

Erin Welsh

Hello listeners. Before we get to the episode we want to take a moment to address the June 24 2022 Supreme Court decision to overturn Roe vs Wade.

Erin Allmann Updyke

This decision stripped away the right to have a safe and legal abortion. Everyone should have the freedom to decide what's best for themselves and their families, including when it comes to ending a pregnancy.

Erin Welsh

This decision has dire consequences for individual health and safety and could have harsh repercussions for other landmark decisions. Abortion is healthcare and restricting access to comprehensive reproductive care including abortion threatens the health and independence of all Americans.

Erin Allmann Updyke

You can learn more by visiting choice.crd.co. That's choice.crd.co.

Erin Welsh

And if you're able to support others, please consider donating to abortion funds.

Erin Allmann Updyke

We encourage you to speak up, take care, and spread the word.

Erin Welsh

She turned her head from side to side with a gentle movement full of agony while constantly opening her mouth as if something very heavy were weighing upon her tongue. At 8:00 the vomiting began again. Then she began to groan, faintly at first, her shoulders were shaken by a strong shuddering and she was growing paler than the sheets in which her clenched fingers buried themselves. Her unequal pulse was now almost imperceptible. Drops of sweat oozed from her bluish face that seemed as if rigid in the exhalations of a metallic vapor. Her teeth chattered, her dilated eyes looked vaguely about her, and to all questions she replied only with a shake of the head. She even smiled once or twice. Gradually her moaning grew louder. A hollow shriek burst from her.

She pretended she was better and that she would get up presently but she was seized with convulsions and cried out, 'Ah! My god! It is horrible!' Then the symptoms ceased for a moment. She seemed less agitated and at every insignificant word, at every respiration, a little more easy. He regained hope. His colleague was by no means of this opinion and as he said of himself never beating about the bush, he prescribed an emetic in order to empty the stomach completely. She soon began vomiting blood. Her lips became drawn, her limbs were convulsed, her whole body covered with brown spots, and her pulse slipped beneath the fingers like a stretched thread, like a harp string nearly breaking.

After this she began to scream horribly. She cursed the poison, railed at it, and implored it to be quick and thrust away with her stiffened arms everything that Charles, in more agony than herself, tried to make her drink. Emma, her chin sunken upon her breast, had her eyes inordinately wide open and her poor hands wandered over the sheets with that hideous and soft movement of the dying that seems as if they wanted already to cover themselves with the shroud. Her chest soon began panting rapidly, the whole of her tongue protruded from her mouth, her eyes as they rolled grew paler like the two globes of a lamp that is going out so that one might have thought her already dead but for the fearful laboring of her ribs shaken by violent breathing as if the soul were struggling to free itself. Emma raised herself like a galvanized corpse, her hair undone, her eyes fixed staring. She fell back upon the mattress in a convulsion. They all drew near. She was dead.

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

Aye aye aye, Erin.

Erin Welsh: Yeah. So that was heavily edited down from the last chapter, sorry for the spoilers but the book has been out since the 1850s. Madame Bovary by Gustave Flaubert. And yeah, the lead character dies of arsenic poisoning. Self-inflicted.

Erin Allmann Updyke: Wow.

Erin Welsh: Yeah.

Erin Allmann Updyke: I have a question.

Erin Welsh: Okay.

Erin Allmann Updyke: In that book does she take arsenic for a long time or does she just take a big dose of it?

Erin Welsh: She takes a big dose of it from what I can tell.

Erin Allmann Updyke: Interesting.

Erin Welsh: I attempted to read it but I didn't start it early enough and I gave up.

Erin Allmann Updyke: Yeah, that's fair.

Erin Welsh: But yeah, I'm excited to see how the description there stacks up against what we know about arsenic poisoning from the biology section.

Erin Allmann Updyke: Yeah, me too Erin.

Erin Welsh: So maybe not super close. Cool, cool, cool.

Erin Allmann Updyke: Maybe not.

Erin Welsh: I mean come on, it's a novel, you have to allow some literary license, right?

Erin Allmann Updyke: 100%. Yeah.

Erin Welsh: Okay, let's let's dive in. 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 arsenic obviously.

Erin Welsh: Obviously. It's going to be really interesting, there's a lot of fun trivia, I'm thrilled to learn about how it works. But first should we, is it time, can we?

Erin Allmann Updyke: It's quarantini time!

Erin Welsh: It is. What are we drinking this week?

Erin Allmann Updyke

This week we're drinking The King.

Erin Welsh

We're drinking The King.

Erin Allmann Updyke

The actual king.

Erin Welsh

The actual king. Arsenic is commonly known as the king of poisons and also the poison of kings.

Erin Allmann Updyke

Which I did not know and I really love.

Erin Welsh

Yeah. And so we just decided to keep it simple and keep it sweet with The King.

Erin Allmann Updyke

The King. And what's in the king, Erin?

Erin Welsh

What's in the king is essentially a Midori sour.

Erin Allmann Updyke

Fantastic.

Erin Welsh

Yeah. We had to have something green because as you'll learn arsenic was used as a colorant for different shades of green a lot during the 19th century. And yeah, Midori ticks that box.

Erin Allmann Updyke

Very green.

Erin Welsh

Yeah. And essentially a Midori sour is Midori, lemon juice, lime juice, soda water. And we'll post the full recipe for The King as well as the non alcoholic placeborita on our website thispodcastwillkillyou.com as well as on all of our social media channels.

Erin Allmann Updyke

On our website thispodcastwillkillyou.com the things that you can find there are numerous. They include our merch and our bookshop.org affiliate account and our Goodreads list as well as Bloodmobile, our music, and transcripts for all of our episodes and all of the sources that we use in every episode. You can find our Patreon, you can find really you name it, it's probably on our website.

Erin Welsh

That's true, that's true. All right, I think that's all the business that we have. So can we get started?

Erin Allmann Updyke

I would love to right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

So Erin, when I started researching for arsenic immediately right off the bat I got really heavy mercury vibes meaning I was way out of my league. And it turns out that we don't have a lot of specifics just like with mercury.

Erin Welsh

Okay.

Erin Allmann Updyke

But I will tell you everything that I learned and then I can't wait for your questions that I probably won't know the answer to.

Erin Welsh

Can't wait to ask them.

Erin Allmann Updyke

I know, it's my favorite part. So arsenic is a metalloid. What is a metalloid, you may ask? Because that's certainly what I asked, everyone, because chemistry really is something that makes me nervous. But I'm going to do my best and it means that I'll explain it as if you know nothing because we all know nothing. Let us go. A metalloid is not quite a metal and not quite a nonmetal when we look at the periodic table of elements. So I feel like most people probably have a sense of what a metal is, even if you don't remember back to your high school chemistry class, like what the definition is. If you give somebody a chunk of something and say is this metal or no? They'll be like is it shiny, is it solid, does it look like metal, etc? So those are the kinds of things that make a metal a metal, right, they're generally shiny or metallic or lustrous. Metals are generally good conductors of heat and electricity.

Non metals can be anything but in general they're not as good of conductors, they're less good than metals. And metalloids are somewhere in between. It turns out that there's no good consensus definition of what makes a metalloid a metalloid, it's not a very clear term but it's still used in a lot of chemistry textbooks. And the most common elements on the periodic table that are considered metalloids are boron, silicon, germanium, antimony, tellurium, and of course arsenic. So arsenic is an element like carbon or lead or mercury, it just happens to be somewhere in between carbon and lead and mercury in that it's not a non metal and not a metal, it's a metalloid. And much like carbon, arsenic as it turns out exists in what are called different allotropes. I learned so many interesting facts about arsenic.

Erin Welsh

Allotropes, I have not come across that word but I love it.

Erin Allmann Updyke

Yeah. It's a really fun word. It basically means that it can form different crystalline structures that look differently, the same way if you think of carbon atoms can form diamonds or graphite, right. Same atoms, different structure, looks totally different. In the case of arsenic there's gray arsenic, black arsenic, and yellow arsenic. Gray is the form that looks the most like a metal and tends to act the most like a metal. It can be a semiconductor so that's very useful in a lot of industrial settings which I'll get to. And arsenic is often used in metal alloys for that reason. And just like our friend and another element that we've talked about on this podcast, mercury, arsenic also exists across the earth in various compounds, both organic compounds like carbon-based compounds and inorganic or no carbon involved compounds.

And if you remember our mercury episode as well as our lead episode which was a very long time ago now, the toxicity of elements like arsenic depends in part on what form we get exposed to as well as of course whether we're being exposed to small amounts over long periods of time like a chronic exposure, or a big hefty dose all at once like an acute poisoning. And it turns out that with arsenic this is very important. The type of arsenic that you're exposed to really determines the toxicity. And being not a chemist, I tried to not get too bogged down in oxidation states and valances but it turns out that that's what's really important when it comes to arsenic.

