

December

Hi, my name is December. I'm 29 and I was diagnosed with myalgic encephalomyelitis/chronic fatigue syndrome or ME/CFS a week before I turned 26. I was always kind of a sick kid. I never had a quarter in school where I didn't need to take a day or more off due to illness. At the time that was trucked up to a poor immune system. As I got older, I think professors and classmates thought I was being lazy and skipping class rather than being sick. If I had any illness, it would take me out for a lot longer than the average person. I would just stay in bed and barely be able to do homework. Missing a few days here and there was enough to make me look for a doctor or think that there was something wrong. Looking back, these sick days were likely the result of having undiagnosed ME/CFS.

In March of 2020 I got infected with COVID-19 and that triggered my ME/CFS. I wasn't able to clear the COVID so I had a fever on and off for about a month. It would go down with Tylenol and then come right back up. Even after the fever stopped, the pain in my neck and my back was unbearable to the point that I couldn't stand up more than several minutes unaided. I couldn't leave the house for very long. I kept thinking well you've been in bed for months, so you're unconditioned, you have to build your strength back up. And I would try to push myself a little bit and every time I did, I would have a massive backlash. I would just be exhausted the next day. It would feel like I ran a marathon and all I did was go to the grocery store. I would have all this pain in my back and my hips like I had been beaten up.

I had a lot of brain fog. I would lose words or walk into a room and forget what I was looking for. I couldn't remember simple instructions without writing them down. I couldn't have conversations because I would lose the start of a sentence by the time I got to the end. At my absolute lowest, I couldn't wash my hair by myself. I was in too much pain to raise my arms for that long. The worst part was that I couldn't get better with sleep. Some days I would sleep for 10 or 12 hours and wake up and still feel exhausted. I saw a rheumatologist who ordered X-rays, MRI, CT scans and none of them showed anything abnormal. It's pretty scary to know that something is wrong and have no way to prove it. She was very terse and diagnosed me with fibromyalgia which is largely untreatable. The doctor didn't have any advice for making the pain better. I got the feeling she thought I was malingering.

So I went to a different doctor. Thankfully, I saw a second rheumatologist at Johns Hopkins Hospital who specializes in chronic fatigue. He diagnosed me with myalgic encephalomyelitis/chronic fatigue syndrome. And because rheumatological diseases are buy one, get two free, he also diagnosed me with postural orthostatic tachycardia syndrome or POTS and Ehler-Danlos syndrome. That seems like a lot but they all interact with each other. Having EDS means that my collagen isn't formed correctly, so the valves in my veins aren't strong enough to keep the blood in my upper body when I stand up. When I stand up I get incredibly weak and dizzy, which is the POTS. Because I have POTS, standing up makes my heart rate go through the roof. Stand up, get low blood pressure and my heart rate hits 140 BPM just from standing. That means my body is working harder which triggers post exertional malaise from the chronic fatigue. And the fibromyalgia is just the icing on the top that makes all the pain a whole lot worse.

So these disorders really fit together and feed off each other and I have to treat all of them together. It took a long time to suss out my body's new limits and what will set off the post exertional malaise. I used to be able to go on hikes and now I have to sit down and rest every quarter mile or use a cane. I've had to figure this out by trial and error. Oh, can I go to the grocery store and go out to dinner with my family? Can I do laundry and good work? If I guess wrong, I get knocked out for a day or more. The thing with ME/CFS is that it's not just physical labor that causes fatigue, it can be going out to the movies or just hanging out with friends. It can be completely mental and not at all physical. I took the GRE and that took about as much out of me as walking a mile. I took it and immediately went to sleep. Anything that takes energy can leave me with this post exertional malaise.

It took me a really long time to figure out where that limit was and how not to cross it. I will have to cancel plans because I'm too tired and I know if I exceed my limit, I'll be a mess the next day. Try explaining to your boss well I can't come in because I overworked myself. So I have to prioritize my work and be strategic about how I use my energy. If I know I have work the next day, I can't hang out with friends or do anything the night before. It's difficult to come to terms with having the energy of a 90 year old in your 20s. I think the hardest thing about having ME/CFS is the number of people who don't believe it exists. You can't point to a lesion or tumor and say this is the cause of my problem. A lot of people think it's an excuse for laziness. When you hear chronic fatigue, you assume it's just being tired but it's so much more than that. It's really and truly a bone deep exhaustion that prevents you from doing much of anything, including thinking.

It's not as simple as just going to bed at a regular time. I can't push myself through it the way that someone with a sprain can still walk on a sprain. It's a condition that impacts everything about how I live my life. I've been really fortunate with my doctors. I now have a medication regime that helps. I take atenolol and midodrine for my blood pressure. The midodrine helps me to stand and walk unaided for longer. I go to physical therapy once a week to strengthen my muscles. The muscles keep my ligaments in place so my joints aren't slipping as much from EDS. Now I can go to physical therapy, lunch with friends, and work in the same day. I'm able to walk longer even if I still need my cane sometimes. Right now most of my symptoms are managed and I'm finally at a point where I can start looking at my future.

Katie Walters

Myalgic encephalomyelitis took my bones when I was sleeping, crept in while I was resting, breathing deep against my pillow or the paper of the books I could no longer read. It grew inside me, drank my mitochondria like wine, took an angle grinder to my spine and wore me away like twilight. I got sick at uni in a small room where nobody could hear me cry or permit me to, my nervous system quit while I was working in the library, while my legs were burning like the oven door against my forearms and the stove top where I made myself curry for the first time. Independent, embryonic. I was 19. November was cold that year and January was colder, as fresh and new as hours and as stark and clean and painful as my fading autonomy. I tried to crystallize it in an essay or a poem in biro ink and off brand toothpaste like if I wrote it right, I could write myself well.

And when the rain fell in February, I fell at the supermarket and at the train station and on the stairs, swallowed the stones in my throat, chose not to dare question why it was that I kept falling and got back up. Because strong people don't get sick, you stick it out, you do not quit. And when the elevator is out of service, you use the stairs. I never knew how high the curb was until I could not climb it. We searched for my bones in decomposing diagnoses, degrading medication on my tongue, took blood tests of my bloodlines and on the coastline tried to calcify my insides strong again. Put our hands in the wet sand to build a tibia. Shoot my sternum like a castle, clavicle and mandible and cranium. Starlight and seafoam and gone. My bones are in the Rotunda Museum under the skin of the Gristhorpe man. We walk where he walked and I walk no longer, pressed behind glass; my skin tight as leather, my bones are in the limestone cliff's edge grown from sediment, calcium carbonate, cycling infinite ground down to shale.

My bones are food for minke whales and I am lying in bed and ugly like a princess, limp and formless and rolled out to sea. I am blue badge on double, yellow as Pepsi Max and heavy metal, flat on the back seat, looking through the windscreen where the starlings will dance until nightfall. My bones are a murmur of starling, dark and undulating, the shapeless shape of nature, inexplicable, impermanent and strong. And I will not be another bleeding tragedy, another DWP dispensability, too many of us have already died. We build on their bodies, defiant. I am driven by duty and fury and I want you to know that I am broken because they could not contain me whole. Chronic fatigue took my bones and they grew fragmented, transcendent, and new. I am F fragile, grounded, bound by dropped curbs and sick insides. But my bones, oh my bones are the sky.

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Thank you so much December and Katie for sharing your firsthand account and your incredible poem with us. I'll also post a link on our website to a video recording of another of Katie Walter's poems which is also accompanied by just lovely music. Thank you again.

Erin Allmann Updyke

Yeah. Thank you so much.

Erin Welsh

Hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allmann Updyke.

Erin Welsh

And this is This Podcast Will kill You.

Erin Allmann Updyke

Welcome to this episode.

Erin Welsh

As promised, we are taking on myalgic encephalomyelitis/chronic fatigue syndrome this week.

Erin Allmann Updyke

Yeah.

Erin Welsh

I hope we don't have to keep saying, we're just going to say ME/CFS, right?

Erin Allmann Updyke

Yeah, ME/CFS.

Erin Welsh

Okay.

Erin Allmann Updyke

And we can talk about the issues with the name. Are you going to get into that like controversy about the name?

Erin Welsh

A little bit.

Erin Allmann Updyke

Okay.

Erin Welsh

Like I'm going to mention it. I think it's like a longer conversation than probably we're going to have here.

Erin Allmann Updyke

Yeah.

Erin Welsh

But definitely it's something that I want to get into.

Erin Allmann Updyke

Yeah. So it's going to be, as we always say, a big episode but I am glad that we are covering it. I was very nervous to cover this episode.

Erin Welsh

Me too.

Erin Allmann Updyke

But we are going to do our best. And I learned a lot in researching for it, so hopefully people get a lot out of it.

Erin Welsh

Yeah, I agree. I think both this one and the long COVID episode from last week really have made me think a lot about diseases and how we classify disease vs health and what is illness vs condition vs all of these different things that are like very fluid.

Erin Allmann Updyke

Yeah. Before we can get into all of that though-

Erin Welsh

Yes.

Erin Allmann Updyke

It's quarantini time.

Erin Welsh

It is. It is. What are we drinking this week?

Erin Allmann Updyke

We're drinking The Understatement.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yep. It'll make a lot of sense I think when we talk about the name chronic fatigue syndrome especially.

