

Erin Welsh	"The patient goes to bed and sleeps quietly til about two in the morning when he is awakened by a pain which usually seizes the great toe but sometimes the heel, the calf of the leg, or the ankle. The pain resembles that of a dislocated bone and this is immediately succeeded by a chillness, shivering, and a slight fever. The pain goes gradually more violent every hour and comes to its height towards evening, adapting itself to the numerous bones of the tarsus and metatarsus, the ligaments whereof it affects. Sometimes the gnawing of a dog and sometimes a weight and constriction of the parts affected, which become so exquisitely painful as not to endure the weight of the clothes nor the shaking of the room from a person's walking briskly therein. Things worsen til about 24 hours from the first approach of the fit. The patient is suddenly relieved and now being in a breathing sweat, he falls asleep. And upon waking finds the pain much abated and the part affected to be then swollen, whereas before only a remarkable swelling of the veins thereof appeared as is usual in all gouty fits."
TPWKY	(This Podcast Will Kill You intro theme)
Erin Allmann Updyke	I can't express how much I love that description. It's so good.
Erin Welsh	It's so good and it's so old. It's centuries old. So that was written by Thomas Sydenham and that was around I believe the late 17th century.
Erin Allmann Updyke	Wow.
Erin Welsh	And I got that directly quoted from a book titled 'Gout: The Patrician Malady'.
Erin Allmann Updyke	It just makes me so excited for the history of this one.
Erin Welsh	I am so excited for this episode that I almost forgot to say that 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	And today we're talking about gout!
Erin Welsh	We are. There is so much more to this disease than I ever realized at least in terms of the history. I'm excited to tell you all about it.
Erin Allmann Updyke	I can't wait because I know not even one single thing about the history of gout but just knowing how it develops in the body, I have no doubt that it is like deep roots and it's such a classic presentation that it's going to be so fun.
Erin Welsh	Well before we dive in, should we get down to business?
Erin Allmann Updyke	We should. It's quarantini time.
Erin Welsh	It is indeed. What are we drinking this week?
Erin Allmann Updyke	We're drinking Crying Gout Loud. I tried to really separate those words.
Erin Welsh	It's amazing. I love this. We had one of the longest lists of possible quarantini names I feel like.

Erin Allmann Updyke: Like gout puns.

Erin Welsh: Yeah, they weren't good.

Erin Allmann Updyke: No, none of them were good.

Erin Welsh: Except for Crying Gout Loud. What is in Crying Gout Loud, Erin?

Erin Allmann Updyke: Listen, it's basically like a stout based beverage.

Erin Welsh: Yeah.

Erin Allmann Updyke: We'll probably have some coffee flavoring in it. It's going to be fantastic and very high in purines.

Erin Welsh: Very high in purines. If you do have gout, you might want to stay away from this one or make some substitutions.

Erin Allmann Updyke: Yes.

Erin Welsh: Yeah.

Erin Allmann Updyke: We'll post the full recipe for the quarantini as well as the non alcoholic placeborita on our website thispodcastwillkillyou.com and all of our social media channels.

Erin Welsh: On our website, you know what you can find, check it out. There's lots of stuff there.

Erin Allmann Updyke: I love it.

Erin Welsh: I do have one piece of business that I wanted to mention at the top here and that is a pronunciation situation. So in our bends episode, I kept pronouncing the structures where you dig out to build the bridge pillar stuff-

Erin Allmann Updyke: Tubes that go down and down and down, yeah.

Erin Welsh: Exactly. I kept calling those ky-sins and I did do my due diligence, I thought, by looking up caisson pronunciation on Google, pressing the little play button and imitating the voice there.

Erin Allmann Updyke: The Google voice.

Erin Welsh: Turns out that Google voice had led me astray.

Erin Allmann Updyke: As they do.

Erin Welsh: And the real pronunciation as several listeners pointed out, thank you, is kay-sin. So there you go.

Erin Allmann Updyke: So there we go. Anything else?

Erin Welsh

I don't think so. Can we get started?

Erin Allmann Updyke

Let's get into the biology of gout right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

So gout is going to be a fun one in terms of the biology at least. And I again can't wait for the history section. But gout is a condition where on the one hand we know exactly what is causing it, we know exactly what causes the symptoms, we know almost all of it. And at the same time we know almost nothing, slight exaggeration, but very little about the kind of real underlying causes if you get down into the nitty gritty. So what I'm saying is that I am going to tell you in this section exactly how gout happens, I'm going to go over in detail the steps of gout formation from preclinical to actual clinical disease, what is happening in your body. But what I will not be able to tell you, Erin, which I know you want to know, is why gout happens. Okay?

Erin Welsh

Okay. I can come to terms with that.

Erin Allmann Updyke

So let's get into it. Gout is a form of inflammatory arthritis which means inflammation of the joints that's primarily driven by that inflammation itself as opposed to an osteoarthritis which is when you have degradation of the cartilage and bones rubbing together, etc, etc. There's a lot of different kinds of inflammatory arthritis, rheumatoid arthritis, psoriatic arthritis, etc. Gout as it turns out, which I did not know, is actually the most common form of inflammatory arthritis that affects adults. The most common one.

Erin Welsh

I mean actually that... So over the past couple of weeks while I've been researching gout and I would happen to mention to someone oh, I'm doing an episode on gout, without fail it was either oh, I've had gout or oh, I know someone that has had gout. And I'm learning so much about how many people have ties to gout. I have ties to gout. I have family members with gout.

Erin Allmann Updyke

Same. Same. My grandpa had gout really bad.

Erin Welsh

Yeah. Yeah, mine did too.

Erin Allmann Updyke

Yeah, I did not realize how common it is. So gout at its core is the result of the deposition of crystals of monosodium urate, so urate crystals in the joint space, and then our inflammatory response to these crystals. We're going to go there in detail but first let's talk about what it actually looks like. What does it look like when someone has gout? Y'all got a really good primer on it in that firsthand account because it was a perfect classic description of gout. It's often described, and when I say often I mean this is a board reviewed question in medical school, it 100% of the time starts like this. Ready?

A 65 year old man comes to your office with sudden onset pain and swelling in his left big toe. He said that he ate a steak and had a beer for dinner last night. He woke up this morning, like in the middle of the night, and he couldn't even stand the weight of the blanket on his foot, it was so incredibly painful. When you examine it it is warm, it's hot to the touch, it's red, it's super swollen, like the joint between his toe and his foot are just really swollen. And if you could touch it you might feel some fluctuance in that space, you might feel some fluid but it's so tender that you really can't even do an evaluation. Boom, answer C, that's gout.

Erin Welsh

And studying over.

Erin Allmann Updyke

Exactly. You're welcome, you all passed your boards. Of course it's not always that simple but gout typically is considered a monoarticular, so one joint or oligoarticular, so a few joints rather than something like there are some other inflammatory arthritis that maybe affect many joints in your hand and might affect both of your hands symmetrically.

Erin Welsh

That is very interesting. And so you will have gout at one time in one joint or just a couple of joints?

