

TPWKY

This is Exactly Right.

Erin Allmann Updyke

"Among the blossoms waits a jug of wine. I pour myself a drink, no loved one near. Raising my cup I invite the bright moon and turn to my shadow. We are now three. But the moon doesn't understand drinking and my shadow follows my body like a slave. For a time moon and shadow will be my companions, a passing joy that should last through the spring. I sing and the moon just wavers in the sky. I dance and my shadow whips around like mad. While lucid still we have such fun together but stumbling drunk, each staggers off alone, bound forever, relentless we roam, reunited at last on the distant river of stars."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Wow.

Erin Allmann Updyke

I really like that little poem.

Erin Welsh

I do too.

Erin Allmann Updyke

So that poem was by Li Bai also known as Li Po who was according to this source one of the greatest poets of China's Tang Dynasty or of all of history perhaps. Li Bai was a martial artist, and academic genius, and also a lover of wine and a member of the group Six Idlers of the Bamboo Brook which was a group dedicated to literature and drinking. And in general people at the time would only indulge socially so this poem, one of his most famous, is exploring the problems of drinking alone.

Erin Welsh

Yeah. All the way back from the 8th century.

Erin Allmann Updyke

The 8th century. And the poem that I read was translated by David Bowles from the original Chinese and we'll post the link on our website.

Erin Welsh

Yeah. Well hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allman Updyke.

Erin Welsh

And this is This Podcast Will Kill You.

Erin Allmann Updyke

It is and it's a big episode for a couple of reasons.

Erin Welsh

Reason number one is that it's our season finale.

Erin Allmann Updyke

It's our Season 4 finale.

Erin Welsh

Yeah, four seasons, four finales. This is a big one.

Erin Allmann Updyke

Can you picture us four years ago when we were doing our first season in my back bedroom in our tiny house? Could you ever have imagined that we would be here doing this now, Erin?

Erin Welsh

You know what? I don't know if I like dared to hope that we would still be doing it.

Erin Allmann Updyke

Yeah.

Erin Welsh: But I think it's kind of funny because I think that neither of us maybe would've been that surprised cause we had lists of episodes we wanted to cover up to like five seasons worth all the way back then.

Erin Allmann Updyke: Spoilers.

Erin Welsh: I think the thing that would've really shocked us and we would not have believed is our listenership being so incredible and so supportive and so wonderful.

Erin Allmann Updyke: Totally. Yeah. It's you all listeners, thank you so much, we would not be still making this podcast without you. Or if we were it definitely wouldn't be as much fun.

Erin Welsh: Yeah. It's true. Yeah so after this episode, don't worry, we will be coming back. So it's kind of not that sad in a way.

Erin Allmann Updyke: It's not.

Erin Welsh: Because it would be a lie to say that we're not looking forward to the break a bit.

Erin Allmann Updyke: No, we are highly looking forward to it.

Erin Welsh: Yeah, just a little bit of time to rest our brains and to get some other stuff done in the background. And if you're looking for more of TPWKY to fill that need while you're gone, you should definitely check out our reading lists, our bookshop.org affiliate account, our Goodreads list which by the way I'm not allowed to add anymore books, I've capped it at 100. I've added 100 books so far and so I can't add anymore. And so if there's a helpful listener out there that wants to add the books that I mentioned, that would be lovely.

Erin Allmann Updyke: That's hilarious, oh my goodness.

Erin Welsh: Problems of a podcaster.

Erin Allmann Updyke: Okay so that's one of the reasons that this is a big episode, the other reason is because today we're talking about alcohol.

Erin Welsh: Alcohol.

Erin Allmann Updyke: Like all of it, just alcohol.

Erin Welsh: Yeah. You know it sounded fun. It still sounds fun.

Erin Allmann Updyke: It sounded manageable.

Erin Welsh: Yeah, yeah.

Erin Allmann Updyke: We'll see if it was.

Erin Welsh: Yeah. You be the judge.

Erin Allmann Updyke: Yeah, you guys tell us.

Erin Welsh: Well it wouldn't be an episode of TPWKY or just an episode of a podcast about alcohol without a quarantini.

Erin Allmann Updyke: Exactly!

Erin Welsh: So what are we drinking this week?

Erin Allmann Updyke: We're drinking Pour Choices. Get it? Like P-O-U-R. I think this is the second pour-related pun that we've done.

Erin Welsh: This season, yup.

Erin Allmann Updyke: This season. But it's a really good one.

Erin Welsh: It is, it is a really good one. And in addition to having a really good name, it's also a really fantastic drink and I'm not exaggerating.

Erin Allmann Updyke: Tell us what's in it, Erin.

Erin Welsh: So you start with mead and we chose mead because mead is one of the oldest alcoholic beverages, also known as honey wine. And then we kind of did a little fun side step, we're doing a shrub.

Erin Allmann Updyke: A shrub!

Erin Welsh: And if anyone hasn't had shrub before, it's basically like drinking vinegar.

Erin Allmann Updyke: Yeah.

Erin Welsh: You make a little recipe with macerated fruit usually or pulped fruit and then some sort of sweetener and then vinegar and some spices if you want. And you let it sit and then you filter it out and it's absolutely delicious. I made a shrub for this of honeycrisp apples and honey, apple cider vinegar, the zest of a lemon, allspice, anis, and cinnamon sticks.

Erin Allmann Updyke: Yum. Also don't be afraid of the sound of a vinegar drink, it's actually delicious.

Erin Welsh: It's really complex and delicious and you can do so much with them.

Erin Allmann Updyke: Yeah, it makes a very good placeborita and don't worry, we'll post the full recipes for that quarantini and the nonalcoholic placeborita on our website thispodcastwillkillyou.com and ll of our social media channels.

Erin Welsh: We will. Other business.

Erin Allmann Updyke: Other business.

Erin Welsh: Our website. There's lots of good stuff on there, you can find all of our sources for all of our episodes, you can find links to like I said our bookshop.org affiliate account and Goodreads list, you can find links to Patreon, to our merch, to transcripts. And also I am excited to announce that Bloodmobile, who provides the music for this episode and all of our episodes is now on Spotify.

Erin Allmann Updyke: Yay!

Erin Welsh: And we will post a link to that as well. So definitely check all of that stuff out.

Erin Allmann Updyke: Is that all of our business today, Erin?

Erin Welsh: I think so.

Erin Allmann Updyke: All right.

Erin Welsh: Should we dive in? Can we dive in?

Erin Allmann Updyke: I think that we can. We'll take a sip and a break and then get to it.

Erin Welsh: Perfect, perfect.

TPWKY: (transition theme)

Erin Allmann Updyke: So alcohol. By which I mean, Erin, ethanol. I'm assuming that's what you mean.

Erin Welsh: Yeah.

Erin Allmann Updyke: Okay good.

Erin Welsh: Yeah, by the way I think we're gonna be using these interchangeably throughout?

Erin Allmann Updyke: Mm-hmm.

Erin Welsh: Okay.

Erin Allmann Updyke: For sure, yeah. Ethanol is the form of alcohol that we drink, it's the form that's used for recreational purposes. So when we say 'alcohol' that's what we're talking about in this context. All right. So ethanol, alcohol, is a psychoactive drug. I think it's important to frame it that was because A) that is in fact what it is, and B) it's not uncommon that we frame it either as something completely harmless or fairly harmless or on the flip side as a recreational substance or something that is really bad, right.

Erin Welsh: What is the definition of psychoactive drug?

Erin Allmann Updyke: So glad you asked, Erin. I actually don't know if I have a formal definition but it's a substance that acts directly on the brain, on the central nervous system.

Erin Welsh: Okay.

Erin Allmann Updyke

Can you remember something else that we covered on this podcast that is also a psychoactive drug?

Erin Welsh

Caffeine.

Erin Allmann Updyke

Caffeine! Yeah, exactly. So alcohol has direct effects on our brain both in the short and the long term that are not only important to understand but are also fascinating. As per usual I'm not going to be able to cover it all and alcohol affects a lot more of your body than just your brain but for most of this episode I'll be focusing on the effects on the brain, I'll get in a little bit to some of the long term effects on other organ systems. So let's get into it. Here's how I'm gonna break this down. First I'm gonna talk about the direct effects of alcohol in kind of the short term and how it produces what we all know of as drunkenness. And then we'll talk about one of my favorite parts which is the dreaded aftermath, the hangover.

Erin Welsh

Yeah.

Erin Allmann Updyke

All right. And to discuss that we do have to get a little bit into the metabolism of alcohol but I promise I'll keep it biochemistry light. And then Erin, I wanna hear from you about how long we've been giving ourselves hangovers.

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

And then at the end we'll wrap it up with the status of alcohol in the world today by at least a couple of measures that I have data on, all right?

Erin Welsh

Okay. (laughs)

Erin Allmann Updyke

So alcohol, ethanol, it's freely absorbed across our GI tract the same way that water is. So it can easily pass through any and all of our biological membranes including of course our blood-brain barrier. So after you drink a beer or a glass of wine or a martini, ethanol rapidly reaches peak concentrations in our bloodstream and tends to go first to areas of high blood flow which includes our liver where it causes lots of damage that we'll talk about later, our kidneys, and what it does in our kidneys is it interferes with water reabsorption, it does this by inhibiting the function of proteins that usually allow water to escape. And so it functions as a diuretic.

Erin Welsh

Why does it do that? Is it just sort of...

Erin Allmann Updyke

The question of 'why' Erin is one I'm never gonna be able to answer in this episode, fair warning. But it interacts with a specific protein called vasopressin and vasopressin normally allows aquaporins to go into our kidneys. But it basically inhibits the function of that in our kidneys.

Erin Welsh

Okay.

Erin Allmann Updyke

So it causes you to lose a whole punch of water, hence you pee a lot. And then of course it also goes to our brain which is full of blood flow for important reasons. So ethanol enters our central nervous system and in truth it acts on so many different receptors in a lot of ways that are very complex and we don't fully understand them despite loads of research. But what we do know is that a large part of the effect that ethanol has is on a specific receptor in our brain called our GABA receptors. And if you think in very basic terms of our brain as having both excitatory, like stimulatory and inhibitory pathways, excitatory ones making you alert and vigilant or whatever and inhibitory ones being more sedating or more calming which is an oversimplification. But what alcohol does is it binds indirectly to GABA receptors which are inhibitory receptors and it makes these more active or more receptive to the effects of GABA. So what that does in practice is it makes us feel more calm.

