Maggie Mills:

Good morning, everybody.

Audience:

Good morning.

Maggie Mills:

Nice to see your bright, shining, smiley, awake faces this morning. Before I introduce Bob, I want to remind everybody to submit polling questions to the Q&A section of the IFM program's app, and we might not be able to get to all of the questions because I think Dr. Hedaya has prepared a very robust lecture for you today, so we'll try to get to as many as we can, but if we can't, he'll make himself available during the break for you to speak with. I'm going to go ahead and introduce Bob right now. Robert Hedaya has been on the cutting edge of medical practice, psychiatry, and psychopharmacology since 1979. He's also been a Functional Medicine pioneer in the field of psychiatry during that time.

He's the author of three books, Understanding Biological Psychiatry, The Antidepressant Survival Guide, and Depression: Advancing The Treatment Paradigm. Bob has been a clinical professor of psychiatry at Georgetown University Medical Center since 1983. During his time there, he's been awarded Teacher of the Year three times for his work, teaching courses on affective disorders, cognitive therapy, and psychoneuroimmunoendocrinolgy. I think I got that right. He's also the founder of The National Center of Whole Psychiatry and The Center for Whole Psychiatry and Brain Recovery.

Dr. Hedaya serves as an editorial volunteer, and has been featured in the local and national media on many occasions. He's also a frequent and internationally recognized speaker, so we're very lucky to have him here, and he's published several articles in peer-reviewed journals. Please welcome to our stage Dr. Robert Hedaya.

Dr. Robert J. Hedaya:

Thank you.

Maggie Mills:

Thank you.

Dr. Robert J. Hedaya:

Okay. Can you hear me? Oh, that's good. Okay. Well, I like to start my talks with a joke, so I came up with one this morning.

I hope you like it. There are three archeologists in a room. First one says, he's bragging about how they have been digging deep, and he says, "We dug 100 feet down and we found copper wires, 100 feet down into the past." The second one says, "We dug 200 feet down, we found fiber optic." Third one says, "We dug 300 feet down, we saw nothing."

They said, "So what's so great about that?" He says, "We had wireless." I was thinking about this joke and I was thinking it's a little bit like PTSD because we're kind of entering into that third layer now. What I hope to convey to you is that PTSD has to be treated in three steps. The first step is alleviating symptoms, second step is fixing the terrain, and the third step is rewiring the brain, because PTSD in a significant measure is about disturbances of information flow and connectivity in the brain, but it really goes way beyond that, but that's part of what I hope to show you.

It's almost like, imagine somebody's in a war zone and a bomb drops, and everything is fragmented and scattered. That's almost like what happens to the brain and PTSD. The bomb is dropped, and there's disconnection between lots of different centers in the brain, and there's a crater in the middle, in the self, and there's a crater in certain structures in the brain, which is part of what we have to heal. I prepared for a 90-minute lecture with 30 minutes of questions and answers, and I understand now that I have 75 minutes, so there are slides on here that are worth going back to if you're interested in PTSD. All right. I'm going to get started.

Okay. Just for people, how many people are actively treating PTSD so I know who I'm talking to? About a third of the audience. Okay. Just to go through some slides in the beginning to just kind of, we'll all get on the same page, what is PTSD? It's a repetitive and unrestrained assault on the mind, the body, the spirit, and it has long-lasting, consequential damage for the person, and their life, and their loved ones, and people in the workforce.

It's really like that bomb I was talking about. This is a quote from a patient of mine who was a Special Ops guy. This guy was in Afghanistan and they were in a village, and they noticed that the enemy was bombing their village, but they wouldn't bomb when there were children in the village, so what they started to do is feed the kids candy, bring candy to the village, and the kids would be in the village all the time, and gradually, he became connected to some of these kids and he actually became attached to one child. This is who he's telling me about, an eight-year old who died in his arms. It just comes back to him in full color, all his senses.

It intrudes into his senses. It's that kind of trauma. He also had other types of trauma that are in the slides, which you could read about, but I asked him, "Do you think this has affected your life?" We've talked a little bit. He says, "You know, I'm very careful. I go into a room."

"I'm always in the corner, looking at the door. I go into a restaurant. I'm at the furthest seat from the door, facing the door, but I don't know, maybe it's affected my life, but I keep going." This is one of the things with PTSD, is that people have it and they don't even know they have it, or if they have it, they don't address it. There are a lot of reasons for that.

One of them is it's minimized, they think they just got to get through, but another reason is they don't trust. They lose trust in the world or aspects of the world, so that's a significant thing. I think there are lots more people. I know certainly in my practice with PTSD than I had recognized early on. This is a slide, which you're not going to read, and you're not going to read it because it is so graphic that you yourself, just in reading it can become traumatized. People who are working with victims of trauma, rape, assault, et cetera, or with veterans, you yourself can become vicariously traumatized over and over and over, hearing these stories, so you have to learn how to protect yourself as well.

The criteria for PTSD are on this slide, duration of one month. You have to have exposure, intrusion, avoidance, arousal, and mood, and cognitive changes. This is a paper you can look up, the Canadian clinical practice guidelines on anxiety, PTSD, and OCD, and there are linkages between these things. It's useful for you to read, so that's why I put that in here. Subtypes of PTSD, so we have the classic type, of course, but then we have different subtypes that are being considered. One of them is complex PTSD, and that is associated with personality disorders, relational trauma, early life trauma.

We have delayed PTSD, which I'll give you a case of that. We have dissociative situation, so in typical PTSD, we have hyperarousal, but in a dissociative PTSD, we have numbing, diffuse numbing, and it's not fully understood why that happens. I have some theories about it, which I'll tell you about. The exposure is directly experienced or witnessed, but again, as I said, it can be vicarious traumatization. You can learn that it happened to a family member, et cetera, and the intrusion is really powerful thing.

The intrusion is recurrent involuntary intrusions of the memory, of the experience, and these can be triggered by cues in the environment that are, in a sense unrelated. They can be intrusions into sleep, nightmares during a period of hyperarousal during sleep, flashbacks of ... Everybody knows about those. Whenever possible, the person wants to avoid these intrusions and this hyperarousal, so they go into avoidance mode, and the avoidance can spread so dramatically that their life obviously can become very, very impaired. Cognition and mood are, in a certain sense, inevitable because as a human being, you are there, you're ...

How many people know about learned helplessness? Great. This is a learned helplessness model, right? You're getting this electric shock if you have PTSD. You're getting this electric shock to your system willy-nilly. It just comes randomly.

You cannot control it. You don't know how to control it. You are like that rat or that dog in the learned helplessness model. You're going to end up having depression because you're helpless, you have no way of controlling it. In part, the depression is a result of that, but also, in part, the depression and the mood and cognitive problems are a result of the changes in the prefrontal cortex, which we will talk about in the frontoparietal tracts, which we'll talk about. Arousal activity, irritability, aggression, suicide attempts, aggression to other people, reckless behavior, startle response, all of this, you know about, but one of the keys is the sleep disturbance in the bottom, which we also will talk about.

In preparing this talk, I tried to condense the theory into a slide that would give you an overview, so I'm going to go through this slide, and then I'm going to tell you how I would change it because I actually, after I had to submit these two months ago, I said, "You know what? I think there's a better way," so here you go, old data. Fake news right here. First of all, you have vulnerability. What are the vulnerability factors? Well, here, I listed kind of three categories, but there's more, prenatal stress, maybe transgenerational, genetic vulnerabilities.

