Using Your Nervous System to Enhance Your Immune System | Huberman Lab Podcast #44

This episode teaches you a lot about the immune system, immune-brain interactions and offers 12 potential tools for enhancing immune system function. I discuss how our immune system works and science-supported tools we can use to enhance our immune system.

I discuss the innate and adaptive immune systems and our various microbiomes-- not just in our gut but also in our nose, eyes and mouth and how to keep them healthy. And I review how specific patterns of breathing and foods maintain a healthy mucosal barrier that is crucial for fighting infections. I discuss how certain neurochemicals called catecholamines enhance our immune system function and how to use specific breathing protocols, types and timing of heat and cold exposure, and, if appropriate, supplementation to activate catecholamines. I also discuss the role and use of serotonin for the sake of accessing the specific types of sleep for recovering from illness, and I discuss how to increase glymphatic \"washout\" of brain debris during sleep. I also review fever, the vagus nerve and the use of atypical yet highly effective compounds for rhinitis (nasal inflammation).

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- Welcome to the Huberman Lab Podcast, where we discuss science and science-based tools for everyday life. I'm Andrew Huberman, and I'm a Professor of Neurobiology and Ophthalmology at Stanford School of Medicine. Today, we are discussing the immune system, and we are also discussing the nervous system, which is the brain, spinal cord, and the connections of the brain and spinal cord with all the organs of the body. We are also going to discuss how the nervous system can be used to activate and control the immune system. Now, about 10, 20 years ago, if somebody said that the mind could control the immune system, they'd probably get laughed out of most academic conferences. And certainly the work wouldn't be published in quality journals, but nowadays there are dozens, if not hundreds of quality peer-reviewed studies on how the mind and how the nervous system can control activation of the immune system. This is a wonderful growing body of research. And just to give you a hint of where we are headed with this, just this last week, there was a paper published in "Nature" which is the apex journal for scientific publishing, premiere journal, extremely stringent, a paper published in "Nature" from Qiufu Ma's lab at Harvard Medical School, explored how acupuncture can reduce inflammation in the body. And I will describe this study in a bit more detail later, but what they discovered was that by stimulating the body in particular ways at particular sites on the body, they were able to liberate certain cells and molecules that

enhance the function of the immune system, and potentially can be used to combat different types of infection. And just to give you another little hint, they found that a particular type of organ tissue called fascia, some of you may have heard of fascia, fascia surrounds our muscles. Just to look at it, you might think it's a kind of useless tissue, it's sort of like a dense bag in which the muscles are contained. Well, it turns out that those dense bags are much smarter than we thought. They don't have a mind of their own, but by stimulating the fascia in a particular location on the body, there's a pathway leading out of that fascia directly to an organ called the adrenal medulla, I'll explain what all this means, that could liberate particular chemicals that had a potent anti-inflammatory effect. So what we're basically saying is that the nervous system acts as a set of highways between the different tissues of your body, calling into action the immune system, liberating particular molecules that can reduce inflammation and lead to faster healing. And I will explain how all of that works as well as some other non-acupuncture methods for activating and enhancing the function of the immune system. So, today, we're going to be talking all about

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healing with the mind in a completely non-mystical, non-abstract sense. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero cost to consumer information about science and science-related tools to the general public. In keeping with that theme, I'd like to thank the sponsors of today's podcast. Our first sponsor is ROKA. ROKA makes eyeglasses and sunglasses that are absolute suburb quality. I've spent a lifetime working on the visual system, and I can tell you that one of the major issues our visual system has to contend with is how to see things clearly in bright environments or dimmer environments, et cetera. ROKA clearly understands the science of the visual system, because one thing that's wonderful about their sunglasses is that you can be in a very bright environment and then walk into a shadowed environment and you don't even notice the transition. Everything is still seen with crystal clarity. Their eyeglasses as well allow you to see things regardless of how bright or dim internal lighting is. I wear readers at night, I wear sunglasses during the day, and ROKA eyeglasses and sunglasses are particularly nice because they're very lightweight, so I often forget that they're even on my face. They also don't slip off if you get sweaty. They

were actually designed to be used while running or cycling. And so I can use them while exercising. They also have a great aesthetic. So you can go from exercising, to dinner or to work, without having to change from one set of glasses to the next. If you'd like to try ROKA glasses, you can go to roka.com, that's R-O-K-A.com and enter the code "Huberman" to save 20% off your first order. Today's episode is also brought to us by Athletic Greens. Athletic Greens is an all-in-one vitamin, mineral probiotic drink. I've been taking Athletic Greens since 2012. And so, I'm delighted that they're sponsoring the podcast. The reason I started taking Athletic Greens, and the reason I still take Athletic Greens once or twice per day is because it allows me to cover all of my basic nutritional bases. It's got the vitamins and minerals that make sure that no matter what I'm eating, I'm covering all of my micronutrient bases. And it has the probiotics, and probiotics we now know are essential for a healthy gut microbiome. And a healthy gut microbiome we know is essential for many important biological functions related to human health, like metabolic needs, endocrine function, immune function, and so on. With Athletic Greens, I can mix that up with water. I usually add some lemon or lime juice. It tastes delicious. I like it very much and I'll drink it once early in the day, and once again later in the afternoon. If you'd like to try Athletic Greens, you can go to athleticgreens.com/Huberman. And if you do that, you can claim a special offer. They'll give you five free travel packs, which make it very easy to mix up Athletic Greens, whether you're in the car, or on a plane, or on the move, and they'll give you a year supply of vitamin D3K2. There is now a lot of data showing that vitamin D3 is important for many biological functions that impact our immediate and long-term health. And most people do not get enough vitamin D3, even if they're getting a lot of sunshine. And K2 is also important or has been shown to be important for heart health and for blood lipid function, et cetera. So, again, if you'd like to try Athletic Greens, you can go to athleticgreens.com/Huberman to get the Athletic Greens, the five free travel packs, and the year supply of vitamin D3K2. Today's episode is also brought to us by InsideTracker. InsideTracker is a personalized nutrition platform that analyzes data from your blood and DNA to help you better meet your immediate and long-term health goals. I've long been a fan of getting regular blood work done for the simple reason that many of the things that impact your immediate and long-term health can only be analyzed from a quality blood test. There's just simply no other body surface marker that you can look at somebody or yourself and say, "Ah, I know that my blood lipids or my cholesterol are good, or that my hormone levels are X, Y, or Z." We really need numbers on those

things to know where they sit. The problem with a lot of blood tests, however, is you get all those numbers back, you don't know what to do with that information. InsideTracker has solved that problem, and they have a very easy to use dashboard where when you get your numbers back, it can tell you for instance, where your numbers are high or low or on target. And they can suggest very specific dietary intervention, supplemental interventions, and behavioral interventions that can allow you to bring those numbers to where you would like them to be. So they've simplified the whole process. And in terms of getting the blood tests, you can go to a local center to get the blood drawn, or they can even send somebody to your house. So, they've made the whole thing very, very easy from start to finish. If you'd like to try InsideTracker, you can visit InsideTracker.com/Huberman

00:07:41 Foundational Tools & Practices for a Healthy Immune System

to get 25% off any of InsideTracker's plans. You just use the code "Huberman" at checkout. Okay, let's talk about the immune system, and the nervous system, and how the two interact, and how you can control your immune system to serve you better. We are going to talk a lot of mechanistic science, a little bit of detail, you'll learn some new language around the immune system; names of the different cell types and so forth, but I promised to make it all very clear, regardless of your background. We are also going to discuss a lot of tools. And I think many of you are probably here because you want to know what you can do in order to boost or enhance the function of your immune system. That's a very reasonable question to ask. I want to begin by just acknowledging that if one were to put that question into the internet, you would get back a lot of answers. And there is now a sort of generic form of that answer that deserves our respect, but is not going to be the topic of conversation today. I just want to tip my hat to it, however, and list off a few of the things that we know set us up to be healthier than we would be if we didn't do these things. So the first of course is the foundation of all mental and physical health, which is to get adequate sleep. Meaning enough sleep, whatever it is for you that you require, to get deep sleep, so it's got to be of high quality, and to time that sleep correctly. Meaning you can't sleep during the day one day, and at night the next day, and expect your system to function well. I've talked a lot about that before on this podcast. You need a relatively consistent sleep schedule most of the time, about 80% of the time, or even better would be 90% of the time. But the realities of life make it that we can't

always go to bed at the same time and wake up at the exact same time. Okay, so we need sleep. We do need sunshine. Why do we need sunshine? Because it sets our rhythm into a regular state where the genes in all of our cells can be expressed at the correct times. We're sort of a factory of cells, if you will, and that factory can only run properly if it knows when certain things should be active and when certain cells should not be active. And the best way to coordinate all of those activities of all the cells is to get sunshine in your eyes in the morning and again in the evening, and not to get too much bright light in your eyes in the middle of the night. That's just foundational. And then any lists that you'll find on any number of websites on the internet would say, "Okay, get good sleep, get sun, get exercise." How much exercise? We should all be getting 150 to 180 minutes of zone two cardio. That's cardiovascular exercise where we can just barely hold a conversation or maybe not, per week. We should be eating well. We're always told we have to get good nutrition. What good nutrition means to you is going to be different than what it means to somebody else. But we acknowledge that food intake and quality of food in particular, avoiding processed foods, that's going to be important. Social connection is important. Hydration is important. You're starting to get the picture. We can take all that, acknowledge it as useful and foundational for mental and physical health. But of course there are many people who still struggle with getting ill too often, or with not being able to heal from physical injuries and wounds, or from various bacterial and viral infections quickly enough or deal with chronic disease. And so, today's really about how you can take all of that information, acknowledge it, and follow it. But in addition to that, there are things that you can do to leverage your nervous system in order to enhance the function of your immune system in very robust ways.

