

Dr. David Liepert:

Basically, uncontrolled inflammation is another way to think of a cytokine storm. That you've got this massive inflammatory response, it becomes self-sustaining, and it, in fact, becomes the problem. Cytokines are meant to be the solution, but uncontrolled, they literally become the thing that's killing us, rather than helping us get better.

Announcer:

Bulletproof Radio, a State of High Performance.

Dave Asprey:

You're listening to Bulletproof Radio with Dave Asprey.

Dave:

On this episode, we're going to talk about pain and inflammation, and how it ties in directly with any sort of infectious situation. Today's guest is a physician with a huge range of experience in things like critical care, but most importantly, specialty anesthesiology, and he works in Canada. He also was chief medical officer and advisor to several different companies, including The DNA Company, which has a subsidiary. In fact, I was introduced to Dr. David Liepert by Dr. Mohammed, who was just on the show and talked about DNA and its effects on your risk of the virus. David, welcome to the show to talk about inflammation and pain.

David:

Thank you very much, Dave. I love the way you opened actually, because it just, it speaks to the fact that pain has a function, and the number one function of pain is to teach us not to do things that hurt us.

Dave:

It makes me happy to hear you say that, because I've said the same thing to my kids. And if they're whining about it, and I say, "Look, kid, when you were 18 months old or one year old and you were learning to walk, the best teacher of all was the fall, because you'd fall over, and it would hurt, and then you wouldn't do that again. And now, the pain that you're feeling when you eat the wrong thing and your stomach hurts, it's just you getting told by the world, 'Don't do that again,' and you can choose to listen or not listen." And it seems so rational, but pain itself is irrational, isn't it?

David:

Well, it just, if you are being chased up a tree by something that wants to eat you, which is where pain first developed its initial function, the pain is a bad thing because it's keeping you from doing the one thing that you've got to do, which is to get away from the imminent threat. But then, after you've been through that imminent threat, after you've survived that imminent threat, you need to take time to recover and heal. You need to protect the part of you that's been wounded, and you need to know not to get too far away from the tree next time so that you can climb faster, and that's both the short term and the long term function of pain as a survival tool.

David:

My kids, I've had the same experience with my kids actually, they always hated me when they were going through school, because every time they made a mistake, I was really happy. If you get something

right, all you learn was that you were right. If you get something wrong, you learn six things. You learn that you can get something wrong, you learn how you got it wrong, you learn what's wrong, you learn how to make what was wrong, right. You learn how to come back from that, and you learn how not to go there next time. So, you learn a lot more from mistakes and pain than from never having anything bad happen to you either.

Dave:

It's a major parenting challenge to do that. I asked the kids every night, at least, I did for a while, though I'm a little bit off lately, but, "What are you grateful for all that?" But then it's, "What did you fail at today?" And if they don't have an answer, I go, "Oh, that's too bad, maybe tomorrow you'll do something hard. So, we shall see." But it all does come down to pain. And the primordial pain molecule is something that I've written about in, I think it was in Super Human, my anti-aging book. Because, substance P is something that's shared by even simple life forms in humans, a basic pain molecule that seems tied into learning, can you talk about what substance P is, and maybe how we get substance P when we feel like we're failing? Is there an emotional component to it? Walk us through it.

David:

Substance P is very poorly understood, is like people even argue about what the P stands for. Because people think it stands for pain. It actually probably just stands for peptide, although, when it was originally identified, I think it actually stood for preparation. One of the interesting things about pain, you have mu receptors which is the primary narcotic receptor in your body, you have mu receptors on every single cell in your body. Amoebas have mu receptors, your myocardial cells have mu receptors. Parts of you that don't experience any pain whatsoever, have mu receptors.

Dave:

So, mu receptors receive substance P.

David:

No, mu receptors are where the endorphins plug into, the actual painkiller molecules that we make. Because, the number one function of the painkiller molecules is to mitigate stress. When it first started off, it was to mitigate metabolic stress and hypoxic stress. As we've become more complex, that function has just been replicated as we've developed more complex functionalities. And so, the narcotic receptor is there to mitigate the effect of pain on you experientially as a person at every single level. Trouble is, that mitigates your ability to learn from pain as well. And that's where substance P comes in. Substance P is really central in the way our body learns to deal with threats.

David:

It doesn't just pertain to pain either, it pertains to inflammation, it pertains to immune responses, and it pertains very, very powerfully to the experiential learning of pain. That's where a lot of, like you were talking about how you can get substance P from things other than pain, substance P is also evoked when we have extremely painful experiences because it really adds a flag to that experience, so that we experience it much more deeply. Substance P, if you're dealing with an infection, if you're dealing with an injury, the substance P adds a flag to that experience, so that your body knows to pay particular attention, and to learn how to better deal with that next time, so that you learn both as a person, but you learn as a system, from substance P.

Dave:

That's a powerful way to describe the mysterious compound. I always thought that P stood for pain, but that goes to show what I know, not being an anesthesiologist. The interesting thing here is that substance P is also tied to inflammation. And the reason I became aware of that is that I was dealing with a really serious problem with a bite alignment that was causing systemic inflammation. And I learned that even a misaligned bite can drive up substance P throughout the system. And many people have heard of using cayenne pepper to fight inflammation, and cayenne pepper drives down substance P, which drives down inflammation. By the way, that doesn't work if you're sensitive to the cayenne pepper because it has lots of lectins in it. Just so you all know, it's not necessarily good.