There are a few genes we'll talk about, early trauma, relational problems, bullying, how you bond with people, but also traumatic brain injury, immune dysfunction, dysregulation, so there are a number of vulnerabilities. Okay. Then, you've got the ... Actually, a premorbid experience of depression would also be a vulnerability, because that affects the prefrontal cortex, et cetera. Then, you have your trauma, and now you get into a loop.

With the trauma, you get obviously a sympathetic surge, but in general, once you're into the PTSD realm, you will have sympathetic dominance. That involves nightmares and panic, et cetera, hyperarousal, the autonomic nervous system, the locus coeruleus, which controls ... The locus coeruleus if you don't know is a little pea-sized area in the midbrain that has all the norepinephrine cell bodies for the entire brain. They all start there, and that's fed by the solitary nucleus and the raphe nucleus, the serotonergic inputs that keep a constant tone in the locus coeruleus, but when you have overexpression of the serotonergic inputs or various other inputs, you can have kind of a kindling of locus coeruleus, so you can have spontaneous panic attacks, et cetera. Anyway, you're in a sympathetic dominance.

From there, we have amygdala gets activated. The prefrontal cortex becomes deactivated, so the limbic brain, this is a kind of general concept that's really worthwhile understanding, the limbic brain and the prefrontal cortex, your thinking, planning, judging, assessing brain are in a seesaw balance, so when the amygdala, the limbic brain get activated or overactivated, the prefrontal cortex actually becomes deactivated, so you can't really think too well, so you have cognitive problems. You'll experience it as anxiety and agitation. If the prefrontal cortex area is strengthened enough, then the limbic is inhibited. It's really a seesaw. It's more complex than that, but it is actually that way.

It's a reciprocal inhibition. We have limbic activity, and all of this encodes the memory, which involves glucocorticoids, serotonin obviously, lots and lots of factors. I just mentioned a couple of things

here, and then we have downstream effects on the immune system, the gastrointestinal system, the microbiome. The mitochondria are affected by stress, and the HPA axis gets activated immediately, and you have rumination, and intrusion, and helplessness, and depression. Then, all of this is really a cycle because all ... For example, the immune, which I am listing here as the fourth item can actually proceed the first item, right?

It's very hard to put this systems type of thing into a graphic, but that's kind of what I did. It looked pretty good, until I realized that there was a better way of looking at it. This is all true, but there is, I think a better way of looking at it. I'm going to tell you that when the slide comes up. You have to stay awake.

These are five cases. We'll discuss a little bit, some of them today, but these are the different faces of PTSD, and I think it's worth looking at because, of course we know with the veterans, we have a good sense of what that looks like, but with the case, one case I'm going to spend some time on is Pam there on the right. Pam, somebody who I treated and only realized substantially into the treatment that it was PTSD. Darrin is the guy I talked to you about. Paul is a guy, a 58-year old guy who was wrongly convicted of white collar crime, then exonerated, but he was suffering with PTSD. Then, I'll talk about Joan as well.

The lifetime prevalence, 6 to 9%, 1.3 to 12.2. It varies. That's kind of in the U.S. and Canada. Interestingly, the prevalence in war veterans in the United States is about 23%. That's like one out of every four vets has PTSD. In Israel, actually the incidence is much lower, and obviously, they're under constant threat, and there is a question about why that is.

I think it has to do with bonding within the society. I think the vulnerability is fundamentally a cultural vulnerability that we have because in our society, families have broken down, communities have broken down. Obviously, the quality of the food, et cetera is not what it should be. There are a lot of factors that we're a soup that we're all sitting in that make us vulnerable if we have other factors. More frequent in women, onset in the mid to late 20's. There are actually a lot of vulnerability factors.

If you don't treat it, supposedly it kind of burns out after five years and if you treat it, three years. I'm not so sure that that's the case, but that's what they're putting in the literature. What increases the risk? Really, it's people who are inherently because of their genetics, their family, their community, the culture, they're vulnerable for all these reasons. This is a list of people. Included in that is people with TBI, parental PTSD, parental depression, substance abuse, but also you see here socioeconomic status, minority groups, et cetera.

Now, the effect of war on PTSD is pretty ... It's almost a different animal, and why do I say that? This is a study where they did a transcriptome analysis of the genetics of soldiers who went to war, and they saw ... This is not showing properly, but basically, 71% of the genes showed significant changes in their expression, pre versus post deployment. 71% of the person's genes are affected by that.

That's massive. These genes had to do with BDNF, and some serotonergic functions, and immune functions, but 71% of the genes. That's a massive effect. Okay, prognosis. Some people say one-third, more than one-third never recover. I would say it's higher.

I would say, and I actually found statistics, which I'll show you later, that indicate that maybe two-thirds don't recover, but the problem is actually worse, because the disorders that we deal with, many of them are comorbid with PTSD. This is a review of 64 studies of comorbidities that are associated with PTSD. You can see here, I mean, it's quite striking, inflammation, 16 studies, all consistent, earlier mortality, diabetes, hypertension, ulcers, shortened telomere length, and oxidative stress. That was a little bit on the fence, but there were five studies that showed that there was some issues going on there. This is a major problem. This is not a psychological disorder, right?

This is a whole body disorder. This is one of the things that is kind of disturbing because PTSD puts people at a higher risk for dementia. It actually makes a lot of sense. When you look at the neurocircuitry, you see that the frontotemporal areas of the brain are involved, and it turns out, I'm going to speed forward a little bit, that PTSD is associated with increased risk of lots of dementias, but the one that is most relevant or the biggest risk is for frontotemporal dementia. Make sense.

When we talk about the tracts, you'll see why. The bottom line, PTSD is not a psychological illness. It's a physiological illness, masquerading as a psychological illness, and it's important to realize and to convey to your patients because a lot of times, particularly vets, but really many people will feel weak like, "What's wrong with me?" Well, what's wrong with you is an atom bomb was dropped inside your life, and you're dealing with the consequences of that. Current treatments are definitely wanting, that leave us with a lot of people who are not responding.

We have some things we can do for prevention. Two medications have been approved, sertraline and paroxetine for symptoms of PTSD, and then there are a variety of psychotherapies. Prevention for children, if you aim it directly at the children who are high in anxiety premorbidly actually reduces the risk after a traumatic event of developing PTSD. Now, one of the main things that helps prevent and also ameliorate PTSD is social connectivity. As one of my patients said, bonding is the best therapy for depression.

Patients who are isolated, and in the United States certainly, we are more and more isolated, but patients who are isolated, when they have this PTSD, they will ruminate about, "What I should have done," "What I could have done," "This should have happened, that if I did this, this would have happened," et cetera. They're playing this out in their mind, but if you're socially connected, it's been shown that instead of ruminating and trying to process this data inside your own head, you start processing with the people around you, who you trust, who care about you. You're actually, in a certain sense, borrowing their prefrontal cortex. It's a little bit like a parent with a child. I saw it.

I was sitting in a parking lot, a strip mall probably 15 years ago. I'll never forget it. I saw a mother walking with a child. She's holding the child in her arms, and the child is screaming. He's about maybe 18 months, two years old screaming, and she's like, you can see she's containing herself. She's not talking to the child, holding the child, carries the child to the van, opens the door, puts the child in the car seat, buckles him in, the kid's flailing, and she's not saying a word, but you know she's dying.