Erin Welsh

For sure. And in The Understatement, it's based on an existing cocktail. I have to pull up my text to you here because I have forgotten already everything about it. And it's 10 in the morning for me so we're not drinking.

Erin Allmann Updyke

Yeah.

Erin Welsh

Oh, it's based on a real cocktail called the Hugo Spritz and it has Prosecco, elderflower liqueur, soda water, fresh mint. It sounds delicious.

Erin Allmann Updyke

I'm excited to try it.

Erin Welsh

And to be honest I love a non alcoholic Prosecco. I think it's wonderful.

Erin Allmann Updyke

I don't think I knew that non alcoholic Prosecco actually existed.

Erin Welsh

Yeah.

Erin Allmann Updyke

I was just excited about how many non alcoholic like elderflower syrups exist because I've had some that are really good.

Erin Welsh

So many. So many, yeah. I bought non alcoholic Prosecco last year for it to make a quarantini because I was like I don't want to open a bottle of Prosecco and then just have it be-

Erin Allmann Updyke: There.

Erin Welsh: Also I take pictures at like 10 in the morning.

Erin Allmann Updyke: Right.

Erin Welsh: Anyway-

Erin Allmann Updyke: You need that lighting.

Erin Welsh: Yeah, exactly. We will post the full recipe for our quarantini and our non alcoholic placeborita for The Understatement on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) as well as on all of our social media channels.

Erin Allmann Updyke: So check us out there.

Erin Welsh: Check us out.

Erin Allmann Updyke: On our website, you can also find so many goodies. You can find transcripts from all of our episodes, you can find links to our Goodreads list, to our [bookshop.org](http://bookshop.org) affiliate account, to Bloodmobile who does our music. You can find merch, you can find our Patreon. You can find sources from all of our episodes. Wow. I think I got most things.

Erin Welsh: That's pretty good. Firsthand account form, did we talk about that?

Erin Allmann Updyke: Firsthand account form, didn't say that one. There you go.

Erin Welsh: There we go.

Erin Allmann Updyke: So check it out, [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com).

Erin Welsh: Yes.

Erin Allmann Updyke: Erin?

Erin Welsh: Is there anything else that we need to... Business?

Erin Allmann Updyke: Not that we know of.

Erin Welsh: Awesome. Rate, review, subscribe.

Erin Allmann Updyke: Rate, review, subscribe. Oh we need to start saying that more.

Erin Welsh: We do.

Erin Allmann Updyke: We've been told.

Erin Welsh: It really does help us out though.

Erin Allmann Updyke: It does.

Erin Welsh: So please, if you enjoy the podcast, please let us know. Rate, review, subscribe, etc.

Erin Allmann Updyke: Yeah. We really would appreciate it.

Erin Welsh: Let's get started, let's get started.

Erin Allmann Updyke: Okay.

Erin Welsh: Right after this break.

TPWKY: (transition theme)

Erin Allmann Updyke: Myalgic encephalomyelitis or chronic fatigue syndrome. To even begin, we have to define what ME/CFS actually is and to do that is difficult. The definitions of ME/CFS have changed over time and I'm sure, Erin, you'll kind of get into some of this, a lot of this.

Erin Welsh: Oh yeah, oh yeah.

Erin Allmann Updyke: And honestly it's probably not without controversy, like what the true quote unquote "definition" is even at this point. But what I'm going to do right now is go over one specific set of criteria that were the result of kind of like a big analysis I guess of all of the various criteria. And this is from a 2015 Institute of Medicine report. And these are the kind of diagnostic criteria that we use to define CFS or ME-

Erin Welsh: Okay.

Erin Allmann Updyke: When someone presents to the clinic. What I will say is that this specific set of criteria is mostly used it seems in clinical research. And so that's why it's the one that's most often cited in all of the papers that I'm reading. There are a lot of other diagnostic criteria out there that have different symptoms that we'll take into account and we'll get into all of that in a little bit. But like what the heck, for someone who's never even heard of ME/CFS, they're like literally what are you talking about, Erin? Let me tell you.

So these criteria, the diagnosis for a person to meet criteria for ME/CFS includes quote, this is all a quote: "A substantial reduction or impairment in the ability to engage in pre illness levels of occupational, educational, social, or personal activities that persists for more than six months and is accompanied by fatigue, which is often profound, is of new or definite onset, has not been lifelong, and is not the result of ongoing excessive exertion and is not substantially alleviated by rest. Along with post exertional malaise," we'll get there, "and unrefreshing sleep and then at least one of cognitive impairment or orthostatic intolerance."

Erin Welsh: At least one of those two, okay.

Erin Allmann Updyke: Yeah. So either cognitive impairment or orthostatic intolerance, sometimes both.

Erin Welsh: Okay.

Erin Allmann Updyke

So what does any of that actually mean? ME/CFS is a chronic, sometimes lifelong but certainly months, years, years long neurologic disorder that results in significant fatigue and a lot of other symptoms, many of which we don't have a good handle on. That's kind of like what it means I guess. It's really hard to define because of how many different symptoms can be associated with it. And one of the things that this list of criteria tell us, whenever we have a list of criteria like this is that there's no test for ME/CFS. There's no thing that we can do to say definitively ah, what you are suffering from, person who came to the doctor's office, is ME/CFS. This is what's called a clinical diagnosis which is something that's not weird or novel for a lot of listeners of this podcast. A lot of things that we've covered there's not a single test for, there's a collection of criteria. Think about migraines.

Erin Welsh

Right.

Erin Allmann Updyke

There's a number of criteria that you have to meet to have a migraine disorder. So ME/CFS is a neurologic disorder which someone has if they're meeting all of these criteria. But while these criteria highlight some of the symptoms like profound fatigue, like unrefreshing sleep, so someone even if they're able to sleep, they're not getting good rest from that and they wake up not feeling like they've actually rested. Oftentimes there's big disruptions in the sleep cycle. And post exertional malaise, which we talked a little bit about in our long COVID episode because we see that sometimes with long COVID, which means if someone does try to exert themselves despite feeling fatigued, if they go beyond whatever their functional ability is, within 12 to 24 hours they will feel significantly worse, that fatigue will be substantially worse. And it sometimes takes a really long time to then get back to feeling better.

And then cognitive impairment or that brain fog that again we also talked about in long COVID. Or orthostatic intolerance, which we also mentioned, is this thing that happens when your autonomic nervous system is not able to regulate itself well. So that means people might have heart rates that jump 20 or 30 beats per minute when they stand up, they might have blood pressures that tank when they stand up or when they sit down. And so that can lead to a lot of things like dizziness, lightheadedness, even loss of consciousness. This is a lot of different symptoms and it's not even all of the symptoms that are associated with ME/CFS.

Pain is another really common symptom that's associated with ME/CFS. And this can be muscle pain, it can be joint pain, sometimes it can be swollen or tender lymph nodes. We can also see issues with temperature dysregulation, the feeling of palpitations or chest pain, people could have nausea or diarrhea or constipation. You could even have sensory changes like new sensory sensitivities that never existed before. It's a really long list. And one of the biggest critiques even of the name CFS, and I know that you'll get into this, is that the name chronic fatigue makes it sound like it's just being tired.

Erin Welsh

Right. I'm tired. Oh chronic fatigue, you have chronic fatigue? Oh tell me about it. I know what it's like to be tired. I've got a toddler at home or whatever.

Erin Allmann Updyke

Exactly. Exactly, Erin. Oh sorry you're tired. Me too, who isn't?

Erin Welsh

Right, right, right.

Erin Allmann Updyke

And so for this one what I want to do is highlight another quote from this Institute of Medicine report from 2015 because I think it kind of sums up one of the issues with just the idea of fatigue and what it means in the context of ME/CFS. So I'm going to read another quote from this. Quote: "Unfortunately the word fatigue does not convey information about the cause, severity, or chronicity of fatigue or its impact on functionality. Although fatigue is a common experience, it has no unique physiological explanations or objective markers. ME/CFS patients often have a level of fatigue that is more profound, more devastating, and longer lasting than that observed in patients with other fatiguing disorders. In addition, fatigue in ME/CFS is not the result of ongoing exertion, not lifelong, and not particularly responsive to rest." End quote.

Erin Welsh

I think the other objection or like fair point that I've seen made about the name chronic fatigue is that it reduces this incredibly diverse constellation of symptoms down to one thing. And there are some people who would say actually my pain is much worse than the fatigue that I experience or on a given day fatigue could be the biggest thing or pain could be the biggest thing or the sensory changes could be the biggest thing. And so it just kind of like oversimplifies this condition that's incredibly complex and incredibly poorly misunderstood and says extreme tiredness.

Erin Allmann Updyke

Right.

Erin Welsh

And that's like not it.

Erin Allmann Updyke

Exactly, exactly. It's a whole range of neurologic and other symptoms that we don't really understand but are all very real. And so to boil it down to just fatigue, just tired, like it is not accurate nor is it helpful, right. So there's also the critique of like we don't name most diseases after a symptom, right, and so that's kind of interesting as well.

Erin Welsh

That's true.

Erin Allmann Updyke

Yeah. So that's why some people prefer the term myalgic encephalomyelitis.

Erin Welsh

Right.