Erin Allmann Updyke

Exactly.

Erin Welsh

And are they all in the same area?

Erin Allmann Updyke

Great question. Most commonly it's going to be one joint, your big toe joint, so your MTP joint between where your toe hits your foot. So that joint of your big toe is one of the most common spots. Other spots are the joints in your heel, you actually have a lot of joints in your heel and that space really gets a lot of gout, or even along the tendon of your calf or the knees or really any of the toes. And yeah, usually it's going to be just one of those joints, it could be a couple and it may or may not be let's say all joints on your left foot. It might be your toe on your right foot and your heel on your left foot, it kind of just depends.

Erin Welsh

Okay, follow up question.

Erin Allmann Updyke

Okay.

Erin Welsh

You can get recurrences of gout.

Erin Allmann Updyke

Oh definitely.

Erin Welsh

Does it tend to happen in the same joints time after time?

Erin Allmann Updyke

It certainly can but it can definitely pop up in new joints as well.

Erin Welsh

Okay, okay.

Erin Allmann Updyke

And while it's primarily just one or a couple of joints, that's the classic presentation, it certainly can be affecting a lot more joints. It can cause a polyarticular, so many joints flare. And especially if you're so seeing it in a lot of joints than what you might see are a lot more systemic inflammatory symptoms. So things like fevers, chills, overall malaise and just feeling really crappy. Because at the end of the day this is an inflammatory process that's driving the pain and the swelling and so if you have severe inflammation, you're going to feel that in other parts of your body besides just that one joint where those crystals are.

Erin Welsh

Why? I know that I'm asking a why question and I apologize.

Erin Allmann Updyke

No, that's okay.

Erin Welsh

But why generally just one joint?

Erin Allmann Updyke

Let's get into the steps of this pathogenesis and I might be able to answer that question in a little bit more detail. Shall we?

Erin Welsh

Okay.

Erin Allmann Updyke

Okay. So gout develops in phases and there's three main phases. First there has to be hyperuricemia. That means there has to be an elevation in the blood levels of uric acid. So uric acid, urate, as a primer because this is not going to be an organic chemistry heavy episode don't worry. But urate is essentially one of the breakdown products of purines. Purines are one of the nucleotides that make up our DNA. So basically you can think of urate or uric acid as a byproduct of cell or DNA breakdown. It's present at various levels in our body at various times. So for the first steps of gout there has to be an abnormal elevation in urate levels. That step is necessary but by no means sufficient because a lot of people if you just tested random people's blood might have high levels of urate without ever having gout. And we'll get there.

The second thing that has to happen is that urate which hangs out in our bloodstream as a negatively charged anion combines with sodium which is positively charged and forms monosodium urate, which will then crystallize in our bloodstream. They come out of solution as crystals and these crystals deposit in places like our joint spaces. But again these crystals alone are not sufficient either, they're just the second step. But there is a subset of the population that has hyperuricemia, high levels of urate, and if you checked some of their joints you might find MSU or monosodium urate crystals but still no gout. Gout is what happens when our bodies see these crystals and then mount an acute inflammatory response to them. So gout is truly the result of that inflammation attacking those crystals.

Erin Welsh

So you could have the same level of crystals in whatever joint in two individuals and one person could have gout with the inflammatory response and the other person's immune system doesn't react to it and doesn't create that inflammatory response?

Erin Allmann Updyke

You got it.

Erin Welsh

And I'm not allowed to ask why?

Erin Allmann Updyke

I'm going to get a little bit more into this, okay?

Erin Welsh

Okay.

Erin Allmann Updyke

We'll go over these three steps in a little bit more detail.

Erin Welsh

All right.

Erin Allmann Updyke

Because I know we can't just leave it there. Not on This Podcast Will Kill You.

Erin Welsh

No.

Erin Allmann Updyke

Okay so we have these three steps. I'm going to try my best to answer some of the whys of these three steps as we break them down. So why do some people get hyperuricemic? Why do some people have high levels of urate in their blood? It turns out that humans in general have much higher levels of urate than most other mammals in the animal kingdom because of some weird quirks in our evolution that led to the inability to further metabolize urate.

Erin Welsh

I'm going to talk about this a little bit.

Erin Allmann Updyke

I am so excited because when I read that I was like what?

Erin Welsh

Just a little bit.

Erin Allmann Updyke

It's great!

Erin Welsh

It's so fascinating.

Erin Allmann Updyke

Most other mammals can further metabolize urate so it doesn't hang out as a byproduct in their system because they keep breaking it down. In humans, we've lost that ability. It is thought that urate has some biological functions itself, like it may serve as an antioxidant, it might be involved in our innate immune response to some degree, maybe even in maintenance of blood pressure. But that is true for all humans. So why do some of us have even higher levels than others? And there are a lot of different factors that go into this. There are environmental factors, individual factors, dietary factors, genetic factors that all are going to play into what the levels of urate are in your blood compared to your neighbor's or your brother's.

So for example, eating high purine foods like beer, meat, seafood, these things have a high level of purines. This will increase purine degradation and therefore increase urate because that's the end product of purine degradation. It also seems like eating high amounts of fructose as well as alcohol increases purine degradation but what's really cool about this is it's through a convoluted series of steps that are required in fructose and alcohol metabolism. If you remember all the way back to our alcohol episode, how when we break down alcohol we have to use up ATP and then it messes up a bunch of our other cycles. Well fructose does the same thing and both of those end up with an overload of AMP which is then broken down via a pathway that leads to urate. I just find that little bit of biochem kind of fun. And then there are also some other things that you might eat that actually could lower serum urate like coffee, awesome, vitamin C, maybe some other things.

Erin Welsh

Okay.

Erin Allmann Updyke

So that's one aspect of it which is dietary. It does contribute but as I'll talk about later on, it's probably not as big of a player as it's often made out to be which I think is really important as we get into how gout actually affects people's lives because it's a pretty gnarly disease. But there are also a lot of other individual factors like specific disease states, especially kidney disease. We excrete your ate through both our kidneys and to a lesser extent our GI tract. So if you have kidney disease or high blood pressure or you're on certain medications, you might have decreased urate excretion.

Erin Welsh

Okay.

Erin Allmann Updyke

And so that's going to lead to higher urates. Higher BMIs do tend to have higher levels of urate, I do not know what that mechanism is but it is a pretty strong correlation. And then of course there are genetic factors. And these genetic factors likely play the biggest role in terms not necessarily in how quickly we might produce urate but how well we excrete it. So there are a lot of different genetic variants in transporters for urate that are present in both our guts and our kidneys that are strongly associated with variations in serum urate levels. So if you have certain alleles, certain transporter malfunctions, you're going to end up with more urate than your neighbor who doesn't have that transporter in their kidneys. That makes sense?

Erin Welsh

Yeah.

Erin Allmann Updyke

So in short the propensity towards having high levels of urate, while it has a lot of factors, genetic factors probably are a really big driver.