So the basics look like this. Arsenic is close to phosphorus on the periodic table. And so in some forms when it's oxidized in a certain way, it's called a pentavalent form, it's an inorganic form of arsenic that's called arsenate and it really can resemble phosphate which is a form of phosphorus. And phosphate in our bodies is a pretty integral part of human biology. It's the P in our ATP, adenosine triphosphate. And so much like with lead and mercury, what we see with arsenic is that the toxicity arises from its ability to mimic other compounds that our body normally uses and/or its ability to hijack various enzymes or metabolic pathways because of these similarities.

Erin Welsh

It's so interesting that it does that. Because we talk about infectious diseases primarily on the podcast, although maybe not as much anymore, we think of these pathogens as striving to reproduce and survive and that's why they cause infection, that's why they make us sick. But with arsenic it's just like here's this inner thing that just happens to be extremely deadly.

Erin Allmann Updyke

Yeah, right. Exactly. It just happens to have an effect in our bodies because it's similar to things that our body actually needs and uses. But not because we need it in any way, it just happens to be there.

Erin Welsh

Yeah. It's very interesting, yeah.

Erin Allmann Updyke

I know. So that's one way that arsenic can exert its toxicity when it's in its oxidized pentavalent form. Another probably even more common and more toxic form of arsenic is called arsenite and this is the trivalent form, this is what happens when arsenic is in a reducing environment. And this in a very similar way disrupts a number of our biological processes but not by mimicking phosphate in this case but by having a high affinity for what are called thiols or sulfhydryl groups, so sulfur and hydrogen. Turns out that our body has a lot of proteins and enzymes that have these sulfur hydrogen groups on them that are really integral to things like, I don't know, our citric acid cycle which makes ATP to power our cells and a whole host of other very basic and important metabolic functions. So that's kind of the most basic look at arsenic.

Erin Welsh

And in terms of whether it happens to mimic thiols or phosphate, that just is in the way that it's formed these...?

Erin Allmann Updyke

It basically just depends on which form of arsenic you're exposed to.

Erin Welsh

Okay.

Erin Allmann Updyke

And which form you're exposed to will depend on what that arsenic is doing in the environment, whether it's a high oxygen environment or a low oxygen environment, blah blah blah. And all of those are inorganic forms of arsenic. Organic arsenic, organic compounds that contain arsenic can be found in really high concentrations in things like shellfish but it turns out if we get exposed to arsenic that's already bound to organic compounds, we actually don't see a lot of effects from it. It actually is very nontoxic which is interesting and different than what we saw in mercury which I think is just fascinating.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

And these different forms of arsenic and the different things they mimic and all of that, that must lead to different symptoms if it's disrupting different parts. Or is it because it's all kind of in the same pathway?

Erin Allmann Updyke

So let's get into that, shall we?

Erin Welsh

Okay.

Erin Allmann Updyke

Let's get into the symptoms and then maybe it'll kind of get at that question.

Erin Welsh

Okay.

Erin Allmann Updyke

So when we encounter arsenic in any of these various forms, we generally absorb it into our bloodstream and it goes to anywhere in our body but it's often stored in places like our liver, our heart, our lungs, our kidneys are really important for excreting arsenic. It can also be found in our skin, really it's everywhere. And our bodies have a lot of enzymes that actually function to break down arsenic to metabolize it into a form that we can then excrete it. But it turns out that one of these forms which is known as methyl arsenite or mono methyl arsenite, blah blah blah, this form is also very toxic. So our bodies are dealing with arsenic by quote "breaking it down", methylating it really. But then that is also toxic. So it doesn't just get rid of it automatically.

Erin Welsh

So then what happens to it?

Erin Allmann Updyke

It builds up in our bodies and causes all these symptoms that I'm about to talk about.

Erin Welsh

Oh, okay.

Erin Allmann Updyke

Yeah, so it acts just like arsenic even though organic arsenic from a shellfish doesn't.

Erin Welsh

Weird.

Erin Allmann Updyke

I know! It's so bizarre. So we get exposed to arsenic generally via food or water. So contamination of food sources and drinking water from arsenic which comes from honestly anywhere, it's found in the soil, it is ubiquitous across this earth. Although as we'll see later on it's certainly not evenly distributed across the globe but it can be found in groundwater kind of worldwide. And oral route, so ingesting it, is the primary way that people get exposed. In industrial settings you can get exposed via inhalation and it's unclear whether you can really absorb much of it through your skin, it seems like mostly no but if you're handling it all day all the time and you have it on your skin, you can potentially then ingest it from your hands. But everyone is being exposed to arsenic at at least some level. So let's talk about what we see in terms of symptoms because as with everything we've talked about in terms of toxins on this podcast, the dose determines the poison or whatever. Right?

Erin Welsh

Well said.

Erin Allmann Updyke

Thanks, I tried. So our firsthand account perhaps described an acute arsenic poisoning episode and I say perhaps because Erin, that firsthand didn't sound like what I'm about to describe.

Erin Welsh

That's so funny because when I came across it in a book I read about arsenic for this episode it was like yeah and then you know in Madame Bovary it's actually a very excellent example of what arsenic poisoning is like.

Erin Allmann Updyke

How fascinating. I will say that most of the papers that I read really did not focus on acute arsenic poisoning.

Erin Welsh

It was more chronic. That makes sense.

Erin Allmann Updyke

Yeah, the highlight is very much on all the chronic. So maybe I just didn't find good enough old timey descriptions of arsenic poisoning.

Erin Welsh

I mean just pick up basically any Agatha Christie novel and you'll find it in there.

Erin Allmann Updyke

Yeah. Well what I found is that arsenic poisoning in some ways can look a lot like a lot of other poisonings in that within a matter of minutes to hours after ingestion you have intense abdominal pain, you have a lot of GI symptoms, a lot of abdominal pain, vomiting, diarrhea. The diarrhea can actually be very profound, I saw it described as cholera-like. Remember back to that episode. So that's like a rice water, just pure water stool. And basically in high enough doses this arsenic is kind of just ripping its way through your intestinal mucosa, so you're losing a lot through your guts. And because of all these losses you can end up seeing hypotension, so drops in your blood pressure which can be from dehydration and volume loss from this profuse GI losses.

This can then cause electrolyte abnormalities because you're losing your electrolytes through your diarrhea, through your vomiting. And that can cause your heart to stop functioning properly because without the right balance of electrolytes your heart can't send the signals that it needs to to beat in sync. So then you can have death because of arrhythmias if you have a high enough exposure. There also can be a lot of neurologic symptoms but from what I read usually, though not always, the neurologic symptoms tend to happen more like weeks, days or weeks after exposure, can cause things like numbness, tingling, muscle cramping, a lot of different neurologic effects. But these tend to not be as acute onset as the GI effects.

Erin Welsh

And these neurological symptoms are part of the acute thing, it's just part of the recovery phase?

Erin Allmann Updyke

Not necessarily recovery but there also can be seen in more like subacute, so maybe you're exposed to kind of high doses for a number of days in a row or something like that. And you can even see them after very, very long term exposures. So it's kind of just like arsenic is having its effect on your nervous system which we'll talk about in more detail but it's happening all at once after that exposure, once it's made its way into your nervous system.

Erin Welsh

Right, okay. What's the half life of arsenic in the body?

Erin Allmann Updyke

Great question. It can vary, it tends to be on the order of many hours to a few days, like 2-4 days. That's for the inorganic forms. But once it's methylated in our bodies, once our body tries to break it down, it can actually persist for a bit longer.

Erin Welsh

Interesting.

Erin Allmann Updyke

Yeah.

Erin Welsh

Interesting that our bodies... What is the benefit of our bodies actually breaking down arsenic?

Erin Allmann Updyke

Well that's a very good question. I think it seems to make it easier to excrete via our kidneys.

Erin Welsh

Okay.

Erin Allmann Updyke

However it also can have bad effects on our kidneys.

Erin Welsh

Yeah.

Erin Allmann Updyke

And I think it's probably in part just our body's natural reaction to stuff that gets absorbed, right. Our body methylates things. It sees something and it's like, 'I'm going to methylate you. Hey, you look kind of like a phosphate.' You know?

Erin Welsh: Right, okay.

Erin Allmann Updyke: So it's not necessarily... Yeah, I don't know. It's a good question. So that's kind of the acute phase. From what I read acute poisoning especially at high enough doses to result in death tends to happen at levels very, very high. So I hate environmental levels because it's like parts per billion and micrograms per etc. But 60,000 parts per billion which is 60,000 micrograms per liter.

Erin Welsh: I can't imagine, it's very difficult to visualize.

Erin Allmann Updyke: It is. That level is about 10,000 times higher than 80% of the drinking water in the US for example. So it's really, really high doses.

Erin Welsh: Okay.

Erin Allmann Updyke: But even much lower doses like 300-30,000 parts per billion could cause pretty significant effects, right, make you feel pretty sick.

Erin Welsh: Right. But there is a level as a safe level because our body will methylate it and kind of kick it out of our systems and excrete it?

