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POST VIRAL SYNDROME AND ME/CFS: WHAT EVERY CLINICIAN NEEDS TO KNOW

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[video transcript]

(00:00:09):

Dr. David Kaufman is our speaker today for the course on Post-Viral Syndrome and Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome: What Every Clinician Needs to Know. After earning a BFA from New York University School of the Arts and Filmmaking and MA from Teacher's College at Columbia University in Education, and his MD from New York Medical College, Dr. Kaufman completed his internal medicine residency training at St. Vincent's Hospital and Cedical center in New York City. He began his internal medicine practice in Greenwich Village in New York City, just as the epidemic that came to be known as HIV/AIDS exploded. With St. Vincent's at the epicenter of this outbreak, he became deeply involved in the care for HIV positive patients and in the research aimed at discovering ways to treat both the opportunistic infections they were dying from, and the virus that was causing the destruction of their immune systems. In addition to his private medical practice, he was the medical director for one of the largest HIV centers in New York state and the Director for HIV Clinical Research at St. Vincent's. In 2012, Dr. Kaufman joined the Open Medicine Institute where he was the Medical Director for the Open Medicine Clinic. In 2017, he opened a new clinic, The Center for Complex Diseases, with a focus on patients suffering from ME/CFS, dysautonomia, autoimmune diseases, and chronic infectious diseases, including tick-borne diseases, small intestine bacterial overgrowth syndromes, and mast cell activation syndrome. He is a member of the ME/CFS Collaborative Research Center at the Stanford University Genome Technology Center, a member of the US ME/CFS Clinician Coalition, and an active participant in several national clinical networks that focused on ME/CFS, mast cell activation syndrome, and autoimmune diseases. Thank you so much for joining us today, Dr. Kaufman, and now I will turn it over to you.

(00:02:02):

Thank you, Mark. And I have no disclosures and I want to thank CEI and ME Action for inviting me to do this webinar. So these are the objectives today. Basically what I would like to, and hope to do, is help other physicians understand what ME/CFS is, and also give us sort of preview of what I'm afraid is going to happen as a result of COVID-19 and post COVID syndrome, also being called long-haul COVID. I hope that I can explain more than just ME/CFS because it's my belief that the underlying illnesses are not well understood, and that's why it does not get the attention and care that patients need.

(00:02:54):

So the point here is it's pretty clear from what I've written, as you may all know, most patients with chronic fatigue syndrome are just not carefully listened to. And I'm going to try to make the case that you need to listen. You need to take a careful history and be a true detective and bring your clinical skills to bear. If their answers are not obvious, that doesn't mean you just roll your eyes. And it's all the more important now because of the post COVID-19. I think, as I'll tell you in some later slides, we are witnessing a post pandemic chronic fatigue syndrome event. So I think it's a huge and scary thing. We

need to understand it. So just some quick statistics, these are already outdated. I think we updated them three days ago, but they're already outdated.

(00:03:54):

My guess is that we've now passed a million deaths globally. The US is a catastrophe, as you all know, with over 7 million cases and growing daily, we now are experiencing another surge all through the country in different areas. The death rate has now gone to 205,000. The percentage of deaths may be somewhat decreasing because physicians and hospitals have learned a phenomenal amount of how to take care of these patients. But nevertheless, the numbers are pretty terrifying and we are now entering flu season and cold weather, and people will not be able to distance as easily outside. So I fear that this will get much, much worse. Please take a look at the bottom line here to compare. This is a statistic generated out of the CDC estimated, 1.7 to 3.4 million cases. I think that's a pretty important statement because basically it's we don't know. If you think about it, look at the range of cases, which implies a lack of clear diagnosis, which is probably a result of patients not being properly diagnosed. And the death rate is unknown, partly because of the poor tracking of statistics, and partly because many of the deaths are probably attributed to other causes, including suicide, unfortunately.

(00:05:21):

So I'm going to start with a few slides on post COVID-19. I don't know what name to give it. I personally just dislike the term 'long haulers.' It's almost as bad as the term 'chronic fatigue syndrome.' I think post COVID-19 syndrome would be better, in any case it's there. So this is a study out of Italy. I chose this one because Italy, after China, was early on with the pandemic and had a huge impact, especially in Northern Italy, and looking for post COVID syndrome statistics, we need a time period. So here at 60 days and if you look at this, a third to a half of the patients have ongoing symptoms. There's a new study that just came out from Korea that showed nine out of 10 patients had ongoing symptoms. And there was another statement from the CDC recently that one third to two thirds of patients had ongoing symptoms. But it's important to understand that the time that we're looking at is short. Okay. As you'll see in a minute, there's a definition related to chronic fatigue syndrome that says you have to have symptoms for at least six months. So for a huge number of the COVID-19 patients we're not even near the six month mark. I think six months from now, we will have a better picture, a clearer idea, of what the syndrome will be like. And I don't think it will be pretty. And we have got a lot of work to do.

(00:06:57):

Most of the symptoms, or many of the symptoms in post COVID, are very, very, very similar to ME/CFS. Fatigue obviously is the biggest. This is a quote from Dr. Fauci. I won't read you the whole quote, you can read it at your leisure, but basically what he's saying is yes, post viral syndrome and post COVID is and will continue to look like ME/CFS. My takeaway from that is that we, as physicians and healthcare providers, better get our act together and realize how significant this is. I am already well aware of patients who had COVID seeing physicians and sadly being told, Oh, just give it time, go exercise, it's just fatigue, you'll get better. Already not getting the picture and beginning to look at these patients as CFS patients, we have to change that.