Erin Allmann Updyke

There are other people who object to that because encephalomyelitis means that you have inflammation specifically in the brain and the myelin, which is the sheaths that cover our nerves. And we see some evidence of inflammation, we'll get into it, but perhaps not in everyone. Is it truly the inflammation? So it's just a little bit like some people say that it's not perfectly accurate.

Erin Welsh

Right.

Erin Allmann Updyke

But others argue that it sounds a lot more medical which makes it sound more quote unquote "legit" so maybe people take it more seriously rather than just being tired.

Erin Welsh

But then that's really frustrating because we should take things seriously whether or not they sound medical.

Erin Allmann Updyke

Shouldn't we, shouldn't we, Erin?

Erin Welsh

The TL;DR is that we don't have a good name or umbrella term for this. So we're just going to say ME/CFS.



Erin Allmann Updyke

ME/CFS.

Erin Welsh

Until we can do better.

Erin Allmann Updyke

And we did our best to define it, which is still probably inadequate. So that is like how we define and kind of what the main symptoms of ME/CFS are. So what I want to try and get into, even though just fair warning, we don't have a lot of information about what is going on in ME/CFS. So what I want for everyone to get out of this, like understand from this is that ME/CFS is a neurologic disorder. It is a disorder that has biologic underpinnings that just because we don't understand does not make them not real. And I think that that's the most important thing that I could possibly highlight from everything that I read about ME/CFS. Just because we don't yet know what is going on does not mean that nothing is going on or that this is a psychosomatic disorder or that this is a somatization disorder and that has been a huge issue. I know you're going to talk about it, Erin.

Erin Welsh

Oh yeah. Yeah.

Erin Allmann Updyke

This is a real thing. I hate that I even have to say that but I think I do. It is a real thing. There is a lot going on biologically that we're still trying to understand, so let's get into it to see what we know so far about how ME/CFS happens and what's going on in the body when it's happening.

Erin Welsh

Yeah, I already have so many questions and I want to know so many things. I'll just avoid asking you all the questions right now and wait for my moment.

Erin Allmann Updyke

You can ask me so that I can answer them one at a time with ooh, great question, I don't know.

Erin Welsh

There we go, there we go.

Erin Allmann Updyke

So the first question is kind of how does this happen? ME/CFS is not something that someone has for their entire life from birth til death, though it is a chronic disorder. A lot of studies point to the links between infectious diseases, especially viral diseases, and the development or the onset of ME/CFS. The problem is we don't have a single identified viral or other infectious disease that we can point to that say this is the cause of ME/CFS. Epstein Barr virus has been implicated, HHV-6, human herpesvirus 6, the causative agent of roseola has also been implicated. We now know from our long COVID episode that SARS-CoV-2 can cause a long COVID which many people meet criteria, these diagnostic criteria for ME/CFS during their long COVID illness. And overall up to 80% of cases of ME/CFS are associated with a known or like pinpointable prior infection of some kind and usually a non-specific kind of like flu-like illness. But not all of them.

Erin Welsh

I also came across brucellosis.

Erin Allmann Updyke

Brucellosis, sure. Ross River virus, Q fever, a lot of these different viruses and bacterial illnesses that we know are associated with post acute infectious syndromes of one kind or another, a lot of those post acute infectious syndromes, people would meet criteria for ME/CFS.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

So I can't stop myself.

Erin Allmann Updyke

Please.

Erin Welsh

Is it thought that the mechanism is the same for all of these infections and how it triggers ME/CFS?

Erin Allmann Updyke

This is a really good question, Erin. I don't think that there is a consensus at this point. One of the papers that I read, and I'll link to it, argues that we can't say that ME/CFS is caused by all of these multiple different disorders. In fact, their argument is that it is enteroviruses, specifically enteroviruses that are the most likely culprit. And so things that result, post acute infectious syndromes that result from other viruses or bacteria should not be conflated with ME/CFS. That is their argument.

Erin Welsh

Interesting. And that is because it can sort of muddy the waters of clinical trials?

Erin Allmann Updyke

It's really interesting because at this point because all we have are these kind of still rather non-specific diagnostic criteria, right, I mean they are fairly specific, like you have to meet XYZ criteria for six months with post exertional malaise, etc. But I think it gets at the question of what you're asking, Erin, which is what is the underlying mechanism? Because if it is different, if it is different mechanisms that are causing similar symptomatology in these different infections, then it really matters to classify them differently because our treatment options are going to be different. If the underlying mechanisms are the same, then having one big umbrella term helps us because we can get a lot more data from larger groups if we're looking across all of these different infections. I didn't get a sense from all the literature that I read that we have an answer to that underlying question yet.

Erin Welsh

Okay.

Erin Allmann Updyke

Maybe with all the more data that we have now on long COVID we'll get closer to that. But at this point we don't have it. And I think there's people that argue kind of both ways, that people who meet criteria for ME/CFS due to long COVID should be called ME/CFS and there are other people who say no, this is something different and we should treat it as something different.

Erin Welsh

So yeah, I think it's a really interesting sort of conundrum.

Erin Allmann Updyke

Yeah.

Erin Welsh

And it's like maybe we just do all these clinical trials and then include that as a factor.

Erin Allmann Updyke

Right. I mean I think what is important is trying to not forget about it, right?

Erin Welsh

Right.

Erin Allmann Updyke

Because at some point, can we have enough data to like really get down into the nitty gritty and disentangle those? Hopefully.

Erin Welsh

Well and that's I think really interesting and where long COVID comes into play is because if we can figure out the mechanism for long COVID, that could then sort of open the door to be like okay, is this the same mechanism for enteroviruses that seem to trigger ME/CFS or Epstein Barr virus or whatever, whichever virus or pathogen?

Erin Allmann Updyke

Right. Exactly. Exactly. Will we someday not have the diagnosis of ME/CFS at all? Will we have long COVID and long EBV-

Erin Welsh

Long EBV, yeah.

Erin Allmann Updyke

And long HHV-6 and long enterovirus? I don't know, maybe. Who knows? But it gets even a little bit more complicated in that sometimes cases are reported to not be associated with infection at all and sometimes are associated with things like significant trauma, either physical trauma, psychological trauma, major surgeries, or even other like immune system changes that someone undergoes. Now the paper that I read that argues that enteroviruses are the most likely culprit argues that enteroviruses are often asymptomatic. And so could it be that there is in fact an enterovirus infection and then a trauma that ends up triggering the presentation of ME/CFS? Again, we don't know right now, we don't know.

But what we do know is that to meet the criteria for ME/CFS, there is kind of a time point at which, and it might be gradual, but there is a time frame in which someone is more well and then less well, right. And that I think is part of the important criteria for how ME/CFS is defined and why when there is an infection that we can pinpoint to, it makes that time point a little bit more identifiable. And so sometimes people might point to a trauma. Was that trauma the trigger? We don't know but it's something that's identifiable where things are different thereafter.

Erin Welsh

Okay.

TPWKY

(transition theme)

Erin Welsh

Another question for you.

Erin Allmann Updyke

Okay.

Erin Welsh

When we do have a clear infection that we believe is responsible for a particular person being diagnosed with ME/CFS, what's the time frame there? Or is there a general time frame? How does it differ across these different pathogens? Part 1, 2, 3, 4 of my question.

Erin Allmann Updyke

Great question. I don't know.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah, I don't know. And I think because a lot of times there isn't an identified infection, it's not like oh I got flu and then I got this. It's like oh I was sick with something, I never went to the doctor, etc, whatever it was and then I never got better. Or I was sick and then within a month I was significantly worse, something like that.

Erin Welsh

Okay, interesting.

Erin Allmann Updyke

And we definitely don't know in terms of like the different infections, we don't know.

Erin Welsh

Okay.

Erin Allmann Updyke

So what do we know about like what's going on immunologically? I said that there's inflammation happening, like what is the underlying pathophysiology? Of course I could give you the short answer which is we don't know. But of course I will give you more context than that. Because again, this is something that has a lot of known biological changes, we just don't understand what the unifying factor is or like what the pinpointable pathophysiology that underpins it all is. And maybe that's because we're dealing with multiple syndromes. I don't know. But let's go over what we know about all of the various biologic changes that we see in people living with ME/CFS that we know are happening.

Broad strokes, we see large scale changes in the immune system. So we know that this is at least in part an immune-mediated disorder. And we talked about this a little bit in our long COVID episode because that's most of the data for long COVID as well is that this immune dysfunction plays a big role. One big paper that I looked at that came out in 2023 really tried to drill down into these immune markers. And what was really interesting about what they found is that if they looked just at people living with ME/CFS as a huge cohort compared to healthy controls, what they found overall was a huge reduction in immune markers, both pro inflammatory and anti inflammatory cytokines and things like that.

But when they drilled down even further and separated out people who had ME/CFS for a shorter time, less than three years, compared to people who had had it for more than three years, it was almost the opposite. People who had ME for three years or less had significantly higher pro inflammatory cytokines and lower anti inflammatory cytokines compared to healthy controls and compared to those who had ME of longer duration, who had lower levels of everything.

Erin Welsh

Right. Like sensitization response.

