

Becca

Hi everyone. My name is Becca and today I'll be sharing my experience with celiac disease. I do want to note here that a good portion of this story is actually going to be about the impact of celiac on my mental health, which is an aspect of the disease that isn't talked about as much as the quote unquote "physical symptoms" are. When I was in sixth grade, so about 11 years old, I started to get really bad stomach aches. I missed a good bit of school because of this which prompted my parents to take me to see my pediatrician. My pediatrician recommended that I go get blood work done. I was terrified of needles at this age and obviously did not want to hear this. But I do remember my pediatrician saying in passing that it could be celiac disease but that she was pretty sure it wouldn't be. After a very traumatic blood test for everyone involved, my pediatrician called my home a few weeks later to let me know that my blood work had tested positive for celiac. I then had to get a biopsy of my small intestine to confirm this.

The biggest thing that I remember from this period was being absolutely terrified of the biopsy. I don't even think it had even processed yet that I could have an autoimmune disease triggered by my favorite foods. I was a kid, so the idea of going to the hospital and getting an IV dominated my understanding of the situation. And the biopsy was really hard. I drank an obscene amount of water beforehand to make the veins in my arms easier to access but it didn't work and the nurse had to use the veins on my hand to get in the IV. I even had to be wheeled out of the hospital because it took a while for the anesthetic to wear off. But after all of that, the results came back positive and confirmed officially that I had celiac disease.

celiac is an autoimmune disease that prevents the body from properly digesting gluten, which is a protein that is found in wheat. The only treatment is to stop eating gluten which is exactly what I did. The good thing is that within a month or so of going gluten free, I did start to feel better. I hated the new food that I had to eat because it was bland but I could at least recognize that my body wasn't in nearly as much pain as it used to be. I had more energy. The awful cramps that made me feel like my stomach was eating itself grew more infrequent. There was however a significant mental impact of celiac disease that I want to highlight.

I was diagnosed with celiac right when I was hitting puberty as a girl in the early 2010s. And even though I was only 11, I was already acutely aware of the seeming requirement for people like me to be small and thin. I was already self conscious of my body and I want to note that celiac did not cause all the issues I would develop with food and body confidence. However it definitely exacerbated them. Suddenly food which I'd already had a tense relationship with became really bad and not just bad but harmful. Because of celiac disease, food actually hurt me. It felt like I had been failed, not just by food but also by my body. I received all of my early treatment and tests at a children's hospital and this included a specialized meeting with a dietitian who explained celiac to my parents and me, including what foods to avoid, possible meal plans, and how to identify gluten and seemingly unsuspecting food products.

Gluten can go by many terms. Maltodextrin, rye, malt, to name a few. So I had to get really good at reading the ingredients lists on foods. Unfortunately the calories were always right by the ingredients. Food became a point of stress. Eating was no longer fun but rather a minefield that I had to navigate for every meal and every snack. I still can't really express how much this altered my perception of food and its relationship to my body. In short, food became my enemy. Unfortunately I also started to lose weight. During my first year post celiac diagnosis, I did not gain any weight despite growing a few inches. And I actually remember proudly telling one of my middle school friends that I hadn't gained weight for an entire year. I was 12 and I was so proud of that.

I also grew really self conscious about my eating habits. I hated having to ask for accommodations in restaurants or when over at a friend's house because I didn't want people to perceive my body as a problem. And I so strongly associated my body with celiac that any sort of conversation about food was immensely stressful. Again, while celiac disease did not necessarily cause my fractured relationship with food, it made it so much easier for me to continue to view food as my enemy.

When I went to college, celiac became even more problematic. As many people with food allergies and intolerances will know, colleges don't necessarily have the best reputation for dietary accommodations. The freshman 15, which is in and of itself a wildly problematic term, did not happen to me. Instead I lost weight. I had to walk about 10 minutes to get to the nearest campus dining hall and then the only option for me was rice and bland vegetables. It was really easy to skip meals and supplant that with going to the gym and I became anorexic. This continued through COVID when suddenly I was living back home and cooking my own meals. I rapidly gained weight within the first few months of lockdown, which in and of itself was terrifying. But that's what happened when I finally started eating three meals a day and making food that I actually wanted to eat.

It's been about three years since I was able to acknowledge how much celiac disease negatively affected my relationship with food. I had to see a therapist that specialized in eating disorders as well as a dietician who had experience working with clients like me who had food intolerances. I would love to say that this all immediately solved my problems but that wouldn't be true. I am however better at eating gluten free meals that are filling and nutritious. And although it's not perfect, I do have a better relationship with food now than I did as a teenager. When I was first diagnosed with celiac, it seemed like a relatively easy thing to treat. I thought all I had to do was stop eating bread. And I wasn't the only one who thought this. I actually remember people sort of brushing my diagnosis off or saying that they were thinking of going gluten free to lose weight. After all, I was diagnosed with celiac right when it became a sort of trendy dieting fad.

I didn't realize how much it would influence my entire understanding of food as a necessary component of my life that had seemingly become very, very evil. I would love to see more support offered for children, especially girls, who are diagnosed with food related intolerances and diseases at a young age. With celiac specifically, it's never just bread that you have to cut out of your diet. Rather the diagnosis means an entire shift in your understanding of food as the thing that is supposed to help you but seemingly only manages to hurt you instead.

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Becca, thank you so much for sharing your story with us. There are just so many important aspects that no matter how much research you can do, it just doesn't... Like the lived experience and learning about that is so important. So thank you.

Erin Allmann Updyke

Yeah. We really, really appreciate it so much.

Erin Welsh

We do. 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

Today we are talking about celiac disease.

Erin Welsh: We are indeed.

Erin Allmann Updyke: I'm excited nervous about this one.

Erin Welsh: Why nervous?

Erin Allmann Updyke: I think just because it's so complicated.

Erin Welsh: Yeah.

Erin Allmann Updyke: Like the biology is more complicated than I even realized. And so I'm nervous to explain it well.

Erin Welsh: Well I think you're going to do a great job as you always do.

Erin Allmann Updyke: Aw, thanks.

Erin Welsh: And we're going to learn more than we knew at the beginning of this episode like always.

Erin Allmann Updyke: More than we bargained for.

Erin Welsh: Yeah. Also always. Yeah, I am really excited for this one too. I feel like not only is it sort of just like us getting back into the groove of our regular format-

Erin Allmann Updyke: Yeah.

Erin Welsh: But also I really enjoyed doing the nontraditional format anyway.

Erin Allmann Updyke: Same.

Erin Welsh: But this is a really interesting topic with so much to unpack in terms of evolution, in terms of diet culture, in terms of stuff like that. And just as a forewarning, I'm not going to get into every last bit of all of that. But also celiac is just a really fascinating topic.

Erin Allmann Updyke: It really is.

Erin Welsh: There is really much to unpack and I don't know really anything about the biology, as per usual, and so I'm excited to learn about it.

Erin Allmann Updyke: I can't wait to tell you about it. I know nothing about the history.

Erin Welsh: Well but before we do all of that, I suppose we should probably do quarantini time?

Erin Allmann Updyke: It's quarantini time for sure.

Erin Welsh: What are we drinking this week?

Erin Allmann Updyke: We're drinking No Grain, No Pain. Get it? Because celiac, gluten. You'll get it, we'll get it. We all get it.

Erin Welsh	I am so proud of the name for this drink.
Erin Allmann Updyke	It's a good one. It really is.
Erin Welsh	I love it. And also the recipe is delicious, right? It's basically a rhubarb Mojito. So you've got like rhubarb, mint, lime juice, rum, maybe a little bit of orange liqueur. Yeah.
Erin Allmann Updyke	Fantastic. You can find the full recipe for that quarantini as well as our nonalcoholic placeborita on our website <a href="http://thispodcastwillkillyou.com">thispodcastwillkillyou.com</a> and on all of our social media channels. Do you follow us there? Check us out. We've got recipes.
Erin Welsh	We do have recipes. You should definitely follow us there. On our website, you can find all sorts of cool things like transcripts, like links to merch, links to our <a href="http://bookshop.org">bookshop.org</a> affiliate account, our Goodreads list, music by Bloodmobile, a firsthand account form, a contact us form. I mean there's just some good stuff you can find. So check it out.
Erin Allmann Updyke	Check it out, check it out. Go there.
Erin Welsh	Can we learn about celiac disease now?
Erin Allmann Updyke	I would love to. Let's take a quick break and get into the biology of it.
TPWKY	(transition theme)
Erin Allmann Updyke	I struggled a little bit with how to structure this biology, Erin, because there is a lot of detail that I could potentially get into, like very nitty gritty biology. But so let's start from the very beginning, shall we?
Erin Welsh	Let's do it.
Erin Allmann Updyke	What actually is celiac disease? Like when someone says those words, what do those words mean really? Celiac disease is an autoimmune disease. It is an autoimmune disorder. We've covered autoimmune disorders on this podcast before and we'll get into the specifics of what the autoimmunity is in celiac disease. But at its core, it is your body attacking itself. First, your body starts attacking gluten and in so doing it creates this inflammatory state that ends up killing a bunch of your small intestine cells. That's the end result. So let's get into the steps of how kind of this all happens. And to do that, I think we have to start with like what is gluten?
Erin Welsh	Erin, what the heck is gluten? Like I didn't even think to look at when people learned what gluten was but I feel like it was the 1800s. I don't know. But anyway, what is gluten?

