Welcome to the Huberman Lab podcast where we discuss science and science-based tools for everyday life. I'm Andrew Huberman and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today we're discussing alcohol, one of the most commonly consumed substances on the planet Earth. She mentioned that both humans and non-human animals consume alcohol, either for recreational purposes because they like the feeling that it gives them, or for medicinal purposes, or for other purposes that we'll discuss. We are of course going to discuss the effects of alcohol on our biology, ranging from its effects on individual cells, on organs, and organ systems in our brain and body. We are also going to discuss the effects of the effects of alcohol. That is, what being inebriated really does to our thinking and our behavior and how it does it. And we are going to address what seems to be one of the more common questions out there, which is whether or not low to moderate amounts of drinking are better for our health than zero alcohol consumption at all. And of course we will talk about severe alcohol intake, binge drinking. We will also talk about hangover and what science says about ways to reduce the effects of hangover, either by doing things that are inoculatory, meaning before you drink or while you drink, as well as things to do if you happen to have a hangover. We will discuss some of the genetic differences for alcohol and alcoholism, and we will discuss alcohol consumption in young people, and how that can be especially detrimental for reasons that I think are going to be quite surprising to most of you. My goal is that by the end of today's episode, you will have a thorough understanding of what alcohol does to your brain and body and that you will be able to make informed decisions as to whether or not you should be consuming zero absolutely no alcohol, small to moderate amounts of alcohol, and again, we'll define exactly what that means, small to moderate amounts. And if you or somebody else that you know is consuming excessive amounts of alcohol that are clearly detrimental to your health, some of the better routes and resources that you can use in order to remove that dependence and or consumption. I'd like to preface all of that by saying that today's discussion is really geared toward giving you information. It is not about judging alcohol intake or lack of alcohol intake. I just want you to be able to make the most informed decision about alcohol possible. I'm pleased to announce that the Huberman Lab podcast is now partnered with Momentus Supplements. We partnered with Momentus for several important reasons. First of all, they ship internationally because we know that many of you are located outside of the United States. Second of all, perhaps most important, the quality of their supplements is second to none, both in terms of purity and precision of the amounts of the ingredients. Third, we've really emphasized supplements that are single ingredient supplements, and that are supplied in dosages that allow you to build a supplementation protocol that's optimized for cost, that's optimized for effectiveness, and that you can add things and remove things from your protocol in a way that's really systematic and scientific. If you'd like to see the supplements that we partner with Momentus on, you can go to livemomentus.com slash Huberman. There you'll see those supplements, and just keep in mind that we are constantly expanding the library of supplements available through Momentus on a regular basis. Again, that's livemomentus.com slash Huberman. Before we get into today's content in detail, I just want to answer a commonly asked question about alcohol consumption and the brain. And the question that so often comes up is whether or not low to moderate amounts of alcohol, maybe one drink a day or one or two drinks a day kind of thing, whether or not that is bad for your brain, in particular, whether or not it causes degeneration of neurons or nerve cells. Now, the reason that question comes up so often is because for many years, it's been known that high levels of alcohol consumption, so 12 to 24 drinks per week or more, is certainly causing neurodegeneration, in particular of the so-called neocortex, the outer layers of the brain that house associative memories, that house our ability to think and plan, that house our ability to regulate our more primitive drives according to context, et cetera. So to make very clear, drinking a lot, so having three or four drinks per night, every night of the week is clearly bad for the brain. A recent study, however, finally addressed the question of whether or not low to moderate amounts of alcohol consumption can cause brain degeneration. The title of the study is associations between alcohol consumption and gray and white matter volumes in the UK biobank, the United Kingdom biobank. First of all, gray matter are the neurons, the so-called cell bodies that house the genome of the cells, et cetera, and white matter is the connections, the fibers, the so-called axons of neurons. And it's called white matter because that tissue is surrounded by a fatty tissue called myelin, which allows nerve cells to communicate with each other very quickly. So what this study did is it looked at the brains, both the gray matter and the white matter, of more than 30,000, and even more than 35,000, generally healthy middle