Erin Allmann Updyke

Exactly, exactly. And so what we see from this is like that's major immune dysregulation, right? That's like pro inflammatory ramping up and anti-inflammatory ramping down, which is consistent with some studies that have looked at imaging studies that sometimes, not like a typical MRI or something like that but kind of very specific and nuanced imaging studies that can see things like neuro inflammation happening in people with ME. There's some kind of immune dysregulation going on. There's also evidence of things like dysfunction in some of our immune cells and not just cytokines. So things like natural killer cell dysfunction. Natural killer cells are a type of T cell that are mostly responsible for killing infected or cancerous cells, so they're really good at fighting off viruses specifically. And we can see disruptions in those, like they're not functioning as well. And reductions in our activated T cells, high again T cell exhaustion. There's a lot of like potential in terms of what immunologic changes we see in people with ME/CFS.

But we also see other things. We see things like a lower than typical cortisol level in people with ME/CFS compared to healthy controls, quote unquote "healthy controls". Now here's where it gets really interesting. A lot of these immune markers, like these cytokines and things, they don't test for at the regular doctor's office. You can't ask your doctor to order you like an ILA test or a natural killer cell function test. That's not something that is easily order for most physicians. Cortisol is but we can't diagnose ME/CFS with cortisol numbers because while they are often and not always low, they're not necessarily outside the normal range on lab values. They're just at the lower end of what is typical or what is normal on those lab values that you see in your MyChart or whatever.

And so the suggestion here, the thought is that cortisol, we think of cortisol as a stress hormone, right? It's a steroid that we fight our flight, we release cortisol, right? But cortisol is released in times of stress in order to help lower inflammation and reduce our immune activation, right. It's in response to stress to be like ooh, back it off a little bit.

Erin Welsh

Okay.

Erin Allmann Updyke

So low levels of cortisol means that one of two things.

Erin Welsh

Oh yeah.

Erin Allmann Updyke

Either it's causing a disruption to our axis, our hypothalamic pituitary axis that produces and controls these hormones or it is the result of a dysfunction in this axis. So our brain to adrenal axis is somehow not working. Is it the cause or the consequence? We don't know. But the end result is an increase in inflammation and an increase in immune activation because the cortisol levels are not enough to suppress it. But not low enough that we can like diagnose it based on cortisol levels.

Erin Welsh

Okay. So I have a question.

Erin Allmann Updyke

Okay.

Erin Welsh

So if this is a... Because I've come across this too, the sensitization, sort of pro inflammatory of your immune system. If we suspect that that is a strong contender for a mechanism that's causing all of these symptoms, is there anything we can do about that? Like are there... You know what I mean? Like to suppress this immune response or to raise cortisol levels or how do we approach that?

Erin Allmann Updyke

Yeah, we can talk more about it in a little bit. I'm going to talk about all of the different options that we have for treatment. The short answer is both yes and no. Like yes, it means that if we can identify what these specific immune things are, can we target those specifically? Potentially. So far there isn't like one medicine that we know of that can like raise your cortisol just enough to be able to treat it and treating people with steroids doesn't generally help. So just giving them more doesn't generally help in studies that have tried that.

Erin Welsh

Okay.

Erin Allmann Updyke

So yeah.

Erin Welsh

Okay. So that's not the whole answer.

Erin Allmann Updyke

Theoretically yes. And that is why these kinds of studies to investigate like what is going on, what is the underpinning? Why is this cortisol just a little low? What is driving it? Is that the main, like is that just an indicator of dysfunction or is that the dysfunction itself, right? We don't know. Does that make sense?

Erin Welsh

Yes.

Erin Allmann Updyke

Okay. There's more though because there always is. There's also evidence in ME/CFS of dysfunction in the production of energy. Our body has to produce ATP, right, to do anything. Like for our cells to be able to function, we have to produce energy in the form of ATP. In people with ME/CFS, we see increases in things like reactive oxygen formation and reductions in things like biological antioxidants. And it gets too, too nitty gritty, the list goes on. But the bottom line is that these disruptions make it so that our production of ATP and our actual metabolism, intracellular metabolism is a little screwy and the end result is again a proinflammatory state.

Erin Welsh

Yeah. Why is it pro inflammatory if you break down some mitochondria?

Erin Allmann Updyke

So reactive oxygen species are pro inflammatory. Our immune system is going to react to those because a lot of bacteria make reactive oxygen, etc, blah, blah, blah. Antioxidants are going to reduce inflammation. So yeah. That's that part of it.

Erin Welsh

Okay.

Erin Allmann Updyke

So that is what we know so far about ME/CFS and like what the biologic underpinnings are. One thing that I wanted to point out... Oh, do you have a question first?

Erin Welsh

I do have a question.

Erin Allmann Updyke

Give it to me.

Erin Welsh

Okay. So my question is about these blood pressure changes.

Erin Allmann Updyke

Yeah.

Erin Welsh

What? Why? How? Like maybe we should do an episode on blood pressure, period. But I guess we've talked a lot so far, you've explained a lot about like a couple of the different mechanistic possibilities for why we see the symptoms that we see. But what about how those symptoms actually work? So like why would mitochondrial dysfunction or why would of this proinflammatory state lead to changes in blood pressure as we change our posture or sitting up, standing down or whatever? Standing up, sitting down. I can't. Yeah.

Erin Allmann Updyke

Erin, what a great question. You want to guess what my answer is?

Erin Welsh

Oh no! We don't know.

Erin Allmann Updyke

So one thing, one thought, or one hypothesis that we have evidence for is that some of this inflammation is happening, a lot of this inflammation is happening in our nervous system. And your nervous system, specifically your autonomic nervous system is what is controlling your blood pressure and your heart rate. And so if you have inflammation, and I think I mentioned this in our long COVID episode, but if you have inflammation in that vagus nerve and that vagus nerve is not able to function appropriately, then you can have dysautonomia where you're not controlling your heart rate appropriately, you're not compensating appropriately so you're having these wild fluctuations in either heart rate or blood pressure or both.

But to get more than that, like why is it the vagus nerve? Is it also other nerves? I mean yes, probably because we can also see things like sensory stimulation differences. We see things like generalized cognitive impairment which is not probably specific to the vagus nerve but is more about neuro inflammation in other parts of the brain and the brain stem. But it's really this brain stem and vagus nerve inflammation perhaps and dysfunction. Like why is it having so much dysfunction? How? I think if we knew that, then we could better treat POTS or postural orthostatic tachycardia syndrome and ME/CFS and the orthostatic changes that we see with ME/CFS. But we still don't know exactly what it is.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

And gut stuff?

Erin Allmann Updyke

Gut stuff. Erin, great question. There's a huge amount. So ME/CFS, if you meet the criteria that we talked about then you have this diagnosis of ME/CFS. It does not also mean that you can't have other things. And there are a few other disorders that are also very what we call comorbid, so they often occur at higher than typical rates in people who also have ME/CFS. And that is things like IBS and fibromyalgia. And so the gut stuff, we can see both if someone also has IBS or if someone doesn't have IBS and that we really don't understand except that I mean the vagus nerve also innervates your guts and your guts have their whole own essentially nervous system, like all of their own, they're producing their own neuroendocrine hormones and everything. So it is also being affected, we just don't understand exactly how.

Erin Welsh

Okay.

Erin Allmann Updyke

When it comes to fibromyalgia, I want to spend just a minute on this. There is a substantial amount of overlap in the symptoms of ME/CFS and fibromyalgia. And some of the kind of ways in the literature that it's often been kind of distinguished are ME/CFS is more fatigue predominant, or like the Hallmark symptoms, especially that post exertional malaise, and pain, widespread pain is the kind of hallmark of fibromyalgia. That being said, the symptoms, pain, fatigue, all of these symptoms can overlap substantially. And so that has led some people in the research communities to say oh well these are actually the same thing. And it's true that some people end up diagnosed with both things. But from everything that I have read and the way that I understand it, the only drive that I saw in the literature to classify these as the same disease is to say that they result in similar dysfunction like in society, like not being able to live your life the way that you would want to kind of a thing.

Erin Welsh

Okay.

Erin Allmann Updyke

But whenever people have tried to actually look at what we need to look at, the underlying pathophysiological differences that are happening in the bodies of people with ME/CFS or with fibromyalgia or with both of them, they're not the same thing. Like there are different biologic changes, immunologic changes that are happening in ME/CFS, both with and without fibromyalgia and in fibromyalgia like separate from ME/CFS. They're not the same.

Erin Welsh

It just means that we'll be doing an episode on fibromyalgia at some point in the future.

Erin Allmann Updyke

100%. Talk about we don't know. But so what it seems to me in reading through the literature is that the people who are arguing that it should be classified as all the same thing are trying to argue that in both cases these are symptoms without an underlying biology. And so for that we should then treat them the same because the symptoms overlap so much.

Erin Welsh

Interesting.

Erin Allmann Updyke

And that does not seem to hold water based on my understanding of the literature when you actually try and look at the differences in biologic markers that are happening in these two different disorders.

Erin Welsh

Okay.

Erin Allmann Updyke

So just because they overlap and sometimes at significantly higher rates than in someone without ME or fibro, that does not mean that they're the same thing. And at the same time, people who have ME/CFS are more likely to also have fibromyalgia and vice versa. So these are two syndromes that while they have similar symptoms, they are not the same thing and they can both be happening simultaneously.

Erin Welsh

That makes sense.

Erin Allmann Updyke

Yeah. That's all I've got, Erin, for the biology.