(00:07:57):

Alright, I'm going to go into some information on specifically on ME/CFS. So the first slide, the first bullet point is really important. And what's important there are two words, chronic and multi-system. Alright, this is not a sore throat, this is not chest pain or shortness of breath. And that may be why it has been so lost in the healthcare system. Patients come in with multiple complaints and that makes it far more challenging to figure out what's going on. It is a disease that affects as I said, multi-system, central and autonomic nervous system, cardiovascular, gastrointestinal system, and the immune system, but it also affects the joints and the muscles and right down to a sort of metabolic molecular level with mitochondrial disorder.

(00:08:58):

About two thirds of ME/CFS, patients will present with what I'll call a classic history. 'Doctor, I was completely fine, I was 24 years old starting a new business, I got the flu and I've never been the same since.' I hear that story at least two to three times a week, over and over, and every other physician who sees chronic fatigue patients hears that same story. It doesn't mean that they get their flu or their mono, and then they have chronic fatigue syndrome from that moment forward, there is often a waxing and waning pattern, a lag in symptoms. But most patients can tell you when it started. it's remarkable. I'll ask a typical first question, I ask a patient, 'prior to what date were you completely fine?' And they will say 'on July 19th I got sick and they state their illness from that date.' It's quite amazing. So as you probably know, mono is the classic viral infection that patients will describe, that is caused by Epstein-Barr virus. I'm sure most of you know, that nearly the entire population has EBV infection in childhood without symptoms. It's the patients who get EBV when they're a little older that actually have mono and present with illness. So mono is just the tip of the iceberg, and I want to emphasize that mono is only one of the herpes family viruses. The others can be involved as well. And in particular human herpes virus six and CMV are other big offenders in the sense of causing or being related to the onset of ME/CFS. It's often thought that's all, just viral illness starts it, but that is not the case. We all have seen patients with chronic mycoplasma infections and chlamydia infections, and absolutely with tick-borne infections, who evolved into the picture of chronic fatigue syndrome. What I mean by that, I'll get to in a minute, but just to give you a preview, my point here is chronic fatigue is a phenotype. It's a description of symptoms. And what we have to figure out is what's underneath those symptoms, what's causing them. I should add on the GI infections, I've had many patients who returned from trips around the world and they describe a significant or brief gastroenteritis. And it almost clearly dates from that moment.

(00:11:39):

The other third of patients who don't give a nice, clear infection history, there are many other causes, physical and emotional trauma, accidents in particular motor vehicle accidents with head injuries. There's a literature demonstrating how childhood abuse will increase the risk of developing ME/CFS. Vaccines can cause, how do I explain this? Vaccines can cause some of the underlying illnesses that end up appearing as ME/CFS, the classic one most recently is Gardasil, the HPV vaccine, which can cause a quite severe autonomic nervous system dysfunction, and those patients meet all the criteria for ME/CFS. And of course in our increasingly toxic and poisonous world, those exposures are causing more and

more disease. There's a huge literature on the role of environmental toxins causing auto-immune disease, which again ends up fulfilling the criteria of ME/CFS by definition.

(00:12:53):

So there is clearly genetic risk factors as I show in this slide, and there is a female to male, three to one preponderance. Although I actually wonder about that statistic because I do find many men come in and you know, I don't want to get into this too far, but I think men are often far more reluctant to go to their physician and say, 'I'm very tired. I have chronic fatigue.' And so I think it's underdiagnosed in men. It's equally diagnosed across all groups, white, African-American, Latinx, et cetera. And I want to emphasize here as well that there are also infectious outbreaks or what appear to be infectious outbreaks of ME/CFS. So you know, I mentioned in the previous slide about herpes, but there've actually been what I'll call mini epidemics. So the most famous might be the incline village back. I think it was in the late sixties and seventies, when there was a cluster of dozens and dozens of patients in the same location, suddenly developing a picture of ME/CFS. So it's a very complicated process.

(00:14:08):

Okay. So this is an indication of how much illness is out there and I selected lupus and multiple sclerosis on purpose. Obviously because I wanted to point out the funding. Okay. So let's just say an average of 2 million ME/CFS versus 785,000 and 486,000 in the others. And look at the difference in funding. It's a six to seven fold higher for lupus and MS, despite the far smaller population and the far lower prevalence. And these patients, I guarantee you are just as sick. So many, many of us if you remember back to medical school and maybe you had a paragraph about ME/CFS, and then it was probably just called chronic fatigue syndrome. I actually don't remember hearing anything about it in school or learning anything, but one of the things that we may have learned or picked up along the way is that it's a 'yuppie disease.' That was a big term back in the eighties, I guess. And I want to emphasize here that that's completely untrue. I mean, if you look at this, this is a slide that shows you the occurrence rate in the different age brackets, alright. I have seen patients 80 years old and I've seen patients that are 18 years old, and I know of children who are five and 10 years old, who fulfill the criteria for a diagnosis of ME/CFS. And I'll get to those criteria in a minute. So don't assume that if a person comes in and they're 71 years old telling you symptoms that sound like CFS, that it's not. Okay? Really, really important.