00:11:20 Immune System Basics: Skin/Mucous, Innate & Adaptive Immune System

So that's where I'd like to shift the conversation to. The first topic we have to attack is the question of what is the immune system and how does it work? I think many of you have heard of antibodies or killer cells or the various organs of the body that are involved in the immune system, like the bone marrow, the spleen, the thymus, and the lymph nodes. I'd like to just take a moment and do a sort of brief immune system 101; really simple, cover the basic elements of the immune system so that everyone listening or watching this can get a clear sense of how the immune system functions and what its basic parts are. For some of you, this might be too basic. It might be a little bit of background that

you already know. I think for most of you, this information will be new. And I promise you, you don't need a biology or medicine background in order to understand this. It's actually really simple because it is truly elegant in design. You have three main layers of defense for your health. These are the three things that are constantly at work to protect you from invasion and illness from bacteria, from viruses, and from parasites. And the first of those three is a physical barrier that we call your skin. And that might seem kind of obvious, but everything about you is contained in this compartment that is boundaried by your skin. And your skin is a very important aspect of your immune system. If you've ever had a cut, you essentially have a breach of the boundary that is your immune system, and you would notice a number of things would happen. You might get some swelling around that cut. You might get a scab, likely you would get a scab over time. If it got dirty, there were some bacteria that got in there, you might see some accumulation of white blood cells, what's called puss. I know it's kind of gross, but that's what that is. It might take on a yellow tint because of the accumulation of some dead cells there. But basically your skin is the primary barrier through which you keep things from the outside that could harm you from getting to the inside. Now, still in category one, your body and your external surface, you have openings to that surface, right? You're not just a round or a body shaped completely covered up with skin. You have openings, what are those openings? Well, let's start at the top and work our way down. A primary site of potential infection are your eyes. You have your ears, you have your nostrils, you have your mouth. Okay, those are going to be the primary sites by which things can get into your system. And you need to put things into your system; you need to drink and eat, and you need to get light into your system. That's why you have those openings, but bad things, meaning things that can harm you, can get into those systems. And then of course, along the back of your throat, all the way down to your stomach and your digestive system, and through your intestines and out your rectum, you have a tube, that you are basically a series of tubes. I've said that before on this podcast, and this is one such tube by which you extract nutrients from the outside environment. But all along that tube, including your nose and your mouth, it's lined with mucus. And while mucus might seem kind of gross to some of you, the more you learn about mucus, the more you realize that mucus is really, really cool because mucus essentially acts as a filter, as a trap for bacteria and viruses. And it has certain ways of scrubbing or killing those bacteria and viruses. Now, the mucus is constantly being turned over, as we'll talk about later, the chemistry of that mucus is really important in order to make sure that certain things don't

make it into your system, and other things are allowed to move through your system and you can extract nutrients from them. So the reason I'm talking about this first category of barrier for immune system in such detail is I'd like you to envision yourself as a human, of course, but as a human that is a clear entity from everything else. And you have to bring in the right things and you have to keep out the wrong things or kill them. Now, inevitably, bacteria, viruses, and parasitic infections are going to make their way into our body, but whether or not they are killed off or whether or not they take over and cause us harm is going to be determined by layers two and three. So, layers two and three are the so-called innate immune system and the adaptive immune system. So the innate immune system is what I would call the second layer of defense. It's very fast. So whether or not it's bacteria, virus, or parasite, what happens when you have something enter your body, maybe you swallowed it, maybe got in through your eyes, maybe you shook somebody's hand who is carrying a particular kind of illness, and then you wiped your eyes. And I've talked about on this podcast before, very soon after we meet another person, usually within 30 seconds, believe it or not, most people wipe that person's chemicals somewhere on their face or on their body's surface. This has been demonstrated over and over again. If you want to learn more about that, we did an episode all about chemical signaling, where you can learn about it. I know it sounds weird and you might say, "I don't do that," but indeed you do, most of the time most everybody does. Okay, so, this innate immune system is this rapid response when something enters our system and our body doesn't recognize it. It's not food, it's not clean air, it's something that's either a bacteria, virus or parasite. And the innate immune system involves the release

00:17:08 Killer Cells, Complement Proteins (“Eat Me!” Signals), Cytokines (“Help Me!” Signals)

of particular cells that are waiting dormant, ready to attack whatever this invader is. And some of these cell types you've heard of before. The most typical one are the so-called white blood cells. So, the white blood cells will actively go to the site of invasion and will start to encapsulate or try and surround that given invader. The other names of these different cell types are things like neutrophils, macrophages, natural killer cells are just a few of the many types of immune cells. So there's kind of like an ambulance system, but rather than go and try and heal something like a paramedic would, they go there and

they try and surround and kill whatever this invader is. They work in concert with two other assistants, and those assistants are called the compliment proteins. Compliment proteins exist in the blood, and what they do is they travel to sites where there's an invasion and they mark certain things for being engulfed and eaten. So they sort of put an "eat me" tag on it. They basically put a chemical tag onto invaders that then allows those white blood cells, neutrophils, macrophages, natural killer cells to say, "Ah, I need to basically kill this thing, and then wrap it in a body bag and send it off. Kill that thing, wrap in a body bag and send it off." And I'm using the analogy of the body bag, but in the sense it's the right one rather because these cells that come in and kill things, the way they do that is actually to engulf the invading bacteria, virus or parasite. So they actually surround it. And when you see puss or you see infection in maybe a cut on the skin or something like that, or even in an ingrown hair that gets some bacteria in it, that puss and the white part, I know it's kind of gross to talk about, but those are the white blood cells, oftentimes it's dead cells, and that's the dead invader sitting there. So it's trying to create an isolated compartment 'cause it wants to keep it in that part of the body. Okay, so you've got the innate immune system, the compliment comes through blood and helps it by tagging certain things with an "eat me" signal. And then there are the cells that are either damaged from the injury or from the parasite, or are suffering because of the bacteria or the virus itself, and the cells of your body will also release an alarm signal, which is not an "eat me" signal, but a "help me" signal. And those "help me" signals come in the form of what we call cytokines. And the cytokines are things like interleukin-1, interleukin-6, tumor necrosis factor alpha. You may have heard of these things if you are at all curious about or have been learning about the health space, online health space, especially in the last few years, inflammation is all the buzz word now. Everyone's talking about inflammation, inflammation, inflammation. What do we mean when we say inflammation? Well, inflammation is a physical response, but it's also a chemical response. And many times the markers of inflammation that are measured in people or in animal models where this research is done, are things like interleukin-1, interleukin-6, tumor necrosis factor alpha. So when those go up in the blood, it's a sign that somewhere there's a cell that's saying "help me, help me." And is secreting these things which calls in those neutrophils, macrophages, natural killer cells, and white blood cells, okay? And it might help to remember all this, by just telling people that what interleukin means is to communicate, right? So the interleukin is shouting out "help me," the compliment proteins are coming in and saying, "eat this" and tagging the invader

with an "eat me" signal. And then the killer cells and the white blood cells are doing the job of trying to kill off that thing. That's the innate immune system. So, your skin and your mucus lining plus your innate immune system are a beautiful two-layered

00:21:06 The Adaptive Immune System: Antibodies

set of defenses against various kinds of invaders and infections. And then there's the third type, which is the adaptive immune system. And you'll notice that leading up until now, I haven't said the word antibody at all, and that's because it is the job not of the skin or the mucus or the microbiome or the innate immune system to produce antibodies that can recognize specific invaders, but rather it is the job of the adaptive immune system to create antibodies against bacteria, viruses, and even parasites and even physical intruders to your system. So, the adaptive immune system has this incredible ability to show up at the site of invasion or infection or inflammation. It's called there by various cues, including the cytokines that we talked about earlier. And what it does is it actually attaches to and creates a sort of an imprint of the shape of whatever invader happens to be there. So if that particular invading bacteria or virus has a contour that's kind of rippled or kind of spiky or whatever shape it happens to have, it creates an imprint of that. And then, using that imprint in concert with some other cells, creates antibodies that are specific to recognize that invader should the body ever have that invader inside of it again. Now, that's why it's called the adaptive immune system. And in many ways it creates a memory of a prior infection so that these antibodies can be made anytime that same invader comes back again, all right? And so, this is the basis of what we call immunity. This is the basis of what we call an enhanced ability to combat certain types of infections. And it's really a wonderful, and I mean, I can't even state how incredible this really is, that all of our bodies have this capacity, right? We have something called leukocytes. These are essentially white blood cells. We have red blood cells and white blood cells, and they both are derived from the same type of origin cell. It's a stem cell. When you hear stem cell, a stem cell just means a cell that can become many different types of other cells. We sometimes hear about stem cells in terms of people that are getting injections of stem cells or the potential therapeutic effects or potential of stem cells. But we all harbor certain stem cells within us as well, that can become lots of different cell types. And there's one particular type of stem cell, which is the hematopoietic stem cell, which can give rise to red blood cells and white blood cells.

And in general, these reside in the marrow, at least in adults. So, in our bone marrow, we have this ability to make certain cells that can go out when they are called out chemically, they get called out to sites of infection and create antibodies, and then maintain those antibodies in our system, or have a memory of that particular infection so that if the infection comes back again, we can kill it off immediately. And it doesn't have to pass through these multiple stages of first, the innate response, then the adaptive response, taking some time. Now, there are a lot more details to the adaptive immune system, but I just want to emphasize a few points that might be relevant. First of all, the name of the antibodies that are created sometimes come in the form of IgM and IgG, things of that sort. This isn't a full deep dive immunology class, but Ig stands for immunoglobulin, okay? So the immunoglobulins are a part of the adaptive immune response in creating antibodies. If you hear IgM, the IgM is the first of the adaptive immune responses, and it tends to come on earlier. So if somebody is immunopositive for IgM for a particular type of viral or bacterial invader, that means that it was a fairly recent infection. Later, one creates... The adaptive immune system, I should say, creates an IgG, which is the more stable form of the specific antibody that's going to recognize a given invader. So IgG tends to come up a little bit later. So, just to recap, something gets into your system through your eyes, through some hole in your skin, a cut, through your mouth, sexually transmitted diseases come in through the mucus membranes that are on the genitalia or in the genitalia, sexually transmitted disease, airborne disease, gets into the mucus, somehow gets into the bloodstream. Then there's the innate response, which is a more general response of trying to contain and combat the infection or invader. And then the adaptive response is the one that generates the antibodies. First, the IgM response, the immunoglobulin-M response, and then the immunoglobulin-G response, IgG response. So, how do we keep these three barriers or these three defense systems to infection tuned up? Well, leaving aside the list of things that I mentioned before that generally enhances their function, things like sleep and sunlight and good nutrition, et cetera, the sort of generic things for good health, one of the key ways we can do that is to keep that mucus lining in really good shape. And what does that mean? Well, the mucus lining needs to turn over quite often and it needs to be the correct chemistry to be a trap for the bad stuff and for it to be permeable to the good stuff, to the nutrients that we need. And it is now very clear from hundreds, if not thousands of studies that the best way to do that is to maintain a healthy so-called microbiome. The microbiome being these little bacterial organisms that are good for us

that live all along our mucus pathways and even in our eyes. Now, just to be really clear, it's not just about the gut microbiome; we actually have a microbiome in our eyes, we have one that's specific to our mouth, we have a nasal specific microbiome, there's one all along the gut and the species of microbiota that live all along the digestive tract differ from the mouth, to the throat, to the stomach, intestines, into the rectum. It's well-established that there are healthy microbiota that live all along that length, and that they differ along that length. There's also a urethral microbiota, and there's a vaginal microbiota that promotes health of that environment as well. So how is it that one can maintain the healthy microbiota and not favor growth of harmful bacteria, or allow that mucus lining to become too permeable to the bad stuff that can come in from the environment?