Erin Welsh

Okay. But there's another aspect that you talked about where you could have the same levels of urate which means that your excretion would be similar between two individuals but there's still that one person that would get gout and the other person wouldn't. And is that like an immune response?

Erin Allmann Updyke

Let's get into it, shall we?

Erin Welsh

Okay, okay.

Erin Allmann Updyke

Let's move on to step two, right. So step two of the process is the crystal deposition itself.

Erin Welsh

Yeah.

Erin Allmann Updyke

So the crystal deposition takes three steps. It takes reduced solubility. So you have to have high levels of urate that lead to supersaturation of urate in your serum or in the joint space. You then have to have nucleation which if you have ever made rock candy, right? We've all made rock candy?

Erin Welsh

I have not.

Erin Allmann Updyke

Really?

Erin Welsh

I love rock candy.

Erin Allmann Updyke

Oh you should totally make it.

Erin Welsh

I should.

Erin Allmann Updyke

It's really easy.

Erin Welsh

Okay.

Erin Allmann Updyke

You basically just put a string in your cup of sugar water, right, but the string is really important because that's what gives the sugar crystals something to grow onto, to glom onto. And so that's called nucleation, having a site for crystal formation and then you have crystal growth.

Erin Welsh

That makes sense why it would be in one joint then.

Erin Allmann Updyke

Exactly. And so we know that there are specific joints, in particular the MTP joint of your foot, your midfoot, your heel, your knees, that these crystals seem to preferentially deposit. We don't 100% understand this but temperature is probably one of the main drivers of this. If we think back to our bends episode, we know that solubility of things depends a lot on temperature and urate is less soluble at lower temperatures as well as higher pH ranges and where you have higher concentrations of sodium. And so that's why we tend to see joints of the foot, which are cooler, preferentially affected. But also you might have in different joint spaces concentrations of other ions that might be different, especially if you are say overall dehydrated, like might happen overnight and we often see flares peaking overnight or after things like alcohol consumption which dehydrate you as well as provide you purines. And then you also have things like a nidus for crystal formation on joints that might be already degenerated, right, spaces that have more, if you think of it as like texture to them, that's more areas for those crystals to deposit.

Erin Welsh

Gotcha.

Erin Allmann Updyke

Yeah. That is how you end up with crystals. But then of course because 25% of people with hyperuricemia have evidence of crystal formation and they don't all have gout, we get to the real crux of it which is the inflammatory response. Why this inflammatory response.

Erin Welsh

Is this is step three?

Erin Allmann Updyke

This is step three.

Erin Welsh

Okay.

Erin Allmann Updyke

And this is where I don't have the answer to the why. There are a lot of inflammatory mediators and markers that are involved in the inflammatory response. We know some of them. We know that for example IL1B is very pivotal, this is a specific inflammatory cytokine that is released by macrophages that interact with the MSU crystals. We know that this is one of the pivotal steps in starting off a gout flare. We know that neutrophils are very heavily involved, we know that leukocytes are driven to the area. But we don't understand the intricacies of this process and while we do think that it is again largely genetic variants that are determining your individual inflammatory response, we still don't know why some people with these crystals get gout and other people don't. And why do you get that gout flare now and not yesterday.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

What does age have to do with it?

Erin Allmann Updyke

So age is one of the biggest risk factors for gout overall. Kidney function declines with age so you're more likely to become hyperuricemic the older that you get. Joint degradation is going to increase with age so you're going to have more areas where these crystals are likely to deposit. And then it's also kind of a time process. This isn't something where if your urate levels spike one day, tomorrow you're going to get gout. It is still a chronic disease and a disease that increases with age in part because of that.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

Can we talk about soft tissue gout? How does that happen?

Erin Allmann Updyke

I mean exactly the same way, it's just that those crystals deposit say in your tendons instead of in your joint space.

Erin Welsh

How often does that happen compared to joint gout?

Erin Allmann Updyke

It's a good question. I don't have numbers on the specific types of gout and flares in different places but it definitely is a part of a gout picture.

Erin Welsh

Okay.

Erin Allmann Updyke

That classic description of gout, the old man who got it in his big toe, is really common but gout is a much bigger deal than just that picture and it affects a wider range of joints and of body tissues. It's also something that is a chronic disease. So while gout flares themselves are generally self-limited, meaning that each flare even if you don't treat it may last anywhere from 7-10 days, which if you talk to anyone who's ever had gout, that sounds like an excruciatingly long time to be in that much pain. I wouldn't want to leave it untreated for a week. But in general the body does eventually cool down and resolve each of those inflammatory flares. It reduces the pain, it reduces the swelling.

But over time there can be this chronic foreign body response to those collections of MSU crystals and it can result in the formation of what are called tophi which are these subcutaneous, rubbery nodules. Depending on how big they get, they can sometimes have this white chalky cheesy stuff that comes out of the tip that really is like crystals and your inflammatory response to it. And these can and do cause damage to the bone underlying them or the tissues underlying them because these are a result of chronic inflammation and remodeling around these crystal deposits.

Erin Welsh

Right.

Erin Allmann Updyke

The tip of the ear is one of the other places that you see especially these tophi a lot, not necessarily a painful gout flare but you get this chronic inflammation and the tophi formation.

Erin Welsh

Interesting.

Erin Allmann Updyke

Yeah. In general these tophi are painless, they don't necessarily hurt. But again they can cause damage to the bone or the tissues underneath and that joint damage can be painful. But the good news is that there are a lot of different ways that we can treat this, it's a very treatable disease. So in the case of these acute flares, the gout flares, the biggest thing is controlling that acute inflammation and we do that with a combination of different anti inflammatories.

So things like ibuprofen or NSAIDs, steroids if it's a really bad flare because they're very anti-inflammatory, and then there's this medicine called colchicine which is an awesome anti-inflammatory that disrupts tubulin and then interrupts ourselves ability to complete inflammation. It's cool. I like it. And so those are kind of the mainstays of treating these acute flares. But once somebody has had a flare of gout they are at risk for having another flare. And so especially for people who have recurrent flares, like two or three or more flares in a year, the mainstay of treatment is called urate lowering therapy, ULT. Literally we know that the problem is you have too much urate so we're going to bring those urate levels down.

Erin Welsh

Right.

Erin Allmann Updyke

And the number one drug that tends to be used to do this is called allopurinol but there are a number of other drugs that we use to do this and they all work in different ways. Some of them block the formation of urate altogether, some of them stop the kidneys from reabsorbing urate, or some of them are actually enzymes that you take to further metabolized urate in your own system if that makes sense, since our bodies don't do that.

Erin Welsh

Yeah.

Erin Allmann Updyke

So there are a number of different drugs and in general this is the absolute mainstay of treatment is we need to reduce the levels of urate and then we stop this entire process and you can cure gout.

Erin Welsh

That's awesome.

Erin Allmann Updyke

I know, right?

Erin Welsh

That's not how it was for so much of history.

Erin Allmann Updyke

Oh I know. So that brings me to my question, Erin.

Erin Welsh

Yeah.