Erin Welsh

Okay.

Erin Allmann Updyke

And it's a sedating drug.

Erin Welsh

Is that how all sedatives work, like the basic mechanism?

Erin Allmann Updyke

So benzodiazepines are another class of drugs that are sedating that also act on the GABA receptors in a slightly different way but there are lots of other sedating drugs that act on different receptors. It's really complicated.

Erin Welsh

Different pathways, receptors, okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

I have a question about diuretics.

Erin Allmann Updyke

Okay, oh gosh.

Erin Welsh

Do diuretics sort of all function in the same way that alcohol does or lead to the same water loss?

Erin Allmann Updyke

You mean like diuretics like other drugs that we have for diuretics?

Erin Welsh

Yeah.

Erin Allmann Updyke

No. There are tons of different classes of diuretics that all act in different areas of the kidney on different ways.

Erin Welsh

I need to know more about diuretics.

Erin Allmann Updyke

Ooh, we could do a whole episode about diuretics, I love it!

Erin Welsh

Okay.

Erin Allmann Updyke

Okay. (laughs) You know what we could do is do an episode about heart failure and then we can talk a lot about diuretics.

Erin Welsh

Oh, okay.

Erin Allmann Updyke

Okay, yeah. Anyways, back to alcohol. So it makes us feel more calm. It also makes us feel more happy because alcohol also serves to stimulate the dopamine pathways in our brain which are our brain's innate reward system.

Erin Welsh

Mm-hmm, right.

Erin Allmann Updyke

Right. So then how do we generally feel after a glass or maybe two of wine? We feel more relaxed, we might feel a boost in our happiness, we might feel even euphoric or super chatty because of those effects of dopamine, we feel generally good. And then maybe a tequila shot sounds like a good idea. Friends, it is rarely a good idea. And as our blood alcohol content increases, that feeling of relaxation progresses. It might progress to suppression of our anxiety, it might suppress our stress response. But at the same time our central nervous system is also becoming more depressed, we aren't able to think as clearly. We might, through both central nervous system and also just GI-related effects start having some nausea or vomiting, our motor and our sensory systems can start to become impaired and you lose especially that motor coordination. And as that blood alcohol content continues to increase, our brain becomes flooded with ethanol and then the blood flow to our brain is impaired which can cause things like blurry vision, slurred speech, dizziness, confusion, eventually possible loss of consciousness, coma, and even death.

Erin Welsh

Can you put this in terms of blood alcohol content or number of drinks type thing?

Erin Allmann Updyke

Yeah.

Erin Welsh

Which I know varies because tolerance really varies person to person, etc etc.

Erin Allmann Updyke

Yeah. So that question gets at a couple of different things, both how much of the ethanol that you consume is absorbed and how quickly does it take effect as well as what specific concentration of alcohol produces those specific effects. And you're right, there isn't really a clear cut answer because there's a lot of variability. The rate at which alcohol is absorbed across the GI tract varies a lot, for example if you have a full stomach then it's absorbed a lot more slowly, if it's an empty stomach, it's absorbed more quickly. And then you also have not only metabolic differences in how quickly you metabolize alcohol but also tolerance effects depending on how often you drink.

In general though, so we measure alcohol in your blood by blood alcohol concentration. So you've heard 0.08% is the legal limit in the US. At concentrations below 0.08% in general you're not having as much of the motor and cognitive deficits. At concentrations above that, especially approaching 0.1%, that's when you have sedation, impaired motor and sensory. Once you get to 0.3%-0.4% or above, especially above 0.5%, that's when you can see acute alcohol toxicity or death. It's hard to say exactly how many drinks it takes, it really varies person to person.

Erin Welsh

Okay so I feel like maybe this is just something that you hear in college and that's like, 'Oh eat a full meal before you drink and you won't get drunk.' And I always kind of thought well I think it's just you get drunk more slowly or it affects you more slowly. But is there actually a maximum at which your body just can't absorb a certain amount of alcohol in a certain time period and you'll like...you know what I mean?

Erin Allmann Updyke

Yeah, it's a good question. It does seem to be the case that if you have a full stomach it leads not only to slower absorption but over time to lower blood alcohol concentrations. So part of that and I'll get into this a little bit more in a minute is that alcohol is metabolized by what's called zero order kinetics, so the rate of excretion is constant regardless of the concentration. So it could just be that if you're absorbing it more slowly because of a full stomach then you are excreting it at a rate that is such that when you're absorbing it slowly your blood alcohol concentration doesn't rise as high.

Erin Welsh

Right, you keep up with the absorption.

Erin Allmann Updyke

Exactly.

Erin Welsh

Okay. Interesting.

Erin Allmann Updyke

Yeah. Eating does help. And as we can continue talking about, it's important the day after too. So let's talk about it.

Erin Welsh

Yeah.

Erin Allmann Updyke

Shall we move onto the biochemistry of a hangover?

Erin Welsh

Perfect.

Erin Allmann Updyke

So to be eliminated from our bodies, alcohol has to be metabolized which just means broken down. Eventually it's broken all the way down into carbon dioxide and water and at some point can be used for actual energy production. But along the way it's metabolized first into a toxic intermediate. So we already talked about the direct effects of alcohol, so now we get to talk about these toxic intermediates and the aftermath. So alcohol is metabolized first into a compound called acetaldehyde which is toxic in a whole number of ways. It first induces oxidative damage both directly and then as we'll continue talking about it has a lot of other downstream effects as well. Alcohol dehydrogenase is the enzyme that breaks alcohol down into acetaldehyde and while it's present in a lot of our body, primarily alcohol is metabolized in our liver, like over 90% of it. And so this is where acetaldehyde tends to build up and that's why drinking alcohol can have such drastic impacts on our liver.

Erin Welsh

Right.

Erin Allmann Updyke

And result in things like cirrhosis which is chronic liver damage. But since this intermediate is toxic our body obviously wants to get rid of it as quickly as it can so it further breaks it down via another enzyme called aldehyde dehydrogenase, right. And then it breaks it into acetate, further breaks it down, etc etc etc. What's important to know about this metabolism of alcohol, what I think is so interesting, is that this process inadvertently ends up interfering with a whole host of our normal metabolic processes which explains some of the symptoms that you feel when you've been drinking alcohol but also it explains a lot of the symptoms of a hangover which anyone who's experienced a hangover knows these symptoms can last a long time and really make you feel like trash.

So without getting into the weeds too much of the different biochemical cycles, let me just say this. We talked in our diabetes episode about how glucose is one of our main substrates that our body uses, we talked a lot about it. But our cells have a lot of different complex cycles that they use to break down different compounds to create ATP for energy so that our cells can use them. And all of these different cycles are interdependent, they overlap with each other. And by overlap what I mean is that these different metabolic pathways use a lot of the same cofactors. And cofactors are substances that are necessary as part of the chemical reaction but they aren't the actual parts of the chemical reaction, they're like helpers that you need for this reaction to happen.

Erin Welsh

Oof, this is like way flashbacks to cell bio and it's kind of giving me the heebie-jeebies.

Erin Allmann Updyke

I know, I'm sorry. I'm trying to avoid saying like 'the TCA cycle'. I know, okay. So let's get back to alcohol. The process by which alcohol is metabolized first into acetaldehyde and further and further all the way to acetic acid, these steps of metabolism use up certain cofactors in our body and change the ratio of what's available for other essential cycles in our body. So what that looks like is a whole host of screw-ups in the way our body is supposed to do basic metabolism. Okay? So it's not alcohol directly but it's the process of alcohol metabolism and the metabolites themselves that cause a lot of the symptoms that we know of as a hangover. So we can go through some specific examples if you want to.

Erin Welsh

Yeah, I do. But that's really interesting because one of the ways I remember hearing hangovers described is sort of the result of stealing happiness from tomorrow.

Erin Allmann Updyke

(laughs) Yeah! That's kind of true.

Erin Welsh

So you go out, you go drinking, you have lots of fun. And then you have used up the happiness, the ability to kind of have a good day the next day, the night before. Same as with cofactors.

Erin Allmann Updyke

That's so funny. That's exactly what it is, you're using up your body's NAD+ which is happiness. Okay.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. So we can go over some of the specifics.

Erin Welsh

Okay.

Erin Allmann Updyke

If you want to.

Erin Welsh

Yeah.

Erin Allmann Updyke

All right.

Erin Welsh

Of course.

Erin Allmann Updyke

Great. So one of the things that happens as a result of stealing these happiness cofactors is that the metabolism of alcohol ends up blocking the process of gluconeogenesis. This is the process by which you make more glucose in your body in times when your glucose is low. So without the ability to do this you end up with hypoglycemia which we talked about in our diabetes episode that can make you feel shaky, it makes you feel super hungry, probably nauseous, weak, trembly. But the thing about this is it's not always even a true hypoglycemia, it's what's called a relative hypoglycemia because you're not able to make glucose from what you already have available in your body because you're missing these cofactors. And on top of that because of missing these cofactors you're also not able to undergo the right kind of catabolism to use what you do have already.

Erin Welsh

Wow. Water, water everywhere, nor any drop to drink. (laughs)

Erin Allmann Updyke

That's exactly what it is. The metabolism of alcohol as well as some of the actions of alcohol itself on our brain also uses up all of our body's glutamine stores. Glutamine is an amino acid which is used to make proteins, it's also an essential neurotransmitter in our brain. So by using up all of our glutamine it makes us feel very tired and then as our body makes more and our glutamine can rebound, it can lead to things like tremulousness, anxiety, restlessness, things that we might see in alcohol withdrawal syndrome. We already talked as well about how alcohol is a big diuretic so then you likely are going to end up dehydrated which might make you awful in and of itself, also give you things like a headache. In the mid to longer term the metabolism of alcohol also inhibits the breakdown of fatty acids which means you have a bunch of fat, like little chunks of fat floating around and your body then stores those in our liver which causes further damage to your liver because of this inflammatory response to this fat.

