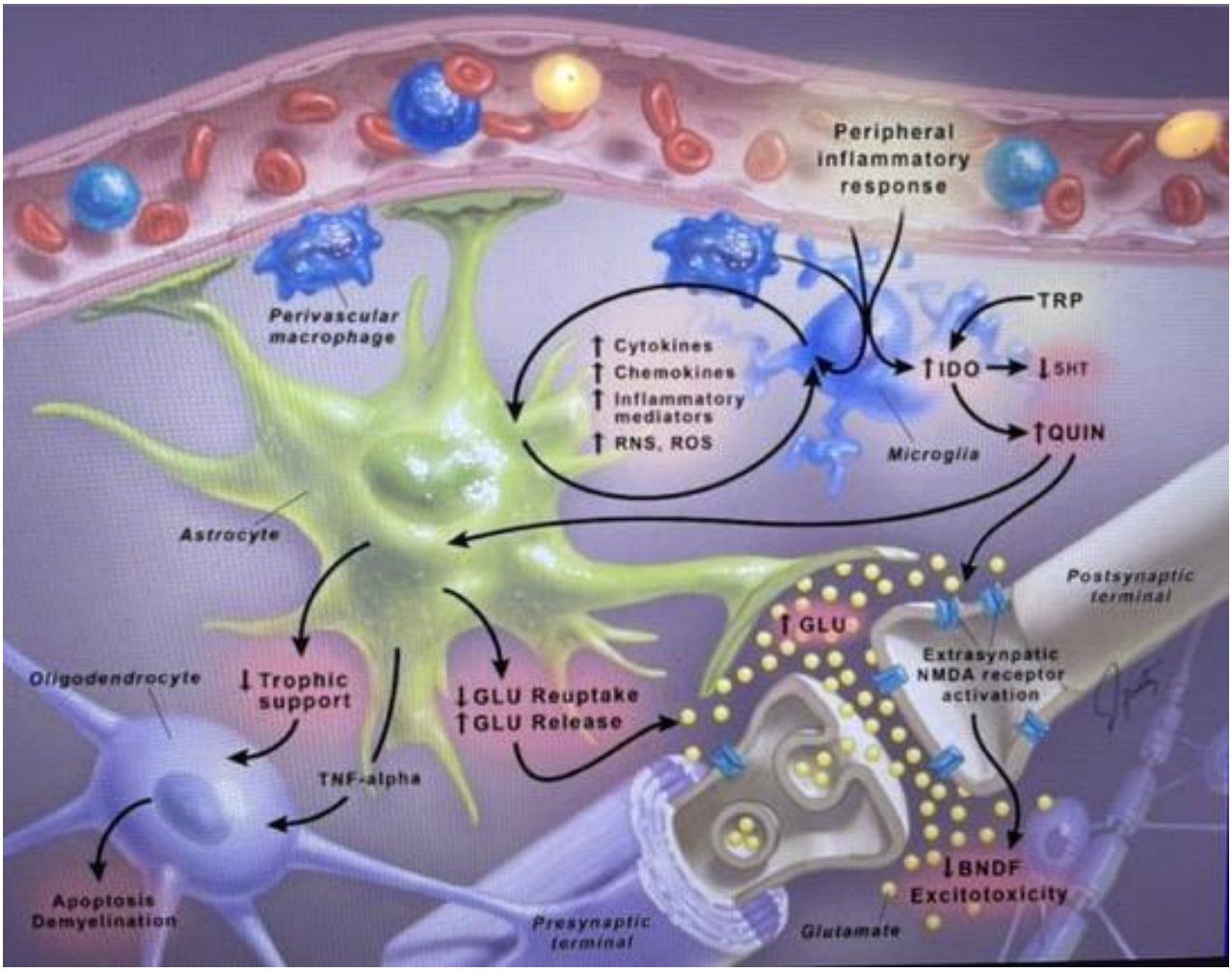
even psychosis. In this blog we will focus on why Coronavirus SARS-CoV-2 is one such culprit.

Long COVID Psychiatric Symptoms

In our practice, and reported by colleagues elsewhere, following a COVID infection there are a number of patients presenting with psychiatric symptoms for the first time, as well as previously stabilized patients that had dramatic worsening of their symptoms. Long COVID's psychiatric manifestations can include brain fog and other cognitive problems, persisting fatigue, depression with an inability to experience pleasure, anxiety, as well as other disturbances such as psychosis, suicidal feelings, OCD, PTSD, and insomnia.

How Does the Coronavirus Cause Psychiatric Symptoms?

Emerging scientific evidence suggests that SARS-CoV-2 affects the brain in a number of ways. Although somewhat rare, the virus can infect the brain itself, which can be associated with movement disorders, stroke, and other neurological disorders. This is more likely with those patients who are hospitalized, where 21% show signs of brain infection on brain imaging tests. What is far more common, particularly among patients with mild to moderate symptoms of COVID, is **chronic brain inflammation** resulting from prolonged immune system activity. Below is an infographic I will use to explain what happens. At the top is a blood vessel feeding the brain, and below the vessel are four types of brain cells:



1. **The microglia** (in blue) – there are one trillion microglia in your brain, and they are the brain's immune system cells
2. **Astrocytes** (in green) – these are the "nurturing cells" in the brain that support, nourish and protect all the other cells
3. **Oligodendrocytes** (in purple) – these important cells lay down and repair the myelin sheaths – the insulation surrounding neurons – to keep firing neurons from "short-circuiting" one another
4. **Neurons** and their synapses (purple myelin surrounding white cells) – probably already familiar to you, there are "only" 100 billion neurons in your brain, which communicate with one another across one thousand trillion synapses in circuits that help create emotions, thoughts, and behaviors.

Keeping in mind the infographic above, here's how chronic brain inflammation develops. As your body's immune system fights the coronavirus, inflammatory molecules like IL6 and TNF Alpha travel through the blood vessels, and then cross from the bloodstream through the blood-brain barrier into the brain. Once inside, they signal to the microglia that "uh-oh, there's an infection coming." The microglia then ramp-up their metabolism,

change their physical form into a “warrior state,” and begin to release all sorts of signaling molecules into the surrounding tissues like free radicals. These molecules then attract white blood cells to enter the brain from the bloodstream (like the two “perivascular macrophages”seen above, also in blue). This is part of the normal acute inflammation process needed to kill off viruses that invade the brain. But what happens when it becomes chronic inflammation? Here’s where long COVID begins to develop.

Macrophage is translated as “big eater.” They and the microglia start “eating” what is around them, damaging the astrocytes which stop nourishing and start releasing excessive amounts of glutamate (a toxic neurotransmitter). This causes the oligodendrocytes to self-destruct, so they can no longer repair the myelin insulation surrounding the neurons. Without their support systems in place to protect them, those poor neurons and synapses get battered by the inflammation and oxidative stress. They lose their “BDNF fertilizer” and not only become damaged, but in extreme cases even healthy neurons get gobbled up by the microglia. This damaging cycle perpetuates itself, resulting in the long COVID psychiatric symptoms mentioned above.

Treating COVID Brain Symptoms: Tom's Story

Tom was a 20 year old college student who presented with brain fog, depression, anxiety, fatigue, panic attacks and gut symptoms including gas, bloating, diarrhea and abdominal pain. All of these symptoms followed his COVID infection a year earlier. He had already seen a couple of psychiatrists, and had been prescribed medications, but hadn’t improved. He felt hopeless, had trouble meeting the demands of daily life, and just wanted his old life back.

To help evaluate and treat Tom’s debilitating condition, we enrolled him in our Root Cause Psychiatry Program, where we implemented a variety of diagnostic tests. In Long COVID patients, these may include:

- A genetic test through a simple cheek swab which helps us more precisely prescribe a medication to help alleviate the symptoms of brain fog, depression or anxiety.

- A microbiome stool test, as 70% of our body's immune system resides in the gut, and healing the gut improves the immune system dysregulation behind long-COVID.
- A test of cellular health that helps us create a nutritional psychiatry approach to improve cellular energy production, and repair damage caused by inflammation
- A cytokine panel, IncellKINE, that looks at inflammatory chemicals in the blood, and uses Artificial Intelligence to recommend targeted medications to reduce their numbers
- A test that measures antibodies that attack brain cells, The Cunningham Panel, leading to recommendations for immunotherapy, which is generally combined with psychiatric medication

Tests for other viruses or bacteria that co-infect, or are reactivated from prior infections, like Lyme, Strep, Herpes, and others

How We Treated Tom's Long COVID Depression, Anxiety and Brain Fog

Based upon Tom's symptoms and genetic testing results, we began him on the antidepressant Trintellix, which treats depression and also has numerous immune system modulating effects; and a methylation support product (good methylation is essential for a healthy immune system), which helped him improve about 50% after one month. He was found to have gut inflammation (caused largely by gluten intolerance), leaky gut syndrome, and cellular mitochondrial dysfunction, so our functional nutritionist, Julie Wendt, began him on a regimen of nutrients, supplements, and a gut-healing protocol. After about three additional months these interventions brought about a 70% recovery. Based upon the results of his cytokine and anti-brain antibody panels, we referred him to an immunology group who then added an immune modulating medication, Rituximab, to the interventions we had initiated. This combined approach achieved a 90% recovery five months later. After nine months of treatment Tom entered CBT therapy to reframe the trauma caused by his COVID, and we are optimistic that he will have a full recovery.

Your Mighty Moody Microbiome

Your Microbiome – An "Invasion of the Body Snatchers"?

My Dear Reader, are you a spiritual person? Do you ever have spiritual experiences when you feel a sense of wonder and awe while walking out in nature, or when contemplating the exquisite complexity of each living being? I know I do. For example, I feel awestruck that each cell in our body contains 70 trillion atoms comprising 2 trillion molecules, whose complex interrelationships are "composed and conducted" by our DNA, creating a grand symphony within each living cell. And then add in an additional layer of symphonic complexity: each of the 32 trillion cells in our body interrelates with one another to create an even greater majestic symphony—that of a living human being!

Today I will introduce you to an equally extraordinary marvel and layer of complexity within your body: your microbiome, comprised of the 90 trillion microorganisms, each of which are intimately related to the functioning of your 32 trillion cells. In our new series, "Your Mighty Moody Microbiome," you will learn how the DNA in these microorganisms is an extremely important "manufacturing plant" that also helps regulate the DNA in your body's cells, and how you can use that information to improve your emotional health. As we journey together, perhaps you too will experience a sense of wonder and awe, and something spiritual alongside me. Let's get started…

One of the best parts of returning from a summer vacation is undoubtedly sharing all of the wonderful memories with friends and loved ones upon your return. I adore hearing of others' travels far and wide, across our abundant, beautiful earth. Like me, many of my friends are avid nature lovers, whose vacation pursuits usually crystallize around the idea of getting out of town and deep into the wild for as long of a stint as time will allow. There are many reasons to connect with the great outdoors, but for me, there is one element I particularly enjoy: I simply love sitting back after a long day spent fishing or walking and letting my eye adjust to the subtle workings of the natural world that surrounds me. Suddenly, I can see not just the trees but the birds inhabiting them, making their home

there and in return spreading tree seedlings or berries far and wide, ensuring survival. I can see not just the flowers, but the bees nesting within, harvesting their pollen. A friend of mine recently came back from a scuba diving trip in Bali, and he told me similar stories: underwater, he spotted bigger fish getting "cleaned" by smaller fish, sea anemones attached to hermit crabs, feeding on their leftovers, and in return, protecting the crabs from octopuses and other dangers with their spikes. Reflecting on the wonderful interconnectedness of nature is a good reminder that we exist in a context much larger than our own… in fact, larger than we ever could've imagined.

It was the English poet John Donne who first wrote the words: "No man is an island." While we can understand this conceptually, our American culture remains deeply imbedded in the idea of rugged individualism—that we don't need anyone or any *thing* to make us happy. These messages often focus on people and things, rather than other creatures of the natural world, like the sea anemone depends on the crab. However much we may think of humanity as separate and above the laws of nature, we remain very much within the very same ecosystem as our animal relatives. And, as we are only beginning to understand, we don't need to look very far outside of ourselves at all to appreciate our connections to other species. In fact, we need only look within. Inside each and every one of our bodies resides an entire universe of microscopic organisms; so numerous are these inhabitants that they outnumber our own cell count 3 to 1. In prior blogs, we discussed the microbiome. This blog marks the beginning of a series that widens the lens. For the next few weeks, we will be talking about the holobiont—the entire study of microbes living in our bodies, from the gut to the mouth and beyond. We will also integrate some of this knowledge with some of the genetic variants assayed by Genomind's Mindful DNA test. Reader: this is truly the frontier of scientific research. In the coming decades, we may be able to treat any number of mental and physical health ailments using the holobiont exclusively. I am thrilled to dig into this exciting new topic. However, every journey must start with a single step—so let's get to know the holobiont, what it is, and what it does!

The Holo-what? The Holobiont, Defined

Like many scientific terms, the holobiont cannot be fully understood without first having a solid underpinning of the context in which it arose—and the primary context we must get to know in this case is the natural workings of symbiosis. First coined in 1879, symbiosis is defined simply as two separate organisms ("symbionts") living in close association with one another, and typically engaging in a mutually beneficial relationship (known as mutualism). The examples of inter-species interactions I described earlier are all examples of symbiosis. The tree could just drop its seeds on its own, sure. But the help of small birds greatly enhance the potential for that seed to spread—and the bird gets fed in the process. Of course, not all symbiotic relationships are mutual. Sometimes, just one species benefits, with the other remaining unimpacted (this is known as commensalism). Other times, one species benefits, while the other is actively harmed (parasitism—think of roundworms in animals).

Humans, too, engage in symbiosis every single second of every single day—from birth until death—without even seeing the symbiotic processes take place. The countless symbiotic interactions happening between our bodies and the microscopic organisms living within it is known collectively as the holobiont. The term was officially introduced in 1991 to define the interactions involving a single host and a single symbiont, but was extended to define a host and all of its associated communities of microorganisms. What, exactly, is the extent of these interactions? The answer may blow you away. Our human genome consists of about 20,000 genes. Our hologenome—or the sum of our genome and all associated microbial genomes—contains *33 million genes* from our microbiota alone.

As this fascinating scientific paper on the topic states, "It is becoming increasingly clear that the development, growth, and health of macroorganisms (like us humans) are influenced by the complex microbial communities they host that shape their ecology and evolution. Biology is indeed undergoing a paradigm shift, where individual phenotypes (our physical characteristics) are seen as a result of complex interactions resulting from the combined expression of the host and associated microbial genomes."

No man is an island, said John Donne… but who would have thought centuries ago that no man is biologically autonomous? Our bodies look so individualized from the outside—but the truth is, we have more foreign cells in our bodies than we have cells we can call our own. And these foreign cells contain 1650 times as many genes. We are a walking host for trillions of other organisms!

The Holo-Why? Why Should I Care about the Bacteria Living in Me?

History often looks back at the past and cringes at the mistaken ideas that have since been corrected. One of the greatest cringhes waiting for the next generations pertains to our ideas regarding the bacteria living within us. For decades, we believed all bacteria was bad bacteria. We tried to kill off these little microbes with antibiotics and worse. Only now are we beginning to see what an incredible ally this inner-universe could be to us—and that includes our present and future mental health outcomes.

In addition to the microbiome community living in our gut, we all have microbiome communities on our skin, in our mouth, in our urethra and bladder, and even in our lungs. And women also have microbiota in their vaginas. Most often, these bacterial communities engage with us in a mutually beneficial relationship—they help us feel good, and we feed them. However, if we have an unhealthy microbiome, we can encounter a state of dysbiosis. For example, if our gut microbiome is unhealthy, we may encounter allergies, hormonal changes, and have trouble losing weight. Each of these affects our mental health, both directly and indirectly—in fact, our mental health and our microbial health are engaged in a symbiotic relationship themselves. Our body can affect our mind via symptoms previously mentioned, and our mind can affect our microbial health just the same: diet, exercise levels, and hygiene, for instance all may shift depending on the state of our mental health—and each of these factors can play a role in keeping our microbiomes healthy or throwing them into dysbiosis.

Your Microbiome: Body Snatcher or Health Promoter?

Whether between our bodies and the microbes living within, or our microbes and our mental health, when symbiotic relationships fail or become more difficult, entire ecosystems are thrown out of equilibrium—including the individual ecosystems that comprise the emotional and physical you and me. **Dysbiosis will "snatch away" the health of our 32 trillion cells!** As we've previously seen in our discussions of the biopsychosocial model, our biology, psychology, and environment all play a role in our mental health, and coming to understand all of the ways our genes interact with our microbiome, to create profound effects on our emotional and physical wellbeing, will be an absolutely crucial element of treatment in the future.

Reader, I'll put it plainly: if you want to have a clearer picture of your mental health and wellbeing, you should care about your holobiont. It will lead you to exciting new places, many of which we will explore in our upcoming blogs. Follow along—and give yourself a head start on creating a healthier future for you and those you care about.