Erin Allmann Updyke

Which is like hello, how did we get here?

Erin Welsh

I can try to answer that at least. Well I'll answer something..

Erin Allmann Updyke

Okay, great.

Erin Welsh

Right after this break.

TPWKY

(transition theme)

Erin Welsh

Today we may think of gout as a relatively straightforward disease. We know what causes it, at least the immediate cause, and we know how to treat it and cure it. Most of us probably don't think all that often about gout unless you had it or you have it and you're in the middle of a flare. But for much of its history, and talk about a long history, gout was anything but simple and straightforward. Gout held incredible meaning, used to distinguish you from your peers or teach you a lesson about the dangers of overindulging.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

It was used in political and religious allegories, plays and poems were written about it, gout was the focus of many paintings and comic illustrations, and an entire industry was centered on peddling cures for it, most of which did nothing of course. Gout's widespread prevalence and unknown pathology were just a couple of reasons why so much attention was focused on it but another reason was who tended to be diagnosed with it. Gout had a reputation for affecting wealthy men who ate their fill of rich foods, drank more than their share of fortified wine, and had a lot of sex. And it was this stereotype of gout that not only drew so much medical attention to it but shaped the way that gout was talked about and perceived. Gout for a lot of its history stands in sharp contrast to many other diseases where diagnosis meant that you had done something wrong or that you yourself were wrong in some way, less than. Whereas to be diagnosed with gout meant that you were a genius, a gentleman blessed with this most aristocratic of diseases.

Erin Allmann Updyke

Fascinating.

Erin Welsh

I know. And we can compare this to some 20th century ideas about cancer for instance, where there was thought to be a cancer-prone personality type. People who were rigid, dull, lacking in emotion were thought to be more likely to develop cancer which is a nice bit of victim blaming.

Erin Allmann Updyke

Oh wow.

Erin Welsh

And of course cancer is just one example of how certain diseases were so closely tied with identity in a negative way and some still continue to be, right. And we've talked on the podcast before about how the language that we choose to describe a disease is very important and can reveal a great deal about how and why the disease is perceived the way it is. And so that's kind of what I want to talk about today or at least a good chunk of it, how people felt and wrote about gout historically and how that changed as political winds shifted or as we learned more about the underlying cause of the disease. But first let's go back in time to see what we can find out about the evolutionary origins of gout.

Erin Allmann Updyke

I love this already.

Erin Welsh

So Erin, in a bit you'll talk about the global prevalence of gout which turns out is quite high, higher than I realized. I read in one paper that prevalence estimates vary from around 1%-6.8%, something like that.

Erin Allmann Updyke

Just depends on the study.

Erin Welsh

Yeah. That's a ton of people. It's a ton of people. Gout, unlike many of the diseases that we've talked about on the podcast, is not a fatal disease but it can negatively impact your life in a number of ways like excruciating pain, reduced mobility, not to mention its emotional impacts. With these negative consequences of gout, why do we see such high numbers from an evolutionary perspective? And also do other animals get gout? They do.

Erin Allmann Updyke

They do?

Erin Welsh

As you said Erin, high levels of serum uric acid can lead to gout and these high levels have also been associated with things such as diabetes, kidney disease, hypertension, stroke, and atherosclerosis among others. So it would seem pretty important to keep those uric acid levels tightly regulated and in a healthy range. And that is done by many animals, like you said, using an enzyme called uricase which breaks down uric acid. Except not all animals have functional uricase. The uricase in humans and some other primates has been rendered nonfunctional due to mutations and this has led to levels of serum uric acid 3-10 times higher than in other mammals. We know that these high levels of uric acid can have negative health consequences but can they also be beneficial? Is that possible?

Erin Allmann Updyke

Can they?

Erin Welsh

Could these higher levels of uric acid have been selected for? Some researchers think so. A few relatively recent papers proposed that higher levels of uric acid could have been helpful for our primate ancestors in the Miocene around 15-20 million years ago who were living in resource limited environments and consuming mostly fruit, since uric acid helps to convert fructose into fat storage. So having higher levels of uric acid through the inactivation of uricase could have helped them survive better.

Erin Allmann Updyke

Interesting.

Erin Welsh

Another hypothesis is that uric acid was retained to act as a powerful antioxidant, increasing the life expectancy of hominids. And researchers think that the inactivation of uricase happened after our ancestors lost the ability to synthesize vitamin C, so that would have also acted as like a replacement antioxidant.

Erin Allmann Updyke

Interesting. Like a redux vitamin C.

Erin Welsh

Yeah, yeah.

Erin Allmann Updyke

Interesting.

Erin Welsh

And yet another idea is that higher levels of uric acid helped our ancestors to maintain blood pressure when they weren't getting a lot of salt in their diets.

Erin Allmann Updyke

Right, yeah.

Erin Welsh

Yeah. However it happened, I think it's interesting food for thought and I'll post some papers about these different hypotheses if you want to read more about them.

Erin Allmann Updyke

Love it.

Erin Welsh

Okay but I also asked another question. Do other animals get gout?

Erin Allmann Updyke

Yeah. And you said yes!

Erin Welsh

Yes. Turns out some absolutely do get gout including other ape species that also lack functional uricase which makes sense. But the most exciting thing I learned was from a paper in 1997 that claims that none other than Sue the T. Rex had gout.

Erin Allmann Updyke

Stop.

Erin Welsh: Yeah.

Erin Allmann Updyke: She had tophi?

Erin Welsh: Well I guess so. I don't remember where on the skeleton but because gout can leave traces on bones then it makes sense that they looked and they were like that looks like gout to me.

Erin Allmann Updyke: Interesting. I want to read that paper.

Erin Welsh: I'll post it. It seems that other birds and reptiles lack uricase so these animals would also be susceptible to the disease.

Erin Allmann Updyke: I love it.

Erin Welsh: Dinosaurs get the gout.

Erin Allmann Updyke: Can you just imagine a T. Rex with gout?

Erin Welsh: I can just imagine how painful. Giant joints.

Erin Allmann Updyke: And they don't have a lot of other limbs to make up for it.

Erin Welsh: No. Yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: All right.

Erin Allmann Updyke: Okay.

Erin Welsh: We know that because of this uricase inactivation, humans have been susceptible to gout for millions of years, all of human history. And study of ancient but more recent human remains backs this up. Researchers have found evidence of gout in mummified remains in Ancient Egypt from 4000 years ago and in remains during Roman times throughout Europe. Gout was one of the earliest described diseases with possible mentions in Ancient Egyptian medical texts. But the first clear depiction of gout comes from none other than our fave the Hippocratic texts from around the 400s BCE.

Erin Allmann Updyke: Love it.

Erin Welsh: Quote: "Persons affected with the gout who are aged, have tophi in their joints, who have led a hard life, and whose bowels are constipated are beyond the power of medicine to cure."

Erin Allmann Updyke: Wow, gosh.

Erin Welsh: I know. Hippocrates referred to it as quote "the unwalkable disease". Yeah.