She's dying, and the kid is getting worse and worse. Close the door, drives off. Three minutes later, another mother walks by with a child, maybe a three-year old, and the ...

PART 1 OF 4 ENDS [00:24:04]

Dr. Robert J. Hedaya:

Maybe a three year old and the child is acting up and "I'm hungry. I'm hungry," raising his voice. She bends down. She says, "It's okay. Oh, I know you're hungry, honey. Let's get something to eat and then we'll go home. We're going to have dinner," and you could see the child start to settle down. What's happening there? What's happening there is that there's a circuit going on between the prefrontal cortex of the mother, the limbic brain of the child and there's ... She's lending her prefrontal cortex to the child and gradually teaching the child, because this happens multiple times in the child's life. She's gradually changing the circuitry within the child, training, the limbic brain of the child to regulate itself.

That's the kind of bonding that gives you resilience, right? That that's the kind of bonding. So if you have that ability to bond and to have that kind of connectivity and do the self regulation, then

you're in a more resilient position. But it's clear that people who have PTSD, who ruminate, who are not socially connected, actually do much worse as actually a predictor of PTSD.

Okay, this is a study that showed that two thirds of people after treatment develop, remain diagnosable as having PTSD. So, okay, so we obviously need more treatments. So what we're going to do now is we're going to walk through the ...

Oh, I'll just mention to you, my timer's not working. So you're going to have to let me know. Otherwise we might be here till noon. Okay.

So we're going to talk about the antecedents triggers and mediators of PTSD. So let's talk about antecedents. So the subjective antecedents would be interpersonal trauma, emotional, physical, sexual abuse, bullying, you know, et cetera, physical injury, disturbed parent-child bonding. I told you about that already.

These are slides, just that the main point of these slides are, many people are talking about, "Oh, I have MTHFR snip, so therefore I have this or that." I'm going to get calls from patients all the time. You know, "I have MTHFR, is that why my daughter is paranoid?" You know, it's so much more complex. And so the point is different genetics offset. You can have snips in lots of things, but it can be offset by other genetics, methylation, protein folding, et cetera.

Genetically, the vulnerability factors that have been identified, the strongest ones are in that top line, the HPA axis. Now the HPA axis is something I really want you to get zeroed in on for treatment of PTSD. So we've got three genes, particularly the first two, the FKBP5 and NR3C1, these, there's really good data on these. So just keep those in mind. Okay, we're going to ... This FKBP5 is chaperone to the NR3C1 and is chaperone for the glucocorticoid receptor and so they work together. The FKPB5 and NR3C1, if you measure these in people which I do as part of the evaluation of the HPA axis, you'll see vulnerability factors. I'm going to show you that in a particular case, but these have a massive effect throughout the body. Because as you know, corticosteroid signaling affects a large portion of our genes. So these guys are almost, almost like a grand central station for stress response.

This is a paper on suicide and suicidal behavior, and one of the things they talk about this paper ... and actually I guess we're going to have a webinar on suicide at some point this year ... this paper spends some time talking about methylation status in particular, over methylation. So over methylation being high levels of SAM-e. SAM-e being the universal methyl donor and what that does, at least this is the theory, we know methylation generally for the most part, but not always silences genes. So if you are over methylated, you have reduced expression of the glucocorticoid receptors, a lot of consequences to that among them increased inflammation, but in decreased signaling in the gluco corticoid pathways, decreased resilience to stress increased agitation, and perhaps suicidal risk. So that's this paper's ... fabulous paper.

This is the special ops guys, methylation panel. So you could see ... Yes, I don't ... Do I have a pointer, you know? Okay. So this is a little tough to see. So look, you see at the top, well, let's, let's start, you see methionine in that black box there? Right? So methionine, as you probably know, it goes into SAM. SAM is the universal methyl donor, and that SAM is converted to S-Adenosyl homocysteine, and that is converting to homocysteine. And then it's recycled with B12 and folic acid back, and that's the methylation cycle, in simple terms, right?

So this guy, his methionine was quite high. You could see that on the top line, on the upper right side of that colorful area of the graph. You can see he's high there, and you could see if you go down to the third line, you'll see the SAM is all the way to the left, right? It's to ... No, it's just backwards, right? It's to your right. It's going down very low. And that means his SAM levels are quite low. And then you go

down to the fourth line in that upper area, and you see how his S-Adenosyl homocysteine is quite high. What's going on here? This guy's got a bottleneck in his methylation cycle.

Methylation's obviously important for many, many things. One of the things is making neurotransmitters. The other thing is breaking down. Neuro-transmitters obviously affects production of proteins. If you're silencing genes, then you have less expression of the genes. If the genes are over expressed, you have over expression of proteins. So this guy, his S-Adenosyl homocysteine was quite high and he clearly, based on his nutrient values, needed a bunch of B vitamins, and I couldn't give them to him. I had to correct the high SAH because when I tried to give him just a little bit of the B vitamins, he became agitated, tiny doses. He became agitated.

So this took about 18 months to normalize because, and I think had to do with his, his gastrointestinal tract, because I looked at his genetics and he ... there's a ... the SAHH or ACH-Y gene it's the same gene. I thought he, for sure, whatever snipped there, and that was the cause of the bottleneck, but he didn't. So that was his situation. So that's pretty extreme, and this was a guy who was in an extreme situation. That's the kind of things you can see.

So this kind of brings up the question of epigenetics, right? How relevant are epigenetics? If you're your grandparent or great-grandparent was in the Holocaust or the Potato Famine or whatever, does this really change your experience really? In animals, we know that it does, but it has not been proven in humans. It is not proven.

Rachel Yehuda, this is a quote from Rachel Yehuda. She's really certainly one of the premier researchers in PTSD, and she says that the studies have not yet demonstrated in humans, that trauma is heritable through epigenetic mechanisms. Logic says it probably is because we see it in animals, but it is not proven.

So these are the antecedents. It's kind of a quick tour through the antecedents. Mediators ... we're going to talk about this as a list of mediators, we're going to start going through the matrix. We're going to start in the center of the mental, emotional, spiritual. We're going to talk a little bit about these four things.

So the person is ruminating. They are in a counterfactual frame of mind. The facts say this, you know, you were exposed to this trauma 10 years ago, you are living in quite a safe environment. You are thinking "What I should have done, what I could have done. If I did this, it would have been this way." That's where your mind is immersed in that, but that is not factual at all. Why is that happening? I think that's happening really because at that point the pathways that I'm going to talk about are already disturbed, and the brain energy is, the information, the connectivity is flowing down the wrong pathways, cognitively.

So social coherence, what does that mean? That's the predictability of your world. The world is inherently not predictable, but we live best when we live under the illusion that it is predictable. I have a theory that if we accept that it's not predictable, and we truly accept that we actually become free. but for the most part, we try to live with the idea that it's predictable, and that sense of predictability is violated by the trauma.

This is a quote from a young woman who came from Mexico when she was 16 without her family, and she was raped a couple of times, wouldn't really talk much about it. Family came back to, came to the United States, a few years later, she was assaulted again and she had two serious suicide attempts. She jumped from the third floor window and survived, and this is what she said, "I'm going to die. I know what the end of this story is, so why not do it now?"