How "Messages from Bugs" Affect Our Mental Health

Reader, have you ever found yourself so absorbed in your thoughts that you forget about the world around you—so preoccupied that you are completely unaware of your emotions and your bodily sensations? I admit, I've experienced many of these moments over the years. Thanks to the ubiquity of smartphones, tuning out is made all the more easy. While our minds can't function without our holobiont—orchestrated by the DNA in our 32 trillion cells and 90 trillion microorganisms—our bodily functions can become an afterthought—something we must lug around to get our brains to go where they need to go, or to show our minds what they want to see (like the latest Facebook post or Instagram message). One great human fallacy of our modern era is to think our brains are responsible for themselves. Reader, if you've been following along with this blog, you'll know that's simply not the case. Our brains coexist with and are enormously influenced by a complex "second brain" inside of us. Resting entirely outside of the brain is a powerful behemoth—an independent yet symbiotic living organism all its own that may decide our desires before we can name them; may create hunger or other cravings; may make us moody and sleepless. It is a symbiosis that promotes health or disease. If we're not careful, it is this organism—not our conscious minds—that has the power to determine our fate. That behemoth has a name: the microbiome, or the trillions of bacteria living in your gut. Those "bugs" are no dummies. They can modify your genetic expression, they can speak to your nervous system, and they can wreak havoc on their home in your own intestinal tract. This week, we're going to take a broad look at how your microbiome impacts your mental health, and why you would do well to take care of it and keep it happy!

Can "Messages from Bugs" Influence Your DNA and Your Destiny?

As we've read in prior blogs, our DNA is not a fixed factor in determining our mental and physical health. We may be born with particular gene variants, but the way those genes

are expressed depends on a series of dynamic environmental factors, many of which can be tweaked, altered, and adjusted. The ability to turn gene variants on or off—or to upregulate or downregulate a gene—is known as epigenetics, which you can read about in our prior blog on the topic here. Epigenetic influencers include factors as large and unwieldy as the cities we live in to more specific factors, like the foods we consume, or the people we love or work with. However, influencers aren't always external—in fact, one of our greatest epigenetic modulators exists inside our own bodies, lining our gut, our skin, our mouth, and more. Your gut microbiota is directly influenced by the foods you eat—and subsequently by the nutrients it can extract to feed itself. In turn, various bacteria found in your microbiome can exert epigenetic effects on your DNA, through a complex set of "messages from bugs." As just one example, elements in the microbiota have been shown to both promote and limit obesity expression—which in turn can have a significant impact on our mental health outcomes.

As an epigenetic modulator, your microbiome also plays a significant role in your immune programming system. Have you ever met someone who simply never gets sick? They likely have a healthy microbiome to thank. If you were born with and cultivate a healthy and diversified microbiome, those trillions of bacterial cells will come to your aid in staving off chronic inflammation and promoting immune cell homeostasis. A dysregulated microbiome, on the other hand, may leave your body chronically inflamed and prone to acute illness and a higher likelihood of diseases. This imbalanced state is known as dysbiosis. Inflammaging can play a role in a number of mental health conditions, including chronic fatigue and dementia. Bottom line: keeping your microbiome in a balanced state is an important component in your DNA expression and mental health outcomes.

How Do These Bugs Impact Your Mental Health?

So, the gut microbiome plays a critical role in our gene expression—and it can help to bolster our immunity. But is there a more direct connection between our gut and our mental health? You bet there is—and it's become so well documented in recent years it's even been given a name: the Gut-Brain Axis. Our gut bacteria aren't just microscopic

mooches, eating whatever nutrients they can get. No: this second brain also sends messages to our first brain —and those messages play a direct role in our mental health. As numerous studies have found, “healthy gut function has been linked to normal central nervous system function”, and a dysregulated microbiome has been shown to have an impact on nervous system disorders, including depression, bipolar disorder, anxiety, schizophrenia, autism, and others. Certain genetic variations tested by the Mindful DNA Assay may also predispose to dysbiosis, including FUT2, HLADQ2/8, stress response genes and BDNF.

We will be looking closely at the connection between our bacteria and our brains in future blogs in this series—including genetic testing of the bugs themselves—nd if you or a loved one is impacted by one or more of these disorders, it’s worth your time to stick around for them.

The Gut-Brain Axis is not the only way our microbiome impacts our mental health, however. A healthy microbe can bolster our defenses against “leaky gut syndrome”, also known as “intestinal permeability”. A healthy microbiome means a healthy gut lining, which in turn keeps partially digested food and nutrients well within the confines of our intestinal tract and helps our bodies absorb those nutrients into our bloodstream. An unhealthy microbiome leads to an equally unhealthy gut lining, which can develop cracks that allow food to seep out and toxins and other bugs to creep into our bloodstream triggering an immune response to these “foreign bodies.” Leaky gut can not only lead to poor physical health, but negative mental health outcomes as well—obesity, chronic fatigue syndrome, and mental illness have all been associated with a leaky gut.

Keeping the many bacterial cells in your microbiome healthy and happy is not only good for your body—it’s crucial to your mental health. Next week, we’ll take an even closer look at how the microbiome impacts our neurotransmitters. Stay tuned!

You're Married to Your Ninety Trillion Bugs – "In Sickness and in Health"

Dear Reader, as a psychiatrist, it's always fascinating to see which time-worn concepts from my field of work find their way into the broader culture. I enjoy observing how cultural movements give rise to pop-psychological "trends", and while it can be frustrating to see certain concepts stray from their original meaning in our field, I believe that, overall, bringing psychological ideas into our daily lives provides a net good to society. That said, I've been watching the rise of self-care with fascination—mainly because of the question implicit in its explosion onto the pop-culture scene: *why now*? I believe the answer lies in two places: first, a growing mistrust in relying upon institutions and the people who serve them; and second, in a long-held truism—if we want to help others, we must help ourselves first—and yet, with our ever-growing list of people and tasks to juggle, helping ourselves first has never felt harder. Have you ever felt yourself brushing off the needs of your own body or mind in pursuit of ensuring the happiness of a loved one? Have you ever taken your own body for granted while focusing on the health and wellbeing of someone else's? If you recognize the importance of self-care but continue to neglect to put it into practice, then I have good news for you. Today, I am going to tell you about a newly identified organ in your body—an entity that, if nurtured, can protect you from disease, can prevent obesity, can stabilize your mental health—and could possibly even aid in solving an addiction. This entity is entirely distinct from you. However, it also happens to live inside of you. Consider caring for this distinct organism within you as a stepping stone to caring for the living organism that is *you!* If you haven't guessed yet, the entity at hand is your microbiome. In this third installation in our series dedicated to your Mighty Moody Microbiome, we're going to take a look at what factors keep your microbiome happy and healthy—and what factors might be hurting its chances to thrive.

What is a Healthy Microbiome—and What Can It Do for Me?

As we discussed in earlier in this series, the bacteria that live within us are a force to be reckoned with. Our microbiomes contain three to ten times as many cells as the rest of our bodies. The genes of our gut bacteria are 150 times larger than our human genome. Perhaps most tangibly shocking, the mass of our body bacteria can reach up to nearly 3.5 pounds! These bacterial cells can send important signals to our brains. They manufacture neurotransmitters, hormones, and vitamins; they help program the immune system; they facilitate food digestion and maintain the integrity of the inner lining of the bowel to prevent "leaky gut syndrome;" they communicate directly and indirectly with the brain; they epigenetically regulate DNA in cells throughout the body; and so much more we don't even understand yet! If not taken care of, they can cause inflammation, gut problems, obesity, insulin resistance (type 2 diabetes), and so much more. They can even cause neurodegenerative diseases over time. If you've been following this series, you know what makes the microbiome mighty. But what, exactly, makes it healthy? The answer to that lies in the 1000 species of bacteria that may live in our gut. Think, for a moment, of your body as the globe, and those thousand species as the people, plants, and animals. Our globe is stunningly beautiful—and its resiliency for hundreds of millions of years up till this point has been made possible by the incredible abundance and diversity of species. The combination of abundance and diversity allows life to thrive in nearly every realm—and that includes your gut. The answer to what makes a healthy microbiome is actually quite simple: a healthy microbiome is both an abundant and a diverse microbiome, comprised of as many healthy bacterial species as possible, with an absence of "disease-causing bugs" that represent infectious bacteria in the gut, and the destructive inflammation of the gut, the brain, and every other organ of the body that comes along with them.

When a microbiome is healthy, it helps the body sustain cellular equilibrium and homeostasis. When a microbiome is unhealthy—that is, populated with less diverse and/or pathological bacteria—the gut is thrown into a state of dysbiosis, which is linked to many diseases such as inflammatory bowel diseases (IBD), irritable bowel syndrome

(IBS), diabetes, obesity, cancer, cardiovascular disease, and central nervous system disorders such as depression, anxiety, bipolar disorder and dementia. Your microbiome is like a loved one; take care of the relationship, and you shall both reap the rewards. Neglect it, and it can turn against you, leaving your body and mind feeling not quite right—or worse. Three factors specifically can lead to positive or negative gut-health outcomes. Let's take a look at each individually, and as we do, I urge you to consider where you fall in each of these realms, and how you might be a better friend to the Mighty Microbiome living inside you.

You Are What You Eat—and So Is Your Mighty Moody Microbiome

Your Microbiome is "Mighty" in how forcefully and extensively it influences our physical health. It is "Moody" in that it deeply influences our mental health and moods. And it is "Mighty Moody" in that can suffer from its own "rapid mood swings." What do I mean by that? Popular culture has known for decades that diet plays an important role in physical health—but numerous studies are now showing that diet also plays a huge role in our day-to-day wellbeing—heavily influenced by the effects of certain nutrients on the health of the microbiome itself. The reason for that lies in the interplay between the food we digest and the bacteria helping the digestion along. If feed our microbiome a diet that it "loves," we can maintain that critical abundance and diversity of gut bacteria that is crucial for maintaining the homeostasis among and inside of our body's 32 trillion cells. However, if we eat a diet that doesn't sit well, that abundance and diversity will deplete itself and leave us vulnerable. As one article states, "Dietary intake alters gut bacteria, which in turn alters host metabolism, which in turn can lead to host diseases." And as for those "rapid mood swings," **unhealthy changes in your diet can, in fact, begin to negatively alter your microbiome within 24 hours—with a reversion to a flourishing microbiome within 48 hours after changing back to a healthy diet.**

More research needs to be done to determine what specific diets feed your microbiome best—however, initial studies have found that high-fat diets in mice decrease the number of gut bacteria, while fiber-rich diets helps "modulate" the microbiome.

Your Microbiome Knows Where You Live... and It May Be Hurting You

We've discussed the Biopsychosocial Model numerous times on the blog—so it may not be a surprise that it comes up once again in the context of keeping your gut bacteria happy. The environment plays a significant role in our mental health—and one of the ways in which it does so is through influencing our microbiome. Much of what you might call our "baseline" microbiome is environmentally influenced from the time we are born into this world. Children born from vaginal births have more diverse microbiomes than children born from cesarean sections—and those who are breast-fed have more diverse microbiomes than those who are bottle fed. We cannot control the factors of our birth and the months after—but we can control how the environment plays a role in influencing our microbiome for good or for ill in the here-and-now. For instance, there's been growing interest in the fact that rural settings lead to more diverse microbiomes than urban settings. Growing up in a microbe-rich environment, like those close to the Great Outdoors, plays an important role in developing a diverse, healthy microbiome. Urbanization, on the other hand, "leads to changes in living conditions such as increased sanitation and antibiotic use, separation from outdoors, and poor land management practices" that can increase the prevalence of dysbiosis. Likely due to decreased gut microbiota in individuals, inflammatory disorders are higher in urban spaces—as are immunologic disorders like asthma.

Where you live may be helping or hurting your microbiome. This will be a fascinating point of research in the future—and one that will likely have far-reaching implications for our gut-brain connection.

Drugs, Antibiotics, and your Microbiome

If you want to help your microbiome, there's one golden rule you may already be familiar with: don't take antibiotics unless your doctor feels they are absolutely necessary. One study found that some of the most commonly used antibiotics caused up to a 25% decrease in diversity in the gut microbiome. Antibiotics are not the only agents that can have a significant impact on your gut. While antibiotics are known to do more harm than good to your microbiome, curcumin is an example of a supplement that can help your microbiome flourish.

We can influence our microbiome, but our microbiome influences us in turn. One of the most interesting fields of research about these incredible bacteria are the way the microbiome may be utilized in future drug addiction treatment. For example, certain bacteria are "substance abuse related," and in the future perhaps certain intestinal microbiota would be introduced into the gut of a substance abuser to treat their condition by altering their microbiome. Think "Therapeutic Bugs."

Love Your Microbiome and It Will Love You Back!

It can be challenging to take good care of our bodies—but if you think of your microbiome as a distinct organ that wants to help you thrive, a "second brain" as vital to your health as every single beat of your heart, it may be easy to focus your energy on helping it do its very important job. The two of you are so intimately bound to one another, you might think of yourselves as a married couple. "Happy microbiome, happy life!"

In the weeks and months ahead we will dive even further into what your microbiome does to promote health and illness, and what you can do about it to preserve and protect your own well-being, and help to restore your health. Our discussions will include the use of the latest genetic tests such as Genomind's Mindful DNA, and Genova's GI Effects Comprehensive Stool Test.

Ninety Trillion Bugs Cry Out, "Feed Me. Feed Me." Why Should You Care?

Reader, in the spirit of the new school year, I want you to close your eyes and travel back to yesteryear to picture the first day of class. You're running late, and as you enter the classroom, there's one desk left. Your lucky day! As you sit down and place your notebook on the desktop, you detect it—the dreaded wobble. Peering shyly underneath the desk, you determine one of the legs seems to be missing a screw connecting it to the desk itself. Then, you hear the teacher announce the desk you claimed will be your assigned seat for the whole semester. As you shift uncomfortably in your chair, you begin to worry: if this desk leg wobbles at just the wrong moment, the entire thing will topple. You have three options in front of you: You can ignore it; you can place a piece of duct tape over it to try to secure the leg to the desk to the desk itself; or, you can get the help of a janitor to invert the desk, to fully "diagnose" the issue at hand and repair it correctly. Only one of these options, of course, guarantees you a complete repair. Ignoring it will inevitably leave you with a sense of continued insecurity: *will this be the day the desk leg gives out and embarrasses me?* Taping it will do the same: *how long can this little piece of tape hold?* We not infrequently use "band-aids" to treat the "broken bones" in our lives. But if we don't fully repair the fractures- taking into consideration all of their various components and how they work together—we never feel as good as possible. And what value would you place on achieving peace-of-mind?

Within this simple, straightforward thought exercise lies a profound message: the medical world is beginning to see the body itself not as a series of disparate elements—the desk and its legs, so to speak—but as a holistic, dynamic instrument, with elements that coincide, intermingle, and greatly inform one another. In the world of mental health, it is no longer enough to isolate the workings of the brain as the primary receptor for treatment. Revolutionary research is finding that our gut microbiome plays a significant role in both driving mental illness, and also in creating a feedback loop that can perpetuate that illness—and sometimes make it worse. As I have noted in prior blogs, our

32 trillion human cells are deeply influenced by, and interconnected with, on a moment-to-moment basis, the 90 trillion “bugs” that comprise our microbiome. This week, we will continue our series on the Mighty Moody Microbiome by discussing the Gut-Brain Connection—and the many possibilities on the horizon for treating mental illness in both the brain and the microbiome.

A Gut Feeling: Is Your Microbiome Making You Moody?

As we discussed earlier in this series, it’s easy to feel that our entire “Self”, our mind, our awareness, lies in the brain alone. However, our very language points to a different, more accurate truth. When we are in love, we describe “butterflies in our stomach”. When we are worried, we describe a “gut feeling”. When we are about to make a big decision, our loved ones tell us to “trust your gut”. Why is it, if we are prone to believing our ultimate command center lies inside our skull, that we attribute so many of our emotional states to somewhere entirely different?

Almost 2500 years ago it was Hippocrates that first said, “All health begins in the gut”. We’ve known for some time that eating healthy foods is a general tonic for the body and brain—but new research is showing a multitude of other reasons to pay attention to what we feed our gut. For instance, evidence shows that certain nutraceuticals like Omega 3 and Vitamin D have the capability of “improving inadequate response to antidepressants”. Both neurodegenerative disorders, like Alzheimer’s and Parkinson’s Disease, and mood disorders, like anxiety and depression, have been shown to have a gastrointestinal component. Similarly, Post Traumatic Stress Disorder is associated with increased inflammation—a problem that undoubtedly comes under the gut microbiome’s purview. Chronic stress and autism also have gut connections—in fact, there’s almost no mental state that does not also have a connection to the trillions of bugs that live in our gut.