Erin Welsh

Does that mean-

Erin Allmann Updyke

So tell me.

Erin Welsh

It's time for me? Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

Let's take a quick break and then I'll get right into it.

Erin Allmann Updyke

I cannot wait.

TPWKY

(transition theme)

Erin Welsh

Tracing the history of an illness when the definitions of said illness seemed to be under constant revision, it's not the most straightforward thing in the world.

Erin Allmann Updyke

Oh really? I'm shocked by that.

Erin Welsh

When it's been known by so many different names and depending on which name you pick, you could be starting your history back in the 1700s, the mid 1800s, the 1930s, or maybe as recently as the 1950s. When enormous and really seemingly quite contentious arguments have broken out over the potential cause or causes of this illness, you know there's a lot going on. Even right now in February 2024, it seems like this is still very much a story that's being written. And I want to do the best that I can, especially after reading some absolutely infuriating papers that either explicitly dismiss the lived experiences of people with ME/CFS or just talk about how medicine has done that for quite some time.

So last week I started off my bit talking about how patients are rarely centered in stories of science and medicine and how long COVID was a rare and wonderful exception to that. And while it's still absolutely the case that the history of ME/CFS has been shaped especially within the past few decades by patient advocates who rightfully demanded a seat at the table, most of the story that I'm going to tell today has to do with what medicine and the rapidly dividing branches of medicine saw in their patients and how that influenced their definitions of disease. For this telling, I'm going to use names as sort of my guideposts because there's a lot that we can tell from a name, like we've already talked about chronic fatigue syndrome and some of the issues with that particular name. Over the course of about 250 years or so, what we know today as ME/CFS, this condition has been known by many other names. If we start back at the earliest, that name would be febricula. Yep.

Erin Allmann Updyke

I haven't heard that one.



Erin Welsh: Yeah, I had not either. This was described in 1750 by Sir Richard Manningham as quote "little low continued fever, little transient chilliness, listlessness with great lassitude, and weariness all over the body, little flying pains, sometimes patient is a little delirious and forgetful." End quote.

Erin Allmann Updyke: Why is everything little? Like a little, just a little.

Erin Welsh: A little bit of this and a little bit of that. A sprinkling of fatigue, a sprinkling of fever.

Erin Allmann Updyke: I have to say I like the word lassitude.

Erin Welsh: Yeah.

Erin Allmann Updyke: Interesting. And that's called fibratica?

Erin Welsh: Febricula. Don't worry, we're not gonna revisit it. I felt like I had to include it just for posterity's sake or something.

Erin Allmann Updyke: Okay.

Erin Welsh: Yeah. I also have no idea how widely this term was used, it doesn't really seem clear. But the author did make a note, the author of this like from 1750 did make a note that he had seen something similar described in Hippocratic texts.

Erin Allmann Updyke: Okay.

Erin Welsh: So it doesn't seem to be a new illness, not in 1750, nor does it seem to be a new illness in the 1800s, nor does it seem to be a new illness in the 20th century, which is the opposite of what some physicians will have you believe-

Erin Allmann Updyke: Okay.

Erin Welsh: When they describe it as quote unquote "yuppie flu" or "20th century illness"?

Erin Allmann Updyke: Okay.

Erin Welsh: It's good stuff.

Erin Allmann Updyke: We're getting spicy already.

Erin Welsh: Oh yeah. Yeah. Every, well I mean when I say every, I mean like at least in the 1800s and the 1900s, these groups of physicians seem to think that like this is an illness unique to our time and society's place in our time. So the next name along our journey is no exception to this: neurasthenia.

Erin Allmann Updyke: Okay.

Erin Welsh	So I want to spend some time, like a good deal of time with neurasthenia because I think that we'll see some parallels with ME/CFS in the second half of the 20th century especially as it relates to this divide of like mind-body or physical-psychiatric and just like the medical gas lighting that's so prominent, all of that stuff. Okay. So what was neurasthenia? In short, exhaustion of the nervous system, nervous exhaustion. Or if Greek translation is really more your thing, want of strength in the nerve.
Erin Allmann Updyke	Okay.
Erin Welsh	This term had been around since around the 1820s or so but it really took off in popularity in 1869 when the physician George Beard published an article about it. He listed many symptoms associated with neurasthenia like nerve pain, indigestion, headaches, insomnia, depression, and fatigue, especially fatigue after slight exertion and which prevents someone from living the life the way they had before.
Erin Allmann Updyke	Okay.
Erin Welsh	Okay.
Erin Allmann Updyke	It's pretty... Yeah.
Erin Welsh	Pretty in alignment. Being as he was the personal physician to much of the upper and middle class of in the New York neighborhoods where he lived, Beard of course saw social class and gender patterns in who was prone to neurasthenia, essentially wealthy, successful businessmen who became overwhelmed by the fast paced and competitive city living that was a result of the Industrial Revolution and this like growth of capitalism I guess. Or women of the quote unquote "better class" whose already sensitive nervous systems were pushed to the brink with the difficulties of maintaining a household or going out and about in high society. So it was a sensitivity of the upper classes primarily.
Erin Allmann Updyke	Of course. I have feelings about that, Erin. Continue.
Erin Welsh	Oh it was also when a woman got an education and then developed neurasthenia-
Erin Allmann Updyke	Those pesky educations, they're always ruining women.
Erin Welsh	Right, it was oh you studied too much, you learned too much, your body can't handle that.
Erin Allmann Updyke	You gave yourself a migraine and then neurasthenia.
Erin Welsh	Yep, yep. But yeah, this sort of reflects a lot of the other diseases that we've talked about on the podcast and I can't remember any specifically but it's just sort of like the cost of progress, right.
Erin Allmann Updyke	Right.
Erin Welsh	This new society, the way that we're living, the cities, everything, the growth, it's all leading to disease.
Erin Allmann Updyke	I also have to say it gives the same vibes of like you know how every couple of years there's headlines like the video games are destroying our youth!

Erin Welsh: Oh yeah.

Erin Allmann Updyke: And if you look back, there's been headlines about TV doing the same thing, then newspaper doing the same thing, the printing press. Like it's the same thing, guys, over and over.

Erin Welsh: I know.

Erin Allmann Updyke: Like it's not anything new.

Erin Welsh: Right. But Erin, social media is destroying our lives. No, I'm just kidding.

Erin Allmann Updyke: Social media is destroying the youth. Tik Tok, ugh.

Erin Welsh: Tik Tok.

Erin Allmann Updyke: We're on Tik Tok, by the way.

Erin Welsh: We are. Nice shoutout.

Erin Allmann Updyke: Thanks.

Erin Welsh: But yeah, so Beard also I think is really fascinating, counted himself among those with neurasthenia. As a younger professional he had been stricken down but recovered through resilience and possibly electrotherapy. It's not really clear.

Erin Allmann Updyke: Great job, Beard. Way to be resilient.

Erin Welsh: Yeah. But Beard's report spurred others primarily in the US to compile their own case reports on neurasthenia which tended to confirm what Beard said depending on their patient population. So if your primary patient population was the upper middle class of New York City, that's who you thought was going to get neurasthenia.

Erin Allmann Updyke: Right.

Erin Welsh: If you were a rural doctor, then it was people who worked on the farm for very long hours. Like basically everyone was susceptible.

Erin Allmann Updyke: Everywhere you look. Yeah.

Erin Welsh: Exactly, exactly.

Erin Allmann Updyke: Yeah.

Erin Welsh: And also I will say too that it seemed like the distribution or the likelihood of getting neurasthenia was similarly distributed among the sexes, across sexes.

Erin Allmann Updyke: Interesting.

Erin Welsh: So it was like equal rates, males, females. Yeah. But of course also like who you said was likely to get neurasthenia and their reasons for getting neurasthenia very much played into maintaining these hierarchies of class and gender structures of the day. Neurasthenia was seen as the quote unquote "half-sister of hysteria". It was the more respectable diagnosis of the two. So let me just read you a quote from a 1915 paper by Edward Angel. He puts it like this, quote: "The neurasthenic would but cannot; the hysteric could but will not."

Erin Allmann Updyke: Stop it, Erin! Wow. Okay.

Erin Welsh: I know, I know. Isn't that wonderful?

Erin Allmann Updyke: Yeah.

Erin Welsh: It's so nice.

Erin Allmann Updyke: Oh my god. Okay. Interesting.

Erin Welsh: Yeah.

Erin Allmann Updyke: Interesting. I mean hysteria aside, interesting that it does seem like they're saying this is a real thing.

Erin Welsh: Yes.

Erin Allmann Updyke: People can't, they are not well and it's not because they are faking it or it's in their head.

Erin Welsh: They're choosing to be sick.

Erin Allmann Updyke: Exactly.

Erin Welsh: And so that is something that really stuck out to me in researching the history of neurasthenia because you know what Beard thought was causing neurasthenia wasn't, and he did of course say that the the the ills of modern society played a role in this.

Erin Allmann Updyke: Right.

Erin Welsh: But there was a biological mechanism. Beard was a neurologist and around this time neurologists saw anything related to do with the nervous system and as well as psychiatry. So it was sort of this like blended unspecialized focus or like not as specialized as it became in later decades. And so he saw neurasthenia as having a neurological, physical basis. He was inspired by the laws of thermodynamics which really were only formalized in the 19th century-

Erin Allmann Updyke: Okay.