Erin Welsh

Interesting.

Erin Allmann Updyke

So that is why you feel so cruddy with a hangover.

Erin Welsh

It makes sense.

Erin Allmann Updyke

Yeah. So that's all of kind of the acute symptoms of alcohol and hangovers. Of course it's important to talk about long term exposure. Chronic high levels especially of alcohol use can lead to a lot of different health problems and I'll just go through kind of the biggest ones which we've kind of already touched on as well. Cirrhosis, cirrhosis being chronic inflammation and eventual scarring of the liver happens both because like I said of the fats that are deposited causing inflammation as well as direct damage from both acetaldehyde and alcohol in the liver itself. In your brain chronic alcohol use can also lead to a syndrome known as Wernicke-Korsakoff syndrome, have you heard of this Erin?

Erin Welsh

No I don't think so.

Erin Allmann Updyke

So Wernicke-Korsakoff, it's actually two different syndromes that are kind of lumped together as one. It's Wernicke encephalopathy which is an acute and potentially fixable disorder as well as a longer term irreversible dementia that's known as Korsakoff syndrome. Both of these are actually caused not by alcohol directly but by a thiamine or a vitamin B1 deficiency. So this is a syndrome that can occur with no alcohol whatsoever but today because we fortify flour and things like that, over 90% of cases tend to be associated with chronic long term alcohol use. And alcohol results in vitamin deficiencies. I can see your face that you're gonna ask how.

Erin Welsh

Uh-huh. You got it.

Erin Allmann Updyke

So alcohol use results in vitamin deficiencies, not just thiamine but especially thiamine in a few different ways. It can reduce overall absorption of our vitamins by just interfering with our gut. The metabolism of alcohol uses up cofactors, we know that, that are essential in the recycling of thiamine as well as other vitamins as well. The effects of alcohol on our kidneys also causes us to lose thiamine more easily, so we're peeing more thiamine out. And then alcohol use, also in part because of its effect on the kidneys, effects our overall electrolyte balance including magnesium which is an important electrolyte and an essential cofactor in thiamine utilization.

Erin Welsh

It really is all about the cofactors.

Erin Allmann Updyke

It really is all about the cofactors. And then on top of that alcohol itself and acetaldehyde both do cause chronic damage to our brain that can lead to generalized volume loss. So it does a lot of different things in a lot of different ways.

Erin Welsh

Yeah.

Erin Allmann Updyke

So I mentioned already that alcohol is excreted by what we call zero order kinetics. What that means is that no matter how much alcohol that you have in your system, so even at very low concentrations or even at very high concentrations, the enzyme that breaks down alcohol, that alcohol dehydrogenase, has such a strong affinity for ethanol that it gets completely bound up, like all of the ADH, the alcohol dehydrogenase, gets completely saturated with ethanol even at really low concentrations so it's working at its max from day one, right. But we know that tolerance exists and so one thing that it seems is that when alcohol use is chronic it actually serves to upregulate a different type of alcohol metabolism, so it uses a completely different set of enzymes. And this is called the microsomal ethanol-oxidizing system, this is a separate enzyme in our liver that's just basically another way that ethanol can be metabolized. Everyone does it at a low level but in some people or over time for some people, this kind of gets upregulated as a bigger chunk of how much alcohol is metabolized, if that makes sense.

Erin Welsh

Yeah.

Erin Allmann Updyke

And what's really interesting is that along those lines there's actually a lot of genetic variation in alcohol metabolism.

Erin Welsh

Yeah, right.

Erin Allmann Updyke

So there are certain alleles, certain genetic changes that have been identified that result essentially in an increase in that same system that gets upregulated with chronic use. And so this means that some people just genetically are much faster metabolizers of alcohol which is so fascinating.

Erin Welsh

It is interesting. And then there's the flip side of that.

Erin Allmann Updyke

And then on the flip side there's other genetic variants not in alcohol dehydrogenase but in aldehyde dehydrogenase, ALDH, that downstream metabolism and it makes that super slow. What that leads to is a buildup not of alcohol but of acetaldehyde, the toxic intermediate.

Erin Welsh

Yeah, it's not good.

Erin Allmann Updyke

It's really not good. So that's why for some people they have like one single drink and they end up flushed, nauseous, feeling terrible, just bodily feeling awful without even any of the cognitive effects that we attribute to drunkenness. It's like going straight to a hangover.

Erin Welsh: Right.

Erin Allmann Updyke: So there's a lot of genetic and also just individual variation in how people metabolize alcohol. Pretty cool, right?

Erin Welsh: It's interesting and I'm gonna talk a little bit more about it in the history section.

Erin Allmann Updyke: Oh good, I can't wait.

Erin Welsh: Yeah.

Erin Allmann Updyke: So do you have any questions, Erin?

Erin Welsh: I mean so I guess I have lots of questions.

Erin Allmann Updyke: Okay.

Erin Welsh: One has to do with sort of how either the role of genetics or the way that we metabolize alcohol, how that plays a role in addiction. And the other thing is also about alcohol and people who are not yet adults, whether that means exposure while a fetus or exposure while you're young, what are the effects of alcohol on you?

Erin Allmann Updyke: Oh, great questions. So I don't have a good answer to your first question about sort of genetic variation in sort of susceptibility to alcohol addiction.

Erin Welsh: Okay.

Erin Allmann Updyke: That would be a really interesting topic that I just didn't have time to research with all of the other things. But yeah, I feel like the genetics of addiction are really, really fascinating in general. And there is a very strong genetic component to alcohol use disorder but to my knowledge at least from what I found, I didn't see any specific genes that are necessarily related to it, like individual genes.

Erin Welsh: Okay, gotcha.

Erin Allmann Updyke: So it's a lot of probably G by E, gene by environment interactions that seem to affect it.

Erin Welsh: Right, of course.

Erin Allmann Updyke

In terms of the effects of alcohol on the young, certainly anything that affects your central nervous system is going to have more drastic effects on people that are younger. Alcohol crosses the placenta freely the same way that it crosses our blood-brain barrier. So it's able to reach a developing fetus and to reach that fetus' central nervous system. We have very, very good data of the effects of moderate to high levels of alcohol use on the fetus which produces a syndrome known as fetal alcohol syndrome which is a real constellation of a lot of different potential problems ranging from mild cognitive deficits all the way up to more severe or even spontaneous pregnancy loss type complications. I think the thing that's important to point out is that while we have very, very clear data of the harms that can come from drinking moderate to heavy amounts of alcohol during pregnancy, obviously all of these studies are very difficult to do in humans for so many different reasons and a lot of them are sort of epidemiological studies that are rife with things like recall bias, etc.

But in general the kind of consensus among public health agencies is that there is no evidence of a safe level of alcohol consumption during pregnancy. There was a study that came out in 2017 that suggested - and it got a lot of press at the time - that less than 32 grams a week which is two alcoholic drinks, like two glasses of wine a week or something, there was only a modest risk of premature birth and small for gestational age babies. Both of those can carry serious downstream health problems and I'm not sure how long that study actually followed those babies after birth. But other studies have also shown things like an increased risk of spontaneous pregnancy loss but most of those were with 5 or more drinks per week. So we don't have a lot of good data for smaller amounts of alcohol but in general the public health agencies both here in the US and across the world take the stance of no level is known to be safe.

Erin Welsh

I mean that's also sort of the same stance for just alcohol consumption generally, right? I mean I feel like every other week there's this study that's like, 'Oh a glass of red wine, oh no a beer, oh no it actually you have to do this very particular recipe.'

Erin Allmann Updyke

Yeah. It's interesting because if you look at sort of all cause mortality and especially cardiac mortality, there is a kind of J-shaped curve where it seems like 1-2 drinks a week might be a little bit protective in epidemiological studies against cardiac mortality. I think that in general a lot of the public health thought is that there are so many known risks to alcohol that the maybe small evidence that there could be a maybe benefit to cardiac mortality is probably outweighed by all of the other risks if that makes sense.

Erin Welsh

Yeah.

Erin Allmann Updyke

So there's not like super strong data. I don't think in general it's something that is recommended as a thing to keep you healthy by any means.

Erin Welsh

Right, right. That makes sense.

Erin Allmann Updyke

Yeah. But so that's pretty much the biology of alcohol, Erin. It's a lot.

Erin Welsh

I have one more question and it has to do with hangover.

Erin Allmann Updyke

Gotcha, okay.

Erin Welsh

And so if we know what causes hangovers, how do you replenish cofactors besides just time?

Erin Allmann Updyke

Time, Erin.

Erin Welsh: Yeah.

Erin Allmann Updyke: Did you read the paper... I found a paper that was just 18 pages of hangover cures.

Erin Welsh: No.

Erin Allmann Updyke: Oh my gosh.

Erin Welsh: I have nothing about hangovers in my history section.

Erin Allmann Updyke: Okay well I will post a paper that's like 18 or more pages of just old-timey hangover cures, it's amazing.

Erin Welsh: Oh my gosh.

Erin Allmann Updyke: You would love it.

Erin Welsh: Ugh, can't believe I didn't see that.

Erin Allmann Updyke: Yeah, none of them are real. To actually treat a hangover sleep is important because alcohol messes with your sleep cycles and so even if you pass out you're not getting quality sleep.

Erin Welsh: Right.

Erin Allmann Updyke: So sleep is important. Drinking lots of water because you're dehydrated, eating food because you know you're hypoglycemic, ibuprofen or other medicines that are inhibitors of prostaglandin synthesis tend to have at least a modicum of evidence that they're maybe a little bit helpful.

Erin Welsh: Like ibuprofen specifically, not acetaminophen, right.

Erin Allmann Updyke: Right, so acetaminophen is Tylenol which is yeah, going to go to your liver so you don't take that while you're drinking please. Don't take ibuprofen while you're drinking either, I'm talking about the next day.

Erin Welsh: Yeah, yeah, yeah.

Erin Allmann Updyke: There's also some thought that B vitamins, since those are cofactors for a lot of different forms of metabolism, if you replenish those levels maybe. But yeah, none of those have actual data, it's really just time. And also hair of the dog does not work.