Erin Allmann Updyke

Yeah, great question. So gluten is a protein kind of, it's not like a protein, it's a combination of multiple types of proteins. So specifically gluten is combinations of gliadin and glutenins. These are two different types of proteins that together make up gluten, which really is what makes springy bread delicious, right. It's the stretchy, stringy bits that you get in wheat that gives bread that chew if you're eating bread. When it comes to celiac, it turns out that it's one part of this gluten complex, specifically the gliadin proteins. And there's different subtypes that people react to in celiac disease. And it's also a different subset of these gliadins that if you have a wheat allergy that you end up reacting to in a different way. Allergies are totally different than autoimmunity. So fascinating. And there's an enzyme in our body that will become important later called tTg or tissue transglutaminase that helps to break down these proteins in our guts. And this becomes important in celiac because spoilers, this is the enzyme that we end up making autoantibodies against.

Erin Welsh

Okay.

Erin Allmann Updyke

So these gliadin and glutenin proteins that make up gluten, they're found in wheat. And there are other really similar peptides that are found in rye and barley. And they're similar enough that nowadays they're kind of lumped under this category of gluten. And so that's why people with celiac have to avoid wheat, rye, and barley. Oats make another very similar protein but it generally doesn't cross react with the same antibodies as gluten. So even though it's similar, it turns out that most of the time oats are pretty well tolerated and considered safe for people with celiac. I'm not your doctor. If you have celiac, please talk to your gastroenterologist, etc. But yeah, so that is what gluten is. It's just like these combinations of proteins that are present in some of these grains that why do they make a person with celiac start attacking gluten? That doesn't make sense. Why? Why would that happen?

Erin Welsh

Why?

Erin Allmann Updyke

Let's talk about it. So as this is an autoimmune disease, the main underlying issue in celiac, like other autoimmune diseases that we've talked about, like lupus, etc, is the formation of these autoantibodies. And in celiac, you start making these autoantibodies against these gliadin proteins in gluten. But to really get into the nitty gritty of why this ends up triggering the amount of disorder that it does, we have to also understand the genetics that play into celiac. Because with celiac disease, the genetics become super, super important. Over 99%, and I think it's really close to 100% but all of the statistics just say over 99% of people with celiac, have one of two HLA markers. HLA-DQ2 and HLA-DQ8. What do those mean? Because they're all over the celiac literature.

Erin Welsh

Dairy Queen 1 and Dairy Queen 8. What is it? Oh, Dairy Queen 2 and Dairy Queen 8.

Erin Allmann Updyke

Like what type of Blizzard are you getting at your...?

Erin Welsh

Yeah.

Erin Allmann Updyke

No. Let's talk about what is an HLA. Have we talked about HLA ever on this podcast? I don't think that we have.

Erin Welsh

I don't think that we have.

Erin Allmann Updyke

Yeah.

Erin Welsh

But we may have. It's possible.

Erin Allmann Updyke

This is why I ended up getting nervous because this is like a lot.

Erin Welsh

Oh gosh. I also went down a little bit of the HLA rabbit hole and then I quickly was like no, no, like turn around, get back.

Erin Allmann Updyke

Yep.

Erin Welsh

Can't do this. This is not... I mean I dropped my immunology class in college.

Erin Allmann Updyke

We're not going to get too into the weeds but I do think that it's a really interesting and important part of celiac disease. So what are HLA? When you hear these words, what does this mean? HLA stands for human leukocyte antigen. These are just proteins. We all make a bunch of different HLA proteins, we have them in our bodies. They are expressed on the surface of a whole bunch of our cells, including our antigen presenting cells. We talked about antigen presenting cells way back in our vaccines episode in Season 2.

Erin Welsh

Yeah.

Erin Allmann Updyke

It's been a minute. But these are cells that help our immune system by bringing stuff that they find to our lymph nodes or other areas where a bunch of immune cells are congregating. And they present stuff to our immune cells, specifically like our T cells and our B cells, to activate them to start an inflammatory reaction. So they are the cells that go out and gather up things that they find that might be foreign particles in our body, viruses, proteins, gluten, whatever it is. And they bring them and say (British accent) here I have presented something to you, tell me if it's dangerous or not. Right? And then our T cells, which are British always-

Erin Welsh

Always.

Erin Allmann Updyke

React to those things if necessary. Everyone has a variety of HLA proteins. You get half of your HLA proteins from your mom, half from your dad. And then that makes up your HLA component. The two that are involved in celiac, DQ2 and DQ8, happen to have an affinity for gluten, specifically for gliadin proteins. So they have the ability in your guts, because remember from our tonsils episode that our guts have their own entire immune system, so these HLA proteins in our guts find some of this gluten, bring it over to Peyer's patches in our guts where immune cells are congregating, and they're like hey, T cells, what should we do with this? And if you have celiac disease or if you develop celiac disease, your T cells are going to see that gliadin protein and be like we'll destroy them! And go hog wild.

Erin Welsh

Tell me more about Peyer's patches.

Erin Allmann Updyke

Oh, so Peyer's patches are kind of like the tonsils of your guts.

Erin Welsh

I love that.

Erin Allmann Updyke

Isn't it cute? Yeah.

Erin Welsh

How many Peyer's patches are there? Where are they located? How big are they? What's in them? What do they do? Like what are other things that they do?

Erin Allmann Updyke

Yeah. It's literally like your tonsils. It's literally like little patches of immune cells. And so it's where your T cells, where your B cells, and where other immune cells are congregating. I have no idea how many you have or how big they are. They're mostly throughout your small intestine and my histology classes are going to be failing me on more details than that. Because they might be in your large intestine too but I don't remember. But they're in your guts.

Erin Welsh

I have an off topic question about intestines.

Erin Allmann Updyke

Okay. Yeah.

Erin Welsh

Can you tell me a little bit, just like a very simple explanation between the different parts of your intestines and what they do?

Erin Allmann Updyke

Are you really gonna do this to me right now, Erin?

Erin Welsh

No, okay, okay, okay. You don't have to.

Erin Allmann Updyke

I mean so okay, if you start from your mouth, your mouth goes to your esophagus, right, your oropharynx goes down into your esophagus. Your food is going to go through your esophageal sphincter into your stomach where it's going to mostly be digested. From your stomach it's going to pass through another sphincter into your duodenum, which is the first part of your small intestine. Then your small intestine is super long, it's like I don't know, over 25 ft long or something. It wiggles back and forth in the whole center of your abdomen. If you look at a picture of guts, it's the wiggly part in the whole center.

Erin Welsh

Yeah.

Erin Allmann Updyke

Your small intestine has multiple other parts. There's the duodenum and then the jejunum and then it goes down into the ileum which is the last part of your small intestine. Your small intestine is mostly responsible for the continuation of digestion in the first part and then absorption, all of your nutrient absorption is going to happen throughout your small intestine. And then it passes through the ileocecal valve which is the last part of your small intestine and that goes into your colon. That happens right in your right lower quadrant where your appendix is because that's like a little beep that hangs off the edge kind of-

Erin Welsh

Yeah.

Erin Allmann Updyke

Where your small intestine and large intestine combine kind of. And then your large intestine goes up your ascending colon on the right side and then it goes across the top, that's called your transverse colon, and then down your descending colon on your left hand side. And then it wiggles around and that's called your sigmoid colon and then into your rectum and out your butt. Your colon mostly is reabsorbing water, that's like the main function of what's happening in your colon. There's some nutrients that also get reabsorbed there in your colon as well but that's like the main thing that's happening throughout your colon. Does that answer your question?

Erin Welsh

That was beautiful. Thank you. First of all, thank you for such a...

Erin Allmann Updyke

Thank you.

Erin Welsh

It was really impressive that you were like I know everything about this. It's perfect. Secondly, thank you for always answering my ridiculous questions like that.

Erin Allmann Updyke

I love your questions. Just they make me nervous because I feel like I'm going to get it all wrong.

Erin Welsh

I wouldn't know. That's the best part.

Erin Allmann Updyke

But it is important because what we'll see in celiac is that celiac is a disease that affects your small intestine. And so as we'll see when we get to like what are the symptoms that you see with celiac, they're a lot going to revolve around the inability to absorb the nutrients that you need to because of the damage that is done to your small intestine.