Dave:

And given that thing, I had said, "Okay, substance P matters for systemic inflammation." And you're saying almost anything can turn it on, what happens if we turn it off? Do we get less inflammation?

David:

It's, again, one of those very confusing chemicals because the answer is both yes and no. And it's really confounded medical research with substance P. Because, for instance, if you do animal research, you'll see good indications that giving an animal substance P affects their pain behavior. But if you give it to a person, it doesn't affect their pain behavior, in fact, it even increases their experience of pain. And that is likely there because it's there to help you both recover from, but also learn from your experience. And if we could ask the animals what they were experiences, of course, if you're having a reflex to pain and that's keeping you from getting better, the substance P will inhibit that. But then, in return for that, it has to make sure that you still learn the lesson from pain.

David:

And the same thing goes from an inflammatory perspective, that there are some components of the inflammation that the substance P will mitigate, but there are other components of the inflammation that the substance P actually will need to accentuate, so that you actually learn from that experience.

Dave:

Given that our experience of pain as humans is very different than it is in animals, as far as we can tell, and that we have an emotional thinking component around pain, and we wonder about pain coming down the road, but it doesn't appear that any animals, or, at least, most animals are living in apprehension, which can raise their substance P levels or any of the other pain inflammatory markers, but we can, is there something happening now with just the media attention, even before the whole pandemic thing, but just where people are starting to spend more and more time thinking about bad things that can happen, does that drive a measurable inflammatory response in certain markers that you know about?

David:

I don't actually know a great deal about the impact of long-term stress on substance P. Having spoken with Mansoor [Mohammed, Ph.D.], I know that there are certainly significant, even genetic changes that occur from long-term stress. One of the things that I find really interesting about the situation that we find ourselves in right now is, we're dealing with, for instance, COVID, COVID is doing damage by overwhelming us and causing uncontrolled inflammation. The inflammatory response to COVID is actually somewhat protective. The question is, at what point does it become counter-protective, or even

counterproductive, or even producing injury? The same thing is true systemically, that, for instance, social distancing and quarantine are kind of a social form of inflammation. We're all getting farther apart.

David:

But, as we become inflamed by, if you think about Fox News and CNN and MSNBC and all of these information sources that we have is kind of functioning like cytokines. They can actually drive useful inflammation where we get concerned about the things that we should be concerned about, or they can drive counterproductive inflammation where we get concerned about things that we either shouldn't be concerned about, or things that actually we shouldn't be focusing on at all. And we've got both an internal inflammation going on to COVID, and we've got an external inflammation going on to COVID, and we don't actually know what to do about either of those things, and that's driving our stress. And I'm sure that's increasing our substance P levels internally.

David:

I'm not sure that it's really driving whatever the societal correlate to substance P is on the social side. I hope it's driving something useful where we start listening to the people who actually give us the advice that we need, rather than just listening to people who wanted to get us angry about Hillary Clinton or Donald Trump, who, as individuals really, the things that they can do matter, but the focus that so many people are getting into about dealing with this, trying to fix the blame rather than fix the problem, is a truly counterproductive thing both societally, and it's also a counterproductive thing when our bodies are trying to deal with the COVID crisis internally too.

Dave:

So then, let's go into cytokines, which are these inflammatory markers. A lot of people by now, listening to any news network have heard cytokine storm, and that's how the virus gets us. Can you talk about what cytokines are, and what a cytokine storm is, and what's really going on when that happens inside the body? Walk people through the steps of what's happening.

David:

Cytokines are actually very simple chemicals in the human body that our cells use to communicate with each other. And cytokines, they're often defined by what they do, like, there are the chemo kinds that actually affect the way cells move around, there are the lymph kinds that affect the way our lymphatic cells work together. They're communication tools, and they coordinate our systemic response. And when they're functioning well, we actually have a well-coordinated systemic response, so that we respond appropriately to whatever we need to respond to, so that we learn from it, we deal better with it next time.

David:

When we get into a situation like cytokine storm, which I struggled with when I was an intensivist, has really contributed to my ability to deal with cytokines as an anesthetist. When we get uncontrolled release of cytokines, when we get uncoordinated activity of cytokines, when cytokines start feeding back on each other and our body doesn't actually know what to do to make the problem go away, that's when we start getting into what people are now describing as the cytokine storm. COVID's starts slow and indolently in so many people. You'll be sick for a few days, and then it's almost like you go down a stack of cards, that something will happen, and suddenly, you're overwhelmed. And it really looks like

COVID manages to gradually overwhelm our ability to respond, and then, suddenly, our body goes into panic mode, and we get this unopposed cytokine rush, and suddenly, everything is inflamed, and your blood pressure is down, and your lungs fill up with fluid, and your temperature is going through the roof.

David:

And because the body doesn't know what to do to make that go away, that's where we actually are ending up losing people now. Because, we can put them on life support, we can keep them going for a time, but we can't fight against cytokines. We have to find a way to fight with them, to actually get them back on track, to get them back focused on what they need to be doing, rather than just being released in panic mode.

Dave:

If your immune system goes in panic mode, I need to create a lot of cytokines in order to fight the virus or just to respond to it, that creates a whole bunch of cascading steps in the body, that ultimately result in sepsis. Right?