00:28:00 Tool 1: Nasal Microbiome and “Scrubbing” Bacteria & Viruses; Nasal Breathing

Well, as far as we know, there are three main ways to do that. The first two are purely structural and mechanical. It's very clear now from work, some of which was done at Stanford, but elsewhere as well, that the nasal microbiome is particularly good at scrubbing bacteria, at preventing certain types of infections. So, this is a reminder that whenever possible, unless eating or speaking, you want to be nasal breathing, not breathing through your mouth. Your nose is a much better filter for viruses and bacteria than is your mouth. The mouth contains certain structural features, even organs and cell types that can protect against incoming infection, but you don't want to be a mouth breather for a variety of reasons. And there's a terrific book called "Jaws: A Hidden Epidemic," which was written by my colleagues, Sandra Kahn and Paul Ehrlich at Stanford, and Stanford Medicine with a foreword by Jared Diamond and Robert Sapolsky. So it's really a lot of heavy hitters on that book that talks about the increase in infection that one gets when breathing through the mouth, as opposed to the nose. Now, of course, during hard exercise, one breathes through the mouth, that's not necessarily bad. When one is eating or speaking, that's not necessarily bad at all. I guess it depends on what you're saying. That was a joke. But in general, when possible you want to be breathing through your nose. Many people have trouble breathing through their nose because of so-called deviated septums or chronically collapsed sinuses. The best way to dilate those sinuses is actually to breathe through your nose. So it can take a little bit of time, but there is some plasticity to the sinuses. And so, be a nose breather, not a mouth

breather, you will combat more of the infections that you are constantly confronted with. I should mention that we are always bombarded with different types of bacteria, viruses, and parasites in our environment. And the goal of course, is to reinforce your immune system, so you can keep these things at bay and not get sick. There's actually a paper that was published in Cell Reports, "Cell Press Journal," excellent journal that showed that the nasal microbiome, it has particular species of microbiota that are good at fighting off infection. There has not been a direct link between particular patterns of nasal breathing and the nasal microbiome yet, but oxygenation of that environment by breathing through your nose, turns out to be quite important overall for enhancing it as a filter. So don't just think of your nose as something

00:30:33 Tools 2 & 3: (Not) Touching Your Eyes; Gut Microbiome & Fermented Foods

to smell foods and to bring in air. It's also an active filter for things that could invade you. The other way to try and keep out bad things and to avoid getting sick is the advice that your mother, and certainly my mother gave me, which is to not touch your eyes after touching other people or touching other surfaces. And as I mentioned earlier, we tend to do this subconsciously. But the reason to avoid doing that is the eyes are a primary entry point for a lot of bacteria and viruses. You're constantly lubricating the surface of your eyes with the so-called lacrimal glands, and tears and things of that sort. If you've ever noticed when you wake up in the morning, you have some sleep in your eyes, you know the kind of crusty stuff in the corners of your eyes or on your eyelashes, that sleep, that crust are actually dead bacteria that you've successfully battled during the night. Okay, that's what that is. It's not the accumulation of some healthy tissue. It's the accumulation of that your healthy mucus membranes and tears and other things that are specifically combating those bacteria. So, I know that sounds a little bit gross, but that's what that is. So you're wiping away the casualties of a battle that you fought at night. So during the daytime, you don't want to introduce viruses and things to your eyes as much as possible. It is a primary site of entry. This is why people wear goggles in surgical units and things of that sort, to try and avoid getting things into their eyes. Very, very important. And then the third way to keep a healthy line of defense for your entire mucus tract is to enhance the proliferation of good gut microbiota. The best way to enhance the quality of your gut microbiome and the mucus lining that serves as this protective layer all along your body is to ingest two to four servings a day of fermented foods, low sugar

fermented foods. I've talked about this before a bunch of times on the podcast, but these are data from my colleague, Justin Sonnenburg's lab at Stanford Med. And there, I just wiped my eyes. Yep, you got me. But a paper published in the journal "Cell," which is a absolutely spectacular journal, really points to the fact that when people eat fermented foods, two to four servings per day, it helps reduce the activity of certain cytokines. Now, you know what those are, right? Cells make cytokines to call out, "help me, help me." To reduce the amount of cytokines, the so-called inflammatom. Now that doesn't render those cells more vulnerable. The reason they saw a reduction in IL-6 and IL-1, and some of these other cytokines is because when people have a healthy gut microbiome, there are fewer cells in the body being infected from outside infections and therefore less of a reason for cells to be crying out, "help," because they are thriving, not suffering. So, don't wipe your eyes, keep your hands clean, everyone tells you that, right? But keep your hands clean, don't wipe your eyes, be a nasal breather, not a mouth breather, unless you're speaking, exercising or eating, and keep a healthy gut microbiome by eating two to four servings a day of quality, low sugar, fermented foods, things like sauerkraut, things like natto if you can access that. I've tried it before, it's interesting. It's sort of an acquired taste, kimchi, pickles, again, low sugar sources are going to be the sources that are going to be most effective for this. So now you're armed with three ways to enhance the function of your immune system and combat infection that is, I like to think separate from the typical type of information that you get such as get good sleep, good nutrition, good social connection, et cetera. All of that stuff still holds true, but these three other points I think can really make

00:34:20 Some Interleukins Are Anti-Inflammatory

a substantial difference in terms of bolstering the immune system, your immune system. I do want to mention, because these names are going to come up several times during this episode, that while interleukins like IL-6 and IL-1 encourage inflammation, they are these "help me" signals that call in cells to gobble up invaders. There are some interleukins that are anti-inflammatory. And the one that I'd like to highlight in particular, because it will come up again in a little bit is interleukin-10. So not all of the IL, insert number, not all of the interleukins are inflammatory, some are anti-inflammatory.

00:34:56 Sickness Behavior

So that's an important point to keep in mind as we go forward. Next, I'd like to talk about what's called sickness behavior. And indeed there is a category of behavior that we call sickness behavior that is very informative as to the things that we can do to avoid getting sick. Now, this notion of sickness behavior goes back several decades or more. And it's a very interesting way of looking at the function of the immune system, because what it does is it bridges us from this thing that we're calling the immune system where it's T-cells, and B-cells, and cytokines and leukocytes, and it starts taking us into the realm of the nervous system, because of course the nervous system controls behavior. So sickness behavior is a suite of responses that we tend to all undergo when we are feeling sick. So this is going to vary from person to person, but there's some general categories of things that we all do and that happen to all of us after we are wounded or sick or dealing with an infection of any kind. And by examining sickness behavior in some detail, it can be really informative as to routes that we can take to health. So the main thing about sickness behavior is that it tends to involve a slowing of our usual levels of activity. People start to feel lethargic, or they feel like the activities that previously they could do with relative ease are very difficult for them or somewhat overwhelming. The other thing you start to see is that people and animals, by the way, stop grooming, they stop taking care of themselves. Not necessarily stopped showering, although oftentimes that's the case, but they will stop doing their hair, they'll stop putting on makeup, depending on whether or not they did that before, they might stop. Animals will stop licking and grooming themselves. People will stop taking care of their cosmetic appearance. Now it's not just because they don't care how they look when they're sick, it's because there's this overall suppression of certain kinds of activities and an enhancement of other kinds of activities. And this is really important. Sickness behavior is actually a motivated state. It's a state that's designed to accomplish certain things. One of the other features of sickness behavior in addition to being lethargic, loss of grooming, will be a loss of appetite, right? Oftentimes people who have a great appetite normally just won't feel hungry at all. And there are several theories as to why this would be. One prominent idea in the literature is that it's to discourage vomiting and diarrhea, which of course can be infectious to other people. So, that's a theory. I don't know that that's ever been tested directly, but that's one idea. The other idea is that it's simply to harbor more resources for sake of repair. And I want to talk about that because we are all told to get extra sleep when we aren't feeling well or to rest. But just like any good two

or three-year-old constantly asks, "why, why?" Good scientists, good people who are interested in health information should always be asking why. Why should I get more sleep? What happens in sleep that I should get more sleep when I'm sick? Why shouldn't I just push through this? And there are a couple of reasons for this that have been established in the literature. The first is that there does seem to be something useful about slowing circulation when we are ill. One idea that has some data to support it is that when we slow our circulation, our blood circulation, so not running around so much or running it all, but rather lying down, getting extra rest, maybe sleeping, maybe even just remaining still, is that the lymphatic system, which carries a lot of the immune-related cells and fluids, is able to ramp up its levels of activity. So, this is interesting, right? So reducing circulation of the blood, but increasing circulation of the lymphatic system. You've all probably been familiar with the lymphatic system when you're combating an infection, your lymph nodes can get sore. You've got lymph nodes behind your ears, in your groin, your armpits, around your throat,

00:39:08 Some People Seek Care When Sick, Others Want to be Alone

around near your thyroid, in your throat, et cetera. So, that's the other reason. Now, some people, when they get sick, psychologically go into a very vulnerable state where they really, really want people, other people to take care of them. You've probably witnessed this, or you feel this way yourself. About 50% of people have that response. They really want to be taken care of. Now, when you think about it from an adaptive perspective, this makes sense, right? A member of our species is ill and they more or less will cry out for help in one form or another to the other members of their species to take care of them. And of course this will be especially apparent in cases where people are young enough or incapacitated enough that they can't actually get resources on their own. If you've ever been really sick, just getting up and going to the fridge or to the restroom can feel like a monumental task. So about 50% of people report or describe seeking of help and support when they are sick. But you could also imagine how this would be a very non-adaptive response because it increases the opportunity to spread infection to the caretaker. So that's an interesting consideration. Another 50% of people seem to have the opposite response when they're sick. So, somehow, regardless of how they were prior to getting ill, the sickness behavior that's engaged by these neural circuits in the brain, they are indeed neural circuits in the brain, create a stay away from

me. I don't want to be bothered. I want to be left alone. I don't want to be taken care of, right? It's not stubbornness. It's literally a lack of interest or a disinterest in social connection when one is sick. And you see this in animals too, some animals will seek out other members of their species. Others, like my unfortunately now passed away bulldog, Costello. When he was sick I always knew because he would go around the back of the house and he would just hide there. He would just take himself away from everybody else. He did not want to be taken care of. And it was just a natural response to him. I don't think he was trying to prevent me from getting whatever it was that he had. So if ever somebody doesn't want to be taken care of, or if they do want to be taken care of, realize that people tend to fall into these two bins naturally, and animals tend to fall into these bins. Regardless of what species they are, it's about 50/50. And again, this sickness behavior is a motivated state. It's designed to slow circulation of the blood, increase circulation of the lymph, and the other killer cells in the body, reduce the probability of infecting others by reducing, its thought, diarrhea and vomit, but also breathing on others, interacting with others. And in some cases it will activate this, I don't want to call it a regressed state, but many people feel somewhat more... If they are adults, they feel more childlike when they are ill and they want

00:42:00 Sickness Behavior & Depression: Cytokines

to be taken care of very badly. Some of it might be learned. Some of it might be innate. We don't know, but the sickness behavior is very interesting for a couple of reasons. First of all, it mimics another state that has been described in the neuroscience literature, which is major depression. And in both sick individuals, sick from bacterial or viral infection, and in people with major depression, it's been shown that there are robust increases in the levels of interleukin-6 and tumor necrosis factor alpha. So there is an idea now circulating that depression involves these inflammatory cytokines being very active. And we know that illness involves inflammatory cytokines being very active. So if you think about it, the similarity between major depression and being sick ought to be able to point us in a direction of interventions that could help us either prevent illness or move through illness more quickly. But as we head in that direction, because indeed that's the case, I just want to emphasize that sickness behavior is what provides this bridge between the immune system and the nervous system. And what we'll soon see also is that healthy behavior, behavior that allows us to avoid infection, also points to a

clear bridge between the nervous system and the immune system. That it isn't just that we have a brain and body and our organs, and then we have an immune system. That's true, but they're interacting all the time. And this is going to lead us to a place where it's going to be very clear and not at all surprising how certain patterns of thinking and certain behaviors