Erin Welsh

Okay.

Erin Allmann Updyke

So getting back all the way to, I think we were at HLA still. No.

Erin Welsh

Yeah. We were not even in the duodenum.

Erin Allmann Updyke

No. So your T cells are going to respond and start causing damage to your small intestine. It's a little bit more complicated than just gluten being presented because I mentioned already this enzyme called tissue transglutaminase. And this is where I'm not going to get too, too deep into the weeds because while there is a lot that we know about the nitty gritty pathophysiology that's involved here in this intestinal damage that's mediated by this autoimmunity, I'll link to a paper about it, it gets just too detailed for us here. But what is important is that there's this enzyme called tissue transglutaminase. This is something that we all have that helps to break down gluten in our bodies.

But what happens in the case of celiac disease is that as gluten is bound to tTg, what ends up happening is that it makes this gluten protein even more available for presentation to T cells and then those T cells that are like 'this is foreign, we'll destroy it!' ends up also making antibodies against tTg. And that is one of the main autoantibodies that we see, antibodies against your own tissue transglutaminase proteins that then end up triggering this whole cascade of immune reactions that leads to the damage that we see to the small intestine in celiac disease. Does that make sense?

Erin Welsh

Victims of our own immune efficiency.

Erin Allmann Updyke

Exactly, exactly.

Erin Welsh

Yeah. Okay. So basically what happens is that gluten, you eat gluten, it's coming through, something presents it to your T cells and the T cells go attack everything. And then there's a bunch of collateral damage from the T cells attacking not only the cells presenting gluten but also the enzymes presenting gluten?

Erin Allmann Updyke

Yeah. Essentially.

Erin Welsh

Okay.



Erin Allmann Updyke

Essentially that. So really if we step back and look very, very big picture, how does someone end up getting celiac disease? There's three main things that have to happen. One, you have to be born with this specific HLA type, right, either DQ2 or DQ8. And that's going to mean that you're going to happen to be really good at presenting gluten in the first place. Number two, you then have to be exposed to gluten. So what's really interesting about celiac disease compared to most other autoimmune diseases is that we know that specific trigger so specifically I guess, not to use the same word over and over. But for most autoimmune diseases we think or we know in some cases that there are environmental exposures as well as genetic susceptibility, right. But with celiac, we can pinpoint that gluten is necessary for the development of celiac disease and gluten is the trigger that continues to perpetuate and cause damage.

But it's not just those two things, it's not just this genetic susceptibility and exposure to gluten. There's also a third component, something else. And that something else we don't fully understand. It's involved with tissue transglutaminase and creating these autoantibodies against tissue transglutaminase and other enzymes as well, it's not just this one. But there's some other trigger that has to happen that then leads to the eventual presentation and development of autoantibodies against gluten but also against your own cells and your own enzymes that end in this immune activation and damage to the small intestine. Now that third point, the trigger besides gluten, we don't know what that is. We don't understand it.

Something like 20-30% of people have these various HLA types, DQ2 and DQ8. Almost everyone is exposed to gluten, right? Gluten is in wheat, rye, and barley. Across the entire globe, populations depend on these grains. And I know, Erin, you'll talk a little bit more about that from an evolutionary perspective. But it's a very small subset of people who then end up developing celiac disease. So there is some other environmental trigger that we don't fully understand. There are a lot of ideas on what this can be. There's some data that perhaps exposure to gastrointestinal infections including rotavirus might be one of those triggers or one of those things that put you at higher risk. Spoilers, rotavirus vaccination might help protect against the development of celiac disease.

Erin Welsh

I was just going to say and do we have like before/after data to suggest that or like at least regional data?

Erin Allmann Updyke

No, not really, no.

Erin Welsh

Okay.

Erin Allmann Updyke

But there's some evidence in some studies that vaccination might be slightly protective, especially in high risk populations.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. But there is something else, right. And altogether what that means is that we don't fully understand how to prevent celiac disease at this point, which is really important.

TPWKY

(transition theme)

Erin Welsh

Since we don't know what the trigger is that's probably all over the place in terms of when people first recognize symptoms or when people get diagnosed and then there's stories about how long it can take sometimes to get diagnosis.

Erin Allmann Updyke

Right.

Erin Welsh

So tell me about the symptoms. How does one get diagnosed, etc?

Erin Allmann Updyke

Yeah. So a lot of people think of celiac disease as an intestinal disease. And I said already like the main thing is it's going to cause damage to the cells of your small intestine. So it is true that the small intestine is the main site of disease and pathology and therefore also symptoms. But because this is an autoimmune disease, it also shouldn't be too far fetched to convince everyone that there are also extraintestinal manifestations, whole body disease. So let's get into what this all can look like. The most "classic" quote unquote symptom that's associated with celiac disease, and it's also now called classical celiac, is diarrhea. And this diarrhea can be pretty profound because again what's causing this diarrhea is that your small intestine kind of gets destroyed.

Like I mentioned that, because of your wonderful question, Erin, that your small intestine is where we have to absorb all of our nutrients. The way that your intestine does that is they have inside, if you look in your small intestine, these beautiful wonderful things called villi that are kind of like these anemone tentacles lining your whole small intestine. They make this incredible amount of surface area for all of that absorption to be able to happen. In celiac disease, you develop what's called enteropathy which just means damage to that small intestine specifically and blunting of these villi. These are just fancy medical words to say that all of your beautiful gut anemones are flattened.

Erin Welsh

Like a lawn that's been mowed.

Erin Allmann Updyke

Exactly. So you can't absorb all of those nutrients. So in addition to the diarrhea, what we can also see is a lot of weight loss and malabsorption. And this can lead to deficiencies in a whole variety of vitamins and minerals that can then in turn lead to things like anemia and not just one type of anemia. Yes, you can have iron deficiency anemia from not being able to absorb iron but also other vitamin deficiency anemias like B12 deficiency, folate deficiency. And especially in kids, and a lot of the time celiac develops in young kids even if it's not diagnosed until they get older, you can then see growth failure because of how much malabsorption you have.

On top of that you can end up with other symptoms or other entire diseases like osteoporosis which results from not being able to absorb enough calcium. Another common sign is abnormal liver testing which we don't have an exact mechanism for except that that tTg enzyme is also present in the liver. So is it because of damage to the liver from that? I'm not 100% sure. But then with all of this overall malabsorption and literal damage to the small intestine, you can have a lot of abdominal pain and bloating. Sometimes you end up paradoxically having constipation because of just how much overall damage and dysfunction and dysregulation really that we see in the guts.

Erin Welsh

Tell me more about the diarrhea.

Erin Allmann Updyke

What more would you like to know about the diarrhea?

Erin Welsh

Are there characteristic diarrhea like content or frequency or...? Yeah.

Erin Allmann Updyke

Yeah. Not really. Sometimes people can have what's called steatorrhea which means like fatty diarrhea. So that very oily kind. But it's not something that's specific. You could see like a bloody diarrhea but not necessarily, it's not characteristic of celiac or anything the way that it would be for an inflammatory bowel disease which we'll do eventually on this podcast. But that's something like ulcerative colitis or Crohn's which is causing damage not to the small intestine but the large intestine. Asterisks, etc. But in general those are associated with more bloody diarrhea which you would expect to see a little bit less of with celiac but it's not impossible. So there's nothing that makes this diarrhea special I guess or very specific. Diarrhea is a very non specific symptom. And while it is classic, it's not necessary to have celiac disease. Not everyone with celiac is going to present with diarrhea at all. And in addition to these intestinal symptoms, there are also extraintestinal, they're outside the intestine symptoms. And not just all of those complications from malabsorption that I already mentioned, right, the osteoporosis and the anemias.

There are also a few specific extraintestinal manifestations that we see relatively commonly. There's a condition called dermatitis herpetiformis. No idea where it got that name, it's a weird name. But this is a skin blistering condition that is associated with celiac disease. And it's directly related to gluten consumption in someone with celiac disease who may not have any other symptoms that they know of of celiac, meaning no intestinal symptoms except for this rash. And this rash looks like incredibly itchy fluid-filled blisters and vesicles mostly on extensor surfaces. So the front of your legs or the back of your arms or on your butt or your trunk. And they're super, super itchy and look kind of like little teeny tiny blisters everywhere.

And then there are also a handful of neurologic complications of celiac disease, the most well known of which is gluten ataxia. We've talked about ataxia on this podcast before. Ataxia is a movement disorder where you lose the ability to coordinate movements, especially walking, because of damage to the cerebellum or the bottom part of your brain. And this is a neurologic manifestation of celiac disease. For these extraintestinal manifestations, we don't fully understand them or like why exactly are you seeing these or what exactly is the specific like cause and consequence kind of a thing. Which is not surprising. But we do know that these two things specifically are related to celiac disease.