These examples aren’t just interesting correlations. Studies have directly confirmed the feedback loop between mood and gut: one study showed that germ-free (that is

microbiota-free) mice were found to have a greater response to stress on their HPA Axis—which could be reversed by colonization of a specific bacterial species.

The possibilities the connection between the gut and brain might bring to light in terms of treatment are absolutely fascinating to consider. In keeping with the biopsychosocial model of treatment, further study in this area will allow psychiatrists to treat the whole person—their biology, their psychology, and their environment—with greater precision than ever before.

How Does the Gut-Brain Axis Really Work?

The Gut-Brain Axis, the system that connects these two critical messaging centers in our body, has been defined as a "bi-directional communicative and regulatory system involving the brain, central nervous system, and… the gut". "Bi-directional" means that while the brain sends messages down through the nervous system to the gut, the gut sends messages up to the brain as well—that's the feedback loop I spoke of earlier. "Communicative and regulatory system" means just what it sounds like. The brain and the gut communicate with one another along this axis, sending messages back and forth, to regulate both our physiological and emotional states of being.

According to Sarkis Mazmanian, professor of Microbiology at California Institute of Technology, there are three ways our gut can communicate with our brain: through our vagus nerve, which connects our brain and gut together through a network of nerves; through circulating immune cells that are "educated in the gut and then travel to the brain"; and metabolites, "molecules that are produced by microbes in the gut and circulate to regions of the brain where they affect behavior."

Bacteria in the microbiome can, in fact, manufacture and secrete many kinds of neurotransmitters, or otherwise can increase or decrease neurotransmitter production. Lactobacillus can secrete acetylcholine, which regulates mood, learning, memory and attention, and can also increase BDNF—a key neurotransmitter involved in stress resilience, mood regulation, new learning and cognitive functioning. Taking a

genetic test like Genomind's Mindful DNA can pinpoint which of our genes are "risk" genes that, if modified, could help our overall wellbeing. Studying the microbiome-related genes on the Mindful DNA test, at times combined with other laboratory tests, can provide a critical link between identifying those genes and developing a precise gut-focused treatment plan that can bolster our genetic resources and improve our mood, cognition and overall health and well-being!

Pitfalls of the Feedback Loop—How Your Gut Bugs Could Be Making your Mental Health Worse

The feedback loop between our brain and our gut is an overwhelmingly positive thing to understand—and to take advantage of. But it's just as important to understand the consequences that can occur when we take that feedback loop for granted. Science has shown that changes in our gut can contribute to mental illness—like depression, as just one example. But depression itself can also induce further modification of our gut microbiota—which can over time contribute to more severe depression. It makes sense—anxiety, depression, and many other cognitive disorders can cause individuals to stop caring about their diet, when in fact this will likely only exacerbate symptoms. As we frequently point out on this blog, knowledge is power, and the more you understand how you "feed your gut,"—for better or for worse—and how that "feeding" directly impacts the health of your brain—the better you can take care of this important feedback loop… and *feed* it the right way.

Reader, let's go back to that first day at school, where taping a desk leg or ignoring it completely will never leave you with true peace of mind. Similarly, attempting to "fix" one part of our bodies while ignoring the infinite complexity of the trillions of other organisms living inside of us right at this very instant is going to result in compromised health outcomes. We must treat the whole person—and that person's entire Mighty Microbiome—if we are to truly feel well.

Convert Your Microbiome to a "Team Player" to Alleviate Depression, Anxiety and Bipolar Disorder

Reader, pretend for a moment that you are back in school, and these blogs are part of your "Microbiome 101" curriculum—and as your instructor I am about to hand out homework. What do you remember about those loathsome school assignments? Did you prefer book reports over science homework? Story problems over essays? Memorizing speeches over memorizing languages? Whatever your preferences may be, I bet you'd prefer anything over the dreaded group project. Perhaps you cringed at the mere mention of it! After being grouped together, one or two students would inevitably carry the weight of the rest of the group. I can recall on one group project in my school days, one student didn't even bother to show up to the final presentation! In these scenarios, there are natural overperformers and natural underperformers—unfortunately, it's all too often that dumb luck determines which combination you wind up with, and how your assignment will ultimately come together, or not.

Likewise, many of us wish that maintaining or achieving health and wellness in our own bodies would be a solo assignment. Sure, we might ask for the support of our friends and family, but ultimately, we're the ones to do the work—or "turn in the homework" so to speak. However, this couldn't be further from the truth. In fact, our mental and physical health outcomes are very much a group effort—and the biggest player beside yourself lives inside your own body. If you've been following along with this series, you know who I'm referring to—those 90 trillion bacteria that comprise your Mighty Moody Microbiome. Just like group projects from your schooldays, your gut microbiome might very well be an underachiever. It might also be an overachiever. Unlike those group projects, however, in this instance it's not the luck of the draw. If you take care of your microbiome, it will take care of you and your 32 trillion cells. It will keep your body and mind healthy and happy.

This week, we're going to take a look at how your microbiome can be an underachiever—and we'll consider what you can do to make it work for you as an overachieving teammate!

The Manufacturing Plant in your Mighty Microbiome

When we explored our personal human genome in our two blog series, "DNA: I Am Who I am… or Am I?" and "DNA: Nature your Nurture", we took an in-depth look at how certain genetic variants (vulnerability variants) may predispose us to mental or physical health concerns, from addiction to cardiovascular concerns to Alzheimer's Disease and much more. Other variants may bolster us against these same concerns—make us more resilient. Our genes are certainly active participants in our group projects. The trillions of bacteria living in our gut are just as active—and we are just beginning to understand why some microbiomes are more overachieving than others. One intriguing area where the microbiome can over or underachieve for our bodies is in its manufacturing and synthesis of micronutrients like vitamins.

Two examples below provide a preview as to how our Mighty Microbiome works in our favor. Within our gut microbiota there are bacteria charged with producing and synthesizing Vitamin K. Vitamin K2 is an essential player in our heart health: once synthesized, it helps to decrease vascular calcification, lower cholesterol levels, and elevate HDL, all of which contribute to a lower risk of heart disease, stroke and other vascular disorders. If your microbiome can efficiently synthesize Vitamin K2, it certainly qualifies as an overachiever in the continuing group project of keeping you healthy. Your intestinal bacteria also synthesize Vitamins B5 and B12. Deficiencies of these vitamins have been linked to both gut-related health concerns like gastrointestinal discomfort, as well as psychological and neurological concerns like chronic insomnia. If your microbiome doesn't adequately synthesize these important vitamins, it may not be pulling its weight in its participation in maintaining your overall health and well-being.

Your Microbiome and your Metabolism—Friends or Foes?

Another area your microbiome can be an over- or under-achiever is in connection with your metabolism. Metabolism is a term that is used to describe all chemical reactions involved in maintaining the living state of the cells and the organism itself. Your gut bacteria is such a significant player in the regulation—or dysregulation—of your metabolism that scientists now consider interventions that alter the microbiome to be the next frontier in potential therapies for metabolic disorders. As a refresher, processes regulated by your metabolism include glucose metabolism and insulin sensitivity (related to how your cells produce energy to power their myriad functions), as well as storage of fat and feelings of hunger or satiety. A dysregulated metabolism may lead to obesity—making this area of study particularly fascinating.

Metabolism regulates important bodily processes—and hormones regulate metabolism, as well as sleep, mood, reproduction, and many other things. Hormones are produced by our endocrine system, and one of the largest pieces of our endocrine system are our enteroendocrine, or EE, cells that are located in our gastrointestinal system. These cells "sense nutrients and secrete multiple regulatory factors" that influence digestion, intestinal motility, and food intake. As it turns out, our gut microbiome can influence the EE cells in our bodies, including the release of hormones that regulate our metabolism!

This is but one way our microbiota can influence hormone production and secretion to directly impact our metabolic regulation. Microbiota also play a role in creating SCFAs—microbial "end-products" that provide energy for our metabolic processes. SCFAs also aid in producing hormones that impact a wide range of crucial functions in our body, from our appetite to our immune response. Some of these hormones actually help prevent obesity by reducing our appetite!

Studies have found that there is, in fact, an "obesogenic" microbiome—that is, a specific set of gut bacteria that may lead to obesity. In our series about the Mindful DNA genetic test, we covered genes that may contribute to obesity or other gastroimmune disorders.

Your microbiome is a participant in that group effort—and whether it contributes to obesity or not can have huge health implications for both your mental and physical wellbeing.

Can You Make Your Microbiome an Overachiever in Alleviating Depression and Anxiety?

Your mental and physical health are not solo assignments. Rather, your microbiome and other factors are team players in helping you achieve a “good grade” in these areas. Maybe even an “A+” health status. So, if your microbiome is not holding its weight on your team, what might you be able to do about it?

Scientists are still pondering this question—but there are exciting possibilities on the horizon—including stool tests that can help determine what your microbiome is doing for you—and what it could be doing better. Genova Diagnostics offers a stool test and several other tests that answer critical questions about your microbiome. And the Mindful DNA test by Genomind assays genetic variants such as FUT2, HLA-DQ2/HLA-DQ8, and MC4R, that can provide additional answers. Both tests provide actionable information to bring health to your Microbiome, which in turn may help alleviate symptoms of depression, anxiety, bipolar disorder, cognitive impairment and more.

These insights provide intriguing new possibilities for treating physical and mental health concerns. Much more is to be learned about our bodies in this realm, but one thing is for certain: your Mighty Moody Microbiome has a big say in regulating key cellular processes—and we should learn more about what it can do to contribute mightily to our personal health and well-being team!

Leaky Gut ↔ Leaky Brain ↔ Leaky Emotions

My Dear Reader, imagine lying in your bed late into a weeknight. You have to go to work in the morning, yet you can't get to sleep. As you're about to toss or turn for the umpteenth time, you hear something. Not a whispering voice. Not a sneaky scurry of claws from a pawed intruder. No—what you hear is far scarier, almost a guarantee you'll be wide-eyed till morning. What you hear is a "drip, drip, drip". And it's coming from inside the room! These mysterious drip sounds can be a homeowner's worst nightmare. Perhaps it started small: a leak in a shower in the guest bedroom. But the leak grew larger, and suddenly, the problem's not just in the shower but in the floorboards, in the insulation. Perhaps there's mold… perhaps something worse. What's certain is a chain reaction has begun—by the time you hear the drip, who knows how many thousands of dollars in damage one tiny leak has caused? Worse yet, who knows where the chain reaction will finally come to an end—or how you'll be able to fix it?

Now, let me give you an even more fearful example: the leak isn't coming from inside the room… it's coming from inside your very own body! Similar to a leaky shower, a leaky gut can wreak havoc on an unsuspecting individual. But we're not talking about dollar amounts—we are talking about chronic, serious health problems—both physical and mental. Unlike a leaky shower, however, the cause of a leaky gut is no random occurrence. Rather, the cause can be traced back to those trillions of bacteria that make up our gut microbiome. And luckily for us, the solution can be traced there too! In this week's post on our Mighty Moody Microbiome, we're taking a deep dive into Leaky Gut Syndrome, and how our microbiome can both cause it and prevent it.

What's Up With your Leaky Gut?

When some of my patients first hear the term Leaky Gut Syndrome, they scrunch up their noses in a look of disgust (particularly when I bring up "the stool test"). We often consider our intestines—our guts—to be our body's sewer system. Who wouldn't be grossed out by a sewage leak? However, as you've learned from prior blogs in this series, our gut

plays a much larger role in our body's health than simply aiding in digestion. The trillions of gut bacteria living within your intestinal tract regulate digestion, sure—but they are also responsible for our metabolism, our hormones, and even our mental health. When your microbiome is healthy and diverse, the lining of your gut itself allows for safe passage into our bloodstream and brain of numerous nutrients, neurotransmitters, hormones, and more. Like an A-plus student on a group project, nothing slips through the cracks—literally. When your gut bacteria are less diversified or otherwise thrown out of equilibrium, your microbiome enters a dysbiotic state. The lining of your intestines becomes more permeable (more "leaky"), allowing bacteria, incompletely digested food molecules, and toxic metabolites that should stay well within the gut to leak through and enter your circulation. As you can imagine, once your body recognizes molecules have "snuck" into a space where they don't belong, thereby becoming antigens, your immune system is not very happy about it. A leaky gut can lead to chronic diseases such as inflammatory bowel disease and diabetes—but more and more research is showing it can also lead to mental health concerns, including depression, anxiety, autism—and even higher rates of suicide.

How Can a Leaky Gut Impact my Mental Health?

A leaky gut is the point-of-origin in a chain reaction that can set off a series of serious health concerns—including a "leaky brain" that leads to "leaky emotions"—so let's trace how your body gets from Point A to Point B. It all begins with an unhealthy gut microbiome (to learn how to keep yours healthy, click here). Once bacteria and other antigens slowly begin to seep out of the lining of your leaky intestinal walls into your bloodstream, your body's immune cells go on high alert. As you may recall from my prior blog on the topic, one of the favorite weapons of an activated immune cell is inflammation. Recognizing foreign bodies in its system, your immune cells call in the guards, including pro-inflammatory cytokines like IL-6. Low-grade inflammation leads to these cytokines hanging around your body in higher amounts for a longer duration—and here's where things get really interesting. Research has found a correlation between a leaky gut and chronic inflammation… as well as a correlation between chronic inflammation—meaning increased levels of cytokines—and symptoms of depression,

anxiety, and suicidal thinking (the “leaky emotions”). Your “leaky gut” also can cause a “leaky brain” whereby the blood-brain barrier also becomes permeable, which allows damaging molecules to leak into and inflame the brain itself. Besides being a “marker of systemic inflammation”, IL-6 also stimulates our HPA Axis, in turn responsible for fight, flight or freeze response. An overactive HPA Axis is a telltale sign in those who suffer from major depression.

Telling new studies have discovered elevated levels of IL-6 in those attempting suicide, as well as increased levels of inflammation. More needs to be understood—but the picture that is coming to light connecting a leaky gut and depression or even suicide may ultimately save thousands of lives in the near future.

Help! I Have a Leaky Gut! What Can I Do about It?

If you have Leaky Gut Syndrome, the answer lies in the same place as the cause of your problem: your unhealthy microbiome! A gut microbiota suffering from dysbiosis can be rejuvenated by “good” bacteria in the form of probiotics. In fact, studies have shown that patients taking probiotics showed reduced levels of stress and “improved self-reported psychological effects” to a similar degree as a commonly administered anti-depressant. Genetic testing, like Genomind’s Mindful DNA test, can give you and your doctor an idea of what you’re working with genetically—and whether you may be predisposed to a leaky gut through analyzing genes that may place you at greater risk.

Lifestyle modifications can go a long way toward addressing a leaky gut—yet the future of medicine may lie in fecal transplants, which transpose a healthy microbiota onto one in dysbiosis. Studies in mice demonstrate this to be an effective way to treat depression, anxiety, and many other mental and physical health ailments.

A leaky gut causes a chain reaction of events in your body that can go quickly from bad to worse. An unhealthy diet can begin to harm your microbiome in as little as 24 hours, and lead to dysbiosis, but the good news it that these effects can be reversed in as little as

two to four days by eating a healthy diet. Eat healthy, fix the leak—and your body, brain, and loved ones will thank you.

Bad Bugs Bring Civil War and Global Depression

> *"The gut is the seat of all feeling. Polluting the gut not only cripples your immune system, but also destroys your sense of empathy, the ability to identify with other humans."*
>
> *– Suzy Kassem*

Reader, for the last seven weeks, we've taken a deep dive into one of the most promising new fields of study in the scientific world: the microbiome. We've learned that the trillions of bacteria impact our mental and physical health in ways we could never have imagined half a century ago. Indeed, these little critters living inside of us have the power to make us stressed out or help us keep our cool; to keep us healthy or to make us sick; to regulate our hormones or throw them into chaotic disarray, at the expense of our mental wellbeing; and so much more. As it turns out, our brains and our gut talk frequently—ideally, they act like the best of friends. Sometimes, however, they can be the worst of enemies. This week, I want to take what we've learned and put it into practice to show you exactly how an investigation of our gut microbiome can act as the missing piece of the puzzle in determining why a person becomes—or remains—treatment resistant. This week, I want to share the story of Mia. As you'll read in the paragraphs below, Mia and her prior doctors were at a complete loss as to why, suddenly, her depression medication stopped working after 25 years. As it turns out, the microbiome and its intricate connection to our body's immune response, was the ultimate culprit. Thanks to precision psychiatry and various tests, we were able to get to the bottom of Mia's treatment resistance and prescribe lifestyle changes to help her find her equilibrium once again.

Mia's Story: How Undiagnosed Immune Symptoms Can Unravel Your Mental Health

Mia* was 47 and had a 25-year history of depression which, until 18 months ago, had been well controlled by Zoloft (Sertraline). Then, as she put it, "I began to fall apart." Her depression came back with a vengeance and was unresponsive to her psychiatrist

increasing her Zoloft dosage. Her doctor then tried Wellbutrin, Cymbalta, Rexulti and Trintellix—all to no avail. A trial of transcranial magnetic stimulation (TMS) also failed to help her symptoms.