Relationships, we've talked about. Social isolation is a big vulnerability factor and so what do you want to do, you want to help your clients integrate, right? That's part of rewiring the brain. This is

another study showing social connectivity and ties in group ties actually reduce the inflammatory response.

Sleep, I'm going to go through quickly, but sleep is a core symptom, right? Disturbed sleep is a core symptom. Most people with PTSD, don't tell their practitioners that they are suffering and what they're suffering with. You need to spend time getting a very thorough sleep history, really with every patient. What happens in your sleep? You get this reverberating circuit. We have the locus coeruleus, the amygdala, the solitary nucleus, the raphe nucleus. The dream content becomes focused around the event and becomes really agitating, activating, the sleep gets disturbed person wakes up in maybe a panic or something like that.

How do you deal with it? First thing, no benzos, benzodiazepines are contrary indicated. They may increase risk for addiction. There are a number of medications. There are certainly herbal things. There's cognitive behavioral therapy for sleep, which is effective and shown to be helpful. Glycine, theanine, ashwagandha, there's a list here. Craniosacral therapy can be very helpful and cannabinoids can be very helpful. The lecture yesterday ... I forget who gave it, but it was a fabulous lecture on the endocannabinoids. And so all of these things, including a small well-balanced snack before bed, all of these things can be helpful.

CBT has shown to be itself, to be effective and can be used as a time limited treatment and is very helpful in reducing the magnitude of the sleep problems.

Okay, brain networks. So we're moving around here quickly. Okay. So what happens? We have network dysregulation and remodeling The brain circuits that we're concerned with fall into a number of categories. So we'll go through these different areas for a little bit. The prefrontal cortex we talked about that is linking to the amygdala. It obviously links to many different areas, but it's pretty clear this, there are sub categories of the prefrontal cortex, like the ventromedial prefrontal cortex is involved in the dorsal mode, the default mode network, which we're going to talk about. The dorsolateral prefrontal cortex is really involved in the executive function. So there are subcategories, but this is talking a little bit, this slide about that Seesaw balance I was talking to you about, okay.

The amygdala is no matter how you slice it. That's where the crater is. You could also say it's in the HPA axis, but the amygdala has been shown over and over and over again, in almost every study to be hypertrophied. There's increased dendritic branching in the amygdala, meaning this structure in the brain that tells you, is scanning the environment, that's saying, "Well, is this safe or is this dangerous? How dangerous is it?" It evokes fear. It evokes rage, sexual responses. That structure is overactive. It's online and it's working 24/7. So the amygdala is a big, big, big center in the salience network.

The salience network also has the anterior cingulate gyrus, which is kind of in the front here and the insula, and the insula parts of the insula are monitoring also what's salient in your body. So part of the insula is monitoring your viscera and your GI tract. So you might have symptoms in your gut and, oh, my gosh. You know, I have a patient, for example, who I think in a certain sense has a PTSD from medical experiences, not induced by a physician, but you know, being really ill.

She was at her parents' house in Arizona. She got some kind of infection and she couldn't return home out of fear for two months and her practice went down and it was a traumatic event. Now she's scanning her body. Her insula is scanning her body and saying, "Oh, is this a sign of something terrible?" It's just like the vet in the room who scanning the room for dangerous signals.

So that insula, anterior cingulate, gyrus, and the amygdala are your salience network. They tell you what's relevant. That salience network is overactive in PTSD. Although I think in the dissociative type, it may be underactive, but that's just my theory ... I don't know ... but it's scanning, right? So the salience network is overactive, but the central executive network, which is the dorsolateral prefrontal

cortex and the middle frontal gyrus, that that network is underactive. So that's your executive function. That's your ability to think, to plan, to analyze, et cetera.

So think about it. You have PTSD, you can't really think, you can't make judgments. You can't plan. You can't assess because your animal brain, your limbic brain, your salience network is saying, "There's danger everywhere." How do you function? Very, very difficult, right?

Then you have the default mode network and the default mode network, simple terms, you could think of it as it's introspective. It's the part of the brain that's saying, "What's what's going on inside? When I'm doing nothing what's going on inside?" And that's the default mode network involves the posterior cingulate gyrus, so it's not the frontal part, but the posterior cingulate gyrus. And then it involves the ventromedial prefrontal cortex, so it's down here. And the medial temporal lobe, which involves includes the hippocampus.

These are the three networks that are operating and seem relevant in PTSD, right? So you normally, in the best of circumstances, your executive network is in charge. The executive is in charge, okay. The salient network is operating and just kind of checking things out. Default mode network is operating a reasonable degree. So you're monitoring what's going on within yourself.

But once the atom bomb of trauma drops in, this kind of changes. Not only does the information flow change, the paths, the way the cars are going on the highway, they reverse direction. All of a sudden the salience network is in charge. The prefrontal cortex, the executive network has taken a back seat, and in many cases, the default mode network is also taking a back seat to the salience network, because it's scanning for danger. "This was a horrible experience. I have to scan for danger." It's adaptive, right?

The downstream effects of this obviously are not it's quite quite destructive, and so that's kind of, I think, a better model. And I also think it opens a door to understanding why we have some types of PTSD that are we'll call them dissociative, tight? Because this, I think ... I don't know ... I think that the salience network is actually, becomes muted over time, the numbing and the mutedness of it, but it's just the theory.

Main take home in a certain sense is you got to get that executive network, put it in charge. You got to rewire the brain. So, as I said, at top of the talk, you know, you want to, you don't want to treat symptoms. You want to clean up the terrain and you want to rewire the brain, right? So the rewiring we do through cognitive behavioral therapy or exposure, and maybe some other treatments we'll talk about.

So that's kind of how I, I see the situation. I'm going to move through these here. So this is a chart basically showing you the different symptoms and in the cortical areas, what structures are involved and in the sub-cortical areas, what structures. And you see, obviously in red that the amygdala is, you know, a big, big player in all symptoms.

Okay, so this, I'm going to speed through this. It's too bad. This is animated. Okay, the brain is remodeled, I think you understand that, it's remodeled under stress. Lots of things, estrogens are involved in that, BDNF production is involved in that, CRH and the cannabinoids, et cetera. These things are all involved. It's a massive restructuring because the brain is trying to adapt, what it thinks is a dangerous situation, "So there's danger now, let's adapt." Everything has to be changed, right?

When it comes to the therapies that you do, particularly exposure and response prevention, the most important things that you get the clients buy in. If you are putting someone in an exposure situation, it could be the smallest exposure. If they don't have the buy in, and they are not determined to master their problem, then they become ... It's retraumatization because they ... it's not under their control. Right? So what you have to do is you have to teach really well, the appropriate mindfulness

techniques or relaxation techniques. They need some way of terminating the stimulus that they're going to be exposed to and terminating their response to that stimulus. So it's must, must absolutely 100% be sure that the patient has bought into this approach, okay? You can not cajole them into this.

Okay, now, we're going to move into the communication. This lecture may be traumatic, right? We're covering like so much turf here. So the genetics we're going to talk about, I'll show you some examples, but the essential idea is that the HPA axis fails to respond appropriately at the time of the stress because of either previous experiences or genetic vulnerability in these particular genes, probably.

Dealing with the HPA axis is critical. It's a pillar of treatment, it's not the only part of the treatment.

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Dr. Robert J. Hedaya:

It's a pillar of treatment, that's not the only part of the treatment. It is a core part of the treatment. You must assess the HPA Axis. This, you probably have dreams, or nightmares about. You've probably seen this a hundred times.