And then there are other disorders or diagnoses that we might see at higher rates in people with celiac that we don't know if they're causal or not. And that's things like migraines or depression. We even can see recurrent pregnancy loss from undiagnosed or untreated celiac. And having untreated celiac disease during pregnancy can result in babies that are born small for gestational age because of growth restriction. So celiac is not just diarrhea and I feel like that's really important because I think that it can sometimes get kind of tossed aside as not a big deal because it gets conflated with a lot of other conditions.

Erin Welsh

Right. How long does it usually take? Like do the symptoms go from 0 to 60 or is it more of a slower onset? And then how does delay in diagnosis affect sort of long term consequences? And are we good at diagnosing celiac?

Erin Allmann Updyke

Awesome questions.

Erin Welsh

So many questions, just sprinkling them in.

Erin Allmann Updyke

Oh there's such good questions though, Erin. So it's really interesting to try and think about like does it go from 0 to 100? Like what is that kind of time frame? The truth is that because we don't really know at what point someone kind of loses their tolerance to gluten and therefore develop celiac disease. And what I mean by that is that someone might have no symptoms and if they are followed for long enough, let's say in studies where they're looking at kind of like higher risk populations, so either someone who has a known HLA haplotype that's associated and a first degree family relative or something like that, right. So they're in these studies where they're trying to look at when do you develop celiac. They might end up with these antibodies that we associate with celiac disease even before they have any symptoms of celiac disease.

On the flip side, someone might have symptoms for years before getting a diagnosis and then that turns out that all of the symptoms were related to celiac. Or they might not have any symptoms, get diagnosed, and then look back and realize actually no, maybe I did have these symptoms but I just didn't realize that they were symptoms, if that makes sense. So there's not a good answer really to your question. And I think that that's part of what one of the challenges is in trying to understand what are the points at which and what are the real triggers aside from the genetics and aside from the gluten that are associated with the development of celiac disease. We don't really know. And so we don't know when someone is going to develop disease from celiac or not.

But when it comes to how do we end up diagnosing them, for a long time biopsy was considered the gold standard. And that's really to look for those specific types of damage in the small intestine that we see associated with celiac, both visually and histologically. Because biopsy is invasive and not available to everyone and expensive and time consuming and all these things, especially for children, people are kind of moving away from biopsy. Though it is still kind of like, especially if the diagnosis is in question, one of the important parts of a diagnosis.

But there are other tests that are getting better and better as our technologies develop that are serologic tests. So looking just in your blood for antibodies against tTg. So specifically tTg-IgA and those are antibodies that you make primarily in your mucosa. So these are the antibodies that your guts are making against this tTg enzyme. And then there are a few other types of enzymes that we can test for antibodies against as well. None of these are 100% perfect in diagnosis. And a lot of times they rely on thresholds of how high the titer is of these antibodies to be able to make a definitive diagnosis. One of the challenges with all of the types of testing that we have for diagnosis including biopsy is that if someone is already adherent to a gluten free diet, you can't diagnose celiac disease because you're going to have healing of the damage and a reduction in these tTg antibodies. So a negative test doesn't rule out celiac disease if someone is already on a gluten free diet, they actually have to be exposed to gluten for these tests to be accurate if that makes sense.

Erin Welsh

Okay. Question. Kind of follow up question.

Erin Allmann Updyke

Yeah?

Erin Welsh

If you are someone who has celiac disease and let's say that it took a long time to get diagnosed and there's been a lot of damage to your small intestine, how much damage can there be before healing? You can't get back to sort of what things were before the damage began.

Erin Allmann Updyke

Yeah. It's a really good question. I don't have a number on like how likely someone is to have healing based on how long they had symptoms. I don't have that data. But it is true that about 40% of people don't have complete mucosal healing. So right now in terms of treatment, the only treatment that we have is a gluten free diet. The majority of people and some studies say like up to 95%, some studies say even higher than that, will have a complete or near complete resolution of their symptoms of celiac as a result of a very strict gluten free diet. But only about 40% of people have complete healing of their mucosa when you go back and do another biopsy. What are the characteristics that are going to determine that? I don't know. It's a really good question.

But it's something important because a lack of complete healing, like this continued inflammation in your small intestine can put people with celiac disease at risk for certain cancers, especially like lymphomas, T cell lymphomas. Because it is your T cells that are primarily being activated as part of this immune process. But it can also put people at higher risk of things like osteoporosis and hip fractures over time even if they are very adherent to that gluten free diet.

Erin Welsh

Okay, yeah.

Erin Allmann Updyke

Yeah. So that, I mean that is celiac disease in a nutshell.

Erin Welsh

If that's celiac disease in a nutshell, then can you tell me just briefly about the difference between celiac disease, non celiac gluten intolerance or non celiac gluten sensitivity, and wheat allergies?

Erin Allmann Updyke

Yes, I would love to.

Erin Welsh

It's so important.

Erin Allmann Updyke

Because I think it's really important to recognize that there are different entities aside from celiac disease. We know a lot about celiac, we know that it's autoimmune, we have markers that we can test for it, and we know that gluten free diet can be very beneficial and therefore is the standard of treatment. Lifelong exclusion of gluten from the diet is treatment for celiac disease specifically. There are at least two other entities that I think in common parlance get conflated with celiac disease and that is wheat allergy, which is something totally separate, and non celiac gluten sensitivity, which is kind of a nebulous term that I'll talk a little bit about. Wheat allergies are an allergy. And I cannot wait to do allergies on this podcast. But allergies are IgE mediated. So these are antibody mediated responses to an environmental exposure. They are not autoimmune disorders. So there's no formation of antibodies that are attacking yourself in an allergy.

There's the rapid onset and release of antibodies that are preformed against the environmental exposure. In this case, specific and separate gliadin proteins that are present in wheat that trigger an overactive hypersensitivity response. So that is like a totally separate thing and like specific to gliadin proteins that are present in wheat. And there's a lot of really interesting things about allergies, especially that are different as it relates to celiac disease, like exposure when you're young and the development of disease for allergies vs celiac disease that I think highlight that allergies are separate from autoimmune diseases, if that makes sense.

Erin Welsh

Yes.

Erin Allmann Updyke

And then there is non celiac gluten sensitivity. This is a disorder that I think is still relatively controversial in some of the literature but is recognized as a disorder that often presents as kind of irritable bowel-like symptoms. And irritable bowel, again we should cover it someday, it is something that is very nebulous. This could be diarrhea, this could be constipation, this could be cramping, like really bad cramping abdominal pain. And sometimes with non celiac gluten sensitivity we can see other non specific, non intestinal symptoms that tend to start hours to days after eating food with wheat or gluten or from rye or barley, and tend to get better when gluten is eliminated from the diet.

But in non celiac gluten sensitivity in people who have this disorder, there are no identifiable auto antibodies. Endoscopy does not reveal damage to the small intestine. And so this is considered something that we essentially don't have any markers for. And so it's often grouped under the larger classification of kind of functional bowel disorders that are very real in terms of the symptoms that people are having and experiencing. And sometimes people can identify, for example, gluten as a trigger for them. Sometimes people also with non celiac gluten sensitivity do better when they have what's called a low FODMAP diet. And that's a whole beast that we don't have time to get into. But I suspect that someday a lot of these diagnoses that are now under these big umbrella terms are going to be separated out into multiple different syndromes that have different potential causes, if that makes sense.

Erin Welsh

Yeah. Hopefully that makes it more manageable-

Erin Allmann Updyke

Exactly.

Erin Welsh

To understand like maybe it's one thing and then eliminating that one thing. Wouldn't that be great?

Erin Allmann Updyke

Right. Well if it's the one thing that... Sometimes it's... Oh my gosh, I have a lot of feelings about this because a lot of it's probably microbiome mediated. And so then if you have this dysbiosis, you could potentially get better even without having to have lifelong elimination of certain things.

Erin Welsh

Or is it chicken and egg?

Erin Allmann Updyke

Exactly.

Erin Welsh

Is the microbiome composition because of the disorder or is it leading to the disorder? Yeah.

Erin Allmann Updyke

Right. Yeah. But so in any case, it exists as an entity, it is real. People have real symptoms from it and if somebody feels better not eating wheat or not eating gluten, then that's great. That's not what we're talking about today. Today we're talking just about celiac disease.

Erin Welsh

Right.

Erin Allmann Updyke

So Erin, speaking of-

Erin Welsh

And now are we talking about the history of celiac disease?

Erin Allmann Updyke

Can we please? I'd love to know about it.