Erin Allmann Updyke: Right. The World Health Organization has the kind of provisional level of arsenic in drinking water which is the most ubiquitous source and so the one that has that level attached to it is 10, 10 micrograms per liter or 10 parts per billion.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. So that's the number. So we're talking about 60,000. That's a lot.

Erin Welsh: That's a lot.

Erin Allmann Updyke: It's a lot more. But that's kind of the acute poisoning. It's pretty rare nowadays. What's much more common is that someone is exposed to levels that are higher than that 10 parts per billion but still low, like between 50-100 say for example. So people who are exposed to this lower level but still high level of arsenic over a prolonged period of time, one of the most characteristic things that we can see is pigmentation changes in the skin which is fascinating. You get these little patches of skin that can be darker or lighter than your underlying skin tone. And these patches are hyperkeratotic which means that they are these little hard patches, kind of like a wart almost, like a little stuck on patch of skin. And this is caused by your skin actually proliferating in a very abnormal way. And these lesions are precursors to various skin cancers.

Erin Welsh: Oh and so the skin cancer that's associated with arsenic is not just through direct contact on your skin but through any way that you are exposed.

Erin Allmann Updyke: Right. It's not skin contact.

Erin Welsh: Gotcha.

Erin Allmann Updyke: It is ingestion or inhalation but it goes and is absorbed through your whole body and causes these changes in your skin.

Erin Welsh

And you wouldn't expect to see this with an acute case.

Erin Allmann Updyke

Not as far as I could tell because it takes time for your skin to react to it.

Erin Welsh

Gotcha.

Erin Allmann Updyke

Right. Long term ingestion can also cause cardiovascular disease. It can cause something that is called blackfoot disease, it's a very severe form of vascular disease in the feet where the vascular system becomes so severely compromised that you basically lose circulation to your feet and then develop gangrene.

Erin Welsh

Okay.

Erin Allmann Updyke

It can cause heart attacks, it can cause strokes, can cause a lot of different things. So I wanted to try and get a little bit more into the nitty gritty of why it's causing specifically heart attacks, specifically vascular disease. So let me attempt. So I said that this is an element that can affect our enzymes and how our enzymes function. So a lot of what we know about the effects of arsenic in our body are what we think it's doing to various specific enzymes in the systems that we see effects. So for example, cardiovascular damage. We know from epidemiological studies that arsenic can cause some pretty severe cardiovascular damage. It seems like the way it mostly does this is actually by increasing reactive oxygen species and inducing our cells to synthesize a bunch of inflammatory cytokines and a whole host of other largely reactive oxygen-mediated enzymes and effects.

And so the end result is that this arsenic is turning on a bunch of stuff that damages the lining of our blood vessels, that damages that endothelium. And so that's what ends up causing these cardiovascular complications like heart attack. It can cause increased blood pressure because that damage first of all is going to damage our blood vessels. But then it also affects enzymes that cause vasoconstriction, so it causes our blood vessels to go get smaller and smaller and smaller which increases the pressure in our blood vessels.

Erin Welsh

It can do anything.

Erin Allmann Updyke

It can. And then in our nervous system because it's going to get there eventually, this is something that can cross our blood-brain barrier, in our brain again we think it's related to oxidative stress, increase in reactive oxygen, but it can alter the metabolism of various neurotransmitters. So over long periods of time exposure to arsenic can result in impaired memory or poor concentration. Arsenic also causes the cytoskeleton of our cells, the literal kind of bones that form our cells, they're not bones but it's called the cytoskeleton, it can cause that to be disrupted, to basically not be as strong or form in the correct way. And one of our types of cells that really rely on our cytoskeleton are our nerve axons. So arsenic causes the axons of our nerves to degrade which leads to things like neuropathy, which we talked about a little bit already. This can look kind of like a Guillain-Barré type neuropathy.

Erin Welsh

Interesting, okay.

Erin Allmann Updyke

It can also, arsenic, lead to degradation of specific groups of neurons in our brains like for example our dopamine producing neurons. So this can cause a syndrome that looks a lot like Parkinson's.

Erin Welsh

Is it targeted in that way? Or are those just the types of neurons that are somehow more susceptible?

Erin Allmann Updyke

Right, exactly. Because it's not just those, it can also decrease activity of things other than dopamine like acetylcholinesterase, it can cause an increase in cholinergic crisis. Honestly you said it can go anywhere and do anything, that's accurate.

Erin Welsh

Yeah. Okay.

Erin Allmann Updyke

It also affects our kidneys even though our kidneys are what is going to be excreting this arsenic eventually. As our kidneys are excreting this arsenic, they can also get hammered by the effects and then that can have even more of an effect on our blood pressure because it's disrupting our kidneys' ability to regulate our blood pressure, which by the way your kidneys do that for you. Finally, maybe not finally because I'm going to keep going, but another thing that I think is so fascinating is that exposure to arsenic at higher levels can also cause diabetes, very specifically diabetes. I know, your face.

Erin Welsh

Yeah, what?

Erin Allmann Updyke

Okay. So this we have a more specific answer for. It turns out that arsenic decreases the expression of a transcription factor that results in us having increased resistance to insulin, right, basically causing type 2 diabetes. And then on top of that it slows down the metabolism of glucose because of its effects on ATP, right/ Because of the way that it interacts with our metabolic cycles that produce ATP, it disrupts that process and so it interferes with ATP-dependent insulin secretion. So now we're secreting less insulin and we're resistant to insulin. Boom, diabetes.

Erin Welsh

That is incredible.

Erin Allmann Updyke

It's so overwhelming.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. I mentioned blackfoot disease, this is something that is a cardiovascular complication in a way because it's your vascular system just in your feet. And it's actually unclear if this is just arsenic or if this is something more. It has been seen in Taiwan very strongly in association with exposure to arsenic but it hasn't been seen outside of Taiwan with exposure to arsenic. So there's a question is it in combination with malnutrition, is it something else? And the reason I bring this up is because I think it highlights one of the big problems with trying to get at the exact effects of arsenic exposure. Not only is it going anywhere and everywhere and affecting over 200 different enzymes potentially in our bodies but it's also something that we're being exposed to to various degrees in combination with so much else in the environment. So it's never going to be an individual only exposure, arsenic alone.

Just a couple more. Arsenic does cross the placenta the same way that it crosses the blood-brain barrier, so it can have a lot of detrimental effects on the fetus. It can cause spontaneous abortion, stillbirth, preterm birth. There's some suggestion that exposure to arsenic in utero might be associated with increased cancer risk later in life but that's a little unclear. But we do know that arsenic is a carcinogen and what I think is so interesting about arsenic as a carcinogen, arsenic as something that causes cancer, is that we do not know the cellular mechanisms of this. But this is one of the strongest associations especially when it comes to skin cancer as well as bladder cancer, lung cancer, various other cancers.

Erin Welsh

Right. So we don't know the exact mechanism of that abnormal skin growth or cellular growth on your skin or is it just inflammation?

Erin Allmann Updyke

Yeah, it's a good question. It seems like arsenic activates various transcription factors and changes the expression of genes that are involved in cell growth and proliferation or transformation. And so that is then leading you to cancer. Why does it do this in the skin so specifically? We don't know. How is it doing it in the skin so specifically? We don't know. And the same is true for other cancers like lung cancer and bladder cancer that have been associated with arsenic.

Erin Welsh

Wow.

Erin Allmann Updyke

I know.

Erin Welsh

Interesting.

Erin Allmann Updyke

I don't know if that was way too much or not enough but it feels like a lot.

Erin Welsh

I mean it's a lot but I think that that's just also the nature of arsenic.

Erin Allmann Updyke

Yeah.

Erin Welsh

It has profound effects throughout your body. And how much variation is there in terms of susceptibility, like children vs adults? Or yeah, anything else like that.

Erin Allmann Updyke

Great question. Children generally are more susceptible to things like toxins than adults because lower amounts are going to cause an effect on children because they're smaller, because their metabolism is such that that's going to be the effect. But other than that I don't have a lot of very specifics in terms of who is exposed the most or anything like that.

Erin Welsh

Okay.

Erin Allmann Updyke

So that's arsenic, Erin. That was a lot.

Erin Welsh

How do you treat arsenic poisoning?

Erin Allmann Updyke

Such a good question. It's not super easy to do. There are a variety of different compounds that you can use for what's called chelation therapy, especially if someone is exposed to very large amounts of arsenic. And what chelation therapy does is basically bind the arsenic and then allow your body to excrete it without having to metabolize it, etc. So basically just helping your body get rid of it quicker. But otherwise you just wait it out and try to not be further exposed and then treat whatever complications have arisen.

Erin Welsh

I thought I also read something about folate which I thought was fascinating because we just researched folate and how higher levels of folate are recommended for long term more chronic exposure to arsenic. But I don't know why.

Erin Allmann Updyke

I wonder. I don't either but most likely it has to do with the fact that we talked about how important folate is as a cofactor in all of these various metabolic processes.

Erin Welsh

Right.

Erin Allmann Updyke

So it's probably just trying to displace arsenic in a way not directly but allowing our cells to continue their metabolic processes despite the exposure to arsenic.