And the idea is, again, that seesaw balance between the prefrontal cortex and the limbic brain. So, there's a perceived threat, it's not necessarily actual threat, it can be. But it's perceived and then you have activation of the hypothalamus. And then you have the CRH, CRF, and then the adrenal output, et cetera.

So in PTSD, patients have high levels of CRH. And as we learned yesterday, CRH is produced in the hypothalamus, in the pituitary, but it's also produced in lots of parts of the brain. So it's not limited to that area.

So let me tell you about one of the patients. So this is a guy... He's about 37 years old, or so. He's an internet genius, the guy has made millions of dollars. And he got into a lawsuit... Well, Amazon went after him. And they tried to destroy his career. And he was having nightmares. He was hospitalized three times. Multiple addictions. And his memory was impaired and he was intermittently suicidal and on Depakote, which was helpful to him.

The history was, that he had a father who was narcissistic and rageful. Very successful, comes from a long line of successful, bright people. But the father was very narcissistic. And that set him up for abuse by a high school music teacher. And then, in the year preceding his PTSD, all at the same time, as he was dealing with Amazon and thought basically his professional life was over. He was living with a partner, who had borderline personality disorder.

And so she kept threatening abandonment. And accusing him and blaming him. And he was going... Trying to appease and satisfy the rageful father. He tried to say, "Oh, yes, you're right. I'm sorry. I made a mistake. You're right about this, you right..." He was walking on eggshells and she was constantly threatening him.

So he had all these stresses coming into him. When I saw him, his ACTH, adrenocorticotropic hormone was 278. Now the range for that, depending on the lab, basically is 5 to 60. Most people are 15 or 20. He's 278. And he looks Cushingoid, he looks like he's got too much steroid in his body. He's puffy and he's got a Buffalo hump and he used to be a thin guy. And he also had a metabolic syndrome. So I sent him to the endocrinologist, who said he had pseudo-Cushings.

So, I think what had to be happening is that, by the time I saw him, he had been under high levels of cortisol. And that's why he'd look that way.

But what did I see on his adrenals? I saw basically... Relatively... The pattern's a little bit off. When you see the morning cortisol, it's actually low and then he's high, normal in the afternoon. But his ACTH was off the charts.

Now, ACTH is released in a pulsatile manner. So I repeated his as ACTH and it came back and it was about 40. Which is still relatively high, compared to what I see with most people, it wasn't in the two hundreds. But obviously there's some kind of a problem there. How come he's not getting a feedback mechanism to turn that off? So, obviously the HPA axis is playing a role here.

So this is a meta analysis, of the relevance of salivary cortisol in PTSD. And basically the conclusion is, that lower salivary cortisol is a marker... That if you do the salivary cortisol at the time of the trauma, or shortly after the trauma, you can predict who's going to get PTSD. That's how important it is, because it's your stress response.

So it's also associated with increased risk of non-remission. So one of the things that I have found most helpful, is dealing with the adrenals using cortisol.

This is a study on... Basically they used artificial intelligence, to determine whether in fact cortisol levels could be relevant to PTSD and whether they could predict PTSD. And they found that actually it was an accurate and predictive signal. So that tells you, "Okay, this needs attention."

Endocannabinoid system. I'm not going to spend too much time... Were all of you at that lecture yesterday? There were two lectures on endocannabinoids. So they did a great, great job on that. So it's basically, the cannabinoid one receptor that's in the brain. So endocannabinoids... I think one of the most important things, is that, the complexity of the system is astounding. And the changes in the endocannabinoids in normal, physiological, day to day functioning, are subtle. There's a lot of control over it.

So when somebody takes high doses, say smoking a joint, or high doses of cannabidiol, or something like that. You have to realize, that you could be overshooting the mark. So I would say, generally lean towards the lowest, effective dose.

Most patients who use cannabinoids, or THC, or pot, or whatever it is, they really talk about it as self-medication. Because it's actually quite effective. This is a study of Nabilone, which showed 34 to 47 patients with PTSD, had either total, or a significant reduction in their nightmares with the cannabinoids. And so that's pretty significant. And marijuana maybe had a negative rap, but you can't really ignore this data, it's very important.

So, here's a case. It is a woman who came to me when she was 25 and she had postpartum emergence of PTSD. She started to remember the physical and possible sexual abuse. And also the abandonment and relational abuse that she had when she was a child. And it came out after she gave birth and her husband was very non-supportive and she felt all alone, very isolated. And she was being flooded by these memories and she eventually had to avoid all contact with her family, as the avoidance part. And she was having intrusion... Any sense of abandonment, would create a tremendous level of anxiety. And she would actually go into, what she called, a black hole.

And it was quite astounding, because the tunnel vision... She was convinced... It was almost delusional, a temporary delusion. Until we could work with it and break through it. Panic attacks, self-medicating, cutting herself to alleviate these states. So this was a borderline personality disorder. She came to me ostensibly for functional medicine, but she really didn't want any part of it. She didn't want any part of functional medicine. She didn't want any part of cognitive behavioral therapy. What she

wanted, is a healthy bonding experience. So that's what we did, basically. Supportive psychotherapy, that was about what I could do.

I was able to get her on Trileptal, I think it was Trileptal, yeah. And that helped to calm her rage episodes. So that was targeting the amygdala, in my mind. Treated her hypothyroidism, that was reasonable. She was unable to eat in a consistent manner. Obviously important, because not eating properly is a stress on the brain and the body and the HPA axis. But what ultimately was most impressive, was her using low dose marijuana. Which I fought for probably a year. And then, it was so obvious, that she was so much more stable. And we could have so much more reasonable conversations and she could conduct herself in a reasonable way. It was quite astounding.

And I would say out of all of the interventions... At least any medical interventions, that was most astounding. So, I think what I do now, is I check the genetics of the cannabinoid systems, endocannabinoids. And see, do I think there might be use for cannabinoids in this person? And I just started doing that a couple of months ago and actually recommended cannabinoids for someone, based on their genetics. And it worked.

Now, maybe that's a fluke. That's just an N of one, but I think it might be a promising direction to look at that. For some people, the endocannabinoids have a significant effect suppressing immune function. So you have to watch out for that.

I'm just going to mention thyroid, because thyroid is obviously critical. The target that you want for the TSH is... The height would be 1.4. The mean TSH in the United States, in healthy populations is 1.4. If you're dealing with someone with neuropsychiatric issues of any type, you need to make sure that's optimized. And also, you might start looking at the deiodinase enzymes. There are three families that control how much T4 is converted into T3 in the brain. Which we have no way of measuring, unless we stick a needle through the temple and probably not a good idea. Nobody's laughing. So maybe you think it's a good idea? So, thyroid is really important. I think that's critical to optimize thyroid function.

Oxytocin seems, in a small number of studies, to be particularly helpful in people who have low grade or mild PTSD. You can get it at compounding pharmacies. It's just one part of the treatment. This is not going to cure PTSD, but it can help people connect to others. But it only seems to be helpful in the milder forms. If you wanted to measure, whole body, neuro-transmitters, not brain neurotransmitters, in the urine. You'll find significantly higher norepinephrine levels, according to the studies in people with PTSD. Which of course makes some sense.

Methylation, we talked about here.