Erin Welsh: Which I think is really interesting to kind of like take other knowledge developments that are happening around this time and how that influenced medicine.

Erin Allmann Updyke: Yeah.

Erin Welsh: Really cool. But he applied these notions to the nervous system.

Erin Allmann Updyke

Okay.

Erin Welsh

And nervous force in particular. And so if the problem was nervous exhaustion, then the obvious solution would be to get more rest, the quote unquote "rest cure".

Erin Allmann Updyke

Interesting.

Erin Welsh

Which is exactly what it sounds like. So a bunch of retreats popped up across the US, Central Europe, and the UK. These retreats were where people could go to restore their stores of energy in theory. And I want to just side note, I can't, I like was like should I cut this? Is this interesting enough? I find it interesting so I'm going to make you all listen to this.

Erin Allmann Updyke

Okay.

Erin Welsh

But here's my little fun fact. Erin, does the name Charlotte Perkins Gilman sound familiar to you at all?

Erin Allmann Updyke

No.

Erin Welsh

Okay, what about the short story 'The Yellow Wallpaper'?

Erin Allmann Updyke

Nope.

Erin Welsh

Okay.

Erin Allmann Updyke

Sorry.

Erin Welsh

I think I read this in like high school English or something like that, I can't remember where I came across it.

Erin Allmann Updyke

Okay.

Erin Welsh

But 'The Yellow Wallpaper' written by Charlotte Perkins Gilman is an amazing piece of early feminist literature published in I think 1892. And it tells the story of a woman whose husband, a doctor, forces her to rest in a room in a rented mansion after the birth of her baby. She's not allowed to write, she's not allowed to read, she's not allowed to see anyone, just complete and total rest. This is the rest cure. You should definitely read it if you haven't and you can find it for free on the internet, I'm going to post a link.

Erin Allmann Updyke

Okay.

Erin Welsh

But I can't resist reading you a quote from this. Quote: "John," the narrator's husband, "is a physician and perhaps I would not say it to a living soul, of course, but this is dead paper and a great relief to my mind, perhaps that is one reason I do not get well faster. You see he does not believe I am sick. And what can one do if a physician of high standing and one's own husband assures friends and relatives that there is really nothing the matter with one but temporary nervous depression, a slight hysterical tendency, what is one to do?" End quote. It's so good. Go read it, go read it. It's great. Okay. So back to neurasthenia. What was becoming apparent at the turn of the 20th century was that no matter how much rest someone was getting, no matter how much electrotherapy they were receiving, because that was popular for a time, no matter how many quote unquote "Americanitis" tonics they drank, that was a real thing, it was also called Americanitis.

Erin Allmann Updyke

Wait, wasn't there something else that was called Americanitis?

Erin Welsh

Oh I'm sure, I can't remember. Probably.

Erin Allmann Updyke

Oh my gosh, that sounds so familiar. Maybe you just told me that about this while we were researching. I don't know.

Erin Welsh

No, it sounds familiar to me too. I don't know.

Erin Allmann Updyke

I'll google it later.

Erin Welsh

We'll google it. But people didn't seem to be getting any better. And so this then cast doubt on Beard's hypothesis that the root cause of neurasthenia was a nervous system issue, along with the fact that people weren't finding consistent results in like dissected nerves. They couldn't find out where the problem was, they couldn't distinguish someone who had neurasthenia from someone who did not have neurasthenia based on dissections.

Erin Allmann Updyke

Okay.

Erin Welsh

So this led to, by the early 20th century, neurasthenia rapidly falling out of style as a neurological diagnosis. And this was not just because of the rest cure not working, not finding a nerve basis for this disease. But it was also because of medical specialization, especially sort of the division of this field of neurology that kind of went to neurology and then psychiatry. And so this led to this mind-body divide in medicine that hadn't really been there as much before. And what I mean by this is that conditions tended to be described as all physical, where the signs and symptoms were from a physical quote unquote "organic" cause or psychological, where everything was arising in the mind and to get better it was either if you didn't get better, it's because you didn't want to get better.

Before this divide, patients tended to be treated more holistically and all of their symptoms were taken into account, whether objective or subjective, like something like pain. The message became if we can't tell that you're experiencing something real, then it must be all in your head and your physical problems are the result of your mental issues. So like this causal arrow only went in one direction. You're the one to blame because you want to be this way. Or for children, the mother was to blame.

Erin Allmann Updyke

Oh always. Always blame the mother.

Erin Welsh  
This is that same guy who said the hysteric can but will not. So you know it's going to be good. Yeah. Quote: "Timidity, so often inculcated by an overzealous mother, also is one of the early influences which later contributes its share to a neurasthenic diathesis. The forcing process of ambitious mothers is very reprehensible and at times a later cause of disastrous breakdowns." End quote. So it's like and if you read more of this, it's like either too strict, not strict enough, too much education, not enough education. Basically you can't do anything right.

Erin Allmann Updyke  
Moms cannot do anything right and are responsible for 100% of their children's issues.

Erin Welsh  
Always, always. But neurasthenia also faded from sort of public consciousness or at least like popular diagnosis because it was never well defined to begin with. And I think that there is something to that but I also think that it was sort of overused and eventually became broken down into other more specific diagnoses, largely psychiatric. And it did make me wonder how many people who were diagnosed with neurasthenia in the late 19th century would be diagnosed with ME/CFS today. I have no idea.

Erin Allmann Updyke  
Yeah.

Erin Welsh  
But I do think that at least probably a subset did have symptoms that would fit into that category, that would lead to a diagnosis of ME/CFS. Neurasthenia is not a perfect, it's not the originator.

Erin Allmann Updyke  
Right.

Erin Welsh  
It's not the thing.

Erin Allmann Updyke  
It's not like a perfect parallel or anything.

Erin Welsh  
Right. But it is a likely precursor. All right, so now I'm going to skip ahead to the 1930s-

Erin Allmann Updyke  
Okay.

Erin Welsh  
Where we meet our next name. This decade, a series of epidemics of what was initially thought to be polio took place around the world.

Erin Allmann Updyke  
Yes.

Erin Welsh  
You know this. But people realized that this illness was milder than polio, it was more commonly seen in adults, and it resulted in fewer cases of paralysis and death. And so it was designated as quote unquote "epidemic neuromyasthenia". Several of these outbreaks happened in hospitals among staff, like the Los Angeles and Switzerland epidemics in the 1930s, or among military in close contact, also in Switzerland. And I won't list all of the symptoms but among them were initial systemic and meningeal symptoms that were similar to polio, temperature fluctuations resulting in fever, localized muscular weakness, extreme fatigue, sensory changes, pain, recurrence of symptoms, and a long, sometimes years long period of recovery. The cause of these epidemics was still a mystery when another larger scale outbreak of something similar happened in Iceland between 1948 and 1949. So this is 841 cases out of a population of 15,000.

Erin Allmann Updyke  
Wow.

Erin Welsh  
Pretty, pretty high attack rate.

Erin Allmann Updyke

Pretty sizeable.

Erin Welsh

Yeah. And this gave rise to the name Icelandic disease. Again, extreme pain and fatigue was a feature and recovery was long. So one researcher went back like seven years after this epidemic happened and found that only 25% of those who were most severely affected had recovered completely and most still had pain, neurological symptoms, and fatigue. And interestingly, this is where the enterovirus is come in-

Erin Allmann Updyke

Yes. Well polio is an enterovirus.

Erin Welsh

Exactly, exactly.

Erin Allmann Updyke

Yeah.

Erin Welsh

So an outbreak of polio in Iceland several years after this sort of mysterious outbreak failed to take hold in the affected region and children in that affected region who relieved or given the polio vaccine had really high antibody titers, which led people to suggest that what was causing quote unquote "epidemic neuromyasthenia" was some kind of enterovirus related to poliovirus.

Erin Allmann Updyke

Yeah. I mean...

Erin Welsh

And it's entirely possible. Like yeah. In the early 1950s, a few more outbreaks of epidemic neuromyasthenia cropped up in Australia, Florida, South Africa, Denmark, and elsewhere. But the one that would give us our next name took place in London, England at the Royal Free Hospital in 1955. Between July 13th and November 24th of that year, 292 members of the medical nursing and administrative staff of the hospital came down with an unknown disease and 255 were admitted. So throwback to last week and the whole medical practitioner patients lending credence to a poorly understood disease-

Erin Allmann Updyke

Yeah.

Erin Welsh

Definitely had a role to play and a role that would soon be undermined.

Erin Allmann Updyke

Oh dear.

Erin Welsh

Foreshadowing. Yeah. The acute phase of this illness included malaise, headache, swollen lymph nodes, depression, mild sore throat, nausea, GI symptoms, and later dizziness, extreme pain in the back, neck, and limbs, and fatigue. It was clearly contagious but no one could track down the cause and Royal Free disease, which is what it was initially termed, became quote "benign, myalgic encephalomyelitis" to reflect quote "the absent mortality, the severe muscle pains, the evidence of parenchymal damage to the nervous system, and the presumed inflammatory nature of the disorder". End quote.

Erin Allmann Updyke

Yep.