aged and older adults in the United Kingdom, who were drinking various amounts of alcohol. What they found was that even for people that were drinking low to moderate amounts of alcohol, so one or two drinks per day, there was evidence of thinning of the neocortex, so loss of neurons in the neocortex and other brain regions. And I don't say this in order to cause alarm. I tell you this because they are important data, because they reveal, and indeed answer the question that has been burning for so long, whether or not chronic alcohol intake can disrupt the brain, even if the chronic intake is very low. Now we should talk about what the word chronic means, because many people, when they hear the word chronic, think high levels of whatever intake. So they think five drinks a night or ten drinks a night, or people drinking every night. Now in this study, they looked at people who, on average, were drinking one or two drinks per night. So that could be 14 drinks on the weekend. It could be one drink per night. It could be seven drinks on Friday. In other words, on average, one or two drinks per night. And I think many people out there are drinking somewhere between one and two drinks per night, or day of the week, on average. So that would be seven to 14 drinks per week. So this is an important study, because it says that if you're consuming even just seven glasses of wine across the week, it's likely that there is going to be some degeneration of your brain in response to that alcohol intake. Although, as mentioned earlier, we will talk about some of the things that can inoculate against some of that neuronal loss. For those of you that are interested in reading the study in more detail, we put a link to it in the show note captions. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero cost to consumer information about science and science-related tools to the general public. Let's talk about alcohol. Let's just acknowledge that human beings have been consuming alcohol for thousands of years. If you look at the archaeological evidence from Mesopotamia, you'll find that 5,000 years ago people had wine vessels. If you want to know when people first started distilling alcohol, much to people surprised that did not first take place in Ireland, and that's not a joke about the Irish, that you'll see a lot of claims online that the Irish were the first to distill alcohol, but in fact they were not. It was the Chinese that were the first to distill alcohol, and that took place in China in the first century. Alcohol has been used for nutritional purposes, so there are cultures that believe and indeed still believe that the calories in alcohol are useful, although later we'll talk about how alcohol calories are indeed empty calories and what an empty calorie really is, why it's called empty. Alcohol has been used for medicinal purposes, because indeed it does kill bacteria, and as you'll soon find out, the fact that it kills bacteria, because that is absolutely true, it also kills the good bacteria in your gut, and the destruction of the good bacteria in your gut can lead to things like leaky gut syndrome and has all sorts of issues, and their ways to deal with those issues, and we'll talk about those. So alcohol has been used for medicinal purposes, it's been used to clean surfaces, it's used in my laboratory in order to make up so-called reagents to do our experiments, but most humans have been consuming alcohol in order to change their internal state in order to feel differently than they would otherwise. That feeling of being drunk or inebriated or tipsy or lightheaded is something that many not all, but many humans seem to enjoy and pursue even though, typically, it leads to a feeling of being less happy, less motivated, more stressed, etc, when the alcohol wears off. That's pretty incredible, right? I mean, we're talking about a substance that people have been highly motivated to pursue, that are still highly motivated to pursue, to create and to consume, that they'll spend money on, and that's despite the fact that it makes them feel good, and then it makes them feel lousy. Now, some of you might be saying, well, I drink, but I don't drink to excess, and therefore I don't feel lousy. I feel good when I drink, and then it wears off, and it allows me to get through my evening, and then the next morning I'm ready to go. Okay, that very well may be true, I believe those people. And as I mentioned, the beginning of the episode, I'm not here to demonize alcohol in any way, but I do want to point out what alcohol is and how it creates the effects that it does, and then I want to talk about what those effects are when you engage in consuming alcohol, even as often as one or two nights per week, or let's say you're just somebody who has a drink or two on Friday, maybe a few more on Saturday, or maybe you're somebody who consumes all your alcohol one night per week or one night per month. We'll talk about how that's affecting your biology. So let's address what alcohol is and how it affects the cells and tissues and organs of your body. Then we'll take a look at some of the epidemiology, that is how many people are consuming alcohol and how much they're drinking. And then you will be able, I think, to get a good sense of how the alcohol that you're drinking, if you're drinking any at all, is impacting your brain and body, and the choices you