00:43:40 Reduced Appetites When Sick: Protein, Iron, Libido

that we can elect to take can help enhance our immune system function and vice versa. There are two other features of sickness behavior definitely worth pointing out. One is a theory, which is that the reduced appetite, in particular appetite for protein rich foods when sick, is thought to be an attempt, a subconscious attempt, of the organism to reduce the amount of iron that it's taking in. Now, typically the amount of iron intake that's recommended or more or less is for men, it's about eight milligrams per day. For women, it's anywhere from 18 to 27 milligrams per day, depending on whether or not they're pregnant, lactating or menstruating, et cetera, the ranges can vary. But, and indeed, it's true that if iron levels in the blood go too high, like over 45 milligrams per day can be very toxic to the system. But the theory that's prominent in the biology literature and in the health literature is that the reduction in appetite is actually an attempt to reduce iron intake specifically because many bacteria and other forms of infection seem to thrive when levels of iron in the blood are high. And I don't want to see anyone take this too extreme and suddenly do an iron deprivation diet in order to get well. But it's an interesting theory that I'd be remiss if I didn't mention, because it makes good sense. Iron is actually attached to hemoglobin and red blood cells in the bloodstream. Normally that can help us quite a lot. It's also in muscle, I should mention that. Iron can be a sequestered into muscle, and iron serves a lot of important health promoting roles, but by reducing appetite and thereby reducing iron intake, it does reduce the capacity of certain things, including infections to travel in certain compartments within the body. So, again, that's just theory, but I think many of you are probably familiar with not having an appetite when you're sick. The other thing that's very typical of people with major depression is loss of appetite, not always but often loss of appetite. So, here again, we have loss of appetite in sickness behavior, loss of appetite and major depression, and perhaps not surprisingly one of the major symptoms of sickness behavior and major depression that map more or less onto one another is loss of libido or interest, not just in

social interactions, but in sex and reproduction. And so, again, if you think about sickness behavior and depression, they are very, very similar. Okay, so sickness behavior and major depression have certain core features in common. We need to therefore ask ourselves why and how does being sick influence the way that we think and perceive our environment and impact our appetite, whether or not we want to be cared for more or cared for less? Again, people tend to diverge into two different bins there,

00:46:45 Vagus-Nerve Stimulation: Fever, Photophobia, Sleepiness

and believe it or not, the pathway for this has been identified. When we have an infection someplace in our body, and it could be up in our head, it could be a sinus infection, it could be an ear infection, or I should also mention many of these same mechanisms can also be the consequence of a wound or an injury to the body. A back injury or a slipped disc or I guess it's called a herniated disc is the way that you hear it described. When we have that, we can be kind of irritable, we don't want to do certain things and we just want to be left alone. Things are harder. How? Why? Well, there's a known pathway, which is the so-called vagus nerve that connects the body and the brain, signals to particular brain sites to engage this category of motivational state that we call sickness behavior. Many of you have probably heard of the vagus, V-A-G-U-S, vagus. The vagus nerve is a very extensive nerve pathway, as the 10th cranial nerve comes out of the back of the brainstem, heads into the body, and branches out extensively to innervate or connect to many of our organs, including our lungs, our heart, our gut, et cetera. And all of those organs are able also to send neural signals back up to the brain. We sometimes hear of the vagus as the route to calming ourselves down. Unfortunately, that's more or less a myth that I don't know how it got propagated. You have lots of different pathways in the vagus Usually vagal stimulation actually creates more arousal and alertness, although it does have multiple pathways, but there have now been many studies of the vagus in various contexts, including in sickness behavior. And it's very clear that the vagus nerve is the fast pathway by which an infection in the body is signaled to the brain, to a particular location in the brain called the hypothalamus, which harbors a lot of different types of neurons. Neurons, for instance, in the preoptic area that increase body temperature and fever, right? That's one of the most important things is to increase body temperature, it's the body's attempt to kill off this invader because many viruses and

many bacteria don't survive well at elevated heat. That's the function of a fever. A fever actually has a functional role. So, in biology, we like complicated words, so we call anything that increases body temperature or creates a fever, a pyrogen. Many years ago, in my undergraduate years, I was working on pyrogens, injecting something called lipopolysaccharide into the belly, which then gives you a fever. The way it does that is LPS causes an inflammation response in the gut. The gut doesn't know what is happening. The stomach cells don't know what's happening. So they just start secreting the IL-6, the IL-1, all those cytokines, the killer cells migrate into the gut. That's why you sometimes get a stomach ache when you don't feel well, you have a flu, or something like it. A neural signal, electrical signals get sent up to the hypothalamus. The hypothalamus says, oh, I don't know what's going on out there, but there's a signal something's going on. Let's just heat up the body. Let's just start cooking whatever it is out there. And of course you don't want fever to go too high because you can kill brain cells. But within a particular range the fever is a functional and adaptive response, okay? So if you're taking drugs to try and lower the fever that might make you feel more comfortable, but actually that's limiting the response that your body is creating in order to try and kill off that invader. And again, you don't want fever to go too high. This is going to vary depending on age. You can look up online what the tolerable ranges are for fever. But when you're trying to lower body temperature when you have a fever, unless you're heading into dangerous levels of heating up, that's actually the wrong way to take your system if you do indeed want to kill off that invader. Okay, so the vagus nerve is the quick response. It also sends input to areas of the brain that change your perception of the outside world. One of the most obvious of these, obvious once I tell it to you, is photophobia, right? I love bright sunshine. I love bright lights when I want to be alert. We all have different levels of light sensitivity, but most people when they are sick, when there's an inflammation response in the body, they feel like bright lights are kind of aversive. They get a well-described kind of classical photophobia, and that's mediated by a pathway that goes from your eye to an area of your thalamus, called the anterior nucleus of the thalamus. This is work that was done by Clifford Saper at Harvard Medical School. It's really beautiful work. And then from there up to the outer lining of the brain, which is the meninges just sort of on the outside of the brain where the brain starts to interface with some of the other connective tissues. We'll talk more about these later. It can actually create a photophobia and a headache when one is ill. So, here's the pathway: Some invader gets into your system 'cause you wiped your eyes or it got in

through your mouth. You didn't listen to your mother and got in through your eyes. You're feeling sick. Something's going on there. You have a stomach ache because of all the inflammation there, the signal goes up from your vagus nerve. You're heating up with a fever. You've got photophobia because you've activated this pathway by which what would normally be tolerable light is triggering this thalamic nucleus, the anterior thalamus, that's projecting up to the meninges. You got a headache in response to looking at light. It's basically triggering an overall pathway to get you to go into a quiet, dark place and rest. And the last element I'd like to talk about is the rest. There's something that gets triggered from the body to the brain, to the hypothalamus, and we think we know which hypothalamic area it is. It's the supraoptic nucleus, we think. Supraoptic 'cause it's right above your so-called optic chiasm, If you want to look up where that is, it's right above the roof of your mouth. And there are nuclei there that promote the desire to sleep even during the daytime, what would normally be the active phase of your circadian cycle.

00:53:03 Humoral (Blood-Borne) Factors, & Choroid Change Your Brain State

Now, that is really interesting because what's happening here is you've got multiple pathways that are saying avoid light, reduce your amount of behavior, heat up, all the things that are making you sick. This is sickness behavior, and it's going from your body to your mind to make you do the right thing. Now there's also a slow pathway that's purely mediated by the blood, so-called humoral factors. Not 'cause they're funny, but humoral factors are factors of the blood. As you have an infection for many hours or days, the amount of IL-6 and IL-1 and tumor necrosis factor and other inflammatory cytokines is starting to increase such that the total amount in your circulation gets high enough and is communicated to the brain. And it tends to enter the brain through a particular type of tissue that's really interesting called choroid, C-H-O-R-O-I-D. Choroid is really interesting. It's kind of this fluffy tissue that sits in your ventricles. The ventricles are the spaces in your brain, and the spaces in your brain have what's called cerebral spinal fluid in them. The cerebral spinal fluid contains a number of important things, but the choroid starts releasing and responding to these cytokines, the inflammatory cytokines, and then the brain actually starts to experience all sorts of changes in terms of inflammation to neurons, your memory tends to get poor, your cognition tends to get poor. These are transient things most often. Eventually these things will pass, but this is

deep into sickness when you're really feeling lousy. You can't read, you can't watch a movie, you can't do anything. So if you ever get sick and you just can't be bothered by anything, it's probably because you've had that fast response from the body and you've also had the slower response where you literally have a set of tissues in your brain that are sending out these inflammatory signals. And now your whole brain is starting to cope,

00:55:04 Tools 4, 5: Reducing Sickness: Glymphatic Clearance, Pre-Sleep Serotonin, 5HTP

or is trying to cope with this infection. So you've got a slow pathway and a fast pathway. That all sounds really terrible. So, now, I'd like to talk about what you can do to reduce the probability of getting sick. And there are actually things that one can do as you start to get sick and once you're sick, to accelerate the healing process by flipping the equation. Up until now we've been talking about how the body activates certain areas in the brain to create sickness behavior that's very much like depression. You're probably all familiar with this from anytime you've had a cold or a flu or something really lousy or an injury. Now, let's flip the equation and ask what can we do with our nervous system in order to enhance the function of our immune system in order to be able to heal and recover from illness and injury more quickly. So let's say you are in that unfortunate circumstance of waking up one day or coming home, and you've got that tickle in your throat, or when you breathe, your nasal passages don't feel the same way. You've got a little bit of a headache. You're feeling kind of off. We all know what we should do. We should all hydrate, drink some water and go to sleep. Right, that's we are all told, but there are actually things that you can actively do in order to get your immune system to deploy a more robust response at that early phase of potential infection. Let's focus first on the rest component. Yes, of course we are all told that we should take a hot shower and go to sleep, and get nine or 10 hours of sleep. But there's an interesting way of looking at sleep, specifically for its role in enhancing the immune system. And there's a wonderful review, I'll put the review in the captions that looked specifically at the literature surrounding sleep that is different because it occurs in support of the immune system. So normally when we go to sleep, we have slow-wave sleep predominantly in the early phase of the night, and then over time as we sleep longer and longer, we get more so-called REM, rapid eye movement sleep. I talked all about this on the episodes

on sleep. Of course you have slow-wave sleep and REM sleep throughout the night always, but it's the fraction of slow-wave sleep to REM sleep that shifts, and they have different functions, et cetera. There is some evidence that the sleep associated with an infection, in particular, early stage of infection, is associated with elevated levels of serotonin in the brain that either through an adaptive mechanism or for whatever reason, the neurons in the brain of the so-called raphe nucleus start releasing more serotonin. And that serotonin and its related pathways can help enhance some of the immune system function that could combat the infection. There is starting to be some data, and I emphasize starting because it's not a very robust literature yet, looking at whether or not supplementing precursors to serotonin like 5-HTP, which can be taken in a supplement form or consuming foods that increase serotonin naturally. So these would be any foods that contain high levels of tryptophan. You can look up what those are. So, white meat turkey, for instance, certain complex carbohydrates can often be rich with tryptophan. That consuming those foods can enhance the amount of serotonin that's available in the brain and blood and thereby lead to the particular quality of sleep that allows for more deep healing or for when I say deep healing, I mean for a more robust immune response. Now, again, those are still emerging data. What is very clear, however, is that during sleep and in particular, during sleep that's associated with the early stage of any kind of viral or bacterial infection, the so-called glymphatic system is much more active than it would be normally. What's the glymphatic system? The glymphatic system is actually a relatively recent discovery. I mentioned lymph and the lymphatic system earlier, the glymphatic system with a G, is a system in the brain by which debris that accumulates throughout the day, but in particular, debris that accumulates under conditions of neuroinflammation and inflammation of the body, is cleared out or is washed out of the brain. And the activity of this glymphatic system is extremely important for the recovery from infection of any kind. And it's now becoming clear, is important for recovery from traumatic head injury, and maybe even from psychological trauma. So, the glymphatic system can be thought of more or less as a plumbing system that runs through the ventricles, but also mainly through the lining that sits between the brain and the skull and some of the other tissues and things of that sort. The choroid is involved as well. Brain imaging reveals the glymphatic system is very active during deep sleep. And there's this kind of wash out of the glymphatic system. And I am aware of some studies that are ongoing now where augmenting the serotonin system through either supplementation of tryptophan or 5-HTP or even serotonin itself, these are laboratory