Erin Welsh

And maybe you're thinking benign, like why? That just does not reflect accurately this disease at all. And yes, I would agree with you and many other people would also agree with you, including Dr. Melvin Ramsay, which I'll tell you later about in a second. But for now, the benign thing is the least of our problems. Because in 1970, 15 years after this Royal Free Hospital outbreak which people were still not fully recovered from, two papers came out in the British Medical Journal by psychiatrist McEvedy and Beard, a different beard by the way. That said-

Erin Allmann Updyke

He wasn't alive for 100 years?

Erin Welsh

I know. And these papers said essentially they're making it all up. From the abstract of one of these papers.

Erin Allmann Updyke

Oh my god, I'm sorry. I just need to take a breath because I know I'm about to get so frustrated. Okay.

Erin Welsh

Quote: "It is concluded that there is little evidence of an organic disease affecting the central nervous system and that epidemic hysteria is a much more likely explanation. The data which support this hypothesis are the high attack rate in females compared with males, the intensity of the malaise compared with the slight pyrexia, the presence of subjective features similar to those seen in previous epidemics of hysteria, over breathing, etc." End quote. There's more to it.

Erin Allmann Updyke

It's just like we didn't think that you looked that sick and therefore you're making it up.

Erin Welsh

Right.

Erin Allmann Updyke

That's what they're saying. Also you're female.

Erin Welsh

Oh yeah. They absolutely did not attend the statistics class where they learned that an absence of evidence is not evidence of absence. Not the same thing. They ended the article by saying okay yeah, I know, we know mass hysteria doesn't have the greatest connotations but quote "the occurrence of a mass hysterical reaction shows not that the population is psychologically abnormal but merely that it is socially segregated and consists predominantly of young females." End quote. Can you believe that?

Erin Allmann Updyke

They made it so much worse, how do you make it worse? How do you do that?

Erin Welsh

I know, I know. I know.

Erin Allmann Updyke

This is from the 1970s, Erin?

Erin Welsh

1970. Yes. Yep.

Erin Allmann Updyke

Wow.

Erin Welsh

Yep. And just to underline how egregious these papers are, I want to read you something from a 1956 paper about that Royal Free Hospital outbreak speculating on the cause. And so this was by Ramsay, Melvin Ramsay, that doctor that I mentioned who did a lot of work on this particular outbreak. This is 1956, 14 years before. Quote: "It remains to identify this syndrome more precisely but we believe that its characteristics are now sufficiently clear to differentiate it from poliomyelitis, epidemic myalgia, glandular fever, the forms of epidemic encephalitis already described, and need it be said, hysteria." End quote. Apparently it did need to be said and I guess it wasn't said loudly enough.

Erin Allmann Updyke

They just chose to ignore it.

Erin Welsh

They chose to ignore it and those McEvedy and Beard papers became an absolute hit and they led to a decades long battle to get the medical community to recognize that this is a disabling medical condition in need of treatment and care and not just like psychotherapy. Nicknames like yuppie flu or 20th century illness popped up to reflect this disturbingly popular feeling that this was just an imagined disease by people who felt disconnected to their community or who were bored and wanted attention from a doctor, just stressed out. By discrediting the physical basis for this condition, McEvedy and Beard and subsequent doctors set back the field tremendously, making it more difficult to get funding for research, discouraging medical interest in the condition, and breaking the trust that patients have for their healthcare providers. Not to mention what never being believed does to a person.

Fortunately there was still a strong contingent of physicians and researchers who fought against this mass hysteria diagnosis including Dr. Melvin Ramsay, who also got the word 'benign' dropped from benign myalgic encephalomyelitis in the 1980s to reflect that like no, this may not kill you but it is severe, it can be severely disabling, certainly not benign. Ramsay also published the first diagnostic criteria for ME in 1986 and it was like one of the first clear ones that people could finally use to be like this is a diagnosis. And around the same time in the 1980s, the mid 1980s, a couple more outbreaks of what seemed to be mononucleosis happened in the US, specifically in Nevada and New York. And these cases were linked to Epstein Barr virus, leading to the name Epstein Barr virus syndrome. And research later cast doubt on that connection or at least like EBV being the universal cause. I think at this point people were still seeking a universal cause for this.

Erin Allmann Updyke

Right, yeah.

Erin Welsh

Which makes sense.

Erin Allmann Updyke

One thing, yeah.

Erin Welsh

And so the CDC then once that connection was kind of on shakier ground, the CDC came up with the name chronic fatigue syndrome in 1988 to be more quote "neutral and inclusive". And like we've talked about the issues with this name largely with being stigmatizing and trivializing. And so hopefully we'll be getting another name change in the future. And hopefully that will take patient opinions into account.

Erin Allmann Updyke

Wouldn't that be nice?

Erin Welsh

And like maybe have people with ME/CFS be part of the conversation. Anyway. So ME/CFS finally began to gain some broader medical support in the 2010s. The 2010s, not that long ago.

Erin Allmann Updyke

Wow. Yeah, wow.

Erin Welsh

Yeah. As studies came out showing immunological differences in people with ME/CFS compared to those without the condition. And this was a really important development because it meant finding new avenues for treatments, conducting clinical trials, and developing treatment plans which up to this point had pretty much focused solely on mental health strategies as opposed to a biological approach. Of course I really want to emphasize that addressing the mental health aspect of this and other chronic diseases and just like life in general is a critical part of treatment. But the labeling of this disease as solely of psychological origin as a result of too much stress, it shuts down other avenues of research or treatment which could bring much needed relief to someone.

And I understand the argument that this tendency of medicine to declare a disease quote unquote "legitimate" only if it has a detectable biological as opposed to mental origin just further stigmatizes mental illness. But I think the point is bigger than that, that maybe by fixating so much on this mind-body divide and the need to categorize things as psychological or biological does a disservice to everyone, patient, physician, researcher alike. We know that our mental health can affect our physical sense of wellbeing and we likewise know that our physical health can very much affect our mental sense of wellbeing. The road can go both ways and it can be entirely parallel, as in our physical health may have nothing to do with our mental health at any given moment and vice versa.

ME/CFS has shown, over the centuries really if we go back to neurasthenia, that we miss the big picture if we're obsessed with the individual parts. Categorizing ME/CFS solely within psychiatry has invited victim blaming and gaslighting where a healthcare provider can say your test came back normal, there's nothing wrong with you. You just lack the resilience to deal with the modern world. Oh the CBT I've prescribed for you isn't working? It's because you're not trying hard enough. And to persist with that approach, solely with that approach when we have evidence to the contrary, evidence which you thoroughly explained, Erin, it's regressive. It takes us back to at least the mass hysteria of the 1970s, if not straight up back to Freud. Do we really want to be with Freud at this point? Please, like let's not. And similarly medicine as a field I think has really underappreciated at least until recently the mental health impacts of diseases, chronic diseases in particular. The bottom line that I'm trying to make with all of this is that I am once again asking you to believe people, to listen to people, and to remember that we don't know everything.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so with that, Erin, I'm handing it over to you.

Erin Allmann Updyke

Oh what a place to take over from. I agree entirely. Let's take a quick break and get into more honestly of the same and some numbers what we're dealing with right after this break.

Erin Welsh

Cool, cool, cool.

TPWKY

(transition theme)

Erin Allmann Updyke

You're not going to be surprised to know that we don't have great numbers.

Erin Welsh

What?

Erin Allmann Updyke

But let's talk about what we have. In the US, most public health agencies and the CDC estimate that between 836,000-2.5 million people, just a pretty huge range there-

Erin Welsh

Yeah.

Erin Allmann Updyke

In the US are living with ME/CFS.

Erin Welsh

Okay.

Erin Allmann Updyke

A significant number of people who likely meet these criteria have never gotten a diagnosis.

Erin Welsh

So can you tell me more about that?

Erin Allmann Updyke

Yeah. I can also tell you more because there is also a difference in severity. It cannot be stressed enough I think how debilitating ME/CFS can be. And at the same time there can be a wide range. So it's estimated that only about 5% of people recover to their pre existing, like pre illness baseline. So almost everyone who has a diagnosis or who meets criteria for ME/CFS will not fully recover. About 25% of people with ME/CFS are estimated to have severe or very severe CFS or ME, meaning that they are house bound or bed bound. They are so ill that they can't leave their house, they cannot do things like go to the grocery store. Sometimes they don't have the strength to get out of bed like we talked about in long COVID. This can be a severely debilitating disease for about 25% of people with ME/CFS which means that 75% of people are struggling with very similar symptoms and somehow still functioning, which is like it's just so depressing I think.

Because the other thing is that when we look at the statistics in terms of who gets diagnosed with ME/CFS, across the board it's a significantly higher risk factor to be assigned female at birth. People assigned female at birth are like 1.5-2x more likely to have ME/CFS than people assigned male at birth. What are the biological underpinnings of that? We still don't know, right, and we've talked a lot about these kind of like sex differences in disease, things like migraines, things like long COVID.

Erin Welsh

MS, lupus.

Erin Allmann Updyke

Exactly. Yeah. We don't know necessarily what these biological underpinnings are, lupus. But it exists, right? People assigned female at birth significantly more likely to have ME/CFS. But also you are significantly more likely to be diagnosed with ME/CFS if you're white than if you're a person of color. Is that a biological basis or is that lack of access? Is that lack of recognizing? Is that lack of being able to get a diagnosis because nobody believes you in the healthcare system, right? So there's a lot, there's a lot. It's also suggested, and I think that this is like we've talked a lot on this podcast about how we don't like to just look at the economy or the numbers of dollars lost.