David:

Well, sepsis is one way to get into cytokine storm. Sepsis is basically, the assumption is that you're infected with something. You can also get into a cytokine storm from just massive trauma or bad burns, anything that causes a massive inflammatory response can trigger a cytokine storm.

Dave:

Got it. So, you're saying that the sepsis is the cause of the cytokine storm? Or, do you get a lot of cytokines as the infection grows and grows and grows, until they're at a certain storm where it becomes self-replicating?

David:

Yeah. Basically, uncontrolled inflammation is another way to think of a cytokine storm. That you've got this massive inflammatory response, it becomes self-sustaining, and it, in fact, becomes the problem. Cytokines are meant to be the solution, but uncontrolled, they literally become the thing that's killing us, rather than helping us get better.

Dave:

I like to think of the controlled burn in a forest, the way people who do old style forest management. Every summer or spring or fall, whenever they would do it, they'd go through and they would burn the underbrush. And it would go through quickly, and it was okay, normal cytokine behavior. And then, you let that stuff build up or it's a really dry summer and you get the big trees catching on fire, you get this big storm and it's not how it was meant to be. So, they're both fire, they just work in different ways. And the reason I'm a fan boy of cytokines is that I had chronic autoimmune inflammation, in part from toxic mold and just from other things, for most of my life, especially growing up, and I very actively manage my cytokine levels.

Dave:

So, I know which herbs you can take, which practices you can do. And I walk around, and I'm not a size 46-inch waist guy, and my brain works really well, and I very rarely get sick, when I used to get sick all

the time. So, it's been profoundly transformative. But, for me, the biggest measure of my cytokine levels is muffin top. If I wake up and I'm swollen around the midsection and my joints hurt, I'm like, "Oh, I allowed one of these things to get out of control. And it's something I did, that's my fault." Now, if I got infected with a virus or a bacteria, whatever, it's still something I did, it's my fault. I exposed myself to it, or I didn't have an immune system that was intact enough to deal with it. So then I take a corrective action.

Dave:

And now, that's a long description about this, this managing a cytokine storm. You are seeing patients, or preparing to see patients who have COVID and are experiencing cytokine storm. And you are an expert in cytokines because you're an anesthesiologist. How do you think about approaching the care for someone that have, either someone who doesn't want to get the virus, someone who's in the early stages, or someone who's at the hospital? Walk me through your picture in your head of what you do for each of those things, knowing that you don't want cytokines out of control.

David:

Starting at the first level, the stuff that you're talking about, where you're just dealing with your chronic inflammation level, that's actually where Mansoor, who you had on your show last week, and I started working together. Because, his company was really looking at metabolic markers associated with chronic disease, and particularly, chronic inflammation, and even more particularly, chronic endothelial inflammation. He was looking at the reason why some people end up with chronic inflammation, hypertension, type 2 diabetes, all of that seems to be driven by a chronic inflammation in our systems, that, in fact, can be genetically coded for. Some people, have an increased predisposition to different pathways of developing chronic inflammation.

David:

And the company that I've been helping build My Pain Sensei, we've actually created a chronic pain self-management system for patients to use, but we've created it with IBM. And it's part of a massive database undertaking really, linking people's experiential history of chronic pain with different therapies and different functional outcomes. Because one of my big frustrations in medicine is, we're so frequently focused on economic markers of outcome, very rarely do we have a system that actually is just looking at people and working with them and figuring out, how are you really doing? So, we built My Pain Sensei to do that. But of course, we're very focused on chronic inflammation, and chronic neuropathic pain, which is a form of neuroinflammation.

David:

And The DNA Company has done all of this foundational work looking at things that increase our susceptibility from an immune perspective, things that are genetically coded, things that increase our susceptibility from a metabolic perspective. We may have a disorder of methylation, we may have a disorder of intracellular detoxification, we may even have an increased tendency to some sort of mitochondrial dysfunction. All three of those things, can contribute to a chronic metabolic inflammatory state, that, yes, it gives you a predisposition to chronic pain, either inflammatory or neuropathic, and that was groundbreaking in and of itself. But then, when COVID came along, and Mansoor looked at the data, and the same metabolic markers and diseases that are associated with an increased risk of an extremely bad outcome from COVID, are the diseases and metabolic markers that are associated with the things that they've been studying from a genetic perspective.

David:

And so, the first step is to identify what your risks are, and deal with those, even at a foundational level, so that you make sure that your immune system is functioning as well as it can, so you can resist COVID as much as possible. Make sure that your metabolic inflammation is at the lowest level possible as you have done, and identifying why you may be someone who runs a higher level of metabolic inflammation. In your case, it sounds like it was chronic mold exposure. Other people, it'll be something internal. Identifying those things and shoring your body up so that your cytokines aren't already tired from fighting this chronic state.

Dave:

So, you make yourself more resilient by lowering your cytokine levels to normal. Now, how would someone listening say, "Okay, I think I'm okay. My joints are a little sore sometimes and I have to make some pains and some muffin top, but I don't really have cytokines"? It's like when people say, "Yeah, I'm healthy." And you look at their labs, and you're like, "Ah, you're not healthy, you just think you are." How would you go about knowing what to do, if you're right now listening, saying, "Okay, I'm in. For the first time in my life, I want to control my cytokines, what the hell do I do?" We're not going to go and get lab tests for that right now. Give me the short list.