might want to make about how and when to drink alcohol, or even if you want to eliminate alcohol altogether. So some basic chemistry and biology of alcohol, and again, I'll make this very clear, even if you don't have a chemistry and biology background, because of the structure of alcohol, it is what's called both water soluble and fat soluble, translated into what's meaningful for you. What that means is when you drink alcohol, it can pass into all the cells and tissues of your body. It has no trouble just passing right into those cells. So unlike a lot of substances and drugs that actually attach to the surface of cells to receptors, as they're called, low parking spots, and then trigger a bunch of downstream, like domino cascades of effects. Alcohol actually has its own direct effects on cells, because it can really just pass into those cells. So it's water and fat soluble, and the fact that it can pass into so many organs and cells so easily is really what explains its damaging effects. I should mention that there are three main types of alcohol. There's isopropyl, methyl, and ethyl alcohol, and only the last one, ethyl alcohol, or ethanol, is fit for human consumption. However, it is still toxic. It produces substantial stress and damage to cells. I'd love to be able to tell you otherwise, but that's just a fact. Ethanol produces substantial damage to cells, and it does that because when you ingest ethanol, it has to be converted into something else because it is toxic to the body. And there's a molecule inside of all of us called NAD, and you may have heard of NAD because it's quite popular. There's a lot of discussion about NAD in the longevity literature right now. NAD is present in all our cells from birth until death. The levels of NAD tend to go down across the lifespan. There are ideas that increasing levels of NAD may extend lifespan. A lot of that is still controversial, or at least we should say is ongoing in terms of the research. But nonetheless, when you ingest ethanol, NAD and related biochemical pathways are involved in converting that ethanol into something called acetyl aldehyde. It's broken down into acetyl aldehyde. And if you thought ethanol was bad, acetyl aldehyde is particularly bad. Acetyl aldehyde is poison. It will kill cells. It damages and kills cells and it is indiscriminate as to which cells it damages and kills. Now, that's a problem, obviously, and the body deals with that problem by using another component of the NAD biochemical pathway to convert acetyl aldehyde into something called acetate. Acetyl is actually something that your body can use as fuel. And that process of going from ethanol to acetyl aldehyde to acetate does involve the production of a toxic molecule. Again, acetyl aldehyde is really toxic. And NAD, and if we want to get technical, it's the NAD to NADH ratio, and that chemical step is the rate limiting step to ethanol's metabolism. What does that mean for you? What that means is that if your body can't do this conversion of ethanol to acetyl aldehyde to acetate fast enough, well, acetyl aldehyde will build up in your body and cause more damage. And it's important that your body be able to do this conversion very quickly. And the place where it does that is within the liver and cells within the liver are very good at this conversion process. But they are cells and they are exposed to the acetyl aldehyde in the conversion process. And so cells within the liver really take a beating in the alcohol metabolism events. So the key thing to understand here is that when you ingest alcohol, you are, yes, ingesting a poison. And that poison is converted into an even worse poison in your body. And some percentage of that worst poison is converted into a form of calories that you can use to generate energy, generate ATP. And the reason why alcohol is considered empty calories is because that entire process is very metabolically costly, but there's no real nutritive value of the calories that it creates. You can use it for immediate energy, but it can't be stored in any kind of meaningful or beneficial way. It doesn't provide any vitamins. It doesn't provide any amino acids. It doesn't provide any fatty acids. It's truly empty calories. I know some people talk about sugar is empty calories, but sugar actually is a far better fuel source than alcohol or acetate. But nonetheless, when you ingest alcohol, some percentage is being shuttled into a worse poison and some is being shuttled into a fuel source. Now, the important thing to understand is that it is the poison, the acetyl aldehyde itself, that leads to the effect of being inebriated or drunk. I think most people don't realize that that being drunk is actually a poison-induced disruption in the way that your neural circuits work. And so we should ask ourselves which neural circuits, what brain areas, what body areas involved in feeling drunk or inebriated. Now, in thinking about this state of being tipsy or happy or really drunk or a little bit drunk, I want to mention something I think most people aren't aware of. And that's the fact that for people that are regular drinkers or that have a genetic predisposition to alcoholism, when they drink, they tend to feel very energized and very good for longer periods of time. Again, people have a genetic predisposition to alcohol or people who are chronic drinkers or even just, if you recall, chronic