Erin Allmann Updyke: Are you going to tell me where the word gout comes from?

Erin Welsh: I am, I will.

Erin Allmann Updyke: I can't wait. When you said like Hippocrates said gout, I was like how did he get the word gout?

Erin Welsh: That was definitely a translation. Probably podagra is what he would have called it.

Erin Allmann Updyke: Okay.

Erin Welsh: I'm not sure actually because I think gout wasn't used until like 1100 or that's the first mention of the word gout. It comes from Latin, I'll get into it.

Erin Allmann Updyke: Okay, cool.

Erin Welsh: But it's this early on the time of Hippocrates in its first clear description that gout already had a rough outline of the reputation that would follow the disease all the way through to the 18th and 19th centuries. In Ancient Greece and Rome it was said to be a disease of decadence and was used as an illustration for the consequences for a society that had started to indulge. Nero's advisor Seneca wrote in the first century CE that the increase in gout in general but especially in women signaled a decline in the morals of the time.

Erin Allmann Updyke: Oh my goodness.

Erin Welsh: Quote: "In this age women rival men in every kind of lasciviousness. Why need we then be surprised at seeing so many of the female sex afflicted with the gout?" Yeah, it's great. Although we don't have stats for the prevalence of gout during Roman times, one author suggested that the high rate of lead poisoning could have exacerbated gout or made it more prevalent due to the impact on kidney function on hyperuricemia. What do you think about that? Plausible?

Erin Allmann Updyke: I would have to remind myself of our lead episode.

Erin Welsh: Same.

Erin Allmann Updyke: But it totally makes sense because yeah, if you have anything that's going to increase your incidence of kidney disease, you're going to increase gout.

Erin Welsh: There you go.

Erin Allmann Updyke: Yeah.

Erin Welsh: So possible. The Hippocratic Texts wrote that it was caused by a sedentary lifestyle with too rich a diet and too active a sex life. And general rules were laid out as to who was susceptible, women who had gone through menopause and men after they've had sex for the first time.

Erin Allmann Updyke: Okay.

Erin Welsh

Gout or specifically podagra from the words for foot trap was referred to as quote "the rosy daughter of Bacchus", who is the god of agriculture, wine, and fertility, and Venus, the goddess of love, beauty, desire, sex, etc. Greek-Syrian playwright Lucian wrote a satirical play about gout called Trago-Podagra in which a man with gout and his doctor do battle with the heartless demon goddess Podagra. And this wasn't his only play about gout which I just love. Another was titled Swift of Foot and the main character, the title character, was a fast athletic young hunter who laughed scornfully at people with gout saying they were exaggerating and it was no big deal. So of course the goddess Podagra cursed him through his feet and claimed her victory. Quote: "I have a name men dread and loathe to hear. They call me gout, a fearsome scourge to men. I bind their feet in sinew knotting cords when I have swept unseen into their joints."

Erin Allmann Updyke

I love it.

Erin Welsh

It's amazing. Of course gout was not really thought to be caused by a vengeful goddess. Under the humoral theory which was developed by Hippocrates and later Galen in ancient times, in the body there were four humors: blood, yellow bile, black bile, and phlegm. And when those humors got out of balance disease would result. One of these diseases being gout which was thought to be caused by a buildup of phlegm at the joints, preventing the rest of the humors from flowing as they should. The humoral explanation for gout persisted for hundreds of years and it's actually how gout got its name. So the word gout, like I said, comes from the Latin word 'gutta' for drop, which refers to the belief that one of the humors dropped into the affected joint. It's not that exciting of an explanation.

Erin Allmann Updyke

But interesting.

Erin Welsh

But it is, yeah. But I also should point out that it didn't have to be a joint. Gout was very widely used to describe any manner of things and it's likely that many historical references to gout may not actually have been gout as we define it today. Anywhere there was thought to be a buildup of phlegm or other humors you could have gout, like a gouty migraine or gouty hemorrhoids. This combined with the fact that gout grew to become a fashionable disease. Like were you really a member of the aristocracy if you didn't have gout? It makes teasing apart real gout from not gout a bit difficult. But in any case it seems likely that gout has historically been a very prevalent disease, given just how much it was written about in ancient times by all the famous medical writers and how many treatments there were. Let's go through a few of those.

Erin Allmann Updyke

I feel like it's been a little while and I can't wait.

Erin Welsh

It has, there are some good ones in here. I'm excited about it. All right, well you've got your classics, right. Bloodletting, diuretics, emetics, purgatives, some straightforward lifestyle changes like exercise and a lean diet. Staying away from wine, mead, and sex for awhile. Again with the sex. Or a bit more adventurous, going on a sea voyage since that would force you to eat fish rather than red meats and seasickness would be a great way of relieving the symptoms.

Erin Allmann Updyke

Ah yes.

Erin Welsh

And finally if you were truly desperate, you could scorch the veins above the affected region. Sounds horrible.

Erin Allmann Updyke

I'm sorry, what?

Erin Welsh

Yeah. You could boil up a puppy with cucumber, roux, and juniper.

Erin Allmann Updyke

No. No.

Erin Welsh

Nope.

Erin Allmann Updyke

Stop it.

Erin Welsh

Or you could chop up a piece of hard old cheese, soak it in bacon broth, and make it into a plaster which you lay on the affected joint.

Erin Allmann Updyke

I have so many questions.

Erin Welsh

I don't have any of the answers, I'm certain of that.

Erin Allmann Updyke

A hard old cheese.

Erin Welsh

I think the quote was like there is used for hard old cheese.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

None of these ancient treatments likely brought any relief with one notable exception, colchicum, which is from the plant autumn crocus or meadow saffron. It was used as a laxative and as a poison and it also helped to relieve the pain associated with gout. I read that the first mention of colchicum to treat gout was from around 500 BCE but at some point it fell out of popularity and was only picked back up again in the 1700s. Okay, I think we've spent enough time in the ancient world of gout. So let's journey to the golden age of the disease which really begins around the 1600s and last until the early 1800s.

Erin Allmann Updyke

Okay.

Erin Welsh

It was during this time that gout really came into the reputation that had been loosely established in Ancient Greece and Rome. Here gout became known as the monarch among maladies due to its strikingly high prevalence among kings, lords, ministers, and other members of the aristocracy. Philip II of Spain, Henry VIII, George IV, lots of famous Charles', two Queen Annes. Queens Anne? I don't know. Benjamin Franklin, Wilkie Collins, Francis Bacon, Isaac Newton, and Thomas Sydenham, the provider of our firsthand account and also who kicked off a huge interest in gout in the 17th century. All of these famous people and so, so many more had gout. And even though I just included old names, gout is by no means a disease of the past and you can find many more recent names to add such as Bernie Sanders, Jim Belushi, Alec Guinness, and many, many more that I haven't mentioned.

Erin Allmann Updyke

We haven't done this in a while, like name who has the disease. I really love it.