By the time she got in to see me she was in a bad way, afraid of losing her successful career as a real-estate broker and terrified that her husband would abandon her and seek custody of their children. “Dr. Kehr, after 25 years of success with Zoloft, suddenly nothing works anymore to cure my depression. What happened? How can you explain this? What can you do to help me?”

As is often the case with patients like Mia who are treatment-resistant, some underlying contributors had gone undiagnosed—and if you have been reading these blogs (and have become amateur psychiatric sleuths!) you might even be able to list a few possibilities. Here is what stood out in Mia as I took her history of the past 18 months: she had four sinus and ear infections in the past five months, with no past history of these types of infections—and was treated with antibiotics (think immune system compromise and microbiome dysbiosis); she had gained 30 pounds while on Rexulti (think inflammation); she had been under severe job stress to close on some multi-million dollar deals (think chronic stress affecting her fight/flight/freeze HPA axis, which predisposes to dysbiosis); she had been eating more and more carbs to comfort herself (think dysbiosis and inflammation); and finally she complained of chronic fatigue, persistent diarrhea, bloating and gas (dysbiosis strikes again!).

Using Precision Psychiatry and the Microbiome to Treat a Compromised Immune System

To get to the bottom of Mia’s underlying issues, I administered Genomind’s Professional PGx Express and tests for dysbiosis, leaky gut syndrome, and inflammatory biomarkers. Her genetic test revealed that she would likely respond to medications like sertraline but would need higher than average doses, so we increased hers to 300 mg daily and she partially responded. Her blood tests showed elevations of four inflammatory biomarkers, and her GI tests revealed both dysbiosis and leaky gut syndrome. Not only had her

dysbiosis and leaky gut worsened her depression, they also created chronic systemic inflammation, and a weakening of her immune system, which was affecting each and every one of the 32 trillion cells in her body. Arguably, this was causing a "global depression" throughout her body. I worried that she might also be developing an autoimmune disease, where her body's immune system began to attack her body's cells (a kind of "cellular civil war" so to speak) further worsening her depression.

Now, let's take a moment to review the connection between our gut and immunity. As you learned in an earlier blog in our series on the Mighty Moody Microbiome, the gut microbiome plays a significant role in programming our immune system. A healthy, diversified microbiome can stave off chronic inflammation and promote immune homeostasis. However, an unhealthy microbiome—one in a state of dysbiosis—leads to a leaky gut, which in turn allows bacterial fragments, incompletely digested food molecules, and other "foreign bodies" into our bloodstream which triggers our immune response. Consider this: the largest organ of our immune system is our GI tract—and our GI tract happens to be lined with epithelial cells, key drivers of our immune system, which can recognize "invaders" and promote an autoimmune response, or "attack". Often, as in Mia's case, that attack leads to chronic inflammation—which in turn leaves both our bodies and our brains in a compromised state, unable to maintain a normal equilibrium. Given that our gut and our brain are in constant communication, it is not hard to see that a weakened immunity in the gut would lead to equally negative consequences in the brain. It's a terrible cycle—and one that can be difficult to reverse without understanding all the underlying causes.

Luckily, Mia's test result clarified the missing pieces of the puzzle—and helped us create a precise plan suited for her body's needs. We placed her on a Mediterranean diet, elimination diet for food sensitivities (her leaky gut had let undigested food molecules into her bloodstream, triggering antibodies to those foods. By eliminating those foods, we would eliminate the antibodies over time), a probiotic and a prebiotic. Initial results are encouraging, as she is beginning to lose weight, gain more energy, and have more normal bowel movements. I now feel that we are on the right path with her—time will

tell—and I am hopeful that as her microbiome and immune system improve, and as her chronic inflammation abates, those nasty recurring upper respiratory and ear infections will abate as well, and she will fully recover from her depression.

The Care and Feeding of Your Microbial "Pet" with Mental Health Prebiotics

Reader, I have a colleague who dearly loves animals. She's the sort of person who always stops to say hello to the stray cats she sees on the street, and who lets out an audible "Aww!" whenever she sees a puppy waiting patiently at a coffee shop or restaurant as their owner finishes their bite to eat. I've seen her melt so many times in front of a cute animal that I finally asked her—if she loves animals and animals so clearly love her back, why doesn't she get a pet herself? She laughed and responded with a simple answer: "I would love to have a dog or kitty keeping me company at home, but they're just too much of a commitment right now." I had to agree. After all—some parents get an animal for their children to teach them responsibility. Some couples even get an animal to gauge their readiness to have kids together! And some single, divorced, or widowed folks long for the companionship of a pet, but don't want to sacrifice their freedom. It takes time to raise a well-behaved pet. And if you don't have the time to give, or are unwilling to make the effort, a pet can wreak absolute havoc in your household. And no matter what your pet's breed or species, the foundation of responsible pet care is to love them, which includes feeding them a healthy, nutritious diet. But, you might be saying, Dr. Kehr is not a veterinarian… so why does all this matter? For the last two months we've taken a deep dive into the workings of our microbiome—a collection of trillions of microscopic organisms living within our gut. The genetic makeup of these organisms outnumber the genes in our bodies by a factor of 1000:1, and unlike our personal genome, which is fixed for our lifespan, their genome can begin to vary in as little as 24 hours, based upon the foods we eat, the drugs we take, and other environmental factors. They are within us, and yet they are not us. And reader? Just like a pet, our microbiomes can bring us great pleasure and joy, or wreak havoc on our emotions.

The Care and Feeding of Our "Pet Microbiome" to Help with Anxiety, Depression and Bipolar Disorder

Just like a regular pet, we should all treat caring for our microbiomes as a big responsibility—after all, those trillions of bacteria play a role in everything from our mood to our metabolism; producing neurotransmitters, vitamins, hormones, foods for our cells to produce energy, building and maintaining a healthy immune system, and so much more! And just like a regular pet, paying attention to what we feed our microbiome can make it sing our praises, or hate our guts (pun intended)—and create profound consequences for our mental and physical health. As it happens, our microbiomes have a "favorite food"—prebiotics—and the more we understand about them, the happier "pet" we'll have living in our gut!

Why Feed Your Gut?

If a kitty is happy and healthy, you can expect lots of hugs, nighttime cuddles, purrs, and happy meows when you get home. If a puppy is happy and healthy, you can expect a playful companion who gets you out the door on walks, loves to play games, and administers affectionate licks to show you love. If your microbiome is happy and healthy, you may expect increased cognitive functioning, mood regulation, decreased inflammation, decreased chances of developing mental illness or neurodegenerative disorders, a healthy metabolism, and a happy immune system ready to fight off all comers. Talk about an incredible pet—we call it our Mighty Microbiome for a good reason, after all!

As we've discussed at length in this series, our microbiome does so much for us—but just like a little puppy or kitty, if we don't create the conditions for it to thrive, it can make our lives miserable. Now, we must remember: our microbiome is an entirely distinct, living entity within us—and like all living things, it needs to be properly fed to flourish. If we don't feed it the right way, it will become less diverse, and less able to help us fight off pathogens and keep us healthy. So, what should we feed our trillions of little gut bugs? Prebiotics provides a straightforward answer.

Prebiotics Keep your Mighty Microbiome Happy and Healthy

When discussing the microbiome, probiotics and prebiotics are two terms that come up with relative frequency—so I want to clarify at the outset what the differences are between the two. Quite simply, probiotics are living microorganisms, some of which may naturally occur in the gut already. Prebiotics, on the other hand, are defined as a "selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefits upon host health." Far more simply put: prebiotics are the foods that probiotics and your microbiota both love to eat! They feed your "pet" exactly the diet it needs to provide you unconditional (cellular) love.

Here's how it works: non-digestible carbohydrates in our food make their way into our digestive tract, where our gut microbiota eagerly seize upon them and "eat" them—the fancy word for a gut bug eating its carbs is called "fermentation". When our gut microbiota is finished with their yummy prebiotic snack, new substances called short-chain fatty acids are produced from their degradation. These include lactic acid, butyric acid, and propionic acid. Short-chain fatty acids are so small that they are able to diffuse into our blood circulation and affect organs throughout our body, from our brain to our gut and back again! They are also epigenetic modulators of our cellular DNA throughout our body!

These little wonder molecules that appear after our gut is finished digesting the prebiotics we feed it have been found to significantly impact a number of our physical and mental systems. They've been found to mitigate the risk of colorectal cancer by, among other things, improving the integrity of our intestinal tract (playing its role in preventing a leaky gut!). They've been found to improve our immunity by increasing numbers of good gut bacteria while minimizing numbers of harmful bacteria that make us sick. They've been found to have "regulatory effects" on our synaptic functions, our neurotransmitters, and on our BDNF. Studies have shown that prebiotics and their degraded biproducts, short-chain fatty acids, may reduce stress, influence mood, improve memory and concentration, and reduce inflammation. Talk about a happy pet!

Certain genetic variants may predispose to a greater need for prebiotics, given their negative effects on the microbiome. For example, in Genomind's Mindful DNA Professional, the FUT2 gene affects the surface receptors in your gut that allow for the attachment and growth of intestinal microbes and provides an important food source for healthy gut bacteria. If you have a resilient FUT2 gene, your surface receptors are robust, and you have more potential for a diverse—and thus healthy—microbiome. If you have a risk gene, however, you likely have a lower diversity and possible dysregulation of gut microbiota. Those with the risk variant have a 7-14% increased risk of inflammatory GI conditions like Celiac disease or Crohn's disease.

Prebiotics may well be a revolutionary new avenue to help doctors treat patients with mood disorders, stress, anxiety, inflammation and more. And at this point, you may be wondering how the heck you can get your hands on these microbial goodies. Turns out, you don't have to look very far. Prebiotics—those non-digestible carbs your gut bacteria love—are naturally found in a whole host of foods you may already be eating, including tomatoes, soybeans, wheat, onions, asparagus, bananas, beans, honey, fermented vegetables, sauerkraut, walnuts, pistachio nuts, tiger nuts, garlic, milk, oats, artichokes, sugar beets, leeks, chicory, barley, peas, beans, seaweed, and microalgae.

In some ways, thinking of your gut as an incredible pet might make you more inclined to eat a healthier diet. If you realized you had an organism living inside of you that had the power to keep your mood steady and so much more, wouldn't you want to make sure it had everything it needed to thrive? Our Mighty Microbiome is an incredible organism—and prebiotics help your gut bugs help you. Feed them right—they'll thank you for it!

Zombie Gut Bugs – Can You Eat Your Way out of a "Microbiome Depression"?

Reader, I can't remember a time when depression and mental health have been more central to our cultural consciousness. They have finally come out of the closet. Pop psychology is booming, celebrities are increasingly open about their mental health struggles, and even our television shows—from *13 Reasons Why* to *This is Us*—offer intimate, and sometimes controversial, portraits of depression. And yet if you asked any of the patients I see on a regular basis, you'd see very quickly that the stigma of mental illness and depression is still very much alive. When someone has a persisting cough, it's a no-brainer to make a doctor's appointment to see what's wrong. But when someone has persistent anxiety, chronic fatigue, emotional mood swings, or irritability, it often takes months, if not years of denial and delay before they visit a psychiatrist's office to determine the root issue— if they visit at all. There are many reasons for the hesitation, but a primary reason I've witnessed is surprisingly simple and terribly sad: People still feel ashamed. They believe there is something defective about them, that they are damaged goods, and if they only had the will they could "fix themselves" and "be better;" or worse still, feel afraid that if they seek help they will be mocked by friends or loved ones.

Good Gut Bugs Treat Depression

For many patients, taking prescription medication that directly targets their brain – where most of us believe our "personalities" arise—is a stigma within a stigma that can feel something like a personal affront. With all of this in mind, what if I told you that exciting new research suggests sometime in the not-too-distant-future, depression and other mental illnesses could be targeted and treated not in the brain… but in the gut? What if I told you that the 100 trillion bacteria that comprise your microbiome play a much larger role in your mental health and wellness than previously thought—and that treating them, rather than the "you" in your brain, may be a significant boon to recovery? If we as a culture believed our gut bacteria were to blame for our mental health outcomes, would the

stigma of depression survive—or would the outsourcing of blame and shame from our brain to our bacteria turn the stigma on its head? These are exciting questions to consider—and today, I want us to consider them through the lens of Brenda's story. Brenda felt shame at her own depression—but within months, she excitedly told me about her own mental illness, "It's not me, Dr. Kehr—it's my gut bugs!" If our gut bugs are the problem, reader, the answer to treating depression may very well lie in the simple administration of targeted probiotic bacterial strains. Let's see how it all works!

Brenda's Story: Depression is a Gut Feeling

At just 30 years old, Brenda* already held an impressive position in management at an Internet marketing firm. She joined the firm early on, which meant she'd accumulated stock in the company—and it was about to be acquired. To outsiders, it seemed Brenda was guided by a lucky star: at an age where most of her peers are just beginning to truly build their careers and think seriously about saving, Brenda had already reached an incredible peak in her professional life—and she had an equally impressive nest egg to show for it. Yet these were not the first details I learned about Brenda—far from it, in fact. Instead, Brenda stepped into my office with a distraught expression and spoke with an urgency so strong I could practically feel the pressure and stress emanating from her as she spoke familiar words "Dr. Kehr, *something is wrong with me. At times it feels like I'm dead inside, like I've been transformed into a zombie!*" As she described episodes of emotional escalation, anger outbursts, binge eating, suicidal thoughts, mood swings, irritability, long periods of remaining in bed, and fatigue, her face took on an expression of tearfulness and near embarrassment. Self-consciously, she moved on to tell me of her physical symptoms as well: stomach pains, heartburn, acid reflux, belching, a grumbling stomach, and urgent bowel movements. She was also about 20 pounds overweight.

Brenda's mental health concerns were thus twofold: she had symptoms impacting her mood and behaviors, and she had symptoms impacting her physical health. Brenda's mood symptoms dated back to childhood, and since then she'd been treated with stimulants for ADHD as well as lithium, all to no avail. Her family history was positive for

bipolar disorder in an uncle, and her mother suffered from depression. I diagnosed Brenda with rapid cycling bipolar disorder and probable dysbiosis. We performed Genomind's Professional PGx Express Assay on her, which revealed COMT Val/Val, ADRA2A C/C, MC4R A/A, and CACNA1C G/A. These variants pointed toward increased rates of dopamine breakdown, likely poor response to stimulants, difficulty feeling full (poor satiety signaling), and a higher likelihood of mood instability. We also performed a blood test which revealed low estrogen, low vitamin D and elevated inflammatory biomarkers.

Administering a genetic test revealed important indicators about Brenda's mental health. To bring about the fastest possible symptom relief, I began her on Memantine to address her calcium channel variant and unstable moods. But we also urgently needed to treat Brenda's physical symptoms of dysbiosis. Her microbiome was most likely causing her digestive system issues —but I knew it was very likely the dysbiosis itself was serving to underscore or possibly even perpetuate her depressive symptoms. We ordered a stool test to examine my hypothesis.

Depression and Your Microbiome

Microbiome transplantation accounts for some of the most exciting research about our gut bacteria—and transplantation observations have revealed incredible insights about how and where depression manifests itself in the body. Scientists have found fecal microbial transplantations (FMT) from a human suffering Major Depressive Disorder into a microbiome-free rodent causes it to develop depression-like symptoms, from anxiety-like behaviors to anhedonia, or the inability to experience pleasure or excitement. Given that depression has long been thought to be a brain-centered illness, it's incredible to think that our gut bacteria—species that do not even qualify as genetically "us"—could play such a significant role in causing mental illness. Let's take a look at just a few of the ways this may be possible (and for more information, I highly recommend this research article that outlines each of the categories below):

***The Gut-Brain Connection*:** First and foremost, we must recall from a prior blog the significant communication that occurs between the brain and the gut. Study after study has shown that a dysregulated microbiome can lead to significant consequences in the brain and body—so let's keep in mind this intricate and important connection as we move on to a few other causes of depression in the gut:

***Bacterial Metabolism*:** As we previously discussed, our bacteria love snacking on prebiotics, or indigestible carbs. Our bugs can then transform those snacks into short chain fatty acids, or SCFAs, which can cross the blood barrier and move to all different parts of our bodies to send messages that inhibit inflammation and bolster our immune systems—and much more. These SCFAs, in fact, are even involved in neurotransmitter production (you can read more about this in a below section)! However, not all bacteria are capable of digesting those carbs for us. Some bacteria would much rather digest—or metabolize—proteins and amino acids. Just like the digestion of carbs produces SCFAs, the digestion of proteins by our bugs produces many byproducts that are toxic to our bodies and lead to dysbiosis and inflammation. Scientists have found that people with Major Depressive Disorder have elevated levels of gut bacteria that snack on proteins (and therefore elevated levels of toxic biproducts circulating through their digestive tracts), and reduced levels of the bacteria that snacks on carbs (and reduced levels of those helpful SCFAs!)