(00:16:01):

Alright. This slide is, to me, a painful slide. And I actually think that it's not quite accurate, but it's the only one I could find. Okay. So this is describing how long a patient has been sick with ME/CFS and implying how long they were sick before they were finally diagnosed. That's the key point. So think about if you are a patient and you have chest pain and it took you years and years and years to get diagnosed and then realize how chronic this illness is, it's not unusual for patients to come to me as a new patient and say, 'I've been sick for 24 years.' It's rare to find somebody who has been sick only one to five years in my experience. That's why I don't quite know where this statistic came from, but the point is still there, and I really think you need to hear it. These patients have a chronic illness. It lasts a long time, if not their lifetime. And it can be a daily struggle for them. And that struggle is compounded

by how long it takes to get diagnosed. This is a painful slide to look at. Imagine if you had the kinds of symptoms I'll be describing in a few minutes, and it took you 10 years to get diagnosed. And again, my personal experience is that there's no way 78% are diagnosed within one to five years. The typical pattern I see is a patient who has seen five to 20 doctors over the last 10 years before they finally get their diagnosis and make some progress.

(00:17:45):

Okay. Another version of that slide, how many doctors did they see before they were given the diagnosis? Again, I think this is not a hundred percent accurate based on my own experience, but maybe I'm wrong. Maybe I see a selected population, but even so, just look at the number of doctors. Alright. And then the patients end up getting accused of doctor shopping. Sadly, most of the an explanation for how many doctors are seen is that the most frequent diagnosis, as I'll come to in a minute, is depression and anxiety, and the patients are just sort of slowly moved out the door.

(00:18:31):

Okay. So, and this is what I was just alluding to. So patient comes in and says, you know, they have fatigue and they are so tired and when they try to do something, they feel terrible and they have to lie down and they have a sleep disorder and they have aches and pains. Okay. And these are the diagnoses they most commonly get. Alright. So try to picture yourself as a patient feeling miserable and being told these things. Alright. The one that gets me most recently is conversion reaction, which is basically a psychiatric diagnosis, but all of these, all of these diagnoses are basically avoiding the truth of what's going on. The Munchhausen is particularly infuriating. Both as in the way it's accusing the patient of making everything up, and in by proxy this is referring to parents who have a sick child with chronic fatigue and the authorities in quotes, "the authorities" accuse that parent of Munchausen by proxy and they take the child away. And this does happen in this country and in Europe. So I kind of keep emphasizing this, this is not a psychiatric disease. It is not made up. It is not depression. They may have depression, but that's not what's going on. And all people are at risk. This is not a white middle-class disease. Okay. And it's not a disease that only occurs in patients without other problems. Everybody can get this illness. It certainly gets more confusing if they have comorbid illnesses such as HIV or Hep C, but that doesn't change what I'm saying.

(00:20:19):

I told you I was going to keep saying it. So I'm going to say it again. Okay. It is not a psychiatric disease. The other term that patients are frequently told is that, 'Oh, you're just deconditioned. You need to go out and get more exercise.' And in fairness to the physicians, there's such a lack of understanding of what this illness is about and what's going on that they easily can fall into the mode of calling this a psychiatric or an anxiety disorder. 'And you just got to get back in shape, you know, get up and go out, come on, be tough, be strong.' The fact is, if we tell a patient with ME/CFS to go out and exercise, they will get worse. They don't just get tired, they get worse. That's called post exertional malaise, and I'll come back to that in a minute.

(00:21:08):

There's a group, there was a study in Europe, in the UK, called the Pace Trial which has been pretty much debunked. But out of that trial came these two other recommendations, cognitive behavioral therapy and graded exercise therapy. And they are equally unhelpful to patients, if not damaging. There is a difference between graded exercise therapy, which sounds good, but is not. Between the graded exercise and self-pacing, and that's really what we have to work on with patients. Self-Pacing really means you do what you think you can do, but don't go past a certain point and I can come back to that later, but we often use the patient's heart rate as a guide for the pacing. Post exertional malaise is the hallmark of ME/CFS. And as a physician or clinician or a provider, you need to never forget that, it is key to understanding the illness. And it is key to helping patients and discussing therapies that they can do.

(00:22:16):

Alright, let's get down to what it is. So this is a definition, a criteria definition that comes from the Institute of Medicine. That's been renamed The National Academy of Medicine. So it's basically the US CDC criteria. There are other criteria around the world, there is a Canadian criteria. They're all relatively similar. Unfortunately, people use different criteria which can confuse the research, but they're all pretty much the same. And this slide I do want to read and go over. So substantial reduction or impairment in ability to engage in pre-illness activity for six months or more. So basically what that's saying is the patient is not functional. If they were a hundred percent functional prior to illness, they may now be at 70% or 30%, and it lasts for six months or more. It can wax and wane somewhat over the six months, but it's pretty obvious. It's a chronic problem. This is not the fatigue that you and I may experience during our anxiety about COVID or election fatigue or whatever. This is a whole other brand of fatigue. And it's unfortunate the name chronic fatigue syndrome, I think, undermined the understanding of this illness. This is not because you didn't get enough sleep or not because you were a resident and you were up all night. This is a whole other ball game. Alright. Combined with the fatigue is this concept of post exertional malaise, which is fundamental to understanding ME/CFS. Although I will tell you now, I don't think we understand why the patients experience this, this is one of the great gaps in research. But it is extraordinary to see, it occurs not only with physical activity, but cognitive activity. I have patients who will tell me they can keyboard for half an hour, and then they're out for the rest of the day. And I will confess the first few times you hear these kinds of comments in history, you sort of say, wow, that doesn't make sense. Why would a half an hour of keyboarding makes somebody have to sleep four hours or rest in bed with lights out? But it's, it is accurate and true, and you hear it over and over. Patients who say they have to go shopping and an hour of shopping will knock them out for the next two days. So again, this is not fatigue the way you think of it, and this is not recovery the way you think of it. All of the patients have a sleep disorder or virtually all, unrefreshing sleep is sort of a vague description. Most patients will describe either trouble falling asleep and/or staying asleep. And regardless of how much they sleep, when they wake up, they do not feel as if they've slept well. And the last bullet in some ways in my mind is the most important, they need to meet the criteria that they have either cognitive impairment and/or orthostatic intolerance. So cognitive impairment in the ME/CFS world is also called brain fog. This is a patient who says when they're in a conversation, they can't find the right words or they lose track of the conversation. They read a book and they have to reread the same paragraph over and over. You know, in its most extreme forms, I've had patients get lost on their