doesn't have to mean a ton of alcohol, but they're drinking one or two per night or they're every other night type drinkers or Thursday through Sunday drinkers. Those people typically experience an increase in alertness and mood when they drink, whereas occasional drinkers will have a brief or meaning less long lasting period of feeling good when they drink and then more quickly transition into a state in which they're tired or they start losing motor skills, they start slurring their speech. I also want to emphasize this is distinct from tolerance. We'll talk about tolerance later and exactly what tolerance means, but I really want to highlight the fact that when people ingest this poison, because indeed it is poison, the range of effects is very different and you can reliably predict who are the people with a predisposition to alcoholism and who are the people who are more regular drinkers by the contour, the timing of the different effects. And again, people who tend to feel more alert and excited every time they drink, they tend to get a real lift, they become a little life of the party and that lasts a long while. Those people are the ones that really have to be careful about predisposition for alcoholism and those people also need to be careful about the drinking and the amount of drinking that they're doing, even if they're not full blown alcoholics. Now, of course, people who are ingesting alcohol, who are not accustomed to drinking alcohol, have to be concerned about drinking alcohol for other reasons because it can impair motor function and judgment, etc. But in thinking about the biochemical effects of alcohol and what it's doing to the body, what it's doing in all cases is it's consumed into the gut, goes into the stomach. The liver immediately starts this conversion that we talked about before of ethanol to acetyl aldehyde to acetate. And some amount of acetyl aldehyde and acetate are making it into the brain. It crosses the blood brain barrier. Again, the brain has this fence around it that we call the blood brain barrier or the BBB. Many things, most things, thankfully, can't pass across the blood brain barrier. But alcohol, because it's water and fat soluble, just cruises right across this fence and into the milieu, the environments of the brain, which is made up of a couple different major cell types, neurons, nerve cells, and so-called glial cells, which are in between the nerve cells. And we'll talk about the effects on each of those soon. So what happens when alcohol gets into the brain that makes us feel tipsy or drunk and in some people make people feel really especially energized and happy? Alcohol is indiscriminate in terms of which brain areas it goes to. Again, it doesn't bind to particular receptors. But it does seem to have a propensity or an affinity for particular brain areas that are involved in certain kinds of thinking and behavior. And one of the first things that happens is that there's a slight, at least after the first drink or second drink, there's a slight suppression in the activity of neurons in the prefrontal cortex. This is an area of your neocortex that's involved in thinking and planning, and perhaps above all in suppression of impulsive behavior. So if you go to a party and they're serving alcohol and people are consuming drinks, what you'll notice is that a few minutes into that party, the volume of people's voices will increase. And that's because people are simply not paying attention to their voice modulation. And as other people start speaking more loudly, other people are speaking more loudly. We've all had this experience right of going to a party and then you step outside for a moment and go, oh my goodness, I was shouting, you're coming over the next day, you got a sore throat, might be that you picked up some sort of bug, some virus or something. But oftentimes it's just the fact you've been shouting all night just to be heard because as the prefrontal cortex shuts down, people stop modulating their level of speech quite as much. Also notice that people start gesticulating more people start standing up and sitting down more, they'll start walking around more if there's music on people might spontaneously start dancing. All of this is because these areas of the prefrontal cortex normally are providing what's called top down inhibition. They are releasing a neurotransmitter called GABA onto various parts of the brain that are involved in impulsive motor behavior and thought patterns. And as you shut down the prefrontal cortex, that GABA urgent suppression of impulses starts to be released. So people will say things that they want to say without so much forethought about what they're saying, where they might do things that they want to do without really thinking it through quite as much, where they might not even remember thinking it through at all or experience, I should say thinking it through at all. We haven't talked about blacking out yet in the effects of alcohol on memory. But as long as we're there, I'll just tell you that alcohol has a very strong effect in suppressing the neural networks that are involved in memory formation and storage. This is why oftentimes we forget the events of a night out if we've been drinking. One of the more important things to know about the effects of alcohol in the brain is this disruption in top down inhibition, but also that areas