Erin Welsh: No it does not work.

Erin Allmann Updyke: Yeah. Okay, is that it? You have more questions?

Erin Welsh: I think that's it for now.

Erin Allmann Updyke: That was a lot, it was pretty long, sorry. So can you tell me how long have we had a hangover collectively?

Erin Welsh	Oh boy. I can't wait, I will get started right after this break.
TPWKY	(transition theme)
Erin Welsh	Okay. The history of alcohol.
Erin Allmann Updyke	Yes, all of it!
Erin Welsh	Simple enough, right? And I'm going to try to not do the thing that we always do which is apologize in advance for not including every tiny piece of information about the topic we're covering even though I'm like right now I'm actively resisting the urge to apologize.
Erin Allmann Updyke	I know, I do it every time, Erin.
Erin Welsh	I know, it's really hard not to. And everyone knows the drill anyway, right. Like we're not experts and this is not a comprehensive audio textbook on alcohol, it would be very challenging to do that and it would require a whole team of people, not just two people.
Erin Allmann Updyke	Yeah. Two humans.
Erin Welsh	Instead I'm going to tell you what I am going to cover and hope that we all have fun along the way even if I miss some things here and there. And if you're left wanting more, that's great because curiosity is the best and you can check out further reading for the topic on our website post for the episode where we include all our sources and also there is no shortage of books about alcohol as specific as the history of bourbon in this one county and as broad as the global history of alcohol. So there's anything you want. Okay. So what am I going to cover about the history of alcohol? Basically the way that I set this up is to first talk a bit about the evolutionary origins of alcohol metabolism or ethanol metabolism. So when did humans and other animals evolve this ability and how much does it vary across species? And then just kind of play the hits in the history of intentional alcohol production by humans starting all the way back at the beginning thousands of years ago and ending at today or at least the last few decades or so because yeah. There's a lot there. Let's get started.
Erin Allmann Updyke	Yeah.
Erin Welsh	Erin, you answered how humans can metabolize ethanol and what it does to us and all that good and bad stuff. But I wanna get at the why of this. Why we possess this ability, where did it come from and when did it come from under what circumstances. And then I might dabble a bit in another 'why', like why we get drunk. What are the benefits and drawbacks of alcohol consumption from an evolutionary perspective? Do the pros outweigh the cons? But first things first, many, many organisms possess the ability to metabolize ethanol but humans are somewhat unique in that we possess a particular form of that alcohol dehydrogenase gene and it's specifically for if you're interested the alcohol dehydrogenase 4 enzyme. And this form, this mutated form allows us to metabolize alcohol much more efficiently than most other animals, like 40 times for efficiently as compared to the non-mutated version.
Erin Allmann Updyke	Whoa. I did not know it was that big of a difference.

Erin Welsh

Yeah, it's really big. And I say somewhat unique because we aren't the only animals to have this mutation. Chimpanzees, bonobos, and gorillas also have the same type of mutation at the same spot in the gene for ADH4, alcohol dehydrogenase. From this point on I'm just gonna call it alcohol dehydrogenase and acknowledge freely that it is just one of the enzymes, okay, not all of them. But there are other animals that also have the same type of mutation at that same spot and that is the large fruit bat, the common vampire bat, aye-eyes, and koalas.

Erin Allmann Updyke

What? That's such a random assortment.

Erin Welsh

Well or is it?

Erin Allmann Updyke

Oh!

Erin Welsh

(laughs) And then there are a couple other animals, a couple other species of bats that also have a mutation in that gene but not the same exact kind. So we also don't really know beyond chimpanzees, bonobos, gorillas, we're not really sure physiologically vampire bats, the large fruit bat, aye-eyes, koalas, they have different gastrointestinal systems compared to great apes, right. And so whether the function of that mutated alcohol dehydrogenase is the same in those as it is in these great apes, we don't know for sure but there's also some hints that it might be at least somewhat similar. Okay. Basically there's a lot that we don't know about alcohol metabolism in other species but what is the whole point of this section? Okay, it's one thing for a mutation to occur, like it happens all the time, but it's another for it to stick around. In order for that to happen it has to be a useful mutation generally speaking. It could just be drift, whatever. But it turns out that this mutation in the gene for alcohol dehydrogenase appeared in the ancestor of humans, chimpanzees, and gorillas about 10 million years ago. So that's when this mutation, this new enhanced form first appeared.

Erin Allmann Updyke

Okay.

Erin Welsh

And that's right around the same time that our primate ancestor started venturing down onto the ground from the trees, becoming more terrestrial than arboreal. On the ground they would have found a great food source, fallen and fermenting fruit.

Erin Allmann Updyke

That's right, that's right. Okay, yeah.

Erin Welsh

And some of this fruit would have contained ethanol concentrations as high as 8.1%.

Erin Allmann Updyke

Wow!

Erin Welsh

This new mutation which helps us metabolize ethanol more efficiently, it would have been a big advantage in utilizing this new food source and also not getting too impaired by it and getting picked off by predators or your neighbors. So it makes sense that it was retained and then spread throughout subsequent generations, all the way down to modern humans. The other animals that had this mutation, chimpanzees, bonobos, gorillas, aye-eyes, etc, these are animals also known to forage extensively on fruit and nectar which may also be fermented and may also contain ethanol. So it seems as though diet plays a big role in the evolution of these genes for the metabolism of ethanol, why we can process it more efficiently and why some animals have actually lost the ability altogether. So there's a recent study from 2020 by Janiak et al that showed that the gene for ADH4, for this alcohol dehydrogenase 4 enzyme is nonfunctional in some animal species meaning that it was once there and it once worked.

Erin Allmann Updyke

Right.

Erin Welsh

And that it accumulated at least one mutation that would have made it stop working.

Erin Allmann Updyke

Yeah, interesting.

Erin Welsh

And it turns out that there's a pattern among these animals with the nonworking alcohol dehydrogenase, they don't really had nectar or fruit in their diets and so it wouldn't have been that important to keep that functional gene, so relax selection and boom, some of them just lost it. Okay. So I feel like I've already gotten a bit into the weeds here but I wanted to bring this up because I think it's an absolutely fascinating look not just at the evolutionary origins of the way humans metabolize dietary ethanol but also why this ability might vary across the animal kingdom. Like what are you eating and how is that affecting your physiology and the way you metabolize certain compounds?

And I also should end this part with a caveat that is this is just looking at one enzyme for dietary ethanol metabolism. Granted it is the first enzyme that would encounter ethanol after it's consumed cause it's the one that's the first part of your gastrointestinal tract and whatever. And that there are many other enzymes involved that are part of this process and that metabolize other forms of alcohol as well such as some that would be encountered by consuming certain plant leaves for example. All right. So we've now established the likely origin story of our enhanced ability to metabolize alcohol and to some degree why it gave us an evolutionary advantage because it allowed us to use a new food source. Fermentation can actually increase the nutritional value of things, make it more bioavailable I guess.

Erin Allmann Updyke

Yeah, so drink you kombucha, that's what you're trying to say?

Erin Welsh

Uh-huh. (laughs) And also don't forget that it can decrease the prevalence of harmful pathogens and parasites.

Erin Allmann Updyke

Yeah, that's pretty major.

Erin Welsh

It's pretty major. And that's something that became especially more important later on. The importance of dietary ethanol to humans and other primates is also maybe illustrated by just how sensitive we are to the smell of it, a smell that signaled to our evolutionary ancestors, 'Hey, here's some ripe fruit to eat, here's some good food here.'

Erin Allmann Updyke

Interesting.

Erin Welsh

It's interesting to think about what we're more sensitive to in terms of smell, in terms of taste.

Erin Allmann Updyke

Yeah.

Erin Welsh

All of these things might have roots.

Erin Allmann Updyke

Yeah.

Erin Welsh

And let's also not forget that we're sensitive to the effects that it has on our bodies, it makes us drunk, it makes us feel good.

Erin Allmann Updyke

Yeah.

Erin Welsh

It triggers these reward systems in our brains that evolved to encourage adaptive behavior. Like, 'Hey, dietary ethanol is a good food source, keep seeking it out'. And this hijacking of our reward systems, it might have worked out great when the sources of alcohol were limited to the piles of fermenting fruit on the forest floor.

Erin Allmann Updyke

Right.

Erin Welsh

But then once humans began to actually intentionally produce alcohol, some more of the downsides began to appear.

Erin Allmann Updyke

Right.

Erin Welsh

And there still seems to be some debate on when this was, like when humans began to first intentionally produce alcohol. It's like this question of chicken or egg but instead of chicken or egg it's what came first, beer or bread? Did humans begin to settle in large groups and domesticate grains, aka the Agricultural Revolution and then notice that rain-soaked grains produced a fermented alcoholic beverage? Or did they settle in large groups and domesticate grain so they could produce alcohol? Over the past few decades this second hypothesis, the beer before bread one, it's become increasingly popular. Rather than the Agricultural Revolution providing the means and locations for large gatherings for which alcohol might have been produced, those might have led to the Agricultural Revolution. So people started to settle because of the large gatherings rather than being able to settle because of agriculture.

Erin Allmann Updyke

They started to get together, hang out more in groups, eat fermented fruit and be like, 'We should be able to make more of this, why don't we try and do it ourselves here? Let's plant some barley.'

Erin Welsh

Yeah.

Erin Allmann Updyke

What?

Erin Welsh

Yeah. There is some support from archeological evidence such as what we see as Göbekli Tepe, a super old, like 11,000 years old archeological site in what's now Turkey.

Erin Allmann Updyke

Whoa.

Erin Welsh

It's really cool, you should definitely read more about it, I am fascinated by it. And at this site which was constructed at the very beginning of the Agricultural Revolution there's evidence of big fermentation vats and storage basins used to brew beer. And that's not that surprising except for the fact that some archeologists believe that this was not a continually occupied site but more of a site that groups of nomadic hunter-gatherers would congregate at during certain times, so it was sort of a meeting place.

Erin Allmann Updyke

Oh yeah. Interesting.

Erin Welsh

I will say that more recently the supposed transient use of this site has been called into question and some people are saying well maybe it was continually occupied.