Erin Welsh

I know. It's amazing. Many of the gout scholars of this time, of the 1600s, 1700s, they themselves had gout or had close friends that did and I think that carries into the way they wrote about the disease. So in contrast with something like a sexually transmitted infection or a parasitic infection, gout was not anything to be ashamed of or talked about only in whispers. It was a badge of honor, proof that you belonged in the club. Before reading some descriptions of gout from this golden age of gout where it really shines through this reputation, this claiming of gout, I want to read a modern quote from a book about the usefulness of gout. Quote: "So pressing has been the ideological need to reinforce hierarchies of social distinction that the upper crust has even been eager to flaunt marks of debility to signal its exclusiveness."

Erin Allmann Updyke

Wow.

Erin Welsh

So only if you belonged to a certain gender, race, and class were you allowed to have gout and you should be grateful for it. The long recognized heritability of the disease was taken as further proof that gout only affected those who were worthy. Let me read you this quote from Thomas Sydenham's 'Treatise on the Gout' published in 1683. Quote: "The gout generally attacks those aged persons who have spent most of their lives in ease, voluptuousness, high living, and too free a use of wine and other spiritus liquors. And at length by reason of the common inability to motion in old age entirely left off those exercises which young persons commonly use. And further such as are liable to this disease, have large heads and are generally of a plethoric, moist, and lax habit of body and with all of a strong and vigorous constitution and possessed of the best stamina vite."

He then followed that up by saying, because he also had gout, quote: "But what is a consolation to me and maybe so to other gouty persons of small fortunes and slender abilities is that kings, princes, generals, admirals, philosophers, and several other great men have thus lived and died. In short, it may in a more especial manner be affirmed of this disease that it destroys more rich than poor persons and more wise men than fools, which seems to demonstrate the justice and strict impartiality of providence."

Erin Allmann Updyke

Very interesting.

Erin Welsh

Isn't that? Gout was a blessing. Gout was good.

Erin Allmann Updyke

Weird.

Erin Welsh

Very weird.

Erin Allmann Updyke

Very weird.

Erin Welsh

But not surprising I guess when you think about the source, right? Another gout sufferer, Lord Chesterfield, said quote: "Gout is the distemper of a gentleman, whereas the rheumatism is the distemper of a hackney coachman." A quote from 1803 attributed to a fragment from an ancient manuscript goes quote: "Blessed gout, most desirable gout, sovereign antidote of murdering maladies, powerful corrector of intemperance, deign to visit me with thy purging fires." Benjamin Franklin composed a quote "dialogue between Franklin and a Gout" where gout informs Franklin that he brought it on himself and that he's not truly an enemy since he is teaching Franklin temperance. In the late 1600s, early 1700s a Bavarian publisher and engraver, Gottfried Rogg, wrote out a list of 20 virtues of podagra. And I won't read all of them since this is already so full of quotes with more to come but I'll read a few of my faves. Number 1: "The podagra is a fashionable ailment because he who is burdened by it does not run around all over town with other ambitious persons but remains elegantly at home."

Erin Allmann Updyke

Wow.

Erin Welsh

Number 3: "It is humble because it attaches itself to the patient's feet." Number 8: "Taciturn, one size more than one reads while all conversation becomes annoying." 14: "Chaste, since it does not even like to be touched." 17: "It is faithful because it seldom leaves its patient entirely."

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

And 20: "It finally is also majestic. One lies in bed like a king on his throne, one goes to meet no one, one arises for no one, one accompanies no one, and one finally visits no one. Even when one has been visited."

Erin Allmann Updyke

Oh my goodness. How bizarre and interesting.

Erin Welsh

I love it. Yeah and there's more where that came from, it's quite a list. In terms of treatment, while some doctors promised a cure or symptom relief through this or that treatment, most said that gout could not be cured. So many doctors just leaned in more than I've ever seen doctors lean in while doing the research for this podcast. The sentiment was well of course we could cure it but why would we want to? You should be grateful for this disease because not only does it prove that you're a distinguished gentleman genius, it will also act as a guiding hand, teaching you to slow down and take it easy, to learn how to live in healthy moderation. And bonus, as long as you have gout, you'll be protected from developing other more deadly diseases. Because that was a very common belief at the time.

Gilbert Sheldon, who was Archbishop of Canterbury under Charles II in the 1600s, supposedly offered a £1,000 reward to any person who could quote "help him to the gout to cure the distemper in his head" which he worried would kill him. And ultimately it did. And in a sense, I can see why it would be a tempting thing to believe. If you put yourself in the 1600s, you had so many deadly diseases to worry about. So if you got gout, you could take some comfort that while it was persistent and painful, it wasn't going to kill you.

Erin Allmann Updyke

Well I imagine too because it often affects people who are older, you might look at that and think well old people have it so I will live to be old if I have it.

Erin Welsh

Yes.

Erin Allmann Updyke

Like backwards kind of thinking. Yeah.

Erin Welsh

Totally, yeah. Like I should be so lucky to have gout.

Erin Allmann Updyke

Right, exactly.

Erin Welsh

Yeah.

Erin Allmann Updyke

How interesting.

Erin Welsh

Did gout protect you from other diseases? I highly doubt it. But I also don't want to give the impression that gout was a walk in the park. Gout was, is, horrifically painful, like quote "walking on eyeballs" as one person said or quote "no other pain is more severe than this, not iron screws nor cords, not the wound of a dagger nor burning fire." For some like Samuel Johnson it was incomprehensible that gout would be looked at as a blessing. Quote: "At best the gout is only a dog that drives the wolf away and eats the sheep himself, for if the gout has time for growth, it will certainly destroy and destroy by long and lingering torture." While this negative attitude towards gout may have been in the minority during the 1700s, it was becoming increasingly common as the 19th century rolled around.

Gout was still heavily personified but the moral of the story seemed to be changing. Whereas in the couple of previous centuries gout was a lesson for the wealthy to take it slow, in the 19th century it became a symbol of over consumption, of the negative consequences of greed and excess, a rightful punishment in some Christian allegories and a political lesson in others. The government in England was ruled by a system of checks and balances, keyword being balance, and gout was often used to illustrate what could happen when things were out of balance, especially due to a lack of self control or oversight. This shift in the narrative around gout was not a welcome one for those with the disease. In 1771 William Cadogan published a dissertation on the gout in which he labeled gout as a self-inflicted disease entirely with idleness, intemperance, and vexation to blame and without any hereditary component whatsoever. The rebuttals came in strong and fast.

People took issue with Cadogan's explanation as gout being self-inflicted also because it meant that it could be cured or prevented by practicing exercise, temperance, and peace of mind. Everyone knew that gout was impossible to treat. What is this guy talking about? Everyone, including the ancient medical writers, knew that gout was a mark of genius handed down through special lineages. How did Cadogan dare to go against that? Because that was really the biggest issue that people had with his publication, his claim that gout was not at all hereditary impugned gout's honor and denied the meaning that it had held for so long.

Erin Allmann Updyke

Wow.

Erin Welsh

There's so much more to gout than I realized.

Erin Allmann Updyke

So much more. Wow, I love it. I was never expecting to go down this road.