David:

Well, you know what? This is where biohacking comes in. This is why I got so excited when Mansoor told me I needed to talk to you. Because, I was speaking with a nurse last night, for instance, she has done the very simple things. And she said, "I didn't know that feeling good was an option. I thought the way that I felt was just normal." And she went and explored the issues that she might be facing with a functional medicine physician. And she got on some simple supplements. We're not talking about any really complex stuff, we're talking about vitamin D, if you need vitamin D, we're talking about vitamin B, if you need vitamin B, different sorts of vitamin B. Because, depending on how you metabolize it, some people don't absorb vitamin D or vitamin E-

Dave:

About a third of us, right? The methylation people. And longtime listeners understand methylation pretty well.

David:

Perfect. I love your audience. So, dealing with all of those things proactively. Try something. What Mansoor has done actually is Mansoor has hacked the genotype.

Dave:

This is Mansoor from The DNA Company. The guy who was just on a couple episodes ago. Okay.

David:

He's actually come up with, I think it's 70-some questions. And we've got a questionnaire that you can go down, and based on your response to like how you respond to insect bites and when you were nine years old, when your dad yelled at you, he could actually give insight into whether or not you need to be on a manganese, or selenium, or B vitamins, and dealing with those issues proactively ahead of time, so that your cytokine system is not already partially depleted. So that your body isn't already dealing with

intracellular toxicity, so that when the virus comes along, you're more able to respond to it appropriately.

Dave:

There's a doctor who put together an ICU in New York, who is making the rounds online, saying, "Look, I've never seen anything like this before. It's almost like my patients are, like someone dropped them off at the top of Mount Everest. They're experiencing hypoxic symptoms. Their lungs work, and sure, we can ventilate them and get a little bit more oxygen into them, but the real issue is that cells aren't taking in the oxygen. What's going on there?" And scratching his head. I heard that, and I said, "Oh, well, anytime I see higher levels of cytokines, in other words, inflammation, you usually see lower levels of mitochondria function. In fact, I would argue that, quite often, the cytokines are triggered by mitochondria who are not working at their level, the level they should be.

Dave:

And so, if there's a problem in the mitochondrial respiration, in other words, our ability to use food and air to make energy, well, then, of course, the air is not getting into the cell if the cells are blocked and doing that in some way. Does pain play a role? Or, does pain play a role in our cells' ability to actually use oxygen? Or, is that just inflammation? Or, is it both?

David:

Our cells are built to be very, very different in the way they look and function from the outside, but the building blocks are the same. They're just assembled differently depending on the function that you need for your cell. So, if you have a tendency to a dysfunctional intramitochondrial redox reactions, that's going to contribute to an increased risk of chronic inflammation. It's also going to put you at increased risk of mitochondrial dysfunction, when you get infected with something like COVID, because viruses actually replicate better in dysfunctional mitochondria with aberrant redox activity. And as your body is struggling with the virus, as the virus takes hold, as the virus starts to replicate better, that virus is using the same substrates that your cell is trying to use.

David:

And so, you end up getting into this spiral, where, yes, you end up going into a chronic inflammation, to an acute inflammation, to a intracellular dysfunction, to a mitochondrial dysfunction. And at point, you develop progressive acidosis. And the more acidotic you get, the less well things function, you're not metabolizing oxygen anymore. Your body is acidotic, it can't eliminate the CO₂ appropriately anymore because you're on a ventilator.

Dave:

We should pause that for just a second. There's a bunch of people who say, "Oh, acidic, alkaline, I need to drink alkaline water for this." Your body gets rid of acidity if you're breathing out carbon dioxide. That's what we're talking about here. We're not talking about, I alkalize with kale or some kind of garbage like that. Correct?

David:

Oh, I wish it was that simple. Oh, I wish it was that simple. I wish there was a way you could actually alkalize yourself. This is a problem inside yourselves, and it's all about maintaining balance. And when you start getting unbalanced, your cells have mechanisms to get themselves back into balance again.

And what we need to do is we need to shore up the ability of the cells to get back into balance, we need to shore up the ability of your body to get back into balance. I hope they come up with a pill for COVID. Plaquenil is really, really interesting because Plaquenil, it was originally derived from cinchona, the Jesuits brought it to Europe.

David:

They discovered that it was effective for malaria, because it's been in Western medicine. They've done a lot of work with it and they've looked and they said, "Well, it seems to reduce chronic inflammation, and so, we started using it in rheumatologic disease." And it seems to be quite effective at reducing the level of metabolic inflammation. One of the problems with Plaquenil although, and one of the reasons why I'm really hesitant about people recommending it for COVID, it's been almost over-refined. One of the issues we have with Western medicine is, Western medicine is very focused on power and purity. And so, Plaquenil is very powerful and it's very pure and it can actually drop your blood sugar levels, because one of the reasons why your blood sugars are high, maybe because you have chronic inflammation. You settle that down, the next thing you know, you're dealing with potentially life-threatening hypoglycemia.

David:

And so, figuring out how to mitigate and settle things down, you were asking how in the ICU, I would start to deal with cytokine storm, I would start with something like a lidocaine infusion. Because, we know that lidocaine infusions reduce IL-6 activity, which is an inflammatory interleukin. We know that lidocaine promotes IL-10 activity. But the nice thing about lidocaine is it does it within the context of a functioning human physiology. It works with our physiology, rather than replacing or fighting against our physiology. And so, we can achieve those things and try to mitigate the effect, rather than completely blocking the effect.