Erin Allmann Updyke

Okay. All right.

Erin Welsh

But there's still more. In the Fertile Crescent some of the earliest archeological sites show tools and grains that are more in line with beer-making than bread-making.

Erin Allmann Updyke Okay.

Erin Welsh Personally, this is my opinion, I feel like it doesn't necessarily have to be one then the other.

Erin Allmann Updyke Right.

Erin Welsh Why can't humans have begun to settle in large groups and domesticate grains for both beer and bread?

Erin Allmann Updyke Right and also what do you do with the grains when you're done fermenting them? You make bread. So you do both.

Erin Welsh You do both.

Erin Allmann Updyke Waste not, want not Erin.

Erin Welsh Exactly. But anyway the point that I'm trying to make here is that humans around the globe have been intentionally making alcohol for a very long time.

Erin Allmann Updyke Yeah.

Erin Welsh They saw this, they tasted it, they recognized it and said, 'I want to be able to have this all the time.' And to underline that, here are some examples.

Erin Allmann Updyke Yes.

Erin Welsh There's a 20,000 year old carving from southwest France that shows a woman, possibly a fertility goddess, drinking out of a horn. Maybe it's been speculated that it was some fermented beverage.

Erin Allmann Updyke Maybe.

Erin Welsh It's thought that some strains of yeast associated with wine and sake production might have been domesticated over 12,000 years ago.

Erin Allmann Updyke Whoa.

Erin Welsh Which is really cool.

Erin Allmann Updyke Yeast domestication now.

Erin Welsh I know.

Erin Allmann Updyke Let me say, wow.

Erin Welsh: Oh yeah. The oldest physical evidence of an alcoholic beverage comes from the Yellow River Valley of China from around 7000 BCE and it was made from wild grapes, hawthorn fruit, rice, and honey. Grapes were domesticated in what is now Georgia from around 7000-6000 BCE. In what is now Iran there's evidence of grape wines in ceramics from 5500-5000 BCE. In Armenia there's an ancient cave site that seems to have been a winery complete with grape-stomping basins, presses, fermentation bats, storage jars, drinking vessels. The oldest surviving recipes is a recipe for beer from 3400 BCE.

Erin Allmann Updyke: Fascinating, Erin.

Erin Welsh: The oldest preserved liquid alcohol was found in China and dates back to 1900 BCE. And there are references to alcohol in our oldest surviving literary document, the Epic of Gilgamesh from 1800 BCE and in our oldest law document, Hammurabi's Code from 1770 BCE which regulated the strength and price of beer and forbade women from drinking it.

Erin Allmann Updyke: Okay, a lot of whoas on that.

Erin Welsh: Yeah. (laughs)

Erin Allmann Updyke: Also we're going way back further than the Ebers Papyrus, is that what you're telling me here?

Erin Welsh: Oh yeah. I'm sure that it's in the Ebers Papyrus, shame on me for not finding it explicitly.

Erin Allmann Updyke: (laughs) Wow.

Erin Welsh: Yeah, I mean the evidence for early and thoughtful production and consumption of alcohol is vast and varied as are the ingredients used in fermentation.

Erin Allmann Updyke: It's so interesting to me that you brought up grapes so early. People were like, 'Hey grapes, grapes make really good alcohol' from like day one? That's so interesting.

Erin Welsh: I know. It's really interesting and I don't know much about the domestication process of grapes but grapes were just one of many ingredients that people use and I'll definitely go into some more of these or at least a list of examples of things that people used later on.

Erin Allmann Updyke: Yes, my favorite.

Erin Welsh: Okay. So now we're in the Agricultural Revolution, we're there.

Erin Allmann Updyke: Okay.

Erin Welsh: I'm taking us there.

Erin Allmann Updyke: All right.

Erin Welsh: And so with this period time of huge change, alcohol took on many other important roles, not just as a food source but also as a medicine or a good to trade, as a component of religious ritual or celebration. Dionysus, Jesus, there were many gods or religious figures associated with certain alcoholic beverages, wine in particular.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

But the availability of alcohol in large quantities also revealed of course its dark side. In many ways these structured rituals or ceremonies at which alcohol was consumed helped to regulate consumption, like they created these boundaries between what was acceptable drinking and what was too much. They weren't free for alls, it was very you wanna be respectful of the gods, you want to commune with them in a way that is the right way. Drinking too much was seen to have negative health consequences, to lead to alcohol dependence, to lead to accidents, and at the very least lead to negative social interactions.

For about as long as humans have been making alcohol intentionally, we have also been issuing proclamations against it. The most famous is probably of course the prohibition of alcohol in Islam which began in the 7th century CE. But even before then China attempted to ban alcohol in the 2nd century BCE and it wasn't necessarily all or nothing. Like in many places alcohol consumption in moderation was fine but excessive drinking was looked down upon. For example there's an inscription on a stadium in Ancient Greece that forbids spectators from bringing wine into the arena which cracks me up cause that is still on every stadium, every concert hall, every whatever.

Erin Allmann Updyke

It is, yeah. You can't bring your own. Oh my goodness.

Erin Welsh

Yep.

Erin Allmann Updyke

That is so funny.

Erin Welsh

Yeah I wonder if they sold it for like \$15 for like 3 oz of wine.

Erin Allmann Updyke

Of course they sold it. Oh my goodness.

Erin Welsh

Humans have long recognized the cost of alcohol consumption even if we've been able to quantify it or understand the nuances of it only more recently. And the costs are substantial. Erin, you went over a lot of them both in the short term and the long term and like you said, most public health officials or groups will conclude that there is no real safe level of alcohol, no tablespoon amount of red wine that's gonna make us live longer.

Erin Allmann Updyke

Right.

Erin Welsh

So that begs the question maybe why do we drink it? And maybe not that so much as why haven't we evolved to dislike it, to undo that pleasure center hijacking? And we kind of have actually. So Erin, you talked a little bit about ALDH, aldehyde dehydrogenase that causes this buildup, these immediate negative effects of a hangover immediately, this buildup of acetaldehyde with these symptoms of facial flushing, hives, nausea, heart palpitations, difficulty breathing, etc etc. Basically it make drinking alcohol extremely unpleasant.

Erin Allmann Updyke

Right.

Erin Welsh

Some people speculate that this mutation which evolved independently in parts of East Asia, the Middle East, and Europe may have evolved in response to the increase in alcohol consumption as a way of curbing the negative effects of alcohol. So looking at one of the evolution events, it originated between 7000-10,000 years ago in East Asia which is around the time that rice-based agriculture was spreading and thus the availability of rice wine. So is this a defense mechanism against drinking too much? It's not clear.

Erin Allmann Updyke

Yeah.

Erin Welsh

If it is, we might expect it to be more widespread than it is if it confers such a strong selective advantage.

Erin Allmann Updyke

Yeah.

Erin Welsh

And other researchers think that it might protect against fungal poisoning and the alcohol is just a side effect of that.

Erin Allmann Updyke

Side effect.

Erin Welsh

Yeah, especially the fungal strains that would have affected stored grains. Or it might protect against tuberculosis. I don't know. But I think the other thing to consider is how we're looking at this equation of the pros and cons of alcohol consumption. In the ancestors of humans the advantages were clear, like I've gone over them right. But did the ability to metabolize alcohol outlive its usefulness? Was it all just backfiring and hijacking after the Agricultural Revolution? The author of one of the books I read for this episode says no, that while there are clear disadvantages to the consumption of alcohol in an evolutionary sense, there are also reasons why it would have been selectively advantageous even after or during the Agricultural Revolution. For a long time, probably at least since humans have been settling in large groups, the primary adaptive challenge that humans have faced is not the environment and overcoming the environment but it's other humans.

Erin Allmann Updyke

Right. It's everything we talk about in this podcast.

Erin Welsh

Uh-huh. And from a more social standpoint, humans don't just need food, shelter, and water to survive, we've evolved to exist in groups where social cooperation, creativity, and tolerance and trust of non-relatives is necessary. The author of this book suggests that alcohol in moderation can help with those things. Quote: "By enhancing creativity, dampening stress, facilitating social contact, enhancing trust and bonding, forging group identity, and reinforcing social rules and hierarchy, intoxicants have played a crucial role in allowing hunting and gathering humans to enter into the hive life of agricultural villages, towns and cities."

Erin Allmann Updyke

It does make you more sociable.

Erin Welsh

It does. So I bring this up not because I necessarily agree or disagree with it but I think it's interesting food for thought or beer for thought. But I also think it shows that it's important to consider how the pros and cons equation of alcohol is specific to a time and place and even to an individual when you're talking about it. Or I also have to say maybe it's not as complicated as all that. This book had a very adaptationist perspective on the consumption of alcohol where there has to be some evolutionary reason for it, some way it increased our ability to survive and reproduced just beyond the fact that we like the way we feel when we drink it.

Erin Allmann Updyke

Yeah.

Erin Welsh

Maybe as my younger sister would say, it's not that deep.

Erin Allmann Updyke

(laughs) Yeah.

Erin Welsh

Maybe the reason humans drink alcohol is just because we like it, right, and that's reason enough for it to persisted for so, so long.

Erin Allmann Updyke

Definitely.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. It makes you feel good, literally.

Erin Welsh

Yeah, exactly. Okay. Evolution talk over. Do you wanna hear a very general history of alcohol?

Erin Allmann Updyke

Always.

Erin Welsh

Okay. Where did I leave off? So I've already covered some of the archeological and historical evidence of early alcohol consumption and production around the world and I think that it shows not only how important alcohol was to many cultures but also how creative humans are at coming up with new ways to make it. For instance in the Orkney Islands people included oats and barley with some additional flavors and maybe a light hallucinogen or two to make a kind of beer.

Erin Allmann Updyke

Spice it up.

Erin Welsh

In Tasmania, sap from a gum tree was fermented and what is now Victoria and Southeast Australia people mixed flowers, honey, and gum into a liquor. In parts of Africa people made banana beer and palm wine which was also made in parts of South Asia. In Mexico people made pulque from the fermented sap of the agave plant and in Southeast Asia people made pie from fermented cassava. And of course there was wine and beer and mead made in many, many different places. Much of the very early history of alcohol is a bit like guesswork but starting around 3000 BCE and on is when our knowledge gets a bit more refined. And this is when we see the spread of technology for alcohol production along trade and exploration routes.