Erin Welsh

Me neither. I'm so glad that this is what I get to do, it's great. Of course Cadogan was wrong in his insistence that heritability was not involved in gout but his dissertation on gout at least to me seems to mark the beginning of a shift in the way that gout was discussed. Beginning in the 1800s, gouty main characters or even side characters seemed to slowly disappear from novels and plays. Gout seemed to be portrayed less and less in comic illustrations and gout became more of a disease to hide rather than wear proudly. It's hard to say precisely why the shift happened. It could coincide with the rise of the temperance movement in England starting around the 1830s or so where overindulgence in alcohol, seen as a risk factor for gout, was also seen as unraveling the fabric of society. Similarly gout began to be described as a trait of disintegration, degeneration.

It could also be that by the early 1800s our medical understanding of gout had advanced, transforming gout from a personality trait into a clinical disease and one with more narrowly defined edges than it had previously, which is another possible reason why the frequency of gout seemed to decline somewhat during this time. Interest in gout had always been driven by the desire to understand the disease, not only what it was, what caused it, how to cure it, but also what did gout mean? What did it say about you if you had gout? And what we see happening in the early 1800s seems to be less focused on those meaning of gout questions with more attention paid to the medical side of things. Of course people had long been interested in understanding gout from a medical perspective, like since they could write about gout, right.

In the 16th century Paracelsus hypothesized that gout wasn't a humoral condition with phlegm and too much phlegm and not enough flow of the other stuff but something caused by a specific condition or poison, the deposition of certain chemicals in the joints. He thought that this quote "bodily tartar" came from food and was released into the body during digestion which explained why overindulgence in certain foods lead to greater build up and ultimately gout. In the 1670s our favorite microscopist Antony van Leeuwenhoek became fascinated by gout and examined some gouty chalk from a relative under the scope, observing that what looked like chalk to us was actually composed of crystals. But it would take a number of years before the significance of this would become apparent. In 1793 a Scottish physician named Murray Forbes suggested that uric acid could circulate in the blood and accumulate in certain parts of the body. And this was confirmed a few years later by William Hyde Wollaston who examined a tophus under the scope and determined that the chalky stuff that came out was indeed uric acid.

Erin Allmann Updyke

Whoa.

Erin Welsh

By the mid 1800s a couple of tests had been done developed to determine whether or not elevated uric acid levels were present in the blood and researchers were beginning to understand how gout could come about, either through decreased kidney function or increased formation of uric acid. Side note, even with this better medical understanding of gout, some people clung to the 'but I'm special' narrative with one researcher suggesting that quote "excessive production of uric acid would account for rich man's gout whereas kidney deficiency would explain poor man's gout."

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

Like come on, yeah. All this new knowledge about gout didn't translate directly into cures or treatment but that didn't mean that there was any shortage of things claiming to cure gout, like Goddard's drops. Quote: "Take human bones well dried and broke into bits together with 2 pounds of viper's flesh. Put them into a retort and distill so you will have a spirit, oil, and volatile salt. Set it in the earth to digest for three months. Then separate oil which keep for use. If you want it for the gout in any particular limb, it is better to make it from the bones of that limb. The dose is 6-12 drops in a glass of canary wine but it has an evil scent."

Erin Allmann Updyke

Nope. No, thank you.

Erin Welsh

Pass. I won't go through more but gout medicine wasn't limited to snake oil but also wacky contraptions. Gout-specific furniture like chairs and stools also had become a thing in the 1800s. Colchicum was reintroduced in the early 1800s also and produced in crystalline form in the 1880s which made dosing more accurate. Although some mystery surrounding gout still remained at the end of the 19th century, particularly the role of heredity and whether there was such a thing as heart gout or metastatic gout, the disease grew more and more demystified in the 20th century as researchers developed a test for specific uric acid levels and began to use corticotropin and prednisone with allopurinol to treat the disease beginning in the mid 20th century. Some people still tried to perpetuate the association of gout with certain personality traits such as intelligence, so I'll link to one paper from 1966 that looked at serum urate concentrations among university professors and found them to be positively associated with certain behaviors like quote "drive, achievement, and leadership."

Erin Allmann Updyke

Oh my god, so many points of bias.

Erin Welsh

Oh no, I'm sure that these were all very unbiased interviews.

Erin Allmann Updyke

Oh totes.

Erin Welsh

And self-assigning characteristics, I don't know.

Erin Allmann Updyke

Yeah. And only studying university professors in the 1960s. Yeah.

Erin Welsh

I think the title of the paper was literally like serum uric acid concentrations among university professors and markers for achievement or something.

Erin Allmann Updyke

Oh my goodness gracious.

Erin Welsh

Yeah. But I find gout's legacy in this way so very revealing. Gout is not at all unique as a disease that has held deeper meaning or is supposed to reveal something about who you are or a disease that only certain people get. We've seen it with endometriosis, we've seen it with hookworm, we've seen it with syphilis, just to name a few. But what's different about these compared to gout is that those were all written about in a negative light for the most part, where to be diagnosed with endo or hookworm or syphilis meant that you were weak or frigid, unclean or unintelligent, immoral or unclassy. You did this to yourself and you deserved what you got. And while gout was discussed in that same way for a part of its history, for the vast majority of it and even persisting into the 20th century, it was a positive thing. The monarch among maladies. And I think it comes down to who was constructing these medical narratives. Gout was written about in such a positive light because those doing the writing often had gout or had close friends with it, they got to choose what they wanted to say about gout.

Erin Allmann Updyke

Yeah.

Erin Welsh

Even though women absolutely can get gout and have gotten gout forever, gout was rarely described in women. Women were rarely if ever depicted as having gout in comic illustrations or anything like that. Why? Because it didn't fit the narrative. A woman with gout? But that would mean that I as a gentleman genius am not special. It cannot be. So while I do think it's essential to avoid stigmatizing and othering figurative language to describe diseases, I also think that it's important to understand why certain phrases or words or images or connotations came to be associated with certain diseases and what that can tell us about the narrators themselves and their historical context.

Erin Allmann Updyke

Yeah.

Erin Welsh

So with that Erin, what's going on with gout today?

Erin Allmann Updyke

Oh my gosh, Erin. What an amazing journey. I can't wait to bring us up to 2022 right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

So in terms of the epidemiology, let's none of us be surprised that I don't have great numbers for you. It's just that's how things go. There was a meta analysis from 2015 or so of 71 different papers and that estimated a global prevalence of 0.6% for gout globally.

Erin Welsh

Okay.

Erin Allmann Updyke

But there's so much heterogeneity in those estimates and there's so many pockets of the globe that aren't included in those because we just don't have really any data. And there's also a lot of variation among different races or ethnicities in terms of gout prevalence as well. So for example in some studies in Taiwanese aboriginal populations and in Māori populations, prevalence estimates are up to 10% of adult populations, 10%. Across the US and Canada most estimates put the prevalence at around 4% of adults which is still very high. In Europe estimates really range depending on what country you're looking at, anywhere from 1%-4%. Whereas in China and South Korea most estimates are at around 1% or less, though those are predicted to rise and will probably get there. But when it comes to much of the rest of the globe, the Middle East, the entire African continent, Central and South America, we don't even have data to estimate how much prevalence we might have.