Okay, this is Darren. This is the guy, the special ops guy. And this is where he was... You see the yellow dots are the improvement. This was at about nine months, to a year. So it's significant, but he's still almost an outlier within... You see that's the 16th percentile there, on you're right, in that graph.

GABA. GABA, again, in the communication part of the matrix, it's not clear what's happening with GABA signaling. There are differing reports, but these are the things that seem to be clear. That there's reduced binding to benzodiazepine receptors in SPECT studies. Reduced binding in the cortex, the hippocampus and thalamus, according to the PET studies. According to other SPECT studies, no abnormalities. But meta-analysis shows, that benzos are contra-indicated in PTSD. And that's really, intuitively for me, I'm a psychopharmacologist. That would be the first thing I would think of, but it's probably not a good idea.

This is something you can look at later. But it's basic message here, is the interaction of these signaling molecules. You see the glucocorticoid receptors, mineralocorticoid receptors, cannabinoid receptors, glutamate, NMDA, AMPA, et cetera.

All right, let's talk a little bit about mitochondria. So, bottom line is, we don't have great evidence in humans that the mitochondria are affected by PTSD. But, the logic is really compelling. So, these are five facts.

Energy is needed to sustain cellular organ responses to stress. That's a fact.

Glucocorticoids and other hormones like pregnenolone, produce and metabolize in the mitochondria. It's a fact.

We know mitochondria respond to stress mediators.

And we also know, that in animals, manipulation of mitochondrial function actually alters behavioral responses to stress.

And finally, the neural circuits involved in PTSD, have to be affected, because the mitochondria is what's driving everything.

So, chronic stress, leads to decreased mitochondrial energy production and morphology. That's a fact.

This is an interesting one, mitochondrial complex IV, cyclo-oxygenase, is most effected by chronic stress. And I find that interesting because, I'm going to show you later a study, it's only an N of one, of using laser treatment of PTSD. And the laser actually activates cyclooxygenase. And the result is, almost immediately increased production of ATP. And very rapid changes in signaling. And so, there are lots of technologies on the horizon for rewiring the brain. And there was a lecture yesterday by David Hagadorn, on qEEG and transcranial electrical stimulation.

My thinking is... But again, not proven. My thinking is, that there's something unique about the laser. Because it's actually providing direct activation in ATP, in the neurons. And in the cells in the brain. So, that's a clear physiological change. What happens when you pass electrical, even low voltage electrical current through the brain? You're priming, you're getting the neurons ready, or maybe with Theta Burst TMS, you're putting them on pause. But this seems to get to the core, because in my mind, energy and ATP is where it's at. Because if you have energy, the body can do great things. But when it doesn't have energy, it struggles. So I'm partial to that.

So, these are animal studies. 23 animal studies that showed... 19 of them showed significant adverse effects of psychological stress on mitochondria. So it's very, very clear, that it has an effect.

Translation to human studies. There are only six observational human studies and they seem to think that it can lead to changes in mitochondria.

So what's the future? So again, I talked about, treat the symptoms, work on the terrain, fix the terrain and then rewire the brain. So, when we rewire the brain, we want to change the patterns of information flow and activity. And we want to rehabilitate the nodes in these three networks. And most of all, want to get that executive network online. Most of all, that's what we want to do. And there are different ways of doing that.

So I think, on that rewire the brain, we have cognitive behavioral therapy. We have, maybe family therapy. Maybe we have exposure. Maybe we have mindfulness. Maybe we have EMDR. We have these therapies can help in the rewiring.

But they're also now these things listed on this slide. Like qEEG guided Neurofeedback, Theta Burst rTMS, qEEG guided laser, transcranial Direct Stimulation. These are new, we don't know what works and how well it works. Maybe it won't work? But they're promising. And so, I think we're waiting for good studies and hopefully we get funding to be able to do these studies.

This is the article... You can actually Google Harold Kraft, PTSD. This is his study, where he used the 810nm laser. And he radiated the brain. The patient shaved their head, it was a woman. And he rated in those red areas over... I think it was 10 or so treatments, relatively high levels of energy. And it was a remarkable recovery. It's one case, but it did work.

Now is this placebo? People do say in the literature, that light therapies have a high placebo rate. But there is data, that actually shows objective... I have data that shows objective changes in qEEG after 20 sessions, pre and post.

In fact, this is one of the reasons I like the laser. Is that, I have a woman with mild cognitive impairment, who I treated. And her qEEG after 20 sessions was improved. And then we stopped the treatment, she was actually normalized. Now, we did the functional medicine thing, but then she had the qEEG and it was still abnormal. We did 20 treatments of laser. And then we repeated that qEEG after 20 and it was essentially a normal brain. There was still some things, but essentially normal.

Then we stopped the treatment and we repeated it in a month, expecting to see a relapse. But we didn't see a relapse. We actually saw improvement. Why? Because the brain... This is my theory. The brain got the energy, the mitochondrial work and had the ATP, to do all the functions that the nerve cells needed to do and the glial cells need to do. So that the repair continued. So, in my mind, I'm partial to laser, but I could be wrong. There's a small number of cases. But it's just a way of thinking about this.

There are clear effects of PTSD on the cardiovascular system, changes in cardiac output and metabolic syndrome I mentioned. I'm not going to spend too much time on these things.

And then we come to defense and repair. So, I have a case of a woman who grew up, again, with a highly successful family, a narcissistic father, but there are plenty of those around. And she was going through life great, Harvard graduate, high functioning, relationships were going well. And then she... Over the years, she accumulated a number of immune insults. Lyme, mold, these kinds of things. And then, after that, what emerged was PTSD. Around her relationship with her father. She can't even talk to him now. So actually, the immune dysfunction laid the groundwork for her PTSD. I'm not saying that it happens with everybody, but it seems to be one path to the problem.

So, this is one of my favorite slides. And the main thing on this is, if you see tryptophan up there... So, you may know this, but I'll say it anyway. Tryptophan normally, it goes down both these pathways and a lot of it will go down the red pathway normally. But when you have inflammation in the body, wherever it's coming from, mold, Lyme, whatever it is. This 2, 3 indole dioxygenase is activated. So you get more production down that red pathway. You get more quinolinic acid. And then, what you end up having, is a lot of glutamate. The astroglia fail to be able to clear the glutamate out of the synapse and you have excessive NMDA activation. So that high level is cytotoxic.

Obviously, your GABA, glutamate balance is off and you're more likely to have anxiety. But the other thing that happens, is that you're not getting as much of the tryptophan going down the 5HTP, serotonin melatonin pathway. So now you have the deficiency of serotonin melatonin. Because you're not producing it.

The other thing that happens with inflammation, is inflammation... The immune system needs zinc, it needs zinc to function. The brain is the organ that usually contains the most zinc. Unless you're an adolescent, it's going into your bones. But that zinc has taken from the brain, in part. And so now you don't have enough zinc. Zinc is necessary for the proper confirmation of the 5HT1A receptors. The serotonin 1A receptors. They don't have the proper shape if they don't have enough zinc. So now your serotonergic neurotransmission is compromised, in terms of its efficiency that way. So you have less serotonin, less efficient communication. And finally, if you...

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Dr. Robert J. Hedaya:

And finally, if you are inflamed, you might have under methylation. Under methylation means that the genetics may be over expressed, in particular, the serotonin transporter. The re-uptake pump may be over expressed and if it's over expressed, that means it's clearing serotonin out of that synapse too quickly, because there's too many of these pumps.