Wine-making knowledge and technology for instance seems to have originated in western Asia like modern day eastern Turkey, eastern Iraq, northwestern Iran, and then was brought to the eastern Mediterranean and Egypt and then onto Crete, Greece, and southern Italy before arriving to the rest of Europe around 2000 years ago, helped along after that point very much by the spread of Christianity which directly led to the spread of wine-making technology throughout the western Roman Empire. Beer production on the other hand seems to have begun simultaneously in many different places such as Egypt and Scotland. In Ancient Egypt wine-making technology seems to have been well integrated into the culture with production seriously ramped up. In 1000 BCE there's a list of 513 vineyards owned by temples mostly in the Nile Delta.

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah, it's like full on production scale type stuff.

Erin Allmann Updyke

Yeah, wow.

Erin Welsh

And there are other writings from Ancient Egypt showing that beer was a common form of payment especially for the lower classes. And from the beginning there seems to have been in many wine and beer-drinking cultures a class structure to these drinks. The wealthy and elite drank wine, the poor drank beer, and the poorest drank water. The inherent greater value placed on wine does make sense in some ways, there was a shorter growing season, it couldn't be produced in the same quantities as beer, and it kept better than beer which was important in long distance trading. And these qualities led wine to be scarcer and thus more valuable than beer which is one of the reasons why wine was included in rituals and ceremonies more often than beer and why it was written about, like we have more ancient writings it seems like or references to wines than we do with beer.

Erin Allmann Updyke

That makes a lot of sense actually.

Erin Welsh

Yeah. And it also led to a class division between these drinks, one that we'll see time and time again throughout history. Beer was cheap, it was consumed by everyone but wine was consumed only by those who could afford it. This attitude carried over into Ancient Greece and Rome where the climate was more suitable for grape growing and beer was seen as the drink of barbarians coming from those northern Germanic tribes, they couldn't grow wine up there so they were clearly not cultured.

Erin Allmann Updyke

Goodness.

Erin Welsh

Yeah. Wine production turned into a full-on industry in Greece, even more so than it was in Egypt. And by 400-300 BCE it took its place alongside olive oil and grain as one of the big three products of economy and commerce in the Mediterranean. In addition to transporting enormous quantities of wine in amphoras, and I mean enormous - so there's one shipwreck I read about that contains 10,000 amphoras which is about 300,000 liters of wine.

Erin Allmann Updyke

Whoa.

Erin Welsh

Yeah, or about 400,000 modern wine bottles.

Erin Allmann Updyke

Whoa.

Erin Welsh

Yeah. And Ancient Greece also had symposia where wine was consumed in moderation with strict rules. The word 'symposium' actually means 'fellow drinker' or 'drinking together'.

Erin Allmann Updyke

I didn't know that.

Erin Welsh

Yeah. And it was first used for these wine parties attended by upper and middle class men from which women were excluded except to serve. And boy does this echo throughout history.

Erin Allmann Updyke

Ugh, I bet.

Erin Welsh

In many cultures throughout history there are laws that deal in some way with restricting women from drinking alcohol, usually on the grounds that women who drink alcohol will commit adultery or be sexually promiscuous or whatever. In Ancient Rome there was a law that allowed a man to divorce his wife if she had been drinking and alcohol consumption by women could also be punishable by death which is what happened to one woman, death via starvation in her case, who had been caught not drinking but just caught with the keys to the wine cellar.

Erin Allmann Updyke

Oh my goodness gracious.

Erin Welsh

In the early Middle Ages in Europe, women in a household were the ones doing the brewing primarily, it's why you heard the term alewives or brewsters and so it would be beer made at each house, right, each household had their beer. But this changed starting in the 1400s when women were essentially excluded from making beer as beer began to be made in commercial production facilities rather than in individual households as cities grew.

Erin Allmann Updyke

Right, once it became a job rather than a household job.

Erin Welsh

A chore, right.

Erin Allmann Updyke

Yeah.

Erin Welsh

Commercial brewing was regulated and required licenses which women were forbidden from applying for and this also marked the start of taverns. The first tavern license in London was actually in 1189 which just is like really old.

Erin Allmann Updyke

Whoa. Yeah.

Erin Welsh

But also women were forbidden from entering taverns as well for the most part.

Erin Allmann Updyke

Okay.

Erin Welsh

And these shifts to exclude women from beer production, they weren't just accidents of history like a natural consequence but intentional misogynistic exclusion which is pretty easily seen in the depictions from this time showing women brewers as dishonest and unhygienic and women who drank in taverns as immoral.

Erin Allmann Updyke

Of course.

Erin Welsh

And this whole thing gets repeated again in Europe in the 1500s or so when distillation began to be widespread with women starting small scale distilleries and then being shoved aside because they were forbidden to have licenses. But that's getting a bit ahead of things. The Middle Ages in Europe led to an increase in beer and wine-making technology, a shift towards commercial production of these alcoholic beverages, and a big growth in long distance trade as the preservation of wine and beer improved for example through the addition of hops to ale. All of these things marked a shift where alcohol had moved beyond just being something reserved for rituals and the huge spread of Christianity had certainly cemented wine as a sacred part of ritual by this point, or for just personal household consumption.

Alcohol at this point was now a key part of the economy. Alcohol production and consumption began to be taxed and those taxes funded many a government and the growth of cities and trade also led to a larger consumer market where variety was demanded. People wanted to choose what they drank, what vintage, from what region, and some places began to specialize in this, they began to be known for their wine or beer. And then distilled spirits entered the picture.

Erin Allmann Updyke

I'm excited for this.

Erin Welsh

Distillation is a fairly old concept with fairly old technology. Experimental distillation was practiced in Ancient China, India, Egypt, Mesopotamia, and Greece with the technology most probably originating in the area around the border between modern Pakistan and India. But it wasn't really until the 13th century in China and the 16th through the 18th centuries in Europe that it became widespread. Brandy distilled from wine was the first spirit produced in large quantities in Europe and there was whiskey, gin, vodka, and others that followed. Production of distilled spirits became especially popular in places where the climate had prohibited growing grapes for wine.

So for instance vodka, meaning 'little water', was developed in northeastern Europe in what is now parts of Russia, Poland, Belarus, and Ukraine. Rum on the other hand which was not the first liquor made from sugar cane, there were earlier ones in China and India, rum was made in the sugar plantations in British and French colonies in the Caribbean by distilling molasses which had increased in availability due to the huge numbers of people they were enslaving. This rum would then be used in trade and this is where distilled spirits absolutely were far superior to wine or beer for long distance travel.

Erin Allmann Updyke

Right.

Erin Welsh

And rum would also be added to water barrels on boats with each member of the crew getting a ration of rum which is sort of how sailors and pirates around this time came to be so associated with the drink. And contrary to popular belief, the puritans drank their fair share of alcohol. Mostly I bring this up because I wanted to include these numbers as just a visualization of how much alcohol people brought with them on journeys.

Erin Allmann Updyke

Okay.

Erin Welsh

On the puritan ship Arbella which carried around 700 people from England to Massachusetts in 1630, there were 10,000 gallons of wine, 42 tons of beer, 14 tons of water, and 12 gallons of brandy.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

Yeah. (laughs) Yes. The introduction of distilled liquors was kind of huge and it really changed the way people interacted with alcohol. Historically beer and wine averaged maybe 2-4% or 6-12% respectively, it's actually much more alcoholic nowadays, like your standard beer or wine is more alcoholic than it used to be. But distilled spirits, they can be incredibly alcoholic, right.

Erin Allmann Updyke

Right.

Erin Welsh

I mean I would say the range was typically 20%-100%, just pure ethanol.

Erin Allmann Updyke

Yeah.

Erin Welsh

And this was an amount of ethanol in any distilled spirit far beyond what our primate ancestors had ever encountered.

Erin Allmann Updyke

Oh my goodness, yeah.

Erin Welsh

And some people used that to their advantage. The role of alcohol in colonialism is obviously deserving of much more attention than I can give it here but I do wanna mention some of the ways that European colonizers used alcohol to subjugate and control the people whose lands they invaded. Generally speaking most of the places that Europeans sought out to colonize already had a relationship with alcohol. Alcohol like I said had almost a global distribution at this point with one notable exception in North America where fermented beverages were less common although not entirely absent and rituals did not typically include alcohol but that's painting with a very broad brush and there are exceptions to that.

But when Europeans invaded those places whether they had a relationship with alcohol or not, they didn't drink the local fare but rather they just drank the alcohol that they brought with them, wine, beer, spirits. And when they set up permanent settlements there they often planted vineyards or build breweries to make beer and wine for trade, for religious ceremonies because most colonizers practiced Christianity, and to just drink themselves. But it wasn't drink and let drink, it was let's ban all of the local drinks because they weren't mentioned in the bible. Oh that didn't work? Okay, well let's just tax only those drinks instead.

Colonizers also used alcohol as a currency or as payment for workers with the intention of dulling the impact of horrific working and living conditions and keeping them in a state of subordination. It was a weapon, alcohol was a weapon, a tool of colonization. In North America colonizers created and spread the stereotype of the quote "drunken Indian" which was used to exclude and undermine Native Americans from any discussions of government policies or treaties that affected them and was then used as justification to prohibit the sale of alcohol and guns to Native Americans 28 years before the 1920 legislation that led to the US-wide alcohol prohibition. And this specific prohibition wasn't repealed until 1953 which is 20 years after nationwide prohibition ended.

Erin Allmann Updyke

I'm sorry.

Erin Welsh

Yeah. And similar things just like that happened in Canada but with slightly different timeframes. Which brings me to the last part of the history of alcohol I'm going to cover also not in any great detail: prohibition.

Erin Allmann Updyke

Yes!