of the brain that are involved in flexible behavior. So considering different options like I could do A or I could do B, I could say this to them or I could say that I could say to that way or I could say to this way this might be a little more tactful. Those brain areas basically shut down entirely and people just tend to say what they want to say. So the key thing to understand is that when people drink the prefrontal cortex and top down inhibition is diminished. That is habitual behavior and impulsive behavior starts to increase. Now what's interesting is this is true in the short term. So after people have one or two, maybe three or four drinks, but it's also true that the more often that people drink, there are changes in the very circuits that underlie habitual and impulsive behavior. This is really important to highlight so much so that I want to drill into it a little bit more deeply for the person that drinks say every Thursday night or every Friday night or goes out only on Saturdays but every Saturday. There's evidence that there are changes in the neural circuits of the brain that control habitual behavior and impulsive behavior. And they are modified and strengthened in ways that make those people more habitual and more impulsive outside the times in which they are drinking. And when they drink, impulsive and habitual behavior tends to increase even further. This is something that's not often talked about when discussing the effects of alcohol. The effects of being drunk can be bad, right? Can be bad in terms of judgment, motor coordination, certainly driving drunk is a terrible thing, get you or other people killed and so on. But rarely do we hear about the changes in neural circuits from just one or two nights of regular drinking. Again, chronic drinking doesn't necessarily mean every day and every night. It could be the person that simply drinks every Thursday or every Friday or just once a week has three or four drinks or maybe even a few more. That person is going to experience a decrease in this top down inhibition. So an increase in impulsivity and habitual behavior because the break on those behaviors has been removed while they're drinking but also changes in the very neural circuits that allow habitual and impulsive behavior to occur more readily even when they're not drinking. And if you want to know the actual substrate for that, the cellar substrate, I can briefly describe it. It's really interesting. Again, you don't need to know any biology to understand this. What it does is it increases the number of synapses, the actual points of connection in the neural circuits that control habitual behavior. So there's literally a growth of the neural circuits in your brain that lead to existing habit execution, right? The performance of things you already know how to do and a reduction in the neural circuits, where I should say a reduction in the number of synapses over the contacts within the neural circuits that are controlling behavior. So this again is a not often discussed aspect of alcohol intake. Fortunately, it is reversible. So in animals or humans that undertake a period of abstinence of anywhere from two to six months, these neural circuits were returned to normal. Except in cases where people have been chronically drinking large volumes of alcohol for many, many years. And in those cases, while there is some recovery of brain circuitry, after people get sober, meaning completely sober, they stop drinking entirely. There is evidence of long lasting impact of heavy alcohol usage throughout the lifespan. But of course, this doesn't mean that anyone that's suffering from alcoholism or that used to should not continue to focus on their health. You absolutely should always not lost. But for people that have been drinking for a lot of years, maybe you went to college and you drank a lot in those years and your neural circuits change. If there's a period in which you don't drink alcohol again from two to six months and ideally longer, those neural circuits can then be remodified back to their original state. So let's consider some of the other neurochemical effects of alcohol in the brain embody. And again, for right now, we're confining the conversation to people that are drinking on average, one or two drinks per night. Now, some people might think that two drinks per night is a lot. And a lot of that will depend on body weight. So for instance, people who weigh 110 pounds for them to ingest two alcoholic drinks is going to be substantially different in terms of the biochemical effects than somebody who weighs 220 pounds. Of course, tolerance will also factor into this genetic background will also factor into this. And indeed, whether or not people have eaten will factor into this. So there are a lot of factors and we'll talk about that for the time being, if you're curious about how food impacts the effects of alcohol and your feelings of being drunk, you may have heard, for instance, that if somebody's inebriated and they want to sober up, they should eat something turns out that does not work. Here's how it does work, however, if you eat something prior to drinking alcohol or while ingesting alcohol, it will slow the absorption of alcohol into the bloodstream. In other words, you won't feel as drunk as fast. For many of you, this probably comes as no surprise. In particular, if that meal includes