***Micronutrient Production*:** Our microbiome is responsible for synthesizing vitamins important to our physical and mental health. For instance, strains of healthy bacteria can synthesize and generate folate and thiamine—two micronutrients known to be implicated in depressive symptoms. Low blood levels of folate and thiamine have been associated with depression. Dysbiosis that results in low production of these key micronutrients could very well be contributing to mental illness.

***Inflammation*:** We've talked much about inflammation on this blog before, but it warrants repeating: dysbiosis can lead to irritable bowel syndrome and a leaky gut, which in turn can lead to significant chronic inflammation throughout our body and brain. But there's

another important element at play when it comes to our gut and inflammation: when our cytokines—the proteins responsible for our inflammatory response—are “upregulated”, our body’s synthesis of serotonin can be impacted—and recall, low serotonin levels can be a key indicator of depression!

***Neurotransmitter production*:** Certain gut bacteria are capable of making the very neurotransmitters implicated in a range of mental illnesses, including serotonin, norepinephrine, and dopamine. One type of bacteria, Bifidobacterium, is particularly efficient at this and is found in lower amounts in people who are depressed. The production of neurotransmitters in our gut is perhaps the most direct way our microbiome impacts our mood—and studies show that supplementation our gut microbiome with probiotics that help produce those neurotransmitters can actually have an antidepressant-like effect. Incredible!

Diet: Our diet can certainly have an impact on our mood through the interaction between the food we eat and our gut microbiome. A diet rich in Omega-3 fatty acids, like a Mediterranean diet, has been shown to reduce inflammation and have an impact on depression.

Treating Brenda’s Gut—and Her Depression

Brenda’s stool test revealed both low diversity and low abundance of bacteria, and the presence of inflammation. With the understanding that Brenda was suffering from gut dysbiosis, I placed her on a probiotic, and a prebiotic, and a Mediterranean diet to address her gastrointestinal symptoms and inflammation, and Vitamin D3 to address its deficiency in her body—this vitamin also has anti-inflammatory properties. The next time I saw her, as she gave me her update, I felt what I imagine it must be like to be a surgeon who rapidly cures people.

“Dr. Bruce, I feel fantastic! Overnight I began to feel physically better with lessening stomach pains, and an absence of heartburn and burping. My urgent need to have a bowel movement went away three days later. The panic attacks are now gone, the mood

swings are mostly gone, my executive functioning is somewhat better, and while I remain depressed the symptoms have lessened a lot."

As we have reported in prior Mighty Moody Microbiome blogs, you can begin to restore health to your microbiome in as little as 24 hours (or begin to damage it that quickly, too!)—and for Brenda this restoration was exactly what happened through her taking probiotics and prebiotics and initiating a Mediterranean diet. Next week, we'll dig in more specifically to the role probiotics can play in treating depression. Stay tuned!

“Powerful Superhero—Mr. Probiotic—Kills Evil Depression Bugs!”

Reader, there’s a common trope in crime movies and television shows that you may be familiar with. Picture this: after a long search, the “Good Guy” detective (or cop or other seeker of justice) finally finds the “Bad Guy” criminal (or fugitive or other person of interest). Perhaps they’re alone in a dark alley. As they size each other up, the Bad Guy starts menacingly moving forward the Good Guy—he sees himself at an advantage. But the Good Guy has a secret weapon—his walkie talkie. Fearfully, and with shaking hands, he presses the call button and mutters, “I’ve found the Bad Guy—but I’m going to need some back up over here…” Just as the Bad Guy pounces, allies of the Good Guy swoop in and overtake the criminal! He’s outnumbered! In an explosive climactic scene, justice wins—and the world is safe for another day.

Lots of movies make it look so simple to take out the bad guy—but there’s another variation of this trope where the “bad guy” isn’t so simply defined. Like the mythological hydra (or the villains in big franchises like Avengers or Mission Impossible), you might cut off one head only to find three more growing in its place. Often, when it comes to our mental health, the Bad Guy is more hydra than one-off character. When it comes to fighting depression, “send in the back-up!” has often meant deploying an anti-depressant directed at the neurotransmitters in the brain. But the future of mental-health “back-up” may be in a different sort of pill—one filled with real-life “fighter bacteria”, rather than chemicals. By bolstering your microbiome, probiotic supplements may just play a critical role in fighting off the hydra of depression once and for all. Let’s take a look at the new “Good Guys” and how they can strengthen our mental health outcomes!

The Hydra of Depression—And How the Microbiome Comes into Play

As we previously discussed, depression is increasingly being discussed in the news and portrayed in pop culture. Bringing awareness to the realities of this mental illness is

crucial in our collective fight to understand and manage its impacts—because this is an illness that's only projected to grow in the coming years. Depression already affects almost 400 million people across the globe. Approximately 20% of the population will suffer from it at some point in their lives. Major Depressive Disorder is already one of the largest causes of health-related disability, as well as one of the costliest of all the mental health disorders—and rates are increasing among younger individuals.

For Many Who Suffer from Depression, Antidepressants Simply Don't Work

Yet, despite its global precedence, treatment of depression remains frustrating elusive for many—up to 60% of patients suffering from depression don't see any improvement from the most common pharmacological treatments targeting neurotransmitters. SSRIs and SNRIS simply don't work for the majority of patients suffering from depression! Over and over again, I've seen patients who all want to know: Why is treatment so difficult—and why do they remain treatment-resistant, after seemingly trying everything?

There is No Such Thing as Depression—There are Many "Depressions"

The reason is deceptively simple: Depression is not a single bad guy—it's a hydra. There are many "depressions" and the unique underlying contributors for each depressed individual, her or his genetic and epigenetic causes, need to be uncovered and addressed in a thoughtful, systematic way. Unlike what so many believe, depression does not just live in your brain—although it certainly takes up residence there as well. It also lives in your HPA axis, your immune system, and in your gut. Let's take a quick look at each of these four "heads" of the hydra of depression:

- In your brain, low levels of neurotransmitters like serotonin, norepinephrine, and dopamine can play a role in depression. Treating those with SSRIs, SNRIs, NDRIs, or Multi-Modals can bring some improvement—but for many, antidepressants alone aren't the only answer, because their depression lives on in one of the three other "hydra heads".

- Your hypothalamus-pituitary-adrenal axis plays a critical role in your response to stress—so it's easy to see how a dysregulated HPA axis may lead to complications. When your HPA axis is over-active, it can lead to higher levels of stress hormones pulsing through your body, and those hormones can also impact your depression. These stress hormones also harm your microbiome.
- Your immune system is meant to keep you healthy—but many depressed patients exhibit dysregulated immune systems, and chronic inflammation may be to blame. As we've discussed in prior blogs, chronic inflammation can wreak havoc on our mental and physical health. And in our brain, as our microglial cells become activated and drain surrounding neurons of their energy resources, those "underpowered neurons" contribute to the emotional, cognitive and behavioral manifestations of depression.
- Last but certainly not least, depression can live and breed in your gut—and thanks to what we now know about the gut-brain axis and the ways in which those two command centers are able to communicate with each other, if your microbiome is dysregulated, your mental health will likely suffer the consequences.

As you can see, depression is a complex, whole-body illness which can manifest in different ways in different people. Successful treatment must be tailored to the individual's unique genetic makeup and epigenetic needs—but in many cases, success means treating not just one part of the hydra but many. And that's where probiotics come in—because if we've learned anything from this series, it's that our Mighty, Moody Microbiome is a powerful and distinct force in our bodies—and sometimes, sending for backup to reign in a dysregulated microbiome is the missing piece of the puzzle that many patients have been looking for.

Why Probiotics are Your Gut's Ultimate Superhero Ally

Here's another common trope in those "bad guy" movies and TV shows: one bad guy in a group of villains doesn't *really* belong. Perhaps he started out good, and something along the way brainwashed him into thinking he, too, was an evil force. These bad guys are sometimes the most susceptible: they just need to be reminded of their goodness—and the good guy doing the reminding often has a secret quality that makes them more trustworthy. In Marvel's Captain America, the character of Bucky was once known as Steve Roger's (The Captain himself) best friend and ally. But literal brainwashing turned him to the dark side—and only Steve could turn him back, reminding him who he really was. In our very own bodies, the gut bacteria comprising our microbiome can be a force

of good or evil. But when our microbiome is dysregulated, the “good guys” that can swoop in and save it from the dark side are bacteria themselves! Probiotics are defined as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.” These live organisms can give your dysregulated gut a strong, positive message to shape up and behave.

Studies have shown that the microbiomes of depressed individuals are qualitatively different than the microbiota in healthy people. Studies have also shown that fecal transplants of microbiota can also “transplant” depressive symptoms from organism to organism. Lastly, study after study has shown that the impact of probiotics in treatment of depression have been so notable that some are moving to call these little bacteria “psychobiotics” rather than “probiotics” to reflect their incredible impact on our mental health. The gut-brain axis is bidirectional—meaning that your gut sends messages to your brain just as your brain sends messages to your gut. Feeding your gut good bacteria through probiotics can improve dysbiosis—and your gut will relay its newfound “good guy” status straight to your brain!

Probiotics + Your Gene Variants = A Roadmap to Good Health

Certain genetic variants may predispose to a greater need for probiotics, given their negative effects on the microbiome. For example, in Genomind’s Mindful DNA Professional, the FUT2 gene affects the surface receptors in your gut that allow for the attachment and growth of intestinal microbes and provides an important food source for healthy gut bacteria. If you have a resilient FUT2 gene, your surface receptors are robust, and you have more potential for a diverse—and thus healthy—microbiome. If you have a risk gene, however, you likely have a lower diversity and possible dysregulation of gut microbiota. Those with the risk variant have a 7-14% increased risk of inflammatory GI conditions like Celiac disease or Crohn’s disease. In addition Mindful DNA tests for HLA-DQ2/HLA-DQ8 genes that put you at increased risk of suffering from Celiac disease. The DQ2 and DQ8 haplotypes (genes inherited from a single parent) are strongly associated with the disease, and the DQ5 haplotype is carried in 90-95% of all Celiac patients. This

disease can impact your entire body, from your energy levels to your brain functions—and the sooner you know whether you suffer from a gluten sensitivity, the sooner you can make those gluten-free changes to your diet to feel better. In addition, probiotics may help lessen the impact of dysbiosis that was induced by gluten-promoted intestinal inflammation.

Sometimes we could all use a little superhero back-up when fighting off the “bad guys”. And when it comes to the “bad guys” causing our depression, probiotics can be a huge addition to the “good guys” team. There’s plenty we still have to learn about the administration of probiotics in treatment of depression—but in my own experience as a psychiatrist who evaluates and treats the Whole Person, treating my patients’ guts in addition to their brains has not uncommonly led to significant improvements in their mental health.

Villainous Gut Bugs Bedevil Bipolar Patients?

Reader, are you in awe over the effects of those 100 trillion bugs that live inside of us in promoting our health, or contributing to many of our chronic diseases? I know that I am. In that spirit, did you know that there may well be more genes in our microbiome than stars in the universe?

Here is an amazing fact… happy and healthy mice raised in a sterile environment, who have no microbiome, become depressed when they receive a fecal transplant from a depressed human!

We previously discussed the cinematic tropes of heroes and villains. In the spirit of Halloween, I'd like to continue this week by discussing another trope, found in nearly every classic horror plot, from *The Telltale Heart* to *Scream*. The trope goes like this: you recognize the antagonist. Perhaps you hide. But suddenly, you get the creeping sensation that the evil villain isn't outside at all: *he's inside the house*. Worse yet, he's inside your very room! But there's something worse even beyond that: What if the villain is inside your very own body?

Thus far in our series on the microbiome, we've considered our gut bugs as a team-player, as a pet, and as a villain that probiotics could "conquer" with a one-two punch. But sometimes, our microbiomes may play the role of a different type of villain—one that lives discretely inside our bodies and influences our other bodily systems to impact our mental health for the worse. This week, we're going to investigate the microbiome's role in bipolar disorder and mania. Reader: the gut bugs living within us may have an insidious effect on our mental health… but take heart. Even this villain can be conquered through personalized medicine and targeted care.

Is There Such Thing as a Leaky Gut Bipolar Microbiome?

As previously discussed, depression is a multifaceted mental illness that has multiple points of origin throughout our bodies, including our brain, our gut, and our immune

system. Bipolar disorder lives in the body in a similar way, and as with depression, there is often a genetic component to the disorder, which can be better understood through genetic tests like Genomind's Professional PGx. But the two illnesses have significant differences in terms of their outward manifestation. Individuals with depression report feelings of not just sadness but emptiness and worthlessness. While depressed patients might feel better some days than others, their mood and their energy levels remain low. Individuals with bipolar disorder also feel that sense of emptiness and have deep "low" periods—but they also have periods of hypomania or mania, where they seem to be overtaken by a restless, relentless energy. Studies have shown patients with depression have a markedly different microbiome than individuals without depression—and now research suggests that patients with bipolar disorder have distinct features in their microbiome as well that differ from the rest of the population.

As with depression, patients suffering from bipolar disorder display reduced levels of microbial diversity in general, and also exhibit higher levels of intestinal inflammation and symptoms of a leaky gut. But the microbiomes of individuals suffering from bipolar depression also have one distinct feature in common: they have a significantly lower amounts of two types of bacteria known as *Faecalibacterium and Ruminococcaceae* when compared to healthy individuals without the disorder. Higher levels of these bacteria have been associated with better sleep, better mood, and better overall health. Significantly, these bacteria have also been shown to have anti-inflammatory properties—if you've been following along with the blog, you know chronic inflammation is one of the causes of numerous negative health outcomes…. In other words, the more anti-inflammatory gut bugs, the better! Lower levels *Faecalibacterium* have been associated with many negative health outcomes such as Leaky Gut Syndrome, ulcerative colitis, irritable bowel syndrome, colorectal cancer, and diarrhea. Higher levels of *Faecalibacterium* offer improved health outcomes—and indeed, early studies indicate that therapeutically increasing this bacteria in bipolar patients could lessen the burden of the disease.

Low levels of *Faecalibacterium* are not the only biological contributor to bipolar disorder, however—like a villain that is wreaking havoc inside the house, a dysregulated microbiome can also disrupt numerous mood-regulating systems within your brain, as we will now explore.

How Your Bipolar Gut Bugs, Your Immunity, and Antibiotics Perpetuate a Vicious Cycle of Dysregulation

Bipolar disorder has been increasingly associated with abnormalities in the body's immune system—more specifically, in periods of mania, patients' immune systems display significant alterations before returning to normal levels. But studies have also shown that individuals undergoing an episode of mania have an "increased rate of recent antibiotic exposure compared to a normal population." This raises questions about the interrelation between a patient's immune system, microbiome, and bipolar disorder. Because many bipolar individuals suffer from dysbiosis and a leaky gut, they may be at greater risk of bacterial infection, which then leads doctors to prescribe antibiotics. But antibiotics themselves have been known to diminish the health and diversity of a patient's microbiome, which essentially perpetuates or worsens an already compromised immune system.

The connection between antibiotics and mania has been made enough times that a name has been given to it: "antibiomania". However, more research must be conducted to determine the precise mechanisms at work between these factors. If antibiotics worsen symptoms of bipolar disorder, what alternatives could be prescribed to mitigate their effects? Further, studies have shown that overstimulation of the immune system can contribute to bipolar disorder. If mania is at least partially rooted in immunological abnormalities, could the answer to easing bipolar disorder possibly lie in treating the immune system by treating the gut? As we've learned in this series, the gut plays a major role in bolstering our immunity. Understanding the cycle of immune system compromise, the gut microbiome, and antibiotics will be a crucial factor in future treatment of bipolar disorder.

In the future, will patients suffering from intractable bipolar disorder symptoms receive a fecal transplant?

Probiotics to the Rescue!

Every year in the United States, 3 million people are diagnosed with bipolar disorder. Typical treatment may involve prescription of antipsychotic medication or mood stabilizers and regular psychotherapy. But the frontiers of medical research suggest that treating bipolar disorder by treating the microbiome could provide an alternate therapeutic route. As with depression, in bipolar patients probiotics may provide a mighty answer to the villain lurking in our own bodies. Administration of *Faecalibacterium* and Faecalibacterium and Ruminococcaceae could help bolster bipolar patients' lower levels of the bacteria, and taking probiotics more generally eases the symptoms of a leaky gut. Finally, if antibiotics do indeed play a role in the disease, probiotics could act as a protective agent against the destruction of the microbiome they cause.

The time is ripe for more research about the connection between bipolar disorder and the microbiome—but what we know now is promising in terms of what solutions lie ahead.