Erin Welsh: That makes sense.

Erin Allmann Updyke: Right. Ooh that's interesting though.

Erin Welsh: I know, connections.

Erin Allmann Updyke: Yeah. They're all around us. So Erin, speaking of connections, how did people connect the dots? How'd they figure out what arsenic was and then figure out that it's such a great killer of people?

Erin Welsh: I will try to answer those right after this break.

TPWKY: (transition theme)

Erin Welsh: Like we talked about earlier, arsenic is often called the king of poisons and the poison of kings. It is perhaps the most infamous and famous of all poisons and the one most synonymous with murder. And it could be said that the history of all intentional poisonings is really the history of arsenic.

Erin Allmann Updyke: What? Why?

Erin Welsh: It was so... Well we'll get to it, we'll get to it.

Erin Allmann Updyke: Okay.

Erin Welsh: And you'll see that it does make sense as an intentional agent of poison.

Erin Allmann Updyke: Okay.

Erin Welsh: And as I'll also talk about later on, arsenic does deserve this notoriety. But like with all poisons that we've covered on the podcast, there is so much more to this chemical than just its role as a plot device in an Agatha Christie novel or its use by the Borgias to amass wealth and power in 15th century Italy.

Erin Allmann Updyke: What?

Erin Welsh: Alongside arsenic's potential for murder is also of course its potential for healing. It has been considered an important medical substance for years, though whether it was more harmful than helpful is in question for much of that time and it's still in use today as a treatment for some cancers which is pretty awesome. But the other enormously important side of arsenic is what happens when you come into contact with arsenic unintentionally whether through occupational exposure, environmental exposure, or through drinking water that is expected to be safe and clean. And these three main faces of arsenic as an intentional poison, as a historically questionable but present day effective medicine, and as an environmental contaminant are the three themes that kind of make up this history section.

And initially I was going to split up the discussion along those lines. First I'd talk about arsenic and murder and then I'd talk about arsenic and medicine and so on. But as I read more I realized just how intertwined these roles of arsenic all are. For instance, the rise of arsenic as a murder weapon in the 1800s in Britain and its inclusion among many patent medicines came about because it was more available from mining, which of course led to more occupational exposure as well as environmental exposure when it was used as for instance a dye, a colorant. So let's get started on this rich history of arsenic.

Erin Allmann Updyke

Ooh, I can't wait.

Erin Welsh

Like you said Erin, arsenic occurs naturally all over the world with apparently a good deal of it coming from volcanoes in its natural form.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. And typically you won't find arsenic in its elemental form in nature. It exists in over 150 different minerals and is usually found as a sulfide compound commonly realgar or orpiment, I'm not sure if I'm saying those right, probably not. And although arsenic is widely distributed like we mentioned, it's not necessarily evenly distributed. And mining has played a big role in both the uneven distribution of arsenic in the environment as well as the high concentrations that we see in the soil, the water, in the air of some regions. But even before mining and industry unloaded tons of arsenic everywhere, some humans lived in naturally arsenic-rich environments and their constant exposure may have left a genomic signature.

Erin Allmann Updyke

Stop it.

Erin Welsh

So you talked about how we have a gene that is like a methyltransferase, right. It adds methyls to whatever. And this gene is really important in metabolizing arsenic so that we can excrete it safely. There is some very cool research looking at this gene which is called AS3MT, if you're curious it's the arsenic + 3 oxidation state methyltransferase gene. And this research has found that in some populations that have historically lived in areas with high arsenic concentrations in drinking water, particularly in some parts of the Andes in South America, it seems that you're more likely to see a protective version of this gene, one that helps with more efficient arsenic metabolism. So you can be exposed to higher levels of arsenic without getting as sick as you would without that version.

Erin Allmann Updyke

Fascinating.

Erin Welsh

Which is so cool.

Erin Allmann Updyke

Yeah.

Erin Welsh

And I think that this is one of the earliest or one of the only known examples of humans adapting to toxins.

Erin Allmann Updyke

Yeah.

Erin Welsh

So cool.

Erin Allmann Updyke

How interesting.

Erin Welsh

Also there is evidence of high arsenic exposure that's been found in remains of people who lived in the Atacama Desert in Chile around 7000 years ago. So yeah, humans have been exposed to arsenic for a very long time even before mining, which isn't to say that mining hasn't played possibly the largest role in exposure nowadays and historically. But when did humans start noticing the negative health effects of arsenic? Probably as soon as we started working with this stuff which was around the Bronze Age, which began 3300 BCE. The Bronze Age is called this because it's when people began to create, guess what? Bronze.

Erin Allmann Updyke

Yeah. And what's bronze?

Erin Welsh

Bronze. Bronze is an alloy consisting mostly of copper along with tin and sometimes other nonmetals or metalloids.

Erin Allmann Updyke

Okay.

Erin Welsh

Most metals aren't just hanging out there in their pure form, they often co-occur with other things like arsenic. And an observant smelter would have noticed that what you find with your copper naturally could influence the quality of the alloy that you produced, how strong it was, how durable it was, etc. And arsenic and copper happened to be a great combo, which is something that you would be like I'm storing that little fact away for later because I'm going to have better bronze than the other person.

Erin Allmann Updyke

Yeah.

Erin Welsh

And this observant smelter would have also probably noticed that when they did their smelting with this combo, the oven was full of noxious fumes and the more they worked with it, the worst they felt.

Erin Allmann Updyke

Yeah. Because the fumes are pretty bad.

Erin Welsh

Pretty bad. They also may have noticed that smelters tended to not live quite as long as their non smelting buddies. One paper I read suggested that arsenic poisoning in metal workers represents the very first occupational exposure.

Erin Allmann Updyke

Wow. Bold claim.

Erin Welsh

It is a bold claim but if you were smelting, you would come into contact with arsenic almost immediately.

Erin Allmann Updyke

Oh yeah.

Erin Welsh

I'm sure we could make arguments for other occupational exposures, there are many different occupational exposures.

Erin Allmann Updyke

Yeah.

Erin Welsh

In any case people have been exposed to arsenic in an occupational setting for a long time.

Erin Allmann Updyke

Yeah.

Erin Welsh

The Greek god of smiths Hephaestus and his Roman counterpart Vulcan are often depicted as limping and kind of hunched over. And there's been this long debate over what might be the cause of that limp. Some people have speculated it's because smiths were known to suffer the ill effects of working with toxic metals such as lead and arsenic and so he was depicted with a limp in recognition of that.

Erin Allmann Updyke

I love that, Erin.

Erin Welsh

Whether or not Hephaestus' limp was supposed to represent arsenic poisoning, humans have been aware of arsenic in its various forms for centuries. Take the etymology of the word for instance which starts somewhere around the Persian word 'zarnikh' which means yellow orpiment, which is this brightly colored compound of arsenic and sulfur. Zarnikh was then translated into the Greek word 'arsenikon' which was related to another Greek word 'arsenikos' meaning masculine or potent. And eventually that became arsenic. And that's only a little bit of a snippet of the etymology. So I think that kind of is a good indication that not only was arsenic widely known in many parts of the ancient world, it was also known in the ancient world for a very long time. Arsenic in its many forms was used in the ancient world not just to make copper alloys but also as a hair remover for leather working or to create a silvery surface on mirrors and statues, as a dye or a cosmetic or as a medication for all sorts of things, lice infestation, abscesses, constipation, tuberculosis, ulcers, cough, shortness of breath, and so on.

Erin Allmann Updyke

It does it all.

Erin Welsh

It does it all. The first exposures to arsenic may have been of an occupational nature but the growing range of uses for arsenic meant that anyone was at risk. And some scholars think that arsenic poisoning in the ancient world was incredibly unbelievably widespread. Not necessarily poisoning in the murderous sense however, the most common forms of arsenic that people worked with, this realgar and orpiment which I have mentioned before, are insoluble and brightly colored which are two qualities that would make them pretty poor murder tools, at least if you wanted to get away with it.

Erin Allmann Updyke

Okay, Erin.

Erin Welsh

Arsenic trioxide or white arsenic or ratsbane on the other hand, those are all names for the same thing, is a powder that dissolves in water, is colorless and tasteless.

Erin Allmann Updyke

Erin.

Erin Welsh

Does it get better than that? Yeah.

Erin Allmann Updyke

No, not when you're trying to murder somebody.

Erin Welsh

This form of arsenic, this arsenic trioxide or white arsenic was known to the ancient world as were the means of producing it but it didn't seem to be the top pick for intentional poisonings in Ancient Greece or Rome. That honor would go to wolfsbane and hemlock.

Erin Allmann Updyke

Okay.

Erin Welsh

It was probably used here and there such as by Agrippina The Younger and her son Nero to get him to the coveted position of Emperor of Rome. But it really only began to gain notoriety in the 1400s and 1500s thanks to the Borgias. Who were the Borgias, someone might ask?

Erin Allmann Updyke I remember learning about the Borgias.

Erin Welsh In what class?