carbohydrates, fats and proteins, the inclusion of all three major macronutrients seems to slow the absorption of alcohol into the bloodstream far more than having any one of those or two of those macronutrients present. Now, if you are already inebriated or you've had a glass of wine or a beer and you eat something, chances are that alcohol has already made it into your bloodstream because it moves into the bloodstream so quickly, again, it's fat, soluble and water soluble. So within minutes, if you have an empty stomach within five to 10 minutes, that alcohol is going to be within your bloodstream and distributed throughout your body, maybe even faster depending on the type of alcohol and your metabolism. But if you're already drunk and you eat something, it's not going to sober you up more quickly, but it certainly will blunt the effects of any additional alcohol that you might consume. And if you're somebody who is concerned about getting too drunk too quick, even from a small amount of alcohol, having some food in your gut can certainly be beneficial. Now, that's food in alcohol and the absorption of alcohol. But let's go back to talking about the biochemical and neurochemical effects of alcohol in the brain. We talked about top down inhibition and we talked about habitual and impulsive behavior circuitry. There are also dramatic changes in the activity of neurons that control the release of so-called serotonin. Serotonin is a neuromodulator. It changes the activity of neural circuits and many neural circuits in particular those involved in mood and feelings of well-being. Recently, there's been a lot of interest in serotonin because of a study that was released that showed pretty conclusively that serotonin levels can't really explain depression and depression-like symptoms. I want to make it very clear that although that study did show that serotonin levels are not necessarily associated with depression, the study was interpreted by many to mean that SSRI selective serotonin reuptake inhibitors, which have the net effect of increasing serotonin, increasing serotonin, so these are things like prozac, etc. That those drugs are somehow not helpful because they increase serotonin and serotonin isn't involved in depression. That logic doesn't really hold together. So I'm going to use this as an opportunity to just clarify what really occurred there. And then we'll talk about how serotonin relates to alcohol consumption in things like feeling good and in depression. The key thing is this, SSRIs can help alleviate depression. That's right, SSRIs can help alleviate depression. They are often not always associated with side effects, dosage is very important, etc. But they probably support relief from depression by changing neural circuits, not necessarily by increasing serotonin itself. That is increasing serotonin with these drugs, likely change the neural circuits involved in mood, allowing people to feel better through so-called neuroplasticity, which is the brain's ability to change itself in response to experience. So there's a bit of confusion and again I'm using this episode on alcohol to highlight some of the confusion because I think it's timely, because the study just came out and there's a lot of chatter about this out there. That when people are depressed, it's not necessarily because serotonin levels are low. However, if serotonin levels are increased with things like prozac, zoloft and other SSRIs, oftentimes there is, yes, a relief from depression. But that's probably not because of restoring serotonin levels per se. It's probably because serotonin facilitates the changes in neural circuits that need to occur in order for people to feel elevated mood. So again, that's a bit of a tangent in a sigh, but I do think it's a vital one for people to know about. Again, if you're thinking about taking SSRIs, you're currently taking them and you've heard this news, definitely talk to your doctor. Again, there is great utility for some of these SSRIs and also in conditions like OCD, they've been shown to be very beneficial, so we really don't want to throw SSRIs out as a potentially valuable treatment. Getting back to the effects of alcohol on serotonin, it's very clear beyond any doubt that many of the circuits in the brain that are involved in mood and feelings of well-being and also sort of self-image in how we see ourselves, employ the neuromodulator serotonin, and alcohol when we ingest it, and it's converted into acetylaldehyde. It goes and that acetylaldehyde acts as a toxin at the very synapses, the connections between the serotonergic neurons and lots of other neurons. In other words, when we ingest alcohol, the toxic effects of alcohol disrupt those mood circuitries at first making them hyperactive. That's right, making them hyperactive is why people become really talkative, people start to feel really good after a few subs of alcohol, at least most people do. Then as they ingest more alcohol, or as that alcohol wears off, serotonin levels and the activity of those circuits really starts to drop, and that's why people feel less good. Typically what they do, they go and get another drink, and they attempt to restore that feeling of well-being in mood. Typically what happens is that as people ingest the third and fourth, maybe even the fifth drink, there's an absolute zero chance of them recovering that energized mood. Most people