way to driving somewhere. When you speak with them, if they are significantly ill with brain fog, their speech is slow, their thought processes slow, there'll be long pauses in the conversation. And the orthostatic intolerance is a huge issue, which I'm going to come to in a minute, which describes difficulty when standing, when vertical, with the blood pressure and heart rate. And it's probably a major cause of the cognitive impairment in terms of hypoperfusion.

(00:26:22):

Alright. Let's try to go over the post exertional malaise for a minute. I do want to emphasize again, I don't think we understand what's causing PEM, for me is that is the biggest mystery that still needs to be solved. Alright. So by definition, it's a worsening of symptoms after physical or cognitive effort. And I should emphasize it's after physical and cognitive effort that would not in any way impact a normal person, a healthy person. Like I said, this is keyboarding for half an hour, or this is getting up and making a cup of coffee for some patients. They're not making this up. It's very real. That PEM to make things even more confusing is not necessarily right after the activity. There's often this very puzzling delay. So they may go shopping on Monday and on Tuesday they're bed bound for two days. Why there's the delay? Why some patients take a day and some patients take three days to recover is not clear. The third bullet point is obvious. I'm trying to say I would challenge anyone listening to this who does not have ME/CFS, that you don't get tired or have post exertional malaise by walking or getting dressed or doing these other things. The showering complaint is classic. And for those of you that might be seeing patients, I would urge you to include it in your history of questions. Ask the patient how they feel when they take a shower. Most of these patients will say, 'Oh, I only take a shower once a week. It's too hard for me to stand. I use a chair in the shower. I can't lift my arms above to wash my hair' is a classic. What we know from the lab and from studies is that there's an impairment of aerobic metabolism and reduced anaerobic threshold. So for a healthy person who might exercise for 15 minutes before they develop anaerobic metabolism, these patients may exercise for three minutes and get their heart rate to 105 and then they're already into anaerobic metabolism, which is obviously less efficient. The orthostatic stress is a major part of this illness, as I mentioned before, and I believe a major cause for PEM, but we don't have the lab data for that. And most of all is this question of mitochondrial dysfunction. I think we all believe that, and we have evidence of it, but we don't understand fully what's going on. I suspect it's related to the initiating viral illness and subsequent auto immunity, but we just don't know for sure.

(00:29:14):

Again just focusing on the issue of post exertional malaise. So there are many other fatiguing illnesses. I've obviously named a few, lupus, multiple sclerosis, rheumatoid arthritis, and mono. Those patients do not really experience post exertional malaise, and their fatigue is a different quality. Except maybe for mono, and acute mono patients who say they're bed-bound for two months. The PEM is unique to this phenotype and by phenotype, I mean ME/CFS. But we also see it in Gulf War illness and long COVID or long haulers or post COVID syndrome. And I think that's a key point to understand, there are some similarities between these chronic post viral or post toxic exposure illnesses. Patients with SARS and MERS and Ebola do actually have a fairly similar CFS picture, but the numbers are very small and it's not well reported in research, but if you actually look at the literature, those patients report the same post

illness symptoms. I've said this already a dozen times about post-exertional malaise as being defining and disabling, but it's worth repeating every day because it is so key to the diagnosis and to the management.

(00:30:39):

Alright, let's talk a little bit about brain fog. I think the medical community struggles with this, as they do struggle with the ME term, myalgic encephalomyelitis. It sounds very neurologic, but then the patient sits in front of you and says, 'well, I have brain fog,' but they can talk to you and listen to you. So you sort of easily can slip into the, 'Oh, there's nothing wrong with this patient' mode that could not be further from the truth. I have patients who built companies, who ran businesses, who were elite athletes, who have PhDs and MDs, and they have trouble talking and keyboarding at the same time. They have trouble multitasking. They can talk to me and suddenly they just can't find the right word. All of the things I have listed here are typical complaints. And what I will warn you is that often in your initial interview, you might not see that. You have to basically believe the patient when they describe it.

(00:31:48):

Autonomic nervous system dysfunction is a huge piece of ME/CFS. And I think it is a major driver of the illness. And I want to emphasize here and I will emphasize it from here on in that all of these different pathologies interact with each other. Think of them as sort of bi-directional, they're cross-talking, so a hypoperfusion meaning a decreased blood flow to the brain and the core muscles increases the risk of experience of brain fog and cognitive impairment. It increases the occurrence of muscle weakness and fatigue because you're not getting enough blood flow. POTS, postural orthostatic tachycardia, POTS is a classic presenting symptom defined as a heart rate bumping up over 30 beats when you go from lying to standing. It is present. I find it in virtually almost every single patient. You just have to look for it.