“Don’t Shoot the Messenger!” How Microbiome Crosstalk Influences Your Emotional Health

Reader, it’s a phrase that’s been used for thousands of years, used as a code of conduct during ancient wartimes, and written by everyone from the Ancient Greeks to Shakespeare: “Don’t shoot the messenger!” This timeless metaphor persists because it gets at something fundamental in our nature: when we hear news, whether good or bad, we often react with strong emotions—and when it’s bad, we have an impulse towards blame. In recent weeks, this metaphor has become increasingly relevant on a national scale. With politics being as dysfunctional as they are, and talk of impeachment framing the headlines, some have an impulse to blame the modern messengers of our day: the journalists. We get angry when we hear messages we don’t like—and that emotion stems from a deeper place than just irritation at perceived biases in the media – perhaps it stems from our anxiety over the deteriorating quality of communication between our political leaders – which threatens the very health of our democratic republic. This toxic multimedia “crosstalk” can begin to affect our emotional health. Simply put, this continuous communication begins to chip away at the very fabric of our emotional well-being. And since we feel emotionally threatened, we may want to lash out at the messenger – perhaps a reporter, newspaper or loved one with a different point of view.

If you’ve been following this blog series, you know what question comes next: “Dr. Bruce, how could this possibly relate to my mental health?” It’s simple. “Don’t kill the messenger” relates directly to the workings of our own body. Our microbiome’s “crosstalk” naturally creates millions of “messengers” that report the “news” out to our 32 trillion cells, down to the level of our very DNA. And just as the news can alter our minds and beliefs, the “news” being delivered to our cells has the epigenetic power to change the expression of our genes – to turn them on, turn them off, or regulate them in other ways. And when our gut bugs are in dysbiosis (when they are not healthy), our genetic expression can be changed for the worse, negatively affecting the production of trillions of essential

molecules inside each cell. How does our microbiome have such power to change our DNA? Let's dig in to find out!

What is Epigenetics?

While our DNA may seem like the most stable thing about us, how it expresses itself – what it produces – is in fact anything but certain. Each and every one of our genes can be turned on or off based on triggers found in our environment—including the rich environment that lives inside our own bodies. The change that can occur in gene functionality is known as "epigenesis", and the field that studies those changes is called "epigenetics".

The role external and internal factors can play in modifying the expression of our genes—and the power we have to harness those factors to benefit our mental and physical health—is so important to the future of precision medicine that we've not only dedicated blogs to epigenetics, but have used the term to frame entire blog series. However, while we have discussed epigenetics broadly on the blog, we've not taken a look into the specific mechanisms that allow a gene to change its expression. To use our messenger metaphor, you can't send a letter without a mailbox to receive it on the other end, and you can't share the news without an active listener. If "messengers" are sent from the microbiome to our cells, what mechanism is receiving them and processing their important messages?

In this blog, I want to focus on two biological factors that can lead to epigenesis: DNA methylation and histone modification. DNA methylation can downregulate or turn off the expression of a gene. DNA demethylation reverses this process to upregulate or turn on the expression of a gene. Histone modifications are changes occurring to a cell's histones—proteins that DNA coils around to form chromosomes—which can in turn lead to activation/inactivation of a gene and other epigenetic outcomes. These two factors create the foundation for epigenesis, and epigenesis itself can turn on genes that lead to

health outcomes ranging from addiction and substance abuse to higher rates of depression and stress.

Now that we understand the "receiving" mechanism for epigenetics, let's take a look at the messengers themselves: those little, microscopic entities that arise from our gut microbiome and help shape our DNA destiny.

How Your Microbiome's Messenger Microbes Play a Role in Epigenetics

As we've read in prior blogs in this series, the trillions of bugs comprising our gut microbiome play a significant role in our mental and physical health. Those gut bugs are capable of "speaking" to our brain through the Gut Brain Connection, and, as numerous studies have indicated, the messages sent from a healthy microbiome are significantly different from those sent from a microbiome in dysbiosis. Our body "listens" to those messages about our gut through the process of epigenesis—but who, exactly, is doing the talking and what are they saying?

Our gut bacteria are hugely efficient manufacturing plants, and among their many products are "microbial metabolites." Two examples of these metabolites are B vitamins, and short chain fatty acids, or SCFAs. Each of these metabolites is a "messenger" that plays a role in the epigenetic modification of our genes. Our body's own cells cannot manufacture B vitamins—instead, we rely on our microbiome to synthesize them for us. B vitamins, including riboflavin, niacin, biotin, and folate, are produced by our gut bugs—and each acts as a unique cofactor of enzymes that modify histones in our chromosomes. Specific B vitamins—riboflavin and folate—also impact MTHFR, which plays a large role in epigenetic regulation through DNA methylation. Low levels of MTHFR can lead to lower production of serotonin, dopamine and norepinephrine – contributing to a greater vulnerability to developing depression —and low levels of riboflavin and folate lead to low levels of MTHFR. And what leads to low levels of B vitamins in our gut? An unhealthy gut microbiome – one that is in dysbiosis!

If you'll recall from a recent blog, SCFAs are what our microbes produce after we feed them food they like, namely prebiotics. These SCFAs become an important energy source to increase energy production in our cells. They also act epigenetically on histones to turn on genetic production. A reduction of SCFAs has been associated with diseases such as depression, bipolar disorder, obesity, diabetes, autoimmunity, chronic inflammation, and intestinal diseases such as ulcerative colitis (UC), Crohn's disease (CD), and colon cancer. One SCFA in particular called butyrate has garnered significant attention for its role in epigenesis. Butyrate is a key enzyme known to regulate gene expression through histone modification—and low levels of butyrate produced by our gut can lead both to variances in gene expression and to an increased intestinal permeability also known as "leaky gut". Decreased levels of butyrate have also been implicated in obesity—which has its own mental health implications.

SCFAs and B Vitamins each play messenger roles and "talk to" the DNA inside our cells —and our genes respond and produce more or fewer molecules essential for the maintenance of life itself. Like any messenger, these microbial metabolites shouldn't be blamed for poor health outcomes—instead, the fundamental problem lies in the society from which they arise: namely, a dysregulated gut. A healthy microbiome simply sends different messengers to our chromosomes than a microbiome in dysbiosis. And a good place to start if you want your gut messengers to convey happier news is to take care of your microbiome and treat it kindly—by feeding it what it likes (like prebiotics!) and by sending in those probiotic "troops" to help get it into shape if needed.

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Taking advantage of the power of epigenetics to optimize our health is the future of medicine—and paying attention to which messages from our gut bugs promote healthier genetic expression is already becoming a crucial tool in the psychiatrist's toolbox. For better or for worse, our gut microbiome is constantly speaking to us—and we'd do well to listen to exactly what it is saying!

Autistic Gut Bugs?

Reader, with Daylight Savings Time behind us, and long winter nights ahead, what better time is there to talk about the one activity that unites us all? No, I'm not talking about readying ourselves for the holidays—I'm talking about cozying up with a blanket and a good book! Admittedly, when perusing the bookstore shelves, I tend to gravitate towards nonfiction and literary fiction—but I have a soft spot in my heart (and my soul) for books about the mysteries of the universe, including the greatest mysteries of all—the origins of consciousness and of life itself. In these books, where a deep scientific mystery must be solved, they tell the stories of brilliant scientists who, "standing on the shoulders of giants," pull the pieces of the puzzle together in a way that creates awe and wonder. Perhaps I gravitate toward these mysteries because of the problem-solving nature my work: when I see a new patient who is suffering, the underlying causes of their emotional pain is a mystery I seek to solve. Every mystery can be solved with finding the right set of clues—and the difference between a great "detective" and a bumbling one often lies in knowing where to look. When it comes to the mystery of mental illness, it was often thought those clues were predominantly found in the brain. In reality, mental illness is a genetic and epigenetic whole-body experience, and the search for clues should be conducted accordingly. One of the biggest mysteries in the field of psychiatry is Autism Spectrum Disorder—and with pop culture increasingly shining the spotlight on this complicated disorder, the puzzle pieces that comprise it are certainly some of the most controversial. But research now suggests an important clue in solving the puzzle of ASD may be lingering in our gut microbiome, just waiting for a good detective to pay attention. Is it possible to treat ASD by treating the trillions of bacteria in our gut? Let's walk through this mystery together!

The Great Mystery of Autism Spectrum Disorder—and How One's Microbiome May Play a Role

We know from prior blogs in this series that depression is a complex disease as it lives in multiple places in the body, including our brain, gut, and immune system. Bipolar

disorder is much the same. Like these two mental illnesses and so many more, Autism Spectrum Disorder, or ASD, also lingers throughout our body—but, as the name would suggest, ASD is so vast and varied in terms of its manifestations that there is no one "disorder" but many that fall under this umbrella category. While the developmental disorders that fall under ASD vary in terms of their type and severity of symptoms, they do share a core group of characteristics, including the display of repetitive and restrictive behaviors and difficulty in communication and interaction with people. ASD effects 1 in 59 individuals in America—yet despite its prevalence, the causes of the disease remain poorly understood. Factors that have thus far been associated with ASD range from the genetic to the environmental, from nutritional deficiencies to nutritional overloads, to virus exposures to immune system dysfunction to allergies. To demonstrate the variability in just one of these categories—the genetics of autism—ASD has been associated with more than 100 genes, and roughly 400 genes may be associated with ASD susceptibility. Some of these genetic variations, like CACNA1C, ANK3, BDNF and COMT, are analyzed in Genomind's Professional PGx Express. To revisit our detective metaphor, you might say the search for a root cause of ASD is like searching for a single clue in a city the size of Manhattan. When mapping your search for answers, it's hard to even know where to begin!

That's why the following fact is so significant: In the last few years, more and more research has found a significant connection between the gut microbiome and ASD. A considerable number of patients with ASD also have gastrointestinal dysfunctions, and—here's the kicker—*severity of GI symptoms in individuals with ASD correlate strongly with the severity of their ASD!* To me, this amounts to finding a needle in a haystack: determining the link between the gut and ASD could lead to a revolution in our understanding of the disease—and to novel therapeutic approaches. Luckily, researchers have already begun to undertake this work—and they've offered some interesting insights.

Leaky Gut—Autistic Crosstalk

Bacterial composition of the microbiome can vary drastically between a healthy patient and a patient with mental illness, with the latter often suffering from a dysbiotic gut in addition to the symptoms of their disease. Because of what we know about the gut-brain axis—namely, that our gut can carry messages up to our brain that can not only impact our mental health but can even epigenetically alter the expression of our genes—we know that an unhealthy microbiome, one in dysbiosis, fails to create the right messenger molecules, thereby conveying disinformation to and dysregulation of the brain and our entire nervous system. Think of this as "toxic crosstalk" between the gut and the brain. We also know that a dysbiotic gut—a Leaky Gut—can lead to more toxins entering our blood stream (such as bacteria, bacterial fragments, and incompletely digested food molecules), triggering a chronic inflammatory response that further impacts our mental health for the worse. Individuals with ASD often exhibit dysbiosis—and their microbiomes frequently share some key characteristics. First, their microbiomes tend to show reduced microbial diversity, which can often lead to the "overgrowth of harmful bacteria contributing to the severity of autistic symptoms". Second, their microbiomes show higher levels of *Lactobacillus, Clostridium, Desulfovibrio, Caloramator, Alistipes, Sarcina, Akkermansia, Sutterellaceae* and *Enterobacteriaceae*. Third, their microbiomes show decreased levels of *Bifidobacterium*, a genus of gut bacteria that helps to reduce inflammation; as well as reduced levels of *Prevotella, Coprococcus* and *Veillonellaceae*, which are responsible for carbohydrate digestion and fermentation, processes that produce many of those important "crosstalk" molecules like SCFAs—short chain fatty acids—that facilitate communication between gut bugs and human cells, and between the gut bugs themselves . Arguably, this could be understood as "autistic crosstalk" throughout the body.

These are not the only shared traits found in the microbiomes of patients with ASD—but they do suggest the disorder is as much a concern with the gut as it is a concern with the brain's physiology. If that is the case, what solutions might there be by treating the gut for ASD? Let's take a look at two possibilities.

Could Probiotics Ease Symptoms of ASD?

A gut in dysbiosis plays a role in poor mental health. Feeding your gut right with prebiotics and sending in healthy gut bugs in the form of probiotics to whip it back into shape have both been shown to ease symptoms of depression and other mental illnesses—and research is in its early stages to determine whether and to what extent this could be a treatment for symptoms of ASD as well. Early evidence shows that by reducing gut inflammation, probiotics do indeed have a positive impact on children with ASD. It also shows that probiotics can "act via the gut-brain axis to influence neurotransmission and mood states". Because of the diversity of symptoms and causes of ASD, more research must be conducted to determine which probiotics and prebiotics may have therapeutic impacts—but the field is ripe for more hopeful discoveries.

Is "Repoopulating" the Gut—a Fecal Transplant—the Future of ASD Treatment?

If the gut microbiome causes symptoms of ASD, what would happen if the dysbiotic microbiome was entirely replaced with a healthy microbiome? Reader, not only is that a possibility—it could be the future of treatment for ASD and other mental illnesses. Microbiota transfer therapy involves an antibiotic treatment, a bowel cleanse, and a fecal transplant. The process can take weeks, but by the end of treatment, patients have a new "repoopulated" microbiome—and in many cases, that newly healthy microbiome has a huge impact on their mental health outcomes. In a study of microbiota transfer therapy with individuals with ASD, researchers found substantial changes in both gastrointestinal and ASD symptoms by the end of treatment—and the positive changes were sustained weeks after treatment ended. Patients saw an 80% reduction of GI symptoms and a 22% reduction in ASD symptoms as measured by CARS—a system that rates core symptoms of the disorder. As with probiotics and prebiotics and ASD, more studies must be conducted, but microbiota transfer therapies could be the next revolution in precision medicine—as consequential as genetic testing in helping patients become whole and healthy, both physically and mentally.

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Reader, I'm no giant in the field of unlocking the mysteries of the universe, but I do love to solve mysteries of human health and wellbeing—and these promising new fields of research around Autism Spectrum Disorder only further my suspicions that evaluating and treating the microbiome might be the missing link for many mental health struggles—and treatment of those gut bugs could offer healing potential for millions of patients who are suffering. We're homing in on the root of the mystery of ASD—and I can't wait to see it solved!

Can the Microbiome Cause ADHD?

The microbiome is the next frontier of mental health treatment. Studies have demonstrated the connection between the microbiome, the brain, and ADHD. Harnessing the power of that connection may change the future of ADHD treatment.

What is ADHD, and how is the microbiome involved?

ADHD effects approximately 6% of US children, making it one of the most prevalent neurodevelopmental and neurobehavioral disorders. Despite its frequency, we know strikingly little about its underlying causes. ADHD is commonly characterized by hyperactivity and impulsivity, inattentiveness, or a combination of all three—however, like autism, this is a heterogeneous disease that can look very different from patient to patient. That said, there are a few hallmarks of ADHD displayed by a large swath of patients with this disorder—and several can be directly tied back to the microbiome.

Patients with ADHD frequently display increased incidence of gastrointestinal issues and regularly suffer with immune dysregulation, low-grade inflammation, and a leaky gut. These are all warning signs that the microbiome is sending bad signals to the brain. Let's review what we know about GI issues and their connection to mental health:

- First, we know our microbiomes and brains are intricately interconnected through the "Gut Brain Axis", and that our gut bugs can "speak" directly to our nervous system and other bodily systems via the passage of various metabolites, hormones, and other "messenger" compounds from our intestinal tract into our bloodstream.
- Second, we know that the messages sent from a dysregulated microbiome—a "leaky gut", that is—are different than the messages sent from a healthy microbiome.
- And third, we know that the toxins and bad gut bugs found in a gut in dysbiosis can lead to inflammation and trigger an autoimmune response that has further impact on our mental health.

The consequences of a dysregulated gut, of course, are the most obvious ways the microbiome may be implicated in ADHD. But gut bugs are also increasingly implicated in another significant hallmark of the disorder—like the game of Mouse Trap, they may

begin a chain reaction that leads directly to another hallmark trait of ADHD: a dysfunction of the brain's reward pathway.

The microbiome, ADHD, and the brain

Patients suffering from ADHD demonstrate dysfunction in their brain's reward pathway. This pathway plays a critical role in "reinforcement, motivation, and learning how to associate various stimuli with reward"—and to function properly, it relies almost entirely on our body's supply of dopamine. Here's how it works: when we engage in activities that are beneficial to our survival—like drinking, eating, and reproduction—dopamine is released. As we've discussed before on this blog, dopamine is a "feel good" or "pleasure" chemical. It makes us feel joyful and euphoric, and in terms of our reward pathway, feeling good after we partake in an activity leads to a desire to partake in it again and again.

Now, here's where things get interesting. The dopamine release that keeps our reward system pathway regulated is just the end of a long chain reaction of circumstances—and that chain reaction begins in the microbiome. Researchers studying the microbiome have found that patients with ADHD display elevated levels of Bifidobacterium compared to patients without the disease. These increased numbers of gut bugs begin the chain reaction. Bifidobacterium DNA creates an enzyme called CDT, which in turn helps manufacture the amino acid phenylalanine, which subsequently makes dopamine—and dopamine, finally, helps us regulate our body's understanding of reward, incentive, motivation, and positive reinforcement. Whew!—that's quite the Mouse Trap if you ask me—and it all starts in the gut.