Erin Allmann Updyke History. No, I remember in I'm pretty sure it was 8th grade European history, does that sound right?

Erin Welsh Yeah. I feel like that would be right. I mean the Borgias are a very dramatic and titillating part of history.

Erin Allmann Updyke Yeah.

Erin Welsh So this was this family who was super wealthy, super powerful, and whose name became synonymous with greed, adultery, theft, and murder. Specifically murder via arsenic.

Erin Allmann Updyke Ooh I love it.

Erin Welsh The Borgias were said to collect and store poisons like wine, having a poison cellar instead of a wine cellar. They would experiment with different combinations until they found one that they liked.

Erin Allmann Updyke Oh my gosh.

Erin Welsh Their signature poison, la cantarella, was mostly arsenic and they, especially the siblings Cesare and Lucrezia Borgia whose father by the way was Pope Alexander VI, like the pope.

Erin Allmann Updyke Wait, what?

Erin Welsh Yeah.

Erin Allmann Updyke The pope had kids? Okay.

Erin Welsh And these siblings supposedly fed it to anyone who stood in their way. And it seems like there were a lot of people who stood in their way.

Erin Allmann Updyke Okay.

Erin Welsh But I do want to add that many historians nowadays think that a lot of these rumors about the Borgias were exaggerated by contemporary critics. And Lucrezia may have been more of a victim of her family rather than the infamous poisoner that she was painted to be. But regardless of where the truth lies, the Borgias were definitely responsible for putting arsenic on the map as a murder weapon. But they were merely just the first. After the Borgias, arsenic pops up more and more in stories like the one of Giulia Tofana from Naples in the 17th century who sold her signature arsenic poison Aqua Tofana to dozens of people. Or Hieronyma Spira who also sold poison and started a poisoning society in Rome in the mid 16th century where she taught women how to poison their husbands.

Erin Allmann Updyke Oh my gosh.

Erin Welsh

Allegedly. And of course I have to mention Catherine de Medici, Queen Consort of France in the 16th century who was said to have studied poisons extensively, including arsenic, and brought the art of poisoning especially for political gain from Italy to France. And already a pattern emerges with these stories of famous arsenic poisoners. They were all women. Granted they were also mostly all from Italy which did have a reputation for a while as a place with a lot of poisoners in part maybe because there was for a period of time an entire branch of the Venetian government apparently dedicated to poisonings and you could get a job as a professional poisoner.

Erin Allmann Updyke

Wait, wait, wait, wait. Not like investigating poisonings or something like that? It was just like-

Erin Welsh

To poison.

Erin Allmann Updyke

To poison people.

Erin Welsh

Yeah.

Erin Allmann Updyke

How fascinating. I just love learning this history that I once probably heard some of.

Erin Welsh

There's just so much to arsenic, there's so much and this is such a brief tour even though this is a long section, this is such a surface level tour.

Erin Allmann Updyke

I love it.

Erin Welsh

And of course neither of these stereotypes were true.

Erin Allmann Updyke

Right. No.

Erin Welsh

Right, it's not like people were only poisoning in Italy.

Erin Allmann Updyke

Right.

Erin Welsh

And of course women weren't the only ones poisoning.

Erin Allmann Updyke

Yeah.

Erin Welsh

But that didn't stop them from being perpetuated.

Erin Allmann Updyke

I feel like that's still in movies and things, that's still the trope. Like on CSI or Law & Order, you still hear that as a trope.

Erin Welsh

Yep, yep. And there was a study of murders in Victorian England which by the way had fully embraced arsenic as a murder weapon by the late 1700s. And this study showed that cases of poisonings were actually fairly evenly split across genders but that poisonings represented a smaller proportion of murder styles for men who were much more likely to use violent means of murder and were more likely to murder overall. So if that makes sense.

Erin Allmann Updyke

Yeah, yeah, yeah.

Erin Welsh: So when women did murder, even though they took up a smaller proportion of all murders, they were more likely to use poison in their breakdown according to the study.

Erin Allmann Updyke: Right. Got it. Okay, interesting.

Erin Welsh: And when anyone used poison, they grew more and more likely to reach for the bottle of arsenic. Let's talk about why.

Erin Allmann Updyke: Yeah.

Erin Welsh: And to do that let's head to the 1800s. The 19th century has been called the arsenic century but not because everyone and their neighbor was poisoning everyone else and their neighbor with arsenic or rather not just because that. Intentional poisoning via arsenic was a really popular choice during this time in part because the symptoms of arsenic poisoning could mimic several infectious diseases that were super common around this time or even just other diseases.

Erin Allmann Updyke: Yes, okay. I love this.

Erin Welsh: Yeah. Like cholera, right. So you talked about how these GI symptoms are like cholera. That's pretty handy if you're trying to murder someone during a cholera outbreak.

Erin Allmann Updyke: Sure is, yeah.

Erin Welsh: But also not just because of this mimicry but because arsenic was really easily accessible. You could just buy it at the local grocers, the pharmacy, anywhere. But the vast majority of people who became exposed to arsenic during the 1800s, and a whole lot of people got exposed, did so because of their job or simply because they were eating, breathing, and living among the poisonous stuff. During the Industrial Revolution which started in Great Britain and the US around the 1760s or so and lasted until the 1820s, 1840s, the demand for metals grew and grew in order to build these new buildings or build these new machines. And of course to get new metals you have to mine.

At first it seems like arsenic, specifically this super toxic white arsenic, arsenic trioxide, was mainly a byproduct during the smelting of other metals. People had of course recognized its value on its own for a long time but it wasn't until the 1800s that mining for arsenic specifically really took off. The list of things that you could use arsenic for seemed endless and the arsenic industry and mines to produce this stuff grew and grew. For instance, it began to be used as a bright green colorant, it went by the names Paris Green or Scheele's Green.

Erin Allmann Updyke: Okay.

Erin Welsh: Wallpapers were full of the stuff.

Erin Allmann Updyke: Question. You know the book Goodnight Moon?

Erin Welsh: Yeah.

Erin Allmann Updyke: The walls are green. Is that Paris Green?

Erin Welsh: When was Goodnight Moon written?

Erin Allmann Updyke I don't know. It's been around since my mom was little so before the late 1950s.

Erin Welsh I feel like no.

Erin Allmann Updyke Okay.

Erin Welsh It's unlikely to have been at that point Paris Green unless they were living in a house that hadn't been updated since the mid 1800s, late 1800s.

Erin Allmann Updyke How fascinating.

Erin Welsh Yeah.

Erin Allmann Updyke Okay, I'm gonna have to google this.

Erin Welsh Yeah, you should definitely google wallpapers that have Paris Green in them.

Erin Allmann Updyke Okay.

Erin Welsh Because some of them are really beautiful. But it wasn't just wallpapers either. This arsenic green was used in artificial flowers which were often in decorations for hats or dresses and the gowns themselves were often dyed with arsenic colorant.

Erin Allmann Updyke Oh no.

Erin Welsh So you can imagine someone in an arsenic dress dancing and swirling around, not knowing that arsenic was being discharged with every move and you're breathing it in, you're shedding it on the floor, absorbing it maybe into your skin, maybe not. Yeah. There's a comic from 1862 about this that's titled 'The Arsenic Waltz'. And speaking of just discharging arsenic everywhere, let's talk about the wallpapers. Even though wallpaper producers tried to downplay any risk that their arsenic wallpapers posed, such as the famous designer William Morris who by the way was a big investor in the Devon Great Consols arsenic mine which was the biggest source of arsenic in the world.

Erin Allmann Updyke Wow.

Erin Welsh So this is like the head honcho most beautiful wallpaper designs you've ever seen, you can still get actually William Morris designs in all kinds of things. He was all about the arsenic. And even though there was all this downplaying of the risks, reports just kept pouring in of people that would become really sick after wallpapering their room and the only time they would get better was moving out of the room or taking down the wallpaper. And children of course seemed to be especially at risk, crawling around on floors that were coated with a dusting of arsenic from the green wallpaper.

Erin Allmann Updyke Ugh. And just licking everything.

Erin Welsh Licking everything.

Erin Allmann Updyke Yeah.

Erin Welsh: Yep, yep. And this is actually still, arsenic wallpaper is still a problem of course in places that are being renovated or going back through, just like we talked about with anthrax I think because they used to use... Anyway, I can't remember what it was.

Erin Allmann Updyke: Or lead?

Erin Welsh: Could be both. Probably both. Arsenic could also appear in candles, soap, books, glass and glassware, paint, stuffed animals, paper and packaging, fly papers, lampshades, I mean the list goes on and on and on. And so it's pretty easy to see how you could be exposed on a daily basis.

Erin Allmann Updyke: Yeah.

Erin Welsh: But let me read you this quote about arsenic during the Victorian era to finish out the picture. So this is from the medical historian James Horton. Quote: "A great deal of it was introduced purposely into many of the components of everyday life, with the result that people took it in with fruits and vegetables, swallowed it with wine, inhaled it from cigarettes, absorbed it from cosmetics, and imbibed it even from the pint glass. The substance was present in a broad assortment of household items from candies and candles to cookware, concert tickets and preserved partridge heads used to ornament ladies' headdresses."