(00:32:49):

Okay. Neural mediated hypertension, or orthostatic hypertension, is another common finding. It may be caused or related to the POTS, or maybe separate, you know, neurologically separate. There's also a form called hyper adrenergic POTS where paradoxically the heart rate goes up and the blood pressure goes up. All of these are disabling conditions. All of them make the patient miserable and all of them impact all of the other aspects of ME/CFS. Just picture yourself, how you would be, how your life would be, if every time you stood up to walk, you started to feel lightheaded or sweaty or foggy. And they don't always complain. This is important. Patients do not always tell you 'doc, every time I stand up, I get dizzy.' They might say, 'doc, every time I'm standing for three minutes, I start to get foggy.' I'll give you a pearl in terms of diagnosis and history, ask your patient, 'do you feel better when you're standing in line at the cashier in the supermarket, or when you're walking around in the supermarket,' virtually every patient will tell you I'm pretty good when I'm walking around and I'm miserable when I'm standing still. And that's orthostatic intolerance, their muscles are not contracting and their blood pressure is not being maintained. I wrote the symptoms there, but I think most of you understand, okay.

(00:34:23):

So these patients have symptoms in every single category of the review of systems. So, you know, for physicians seeing patients every 10 minutes or 20 minutes, this is your nightmare. Alright, these patients will complain of symptoms in every category. And that's part of the reason I think that you know, it's been an eye rolling disease in the past, but these symptoms are real. You may not see them. You may not be able to see it. You can't see light and sound hypersensitivity, but it's real. Patients come in with eye masks and ear blocks on and it's important to take this history and get this information.

(00:35:13):

So the point here that I'm making is that ME/CFS is a phenotype, right? It is a description of an illness. It's a diagnosis given when a patient meets criteria. It does not tell us how they got there. So I'm going to spend a couple of slides here trying to go over that and make a major point. So, as I said before you know, two thirds begin with a viral infection. I think everybody is familiar with that concept. The rest of this slide is not as familiar and I'd like to emphasize it. So it's become clear that a portion, by no means all, but a portion, a percentage of ME/CFS patients have hypermobility Ehlers-Danlos syndrome, not at all clear why. We can certainly speculate, but I don't think I have time to go into that, but it's worth noting this because you can diagnose this in 60 seconds in your office. And if you think about risk factors, it's another box to tick off. Two thirds have orthostatic intolerance or POTS. I should tell you, by the way, this slide is from my own practice. I took a month of patients and I counted every single visit and the diagnoses they have. A hundred percent of the patients had ME/CFS, these are percentages from that, from that count. Mast cell activation syndrome may not be familiar to many of you. It is a relatively newly understood entity, but look at that, 82% of the patients met criteria and had a diagnosis of mast cell activation syndrome. Similarly, and this was astounding to me when I first learned about it, is small intestine bacterial overgrowth, often misdiagnosed as irritable bowel syndrome, almost 90%. And I suspect it's a hundred percent and it's related to the leaky gut that can occur, the increased permeability. And similarly auto-immune disease characterized by the findings of abnormal antibodies.

(00:37:15):

So how do you figure all this out? As we all learned endlessly in medical school, it's about history, but it's never been more true than for patients like this. My history taking has evolved over the last eight years to the point where I now literally start during pregnancy. I ask some questions that sound crazy to patients, but it's unbelievable what you learn. And I have really combined it all into the history of present illness. In other words, everything seems relevant. So I just put it all together and that's the point of that second bullet. You have to think big, don't ignore anything, tell the patient don't leave anything out. You're looking for clues.

(00:38:02):

So the physical exam is most often benign. Especially if it's the five to 10 minute exam with the patient already undressed in the exam room and lying down. So you haven't seen the patient walk or anything like that. You know, and they seem fine. Okay. But you run the risk of missing all the key things, if that's all you do. Alright. So the first thing here for the dysautonomia, which includes the POTS and orthostatic intolerance, you have to do orthostatics, and doing a 30 second orthostatic like I used to do back in the

day is not going to give you the answer. The NASA Lean Tests. You should Google. That is a poor man's tilt table. Basically patient has orthostatics done for 10 minutes while leaning against the wall. You will not believe what you find.

(00:38:53):

Alright, minute two and three may be fine, but suddenly at minute seven, the patient is diaphoretic and pale and the blood pressure is 90 over 40 and their heart rate is 130. I use this test all the time and I have patients do it at home constantly so that I can titrate medication. It's one of the most important tools in my care. For hypermobility EDS, you can do a Beighton score and you can just look that up on the internet. It's very, very easy to do. It's a nine point test and you can do it literally in 60 seconds. I put in the word about history because you want to find that have you dislocated joints, are you hyperflexible, did you, did you love gymnastics and cheerleading and things like that, but did you get injured easily? Those are all clues, hints, in your detective work. Mast cell activation syndrome is a clinical diagnosis based on what the patients tell us, how did they react to things? Very often, there's a lifelong history of minor symptoms or 'doc, I had allergies as a kid, and I constantly had a runny nose and sore throat and ear infections, and they just thought it was nothing.' And then something tips them over the edge and their mast cell explodes, and they begin to have symptoms. So history is a major piece. It can be diagnosed with labs, which I'll come to in a minute.