studies, is being looked at for its capacity to increase the amount of circulation in the glymphatic system. And the idea is that it might, and I want to underscore might, potentially lead to more rapid recovery from injury and illness and potentially ramp up, if you will, the activity of the immune system. So, it essentially is a ramping up of the activity of the immune system. Now, regardless of whether or not you decide to, for instance, supplement with 5-HTP before sleep or not, I'll talk about what that might look like in a moment, there is a way that you can increase the activity of your glymphatic system under normal circumstances. Because of the mechanics of the glymphatic system, it turns out that if you elevate your heels by about 12 degrees, it doesn't have to be exactly 12, as you sleep by putting maybe a rolled pillow or two pillows underneath your feet, by having the head below your legs. It seems that there's more glymphatic washout or clearance during sleep. And this is without taking any compound to adjust the serotonin system. So I would say if you're not feeling well, yes, take the hot shower. Yes, get into bed and go to sleep, but elevate your feet to try and increase the activity of the glymphatic system. Some might even consider that if you have to be awake, that you might want to be awake with your feet elevated above your head. Now that might not be practical for the workplace, but it might be practical for a short nap during the day or something of that sort. The glymphatic system is not just active during sleep. It's also active during certain phases of waking, in particular when we are in a deep state of relaxation. So as many of you probably know I'm a big proponent of self-hypnosis because of the quality scientific literature on this. If you're interested in self-hypnosis, you can go to Reverie, R-E-V-E-R-I.com. Reverie is a cost-free app for Apple and Android that was developed by my colleague, David Spiegel, and others at the Stanford University School of Medicine, based on quality studies and peer reviewed data, showing that deep states of relaxation can be used to improve pain management, improve transition time to sleep, and a number of other things. You can select the various sort of outcomes that you're seeking using Reverie. It's a great thing especially for people that are challenged with meditation could use, because you just listened to the script. It involves deep relaxation. I would suggest using that script, or the script for sleep, but with feet elevated to increase activity of the glymphatic system. Now, if you do decide that you want to test out this serotonin hypothesis on your own, obviously check with a doctor. I'm not a doctor, I'm a professor. So, I'm professing things, not suggesting things, but 5-HTP is a supplement that I've talked about before on this podcast that I actually do not recommend for most people for sake of sleep, because it can disrupt the

normal architecture of sleep and create a deep sleep early in the night, and then a spontaneous waking with some trouble to get back to sleep. And that's because of the way that the serotonin system and the melatonin system interact. However, under conditions where one is feeling like they might have an infection or an early stage of illness, in that case, 5-HTP might be a useful supplement in order to access these states of sleep that are not typical. They're not the typical deep sleep that you would achieve when you're feeling healthy. These are states of sleep that are specifically there in order to try and repair some of the immune system related inflammation that's occurring. If you'd like to explore the 5-HTP approach and you feel it's right and safe for you, and you've talked to your doctor, it's 300 to 500 milligrams taken about 30 to 60 minutes before going to sleep for the night. That's the typical protocol. Not incidentally, increasing serotonin is also one typical approach for the treatment of major depression. This is the basis for things like SSRIs, selective serotonin reuptake inhibitors, like Prozac and Zoloft, and so forth. The 5-HTP approach is a much milder approach than prescription drug, of course, but will allow more serotonin to be synthesized and/or released. Now, for those of you that are interested in learning more about the glymphatic system, it's a fascinating system, and you might want to do a deep dive there in terms of the behavioral protocols, and what's known about it, there's a wonderful article called "The Glymphatic System: A Beginner's Guide." This is a scientific article. The first author is Jessen is the last name, J-E-S-S-E-N. If you put in "Jessen, The Glymphatic System: A Beginner's Guide," you can access the full length manuscript easily online. It'll show up immediately in your search. And in a really interesting way, the glymphatic system has now also been tied to the iron deposition system. Earlier we were talking about iron and how, of course, getting enough dietary iron is important, but if levels of iron are too high it isn't good for a number of reasons. There's a very interesting article that just came out last year called "Dysfunction of the glymphatic system might be related to iron deposition in the normal aging brain." So, we're starting to see these links between iron levels being too high, the glymphatic system not being active enough and so forth, leading to sickness behavior, inflammation, and maybe even damage to neurons associated with aging. We can flip that on its head and say that increasing the activity of the glymphatic system, feet elevated during deep sleep, maybe even feet elevated above the head while awake, during a nap or doing a Reverie script once a day or something of that sort, could increase the activity of the glymphatic system, lowering iron to a point that's probably below the typical intake during periods of infection, perhaps, I should say, can

enhance the glymphatic system and vice versa. And then you've got this specialized sleep that's related to sickness behavior that seems to have heightened levels of serotonin that might be augmented by ingesting 5-HTP. Again, not on a regular basis. I don't suggest that people take compounds that increase serotonin unless it's prescribed to you for depression or something, but not doing by supplement with tryptophan or 5-HTP on a regular basis, but only under conditions where as I mentioned, you might be starting to feel sick

01:07:03 Tool 6: Hot Showers, Saunas, Baths & Cortisol, Heath-Cold Contrast

or you're coming down with something, or you're combating some sort of infection. So if we consider the advice that we typically get when we're not feeling well of take a hot shower, get into bed and go to sleep, and we've now touched on ways to potentially increase the efficacy of the sleep part through the glymphatic and the serotonin system. What about the take a hot shower part? Is that good advice? Well, it turns out it is, and there's actually a way to do even better. There's a study, a very interesting study, the title reveals where I'm going with this, it's "Effect of a single Finnish sauna session on white blood cell profile and cortisol levels." In this case, it was done in athletes and non-athletes, which is kind of nice. This involves taking athletes and non-athletes and exposing them to sauna. It wasn't particularly hot. It was 96 degrees, which isn't cool, but it's not really hot. Nowadays you hear about people doing very, very hot sauna. The humidity of the sauna, if you want to know, is 15 plus or minus 3%. But basically what they found was that just one 15 minutes sauna session could really increase white blood cell profiles and could adjust cortisol levels in ways that were beneficial for combating infection. And now there are many other studies like this. Now, this should immediately make sense based on what we said before about fever; heating up can actually help combat infection. But for those of you that have listened to the episodes on temperature, what you probably know is that when you get into a sauna or any kind of hot environment, your body is also going to be actively pushing to cool itself off. So, there's probably an increase in heat, there is an increase in heating, but then afterwards your body will cool off, maybe even with a dip below baseline. I do want to provide a cautionary note that if you are already running a fever, getting into a sauna could take your body temperature into dangerously high levels, dangerously meaning you can kill neurons. And once you kill neurons, they do not come back. So, please don't kill your

neurons. I don't recommend getting into a sauna if you're already running a fever. So this would be something to do at the initial stage of an infection or if you're feeling a little bit off. So this is kind of a ramping up or a super protocol of the typical advice of take a hot shower and get into bed. That is good advice. Now we're talking about a hot sauna, probably showering off and then getting into bed, maybe augmenting serotonin. I know many people don't have access to sauna. So, in that case, a very hot bath or shower, don't scald yourself, of course, but as hot as you can comfortably tolerate or right at that edge of what you can tolerate would be a good idea. Some people I've heard are creating saunas in their bathrooms by running hot water and creating a ton of steam. Anything that really heats you up, but not to dangerously high levels is going to be beneficial. If you have access to a sauna, terrific. This again was only 15 minutes. They'd had a cool off session. Would you get more of an increase? People always want to know if you did it twice as much, would you get twice an increase? Those data don't really exist yet. However, if you are interested in maximizing the effects of sauna, it is clear that a cool off period is important. So it's not that a 15 minute sauna is good, and a 30 minute sauna is better. If you are going to take that route of exploring more, it does seem that doing a 15 minute heating period followed by a five to 10 minute cooling period, and then getting back into the heat can be beneficial. And this is interesting. It gets to the mechanisms by which the hypothalamus areas, the areas of the hypothalamus, that is, that generate increases in body heat, the activation of those neurons occurs as you heat up and then were you to just stay in that heated environment, they would actually shut off and some other neurons would be handling the job so to speak. But by getting in and out of the heated environment, you actually force that system to send repeated pulses of these cortisol lowering and white cell stimulating

01:10:53 Feed a Fever & Starve a Cold (?), Adrenaline

signals to the body. Some of you have probably heard the phrase, "feed a fever, starve a cold." I don't know who first said that. I couldn't find the citation, but we hear this. And we can speculate that the reason that phrase, "feed a fever, starve a cold" came to be is because of the adaptive function of fever, that increases in body temperature make it challenging for intruding viruses and bacteria to survive. Even though, of course, highly elevated body temperatures pose a danger to the host organism, to you. Feeding, eating does cause an increase in body temperature through the so-called thermogenic effect of

food. So I can understand the logic of feed a fever. It would mean that when you have a fever, it's your body's natural attempt to heat up and kill some invading thing. And by eating, you would further increase your body temperature. Why you would want to starve a cold, I don't know, however. Maybe it's because when your nasal passages are congested, it's uncomfortable to eat or something of that sort. So the feet of fever part makes sense to me, the starve a cold part is still mysterious to me. I couldn't find any logical reason why that would be good. There are communities out there that believe that fasting is a viable way to combat certain types of infection. Fasting, in particular, prolonged fasts, do increase the amount of adrenaline, also called epinephrin, in the brain and body. And as we'll next explain, epinephrin, adrenaline does have a powerful effect on