Dave:

Do you think there are any emergency rooms today who sees someone who's getting subsidized, who's not doing well with COVID, who've just decided to do a lidocaine drip? I've not heard this in their discussion, I'm in a lot of discussion groups with physicians, by the way, if you're new at this show, I'm not a physician, I just play one on the internet, except, not really. I just, I talk with a lot of them because I care a lot about translating it. Is this common? I know, as an anesthesiologist, it might be common, is anyone else doing this for IL-6? Or, is this a new innovation?

David:

I don't know if anybody's doing it yet. I've been speaking with our intensivists in Alberta and it's being added to our protocol because it just, people know the physiology, and people know that it might help, and it's one of those things that is unlikely to hurt. And so, it's on our protocol, and it will be interesting to see how much of an impact that it has. There will be other therapies that come along. Plaquenil is one of them, as long as you're being careful with it. There are other therapies that are available. You are asking what people could do just themselves at home, and eating good spicy foods. You were talking about cayenne pepper, cayenne pepper does have some function with substance P.

David:

There are, like black cumin, I love black cumin as a spice. I made an African biryani a couple of days ago, and one of the reasons that I used it was because it has some anti-inflammatory properties as well. The

same thing goes with Indian spices and things like turmeric. There are things that we can do just with the ancient pharmacology that we have, that is used in so many places to spice their food, that we can use to improve our resilience, and eat a better diet while we're getting ready to deal with this COVID crisis.

Dave:

I would offer for listeners, there's an episode, probably five or 10 ago, where I talk about IL-6, and I went through about 40 different things that you can eat or take as a supplement that reduce IL-6, and the things you just listed are on there. And black cumin is a very popular middle Eastern spice. I was in Oman and UAE, right before all this happened, and it's on the shelf everywhere. It's pretty cool. And I take capsules full of the oil. Black cumin oil is very potent for this. I just say that regularly because I don't like being inflamed all the time. I love it because few physicians are talking about, "Hey, maybe we do that, and this other stuff."

Dave:

But I want to go back to lidocaine, because you can buy lidocaine cream right now, or lidocaine ointment, and it absorbs very well topically. So, if you were at the beginning of getting sick, whether or not it's COVID or it's just a virus or a cold or something, I'm curious about maybe smearing some on, oh, the trigeminal nerve, jaw, forehead, chest, and just getting some of that in to reduce that inflammation right at the beginning. Have you ever tried that? Does it sound like it could work?

David:

I would be a little concerned about doing that. You mentioned when we were talking earlier about the way you're using lidocaine, lidocaine is one of those chemicals that if you start absorbing too much of it, you can start getting symptoms and side effects that can actually become dangerous or life-threatening. And that's why I'd be leaning towards things like just the vitamin therapy. The system that Mansoor and I are putting together in the Stay Safe app, with the 70 questions, we're really leading people into improving your immunologic function with vitamin therapy, dealing with your inflammatory status with appropriate vitamin therapy. We touched a little bit on things like why Plaquenil seems to be working from a chronic metabolic inflation perspective, but again, it's not something that we would actually recommend.

David:

Lidocaine is one of those compounds that has been, again, very, very, very refined. And if your levels get too high, you can end up having consequences from it. So, I would leave that one in the hands of practitioners.

Dave:

But the difference between an IV dose, I mean, it is an over the counter thing, at least, in the U.S. In fact, I'd buy 5% lidocaine from my local pharmacy here without a prescription in Canada. And we're talking a little bit on the end of your finger for topical use. And it seems like, at those doses, if it was highly dangerous, we probably wouldn't be selling it that way.

David:

Well, and the amount that's in things like the Salonpas and things like that, that you put on your back, I wouldn't be concerned about that, I'd be concerned about people just digging in too deep and starting to give themselves too much of anything.

Dave:

Yeah, because you're marinating in the highest strength that you can get is probably not a good idea because you want dose control if you're really sick. I have found, and I've actually been taught by a functional medicine guy, Dwight Jennings, that the normal couple of pumps of whatever the consumer thing is, over the trigeminal nerve, has been able to reverse, like early onset, I feel like I'm getting a cold, probably because of that IL-6 thing. But it's not going to treat COVID. Could it blunt your response? Or, you're just saying, even that level of doses, from a topical painkiller, muscle soreness kind of rub, even that isn't worth doing? Or, we just don't have data?

David:

We just don't have data at this point. I think that it would be interesting, I think that as time progresses. One of the reasons why we built the Stay Safe app that we've doing is as a data collection tool as well.

Dave:

Can we get that now? Or, is it not available?

David:

It should be there. IBM has promised us next week, so, I would say probably the week after that.

Dave:

Okay. So, it's very close. And that'll be listed probably from the homepage of The DNA Company.

David:

Yes.

Dave:

Okay. Good deal. And The DNA Company does DNA testing for other things like that. I've been working really closely and I'm pretty excited about what's happening with functional genomics and that sort of thing. So, Stay Safe is the name of the app. By the time this comes out in two, three days, I will see. But, okay, people go there...

David:

And it's going to, as much as anything, function as a data collection tool, because people will be participating in it, people will be entering all of their data. We'll have a symptom tracker as well, to give people some advice on how to deal with their systems, both with over the counter and home therapies and some of this functional medicine stuff as well. And then, collecting that information, tracking what's working and what isn't working. And that's the point where we'll actually be able to start answering these questions that you're talking about. Getting ahead of COVID, it's going to require crowdsourcing, way more than we've been doing right now.