Erin Welsh

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

TPWKY

(transition theme)

Erin Welsh

Erin, you just beautifully took us through all that we know about the pathophysiology and the symptoms and the treatment for celiac disease, which as you mentioned pretty much consists of having a gluten free diet or as gluten free as possible. And also what can happen when someone with celiac disease eats gluten, like not good.

Erin Allmann Updyke

Yeah.

Erin Welsh

Probably that's putting it mildly. And while it can be incredibly challenging to find gluten free options in some parts of the world or to ensure that no trace of gluten is in your food, thinking about like having dinner at a friend's house and maybe they don't know that soy sauce has gluten. Which like there are so many things that have gluten.

Erin Allmann Updyke

So many things.

Erin Welsh

That's like why does it? But there are so many kind of random things like Rice Krispies have gluten apparently. How? So apparently the packaged Rice Krispies are not gluten free because they have a malt flavoring.

Erin Allmann Updyke

Wow. Yeah, that'll do it.

Erin Welsh

And so many things have malt in them. There's just a lot. Gluten free is not like oh don't eat bread and pasta.

Erin Allmann Updyke

Right.

Erin Welsh

It's so much more than that.

Erin Allmann Updyke

Yeah.

Erin Welsh

But yeah. And then like you're traveling, all of these things. But in theory, depending on where you live, many people with celiac disease can get a decent handle on their symptoms by avoiding gluten, right. And I know that that can be really difficult depending on where you live, depending on... A lot of the times it's difficult, it's more expensive to eat a gluten free diet, all of these things. But as restrictive and difficult as this diet can be, celiac disease is fairly unique I would say among autoimmune diseases for this, for having this relatively straightforward way to manage symptoms.

Erin Allmann Updyke

Right.

Erin Welsh

It's like we know the problem, we pretty much know the mechanism, we know what's making you sick, and we can do something about it. And again, I know this is a general rule, I know that there are exceptions and that a gluten free diet is not a breeze. But having this option or even knowing that this option exists is actually pretty dang recent in the history of celiac disease.

Erin Allmann Updyke

Oh, I can't wait.

Erin Welsh

And by recent I mean the 1950s.

Erin Allmann Updyke

Wow.

Erin Welsh

It was only then that the link between a gluten free diet and alleviation of celiac disease symptoms was made. Gluten, celiac, 1950s.

Erin Allmann Updyke

Erin, I just have so many questions. Like how? How?

Erin Welsh

How? Okay. Well we'll get there like down the line.

Erin Allmann Updyke

Okay.

Erin Welsh

But first let's go back thousands and thousands of years.

Erin Allmann Updyke

Okay.

Erin Welsh

Because what the heck did people do before then?

Erin Allmann Updyke

Right.

Erin Welsh

Celiac disease has been around forever basically.

Erin Allmann Updyke

In our genes.

Erin Welsh

Yeah. And I'll get into that a little bit more in a minute. And although there has been some discussion of rates of celiac disease increasing and the evidence is mixed, like the rise in prevalence could be attributed to better diagnostics and general awareness. Although there is some suggestion that the more recently developed wheat strains may contribute to have like different types of gluten or more immunologically sensitive or triggering types.

Erin Allmann Updyke

More immunogenic, yeah.

Erin Welsh

Immunogenic. Yeah, there we go. Again, it's not clear. But in any case, celiac disease is certainly not a modern disease and it has been present for thousands of years of human history since grain farming began. Because like celiac disease probably didn't begin before grain farming because there would have been no trigger for...

Erin Allmann Updyke

Right. You just weren't exposed to gluten.

Erin Welsh

Exactly.

Erin Allmann Updyke

Right.

Erin Welsh

Like the potential was there.

Erin Allmann Updyke

Right.

Erin Welsh

But the symptoms were not. So I ask again, what the heck did people with celiac disease do before 1950? Just suffer?



Erin Allmann Updyke: I mean just not eat anything?

Erin Welsh: Yeah.

Erin Allmann Updyke: I mean I feel like did they figure out some foods were making them feel sicker than others without knowing what it was about those foods?

Erin Welsh: So it's really clear. Yeah. And I kind of want to get into that.

Erin Allmann Updyke: Okay.

Erin Welsh: Because possibly but that doesn't really seem to be the case from medical writings.

Erin Allmann Updyke: Ooh okay.

Erin Welsh: Unmanaged celiac disease can wreak havoc on your body, as anyone with celiac disease can probably tell you. It can lead to malnutrition or death in juveniles. In adults it can lead to wasting, malnutrition, greater susceptibility to infections, and direct reductions in fertility. This is a disease with potentially severe, even fatal consequences if left unmanaged. And yet for thousands of years people didn't apparently know that it was gluten that led to their symptoms. And therein lies a mystery, an evolutionary paradox as I've seen it described. What do I mean by that? Like what's the paradox?

The paradox is that celiac disease is common in populations that have a long history, again talking thousands of years, of farming wheat and other grains containing gluten like rye and barley. Given the potentially severe outcomes of unmanaged celiac disease, malnutrition, reduced fertility, even early death, and the fact that celiac disease is highly heritable, meaning that it runs in families, you might expect that as grain farming began more prominent, beginning around 10,000-12,000 years ago when the Neolithic revolution began, celiac disease would become less prevalent as people with the disease in areas where grain was a large part of the diet probably would have had fewer kids.

Erin Allmann Updyke: Right.

Erin Welsh: They likely would have died younger, had more malnutrition which would have made them more susceptible to infections. And since celiac is to a large degree heritable, that would all mean fewer opportunities for those HLA genes to be passed down, those specific ones.

Erin Allmann Updyke: Right. You would expect that this is something that would have been selected against in those grain farming populations.

Erin Welsh: Exactly. But that's not what we see. Hence the paradox. And what's interesting is that I guess we don't know this for sure because we don't have a rate of celiac disease over the time-

Erin Allmann Updyke: Of celiac in the past. Right, right.

Erin Welsh: But I've seen rates of like 1-2% of the population basically. Which is a huge number.

Erin Allmann Updyke: Is it?

Erin Welsh

I mean I don't know. Like I'm not sure enough about the mathematics of HLA genetics and stuff like that and rates of mutation and like all of these different aspects of that. But to me it seems like a lot. I don't know.

Erin Allmann Updyke

It's interesting.

Erin Welsh

It's interesting. Yeah. So what's going on? Like what are some hypotheses? Could it be that celiac disease was not as bad historically? So some people have suggested that modern gluten-containing grains have more or different kinds of gluten that trigger more of an inflammatory response, like I mentioned.

Erin Allmann Updyke

Right.

Erin Welsh

Or that we simply eat more gluten nowadays in processed foods, stuff like that.

Erin Allmann Updyke

That makes sense.

Erin Welsh

Yeah. And I'm not sure if we know enough about ancient grains to make that comparison or even if there was a difference, whether it would have been big enough to have an effect. Maybe it's a contributing factor. But we also know that people with celiac disease in ancient times did get very sick. So for instance we have this quote from Aretaeus of Cappadocia from the second century CE, this is the first known description of celiac disease. Quote: "Emaciated and atrophied, pale, feeble, and incapable of performing any of his accustomed works. But if he attempts to walk, the limbs fail. The veins in the temples are prominent, for owing to wasting, the temples are hollow. But also all over the body the veins are enlarged. Not only does the disease not digest properly but it does not distribute that portion which the digestion has commenced. It appears to me therefore to be an affection not only of digestion but also of distribution." End quote. So he's like you're not absorbing any food and you're not getting nutrients is kind of what I'm interpreting that is.

So we've got that description and then we've also got possible archaeological evidence. So there's a paper from 2010 that describes the skeleton of a woman who died aged 18-20 and lived around 2000 years ago in Southwestern Tuscany. The economy of the city where she lived was based on wheat and olives and she seemed to come from a wealthy family given certain aspects of her tomb, like there was like gold and stuff like that. And this suggested to the authors, to the researchers that she would have had a good amount of wheat in her diet. But despite the evident wealth, she died of malnutrition. And her skeleton shows possible signs of celiac disease like shortness, anemia, dental enamel hypoplasia, osteoporosis, and a deformity of the hip. And I'm not sure how conclusive those, like how vague those symptoms are or how many other things they could possibly be. But the authors suggest celiac as a strong possibility.

Okay, so that was a long winded way of saying that it's probably not that celiac disease was milder historically or just that we eat more gluten these days. So onto the next hypothesis. Does having celiac disease provide a health trade off? So for instance, does it give added protection against certain infectious diseases? This has been suggested for lots of autoimmune diseases like celiac. Essentially the idea is that our immune systems evolved under much different circumstances than most of the world faces today, where infectious diseases were a constant threat and oftentimes a killer. Thanks to vaccines and antibiotics and public health, it's not so much the case these days. And as a result, without that persistent threat our immune systems have become overreactive, like hygiene hypothesis vibes.

Erin Allmann Updyke

Right, right.