01:12:36 Tool 7: Activating Your Immune System w/Cyclic-Hyperventilation, Alkalinity

the various inflammatory cytokines and on the immune system in general. So, let's talk about a behavioral protocol that anyone can use; it doesn't involve any equipment, you don't need a sauna, you don't need anything at all, that has been demonstrated in excellent peer reviewed research to enhance the function of the immune system and actually allow people to combat infection in very dramatic ways. Next, I'd like to do an in-depth analysis of a study that has achieved some prominence out there, not just in the scientific literature, but on the internet, because it relates to how particular types of breathing can impact the immune system and the ability to combat infection. The title of this paper is "Voluntary activation of the sympathetic nervous system and attenuation of the innate immune response in humans." This is a paper that was published in PNAS, which is the Proceedings of the National Academy of Sciences, USA. It's a very prestigious journal. For those of you that know PNAS, you know that there are certain papers published in PNAS, or there used to be that were not peer reviewed. In recent years, I think all of them have moved to peer reviewed papers. So this is a peer reviewed, very high quality study. And I just want to describe the basic contour of the study. I'll explain the findings, and then I want to go in-depth and explain the mechanistic basis for these findings and the protocol that we can all export from these findings. So, here we go. First of all, a couple of terms so that everybody is on the same page. The sympathetic nervous system is one division of our nervous system. It's a set of neurons down the middle of our spinal cord and in our brain that generally lead to a heightened

state of arousal and alertness. It's associated with epinephrin release in the brain and adrenaline release in the body. It's the so-called fight or flight system when it's really active, but it's the system that's active when we are wide awake. And we already talked about the innate immune system. That's that first line of defense after the skin barrier, of course, whereby some infection comes into the body and there's this rapid response of increasing inflammation. And that's also about the time that you first feel lousy. So when you start to feel like, "ugh, I think I've got something. I don't feel right, a headache. I feel nauseous. I'm heating up. I don't feel good." That's the innate immune system kicking in. So what they did in this study, and by the way, I should say they, this first author is Kox, K-O-X, last author, last name Pickkers, P-I-C-K-K-E-R-S. What they did was they exposed human subjects to an endotoxin. In other words, they injected people with E. coli, which is a bacteria which makes people, all people feel terrible. Makes you nauseous, fever, vomiting, diarrhea, it's very unpleasant, okay? These people voluntarily signed up for this study. However, some of the subjects in this study performed a behavioral protocol that can best be described as cyclic hyperventilation. My lab works on these types of breathing protocols. This is not work that my lab did, but basically subjects hyperventilate, followed by breath retention, by breath holds, and I'll explain exactly what they did. They also looked at other forms of behavioral protocols, but let's focus on that one. So, they're comparing controls that do just sort of a basic meditation versus people that do this intense breathing followed by some breath holds. I'm just paraphrasing here, in the intervention group, the breathing group, plasma levels of anti-inflammatory cytokine IL-10, so this is a cytokine that is lowers inflammation, increased after endotoxin administration. And that was triggered by an increase in epinephrin and adrenaline. So, in other words, doing a particular pattern of breathing allowed an anti-inflammatory cytokine to be turned on, whereas that was not the case in the subjects that did not do this particular breathing protocol. And they discovered that levels of proinflammatory TNF-alpha, tumor necrosis factor alpha, IL-6, interleukin-6 and interleukin-8, which you should all be familiar with now, as proinflammatory cytokines were lower in the intervention group. Whereas these IL-10 levels that are anti-inflammatory went up. Finally, flu-like symptoms were lower in the intervention group. So this is an amazing finding, right? These are human subjects. One group of subjects is doing this breathing protocol. The other group of subjects is just meditating. Both sets of subjects have been injected with E. coli. So, you know everyone's getting the same amount placed into their system. This is very, very interesting. And it leads to the

question that every good scientist, two year old or health information seeker asks, which is why? How? How in the world does this work? Why does this work? Well to make a long story shortish, because I am going to go into depth here, the reason it works is because the sympathetic nervous system, the so-called stress part of our nervous system, it's not really called that, but the part of our nervous system that triggers stress from mild stress, to severe stress, even to panic, causes the release of adrenaline and epinephrin in the brain and body. And under normal circumstances, when we have some sort of invading infection, our body is able to push back on that, to resist it by engaging the stress response. So what's happening here is there's a behavioral protocol involving the nervous system, 'cause all behaviors are generated from the nervous system of course. A behavioral protocol that people are deliberately employing that allows them to activate the sympathetic nervous system, which in turn allows them to activate the normal pathways by which immune system function is enhanced. Okay? Now, the reason I'm underscoring this is that the common interpretation of this study is that somehow it blocks the normal immune response, but that's not really what's happening here. Yes, there's a reduction in inflammatory cytokines and there's an increase in anti-inflammatory cytokines, but that's not really the same thing as blocking the immune response. This could just as easily be viewed as enhancing the immune response and combating the intruder, in this case, E. coli. So, let's parse this study a little bit more closely. First of all, what is this magical pattern of breathing? Some of you may recognize this as so-called Wim Hof breathing. Wim, of course the Dutchman. I think his occupation online used to be listed as daredevil, believe it or not, on Wikipedia. That's a pretty cool occupation. Wim is best known for his activities with cold exposure, he holds multiple world records for that, swimming under icebergs and other incredible feats, that you definitely don't want to try unless you're extremely skilled and really know what you're doing, as he does, but also for the use of breath work. The breathing that is so-called Wim Hof breathing is very similar, not exactly the same, but very similar to Tummo breathing, as it's been described historically. In the science and physiology community and in my laboratory, 'cause I run a university laboratory, we refer to it as cyclic hyperventilation, which just means repeated deep breaths in and out. And then there are these retentions. So, because I'm here in the hot seat anyway, I might as well demonstrate it for you so you know what this looks like. There are variations on this, so with respect to Wim, with respect to Tummo practitioners, with respect to the cyclic hyperventilators everywhere, this is one general theme of it. It involves 20 to 30 deep

inhales and then exhales through the mouth, followed by a exhale of all one's air and a breath hold, that's the retention. And then at some point, 15 to 60 seconds later, repeating the 25 or 30 breaths. And then again, a breath hold with lungs empty. There are variations on this, but in our laboratory and in this particular study, it looks something like this. Okay, I'm not going to do the whole thing right now, but it goes something like this. [Andrew deeply breathing] Okay, so let's assume I did that for 30 breaths. I can already feel myself perspiring a little bit. You're heating up, that's the release of adrenaline. It's caused by that breathing pattern, and then exhaling all of one's air, no speaking in between like I'm doing. [Andrew deeply exhaling] And then sitting lungs empty until one feels the impulse to breathe and then repeating for several rounds, two or three or even four rounds. Now some people will also introduce a big inhale and breath hold at the end and find that indeed they can hold their breath much longer than they normally would be able to. Because the trigger to breathe is normally activated by increases in carbon dioxide in our blood. We have neurons in our brain stem and in our various regions of our brain, actually, that respond to when carbon dioxide is too high and trigger the reflex to breathe. But when we exhale deeply, we blow off a lot of carbon dioxide so we don't feel that impulse to breathe come quite as soon. Basically this study looked at people doing these cyclic hyperventilation with retention, 25 or 30 breaths, then the retention, 25 or 30 breaths, then retention, 25 or 30 breaths, then the retention. So, three rounds of 25 to 30 breaths followed by exhale, hold in between of various duration. But in general, 15 to 60 seconds is typical. What happened physiologically? This is one of the reasons I like this study. What happened physiologically? Well, a couple of things. Of course, blood oxygenation drops. You would expect that based on hyperventilation and especially based on the exhale of so much carbon dioxide. We could explain why that is, but blood levels of oxygen drop. The pH, the alkalinity of the body goes way up. This is very interesting. If you look up this paper, you can look at Figure One, Panel C, the pH goes way up. People become alkaline. You've heard before of alkaline water. I hate to say this, I'll probably lose some friends for this, but yeah, don't waste your money on drinking alkaline water. You can't really shift the alkalinity of your body. There are cases where some compartment in your body needs to be more alkaline than the rest. Your gut is a different alkalinity than other areas of your body, et cetera, but ingesting high alkaline water isn't going to shift your overall alkalinity. If someone can send me a quality reference that shows different than I'm happy to revise that statement. But in any case, doing that pattern of breathing that I just described greatly increases the

pH. Greatly, I should say, it doesn't send it off into dangerous levels. It takes it from 7.4 to 7.6, which is a significant increase in alkalinity. So, as pH levels, for those you remember high school or college chemistry, as the numbers on the pH go down, you're becoming more acidic, as they go up, you're becoming more alkaline, okay or more basic. So, these subjects went from 7.4 to 7.6 during the breathing, and then afterwards it returned to normal. But that shift in alkalinity is thought to be important here. So, what's going on here? How is the breathing leading to the shifts in... Or I should say reduction in inflammatory cytokines and an increase in the liberation of these anti-inflammatory cytokines. Well, the authors make some good arguments as to why it's not the shift in pH per se, or the shift in carbon dioxide levels in the blood, but rather it's the release of epinephrin. And there's some good reason to believe why that's the case. It's beyond the scope of this discussion, but that it's actually the release of epinephrin, AKA adrenaline, that's causing this reduction in inflammation. And that's actually supported by something that you've probably experienced before, which is if you've ever worked, worked, worked, worked, worked really hard, or you've been a caretaker for somebody else or studying for exams, and people around you are getting sick and you're just powering through it and you're not getting sick, but then you stop, you turn in your final exam, you stopped taking care of somebody else, or you finally stop and rest or you go on vacation, and then you get sick. Well, you've just experienced the effect that adrenaline, epinephrin can have in activating your immune system by way of the nervous system, in order to keep fighting and combating infection. And that brings us to a larger theme, which is that stress and combating infection or a wound is not one unique system. It's the same stress system that you use to combat psychological stress. So when you're very, very stressed, at least in the short term, because you release so much adrenaline and epinephrin, you're actually better able to combat infections and you reduce inflammation and the whole feeling lousy response, right? Remember reduced flu-like symptoms here. So this pattern of breathing is actually a very useful tool. And I confess, I use this pattern of breathing anytime I am at the initial stages of getting some sort of bug. If I feel like I've been running myself ragged, or if I somehow, for whatever reason, have a tickle in my throat, or I have that kind of sensation in my nose, like I might've caught a bug of some sort, I will do this pattern of breathing. I've been doing it consistently, gosh, for the last four years or more. Now this is just anecdotal reports, but I find that it allows me indeed to either have those early symptoms disappear, or it allows me to just kind of push through and harder, longer. I don't suggest people continue to

push through exposure to infections. Obviously you don't want to infect other people, nor do you want to crash and suddenly get a massive illness of some sort because you stopped doing this breathing. But I do think it's a useful tool. It's a purely behavioral intervention that has been shown here and now there are additional studies on the way, to enhance the function of your immune system and to reduce inflammation. And this is to me, one of the most concrete examples of a zero cost tool that bridges the activation of the nervous system through breathing with the immune system by way of releasing adrenaline and thereby reducing the terrible effects or feelings of lousiness from, in this case, an E. coli infection. Now, I'd like to focus on a couple of important points that I haven't heard discussed broadly elsewhere, which is that the hyperventilation and the breath retention are both important. So you can't simply hyperventilate to get this effect at the level of epinephrin release and reduction in inflammatory cytokines. It's been shown before that the hyperventilation phase and the hypoxia, which is a low oxygen saturation due to the breath retention, they both combine to increase epinephrin adrenaline levels. So, you have to do the 25 or 30 breaths, and then the retention. 25 or 30 breaths then the retention, meaning that the exhale with the breath hold, in order to get the full effect. I'd also want to provide a critical cautionary note. Don't do this anywhere near water or while driving a car. These things might seem kind of obvious, but obviously in the off chance that you black out or something like that, it could be disastrous. So, please be careful. And again, don't try and push the breath hold. The moment you feel the impulse to breathe, just breathe. And it did seem that the three rounds of 25 to 30 breaths

01:29:10 Brain Chemicals & Cyclic-Hyperventilation; Catecholamines, Dopamine

with breath hold retentions in between was the ideal protocol. There's one last very interesting feature of this study that I want to emphasize. And that was that they actually measured the so-called catecholamine concentrations. Catecholamines are things like dopamine, epinephrin, norepinephrine. These are chemicals in your nervous system and body that promote states of alertness, dopamine, of course, part of the reward and motivation pathways. They explored the levels of these molecules in blood, in plasma during and after this breathing protocol. And it was interesting, as I mentioned before, epinephrin showed robust increases compared to the control group, norepinephrine, significant increases occurred in the breathing group, in the cyclic hyperventilation

retention breathing group, of course, but less so. And dopamine levels actually dropped somewhat. But this is very interesting because there's a new and emerging literature largely from Asya, A-Y-S-A Rolls' lab in Israel. What her laboratory has shown is that motivational state and mindset has a powerful impact on various aspects of the immune system that were thought to be independent of the brain and mind and thinking. So this brings us back to something that we discussed at the very beginning of this episode, which is that 20, 30 years ago, the idea that you could heal the body with the mind was considered kind of quackery. I think that there was an intervening period up until now where people might've said, "sure, if you're stressed out, it's going to make things worse." I mean, I think everyone agrees that stress makes every thing worse at some level, outcomes to neurodegeneration, performance in a physical endeavors and mental endeavors. If stress is too high for too long people experience different challenges and essentially every major psychiatric disorder, everything suffers, but in the short term, stress can actually be beneficial in the ways that we just described. And stress, if we break it down is really a neurochemical state, right? It's the release of these catacholamines. And what Asya Rolls' laboratory has shown is that when the so-called dopamine system and at several episodes, I described there are multiple dopamine systems, but the so-called mesolimbic reward pathway involving areas like the nucleus accumbens, et cetera. When the reward system that's associated with dopamine and norepinephrine is activated, you see incredible effects, including for instance, highly significant reduction in tumor size in cancers. Now, why would that be? How is it that mindset, dopamine and tumors, and tumor growth are somehow linked?