(00:40:21):

So I'm going to run through some testing that I do. This will look outrageous to some of you. I would argue that it's comes from this notion of cast a wide net and also that when I see these patients, they've been sick for so long and seen so many doctors that I really dive in right away. I don't do the classic medical approach of stepwise, because I just want to get to the answers quickly. So I run panels to assess their immunologic status. Many, many of these patients are IgG deficient or IgM deficient. Many puzzlingly have B-cell CD19 counts that are below normal. I run viral serology in the herpes family in an effort to see if the numbers suggest reactivation. And I run the usual hormone panels that you might do, plus some others. I find the saliva cortisol test, which I never knew about when I was doing HIV to be remarkably helpful because it's measuring free cortisol at four time points during the day. And many of these patients have a disorder of the hypothalamic pituitary adrenal axis.

(00:41:37):

I run the bacterial antibodies because as I mentioned, mycoplasma and chlamydia are common findings. The strep is there because that can cause autoimmune disease, which can end up presenting as the CFS phenotype. This is what's run for mast cell. There's many other tests, but this is the typical first panel. It's a very difficult panel to get properly run and processed, but it's important. I do tick borne disease testing, if there is clear risk in the history. You need to take the history and you need to find out were they a hiker or a camper? Did they go hunting? Did they have pets? Were they scratched by their cats? Did the cats have fleas? Did the fleas bite the patient? All of that is relevant to this. And then I do run the vitamin levels and remarkably find low levels in many of our patients, probably related to the frequency of SIBO.

(00:42:32):

These are additional labs I run. I'm not saying I run all of these the first visit, although I do a lot of them. The advanced panels here are are extremely helpful with the exception of Celltrend and Cunningham, they're all available through Quest or LabCorp. Celltrend is a incredibly important panel to me from a lab in Germany that looks at 11 antibodies related to autonomic nervous system dysfunction. I do SIBO testing on every single patient because of the incidence that I want to prove it. And I want to see if it's hydrogen and or methane. And I always do the three-hour tests, even though some of the labs push for a one hour or two hour because our patients have a disorder of motility. So they're going to be slower in demonstrating the positivity. And as I mentioned, the NASA lean test, I do constantly.

(00:43:27):

So in that first visit, I will often have made some diagnoses and will begin some treatment ideas based on either suspicion or diagnosis. But obviously wait for more information before moving on to others. So these are the easy first things. As I've said, most patients have orthostatic illness. So the fluid, salt, and compression are helpful. I'm not sure I'm going to have time to go into low dose Naltrexone. That's something maybe we can discuss in the Q&A, or afterwards by email, but it is an extraordinarily important treatment opportunity. Interestingly it was discovered in New York by a doc treating HIV patients. So I was using that before. It is a remarkable drug, remarkable in how effective it can be with pain, gut motility, immune modulation, and brain fog. And then if I'm suspicious of mast cell activation, I will give a trial of treatment during the couple of weeks I wait between visits to get the labs back. And it can be amazing how these simple over the counter drugs will make a patient feel remarkably better.

(00:44:47):

So this is just a quick list of other treatments. I probably shouldn't spend too much time on it. There are numerous drugs for orthostatic intolerance and POTS. The treatment of SIBO is increasingly complicated because it's increasingly difficult to prevent recurrence and heal the leaky gut. So I use many other drugs besides Cifaxim or Rifaximin. The use of antibiotics is pretty much driven by the lab results and the history, sometimes I'll do an impure trial. Mast cell activation, these are additional drugs. I'm sorry, this too much here. And then for the auto immunity, the LDN is helpful, and then some of these other drugs are used as well. Immune modulation also refers to the use of intravenous gamma globulin, among other things.

(00:45:37):

Alright. So at this point, the physicians in the audience who are working in the world of managed care have stopped rolling their eyes, and their headache has gotten worse because how am I going to take care of these patients in 20 minutes? And I agree with you, you can't. That's the answer. Alright. My initial visit with a patient is two hours. So this is a suggestion though, because the real world is managed care. And I have some colleagues who do this. I will tell you that most of them have not felt it's successful, but it's what you got to do. So the initial visit, maybe you only focus on history and the second visit, which you try to bring them back quickly, like two weeks, you do your physical exam and start gathering data. And then third visit, you can begin to try to manage them. This is work that takes a

lot of time. Okay. We need people, physicians to have the time, our healthcare system is not allowing us to do that.

(00:46:38):

So one of the objectives was to talk about treatment advances. It's a sort of depressing objective to try to answer since there's no funding, as I showed you in the earlier slide, there's been very few discoveries. Alright, the NIH and the CDC are slowly waking up but the dollars are sort of a joke. And so most of the research has come from private foundations and private advocacy groups. One of them is Open Medicine Foundation, which I work with. I'm not trying to single them out, but just using them as an example. And they have set up a collaborative research center between Stanford and Harvard, which is pretty sensational and has done some pretty amazing bench work in terms of looking for biomarkers and metabolic abnormalities and metabolomics, as well as clinical stuff.

(00:47:34):

And you know, the third bullet is describing some of that. I would say, and I'm not going to get into it because it's not enough time, and it's controversial, is that there is a recognition, I don't know if I'd say discovery that in a subset of ME/CFS patients, particularly those with hypermobility, they develop cranial cervical instability, which is basically compression of the brainstem, which ends up as a major, as you can imagine, a major cause of illness. And my big takeaway here is that everything I'm describing causes chronic inflammation, by that I mean infection, auto immune disease, mast cell activation, they're all sources and causes of chronic inflammation. And these patients live in a chronically inflamed state, and that is probably related to or maybe related to the development of some of the connective tissue disorders or the worsening of those disorders.