The microbiome and the future of ADHD treatment

Researchers have found that increased Bifidobacterium is the origin point for a dysregulated dopamine/reward pathway—and you can understand why, given its intricate relationship to the process of dopamine creation. And if ADHD lives at least in part in the

gut, then that opens the doors to revolutionary methods of treatment that could offer millions of patients relief from their symptoms.

Tests like Genomind's Professional PGx and Mindful DNA can also contribute additional understanding of these chain reactions, given that they assay the COMT genetic variations associated with ADHD.

Within the microbiome, there is incredible potential for treatment, healing, and recovery. Our gut bugs play an important role in the chain reactions that lead to mental health outcomes—and understanding their delicate interplay with other bodily systems will be an important element of the future of precision medicine.

Psychobiotics and Your Microbiome – It's a Gut Feeling

Researchers have coined the term "psychobiotics" to describe probiotics (live bacteria and yeasts that are good for your health, especially your digestive system) that produce mental health benefits. Some authors would also include prebiotics, which enhance the growth of these health-promoting organisms, as having psychobiotic properties.[i] Studies involving the "microbiome" – the hundred trillion (100,000,000,000,000!) bacteria and other microbes in your body that mostly reside in your gut – are all the rage in cutting edge medical research. From the 1990s to present day, scientists have managed to unravel links between gut bacteria and numerous health conditions including: arthritis, cancer, diabetes, fibromyalgia, multiple sclerosis, and obesity. Today, the emerging field of human microbiome research is also demonstrating that gut bacteria may play an important role in brain development, behavior, and mood in humans. Furthermore, these bacteria are also being explored, and sometimes used, as treatments for anxiety and depression, reducing stress, and improving overall mood.

The Gut-Brain-Axis

Did you know that your body contains "two brains?" The familiar one (the one you are using to read this blog!) is in your central nervous system – but there is also "second brain" – the enteric nervous system (ENS). Both can be involved in determining emotional health or illness.[ii] The ENS is a part of the nervous system located within and controlling the functions of your gastrointestinal system. The relationship between your gut and brain is bidirectional. Many of us can all relate to having a queasy stomach and feeling emotionally stressed before a big presentation, on our wedding day, or when anticipating a visit with family members who seem to thrive on "high drama." At these time of psychological stress, certain brain-related pathways will actually alter the composition of the bacteria contained within your gut. On the other hand, depleting healthy bacteria from

your gut may alter a number of neurochemical processes within your brain, thereby altering your mood.[iv]

There are several main pathways by which signals travel from the gut through the body and cross the blood-brain barrier. Some of those core pathways include the ENS, the vagus nerve (connecting the brain and gut), the immune system and hormones within the gut. Communications between these entities regulate several important functions, including immunity, digestion, metabolism, satiety, and stress reactions.[v]

Dysbiosis (Unhealthy Gut)

If one's body has an unbalanced gut microbiome containing too few or unbalanced probiotics and prebiotics it is known as "dysbiosis." This can happen when a person consumes a nutritionally unbalanced diet, has taken antibiotics that have killed off many probiotics in the gut, has been exposed to toxins, and/or isn't doing a good job managing life stress. The body's intestinal lining may become too porous, a condition called leaky gut, which creates chronic inflammation in the body and eventually may precipitate or contribute to a series of autoimmune diseases and mood disorders too.[vi]

Gut Bacteria and Mental Health

It turns out that bacteria have the capacity to generate many neurotransmitters and neuromodulators found in the brain, like GABA, norepinephrine, dopamine, and acetylcholine. They can deliver these neuroactive substances to the brain via the gut-brain axis. Dysfunction in the gut-brain axis and disruptions to gut health have been linked to psychiatric conditions like anxiety, depression, autism spectrum disorder, schizophrenia and neurodegenerative disorders.[vii] Some microbes are capable of producing serotonin. Taking Bifidobacterium infantis as a probiotic, for example, alters levels of serotonin—just like Prozac.[viii] Dark chocolate acts as a prebiotic, enhancing the growth of bacteria called Lactobacillus and Bifidobacterium which help improve mood.

Probiotics for Your Mood

Probiotics such as Bifidobacterium and Lactobacillus have demonstrated a number of helpful effects for mood regulation.[ix] You can find these bacteria in many foods, particularly the fermented ones (one of my favorites is Bubbies Pickles). These health-promoting bacteria can be found in such items as: yogurt, cheese, Kefir, Buttermilk, sausage, cured meats, wine, vinegar, sauerkraut and sourdough bread.

Now that we know that gut bacteria can influence our brain function, and that the brain influences the composition of our gut bacteria, the next challenge for scientists is to more effectively control this communication to bring about greater health benefits, to both prevent as well as help to cure many chronic diseases. The science of psychobiotics explores emerging strategies for encouraging the growth of brain-altering bacteria in the gut to provide mental health benefits Perhaps as the world of microbiome-based medicine expands, we may find that psychobiotics will be used instead of, or to augment the effectiveness of, many common antidepressants; and that custom “psychobiotic cocktails” will be just another tool for promoting psychological well-being.

Gut Bugs Inflame Your Brain – a Genetic Test Guides Prevention

My Dear Reader, congratulations! By the time you read this, you'll have made it through another Thanksgiving. This uniquely American holiday is perhaps most famously idealized by the Norman Rockwell painting of a perfectly roasted turkey being set on a table full of food, shared by people looking perfectly relaxed and contented. The Rockwell scene makes Thanksgiving look all too easy—but for those of us who have been in the kitchen as the feast is being prepared, we know it can be anything but. In many families, it seems the stress of preparation falls to one person who spends hours frenetically boiling potatoes, compiling the green bean casserole, stuffing the turkey, rolling the pie dough, and setting the table. Does that sound familiar to you? If it does, you surely know what follows: after the meal has been cleared and the leftovers stored away in the fridge, the frantic chef is often the first to fall asleep after the tryptophan in the turkey kicks in! For Thanksgiving guests, the holiday is all about relaxing and enjoying the company of loved ones—but for the host, it can be a day of pure chaos, stress, and exhaustion, from the moment they awaken to the moment their head hits the pillow. It's a real act of love to host Thanksgiving, because ultimately the host misses out on the most enjoyable moments of the day. These momentary stresses of living compromise our near-term contentment, yet we can quickly bounce back. Yet what if that stress becomes chronic? Reader, when our body is in a state of chronic stress, our overactive "fight, flight or freeze" response not only leads to chronic immune system problems (chronic inflammation) it can also damage our microbiome, leading to outcomes far more dangerous and long-lasting. This week, I want to review the significance of chronic inflammation to our health, and how both our microbiomes and our genes play a role.

The Consequences of Chronic Inflammation

In small doses, acute inflammation is a crucial part of our biological defense system in fighting off bacteria, viruses, or other antigens that create damage in the body and brain—

and in our brains the cells leading the charge are called the microglia. When the microglia cells sense danger present, they swoop in and clear things up and repair the damage. They do this by “upregulating”, feeding off the same energy sources that are used to power nearby cells, in order to do their good work. This works wonderfully over short time frames. But when our microglial cells get stuck in upregulation, the result is oxidative stress and chronic inflammation, which ultimately does as much or more damage to our bodies and brains than the damage that acute inflammation is supposed to prevent! As we have learned in prior blogs, chronic inflammation can lead to a multitude of negative mental health outcomes—including “inflammaging” and Alzheimer’s Disease. So how does our body become chronically inflamed? For many, it can start in the microbiome.

Can a Leaky Gut Inflame your Brain?

The trillions of gut bacteria living within your intestinal tract regulate digestion—but they also play a role in our metabolism, our hormones, and our inflammatory response. When your microbiome is healthy and diverse, the lining of your gut is leak-free, allowing for safe passage into the bloodstream of numerous important nutrients, neurotransmitters, hormones, and more. When your microbiome is less diversified or otherwise thrown out of equilibrium, it enters what is known as a dysbiotic state, in which the lining of your intestines become more permeable, or “leaky”, allowing bacteria, incompletely digested food molecules, and toxic metabolites that should stay well within the gut to leak through and enter your bloodstream (think of “sewage” entering your bloodstream and circulating throughout your body and brain). As you can imagine, once your body recognizes molecules have snuck into a space where they don’t belong, thereby becoming antigens, your immune system is not very happy about it. Recognizing the presence of malevolent foreign bodies in its system, your immune cells call in the guards, and the process of inflammation begins. Low-grade inflammation caused by a leaky gut in turn causes a leaky brain whereby the blood-brain barrier becomes permeable, which allows damaging molecules to leak into and inflame the brain itself.

Chronic inflammation is a significant side effect of a leaky, dysbiotic gut and can wreak havoc on your brain—and when a leaky gut is paired with certain risk genes, the impact can be even more consequential.

CD33, TREM2, and Inflammation

The microbiome is one of the root causes of chronic inflammation—and your CD33 and TREM2 genes may add to the problem, if you carry certain variants of these genes as assayed in Genomind's Mindful DNA test. Microglia in the brain fight damage, and CD33 and TREM2 gene variants are both involved in manufacturing receptors that are expressed on the surface of your microglia. These receptors help regulate the activities of those microglia. As such, they both help to regulate your brain's neuroinflammatory pathway. Here is an image that may help you understand, (where "AD" stands for Alzheimer's Disease)…TREM2 is a microglial surface receptor that plays an essential role in removing toxic debris from the brain. The failure of this receptor to function normally is one of a group of core components that may lead to Alzheimer's progression. One variant in particular confers down expression, which pushes your microglia to the dark side, making neuroinflammation more common and causing a three- to four-fold increase in the odds of developing Alzheimer's.

CD33 encodes for a protein found on the surface of microglial cells that act as an essential regulator for microglial activity. Think of your microglia as the Thanksgiving host. In the frenzy of the holiday, the host can usually be found in one of two states: completely stressed or completely at rest. Your microglia are much the same. When the microglia are in a constant state of activity, they don't have much time for anything else. This is your microglia in an inflammatory state—which can lead to both oxidative stress and neuronal damage. When your microglia rest, on the other hand, they're in what is known as the monophagocytic state. This rejuvenating state actually helps to clear the toxic debris found in the brain. CD33, then, is the "on-off" switch between these two states. If you have a resilient CD33 gene that confers a down expression, your microglia are switched "off" more often, leading to a more effective clearance system—and a 10 percent reduced

odds of developing Alzheimer's. A risk gene, however, can lead your microglia to be chronically inflamed, resulting in poor clearance and a dangerous buildup of waste products that can light your brain on fire through oxidative stress and the destruction of cell membranes and many cellular functions.

A Healthy Microbiome, Fecal Transplants, and Brain Inflammation

As we discussed in an earlier blog, someday soon fecal transplants may revolutionize the treatment of dementia. But let's try to prevent that dementia from developing in the first place. A dysbiotic gut and risk variants of your TREM2 and CD33 genes may increase your chances of developing chronic brain inflammation—but there are things you can do right now to reduce those chances. As we've discussed in prior blogs, dysbiosis or a leaky gut can significantly benefit from probiotics and prebiotics; and microdose lithium, vitamin D supplementation, olive oil, omega 3, and a Mediterranean Diet can give your brain a jump start in protecting against dementia. Taking a genetic test like Genomind's Mindful DNA can provide you with crucial information about what gene variants you're working with and can provide valuable information to further your defenses in the fight against brain inflammation and its destructive effects on mood, anxiety, and cognition.

Do Gut Bugs Love Genetic Testing?

Reader: Welcome to Peak Holiday Season! With the Thanksgiving feast behind us and New Years still a few weeks ahead, what lies directly in front of us now are the parties. From work holiday celebrations to parties with friends, acquaintances, and fellow parents, 'tis the season to loosen the notch on one's belt, dig into some holiday treats, and dig out some of the year's best stories to retell at the right moment. This season tends to gravitate between the two extreme emotions of joviality and stress—but right in the middle is a more subtle emotion, but one we are all too familiar with: awkwardness. For every holiday party, there seems to be one or two people whose behavior or stories are just on the verge of throwing the whole milieu out of whack. All it takes is one unseemly comment—or some improper gesture—for the mood to turn from happy and festive to something less serene.

Holiday parties feature lots of moving pieces—and the difference between a good party and a bad one often comes down to a single weak link in the chain (e.g. Bad food? Bad music? "Bad apple"?). When the pieces work together harmoniously, good memories are made—but when one piece does something unexpected, the whole thing can fall into disarray, leaving you with a sinking feeling in your stomach (pun intended). A similar balance exists in our microbiomes. From diet to genetics, lots of moving pieces play a role in determining the health of our gut bugs, and those microbes in turn play a significant role in the health of both our bodies and our minds. And, like the awkward person at a party who says the wrong thing, when one link in the chain determining your gut wellness doesn't play its part, your microbiome can fall into dysbiosis and leaky gut (think of trillions of microbes with a bad hangover)—and the health consequences can be significant. This week, we are going to look at two genes that can have a big impact on your microbiome—FUT2 and HLA-DQ2/8. Certain risk gene variants of each of these genes may throw your gut out of whack—but, like a good party host, with the right resources you can take action to protect your microbiome from taking a sickening swoon!

Your Microbiome: 100 Trillion Microbes Partying in your Gut!

Once thought of as an enemy species, the trillions of microbes in our gut (and in our mouths, our skin, vaginal canals) are collectively known as the microbiota, (their genes are known as the microbiome)—and have proven to be so critical to the positive health influences over our day-to-day functioning that some have even called this system a supporting organ. These little microbes help program our immune system; and manufacture neurotransmitters, vitamins, hormones, and food for their neighbors; and aid our digestion and absorption of millions of nutrients that power our cells and preserve our life. When they are fed what they need, they can help keep our trillions of cells in homeostasis and preserve and protect our brain cells. When they're not getting enough of something—or when they are getting too much—our entire 32 trillion cell body-system gets clogged, our brains get foggy, and our whole body can feel out of whack.

We are just beginning to understand the full impact of our microbiome on our mental and physical health. New studies have shown those trillions of gut bugs play a role in metabolism and weight, as well as in ADHD, depression, autism, Alzheimer's, Bipolar disorder, and other complex mental illnesses. Treatment for these health concerns may well lie in treatment of the microbiome—indeed, probiotics and prebiotics have both shown promising outcomes to the health of patients (for individuals with a dysbiotic gut, you might say these supplements help get the "microbiome party" back on track). But no part of our body acts on its own—and our gut is no different. There are certain genes that can help keep a microbiome in homeostasis—or make your gut less than healthy over time.

Are Your FUT2 and HLA-DQ2/8 Variants Crashing Your Gut Microbiome Party?

Certain genetic variants analyzed in Genomind's Mindful DNA Assay may place your microbiome at risk for dysbiosis. As mentioned in prior blogs, a diverse microbiome is generally a healthier microbiome. The reasons for this are still being researched, but one thing we understand right now is that the lack of that diversity can lead to an array of

negative conditions. The **FUT2** gene affects the surface receptors that allow for the attachment and growth of intestinal microbiota, and provides an important food source for healthy gut bacteria. The "resilient" version of this gene, the "secretors", support these surface receptors that in turn make a diverse microbiome possible. The "risk" version, or "non-secretors" lead to a lower diversity and dysregulation of gut microbiota. Those with the risk version have a 7-14% increased risk of inflammatory GI conditions like celiac disease or Crohn's disease. If you know you have a risk allele on this gene, you can begin to take additional steps to promote a healthy gut—a more plant-based diet, and pre- and probiotics being a great place to start.

When it comes to risk alleles in your personal genetic code, the **HLA-DQ2/8** gene is somewhat straightforward: the DQ2 and DQ8 haplotypes (haplotypes are genes that are inherited from a single parent) are strongly associated with Celiac disease—and the DQ5 haplotype is carried in 90-95% of all Celiac patients. Celiac disease (and for that matter less severe forms of gluten sensitivity) can have an impact on your whole body, from your energy levels to your digestive processes to how well your brain functions; and the sooner you know whether you suffer from gluten sensitivity, the sooner you can make those gluten-free changes to your diet to feel better.

Your Genes, Your Microbiome, Your Mental Health

Reader, any great party host does their homework when crafting their get-together, particularly when it comes to the guest list. The more you plan, the better chances you have to throw a holiday party that people will truly enjoy and remember. So, too, with your health, as to "who gets invited" into your microbiome community to join the party there: the more you understand about the goings on of your own body, from your genes to your microbiome, the more information you have on hand to make the right health choices that will serve you for the decades to come. Genetic tests like Mindful DNA can help you figure out if your genes are working for or against your microbiome—and from there you can plot a course that can help you epigenetically modify the expression of your

DNA predispositions. So, here's to the holiday season—and to good health well into the new year!