David:

One of the issues that we're having with medicine is, we're playing catch-up, and we acknowledge that we're playing catch-up. Because, none of us really know what to do internally, that's why our immune systems are overacting. None of us really know how much to do systemically, and that's why we're all in complete lockdown and in quarantine, because we're using the tools that we have. But what tools are really necessary? What is actually effective? That's a situation where, having a system where we can get some useful advice about how to support our systems through this, where we actually participate with entering our information, participate in the tracking and the feedback so we can all collectively and anonymously know how we're doing going forward so that then we can start to surface what therapies are working, so we can answer questions like, is B vitamin support the answer? is selenium the answer?

David:

It would be really wonderful if lidocaine is something that could actually be used in the way that you described to make a positive difference.

Dave:

Now, I look at this, I'm interested in results, and I'm willing to do things that don't work, as long as they're more likely to work, than doing nothing. Which is not the Hippocratic Oath. And I'm willing to do this on myself. And so, I look at this, say, okay, let's look at this hypoxic thing I talked about earlier from that guy, I know about pseudohypoxia, and something about pain, so, for that, thiamine and magnesium are shown in studies to be useful. So, I could say, "All right, because none of those are proven to work, to make it less likely that you're going to end up in the hospital with COVID."

Dave:

I could say, "Since they're not proven, I'm going to follow with the good Dr. Fauci, who is a chemical apologist, what he's going to tell us to do, and say, 'Since nothing's proven, let's do nothing. Let's just have pizza, beer, and hide in our houses.'" Or, I could say, "Screw that noise, I would like to not be average, so, I'm going to do the things that are likely to make me above average in my ability to handle this. Even a 10% or 20% swing into high resilience mode might save your life, or, at least, make you more comfortable."

Dave:

So, from that, I'm like, "Can I take thiamine and magnesium, oh, and maybe some vitamin C? Yes. Would I love to share the fact in a survey, that I am doing that, and then, at the end of it, say, 'Oh, my IgM test, the one that shows that I have natural immunity, what do you know? It says I have natural immunity, but I didn't notice I got sick.' Let's record that data, let's share it with others, along with some stuff that I'm doing, this is the future of humanity." As far as I can tell, and I love that you're building the app, but right now, there's tons of people who are going to do a ton of stuff that cannot possibly be clinical tested like the medication you were talking about.

Dave:

How do we, as mere mortals without white lab coats and MDs, how do we decide, "You know what? Of course, it's not proven, but it might work, and it's more likely to work than the current path, therefore, I'll do it knowing I may lose my 50 bucks on my bottle of supplements." How do you think about this?

David:

I think about it as something that's absolutely essential in situations like this. You were talking about how a substance P, you thought that P stood for pain. It could stand for pain, it could stand for pandemics. It could be something that drives our systemic learning, so that we learn to learn from each other, rather than just learning from the things that we already think we know. My one big struggle with academic medicine and the way it responds to situations like this is, academic medicine assumes we know what questions to ask. And if we don't even know what question to ask, we're never going to find the right answer.

David:

And that really comes to the fore when you're dealing with a situation like this, where we've never had to deal with the true systemic consequences in our incredibly complex and interconnected society, of the way something like COVID can bring us down, not just internally, but also externally, with exactly the same thing, like internal inflammation and external inflammation and a storm of information that our buddy doesn't know how to deal with, and a storm of information that we don't know how to deal with either. So, yes, that's why we've built this system, so that people can participate in crowdsourcing the solution, identifying what works better than what else, and identifying the simple things that we should do at the foundational level, which is where our genomics insights comes in, so that our system is strengthened as much as possible in response to our own internal vulnerabilities that we may or may not be aware of.

David:

Your listeners are probably more aware of this, you're certainly far more aware, the average person on the street doesn't understand just how much their internal variability can affect the way they respond to things like COVID, or the medications that we use to treat COVID. COVID is a terrifying disease because it just, the flu also has about a 50% asymptomatic carriage rate. 50% of people will walk through the year not knowing that they had the flu. It shares that with COVID. But COVID has a five to 10% mortality rate, whereas the flu has a 0.1% to 0.2% mortality rate. And that's probably partially because it's the first time that we've seen it, but the one thing we can know for sure, this isn't the first time we're ever... or this isn't the last time we're ever going to be exposed to a virus that we've never seen before, and learning how to deal with that better is one of the most important lessons we're going to get out of this crisis.

Dave:

I like it that you describe this whole situation with the virus and you said that the virus is almost perfectly designed to bring us and our health systems down, with this hurricane force cytokine storm. Talk a little bit more about how this type of virus is bringing our health systems down, not just us individually.

David:

Well, we're so afraid of what can happen, because we don't know what is going to happen individually and systemically. If we could identify what patients are going to be the ones who are more likely to have a severe response to COVID, with something like our Stay Safe app, our hypothesis is certainly focused on metabolic inflammation. As the system learns and goes forward, we may identify some other things that are actually increasing your risk as well, and being able learn from and respond to that is a very useful thing. But at this point, we don't know. So, we have to make all these massive preparations for the worst case possible. And at the same time, COVID gets into our body, it plugs into something called

the ACE2 receptor, which is actually the receptor that breaks down angiotensin 2, and deactivates it after it's done its duty helping modulate our blood pressure.