(00:48:36):

Based on that, and I'm nearing the end here, for myself and what I try to talk to other physicians and groups about is that this point that ME/CFS is a phenotype, it's a presentation. And the question is how do the patients get there? You know, and it's a multiorgan, multipathogen driven syndrome that creates chronic inflammation and immune activation, and that ends up presenting as ME/CFS. If we don't look under that label for all the things I was describing, mast cell, dysautonomia, et cetera, we're not going to help our patients.

(00:49:19):

So this is a scary slide that I put together with another physician, a neurologist, to try to show what I'm talking about, what we're talking about. The point here is that these seven entities or pathologies occur, we know they occur. But more importantly, they all interact with each other. So you have mast cell activation, that's going to make more inflammation, more inflammation is going to increase the connective tissue disorder and damage that might lead to a craniocervical instability. If somebody has some brainstem compression, that's gonna make everything explode. So it's very important to see this. This is a little bit different from the way most of us have thought about medicine and healthcare and

pathology. And you can put in this center circle or oval, you can put ME/CFS, you can put Gulf War illness, and I'll propose you can put post COVID syndrome.

(00:50:29):

So this gives you information with the Department of Health. And these are some useful websites and tools for physicians and clinicians taking care of these patients. The first one is the Institute of Medicine information that I described. It's actually very, very good. It's a 300 page document, not only goes into diagnosis, but workup and management. The second bullet is something I've worked on with a couple of dozen other physicians. It just went live at that website, and it's basically our effort to educate and put the information out there. And I would urge you to take a look at that. The third bullet tells you how to do a lean test. It's really easy. I guarantee you'll be astounded if you start doing it in some of your patients. And the fourth bullet is just for more EDS information. I don't know about everyone in the audience, but for me, EDS was a whole new world, as was most of this stuff for me. So I wanted to end with this clip. I don't know if any of you, probably you're all too young to have seen this. This comes from 1989. It's supposedly on a comedy show, but it is profoundly accurate and painfully true. And the the writer of this also had ME/CFS. Okay, Mark.

(00:52:07):

Dr. Bud. Yes. You probably don't remember me, but you told me I wasn't sick. Do you remember? You told me I was just getting old. Sorry, I really don't remember. Maybe you're getting old. Dr. Bud. I really am sick. I have chronic fatigue syndrome, that is a real illness. You can check with the Center for Disease Control. Oh, well, I'm sorry about that. Well, I'm glad, at least I know I have something. I'm sure. Well, nice seeing you. Not so fast. There were some things I have to say. There are a lot of things that I have to say, words can't express what I have to say. What I went through, what you put me through. I can't do this in a restaurant. Good. But I will. Louis who is this person? Look, Miss. Sit. I sat for you long enough. Dr. Bud, I came to you, sick. Sick, and scared. And you dismissed me. You didn't have the answer. And instead of saying, I'm sorry, I don't know what's wrong with you. You made me feel crazy. Like, like I had made it all up. You dismissed me. They made me feel like a child, a fool a neurotic who was wasting your precious time. Is that your caring profession? Is that healing? No one deserves that kind of treatment, Dr. Bud, no one. I suspect that I've been a man I might have been taken a little bit more seriously and not told to go to a hairdresser. Look, I am not going to sit here anymore. Shut up Louis. I don't know where you doctors lose your humanity, but you lose it. You know, if all of you at the beginning of your careers could get very sick and very scared for awhile, you'd probably learn more from that than anything else. You better start listening to your patients. They need to be heard. They need caring. They need compassion. They need attending to, you know, someday Dr. Bud, you're going to be on the other side of the table. And as angry as I am, and as angry as I always will be, I still wish you a better doctor than you were to me.

(00:54:49):

And now we will also open it up for questions. So we have a handful of questions in here. We do have one comment from a participant saying, I feel so heard, and I'm brought to tears after 4.5 years of

exhibiting almost every symptom of crawling on the floor to get to the bathroom, I struggle intensely now to feel heard regarding my thoughts on why I am unwell. And so thank you so much for sharing your thoughts on this presentation. One of the questions we do have is how far off are you from conducting a repurposing type trial with a sponsor? Is it a case of a multitrial arm protocol, or are we still far off from understanding the particular sub phenotypes that this picks up, including patients with hypermobility or CTD?

(00:55:44):

I'm not quite sure I understand the question, repurposing of drugs? Is that what this person's asking?

(00:55:50):

It's typed into the chat. Yeah. How far off are you from conducting a repurposing type trial with a sponsor? Is it a case of a multi trial arm protocol?

(00:56:04):

So I'll probably answer it a little more generally than the person is asking. So it's been virtually impossible to get big pharmaceuticals to do anything in terms of chronic fatigue drug trials, either the drugs are already out there, so why would they spend money on another trial for an FDA indication? And up until recently at any rate, big pharma has sort of avoided any association with chronic fatigue because well, in the same way that most of organized medicine has avoided it. That said because of the work of groups like Open Medicine Foundation and ME Action, and some of the other advocacy groups, there are plans for trials and efforts to get private funding. I'm personally familiar with quite a few of those and they are moving forward. We will be looking at some of the biomarker type research coming out of Stanford, more work looking at the true incidence of craniocervical instability, and in the broader way connective tissue disorder and how it relates to the onset pathology of chronic fatigue syndrome. So I think it's happening, but it needs money. And right now that's all private money. The government just is not really kicking in.