Erin Welsh  
Or a more specific example would be something like sickle cell disease and malaria. So is it possible that celiac disease stuck around despite gluten because it helped fight off a more pressing threat like infectious disease which was becoming in general more common during the Neolithic revolution as population size and density increased? Perhaps. We don't fully know.

Erin Allmann Updyke  
Classic.

Erin Welsh  
Classic. There isn't a whole lot of direct evidence that people with celiac disease are more resistant to certain infections. But there does seem to be some association where the genes or alleles linked to celiac disease like those HLA ones that you mentioned are also involved in inflammation and general immune function.

Erin Allmann Updyke  
Yeah.

Erin Welsh  
Again, I know that's super vague but it's hard to draw firm conclusions from these types of studies. And remember we are dealing with a decently complex disease involving multiple genes or even networks of genes.

Erin Allmann Updyke  
Yeah, yeah.

Erin Welsh  
We know a good amount about the underlying genetics of celiac disease but we don't have the complete picture.

Erin Allmann Updyke  
No.

Erin Welsh  
Especially when it comes to environmental factors.

Erin Allmann Updyke  
Right. And like I shout out HLA-DQ2 and DQ8 but there are other genes that have been associated too that are-

Erin Welsh  
Totally.

Erin Allmann Updyke  
So it's a whole mess.

Erin Welsh  
It's a whole... Yeah, yeah.

Erin Allmann Updyke  
Yeah.

Erin Welsh  
And so that brings me to the third hypothesis which is that celiac disease is kind of a side effect of evolution, as one paper put it. Essentially since there are multiple genetic risk factors for celiac disease, each one of those factors on its own might not be harmful; might not lead to symptoms of celiac disease. And in fact each of those on their own might be beneficial in immune function or something like that. And so it stuck around, it was selected for, it was maintained. And that could have been what happened for different parts of the celiac disease like genetic risk network. So those factors helpful on their own, so they stuck around. Or maybe they were just kind of there not helping, like not good enough to keep around but not bad enough to like be selected against I guess.

Erin Allmann Updyke  
Right.

Erin Welsh: Not helping, not harming, neutral. In any case because of the way that celiac disease is caused by this network of genetic risk factors, that means that celiac disease as a whole may not have been selected for or against. But instead that evolution may have acted on the individual parts.

Erin Allmann Updyke: Right.

Erin Welsh: Hence the idea that it's a side effect of evolution. Does that make sense?

Erin Allmann Updyke: I feel like that totally makes sense especially because like yes, celiac disease is highly heritable but it's also not like most of the genetic disorders that we've covered on this podcast. It's not directly heritable like 1:1.

Erin Welsh: Right.

Erin Allmann Updyke: And like I mentioned, like 20-30% of people have one or both of these various HLA types and the vast majority of them, something like 15% or so of people with high risk haplotypes in studies go on to develop celiac disease. That's not that high compared to everyone who has those haplotypes. So it's complicated.

Erin Welsh: It's complicated. And I think I want to throw out another hypothesis, which by the way none of these are mutually exclusive, right. Like it can be that today's gluten causes more inflammation and some of the alleles associated with celiac disease do help improve immune function and that evolution has acted on the parts, not the whole.

Erin Allmann Updyke: Right.

Erin Welsh: More or less. And the last hypothesis I'll throw out there is that what if the environmental trigger, the big question mark remaining in celiac disease-

Erin Allmann Updyke: Right.

Erin Welsh: If that has increased in frequency over time.

Erin Allmann Updyke: Yeah.

Erin Welsh: Again, we don't know enough about the rates of celiac disease over millennia but that is something that I think is a possibility.

Erin Allmann Updyke: Yeah.

Erin Welsh: So hopefully that was still interesting enough that even though-

Erin Allmann Updyke: Fascinating.

Erin Welsh: Even though 'I don't know' was the punchline.

Erin Allmann Updyke: I'm sorry, Erin, have you ever listened to one of my biology sections? It's always the punchline.

Erin Welsh: It wouldn't be an episode without it.

Erin Allmann Updyke: No.

Erin Welsh: So that was a much deeper dive into the evolution of celiac disease than I expected to do.

Erin Allmann Updyke: I loved it.

Erin Welsh: But I just think it's so fascinating and I think it shows us that as much as we want there to be neat little stories about evolution that we can tie up with a bow, we don't always get that. Which makes it all the more interesting. Do you know what else I find interesting?

Erin Allmann Updyke: Everything.

Erin Welsh: Yes. The fact that it took until the 1950s for people to make the connection between gluten and symptoms.

Erin Allmann Updyke: I have so many questions.

Erin Welsh: Yeah. Okay. So I mean there are factors and some people's symptoms persist despite a strict gluten free diet. Plus gluten isn't everything. So some of these things might have made it more difficult. But still. So let's get into how that connection was eventually made.

Erin Allmann Updyke: Yeah.

Erin Welsh: Between Aretaeus' description from the second century CE or so, there was mostly silence on the celiac front for about 1700 years.

Erin Allmann Updyke: Wow. Okay.

Erin Welsh: So there's always an asterisk for these types of things, also I'm pedantic. So I have to self correct. Probably other people wrote about it or recognized it but maybe their descriptions were lost to obscurity or maybe they weren't precise or clear enough to gain traction.

Erin Allmann Updyke: Right.

Erin Welsh: Or it was people who were not in a position to be writing medical texts that were noticing these links and just managing it on their own, right. It's possible. But anyway, in terms of medical literature, enter Dr. Samuel Jones Gee in October 1887.

Erin Allmann Updyke: 1887. Ooh, okay.

Erin Welsh: 1887, yeah. That month, Gee presented a lecture titled 'On the Celiac Affection', a nod to Aretaeus who also used the term 'celiac diathesis' or 'celiac flux', with celiac meaning belly. Quote: "There is a kind of chronic indigestion which is met with in persons of all ages, yet especially apt to affect children between 1-5 years old. Signs of the disease are yielded by the feces being loose, not formed but watery, more bulky than the food taken would seem to account for. Pale in color as if devoid of bile, yeasty, frothy, an appearance probably due to fermentation, stinking, stench often very great. The food having undergone putrefaction rather than concoction." End quote.

Erin Allmann Updyke: Is this why you asked me about the details of the diarrhea, Erin?

Erin Welsh: I did indeed. Yeah, this is exactly why. I mean I just assumed that diarrhea does not come in one shape and size.

Erin Allmann Updyke: No, it comes in many.

Erin Welsh: Right.

Erin Allmann Updyke: There's just not one that's like... That description was beautiful, I don't think it's indicative of everyone with celiac's experience.

Erin Welsh: I just think poop can tell us so much and so I was curious.

Erin Allmann Updyke: I agree.

Erin Welsh: Let's see an episode on poop.

Erin Allmann Updyke: Okay. I don't know. Well okay.

Erin Welsh: What is the history of poop? I don't know. I'm sure there's some good nuggets.

Erin Allmann Updyke: Get it?

Erin Welsh: No pun intended.

Erin Allmann Updyke: Yeah, pun intended.

Erin Welsh: Okay, okay. Anyway, so that description is now still hailed as like this was a very clear description of what was probably celiac disease, right.

Erin Allmann Updyke: Okay.

Erin Welsh: So Gee wasn't sure what caused the disease. Quote: "The causes of the disease are obscure. Why out of a family of children all brought up in much the same way should one alone suffer?" Nor was he certain about its pathophysiology. Quote: "Naked eye examination of dead bodies throws no light upon the nature of the celiac affection. Nothing unnatural can be seen in the stomach, intestines, or other digestive organs. Whether atrophy of the glandular crypts of the intestines be ever or always present, I cannot tell." End quote. But he did have a suspicion. Quote: "If the patient can be cured at all, it must be by means of diet." End quote. Gee suggested among other things a diet consisting solely of mussels.

Erin Allmann Updyke: Sorry, mussels like the bivalve?

Erin Welsh: Yes, exactly like that.

Erin Allmann Updyke: Okay. Interesting.

Erin Welsh: So that was just like one of the diets that he discovered worked for one person.

Erin Allmann Updyke: Okay.

Erin Welsh: 3-4 pints of donkey milk daily.

Erin Allmann Updyke: Okay.

Erin Welsh: No vegetables or fruit whatsoever except a tablespoon or two of mashed potatoes.

Erin Allmann Updyke: Sorry, you're gonna get scurvy.

Erin Welsh: Yeah, I know.

Erin Allmann Updyke: Okay.

Erin Welsh: Meat juices and bread sliced super duper thin and toasted on both sides. So if you slice it really thin and you toast it on both sides, you're good, right?

Erin Allmann Updyke: You're good.

Erin Welsh: You're not. Not good.