David:

And that receptor is particularly present in the lungs, so, it's easy for COVID to get in. It's particularly present in our blood vessels, so, it spreads rapidly. It's particularly present in our heart, because our heart is basically a large complex blood vessel. It's also particularly present in our colon. And that's the thing that worries me because our colon is, in a lot of us, just a cytokine storm waiting to happen. Again, if our gut biome is bad, if our gut biome is contributing to our chronic inflammation, then that inflammation that we start to see on our colon, can also put it as increased risk. And that's as yet unanswered question, what role the colon is playing in all of this? All we know is that there's a lot of ACE 2 receptors in the colon as well.

Dave:

That is something that is really of concern for people who vape or smoke. Because, if you use nicotine via those pathways, we think the virus gets in via the lungs, you get a lot more ACE2 receptors, and that probably explains why people who smoke have a much higher chance of getting sick and dying from this. Is there something you would do as a medical doctor, if you knew someone was a smoker and was starting to have symptoms, versus wasn't a smoker, would you do like an ACE blocker? Would you put them on some sort of blood pressure lowering medication? Any thoughts about that?

David:

The number one thing is just to tell them to stop smoking. It's just, the big trouble with smoking, it's like, yes, there are the nicotine effects, but there are the direct effects of the carbon monoxide. That it's just, if you quit smoking, three days later, it's as if you got a big blood transfusion. That carbon monoxide actually contributes to your mitochondrial dysfunction because carbon monoxide is a very specific toxin for the mitochondria. And so, exposing yourself to carbon monoxide from your smoking is so risky at so many levels, but it's also a really quick intervention that you can make to increase your ability to resist and respond and recover from something like COVID.

Dave:

Some people are suggesting that you might want to take an ACE2 inhibitor to lower your risk of COVID. Do you think there's any validity to that?

David:

I have absolutely no idea about that. I know it's a question people are looking at, I'm a little concerned that there's no answer yet, because it's a pretty obvious go-to. As soon as we knew that COVID plugs into the ACE2 receptor, we know the function of these two receptor, we know that it's increased in people on actually a wide variety of drugs. These are questions that people started asking immediately, even from the academic medicine side. It's a question that they know to ask. And they're asking that question and we're not getting any answers yet, which makes me think that there's probably not a lot there.

Dave:

How do you approach a pandemic like this, as a working medical professional, who has to go in and do emergency procedures on a regular basis? You're dealing with someone who looks like they might be

really critical, and you're saying, "All right, the normal stuff we have is we don't really know whether anything works." So, anything you use is almost by definition either off-label or experimental, how do you go through the process? I'm asking you as a proxy for what you're trained to do in medical school, but how do you go through the process of saying, "You know what? I guess I'll give this guy some vitamin C," or, "I'm going to try," in your case, "I'm going to try lidocaine, because it's unlikely to harm, and the guy looks like he's going to die anyway"?

Dave:

What level do you have to hit, to say, "You know what? Here, have some ACE2 stuff, I don't know what else to do, let's just try it"? And I guess I'm asking you as a Canadian doctor, the answer is different for an American doctor because of liability. But just walk me through the decision tree in your mind when you're dealing with a pandemic situation like this.

David:

Well, it's just, this speaks to how I was trained at Stanford University when I was learning to do ICU medicine down there. You fight the battles you know how to fight, you win the battles you know how to win. If you don't know what to do, it's like, you've seen the movie, Frozen 2, if you don't know what to do, do the next right thing. It's actually a really good rule to live by. It's a really good rule to make medical decisions by. Don't do things that you know are wrong. If you see a problem, fix the problem. If you know ways that you can improve someone's functioning, yes, do that thing.

David:

For instance, lidocaine infusion, I know that if I've got someone who's got a breathing tube in place, being on a lidocaine infusion, if nothing else, it'll help them be more comfortable with that breathing tube, and it will have less hemodynamic consequence, it will have less effect on the blood pressure than some of the other agents that I could choose. And so, I would make the decision to use that, before I made the decision to use a drug like propofol, for instance, because propofol does have some effects on, particularly in the long-term, on the way your body deals with redox reactions, even at the mitochondria level. So, the deeper you dig into the physiology of all of these things, the more effective you can make an effective treatment plan, that even if you don't know what to do, you can still choose to do the next right thing.

Dave:

Does it have much of an influence if a patient comes in the door and says, "Doc, I know there's stuff that's the standard tree that you go down, if that stuff doesn't work, I like to be a guinea pig, I like to be an experimentalist, you have permission to do things that might work, if you've got no other options." Does that make you feel more comfortable and more safer? Or, are you of the mindset that like, "Hey, once you're on my table, you do what I say"?

David:

One of the ways that I've always practiced medicine is, I try to deal with a specific concern that a patient may bring to me. Because, if they're worried about something, that's the thing that they're worried about. It maybe something that I don't tend to worry about, but I try to pay particular attention to that, to honor their expectation. And similarly, I try very hard to fulfill the expectation or the need of the patient, even if they come to me with some therapy that I may think is potentially off the wall. First of

all, I'll probably learn from it. Second of all, I have this sense that sometimes people know more than they think they know.

David:

Are you familiar with the Rumsfeld rules of knowledge? There's the stuff that you know you know, there's the stuff that you don't know you know, there's the stuff that you know that don't know, but it's the stuff that you don't know that you don't know that's going to get you.

Dave:

Right.