Erin Allmann Updyke: Oh my gosh.

Erin Welsh: "Christmas tree ornaments and children's stuffed animals no less were often arsenical and the money used to purchase all of these products was itself sometimes contaminated."

Erin Allmann Updyke: How fascinating, Erin.

Erin Welsh: I had no idea the extent to which arsenic was in everyday items.

Erin Allmann Updyke: I would never have guessed, never have guessed that.

Erin Welsh: I know, I know. And I don't know if the word candy popped out to you in that quote because it did to me because what on earth?

Erin Allmann Updyke: I love candy.

Erin Welsh: Well the candy thing refers to the use of arsenic as a dye to make candies green.

Erin Allmann Updyke: So I just googled Paris Green real quick.

Erin Welsh: Yeah.

Erin Allmann Updyke: It's a gorgeous color.

Erin Welsh: Oh it really is, it's beautiful.

Erin Allmann Updyke: It's such a green, green, green.

Erin Welsh: Yeah.

Erin Allmann Updyke

So I get it. I mean I'm not advocating for it but I get how once you found something that makes that color it's going to be a high bar to stop using it because it's going to make you a lot of money.

Erin Welsh

Right, exactly. And that's the thing is that there were so many mines now devoted to arsenic and so it was just like let's find what else we can use this for. But yeah, the arsenic in candies was shocking.

Erin Allmann Updyke

And gross.

Erin Welsh

Intentionally. But there was also a pretty infamous incident in 1858 when an English sweet maker named Joseph Neal accidentally arsenic poisoned about 200 people and 20 of them died. So what happened was that it was really common practice at the time to fill out candies with tasteless inert substances.

Erin Allmann Updyke

What?

Erin Welsh

Yeah, to be like I'm going to add a little bit of sugar just to kind of fill it out a little bit more, save money. And one of these substances was called daft which seems like it was probably mostly plaster of paris.

Erin Allmann Updyke

Oh my god.

Erin Welsh

And the sweet maker mistook, which sounds gross enough on its own, but the sweet maker mistook white arsenic for this daft stuff and poisoned a massive batch of his candies.

Erin Allmann Updyke

Oh no!

Erin Welsh

Yeah. So it was just with white arsenic.

Erin Allmann Updyke

Oh goodness gracious.

Erin Welsh

But even if you avoided these tainted candies or any of these other things, how could you have lived in the late 1700s and 1800s and not been exposed to arsenic, like high levels of arsenic?

Erin Allmann Updyke

Yeah.

Erin Welsh

In the 1950s some hair samples of Napoleon who died in 1821 of stomach cancer supposedly, this is like the fourth time Napoleon has been mentioned this season.

Erin Allmann Updyke

I know, I was just going to say can we put a compilation together of every time that you mention Napoleon?

Erin Welsh

Yeah, I would love that. But Napoleon's hair was tested in the 1950s and found to contain high amounts of arsenic which led some people to conclude that he died of intentional arsenic poisoning.

Erin Allmann Updyke

What? I feel like another episode you said he died from a different thing that we talked about.

Erin Welsh
I'm sure. Probably. Because the other thing too is that's a very fun and interesting hypothesis and it could be true but I think there's some debate over whether it was intentional and whether there were high enough levels to actually cause him severe illness and especially death. Because there was definitely arsenic in the wallpaper on his living room walls and also there was probably arsenic in everything.

Erin Allmann Updyke
Everything.

Erin Welsh
Just everything.

Erin Allmann Updyke
Yeah. In his candy.

Erin Welsh
In his candy.

Erin Allmann Updyke
I'm sure Napoleon ate candy.

Erin Welsh
I feel like he had to have.

Erin Allmann Updyke
He had to have a sweet tooth.

Erin Welsh
But even if Napoleon wasn't around enough arsenic for it to kill him or make him seriously ill, plenty of other people were, especially those working directly with the substance. Let's start right at the source: arsenic mines.

Erin Allmann Updyke
Yeah.

Erin Welsh
Every step along the way, from the dust inside the mines to the toxic gasses produced in the smelting process to the packaging of the arsenic for future sale, workers were exposed to outrageous amounts of arsenic and many mine employees became too sick to work which led to an increase in applications to the government under the poor laws which made the government wonder whether there might be something about these mines making people sick. So they began an investigation into the health effects of arsenic mines and surprise surprise, they found that there was no ventilation or protection and that continuous exposure was really dangerous especially also in terms of lung cancer they found.

Erin Allmann Updyke
Yes.

Erin Welsh
Okay.

Erin Allmann Updyke
Yeah because in a mine you're being exposed to it primarily via inhalation rather than ingestion.

Erin Welsh
Right.

Erin Allmann Updyke
And so it's going straight to your lungs and causing damage there. Hence the lung cancer. Totally.

Erin Welsh
Right. Despite this, nothing was really done about it.

Erin Allmann Updyke
Yeah, I'm not surprised based on this podcast.

Erin Welsh	Yeah. And this is a common theme in the history of arsenic that we'll see repeated time and time again. Like wallpaper. By the 1850s people had grown suspicious of arsenic-laced wallpaper and demanded investigations into just how much of a risk it actually posed, starting with the wallpaper factories. Unsurprisingly these investigations turned up tons of health problems in these crowded and poorly ventilated factories where this wallpaper was produced. Factories which I might add were mostly staffed by children.
Erin Allmann Updyke	Oh no.
Erin Welsh	The majority of the workers that would actually paint the wallpaper were children and over half of these children were under the age of 13.
Erin Allmann Updyke	Oh no.
Erin Welsh	But even though these investigations confirmed what many people had already suspected, no changes were really made to the manufacturing process to try to reduce exposure. If someone did get sick from arsenic exposure in one of these factories, it was usually blamed on the worker. Oh, you didn't clean your hands well enough. Or oh, you shouldn't have licked your paintbrush, which was reminiscent of the radium girls, right.
Erin Allmann Updyke	Yeah.
Erin Welsh	And of course wallpaper production was just one of many industries where arsenic was commonly used. Another one was the artificial flower trade. This was actually a booming industry in the 19th century where workers who were primarily young economically disadvantaged women would spend all day in crowded rooms decorating hats and dresses with these artificial flowers and leaves and fruits, many of which had been died this beautiful green, this beautiful Paris Green or Scheele's Green with these green arsenic dyes. The business owners weren't required to tell their employees that they were working with a potentially deadly substance or give any safety guidelines on how to handle it. Or if those requirements did exist because eventually they did in some places, they weren't really enforced. The attitude at the time was well if you didn't want to work with arsenic-laced flowers then find another job.
Erin Allmann Updyke	Oh my goodness gracious.
Erin Welsh	Yeah, it's classic. Completely ignoring that many workers didn't have this luxury of choice. Besides proving useful in decorating hats and walls with its vivid green color, arsenic was also found to be a stellar pesticide and naturally it was used everywhere. Tobacco for a long time, absolutely chock full of arsenic.
Erin Allmann Updyke	Yeah, I read that. Yeah.
Erin Welsh	Yeah. Grains used in beer, an outbreak of arsenic poisoning in England from tainted beer finally prompted them to put a limit on how much arsenic you could spray. But the US, which was a much bigger user of arsenic, lagged far behind.
Erin Allmann Updyke	Not surprising.
Erin Welsh	At least until a British family got arsenic poisoning from apples that had been imported from the US. And so they finally agreed to lower arsenic spraying levels but only on apples that were to be exported.

Erin Allmann Updyke

Oh cool.

Erin Welsh

Yeah. It's awesome.

Erin Allmann Updyke

Yeah.

Erin Welsh

And I'm very curious to hear we stand in terms of arsenic use in agriculture today because I know that so much land is contaminated with arsenic either in soil or groundwater because of how much it was used as a pesticide in the past. And not just to spray crops but also to protect sheep from pests which probably harmed the sheep as much as it did the worker who had to hold this wriggling animal in this arsenic solution and press it into the wool of the sheep with their bare arms for hours and hours every single day.

Erin Allmann Updyke

Oh no.

Erin Welsh

And many of these people eventually developed skin cancer from this constant exposure to arsenic of course.

Erin Allmann Updyke

Okay.

Erin Welsh

Arsenic was used extensively in taxidermy in the 19th century. The arsenic-based soap that somebody came up with was the soap, it was the first one that actually seemed to work and not just leave you with a rotting carcass.

Erin Allmann Updyke

Like used to clean the animal once you skinned it or something?

Erin Welsh

That's what it seems like, yeah.

Erin Allmann Updyke

Ew.

Erin Welsh

Like the pelt.

Erin Allmann Updyke

Yuck. I have literally never thought about what it takes to taxidermy preserve an animal.

Erin Welsh

That could be a fun episode.

Erin Allmann Updyke

It could be. And that kind of makes sense that they would use something gnarly.