Erin Allmann Updyke: But no fruits and vegetables except mashed potatoes? Do you have to put donkey milk in the mashed potatoes?

Erin Welsh: No idea about the mashed potato recipe, was not in any of the papers that I read. There was another paper from the 50s I believe that did have recipes in it. Just FYI.

Erin Allmann Updyke: Oh, love that.

Erin Welsh: I know. And so he was right in the general sense of things but not the specific.

Erin Allmann Updyke: Yeah.

Erin Welsh: It was diet related.

Erin Allmann Updyke: Right.

Erin Welsh: But not mussels only.

Erin Allmann Updyke: Not mussels, donkey milk, and bread.

Erin Welsh: Not no vegetables. Yeah. But Gee's observations caught on and several other physicians began reporting on the celiac affection as it was called, including Dr R. A. Gibbons who wrote in 1889, quote: "This causes a serious alteration of the digestive process. The food is too readily decomposed and the absorption into the blood of deleterious elements produces the profound ill health from which patients attacked by this disease suffer." End quote. Over the first couple decades into the 20th century, people continued to try to unravel the mystery of celiac disease and got so close to solving the puzzle but ended up sad and frustrated. Like G. F. Still who was rightly convinced that it was a digestive disease due to diet and even recognized that quote "unfortunately one form of starch which seems particularly liable to aggravate the symptoms is bread." End quote. Something that even Aretaeus hinted at nearly 2000 years before. But did Still try a bread free diet? Not that I could tell. Yeah.

Erin Allmann Updyke He's like oh man, seems to me like bread is doing it. But let's figure it out by looking somewhere else.

Erin Welsh Yeah. And so somebody else, Sidney Haas in 1924, introduced a banana diet which seemed to help. At least he claimed that the eight individuals who received the banana diet were clinically cured and the two who did not receive the banana diet died.

Erin Allmann Updyke What's the banana diet, please?

Erin Welsh Oh okay. It wasn't bananas only.

Erin Allmann Updyke Okay, thank god.

Erin Welsh Just 4-8 a day.

Erin Allmann Updyke Eight bananas a day? It's a lot of fiber.

Erin Welsh It's a lot of fiber. Sugar free, no bread, no crackers, no cereals, no potatoes.

Erin Allmann Updyke Okay.

Erin Welsh And it included a daily castor oil cleanse and colonic irrigation.

Erin Allmann Updyke My god. Like you're so right on so many things and so wrong at the same time!

Erin Welsh Because bananas are just sliding straight through your entire digestive tract. Like castor oil cleanse? No!

Erin Allmann Updyke I mean you'll be good on vitamin D, so that was probably important honestly.

Erin Welsh I feel like there's gotta be at a certain number of days of the banana diet, there's gotta be some sort of like overabundance, some sort of toxicity that you're getting from too many vitamins.

Erin Allmann Updyke It's a lot of potassium, yeah.

Erin Welsh Yeah. Do you always think of potassium from Honey, I've Shrank the Kids? Honey, We Shrank Ourselves.

Erin Allmann Updyke Honey, We Shrank Ourselves, 1000%.

Erin Welsh Yes.

Erin Allmann Updyke It's the only reason that I know that bananas are the source of potassium.



Erin Welsh

Me too. I always think of it. Okay. Anyway. So there's a lot that we could unpack about that paper and the banana diet. But putting that aside, people were beginning to circle around the connection between gluten and celiac disease. It's likely that somebody would have gotten there eventually but rather tragic circumstances ultimately provided the evidence that clearly demonstrated this link. In the winter of 1944-1945, food shipments were blocked to the western part of the Netherlands by German forces, leading to a famine affecting millions of people with ultimately around 20,000 deaths, estimates vary. The availability of wheat and rye dropped to near non-existent during this time. And one Dutch pediatrician, Willem Karel Dicke, noticed that his patients with celiac disease actually improved during the famine when they did not have access to wheat and rye.

And then when Swedish planes dropped bread into the Netherlands to help relieve this food shortage, those same kids experienced a relapse and got worse. And so Dicke put two and two together and realized that it might be wheat and rye and barley that was causing the problem and later showed that it was wheat flour and not wheat starch. Ultimately pointing towards gluten as the causative factor. Yeah. But apparently, so kind of when we're talking about like well how did people not realize this? Maybe they decided on an individual level. Apparently years before in 1930, Dicke had a patient who had celiac disease whose mother told him that when she removed bread and biscuits from her kid's diet that they got better. So I feel like probably a lot was like that.

Erin Allmann Updyke

Interesting.

Erin Welsh

But in any case, once Dicke had presented his observations, the use of a gluten free diet to treat people with celiac disease, it like took off tremendously.

Erin Allmann Updyke

Wow.

Erin Welsh

Because it was so, I mean it's so effective, right.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

And all that was left to do is figure out the mechanism, the diagnostic criteria, molecular test, the heritability of the disease and so on.

Erin Allmann Updyke

All the other parts.

Erin Welsh

All the other parts of the puzzle. Over the second half of the 20th century, many of those parts were found or were put together by research teams all over the world. And I'm not going to go into the nitty gritty of the history of discovery of those. But instead what I want to do is wrap up this history section by talking very briefly about the gluten free trend that really took off around 2010 or so. As with most health related things that make headlines or become trendy, it's a mix of fact, fiction, and people wanting to make money. We should honestly do a full episode on the gluten free diet.

It's not clear to me what initially propelled this gluten free diet to the wild popularity that it achieved. But around this time, around 2010s or so, is when non celiac gluten sensitivity was finally recognized as a real thing by much of the medical community. And following that were a bunch of articles and books that perhaps took this and ran with it a bit too much, overstating the extent to which a gluten free diet could improve the health of those who do not have a diagnosed gluten disease or sensitivity. Saying things like eliminating gluten will make you live longer, it will improve your brain health, it'll improve your relationships, it'll improve everything, right.

Erin Allmann Updyke	Everything.
Erin Welsh	And it's what we see with so many diet fads, it's what we see with so much health trends. Like it's a constant.
Erin Allmann Updyke	It's a diet fad like every other diet fad.
Erin Welsh	Exactly.
Erin Allmann Updyke	That's what it is.
Erin Welsh	Exactly. And then there was kind of this backlash, right, where people were like oh your gluten doesn't mean anything, blah, blah, blah. And there were a couple of fair points I think to the backlash against the gluten free diet but not very many fair points. Because first, so here are the fair points. First, there have been studies that show that people who do not have gluten intolerance or sensitivity can experience nutritional deficiencies with this restricted diet. Like it can actually impact your health negatively if you do not have gluten sensitivities or intolerance. And secondly, it has led to the spread of shaky or unsupported pseudoscientific claims about the link between gluten and overall health, again for people without diagnosed gluten disorders. The spread of those claims and sort of this like oh well this one trick, doctors hate this one trick.
Erin Allmann Updyke	It's the lose 10 lbs of belly fat or whatever.
Erin Welsh	Right.
Erin Allmann Updyke	10 lbs. It's the banana diet all over again honestly.
Erin Welsh	It's the banana diet all over again, yeah. Exactly. And this is like again, fad diets in general are horrible for this type of pseudoscience and the spread of pseudoscience. However the road to diagnosis for a non celiac gluten sensitivity or celiac disease can be a really long one. And so this diet provides a way of managing potential symptoms or seeing if gluten might be the issue or part of the issue for you. Secondly, a gluten free diet does bring about huge health improvements for those who can't eat gluten. Necessary. Like it is absolutely necessary. And thirdly, it has done a great deal to raise awareness I think of gluten intolerance and sensitivity and it has led to increased availability of so many more gluten free products which prior to 2010 were not nearly as numerous. And again, with the caveat that this is not globally, this is in certain regions of the world. But I do you think that raising the awareness... And we still have a long way to go. Just the fact that like when I was researching this, there are so many products that have gluten that I'm like but why does it have to have gluten?
Erin Allmann Updyke	Well and I feel like that is so true. And then on the flip side, there's so many products that now have the label of gluten free that I'm like an orange never had gluten in it. Why does that have to be on the label?
Erin Welsh	Yes.
Erin Allmann Updyke	Because it just makes things more confusing.

Erin Welsh: It makes things more confusing. I mean a lot of it is a marketing thing which is really predictable but frustrating. And so I think it's like a little bit of a trade off. I mean I think it's probably net positive for people who have gluten sensitivities or celiac disease because it's like oh yes, gluten. Like did you know the word gluten before 2010?

Erin Allmann Updyke: Right.

Erin Welsh: I'm not sure that I did.

Erin Allmann Updyke: Probably not.

Erin Welsh: Yeah.

Erin Allmann Updyke: Unless you were a baker.

Erin Welsh: Yeah, exactly. Right, right.

Erin Allmann Updyke: Yeah.