01:32:10 Mindsets & Immune Function; Yes, You Can Worry Yourself Sick

We now know how this occurs largely through the incredible work of Asya Rolls and others. So, now I'd like to turn our focus to how it is specifically that certain mindsets impact the immune system in ways that we can actually point to specific biological pathways and also specific protocols related to mindset. I guess a simple way to frame all this would be to say that most of us are aware that yes, indeed, you can worry yourself sick. We've been told that, you're going to worry yourself sick. And actually there was a paper published in "Science," again, one of the top three journals out there, the top three really being "Nature," "Science," and "Cell." And then other of course, excellent journals exist, but this was a paper that came out in "Science" last year. First

author is Kataoka, K-A-T-A-O-K-A, describing psychogenic stress and fever. So this was looking or asking the question, are there areas of the brain that actually underlie this notion that we can worry ourselves sick? And they discovered a new pathway and they were able to both activate this pathway independent of worry and stress and see illness occur, and they were able to inhibit this pathway, block activity in this neural pathway and prevent psychogenic fever and the worrying of oneself sick. So, they were able to do this in a very controlled way. I'll just mention the pathway in case you want to look it up in more detail. This is a corticolimbic pathway. So, just to orient us, the cortex is more or less the outer shell of the brain. It's involved in thinking and sensation and perceptions and learning and maintenance of a lot of memories are stored there. We all hear that you learn and remember in the hippocampus, that's the initial site of learning and memory, but then that information, believe it or not, is passed off to the cortex where it's stored in kind of a long-term hard drive type storage. So the corticolimbic pathway is one in which your thoughts, your prior experiences can literally in a structure way, feed down onto the areas of the brain that control very basal processes, including temperature regulation. So this is a corticolimbic hypothalamic pathway. We talked earlier about the hypothalamus as controlling temperature and a lot of sickness related behavior, right? Remember vagus up to the hypothalamus and all the sleep more, less appetite, fever. Okay, that's all in the hypothalamus. This is a top-down corticolimbic hypothalamic pathway, and it has a fancy name. It's the dorsal peduncular cortex, dorsal tinea tecta. The short of that is the DP/DTT. Let's just call it the DP/DTT, to the dorsomedial hypothalamus. A lot of D's. It shouldn't mean anything. It doesn't really matter what we call it. But what's important is conceptually it's a pathway that originates insights to the brain that are associated with thinking, with emotion and with prior history, and feeds directly into an area of the brain that's involved in basic physiological subconsciously controlled processes. So, that's incredible, right? And it points to a physical pathway by which the way we think about something changes something core about our physiology. Now, in some ways that shouldn't be surprising, right? If you think about something that excites you, your heart rate can increase. You think about something that terrifies you, your heart rate can increase. So the idea that thinking controls our physiology is not a new concept at all, but somehow human beings, we have been challenged with the idea that we could actually think ourselves into being sick. But this paper from Kataoka shows that if you expose somebody to a psychological stress, you can actually activate this pathway and create a fever. And how do they do that? Well, you can do this by exposing

subjects to a very stressful real event, and you cue it through our associative learning. So, maybe, like my PILOT V5s, which I love so much, we could traumatize me to the PILOT V5 if I had some horrible experience happen to me while I'm looking at and concentrating on the PILOT V5. Then you take away the horrible experience, you give me the PILOT V5, and I start to experience a lot of the symptoms associated with that terrible event. They were able to do this using sickness inducing stimuli and so forth. They did all the various derivations and identified this pathway that when activated, even in the absence of some horrible event, could create fever and illness-like behavior and so forth. And if they blocked certain stations along this neural pathway, they could block that effect. So this is really concrete evidence, proof, if you will, that there are dedicated pathways in the mammalian brain, your brain and mine, that allow us to turn thoughts into illness.

01:37:00 Tool 8: Healthy Mindsets, Hope, Dopamine; Tool 9: Tyrosine; Tool 10: Cold Exposure

That's kind of a depressing idea. What about the inverse? What about turning thoughts into health? Well, that's the work of Asya Rolls. They explored the well-established psychological phenomenon that when cancer patients or very ill people or people who are suffering from very debilitating injuries, when people had a reported a sense of hope, their rates of recovery were much higher, right? Sounds very subjective. But what is a sense of hope? A sense of hope is a sense of the future. A sense of the future is tightly associated with the dopamine system. Dopamine, again, being this molecule of reward and motivation and movement, but movement and motivation are about things that are beyond the confines of our skin and are about the future. And so what they've discovered and through other studies from other groups have discovered is that stimulation of the dopamine pathway, either simply by thinking about a future, ideally a positive future, but thinking about a positive future leads to activation of the so-called mesolimbic reward pathway and could reduce the size of tumors, could accelerate wound healing, could greatly accelerate the passage from a state of illness to a state of health and wellbeing. So there are many, many studies now starting to wick out related to this. There's also the idea that augmenting the dopamine system can increase the rate of healing. And so, there are individuals out there who opt, for instance, to take things that increase dopamine. Now, obviously drugs of abuse would not be a good idea

in this context, even though they increase dopamine, they lead to big crashes, they have addictive properties, et cetera. I've talked before on this podcast about things like L-tyrosine, taking anywhere from 500 to 750 milligrams can increase dopamine because tyrosine is a dopamine precursor, of course. Things like Mucuna pruriens, which are L-dopa, the immediate precursor to dopamine. Some of these will lead to somewhat of a crash in certain individuals. Other people tolerate them a little bit better. Again, you have to talk to your doctor, you have to figure out what's right for you. If you have bipolar or mania or schizophrenia, these things, I would not recommend them at all. I'm not recommending them at all, I'm just mentioning them for potential exploration if it's safe and right for you. But the point is this: the dopamine system, when activated can accelerate healing, it can accelerate the recovery from injury of all kinds. And that shouldn't come as a mystery or surprise result to us. It's because this reward pathway and the fact that it's related to a sense of the future seems to liberate entire systems within the body that make inflammatory cytokines go down, and anti-inflammatory cytokines go up. Exactly as was demonstrated in the beautiful PNAS study where breathing, cyclic hyperventilation, was used to increase epinephrin, increase norepinephrine, and to augment the catecholamine system. So, I think that the bridges between these studies are really relevant. In one case, I'm talking about potentially taking an over-the-counter compound to increase dopamine to accelerate healing. In another case, we're talking about using breathing. There's also the use of cold water exposure to increase dopamine. I talked about this several episodes ago, but it's been shown that immersing oneself in cold water up to the neck or so. How cold? Well, it depends on what you can tolerate, but uncomfortably cold, but not so cold that you become hypothermic, but where it's challenging to get in, but you can stay there for three to 10 minutes or so, has been shown to lead to very significant, up to doubling or more of baseline dopamine levels and epinephrin levels that go on for several hours. This may be the basis for why people will do cold showers or ice baths and then get into a sauna. So, what's called cold-heat contrast therapy, as a way to augment these neurotransmitters. Today, we've been talking about how these neurotransmitters can be used to enhance the function of the immune system. And so just keep in mind that anytime you're talking about increasing neurotransmitter levels, that can be done pharmacologically through supplementation, or the can be done behaviorally through exposure to cold water, for instance, or it can be done even just simply by breathing in a particular way, cyclic hyperventilation followed by retention. The catacholamines,

noradrenaline, dopamine, and norepinephrine are the bridge of activation for the immune system and the nervous system. They are the way that the nervous system calls out to the immune system, "Aha, we have a problem. We need to counter this." So you can think of them, them meaning dopamine, epinephrine, and norepinephrine, as being able to deploy larger amounts of immune cells,

01:42:05 Once You're Already Sick: Accelerating Recovery; Tool 11: Spirulina, Rhinitis

all the types of immune cells that we talked about at the beginning of the episode. Okay, so thus far, we've been discussing how one can prevent getting sick or when one starts to feel ill, how one might be able to shorten the course of that infection by ramping up the activity of the immune system. But what about when you're already experiencing symptoms? The runny nose, stuffed up nose, congestion, headache, et cetera. Well, there are many ways to address that at the symptom level. You're probably aware of all the over the counter medications, many of which focus on the epinephrin system. Things that are of the Sudafed variety prevent or reduce congestion because of the way that they cause release of epinephrin, and some of the effects on dilating the bronchioles and dilating the nasal passages and so forth. I'm not going to speak to whether or not those are good or bad choices. They do have a couple of effects that are not so great for the course of treating the underlying cause, which are first of all they can cause dehydration. So you have to make sure that you're hydrating well, both fluids and electrolytes, and they also can interfere with sleep because as I've talked about in the episodes on sleep, one of the hallmarks of deep sleep and in particular REM sleep is that epinephrin, adrenaline levels are low. This is what allows you to have intense, often very emotionally-laden dreams during REM sleep and not act those out. And low adrenaline, epinephrin during REM sleep is basically a signature, a neurochemical signature of the REM sleep state, which is so vital for emotional and physical repair and so forth. So, the fact that they can inhibit sleep, the fact that can cause dehydration, the fact that they can make people feel kind of lightheaded and jittery makes them not terrific choices for a number of people. There is an interesting alternative choice. And when I say alternative, I do mean alternative. The choice that I'm referring to is spirulina, which is actually a form of algae. Years ago, I think when I first heard about spirulina, it sounded very much of the kind of 1970s, 80s health food store variety. It seemed really kind of mystical and wacky, but actually now there are some really nice studies and some data, and also an

understanding of the mechanism by which spirulina can have potent effects in reducing what's called rhinitis, which is a fancy word for congestion of the nose and an inflammation of the nose. Basically, anytime you hear a word that includes "itis," at least if it's in the medical or health context, it generally means inflammation of some tissue. So rhinitis just being inflammation of the nasal passages, but that's one of the most uncomfortable symptoms of any kind of infection. So there are two studies I'd like to highlight just very quickly. One is the effects of spirulina on allergic rhinitis. And the other is a clinical comparison to the efficacy of spirulina platensis, that's a technical name, and cetirizine for the treatment of allergic rhinitis. These looked at humans, so this is not a mouse study, this is a study on humans. Both sexes, so males and females. In one case, looking at 100 plus subjects, 129 subjects. The other, 65 subjects, so decent number of subjects, randomized trial, double blind. Both cases saw significant decreases in nasal obstruction, improved ability to smell, improved sleep, daily working inflammatory cytokines were reduced as well, reduction in nasal itching, all the stuff that you'd like to experience, I can imagine, after taking two grams, two grams, not milligrams, but two grams of spirulina. Sometimes had to be taken for a short while before the effect kicked in. So, that's pretty impressive, I would say, but it doesn't really speak to mechanism,