Now, another reason for less serotonin. What happens with less serotonin? Anxiety, impulsivity, obsessiveness, all the anxiety disorders. So this is a very important pathway and it's triggered, and there are lots of other ramifications to this, but it's triggered in inflammation. That's why we have to look at inflammation and that's why your job when you're dealing with someone with PTSD is to really find the source or sources of the inflammation. That's critical, you've got to do that. That also impacts the HPA axis and if the HPA axis is already compromised, you have less cortisol, you even have more inflammation. So you can see this is like such a vicious cycle.

Now, the other thing is, if you have the FKBP5 or NR3C1 now you're not even transducing the gluco corticoid signal that you do have. So it's a perfect storm, right? So this article says that there's evidence that PTSD is underpinned by the presence of systemic low grade inflammatory state and it may be the mechanism associated with the increased risk as it was in this patient that I just told you about who had the narcissistic father.

Here's this chart again. So the inflammatory obviously is associated with the gut. It could be associated with the lungs. It could be associated with the HPA axis. This is all linked together and it feeds all the way back into the person and their experience because they feel terrible. So not only in hyper alert, hyper arousal mode, or maybe disconnected from the world, but their body is inflamed, everything is inflamed and their nutrient levels go down, et cetera.

GI disorder is quite common. Now I'm going to go through this. There's a logic, I'll go through this quickly. There's a logic to whether the microbiome is playing a role in PTSD. Is it causal? Is it a casualty of the war? Could be both but we don't actually have evidence. This slide shows that the measures of overall microbial diversity were similar among people with PTSD and traumatic exposed individuals who were controlled but didn't develop PTSD here. Here they say there's decreased total abundance of actino bacteria, et cetera. I actually have seen in some of my patients that that's actually not true. So we need a lot more study on this. It has to be playing a role because we know the microbiome is affected by stress. That's a fact, right?

What is its exact role? That's yet to be dealt with. Now this doesn't mean you ignore the microbiome because it's obviously, it's in the gut. The gut is central. We have to deal with the microbiome, but this is about the idea of whether it is causal or we can tease out exactly what's going on. We're not there yet.

So let's talk a little bit about nutrients. So optimizing nutrients and that really means macro nutrients, right? The macronutrient balance and the micronutrient balance is critical because if you don't have the ingredients to make molecules to make neuro-transmitters, immune function, everything suffers, right? You can't make a Big Mac without the ingredients, right? So you can't make a neurotransmitter. You can't make the molecules you need, the hormones, without the proper ingredients. So, that's what this slide is saying.

And these are lists you can go through. But what I want to focus on a little bit is on zinc and zinc is in an inverse balance with copper. Zinc, as I mentioned, influences serotonergic neurotransmission, especially the 5-HT1A receptor. It's most present in the hippocampus, the frontal cortex and the

amygdala and the olfactory bulbs. So hippocampus, frontal, and amygdala, those are areas we're obviously concerned with in PTSD and depression, right?

Zinc also modulates the balance between gaba and glutamate, so it's important there. And zinc, low zinc, is actually a predictor of treatment resistant depression and actually, you can improve response to medications for depression by using zinc. So it's pretty important.

The other thing I'll say is the... Well, I'm not going to say it, we're running out of time. Now you're wondering what I'm going to say, right? Zinc seems to be geographically relevant. Those who live in Pennsylvania, people come to me from Pennsylvania, they don't have zinc deficiency. I think where the crops are growing, I don't know. But in Maryland, tons of zinc deficiency. There are certain populations that are vulnerable to it. The pregnant women or postpartum or adolescents or people who have a lot of inflammation will tend to have low zinc. People on birth control pills.

This is just a cautionary thing. B6 in excessive doses can cause very vivid dreams. If you have someone who's already having nightmares, be alert to that because it'll happen. They'll take one dose one day and boom, that night they'll notice a change.

Okay? This is something that is say debatable. My idea is this. I think you need to treat, you need to assess all areas of the person's life, all areas on the matrix. You need to know what's going on in all of those areas and then treat them in as fast a sequence as possible to get the fastest improvement. Now that is a hard task. It requires a helper, but you get the best outcomes. I think obviously in some cases that doesn't work, but that's my preferred mode. I know there are other people who will stand up here and say to you, "Just do the next best thing and then see how it goes and then do the next thing and see how it goes and then you'll get great results."

They're wrong. Okay. No, sorry. No, they're not wrong. It probably works in their hands, but that's just the way my mind works. And I feel that physiologically it makes sense because if you're trying to change the homeostatic balance of a system that is stuck in a loop, a reverberating loop, you have to intervene in as many places at once if you want the fastest response and I think a fast response is critical in a lot of the things we treat.

It's not critical if you're dealing with someone who has generalized anxiety for 10 years, you have time, but in PTSD with the increased mortality and the increased comorbidity and these circuits being... the groove in the record is getting deeper and deeper and deeper, you need to move fast. Just like you would want to in someone with mild cognitive impairment, you don't want to take one step and then... Time is not your friend. That's my approach to it and I think you should consider it, but it's taxing to you, the clinician. It's taxing to the patient but it does get the quickest and best results.

Okay. These are just about really reiterating a lot of what we're talking about. This is a little bit of a review of the psychotherapies. This is some lists of other psychotherapies. EMDR, something that has some good evidence, not as good as cognitive behavioral therapy or exposure. Social ties, we talked about. Actually some of these were supposed to be hidden. Mindfulness, also useful.

So this is a case that I wanted to spend some time with. So this woman came to me. This was in October of '99 and she was 40 years old, mother of two, and she was complaining of depression for the previous five years since she moved to the DC, Washington DC area in 2012. That doesn't make sense, anyway, five years before I saw her, she moved to Washington DC. Her motivation was low. She was suicidal. She was trapped. She had a bad marriage anhedonic. Her concentration was poor. She couldn't think.

You might listen to these complaints and say, "Boy, there's some cognitive decline going on." And there is she. Her prefrontal cortex is not really functioning. Her brain wasn't functioning. Couldn't comprehend new facts, unable to come up with new ideas, intrusion, memories of her father, intense

exhaustion around that. She'd have a memory of a father and then she would get disturbed and upset and then hyper arousal and then exhausted. Trouble with sleep and the exposure was father's rage, but I didn't actually put all this together until into the treatment several months. She had migraines, severe fatigue, et cetera. And she said, this was a tip, right? "By the way, my symptoms are much worse after my husband yells at me." I don't think I picked up on it quickly enough.

This was her history. You see asthma as a child, so some kind of inflammatory vulnerability. She wasn't eating too well. She had an ulcer. We talked about that kind of problem. Pneumonia in '97 and depression, as we said. PMS, migraine and she was on lithium, serzone, which is a relative of trazodone, affects her and this synthetic birth control and occasional use of Imitrex.

So my diagnosis was major depression, late onset. Got her off her birth control pills, decided to use bioidenticals, if we needed to reduce, that should say serazone. EPA fish oil, gave her a gram and put her in exposure therapy. What did exposure therapy mean for her? It meant going into couples therapy with her husband so that she could start to deal with the terror that she experienced around his raising his voice. Worked up her thyroid, zinc, copper, et cetera, stool, et cetera. This is what we found.