Erin Welsh

Specifically prohibition in the US. So don't get too excited, there's not that much detail, I'm so sorry. Like I mentioned a long time ago in this episode, people have been trying to ban or limit the use of alcohol for about as long as we've been making it with some bans or restrictions more effective than others. And I'm going to focus primarily on the trend towards prohibition that began in the late 1700s, early 1800s and then culminated in the early 20th century in places like the US, Russia, Mexico, Canada, Belgium, Japan, and Finland among others. It was surprisingly widespread, more than I had realized. Starting around this time, starting in the late 1700s, morality around alcohol began to change possibly due to the increasing availability of safe drinking alternatives such as tea or coffee, see our caffeine episode, and also the growth of distilled spirits which was seen by many as a negative consequence or a negative thing.

The gin craze in parts of England which is a thing that happened took place between 1700 and 1750, this may have had something to do with it but many accounts are super exaggerated and probably just an example of moral panic. But essentially what happened was that gin, by gin I mean all grain-based alcohol not just juniper flavored, it increased in popularity in England from around 1700-1750 following a brandy shortage and this led to people saying that women were unable to resist the call of gin and that they were leading their unborn children to be addicted. It was a lot of, 'Oh gin is disrupting family life and the father has to care for the children, crime and immorality are on the rise,' etc etc. Overall the gin craze seems to be more of a class and gender war which is not that surprising considering how drinking had long been portrayed, right.

If you were poor it was a criminal issue, if you were rich it was a moral failing. But don't worry, all is forgiven, tomorrow is a new day. These class distinctions around drinking and moral panic about alcohol consumption by women sort of fed into each other especially as industrialization meant denser populations in cities and a larger working class, both of which alarmed the wealthier classes who wanted to shut down the bars and taverns and public houses that were frequented by the working class which the wealthier classes saw as the breeding grounds for criminality, especially the consumption of distilled spirits playing this big scary role. And the consumption of distilled spirits did massively increase, like I said it changed the relationship between humans and alcohol. So over the 1800s for example in Paris, although this trend is repeated in many other places, per capita consumption of pure alcohol from spirits rose from 2.9 liters in the early 1800s to 5.1 liters in the 1840s to 9.1 liters in the late 1800s. So that's like if you just take what they were drinking and then calculated the pure alcohol concentration of it.

Erin Allmann Updyke

Okay.

Erin Welsh

With the introduction of distilled spirits there was a lot of like, 'Okay this is scary, there's too much drinking but alcohol is here, it's been such a part of our lives, maybe drink in moderation.' And that was sort of the temperance movement, that's what it started out as, just drink in moderation and try not to over consume. This gained a lot of traction in the second half of the 1800s with a push to replace alcohol with tea or coffee or hot chocolate or water and then starting in the early 1900s it turned into just prohibition, no alcohol, period. Eugenists took up the cause kind of by listing alcoholism which was first used as a term in 1849 by Swedish physician Magnus Huss, they listed alcoholism as an undesirable trait that shouldn't be passed onto offspring.

Erin Allmann Updyke

Oh dear.

Erin Welsh

Always.

Erin Allmann Updyke

Yeah, I know.

Erin Welsh

Always.

Erin Allmann Updyke

Always.

Erin Welsh

There's always a tie to eugenics. And morality statistics were used to support the claims of anti-alcohol writers.

Erin Allmann Updyke

Morality statistics? Okay.

Erin Welsh

Yeah, I know. I know. A big turning point came in WWI. During that time there was a change in the gender balance of some pubs where women who were increasingly joining the workforce began to go, they began to actually frequent these bars and taverns and pubs. And this led of course to increased regulations on drinking and fewer operating hours. I read a quote in one of the books for this episode, it was something like men have always historically been anxious about the consumption of alcohol by women which I think is a very, very valid statement.

Erin Allmann Updyke

(laughs) That's so interesting.

Erin Welsh

Alcohol was viewed also during this time as weakening the soldiers and the morale of those at home. By 1916 45 US states had enacted prohibition statutes. The social cause of prohibition had been turned into a political one as politicians realized how strongly people felt about the issue, like strong enough to get them on their side to vote.

Erin Allmann Updyke

Yeah.

Erin Welsh

And on January 1, 1920 the 18th Amendment took effect which banned the production, sale, transportation, and importation of alcohol for beverage purposes. And if you wanna know more about that part of it there's a whole Ken Burns 5.5 hour documentary on prohibition in the US which I did not watch but I want to. But from the research I did it seems that the long and short of it, this period of prohibition, it didn't actually seem to slow drinking rates all that much but what it did seem to do was maybe normalize social and public drinking which had been under attack for the preceding decades as the temperance movement and prohibition movement sort of ramped up. And it also made drinking less gendered with more women attending speakeasies than they had attended bars in the years before prohibition. There was also an increase in unsafe alcohol production and consumption since there was no regulatory oversight to ensure that people weren't drinking just methanol rather than ethanol for instance.

Erin Allmann Updyke

Yeah. Big deal.

Erin Welsh

And 13 years later it was repealed by Franklin Delano Roosevelt, FDR, largely because of a need for tax revenue which grew actually incredibly, it was a big source of tax revenue in the years after. And FDR ran on a repeal platform, still a political issue back then, and he won pretty handedly probably in part because of the way people had come to see prohibition which was as an unwelcome intrusion into the private lives of US citizens. Most countries that attempted some form of prohibition or other did so in a fairly short window of time from around 1914-1933 with most never making it off the ground or ending up being repealed, showing how difficult or even impossible it is to ban any commodity or service for which there is significant consumer demand and that often regulation and education and oversight might be more helpful than anything. I don't know.

Erin Allmann Updyke

Yeah.

Erin Welsh

It feels ridiculous that I am going to try to sum up the rest of the 20th century in alcohol in like two sentences but that's just how big the history is.

Erin Allmann Updyke

Yeah.

Erin Welsh
Since prohibition our relationship with alcohol and our understanding of it has changed quite a bit. Yes, our good old friend Louis Pasteur discovered the process of fermentation in the mid 1800s which kicked off germ theory but it wasn't until the 1940s that we understood the exact mechanism of fermentation which allowed for quantification of blood alcohol content and more specific guidelines for what could be considered quote "safe consumption", minimum drinking age was instituted in some places. Attitudes towards alcohol on both individual and cultural levels became more nuanced as we gained a better handle on what it does to our bodies, to our health, to our relationships with each other. Alcohol use disorder has been increasingly part of the discussion. Alcoholics Anonymous was first founded in 1935 and the stigma surrounding not drinking for whatever reason you choose has also lessened somewhat although still kind of a long way to go there.

Erin Allmann Updyke
Yeah.

Erin Welsh
Like when someone says, 'Oh I don't drink alcohol.' And someone just goes, 'Why? Why don't you drink alcohol? Come on, have you tried it before? You should try it.'

Erin Allmann Updyke
Yeah.

Erin Welsh
Maybe don't do that. Alcohol is a complicated subject. The biology is complicated, the history is complicated, our feelings about it are complicated.

Erin Allmann Updyke
Yeah.

Erin Welsh
And I'm sure that the current status is also complicated.

Erin Allmann Updyke
Yeah.

Erin Welsh
So Erin, what's happening with alcohol today?

Erin Allmann Updyke
Ooh, let's try and find out at least. Right after this break.

TPWKY
(transition theme)

Erin Allmann Updyke
So we'll just go over, I don't know, maybe the worst of it at first and then try and end on a semi higher note. I don't know, let's see what we can do here.

Erin Welsh
Okay.

Erin Allmann Updyke
Okay. So looking first at the US, in a paper from 2019 I found that between 2006-2010, so this is kind of old data still, the annual number of alcohol-associated deaths in the United States, so this encompasses anything from things like drunk driving or accidents where alcohol is involved but also things like cirrhosis or more chronic causes of alcohol-associated death, etc. Just any kind of alcohol-associated death in the US was about 88,000 a year which represents almost 10% of all deaths in the United States.

Erin Welsh
Wow.

Erin Allmann Updyke
Yeah. That's a lot higher than I realized.

Erin Welsh
Yeah.

Erin Allmann Updyke

In 2010, and remember that costs in the US have to be taken with a grain of salt, but the estimated alcohol-related costs in the United States were almost 250 billion dollars, 77% of which were attributable to binge drinking.

Erin Welsh

Okay. Yeah we didn't really talk about binge drinking.

Erin Allmann Updyke

Yeah, we didn't. Binge drinking is very bad. If we take a broader perspective and look worldwide, worldwide according to the World Health Organization about 3 million deaths every year result from harmful use of alcohol which worldwide represents 5.3% of all deaths.

Erin Welsh

Wow.

Erin Allmann Updyke

And overall about 5.1% of the global burden of disease and injury, so the disability-adjusted life years measure is attributable to alcohol which is way more than I would ever have guessed. And what is important is that if you actually look back a little bit further there's a paper from 2004 from the World Health Organization, cause that data that I just said is from 2018, but a 2004 paper estimated that 1.5% of global deaths were attributable to alcohol and 3.5% of disability-adjusted life years were associated with alcohol. So that's a huge change.

Erin Welsh

Yeah, what's happening?

Erin Allmann Updyke

Yeah, that's a good question. I don't have the answer to that. Is it better reporting where we're getting better at identifying not just acute but also chronic causes that are associated with alcohol? Is it better awareness of the types of deaths that we might be contributing to alcohol? Or is it because alcohol use is increasing? I don't have a good answer for it quite honestly.

Erin Welsh

Interesting.

Erin Allmann Updyke

It is interesting. And so you mentioned at the end of your history section Erin, alcohol use disorder. So the DSM-5 which I think that we've talked about on this podcast before, right.

Erin Welsh

I think so, I think a long time ago.

Erin Allmann Updyke

A long time ago. The DSM-5 is in the United States the manual of psychiatric diagnoses. It encompasses very specific criteria on how to diagnose a whole number of psychiatric diagnoses including what is now called alcohol use disorder. And I won't go through the very specific criteria but essentially they all tend to revolve around things like trying to cut down on drinking and not being able to or taking in alcohol in larger amounts or over a longer time period than was intended, missing out on personal or occupational or social obligations because of alcohol use. Basically alcohol use interfering with your daily life as well as symptoms of tolerance or withdrawal symptoms which we didn't even get into in detail but withdrawal symptoms are actually really important because alcohol withdrawal, unlike withdrawal from a lot of other recreational substances, can actually be fatal in and of itself.