Erin Welsh

Yeah, it does. And during the 19th century was this huge time for natural history and taxidermy as people travelled to new places and brought back animal specimens to fill museums, used to have collections, collections, collections.

Erin Allmann Updyke

Yeah.

Erin Welsh

And its legacy lasts today for people who work on these historical collections in museums, right.

Erin Allmann Updyke

Wow, yeah.

Erin Welsh

They have to take special precautions to make sure that they're not being continually exposed to these arsenic specimens.

Erin Allmann Updyke

Arsenic. Wow.

Erin Welsh

Yeah. And the success of arsenic in taxidermy led to it being used also in embalming starting in the early 19th century. But it didn't last too long as an embalming agent for two reasons. One was that people were worried about the negative health impacts of working so closely with the substance.

Erin Allmann Updyke

Okay.

Erin Welsh

Sidenote, John Snow of Broad Street pump and cholera epidemic fame published a letter in the British Medical Journal in which he described the dangers of working with cadavers because of their toxic arsenic embalming contents. Yeah. But the other reason that arsenic in embalming was short lived was that if you used arsenic to preserve a body, how would you be able to tell whether that person had been murdered using arsenic? You couldn't. And this was a problem because people were certainly still committing murder with the stuff.

Erin Allmann Updyke

How interesting.

Erin Welsh

As I mentioned white arsenic is tasteless, colorless, dissolves in water, can be given over time to mimic a chronic illness, and importantly during a good chunk of the 1700s and 1800s was super easy to obtain. In England until 1851 there were no legal restrictions on the sale of poisons.

Erin Allmann Updyke

Wow.

Erin Welsh

So you could pop down to the corner store for some arsenic-based rat poison or head over to the pharmacist's and pick up Fowler's solution which was a medication who's featured ingredient was arsenic. It was also used well into the 20th century. It was bad news, yeah. So of course people used arsenic for murder. One of arsenic's nicknames was inheritance powder.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

There are many stories that can explain why it would be called that but I'll just briefly mention one which is that one of the signers of the US Declaration of Independence, George Wythe, was likely poisoned along with two of his employees by his grandson because he had threatened to cut him out of his will.

Erin Allmann Updyke

Oh my.

Erin Welsh

Juicy.

Erin Allmann Updyke

The family dramas.

Erin Welsh

And as much as I'd like to go through a long list of all of the famous arsenic murder cases, I'm only going to mention a few that played a role in the development of a test for arsenic. However if you are interested in reading more about these other infamous cases such as a town in Hungary where dozens of arsenic murders happened over the course of decades, like dozens and dozens, or the 2003 mass poisoning of churchgoers in Maine, then I will recommend the book 'King of Poisons' by John Parascandola. Another attractive feature of arsenic as a poison for much of its history was that you couldn't test for it. You couldn't say, 'Your Honor, this was clearly a case of arsenic poisoning and not cholera as the defendant claims.' Or whatever you would say.

Of course people still got convicted based on witness testimony or a confession or a coerced confession, but the scientific proof of arsenic poisoning would have to wait until the 1800s. There's an asterisk that I have here because there is one case in England in the 1750s where a chemist claimed to successfully test for arsenic but it's not clear whether he actually did it and if it did anything and the accused, a woman who allegedly poisoned her father for preventing her elopement to an already married dude, was convicted despite of this nonspecific and probably useless test and she was hanged.

Erin Allmann Updyke

Wow.

Erin Welsh

Anyway, the first actual test for arsenic in cases of poisoning was developed in the 1830s by an English chemist named James Marsh. And Marsh had been called on to try to test for arsenic in a case of suspected poisoning where a grandson was accused of murdering his grandfather by slipping some arsenic into the coffee. See it's common. It happened a lot. And Marsh was able to produce a yellow precipitate from the stomach contents of the dead man which was characteristic of arsenic but the jury was not convinced and the defendant was acquitted. Later on he did admit that he actually murdered his grandfather.

Erin Allmann Updyke

Wow.

Erin Welsh

And so Marsh, this chemist, was really frustrated by the acquittal and also by the jury's kind of disregard for his test. He was like it was clearly arsenic poisoning, what do I have to do to convince you that this is a reliable test that you should use?

Erin Allmann Updyke

Yeah.

Erin Welsh

And so that's what he devoted his time to. He wanted to try to make a new and improved and reliable test for arsenic. And he did it. And I won't go into the how of the Marsh test because it's probably confusing and beyond my chemical knowledge scope for sure. But the important thing was that it worked and that it could be reproduced in other labs. Later improvements made arsenic even more easily detected, either by making this test better or building a new test from scratch. But did these tests do anything to affect the rate of poisonings?

Erin Allmann Updyke

I'm gonna guess no.

Erin Welsh

Yeah. It's unclear.

Erin Allmann Updyke

Okay.

Erin Welsh

Even after the laws restricting the sale of arsenic were passed in England in 1851 like I said, people continued to use it as a weapon mostly because these laws were really difficult to enforce. By the time that intentional arsenic poisonings were on the decline, they had already left their mark in public consciousness and pop culture. When I think arsenic I think Agatha Christie, I think Murder She Wrote, I think old cozy murder mystery books which is one of my favorite genres of books. Somebody tallied the different poisons used in works of detective fiction and arsenic came in third behind cyanide and mushrooms.

Erin Allmann Updyke

Wow. Yeah, okay.

Erin Welsh

And in Agatha Christie's books alone arsenic is mentioned either as a plot point or suspected poisoning or just in passing in nearly a quarter of her novels.

Erin Allmann Updyke

Wow.

Erin Welsh

Which is a lot. Also I just love Agatha Christie so much. Our firsthand account of course was taken from Madame Bovary, published in 1856, also featuring arsenic heavily. I just finished a couple of days ago 'We Have Always Lived In The Castle' by Shirley Jackson who also wrote 'The Lottery' and 'The Haunting of Hill House' and arsenic is a main character in 'We Have Always Lived In The Castle' which is by the way such an amazing book, I loved it so much.

Erin Allmann Updyke

Okay. I put it on my list.

Erin Welsh

And I also have to mention 'Arsenic and Old Lace' which is a play later made into a movie in the 1940s. The premise is absolutely absurd. These two old sisters rent out a room to elderly men that have no friends and no family and then the sisters poison them out of kindness.

Erin Allmann Updyke

Out of kindness!

Erin Welsh

Out of kindness. And their poison of choice was not just arsenic, it was a blend but arsenic was heavily featured along with strychnine and just a pinch of cyanide in some elderberry wine. And then the sisters' nephew finds the bodies and chaos and hijinks ensue and it's fun times. It's based on a true story by the way of someone who owned a boarding house and would do this.

Erin Allmann Updyke

I feel like boarding house murders are a thing I have read a lot about.

Erin Welsh

Oh for sure, for sure.

Erin Allmann Updyke

Yeah.

Erin Welsh

I also love not just how often arsenic appears in books and movies but how creative some of its uses are. Like a murderer infusing candles with arsenic so that when they were lit they would poison the intended victim.

Erin Allmann Updyke

Wow.

Erin Welsh

I know. Or my favorite, taking small amounts of arsenic to build up an immunity à la Princess Bride and iocane powder. And this building an immunity to arsenic may be based on the so-called arsenic eaters of Styria which is a state in southeastern Austria. So people in this region would allegedly eat small amounts of arsenic to make their skin look better or to be better able to climb at high altitude.

Erin Allmann Updyke

What?

Erin Welsh

And this rumor or this legend grew really, really famous in the 1800s. Did they actually exist, these arsenic eaters? Hard to say. But whether or not they were real, their legend had tremendous influence on the use of arsenic in the 19th century when people were either poisoning their spouse or grandparent with the stuff, inhaling it while working in the mines, ingesting it with their candy, or absorbing it from their wallpaper or cosmetics. Eventually the prevalence of arsenic in commercial goods or as a murder weapon started to decline in the 20th century but that's certainly not the end of arsenic's story. And don't worry, I'm nearly done.

Sticking with the three themes of arsenic as an intentional poison, a medicine, as an environmental contaminant, the 20th century saw arsenic being developed but not extensively deployed as a chemical weapon during WWI in the form of something called lewisite which is also how I believe we started to develop treatment for arsenic poisoning in anticipation of its use as a weapon. The 20th century also saw the emergence of arsenic as a truly effective medicine, first as a treatment for trypanosomiasis, then the first effective treatment for syphilis in the form of salvarsan, and later as a treatment for a certain type of leukemia called acute promyelocytic leukemia. And arsenic is to this day a hugely important and prevalent environmental contaminant. And Erin, I'm sure you'll talk more about this but arsenic in drinking water poses a threat to tens of millions, maybe hundreds of millions of people around the world today.