(00:57:29):

We have another one here. What dose of naltrexone do you recommend as a starting dose?

(00:57:35):

So I usually start with between 0.5 milligrams and 1.5, depending on the patient. It's a soft decision, if the patient, if they're nervous about drugs and many of these patients are very sensitive to medication, I'll start with a lower dose. If they already have a sleep disorder that is major, LDN can affect sleep. So we'll start low, but most of the time, 1.5 is fine and we titrate up over a period of weeks to 4.5. That's a target dose. It's not necessarily the final dose. And one more thing I should add is if the patient has tolerated it, and almost all do, give it months, give it two to two to six months before you give up on it. It's an extraordinary drug. It really helps a lot of people.

(00:58:28):

Here's one, if someone has a CYP 450 or mutations that suggest metabolism of drugs being different, can one still take LDN?

(00:58:41):

Yes. I've not seen any CYP SNP issues affecting LDN. And I'm not actually sure if we know that information for naltrexone, I'd have to check that myself. Since we taper off, I mean, understand that the usual dose of naltrexone given to block opioid receptors in people using heroin is 50 milligrams. We're using a dose of a 10th of the dose, so I'm not sure this is going to be an issue.

(00:59:13):

And one is, can you describe mast cell activation syndrome?

(00:59:19):

Well in 25 words or less, it is itself a multi-system multiorgan disease. Mast cells are everywhere in our body, when they are disordered they are trigger happy and they degranulate. And when they degranulate, they release over 200 cytokines or chemicals. Since mast cells are everywhere and since the cytokines circulate, you have your nightmare of nightmare of nightmares, review of systems patient who has things that make no sense. Classic typically they'll say I can only eat three foods. Everything else makes me sick. Or I walk into a department store and I suddenly get brain fog, headache, and want a puke. It is a challenging, challenging disease, but once you learn about it, you will be amazed how many people have it and how much you can do to make them better.

(01:00:19):

Thank you for that. We have questions just kind of keep rolling in. Some of them are a little bit briefer than others. So I think if you have a more detailed question we're going to have you possibly reach out to Dr. Kaufman directly with his email. One of the more brief questions is how do you discern between ME/CFS and fibromyalgia?

(01:00:44):

So fibromyalgia pretty much has its own definition in terms of focal areas of pain or tenderness, point tenderness. Fibromyalgia patients usually do have fatigue. Honestly, in my practice, I don't think I see patients who only have fibromyalgia. They all have a spectrum of illness. So to me, ME/CFS is a spectrum illness, can they see me Mark? Yes. Okay. So fibromyalgia is on the left, but it's got some of the characteristics of ME/CFS. Full-blown ME/CFS is over here, but it's a spectrum. So I don't make a huge distinction.

(01:01:33):

Which specialties if any, are appropriate to refer potential CFS patients to?

(01:01:42):

So that's a great question. So I'm a general internist, although I cut my teeth, so to speak with HIV, and I think in a way that was enormously helpful preparing me for ME/CFS. I would say to you that with a few exceptions, well I'll use the the Clinician Summit, that US ME/CFS Summit, every doctor in that group I think is an internist or family practitioner. And the point I'm making is that as internists and family practitioner, we're sort of trained to have a wide net, to think multi-system as opposed to most cardiologists who might just think of heart and most neurologists who think of brain, and sadly, it's been very, very difficult to find sub-specialists to help with these problems. So, you know, most neurologists just don't sort of get it. I don't mean to say something bad, but that's just what I've found and similar with the other specialties. So I would say generalist first, if you can find a good neurologist, I think that would be incredibly helpful.

(01:02:59):

Okay. Thank you. We have many, many questions in the chat, and I think just in the interest of time, unfortunately, we are not going to be able to get to all of them. I would encourage everyone who is on the call, I put Dr. Kaufman's email address into the chat box. You can ask your questions directly to him. We have a fair number of providers, Dr. Kaufman, who share their experiences and the same sentiments along the lines that they weren't taught this in medical school. And it's really quite unfortunate that is the case. Many people are very grateful for the presentation, they feel seen and heard. Thanks to this presentation legitimising the syndrome. Can you share what over the counter drugs you suggest for mast cell activation syndrome?

(01:03:52):

Sure. Histamine one receptor blockers, which are your classic anti-histamines. Claritin, Alegra, Zyrtec, Benadryl, of course, but that tends to make people sleepy. I tend to use Alegra because it seems to have the least side effects. And then H 2 blocker, histamine two, is Pepcid. Fomitadine, I used to use Zantac, but that's taken off the market. It's hard to find fomitdaine, because it looks like it has an efficacy for COVID. So it's been sold out everywhere. So H 1, H 2 blockers, and then Quercitin is a flavonoid, plant flavonoid, over the counter that stabilizes mast cells and decreases their degranulation.

(01:04:32):

Okay. Alright. Well, thank you so much, Dr. Kaufman. I can try and compile these questions. And again, if you are a provider who would like to speak more directly with Dr. Kaufman, you can email him directly. I will also make the slides from this presentation available to everyone, as well as the flyer for the upcoming M E course that will be delivered by the department of health here in New York state. And it will focus a little bit more on some of the hard science and research behind chronic fatigue syndrome as well. Okay. Thank you very much. Yes. Thank you so much. And everyone, please have a great afternoon.

[End]