Erin Welsh

Right.

Erin Allmann Updyke

At the same time, what I think is astounding is that a lot of studies suggest that only about half of people with ME/CFS are able to work at all and about 19% of people with ME/CFS are able to work full time. And like I do not think that we should base someone's worth on their ability to work full time, especially in America where our work culture is ridiculous. Your worth is not tied to your productivity. At the same time, for an economy that is hugely important. How are we ignoring up to 2 million people, half of whom can't work because of how debilitating their real illness is? Like how are we ignoring this to the extent that we're ignoring it? How is this still not taught in most medical schools? Because by the way it's not, it's not on the curriculum for most medical schools. I didn't learn about ME/CFS until I was in residency.

Erin Welsh

I'm sorry, what?

Erin Allmann Updyke

Yeah. I had a patient who has ME/CFS and that was the first time that I had heard the term myalgic encephalomyelitis because it was not taught at my medical school.

Erin Welsh

I am speechless.

Erin Allmann Updyke

Yep. Yeah, you should be. And that's not just me saying that, that is straight from the CDC website that it is not on the curriculum for a lot of medical schools, not just mine.

Erin Welsh

So 2 million people, up to like over 2 million people in the US.

Erin Allmann Updyke

And we wonder why people can't get a diagnosis. Okay. If you've never heard of it, you can't diagnose it, right. If it's not on your differential, then it doesn't exist. And that's just the US. Globally the estimates are all over the place, they are not great. Most studies cite anywhere between 17-24 million people likely live with ME/CFS. A lot of prevalent studies try and estimate like global prevalence at around 1%. But again, who knows? We just don't have good data on this. But what we know is that we are talking about millions of people who are living with a debilitating illness. And at this point we do not have any specific treatments for ME/CFS. We have nothing that approximate a cure, we have nothing that targets the underlying dysfunction because we still don't know what that underlying dysfunction is or how many different disorders there might be that we are calling ME/CFS. So that doesn't mean we have nothing, hope is not all lost. Right now treatment largely focuses on symptoms and getting back to functionality.

Erin Welsh

Okay.

Erin Allmann Updyke

An important thing that I want to mention at the top is that it used to be the case that something called graded exercise therapy or GET and CBT, cognitive behavioral therapy, which I love for indications like anxiety or depression or panic disorder that have really good evidence, are not effective for ME/CFS, period. They used to be recommended mainstay of treatment, no longer, that is not the thing. One thing that is often recommended as treatment and most of the data suggests that it is helpful is something called pacing. And this is kind of like I think of it as the opposite of a graded exercise therapy. It's not trying to increase your activity, it is trying to do only the amount of activity that you can without exerting yourself to the point that you end up with post exertional malaise. Because with someone with ME/CFS, if they exert themselves to that point the recovery can be immense and it can take significantly longer to then get back to just where you were before you exerted yourself.

Erin Welsh

I was thinking about this pacing and how difficult, like how do you know-

Erin Allmann Updyke

Yep.

Erin Welsh

That you pushed yourself too far until... Yeah.

Erin Allmann Updyke

It's so hard. I think one of the things that's so hard is that it relies so much on someone having to be so hyper aware of their abilities in a way that most of us are not.

Erin Welsh

Right.

Erin Allmann Updyke

Like I don't think that hard about what I could or couldn't do. And so someone living with ME/CFS, they have to do that for themselves all the time. Like that alone, that cognitive load is exhausting, right?

Erin Welsh

Yeah.

Erin Allmann Updyke

So yeah, that is really difficult. But pacing can be really helpful in alleviating that fatigue and in avoiding that post exertional malaise. Things like CBT could still be helpful in combination with other treatments if there is comorbid anxiety or depression. Because like you mentioned, Erin, mental health in living with chronic disease can severely be affected just by living with chronic disease, right. And then we get into kind of more medicine, I guess, based treatments of like how are we trying to target some of these underlying biologic changes that we know are happening. And here there's a whole range of things that have been tried, some of which have evidence that they're beneficial, a lot of which are still under investigation. But that doesn't mean that people might not be using them already.

And so this includes even things like using antivirals to try and target herpes viruses in people who have high viral loads, that has been shown to maybe be beneficial for some people with ME/CFS. A really interesting one that has a lot of good data again for some people with ME/CFS is using low dose Naltrexone. Naltrexone is a medicine that we also use for treatment of like alcohol use disorder or opioid use disorder and things like that. I don't need to get into the mechanism but using it at really low doses helps target inflammation and bring inflammation down overall because while it targets opioid receptors, it also targets other receptors that help reduce inflammation. There's also been other immune modulators that people have tried to target if there's autoantibodies that are going on for some people perhaps. You kind of asked are there immune system things that we can do, people have tried.

But the other big category that I think is really promising and needs a lot more research because at this point most of these treatments are in the stage where they're kind of supplements that are non FDA regulated and they're not treated as pharmaceuticals yet, but that is using things like antioxidants and metabolic precursors. So that means things like ubiquinol which is reduced CoQ10, anyone who shops at Costco might see that you can buy CoQ10 on the shelves. Right. Lots of people take it-

Erin Welsh

Is Costco the only place where you can get it?

Erin Allmann Updyke

No. It's just where I've seen. Costco has such a huge supplements area.

Erin Welsh

Oh yeah.

Erin Allmann Updyke

You can't ignore it.

Erin Welsh

Yep.

Erin Allmann Updyke

And we have feelings about supplements, we're going to do an episode on it later.

Erin Welsh

We are, yeah.

Erin Allmann Updyke

We are. But in this case there is evidence that things like ubiquinol and selenium or even using NADH, which again these are all precursors in those energy metabolisms that our cells are doing, in a lot of cases these are helpful in reducing the symptoms of ME and CFS. But again, we'll get into the issues with supplements and the fact that they're not necessarily FDA regulated. So how do you know that you're getting a good one? That's part of the issue here is like these things need to be researched so that they're FDA regulated so that we know that people are getting things that are actually going to help them based on the data.

Erin Welsh: Right.

Erin Allmann Updyke: So there's a lot of work I think being done. And the other huge area of research that will help us eventually develop better therapeutics is trying to identify biomarkers because that will help us with the diagnostics, right, being able to more definitively diagnose someone with ME/CFS or distinguish maybe between these different variants perhaps of ME/CFS. But also eventually then develop therapeutics to target if there are biomarkers that are targetable. Like can we reduce this specific inflammatory cytokine? Can we increase these T cell functions? I don't know, we don't have that yet but that is where I think the research is going and needs to go to be able to actually help people the most.

Erin Welsh: Yeah.

Erin Allmann Updyke: That is what I know about ME/CFS.

Erin Welsh: There's a whole lot we know and a whole lot we don't know. Surprise, surprise.

Erin Allmann Updyke: As per usual.

Erin Welsh: And speaking of stuff we do know, sources?

Erin Allmann Updyke: Sources.

Erin Welsh: Okay. So I have so many sources, Erin, it is overwhelming. And I just wanna before I want to preface this by saying that there are a lot of sources that you will find on our sources table on our post for this episode and not all of those sources are like for information that is useful or helpful or accurate but it's more about like showing how far we've come. So for instance, I have cited those papers from 1970 that said that ME/CFS is mass hysteria.

Erin Allmann Updyke: Right.

Erin Welsh: So just keep that in mind. But I will say that one of the best sources for sort of tracing the history of ME/CFS is called 'Beyond myalgic encephalomyelitis/chronic fatigue syndrome: redefining an illness' and this was published by the Institute of Medicine in 2015.

Erin Allmann Updyke: I can also vouch for that, it was a really great source for some of the biology as well. If you want more details on the immunology of ME/CFS, there's a paper from Horning et al in 2015 called 'Distinct plasma immune signatures in ME/CFS are present early in the course of illness,' As well as a paper from 2023 by Maksoud et al that was 'Biomarkers for myalgic encephalomyelitis and chronic fatigue syndrome: a systematic review'. But we will post the sources from this episode and all of our episodes because there's so many more-

Erin Welsh: So many.

Erin Allmann Updyke: On our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) under the EPISODES tab.

Erin Welsh: Thank you again so much to the providers of our firsthand accounts. It really does mean so much to us and to our listeners.

Erin Allmann Updyke: Yeah. Thank you so much for being willing to share something so personal in your stories. We really appreciate it.

Erin Welsh

Thank you to Bloodmobile for preventing the music for this episode and all of our episodes.

Erin Allmann Updyke

Thank you to Tom and Lianna for the wonderful audio mixing.

Erin Welsh

Thank you to Exactly Right.

Erin Allmann Updyke

And thank you to you, listeners. We hope that you liked this episode. These two, this kind of series a little bit, kind of, ish.

Erin Welsh

Yeah. Miniseries. Let us know what you think.

Erin Allmann Updyke

Yeah.

Erin Welsh

And a big thank you as always, so much thank you to our wonderful patrons. We appreciate your support so, so very much.

Erin Allmann Updyke

So much. Well.

Erin Welsh

Yeah, I guess until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.