Erin Welsh

Interesting.

Erin Allmann Updyke

Yeah. And gout, like we mentioned at the top, is very strongly a disease of aging. Not only because it tends to happen after we reach certain ages but also because the risks continue to increase with age. And so while we don't have great numbers on prevalence and we have even less great numbers on incidence, like how many people are being diagnosed every year with gout, there are suggestions based on the data that we have that in general rates are on the rise and that probably has a lot to do with our overall aging global population.

Erin Welsh

Okay.

Erin Allmann Updyke

But one big problem with this, especially when we talk about a chronic disease that we have a cure for that is a global human problem, is that it's estimated that only about 1/3 to 1/2 of people who have gout, even if they've been diagnosed are on urate lowering therapy, only about 1/3 to 1/2 of people. And many people who may get started on it might not take it as necessary to be able to actually reduce their urate levels and reduce their risk of further gout flares.

Erin Welsh

Is this primarily financial barriers?

Erin Allmann Updyke

Yeah, a lot of its financial, a lot of it's just lack of diagnosis or lack of access to these medicines even though they're not very fancy or new medicines necessarily.

Erin Welsh

Right.

Erin Allmann Updyke

There are especially for the one, allopurinol, there is a caveat to that in that there is a very strong hypersensitivity reaction that some people have. So you kind of have to make sure that people aren't genetically predisposed to have a really bad reaction to that specific medicine. But there are a lot of other options for urate lowering therapy, that's just the one that we tend to use in the United States.

Erin Welsh

Okay.

Erin Allmann Updyke

And it's really interesting to me, Erin, how much you talked about the way that gout was perceived historically. Because when you read about it today and how gout is often perceived today, there is a lot of stigma surrounding gout and there's also very strong biases that it sounds like have persisted throughout time and continue today in that it's very easy to think of gout as just a disease of old men.

Erin Welsh

Right.

Erin Allmann Updyke

Or old men who drink too much or make poor choices in their diet or have let themselves go and it is a them problem.

Erin Welsh

Yes.

Erin Allmann Updyke

And that quite frankly is how a typical gout patient is still portrayed in the medical literature today. Go back to our typical board question, right. And a couple of things that I wanted to point out about this is not only like you were saying Erin, it does no good to stigmatize these diseases, any disease, but it's also so important for gout that these dietary factors or even things like body weight BMI or adipose tissue mass, these things that we know that can contribute to gout, to use them as a way to blame people for their own conditions is not only amoral but isn't even correct, especially when it comes to gout. Because we know from data that dietary changes don't reduce the incidence of gout. We have good evidence to show that, that dietary changes don't reduce serum urate levels significantly enough to reduce your risk of gout flares if you already have gout. There are so many genetic components to this that it is not accurate or useful to put the blame on individuals or their habits as the cause of their disease. Because this is a chronic disease that can have lifelong detriment if it causes joint damage. Yeah, it's very upsetting.

Erin Welsh

Yeah, absolutely.

Erin Allmann Updyke

Yeah. And I think that that is something that happens with gout. And so it does lead to a lot of under diagnosis probably especially in women or in females because it is typically thought of as this one specific presentation of a disease and if you don't fit that exact description you might never get a diagnosis and you might never get started on therapy.

Erin Welsh

Which can just exacerbate things.

Erin Allmann Updyke

Exactly, yeah. So gout. That's gout today. In terms of what I'm excited about with the future directions and research, I mean we know so little that there's so much out there that we could do. But I wanted to shout out a fun paper that I found because whenever I find a fun paper, let's talk about it.

Erin Welsh

Love it.

Erin Allmann Updyke

It was a 2021 paper that was looking into nothing other than the microbiome as it relates to gout.

Erin Welsh

Fascinating!

Erin Allmann Updyke

I know! It had some really fun and interesting findings related to gut microbiome dysbiosis and its possible relations to gout. It's one paper, it's very early in the game, that paper doesn't claim to have all of the answers. But there have been other studies that have linked changes in the gut microbiome especially in not just what bacteria are here but in the actual functional alterations, so shifts in the major products or the major jobs that our bacteria are doing in our gut and the ratios thereof.

Erin Welsh

Right.

Erin Allmann Updyke Associations with those functional shifts and other autoimmune forms of arthritis. And so this paper was kind of like let's look if there's anything with gout and it seems like there could be. So it's early in the game but you know how I just love the microbiome story.

Erin Welsh I do too.

Erin Allmann Updyke So I feel like there is a lot of room there for really fun and interesting research to come out of this.

Erin Welsh I love that because I feel like that could potentially at least answer a bit of the puzzle that is left remaining about why.

Erin Allmann Updyke Exactly. But why? But why? And why this person and not that person? Especially because while we know that there are genetics, it's not a one gene thing and it's definitely genetics and environmental interactions and so I just love the microbiome as part of that interaction.

Erin Welsh Totally.

Erin Allmann Updyke Yeah. But that's it, Erin. That's gout.

Erin Welsh Totally.

Erin Allmann Updyke Toe-tally.

Erin Welsh Fascinating.

Erin Allmann Updyke Too much.

Erin Welsh Toe much? I'll stop. Should we do sources?

Erin Allmann Updyke Yep, it's time.

Erin Welsh I have a few papers about the evolutionary history of uricase and stuff like that. Tan et al from 2016 is great, as is Kratzer et al from 2014. And for a lot of the gout history I relied heavily on a book called 'Gout: The Patrician Malady' by George Rousseau and Roy Porter.

Erin Allmann Updyke I had actually just a small handful of papers for this episode because I had two that probably gave me about 98% of this episode.

Erin Welsh Nice.

Erin Allmann Updyke And that was a paper by Dalbeth et al from 2019 called 'Gout Primer', it was from Nature Reviews Disease Primers. And another one by Dehlin et al 2020, that was the 'Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors.' There's a couple of others including that gut microbiome paper which was very fun. And we'll post the list of our sources from this episode and all of our episodes on our website thispodcastwillkillyou.com under the EPISODES tab.

Erin Welsh We certainly will. Thank you to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Allmann Updyke

Thank you to the Exactly Right network.

Erin Welsh

And thank you to you, listeners. I hope that you found this episode interesting.

Erin Allmann Updyke

I did.

Erin Welsh

And learned something about gout.

Erin Allmann Updyke

I loved it. I loved this episode.

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 means a lot.

Erin Welsh

It truly does. It really does. And by the way, we only have two more episodes of this season coming out.

Erin Allmann Updyke

Oh yeah, we should warn you.

Erin Welsh

We should warn you.

Erin Allmann Updyke

Yeah.

Erin Welsh

Well until next time and a couple of times after that, wash your hands.

Erin Allmann Updyke

You filthy animals!