Erin Welsh: But yeah, maybe someday we should do like a deep dive on just the gluten free diet or other diet fads. But for now I'm going to turn it over to you, Erin, to tell me about celiac disease around the world today.

Erin Allmann Updyke: Oh, I can't wait to right after this break.

TPWKY: (transition theme)

Erin Allmann Updyke: So thank you, Erin, for saying around the world today because I think that people don't maybe recognize that celiac disease is actually a global thing. It's everywhere.

Erin Welsh: It is everywhere.

Erin Allmann Updyke: I think in part because of the kind of gluten free trend or whatever you want to call it that happened in the 2010s, celiac disease which has in many people's minds been conflated with other forms of gluten sensitivity, has this perception that it's only a disease of the Western world or something. And that's not true at all. The overall pool global prevalence of celiac disease is estimated at around 1.4%, that's like most papers cite around that number. There's a little bit of variation. And it's hopefully not surprising that there is estimated to be some variation of this across the world. Prevalence is estimated, surprising to me, to be a little bit higher in Asia at about 1.8% and a little bit lower to about the same as the global prevalence in South America at 1.3%. And then the European and North American prevalence as far as I can tell is about equivalent to the global prevalence of 1.4%.

Erin Welsh: Okay.

Erin Allmann Updyke: I also want to say, and this is what's fascinating to me when I read this because I still don't quite understand how, the first time in I think six seasons of making this podcast, the main paper that I read for these epidemiology numbers said that they thought that these numbers, this 1.4%, could be an overestimate.

Erin Welsh: What?

Erin Allmann Updyke

I know, right? I've never seen overestimate.

Erin Welsh

Yeah. Okay. So then what does that mean about where these numbers come from?

Erin Allmann Updyke

Yeah. So that's the thing. Because here's the other truth is that a large proportion of people with celiac disease are undiagnosed. So when you look at, for example, like biopsy confirmed prevalence estimates, they're closer to 0.7%. So this 1.4% is a projection estimate based on all of these different studies. But because serologic testing is imperfect and differs from place to place, this paper at least that it might be an overestimate. So who knows? It's somewhere between 0.7%-1.4% globally.

Erin Welsh

Fascinating.

Erin Allmann Updyke

But one thing that is consistent across all of the studies and in all the geographic regions, and you mentioned this Erin, incidence does seem to be increasing over time. This one paper from just a couple of years ago estimated that the pooled incidents worldwide is increasing like 7% per year. So that doesn't mean like 7% globally, it just means like compared to each year. And because celiac is a chronic disease, there's no cure for it, an increase in incidence necessarily means an increase in prevalence. So we have new cases being diagnosed and therefore more people are living with celiac every year. Does that mean that the true number of people who are developing celiac is increasing? We don't know. Because it could just be that we are getting a lot better at diagnosing and recognizing celiac disease. But at this point, we don't have enough data to necessarily disentangle are the rates of disease truly going up or are we just better at detecting it and so we are seeing an increase in rates because of this increase in detection. We don't know.

Erin Welsh

Yeah.

Erin Allmann Updyke

But what is still true today is that there is often a real delay in diagnosis. And hopefully with better and better diagnostic tools and more and more awareness, this delay kind of decreases in time. I don't have perfect numbers on this but there was a survey in Finland that reported at least a three year delay in diagnosis for about half of people living with celiac disease. And three years compared to some other autoimmune disorders that we've talked about might not seem that long. What was endometriosis? Like 10 years I think it was.

Erin Welsh

10-12. I think it's gone down in recent years. Yeah.

Erin Allmann Updyke

Yeah. But three years of not absorbing your nutrients, three years of worsening anemia and osteoporosis, that's a very long time. Especially because a lot of people do develop symptoms of celiac disease when they are kids, like under age 10. Which it means that you have kids that are not growing, that are failing to thrive, and that are having delays in their diagnosis. And adults too because really a lot of people don't develop symptoms of celiac until they're adults. So it kind of is both ends of the spectrum which is really interesting.

Erin Welsh

Yeah.

Erin Allmann Updyke

In terms of the pathways forward for celiac disease, there of course is a lot of research being done on what other factors might be in terms of triggers and how we prevent celiac disease. But one of the biggest areas of research is in therapeutics and specifically in trying to find therapies that don't require a strict gluten free diet. Because while a gluten free diet might be easier to achieve today or easier for some people than for others, there's really nothing easy about it. Like wheat is present globally in so much, even if you don't consider that it's also hidden present in so many of our standard American foods and in packaged foods, right.

Erin Welsh

Yeah.

Erin Allmann Updyke

So not only is it expensive and difficult to stick to it but it also can be socially stigmatizing. And like we heard in our firsthand account, it can lead to these unintentional difficulties in terms of people's relationship with food.

Erin Welsh

Yes.

Erin Allmann Updyke

And with celiac disease especially, even unintentional really small amounts of gluten can trigger severe disease relapse. So there's a lot of interest understandably in developing other therapy options. As of today, 2024, there's nothing that's like out there, there's nothing available. But there are a few big buckets of research that I wanted to just kind of highlight that people are looking at in terms of different strategies. So one is what's called like tolerance induction strategies. And so this is exposures in various ways that try and trick the body into developing essentially tolerance to gluten rather than having this really strong reactivity. There's various types of exposures and exposure to certain proteins and things like that that people are trying. We don't have anything yet but that's an idea. Another idea is using gluten degradation, think like lactase for gluten.

Erin Welsh

Yeah!

Erin Allmann Updyke

Using these glutenases.

Erin Welsh

Okay.

Erin Allmann Updyke

So that people can break down the gluten more efficiently to therefore not expose it in the same way to your T cells and not trigger this inflammatory response. So that's another option.

Erin Welsh

Got it.

Erin Allmann Updyke

Another really interesting idea is inhibiting that tTg. So inhibiting the tissue transglutaminase enzyme which then prevents the activation of those T cells and reduces your inflammation because you're reducing the auto antibody formation essentially. And finally monoclonal antibodies, which more generally are targeting like cytokine and inflammatory responses that celiac triggers rather than specifics of celiac or gluten itself, if that makes sense. There's lots of different options out there, none of them exist for humans today. There's a lot of them that are in either preclinical or in some cases like phase one and two clinical trials. So they're moving through the process. And I think that in the future, like in the next few years we will likely see some of these come to market. And it'll be really interesting to see who gets access to them and how much they end up helping people.

Erin Welsh

Yeah.

Erin Allmann Updyke

So that is celiac disease today, Erin.

Erin Welsh: It's amazing to me how on the surface it seems very simple, very clear, very like okay, this is the thing, this is the thing. But there's so much beneath the surface.

Erin Allmann Updyke: Oh 100%. 100%.

Erin Welsh: Always, always. It's always the lesson.

Erin Allmann Updyke: There always is. So if you'd like to learn a lot more, oh boy do we have sources for you.

Erin Welsh: We do indeed. Okay. I have a lot, I'm going to shout out three. One for the evolutionary history, one for the human history, and one about sort of the gluten free diet. So the first is by Sams and Hawks from 2014 titled 'Celiac Disease as a Model for the Evolution of Multifactorial Disease in Humans'. Then for the history Paveley from 1988, 'From Aretaeus to Crosby: A History of Coeliac Disease'. And then about the gluten free diet by Newberry et al from 2017, 'Going Gluten Free: The history and nutritional implications of today's most popular diet'.

Erin Allmann Updyke: Amazing. I have a few really interesting papers. If you want a deep dive on celiac like nitty gritty, there was a great paper from 2023 titled 'The Immunobiology and Pathogenesis of Celiac Disease' by Iversen et al. It was such an incredible pathophysiology deep dive. I also used the American College of Gastroenterology most recent guideline update which was again from 2023 by Rubio-Tapia et al. Several other papers by them. Another paper by someone that I have worked with in gastroenterology here in San Diego which was really exciting to see the name of someone you know. They don't know me. But anyways, that was 'Celiac Disease' from the Annals of Internal Medicine from 2020. We have so many more papers from this episode and all of our episodes on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) under the EPISODES tab.

Erin Welsh: A huge thank you again to Becca for sharing your story with us. We appreciate it so very much.

Erin Allmann Updyke: We really do. Thank you. Thank you also to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Welsh: Thank you to Lianna Squillace and Tom Breyfogle for the amazing audio mixing.

Erin Allmann Updyke: Thank you to everyone at Exactly Right network.

Erin Welsh: And thank you to you, listeners. Did you learn something? We hope so.

Erin Allmann Updyke: We hope so. I did.

Erin Welsh: I did too.

Erin Allmann Updyke: And as always a special shout out to our patrons. Thank you so much for your support. It really means the world to us.

Erin Welsh: It does. Well until next time, wash your hands.

Erin Allmann Updyke: You filthy animals.