And although it's a global problem, one of the areas at highest risk is in Bangladesh and West Bengal. There in the 1970s a huge initiative was started to try to improve the water supply and reduce illness and death from waterborne pathogens. And so one solution proposed was to use tube wells to tap into cleaner water from the Himalayas. A bunch of international organizations got involved and by 2000 there were close to 11 million tube wells in these regions providing water to 97% of rural residents. And waterborne illness and infant mortality dropped tremendously. But about 10 years after this well building program really ramped up in the early 1980s is when a dermatologist noticed arsenical dermatosis in a patient and he linked it to the water from the tube well. This turned out to not just be a one-off but the beginning of one of the largest scale arsenic poisonings in the world.

In the next four years after this first case, this doctor alone identified over 1200 cases from 61 villages. And since arsenic poisoning can take a while to show up when it's long term exposure, chronic exposure, the extent of the poisoning was not realized until much later on. And really you could argue that we still don't necessarily have a good handle on it even today since the wells are still being used in many places. So this is my quick segue here but speaking of today and what's happening today Erin, can you tell me what we know about arsenic poisonings or arsenic in medicine or arsenic in the environment these days?

Erin Allmann Updyke

I would love to. Let's take a quick break first and then we'll get into it.

TPWKY

(transition theme)

Erin Allmann Updyke

So the World Health Organization actually lists arsenic, and this blew my mind but after that whole history section I feel like this makes a lot of sense, it lists arsenic as the most significant chemical contaminant in drinking water globally, period. The most significant one, arsenic.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. I believe it now.

Erin Allmann Updyke

I know, exactly. When I read that I was like what? And then the history and I was like well...

Erin Welsh

Yeah.

Erin Allmann Updyke

So groundwater contaminated with arsenic is a massive problem worldwide with an estimated, according to the World Health Organization, 140 million people in 50 countries that are currently exposed to drinking water at levels well above what is considered... The World Health Organization still listed as the kind of provisional guideline, meaning they're still looking at this to see if this is actually the best guideline but it's been the guideline for a while now. And that is 10 parts per billion or 10 micrograms per liter. So 140 million people in 50 countries are drinking water that is well above that. How high above that can really, really vary. Like you mentioned Erin, Bangladesh has some of the areas that have the highest values that we've found. In some areas in Bangladesh drinking water has as much as 800 micrograms per liter or 800 parts per billion of arsenic which is so high.

Erin Welsh

Oh my gosh. Yeah.

Erin Allmann Updyke

But in a lot of various rivers, streams, and other freshwater sources, various environmental studies have found as high as several 1000 parts per billion. It just doesn't necessarily mean that that's in the drinking water. But the good news is that especially in Bangladesh where we know these levels have been so high, a lot of progress has been made to try and reduce the number of people that are being exposed. The World Health Organization's most up to date numbers are unfortunately still rather old, they're from about 2012. But then it was estimated that over 39 million people in Bangladesh specifically were exposed to levels over that 10 micrograms per liter in their drinking water and 19 million people were exposed to levels above 50 micrograms per liter or 50 parts per billion, which is a lot higher than what our minimum should be or maximum should be rather.

Erin Welsh

Right, yeah.

Erin Allmann Updyke

And in one area of Bangladesh an estimated 21% of deaths were actually attributed to arsenic poisoning. 21% of deaths.

Erin Welsh

21%?

Erin Allmann Updyke

I know, it's so much higher than I realized.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. Globally mostly the sources still are just various environmental sources. Arsenic is found in rock, in volcanic ash like you said. But anthropogenic sources like mining, the burning of fossil fuels, working in industries like alloy-making, etc. Arsenic-containing pesticides are not really used in the US very much anymore, they're not from what I can tell completely eliminated but the use of them has declined significantly. Arsenic is still used in treating lumber, that's one of the main areas that it's still used as a sort of pesticide. It's for an antifungal. So treated lumber is generally treated with arsenic.

Erin Welsh

Interesting. I did not know that.

Erin Allmann Updyke

Yeah, yeah. So wash your hands. That's why they always say to wash your hands after you're working with treated lumber. It's not necessarily the exposure via your hands but just how much it's easy to get that on your face or mucous membranes after handling it. And one thing that I kind of really was trying to get a handle on in addition to those numbers that I mentioned which weren't really that satisfying to me when I was trying to get a sense of the global state of arsenic epidemiology or whatever I usually do in this section, is that the vast majority of papers that I found, even the ones that seemed from the title that they were going to be talking about the epidemiology of chronic arsenic or arsenic exposure, most of these papers were actually more focused on the mechanistic underpinnings. Like here's what you should understand about the mechanistic effects if you want to study the relationship of arsenic and its various potential effects.

And so it seems like from what I can gather and from the papers that were trying to kind of assess the state of arsenic knowledge, the biggest thing that researchers are really trying to get a better handle on are some of these very specific mechanisms to explain the health effects that I talked about in the biology section. Because as much as we know okay, it can affect these various enzymes, it can react with thiols and sulfhydryls, it can mimic phosphate. Because there is such interactions between exposure to arsenic and exposure to so many other things or things like malnutrition, etc, a lot of the epidemiological studies can result in mixed results especially when you're looking at very low levels of arsenic exposure.

So we know all of those health effects from very high levels of exposure but when we get down to the 10 parts per billion, 15 parts per billion, 5 parts per billion, the data becomes a lot less clear and it seems like a lot of that is because we don't fully understand the effects that arsenic is having on our bodies. So a lot of the research seems to be focusing on that, especially at lower levels of exposure. If we can understand specifically what does arsenic do when it gets into our body and how much does it take to cause that in various people, then you can have more data to say no this really is an acceptable level and this level is not acceptable at all, if that makes sense.

Erin Welsh

Yeah, yeah.

Erin Allmann Updyke

So that is kind of what I researched at least when it comes to arsenic. I tried to look into arsenic in rice because I don't know about you Erin, but when I think of arsenic poisoning I think of rice.

Erin Welsh

Yeah.

Erin Allmann Updyke

And I actually didn't even know why in my brain I had that association.

Erin Welsh

Yeah.

Erin Allmann Updyke

But arsenic is something, it is ubiquitous, but one of the reasons that it can be found in relatively high levels in rice and in things like rice cereal which for a while was touted as the best thing to feed your baby, rice cereal, is because of the way that rice is grown and harvested. So it's not necessarily rice specific but it's the way that rice is grown which is often under flood irrigation. And so in places where you want to be able to grow rice during the dry season, where you don't have as much rainfall, if groundwater is used for that flooding, groundwater can contain a lot of arsenic.

And on top of that the way that rice grows in this flood irrigation happens to be really good conditions for arsenic to be in that form of arsenite, the reduced form, which is very toxic and bioavailable. And so it's easily taken up in the rice and accumulates in the rice in high levels. And then when you dry that rice out, pulverize it, and concentrated into something like a baby cereal where you're exposed to a lot more rice than you would be if you were just eating a bowl of rice, then it's even more concentrated. And so that's how you end up with high levels of arsenic potentially in something like rice or a rice cereal.

Erin Welsh

Okay. That makes sense, yeah.

Erin Allmann Updyke

Rice isn't the bad guy.

Erin Welsh

Right, right.

Erin Allmann Updyke

But yeah, that's a nutshell of arsenic current events, Erin.

Erin Welsh

It's a complicated topic because its distribution is so uneven.

Erin Allmann Updyke

It's so uneven.

Erin Welsh

And it seems like we just don't have a good handle on everything.

Erin Allmann Updyke

No, no.

Erin Welsh

Which is kind of kind of a little scary.

Erin Allmann Updyke

Kind of scary and and all of those things.

Erin Welsh

Yeah. But I feel like we covered a lot of ground in this episode. And I just also wanted to say that if I left out your favorite arsenic trivia or favorite arsenic movie or book or whatever, maybe you wanted to talk about the Anaconda Mine in Montana or how arsenic was used in dentistry forever, please share it on the social media post announcing this episode's release or wherever you want to share it because we'd love to hear more about arsenic.

Erin Allmann Updyke

I love it. Well should we do sources?

Erin Welsh

Let's do sources. I had several, I'm going to shout out two in particular. One by Apata and Pfeifer from 2019 is about the evolution of that variant of that arsenic metabolism gene, that's a really interesting one. And then for the big history section mostly I used a book called 'King of Poisons' by John Parascandola all about arsenic.

Erin Allmann Updyke

I had a number of papers that have so much more detail on what we know about the mechanisms of arsenic and its effects on our body. A couple that I'll shout out, one from Toxicology International from 2011 that was just called 'Mechanisms pertaining to arsenic toxicity'. And then there was actually a great Department of Health and Human Services very comprehensive, it was called 'The toxicological profile for arsenic' and it was from the Agency for Toxic Substances and Disease Registry. And that's really comprehensive and also has some data about what the state of arsenic is in the world and in the US. We will post the full list of our sources from this episode and every one of our episodes on our website thispodcastwillkillyou.com under the EPISODES tab.

Erin Welsh

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. We hope that you liked this one. I think I did. I loved it actually.

Erin Allmann Updyke

Yeah. I really liked it.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. Thanks for listening. And a special thank you to our patrons for supporting us on Patreon, we can't tell you how much it means to us.

Erin Welsh

Yeah, truly. Well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.