01:46:09 Histamines, Mast Cells

but in exploring the underlying mechanisms for spirulina's effects on reducing rhinitis, it's interesting to find that spirulina actually can inhibit the formation and/or activity of so-called histaminergic mast cells, M-A-S-T, mast cells. We haven't talked a lot about mast cells, but they are a very interesting cell type in the immune response. Essentially what they are, are little packets of histamine. And when we have some sort of injury or irritant rather to the skin, so a mosquito bite, for instance, or poison oak or poison ivy, something that causes an itch or something that causes inflammation internally, doesn't just have to be on the skin, these mast are these little bubbles that contain histamine that go to that site [hissing], and release their histaminergic contents and cause swelling and inflammation of whatever cells are affected locally. You might think, well, why would I want to have a mechanism in my body that would cause swelling and inflammation? Ah, well then those cells in turn send out cytokine signals that recruit the very cell types that we were talking about way back at the beginning of the episode, the cells that are

characteristics of the innate immune system that come in, the macrophages and the other types of cells that will come in and gobble up the foreign invaders or will help sequester and move away, say the poison from a bite or from whatever irritant. Again, it doesn't just have to be at the skin surface. I'm describing an example of at the skin, for instance, if you've ever had hives of any kind, that almost certainly involved mast cells. So, and when you take an anti-histamine in order to deal with seasonal allergies, for instance, you're taking a compound that's reducing histamines in mast cells. And spirulina has also been used quite effectively as a way to treat seasonal allergies and some of the symptomatology. Equally on par with some of the major prescription and over the counter drugs for that. One cautionary note, spirulina can carry some side effects for people that have a genetic mutation leading to something called PKU. These people know who they are. They're very sensitive to phenylalanine. These same people cannot drink any sort of NutraSweet or diet soda for reasons that they understand. It can be quite dangerous. It's a rare genetic disorder, but nonetheless, spirulina can be an issue for those people. For most people, the side effect profile is pretty minimal. And just to be clear, I don't have any relationship to spirulina company or anything. I just find it interesting that there are these compounds that sound rather, forgive the phrase, but rather new-agey because they come from a algae, from a plant. But when you look at the underlying mechanism, it makes perfect sense. So that's often what we like to point out here is that if there are these so-called alternative therapies, alternative because most people haven't heard of them, it's always nice if they map to a specific logical mechanism and framework by which that compound would work, as opposed to just some anecdote of, "Oh, I hear spirulina is great for allergies." Well, now we know why, it inhibits mast cells

01:49:22 Tool 12: Acupuncture: Mechanism for How It Reduces Inflammation; Fascia, Rolfing

and histaminergic mast cells in particular. Earlier, I mentioned a new and very exciting study published as a full article in "Nature." Full article means that it is a major finding. At the journal, "Nature," they have letters, which are important findings. They're still very high stringency for getting a letter in "Nature" published. But the full articles, generally there's only one or two per issue in the weekly edition of "Nature." And just last week, there was a very exciting article published from Qiufu Ma's lab at Harvard Medical

School. Qiufu I've known for a number of years. His group has done phenomenal work on the mechanisms of itch and pain and discovering some of the receptors and pathways for itch and pain. And more recently they've been exploring the mechanistic basis of acupuncture. And the title of the article is, "A neuroanatomical basis for electroacupuncture to drive the vagal adrenal axis." And while that's a mouthful, now most all of you are probably familiar with what I mean when I say vagal adrenal axis; vagal meaning of the vagus, and adrenal of the adrenal glands. And so perhaps we should not be surprised, although excited, nonetheless, that when Qiufu's lab looked at stimulation of the body with so-called electroacupuncture. So, these are needles where a small bit of electrical current, low level of electrical current, is passed into the needle and therefore into the body. They located sites on the body that can increase inflammation by way of releasing inflammatory cytokines. These areas included the abdomen, and they found areas on the body such as the lower limbs, or the hind limbs in this case, that can stimulate the vagal adrenal reflex and can lead to reduced inflammation. And what was really interesting is that they figured out that it was activation of nerve endings that resided in the fascia. I mentioned earlier what fascia is, but just to remind you, the fascia is a really thick sheath of tissue that surrounds muscle. If ever you've heard of Rolfing, Rolfing is a form of very intense massage. I've never had this done, but I've heard about this. It involves among other things, actually separating the muscle away from the fascia somewhat. So it's a very, very deep tissue massage. Actually a good friend of mine who had this done told me that it was probably the most challenging physical experience that he had ever been through going through this Rolfing procedure. Maybe some of you have have been Rolfed, as they say, and can report to the experience, whether or not it was pleasant or unpleasant, or you felt benefits or not. In any case, this study isn't about Rolfing per se, but it is about the fascia. And so what they discovered is there's a specific population of neurons. Those neurons have a name, as they often do in science. Name isn't important, but if you want to look it up, it's the PROKR2 neurons, P-R-O-K R2 neurons. And they send a connection deep into the limb fascial tissue, okay? And then they send another connection, the connections we're referring to are axons, neurons have axons. So a wire in one direction that goes into the deep fascial tissue of the lower limb, near the calf and thigh. And then they send another wire up into the spinal cord, into a region of the hind brain in the back of your brain kind of near your neck in the medulla oblongata, that neuron also has a name called the DMZ, doesn't matter. And that neuron connects to the adrenal gland to release our good old friends, the

catacholamines, noradrenaline, adrenaline, and dopamine, or norepinephrine, epinephrin, and dopamine. And their release causes a reduction in inflammation, even in response to an injection of something called lipopolysaccharide, which can actually induce fever. So, what does all this saying? This is saying that activation of the deep fascial tissue causes a chain of neural reactions that leads eventually to the release of norepinephrine, noradrenaline, adrenaline, and dopamine. And once again, lowers inflammation, very much like the breathing study

01:53:40 Mechanistic Science & Ancient Practices

that we talked about earlier in the pattern of cyclical hyperventilation with retention, leading to reductions in inflammation. I can't tell you how happy this makes me. I had nothing to do with this work, but the reason it makes me happy is because I have a particular fondness for when practices that have existed for many centuries or even thousands of years, such as acupuncture, such as respiration work, start to converge with some of the hardcore mechanistic science. And the reason this excites me is not because we want to take science and erase the previous tools and methods of these ancient practices, not at all. And it certainly isn't the case that we just want to name things or rename things with modern science. What's very exciting is when we can discover mechanism that explains why certain practices work. First of all, that validates those as legitimate practices, maybe even insurance will start to cover them, whereas maybe they previously had not, I don't know what the current status is for insurance coverage of acupuncture. I'm guessing there are places that do it, maybe others that don't. I personally am not somebody who receives acupuncture. I have in the past, but it's not that I'm in particular a fan of it, but I think that there are a number of people that have benefited from it. So, I think that's wonderful. Breath work and respiration work is something that I've cultivated as a practice over the years. I mentioned earlier, how I use it to push back on incoming infections and so forth. And now that doesn't sound like total... You know, like just a figment of my imagination, there's actually a mechanism, a published mechanism to explain it. But the most exciting thing to me about all this is that practices that traditionally have been shrouded in complicated language or were the unique domain of the practitioners and relied on phrases like the meridians or the chakras, of which I think is perfectly valid language, but doesn't inform mechanism. And then in a separate community, the community I come from, the community of scientists,

have used language like PROKR2 neurons, medulla oblongata, vagal adrenal axis. And basically no one can communicate with one another because the language is shrouding. What we're now starting to see is that at their convergence is a common mechanism. And with that understanding, what's going to be really terrific is as new protocols start to emerge. So in understanding mechanisms and pathways, and in being able to understand the base set of practices like breathing, like electroacupuncture, and so forth, we can now start to daydream in a very realistic way about the development of new protocols, more effective protocols. Protocols that perhaps one can do at home without needles, perhaps protocols such as the breathing that you can do anywhere, anytime, and be confident that you're actually impacting the IL-6 and the IL-8 pathways, reducing those and increasing IL-10. So we are no longer wandering around in the fog hearing about these magical techniques without understanding why they work, nor are we just seeing a bunch of science that is descriptive, but not mechanistic or pointing to specific protocols. So, I'm just delighted. Again, I had nothing to do with this work, but really terrific work, Qiufu and colleagues. And I also want to acknowledge a journal as prominent as "Nature" for featuring this upfront, because I think it really does mark the beginning of a new path in medicine. And just to underscore that point a little bit further, the National Institutes of Health, of course has a cancer institute, an eye institute, that deal with trying to combat cancer and to cure blindness and so forth. And now they have what's called NCCIH, which has complimentary health. And so, there are good tax dollars being put to the kinds of explorations that we're talking about that undoubtedly are going to lead to better treatments for immunological diseases, neurological diseases, the convergence of the immune system and the nervous system. Very exciting times and I hope that by learning about some of this new and emerging science and hearing about some of the protocols that are either zero cost or low cost, certainly for respiration that's the case or for the use of heat or cold, or maybe even electroacupuncture if you have access to that, that we can really see that we're starting to evolve as a field of health and medicine and science and ancient practices, and that they're really starting to converge

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and have a vector, as we say, in a new and more exciting direction. Once again, we've covered a lot of information today. We learned about the immune system, the adaptive

immune system, the innate immune system, and the nervous system and how those interact. And throughout, we discussed protocols that can allow you to tap into this relationship between the nervous system and immune system, and hopefully avoid and/or shorten the course of any illnesses, injuries, or inflammation that you might encounter. If you're enjoying and/or learning from this podcast, please subscribe to our YouTube channel. And also on YouTube, please leave us a comment. One of the best forms of comments you can give us are suggestions for future topics and future guests to have on the Huberman Lab Podcast. Please also subscribe to our podcast on Apple and Spotify. And on Apple, you can also leave us up to a five star review and leave us a comment there as well if you like. In addition, please check out our sponsors that we mentioned at the beginning of each episode. That's the best way to support this podcast. And we have a Patreon. It's patreon.com/andrewhuberman. And there, you can support the podcast at any level that you like. A few times during this episode, and in many previous episodes, I mentioned supplements. Not everybody needs to take supplements, but many people find benefit from them. A key thing if you're going to take supplements is to know that the quality of the supplements that you're taking is very high and that's not always the case with many supplement brands. That's why we partnered with Thorne, that's T-H-O-R-N-E. Thorne supplements are known to be of the very highest quality and the specificity of the ingredients is very high as well. Meaning what they list on the bottle is actually what's contained in that bottle. They've worked with the Mayo Clinic, all the major sports teams. So, trust is very, very high with Thorne products. If you'd like to see the supplements that I take, you can go to thorne.com/u/huberman. And there, you can see all the supplements that I take. You can get 20% off any of those supplements. And if you enter the Thorne site through that portal, you can get 20% off any of the supplements that Thorne makes. That's T-H-O-R-N-E.com/u/huberman, to see the supplements that I take or get 20% off any of the supplements that Thorne makes. If you're not already following HubermanLab on Instagram, please do so. There I teach neuroscience and health-related topics, sometimes, but not always overlapping with the content of the podcast. We are also HubermanLab on Twitter. And last but not least, thank you for your interest in science. [light music]