Can an "Orchid's" IBS be Solved by a Genetic Test and Happier Gut Bugs?

Reader, there are phrases in the English language that, when spoken, invoke a universal human reaction… and one of them is most certainly, "I think I'm going to be sick." Sometimes, those words are spoken after a big meal, or during a particularly long and winding car journey. Other times, they're spoken in response to an emotional stimulus—right after a breakup of a friendship or love relationship, for instance, or before a job interview. And as a psychiatrist, it's these latter instances I'm most curious about. Why is it that a sudden pang of stress is so often followed by a sudden feeling of illness? What are the physiological and psychological connections between facing an emotional moment and your gut turning itself in knots? When we are in emotional or physical pain, our bodies respond with a spectrum of chain reactions, from subtle (think tears welling up in the eyes) to aggressively obvious (think inflammation from a particularly bad bee sting), designed to protect us—but there can be such a thing as too much, or too little, of a good thing, and that holds especially true when it comes to the protective mechanisms of our bodies. This week, I want to discuss how your genes might be predisposing you to gut dysbiosis—and those "I think I'm gonna be sick" reactions—and what you can do to bring your body back into balance!

Your Orchid Genes, Revisited

We've previously discussed how our genes can predispose us towards being an "orchid" or being a "dandelion." Like the flower for which they're named, orchid individuals are more vulnerable to chronic stress situations and need specific ambient conditions to thrive. They are much more "culture-dependent" than dandelions and do much better in emotionally warmer, personal-growth-oriented, nurturing environments. Dandelions, on the other hand, are genetically equipped to be more adaptable to many different environments—in other words, they can "grow anywhere". But they will never be an orchid. The difference between the two lies in how specific genetic variants affect the

body's HPA axis, which in turn dictates our "fight, flight, or freeze" response to stress. Here's a helpful refresher: the body's response to stress begins in a part of the brain known as the Amygdala. Located deep in the brain's temporal lobe, the Amygdala scans our environment for images and sounds that may pose a threat. If and when it finds a "hit", it immediately triggers another part of the brain known as the Hypothalamus, which in turn triggers the "fight, flight, or freeze" hormonal response along the HPA—or hypothalamic-pituitary-adrenal—axis. The resulting hormonal surge of cortisol and adrenaline is what we experience as stress.

Variants of the body's "orchid genes" can impact every stage of this biological process—and the SLC6A4 gene is especially of note. Serotonin is an important neurotransmitter that helps to regulate our sleep, appetite, mood and anxiety—and SLC6A4 is responsible for regulating serotonin levels in our brain's synapses as well as in our gut. If you are born with an s/s variant on your SLC6A4 gene, you are genetically predisposed to have fewer serotonin "transporters" that help to transport serotonin to the places they need to go after the neurotransmitter is released in your body. Under stress, your brain's synapses flood with serotonin, and if there are not enough transporters, all of that extra serotonin results in more "hits" in your Amygdala that in turn trigger your fight, flight or freeze response.

Scientists have long known the connection between serotonin and the stress response—but studies have now shown that the s/s variant on the SLC6A4 gene can also have dramatic implications to your gut response, too. Could SLC6A4 be the cause of that "I think I'm gonna be sick…" impulse?

SLC6A4, Serotonin, and Your Gut

Orchid individuals possessing an s/s variant on their SLC6A4 gene have fewer serotonin transporters and therefore more serotonin in their bodies. In the brain, too much serotonin can lead to an over-reactive "fight or flight" response. In the gut, too much serotonin can lead to a gut in dysbiosis, irritable bowel syndrome, frequent diarrhea and abdominal pain, and many other difficulties. In healthy guts, serotonin plays several key roles in

regulating the gut, including promoting gut motility, modulating electrolyte absorption, maintaining fluid homeostasis, and regulating your gut permeability. However, studies show that increased serotonin levels result in overactive gut muscles, increased secretion and gut mucosal inflammation levels, and more pain for the patient. One study in particular showed that serotonin release was found to be ten times higher with patients suffering from IBS than those who did not!

Like I mentioned in the beginning of this blog, our bodies have a series of chain reactions designed to protect us—and a flood of serotonin is certainly one of them. But if your body is not equipped to process that serotonin effectively, then you might find yourself saying "I think I'm gonna be sick" a little too often for your liking. If you are an orchid individual, living with an increased stress response can be difficult enough. To compound those issues with issues stemming from your gut microbiome can make life harder. Luckily, for s/s variant "orchids", there may be a light at the end of the tunnel.

Can You Make Your "Orchid" Gut Bugs More Resilient?

If you feel stressed or panicked and suffer from IBS or other gut difficulties, the very first step you can take in the right direction is working with a psychiatrist who can administer a genetic test, like Genomind's Professional PGx Express test, that will shed light on what gene variants you're working with in your journey towards better health. From there, you and your doctor can determine a treatment plan that is tailored specifically to your SLC6A4 variant. New medicines help to quell symptoms of IBS stemming from too much serotonin, and those medicines will become increasingly popular as the medical world moves towards precision medicine. If too much serotonin is leading your gut towards dysbiosis, a diet rich in prebiotics and probiotics may help bolster your defenses. The gut is centrally involved in many of our mental and physical concerns, and the more you know about your body, its genetics, and your own microbiome, the more you may be able to stave off uncomfortable "I think I'm gonna be sick" reactions.

Your Subatomic, Atomic, and Molecular Mental Health

Blueprinting Root Cause Analysis begins with DNA

Reader, where does your "Self" reside, and how is it created and maintained? What about your "Identity?" Do these originate in your brain? Your heart? Your gut? Do they emanate from your 130 trillion human and microbial cells? From your 100 billion neurons and their 10,000 trillion synaptic connections? Many neuroscientists would argue this point of view, and I respectfully disagree. Why? Most of us over our lifespan can identify a relatively stable sense of self, and one or more stable adult identities (parent, adult child, friend, among others.). Yet inside our bodies, at the molecular, atomic, and subatomic levels, everything is constantly changing at unbelievably fast speeds! With constant change comes a continuous opportunity to stabilize or destabilize these events—to improve or worsen the underlying health of our cellular and mental processes. What are the implications of this dynamically changing environment? And if such cellular, molecular, and atomic instability is the case, how can we benefit from a stable sense of self and good mental health? Let's illustrate a few examples of what's going on inside us…

Where does the "Self" reside?

We will begin with the lifespan of the cells in our bodies. Those cells that line your stomach and intestines die off and are replaced every two to nine days. Blood cells, depending upon which ones, are replaced every few days to few months. Heart muscle cells die off and are replaced at the rate of 0.5 – 10% per year, so you may have an entirely new heart created over your lifetime! And while most of the cells in our brain last a lifetime, a large subpopulation of hippocampal neurons (the hippocampus is where emotional regulation and new memory formation take place), constituting one third of the neurons, is subject to exchange. In adults, 700 new neurons are added per day, and these neurons are generated every day even into old age. The take-away message? Virtually every cell in our body gets replaced over our lifespan, which offers vast

opportunities to improve their health, and our mental health, or cause premature cellular aging and cellular death.

What about the turnover of molecules and atoms inside these cells? RNA molecules live an average of only two minutes. For proteins, their half-lives (the time it takes for half of them to be destroyed) ranged from 10 hours to greater than 1000 hours. In a study published in the Annual Report for Smithsonian Institution, scientists found that 98 percent of our atoms are replaced each year.

At the subatomic level, things are even faster and spookier. Inside the nucleus of an atom (like the sodium or potassium atoms inside you), particles can move faster than 46,500 miles per second! An electron around a hydrogen atom (think of all the "H" atoms in the H2O inside you) is a little slower, moving at "only" 13,020 miles per second! And finally, many enzymes in our cells dramatically accelerate molecular and atomic alterations, utilizing quantum mechanical events such as electron tunneling, to enable them to take place in a billionth of a second or less. In fact, plants became "quantum computers" long before we or the Chinese developed them!

With all of this turnover and turmoil, all of this chaos, how can there possibly be any stability—or, for that matter, how can there be any stable life at all? Much of the answer lies in the main "Blueprint" for all of this cellular activity, and for life itself: **our unique DNA.**

DNA: A blueprint to build a better life

Life is a highly organized process that within each life form unfolds over months and years—and DNA is its driving factor. It is for this reason that DNA is also a fundamental key to understanding Root Cause Psychiatry, and how we can use it to build better mental health. So what exactly is DNA, and how does it work?

Now, I admit that DNA can seem like an infinitely complex notion to wrap our minds around. For instance, if we unwound all the DNA in our body and put it end-to-end, it

would be able to stretch to the sun and back over 600 times! And while we may be able to understand that our DNA is a simple "digital information system" made up of sequences of just four nucleotide molecules arranged in pairs (we've seen the double helix images—the pairs constitute the rungs in the DNA ladder!) how are we to fully comprehend that inside each one of our human cells, there exists *3 billion* pairs of nucleotides? And how do we wrap our heads around the fact that we 7.8 billion humans can look and act so differently (consider for a moment how different you are from your siblings, your mother, or your father), yet across the globe each of us shares 99.6% of our genetic code—and that our individuality comes from just 0.4% of that code?

Luckily, in our practical understanding of DNA as a blueprint, we don't have to comprehend the enormity of all this. Simply put, DNA is the code that the cells of our body "read" to create and re-create themselves (and by extension, us!) To more easily understand this process, I encourage you to watch the video below, which does an excellent job of visualizing the inner workings of our cells. As you'll see, genes are sections of DNA that contain instructions for building proteins. Those proteins—made up of amino acids—will eventually determine everything from the color of your eyes to whether you might suffer from anxiety, depression, or other mental illness. They will also manufacture those enzymes I told you about earlier, that accelerate cellular functions a billion-fold.

From DNA to Protein Video

As you watch and listen to this video, you might think that such a beautiful, mechanical "blueprinting" process might point to a mechanistic view of life, and a kind of genetic predeterminism—that our fates are sealed as each of those blueprinted genes (our cellular "code") get read and do their work. But about 20 seconds into the video, the narrator makes a different case. Did you catch it? "When the gene is switched on…"

Now, re-watch the video and consider those mechanical processes in a different light, using the analogy of designing and building a home. Any blueprint, no matter how complex, can be modified further by its architect, and the materials (the building blocks)

used to render its design are almost infinite in their variation. And of course there are the engineers, carpenters, plumbers, electricians, tile layers and so on that can further modify the design by collaborating with the architect to make changes in the blueprint. Inside our cells, the process of reading our genetic blueprint in order to create the proteins that build and rebuild our very selves is one of inputs and outputs. And guess what, reader? You have a big say over those inputs. In fact, you are the LEAD ARCHITECT. While you may be genetically predisposed to certain mental health conditions, there are innumerable inputs that can tell your body to switch “on” or “off” certain genes. And these inputs, including everything from vitamins and supplements to macro and micronutrients to targeted medications to a simple run in the morning, are very much in your control. You can even order Genomind’s Mental Health Map DNA Test Kit, and through a simple cheek swab identify certain genetic predispositions related to mood, stress and anxiety, sleep, and other traits; and learn how to “throw the right switches” to improve your mental health!

You are the lead architect of your own health... but you have helpers!

In closing, as you are the lead architect of your future mental and physical health, I would like to introduce you to a new cast of “root cause analysis experts” who will help you create the blueprint and assist you in building better mental health. While we will get to know each of them in great detail in future blogs, for today their brief bios are:

Your “assistant architects,” including the psychiatrist, nutritionist, naturopath, and other professionals who can help "guide" the process of bringing the blueprint to life.

The “engineers,” including genetic testing, nutrient evaluation, microbiome testing, food sensitivities and systemic inflammation assessment, other important blood-based biomarkers, DNA methylation and other cellular aging tests that will help ensure that as Lead Architect, you will have the information you need to build more robust and resilient mental health.

The "builders," which are the cellular systems and processes by which you can begin to implement the design of your blueprint. This includes epigenetic factors such as methylation and acetylation that turn on and turn off genes, RNA (like in two of the COVID vaccines) that manufactures the proteins, mitochondria that produce the energy that powers all the cellular processes, and subatomic events

The "building materials"—while you can design a beautiful blueprint, the end result is very much dependent upon the materials you use to build it out. The building materials in this series include amino acids, fatty acids, carbohydrates, atoms, subatomic particles, other molecules, macronutrients, micronutrients, unconscious factors that originate in childhood, self-help knowledge, meditation, love and work relationships, sociopolitical factors, spirituality, and more.

You may be thinking at this point, "He has no idea what he is asking of me! This is all so complex and beyond my understanding! I'm no scientist, what is he thinking?" My Dear Reader, fear not! Please recall that I am your Healing Companion, devoted to easing your emotional pain, not adding to it. I will be with you every step of the way on this immense journey, and I will teach you how to become the Lead Architect in building better mental health for you and those you love.

National Root Cause Psychiatry Program

True wellbeing doesn't just rely on the health of your brain. It also relies on the health of your cells, your genes, your gut, your immune system, and so much more.

To truly feel emotionally well, each of these "root causes" must be addressed. And in Potomac's Root Cause Psychiatry program, that's exactly what we do… to help you feel better and *stay* better.

Root Cause Psychiatry treats both your mind and your body—but most importantly, it treats you as the unique individual you are.

Working together as your Root Cause Team, psychiatrists and nutritionist combine their expertise to build a personalized treatment roadmap specific to your biological, psychological, and social needs. Your dedicated program manager, will coordinate and manage every aspect of your care. And your team will meet weekly to answer your questions and discuss your progress.

This process personalizes every step of your journey—and we are honored to be a part of it.

Step 1: Build a Blueprint

To build your treatment plan, we listen to your story and administer genetic, nutritional, gut microbiome, and other comprehensive lab assessments to determine baseline root causes of your illness and blueprint our initial interventions.

Step 2: Address Additional Root Causes

Based upon your initial treatment response, your team may identify additional root causes, add them to your integrative health blueprint, and recommend refinements to your treatment roadmap.

Step 3: Restore your Health from the Roots Up

Your team will then monitor your progress over 12 months and refine the plan as needed. Treatment will consist of specific solutions for each and every root cause of illness or suffering, from medication to dietary recommendations, talk therapy, supplements, and more.

Bruce Alan Kehr, M.D.

Bruce Alan Kehr, M.D. is the Founder and President of Potomac Psychiatry. He has been named a *Washingtonian Magazine* “Top Doctor” annually for many years. In 2019 he was the only adult psychiatrist named “Top Doctor” *by Bethesda Magazine.* He received its "Top Doctor" award again in 2021. Dr. Kehr is also a Castle Connolly Top Doctor five years running, since 2016. In 2021, Under Dr. Kehr's leadership, Potomac Psychiatry was awarded "Best Comprehensive Psychiatric Care Services - Northeast USA" by Global Health & Pharma. Dr. Kehr is an accomplished author whose works have been read by over 1,000,000 people in 206 countries. In 2020 and 2021, his blog was ranked #2 in the nation among the top 50 mental health-related blogs. He is also the inventor and Founder of PainScript, a personalized digital platform for pain management, substance use disorder and chronic care management - an award-winning technology which won the "Best Digital Chronic Care Management Platform - USA" and the “Patient Care Excellence Award 2021”

Learn more about his approach to treatment at his extensive, searchable blog library, or by reading his best selling book, Becoming Whole: A Healing Companion to Ease Emotional Pain and Find Self-Love.”

Disclaimer

The material and information provided within this book does not constitute medical advice, and the strategies and treatment modalities discussed in the sessions may not be applicable to you, your family members, or your friends. No part of the content of this book is intended by the author or publisher to be a substitute for professional medical advice, diagnosis, or treatment by a qualified mental healthcare professional. No physician–patient relationship, explicit or implied, exists between the publisher, author, and you, the reader. This book is not a substitute for a relationship between you, as a patient, and a qualified mental healthcare professional.

The patient stories contained within the book are illustrative of emotional issues faced by many of us as we go through life, and some of the themes presented are universal. Although lessons learned from the treatment of actual patients are included in the stories, the historical events and facts represented have been changed to protect the identities of any real patients and to protect their confidentiality. This includes, among other minor alterations, the names, ages, careers, the number and sex of their children, and the careers of the patients' parents. Consequently, all characters that appear in this work are fictitious. Any resemblance to real persons, living or dead, is purely coincidental.

The information included in each chapter or "session" is for illustrative and educational purposes only, to help you understand what your experience in a psychiatric session might be like. You should not consider such information to be medical advice that is in any way suitable to your circumstances, nor should you treat anything you read in this book as an alternative to medical advice that you receive from a doctor or other professional mental healthcare professional. Any use of the information in this book is at your discretion. Consult a qualified healthcare professional if you have any questions or concerns that relate to your own life situation. You should not delay obtaining medical or mental health advice, dis- regard medical or mental health advice, or discontinue medical or mental healthcare treatment because of any information you read in this book, or any resources cited by the author in the book.

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