Erin Welsh

In what way?

Erin Allmann Updyke

So alcohol withdrawal because of its effects on the brain especially with chronic use of alcohol, the effects on the brain, sudden withdrawal can precipitate seizures which can then lead to death.

Erin Welsh

Okay.

Erin Allmann Updyke

So alcohol withdrawal is very, very serious. And we talked a little bit about this a lot earlier on but in terms of the overall risks of alcohol use disorder, since you talked so much Erin about how all humans for the most part are able to metabolize alcohol in the same way, alcohol is affecting our brains in essentially the same way, hijacking these dopamine pathways. Any human has the potential of being susceptible to an alcohol use disorder, to an addiction associated with alcohol. But we also know that there are variation in things like metabolism, there are genetic components to alcohol use disorder but again I don't know of any specific genes that would make one more or less susceptible per se that we have a lot of evidence for.

Erin Welsh

Right.

Erin Allmann Updyke

And then there are of course a lot of environmental risk factors, especially increased stressors that lead to increased risk, so things like a history of abuse of any kind, household instability, other psychiatric disorders, etc. And I think what's really depressing is that alcohol use disorder and its risk actually peaks among young adults aged 18-25. But of course any age group is also susceptible. I think too, like you said Erin, there's so much stigma surrounding alcohol, alcohol use, alcohol use disorder.

Erin Welsh

Not drinking alcohol.

Erin Allmann Updyke

Not drinking alcohol, right. It goes on so many different spectrums and I think it varies so much culture to culture as well as varying so much over time. So I was trying to find real data on the perceptions and stigma but I didn't really find data on it. But I do think that these sort of dichotomous perceptions of like is alcohol good? Rich people drink alcohol or is it what poor people do?

Erin Welsh

Is it good for you when you drink red wine or is it bad for you when you drink beer or whatever?

Erin Allmann Updyke

Or vodka or whatever.

Erin Welsh

Right.

Erin Allmann Updyke

I think that these sort of dichotomous perceptions really wax and wane over time, so I wish that we could just not stigmatize one way or the other and rather just kind of understand this drug, understand the effects that it's having on our brain and why it's making us feel the way that we feel and understand what it means if we do imbibe vs don't imbibe. I don't know. But that's just me.

Erin Welsh

Yeah. I mean I think more nuanced discussion and that's what I think is really frustrating about a lot of the headlines that you see, whether it's about a glass of red wine or coffee or whatever. It's sort of well here's the soundbite, here's the one bottom line and that is that it's going to help you. And it's way more complicated than that.

Erin Allmann Updyke

It's so much more complicated than that as usual.

Erin Welsh

As usual.

Erin Allmann Updyke

Yeah.

Erin Welsh

And it's never gonna be as simple as I don't know.

Erin Allmann Updyke Right, yeah.

Erin Welsh I feel like the increasingly persistent theme in this season is nuance.

Erin Allmann Updyke Nuance, yeah. It's gonna be our subtitle next season.

Erin Welsh Season 4: Nuance.

Erin Allmann Updyke It is though, it really is especially when it comes to alcohol, you know.

Erin Welsh Right. I found this episode challenging to research on a number of levels, one is the sheer overwhelming abundance of literature about the subject.

Erin Allmann Updyke Yeah.

Erin Welsh But the other is sort of all of the stuff that I found, there was a certain bias to it whether it was pro-alcohol or whether it was anti-alcohol, there was something.

Erin Allmann Updyke Yes.

Erin Welsh And I really don't wanna present my views as the right views or like this is the truth or this is not the truth.

Erin Allmann Updyke Right, yeah.

Erin Welsh I wanted to present a variety of things.

Erin Allmann Updyke Yeah.

Erin Welsh I don't know. But yeah, I found it challenging to do also in thinking about how I feel about alcohol.

Erin Allmann Updyke Right, trying not to put our own biases into it. Obviously we make quarantinis for every one of these episodes.

Erin Welsh Right but we also make placeboritas for every one of these episodes.

Erin Allmann Updyke We do.

Erin Welsh And sometimes they're way more delicious and way more appetizing.

Erin Allmann Updyke Definitely try the placeborita for this episode, it's great.

Erin Welsh It is.

Erin Allmann Updyke No I know, it's a difficult subject to navigate. I will say in talking a little bit more specifically about alcohol use disorder, because I think especially when it comes to alcohol use disorder there is such a heavy stigma with addiction in general. Addiction is so heavily stigmatized.

Erin Welsh	Oh yeah.
Erin Allmann Updyke	So I do wanna mention that we have a lot of new therapies to treat alcohol use disorder. There was a time when we had nothing in terms of pharmacologic treatment and kind of for a while it was like AA was the only thing. And then there was a Cochrane review from 2006 that concluded there was no evidence to show that AA, so that's Alcoholics Anonymous, or any other treatment modality was more effective or even effective at all. And then another review came out in 2020 which media reports were like 'AA and other 12 step programs were the only thing that works and they're the best!' That's how the media reported it.
Erin Welsh	Of course.
Erin Allmann Updyke	But there were kind of a lot of methodological flaws in that analysis and the two studies, the 2006 and 2020 study, they don't really actually use the same outcome measures. And okay maybe this is me expressing my bias but I also found a commentary on the most recent Cochrane review that was pointing out that the studies really just measured the total amount of abstinence, like the total days of abstinence as their main outcome measure. And maybe that's not the best outcome measure that we should be using as treatment success.
Erin Welsh	Right.
Erin Allmann Updyke	Because for one a lot of people might be deterred from ever seeking treatment at the prospect of having to have lifelong abstinence be the only correct outcome.
Erin Welsh	Right.
Erin Allmann Updyke	Non-abstinent goals might be a lot more attainable for a lot of people and also just in general quality of life and psychological well being weren't considered as outcomes in these studies.
Erin Welsh	Okay.
Erin Allmann Updyke	So I will post all three of those articles so that people can freely read and choose and judge them for themselves. But we do also now have a number of different pharmacological treatments for alcohol use disorder. We actually have one that's not great, it's called disulfiram and it basically inhibits aldehyde dehydrogenase.
Erin Welsh	So it's like basically mimicking that form of...
Erin Allmann Updyke	Exactly, of that genetic...yeah. Right.
Erin Welsh	Interesting.
Erin Allmann Updyke	That's exactly what it does. So you have to take it if you plan on drinking or you think that you're going to drink and then if you drink you will feel terrible and you will barf and you'll be flushed and you will feel awful.
Erin Welsh	You'll have all of the symptoms of...

Erin Allmann Updyke

Exactly. So it's not very effective because you just don't take it if you wanna drink. You know what I mean? So it takes a lot of willpower to take that and then know, etc. There are other pharmacologic treatments that interact more directly on your brain to basically decrease the dopamine-mediated reward effects of alcohol so you don't get that feel good reward system as much and it has been shown to reduce alcohol consumption.

Erin Welsh

Interesting.

Erin Allmann Updyke

And then there are other ones as well that seem to have evidence to help maintain abstinence in people who have already started to abstain and want to continue to abstain. And then there are still more that are not necessarily in the US FDA approved but are used in other countries or maybe that are used off label. So I think the overall message is that if somebody feels like they might have alcohol use disorder or like they might want to get help with their alcohol use but they don't know where to look, there is help out there. And I think that's important to know because there's a lot of studies that demonstrate how widespread alcohol use disorder is in the United States and in other countries as well but how few people ever actually seek help for it. Yeah. That's all I have, Erin.

Erin Welsh

Are we done? 2 hours later?

Erin Allmann Updyke

Just 2 short hours.

Erin Welsh

(laughs) I learned a lot this episode.

Erin Allmann Updyke

Yeah, me too.

Erin Welsh

I mean I always do but this one sort of hit a lot of different corners of my brain.

Erin Allmann Updyke

Yeah.

Erin Welsh

Should we do sources?

Erin Allmann Updyke

Yeah we should.

Erin Welsh

Okay. So I read a couple of great papers about sort of the evolutionary origins of alcohol dehydrogenase. One I already mentioned, Janiak et al from 2020 and there's another one from Carrigan et al 2014. And I also read a couple of books, one is by Rod Phillips and it's just called 'Alcohol: A History', it's very thorough. And the other one is by Edward Slingerland and it is called 'Drunk'. And so this is the ones that talks a lot about why humans drink and why we keep drinking. So I will say I have mixed feelings about it simply because I don't know if there necessarily has to be a reason, like an evolutionary reason for all the things that we do or choose to do. Anyway. But I talked a lot about that in the history section. So anyway, Erin?

Erin Allmann Updyke

I have a large number of papers for this episode, a whole bunch that go into way more detail than I did on the pharmacokinetics of alcohol metabolism as well as the chronic effects of alcohol etc. I will post all three of those, the two Cochran reviews and the response commentary to the Cochran review about Alcoholics Anonymous and other 12 step programs and a whole host most including that really great paper of a list of common hangover cures throughout history.

Erin Welsh

I can't wait to read that.

Erin Allmann Updyke

It's really good. You can find all of our sources from this episode and every one of our episodes on our website thispodcastwillkillyou.com.

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 of whom we are so proud to be a part.

Erin Welsh

And thank you to you, listeners. You made it not only through this long episode but also this long season.

Erin Allmann Updyke

Yeah and like three seasons before it too.

Erin Welsh

Yeah. And hopefully you'll wait for us on the other side for Season 5.

Erin Allmann Updyke

Thank you also to patrons who support us on Patreon, we cannot express enough how much it means to us. Thank you from the bottom of our hearts.

Erin Welsh

And in the meantime make sure that you're subscribed to all of our social media channels and to our podcast on whatever podcast app you use so that when Season 5 drops you'll get a heads up.

Erin Allmann Updyke

If you need more podcast in your ears in the meantime, Exactly Right has a whole host of so many shows that you can choose from so definitely check out the other Exactly Right shows as well.

Erin Welsh

Exactly right. Well until next season-

Erin Allmann Updyke

Yeah!

Erin Welsh

Wash your hands.

Erin Allmann Updyke

You filthy animals!