So in her gut, in the assimilation we saw, she had Klebsiella Citrobactor, reduced short chain fatty acids, and importantly, reduced pancreatic elastase. So she wasn't really able to absorb her nutrients effectively. Her fatty acids were imbalanced. Her secretory IGA was low, so there's some kind of immune dysfunction going on there, some food sensitivities. Migraine cleared with diet. She had some nutrient deficiencies and you look at her TSH is 1.89, it's just a little bit up, but look at her free T3, it was 2.2. Okay. So that's subnormal, just a little bit under the normal range, right? And her ACTH was four.

So her pituitary is not really telling her adrenals what to do, that's for sure, right? Histamine was high. That's maybe somewhat of a marker for methylation status, so that would be an under methylation, and interestingly, she's APOE 3/4, right? So there's a little bit of a vulnerability there to Alzheimer's.

This is her third visit in December. She lost five pounds, blood sugars more stable, she's off the Estrogen. She's eating much, much better now. Migraines completely gone, but she still has severe fatigue. Her salivary cortisol is 20. The range is 23 to 45 and the pituitary is not really responding. So I did an MRI and I'm looking probably for a pituitary microadenoma because maybe she wasn't producing enough ACTH to get things going but the MRI was normal and her free T4 was low. TSH was high, but I couldn't treat that. You can't treat the low thyroid till you treat the adrenals because otherwise it would be tremendous anxiety and more adrenal exhaustion.

And then she had the nutrient deficiencies so I gave her some herbs and B5 pantothenic acid, vitamin C, some cordyceps. Obviously controlling her eating. Working at doing some, maybe, mindfulness meditation or HeartMath or things like that. You want to do that to get the adrenals back in shape. And we reduced her Effexor because she's found that sedating, switched her to Remeron twice a day. Anyway, she came on on the sixth session, and she's in a much better mood, but still having instability. And she couldn't tolerate any of the adrenal herbs, but she's the one who said bonding is the best antidepressant.

So she's now she's now reaching out and she's breaking the isolation, right? She's in the therapy with her husband and she's starting to feel some hope and she's starting to connect to people. So that's a sign that things are changing in the way her brain is functioning and it's obviously a reciprocal type of thing. She says she's still walking on eggshells with her husband. She's exercising and I decided to see how she's doing on her cortisol and thyroid.

But in between, I interviewed her daughter and son, because I really want to know, is he really yelling or is she hearing... What's the reality? I know what her reality is, but what's really going on in the family? So the daughter says he gets an evil look on his face when he raises his voice. So that was pretty convincing. The son was also pretty convinced and he said, mother would get mad, father would yell. He was quite worried about divorce. Based on this interview I said the husband needs some treatment. So I got the husband into treatment.

Saw her on the ninth visit in May. She was in a slump. She said he's wearing her down. You can see the cortisol is still low. 24 to 42. DHEA is normal. At that point, I said, I'm going to put her on hydrocortisone. Hydrocortisone is a bio identical compound. This is what your body makes, right? Your body makes 20 to 40 milligrams a day and it releases it with the highest levels in the morning and then the levels go down throughout the day.

If you're interested, I strongly, strongly suggest you read a book by Jeffries called "The Safe Uses of Cortisol." I wouldn't be without it. It's critical. The book is actually... you should buy it with your friends because I think it's going for $270 because it's out of print now, but it's worth reading.

I put her on the hydrocortisone and she did so much better and now she said, everything's helping, but she now can tolerate his yelling and she's able to handle that stress because I'm dealing with the HPA axis. Yes it's maybe, you would say, aggressive, but what choice really did I have at this point? Anyway, she responded quite well. At that point, it became really... Somewhere around there I said, "Whoa, this is PTSD."

Anyway, husband says she's more receptive. She was even warm with him, gave him a hug, and things went along better. I'll move through this. Eventually we tapered the Cortef, rechecked her adrenal axis and her ACTH was still low, but she was doing okay. So we kept going with what we were doing. She was exercising, she was socializing.

Now I got a call from her son who I treated after I treated her. So I treated him maybe eight, 10 years ago. He called me, it must've been two months ago because he wanted a copy of his records. I was like, "Wow, this is amazing. So how's your mom doing?" I wanted some followup. She's doing great. She retired, she opened a pottery shop. The husband is still working in the government. He does a lot of woodworking. He built some contraption and whatever.

And the son who actually started acting out, as soon as the mother got better, the son started to act out, right? Because it's like whack-a-mole, right? What's going on in this family? Mother gets better okay, let's get the son. But he did okay and he called me around the time of the birth of his child. He had just had a child a day or two before. He wanted to know his genetic data so he could use that for his child. So it was really a beautiful followup. So this woman did great.

Now remember, she had APOE 4. She is vulnerable and I'm more and more convinced that these early neuropsychiatric problems are actually harbingers of neurodegenerative disorder. That depression isn't just depression, that it's an early sign of some kind of a weakness in the system, a vulnerability. I don't even want to use the word weakness, vulnerability in the system. It has to be taken that seriously because, and people need to be educated that, yes, okay, it's depression, you got better, but you have a vulnerability. The body takes a hit. We need to strengthen you and you need to redesign your lifestyle going forward if you want to avoid neurodegenerative or other comorbidities that are associated with depression.

I'll tell you this one. This is the guy who was falsely convicted of white collar crime. Had a 2.3 million dollar fine. His ex wife nailed him and he had severe PTSD. Lost his business, et cetera. Had all of these comorbidities. He had SIBO, IBS, infections, adrenal insufficiency, hypothyroid. He had intrusions,

aortic insufficiency. You could see his ACTH 59.4, the upper limit of normal, and this was his cortisol, right? This is what the literature is saying.

This guy had this NR3C1 snips. He had a number of snips. You see that up there? All the way on top. Let's see, here are his snips. So you see two, four, six, eight, right? And so 50% of the genes that were tested for the NR3C1 were variants. So this guy at a young age probably had high cortisol, but over time, his adrenal axis couldn't really put out. And so now he's in a low cortisol state. And so helping him recover that adrenal function, whether it's through herbs, et cetera, or through hydrocortisone, all the methodologies we're talking about here, you can't focus only on one gene, because these are all the genes involved in corticosteroids synthesis, okay. I'm just putting it up there just to create anxiety.

Okay. This guy also had Borellia, Ehrlichia, a lot of stuff. We treated his SIBO, et cetera, used trazdone, exercise. He couldn't tolerate melatonin, which was interesting. A craniosacral we did, et cetera. Navy beans helped him tremendously. Navy beans because we did a study of his microbiome and it looked like navy beans would be good and they reduce his inflammation a lot. So NAC was helpful. There are some data on NAC and PTSD, but there's a lot of data on NAC, growing levels of data on NAC with OCD, substance use disorders, et cetera. It's a useful thing to consider with these patients.

Here are some slides, because I think I'm five minutes over now, that are worth going over about how to approach the HPA axis. This is critical, critical, critical. If you deal with PTSD, you have to, you have to do this, okay. You need to assess all levels and you need to know exactly what you're dealing with, okay? Very, very important. You will increase your success rate. So that's all laid out here and that's the last thing I have to say.

Maggie Mills:

Thank you, Doctor Hedaya. We don't have time for the Q and A, unfortunately, but there were some really, really great questions that came in. So if you are-

Dr. Robert J. Hedaya:

I'll stay around, if you want to bring up some questions.

Maggie Mills:

Yeah, that would be great if you don't mind.

PART 4 OF 4 ENDS [01:35:30]