David:

And it's just being cognizant of that, as I'm dealing with people, I do tend to try to work within the framework and the boundaries that they set for me. So, yeah, bottom line, if someone comes to me and says, "I want you to do this," if I can figure it out how to do it in a way that's safe, I will do that.

Dave:

I appreciate that open-mindedness. And I think a lot of people who listen to the show, are aware that sometimes you go into the medical system, especially emergency situations, and they will follow a set of rules that you might not want. You might say, "Look, I really don't want antibiotics unless it's really important because I've worked for two years on restoring my gut microbiome. Thank you very much." But, the standard is, "Well, we're not quite sure. Here, have some." And so, to be able to have that conversation, I like to coach people on how to have it in a way that doesn't alienate doctors, because your doctor should be your partner in healing. And frankly, if you're unconscious and intubated, it's nice if you, at least, told them ahead of time, "It's okay to give me a little something extra if you need to. Take a risk to save my life. I'm good." And just share the mindset there.

Dave:

I feel like that's worth doing, and I feel like your answer was like, "Hey, it's not going to hurt."

David:

Well, there's a lot of... Again, I don't want to come down hard on Western medicine because it's done a lot of good, but again, the assumption that we should use what has worked in the past, is something that tends to put blinders on, in a way that doesn't always do us the best. And pain is a good example. We started with this conversation about pain, that our societies have been dealing with pain for 6,000 years. And throughout our world, there are all kinds of therapies, other than opium-based therapies. We call opium a painkiller for a good reason, that opium is really, really good for pain control, but only to the extent that it makes the pain totally go away, it can also make you totally go away.

David:

Whereas, in all of our societies around the world, we've got things like, well, for instance, the cinchona root that has turned into Plaquenil, that has an anti-inflammatory function. You were talking about black cumin, that has an anti-inflammatory and analgesic function. There are treatments in India, there are treatments in China, there is a vast array of non-considered therapies out there. And, put that in the context of something like, for instance, acetaminophen. Acetaminophen has been in common clinical

usage since the 19th century. It was originally developed by Bayer, because Bayer was an aniline dye company. They were actually a paint company. They were experimenting with aniline dyes, they found this one chemical that had an anti-inflammatory function, we didn't know how it worked for 100 years.

David:

We were giving it to our children for the last 100 years, only in the last 10 to 20 years as we've started to do research with endocannabinoids, have we even discovered that there is an endocannabinoid system, and that TYLENOL actually interacts with our endocannabinoid system. We're very focused right now on whether or not people should be on cannabis and other cannabinoid derivatives like CBD. We've been using cannabinoid derivatives in our children for 50 years. And because it entered through the pathway of Western medicine, we were very comfortable using it, even though, if you read the textbooks, there are textbooks that were published two years ago, that talk about how it's really not well known how it works, but we've been using this stuff, and yet, there's all of these other therapies that are potentially available to us, that again, yes, we don't know how they work either, but they're safe enough that we use them as foods, and we use them as spices.

David:

It's like, cinchona root is now used to flavor tonic water. And the reason why they call it tonic water is because it's derived from the tonic that was used to fight malaria. And so, there is a tendency to poo poo things that didn't enter through the Western medicine pathway, with less than no cause. Because there's stuff that's in the Western medicine pathway, that we understand less well than we understand the chemicals that make up a lot of our supplements and nutraceuticals.

Dave:

It makes a lot of sense. And that does beg the question, if you had to choose one, take CBD oil orally, or don't take CBD oil orally during the pandemic, which would you do?

David:

At this point, I would take CBD oil.

Dave:

Yeah, I think so, too, because we know it has an effect on lowering inflammation, which is the name of the game. There's an argument for it where it doesn't prove it's going to work, but is it more likely to work than not work, and is it likely to cause harm? I'm not seeing the harm pathway there.

David:

More importantly, it has an effect of modulating inflammation. Remember, I was telling you that the problem is the difference between fighting against something, as opposed to fighting with something. If we're fighting with our body's physiology, if we're fighting alongside our body's physiology, if we're using tools that improve the way our body is able to fight and able to recover, as opposed to just trying to blanketly oppose something that our body is actually trying to do, we're more likely to be in the absence of any certainty about what to do. And again, if data starts to come out, if we start seeing data, there's a lot of people doing CBD oil all across Canada. If we start seeing data that says people who are taking CBD oil are more likely to suffer, then we need to respond to that appropriately.

David:

If we start seeing data on the other hand that say people who take CBD oil are less likely to suffer, we also need to be able to respond to that appropriately as well.

Dave:

Keep on cranking through it, and thank you for the work you're doing in hospitals right now.

David:

Oh, you're very welcome. Thank you for the work that you're doing in the public, it's like you are a positive anti-inflammatory cytokine.

Dave:

Wow, I'm IL-10. I appreciate that.

Dave:

If you liked today's episode, you know what to do. I'd be grateful if you would take, oh, about 10 seconds, and you would go over to iTunes and just leave a quick review, that says, "Hey, this show is worth my time." And if you really like what's going on here, head on over to The DNA Company webpage and check out their work, check out the DNA analysis. They've done mine, you can actually hear discussions about my genes on the show, about what effect that has on my risk, on my inflammation, and I think you're going to find that that's valuable for you as well. And I'm sure we'll get you the link for the new AI testing, it's just a survey you can do that's going to tell you a bunch of things and let you share your knowledge with millions of others, just by sharing what works and what doesn't work. Have a beautiful day.