as they drink more and more will now start to feel more and more suppressed. The forebrain is now shutting down quite a lot, a lot of the motor-cortical areas that control coordinated movement and deliberate movement start to shut down. People start to flur their speech, people start to shuffle their feet, people forget their posture, people start to lean on things, people start passing out on couches. They create depression, not depression of the psychiatric depression sort, but a depression of alertness and arousal, and eventually people will pass out. Now I said most people, because there's a subset of people that have gene variants, or who are chronic drinkers, or who are chronic drinkers and have gene variants, that as they ingest the third and fourth and fifth drink, what happens? They become more alert, they start talking more, they feel great, they have all sorts of ideas about the fun they could have that night, and they're the ones that if you've ever fallen asleep at a party for whatever reason or you're getting tired and you're yawning, you're looking around the room, and like these people are still drinking and parting and they're having what seems to be this amazing time. Often not always, those are the future alcoholics in the room, or those are the people that have a genetic predisposition for alcoholism, or those are the chronic drinkers, the people who have built up enough of a tolerance, or who have the chemical genetic make up such that increasing amounts of alcohol make them feel better and better and better, and of course they too have a threshold beyond which their nervous system will start to get diminished and they'll pass out, fall over, etc. But that threshold is way, way higher than it is for most people. Now this is important to understand, and it's important to understand because I think everyone should know and recognize their own predisposition and kind of risk in terms of developing alcoholism. It's also important to understand because it relates to the phenomenon of blackout. Many people think that blacking out is passing out, but blackout drunk is when people drink and they're talking and doing things, sometimes sadly they'll, or tragically they'll often drive home, or walk home, or they'll hop on a bicycle and ride home, or they'll go swimming in the ocean, all, of course, very dangerous activities to do when people are really drunk, or even a little bit drunk in some cases. So these people will do these sorts of things, and they do them because they have the energy to do them, and they feel good while doing them, but they are doing them while the activity of neurons in the hippocampus, which is involved in memory formation, are completely shut off. And this is why the next day you tell them, hey, maybe we should talk about what happened last night. He said, well, do you remember going to the party? Yeah, I know it was great. We did this. We did this, and then what? And it's very clear, all of a sudden, that they have no recollection of all the things they were doing despite being awake. Now, I wish I could tell you that there's some sort of blood test or other biomarker, even a fingerprint test, that would allow you to determine whether or not you have a propensity to be one of these drinkers that has a predisposition for alcoholism. And if you've ever been black out drunk, and certainly if you've been black out drunk more than a few times, you should be quite concerned. And as we talk more about the more chronic effects and long lasting effects of alcohol consumption, a little bit later in the episode, I think it will become clear as to why you should be concerned. But in any case, there is something that can tell you whether or not you might be in that category versus likely not in that category. And I alluded to this a couple of times already, but I want to be really clear that when people drink, no matter who you are, initially there's that shutting down to those prefrontal cortical circuits. There's a gradual shutting down of the circuits, the control memory. But then people divide into these two bins. And these two bins are the people who after more than a couple of drinks start to feel sedated. And the people who after more than a few drinks do not start to feel sedated. Now of course, there's going to be differences created by how quickly people are drinking, whether or not they're combining different types of alcohol, the types of alcohol, etc. But in general, that can predict whether or not you're somebody who has a predisposition for alcoholism or not. One also very interesting finding is that alcohol changes the relationship between what's called the hypothalamus and the pituitary gland and the adrenals. Now the hypothalamus is a small collection of neurons about the size of a large gumball sits above the roof of your mouth. And it houses neurons that are responsible for some incredible aspects of our behavior and our mindset, things like rage, things like sex drive, things like temperature regulation, very primitive functions, including appetite thirst, etc. Alcohol, because it can go anywhere in the brain, remember it's water and fat soluble, has effects on the hypothalamus. The hypothalamus normally provides very specific signals to what's called the pituitary gland. This is a little gland that actually sticks out of the brain, but it receives instructions from the hypothalamus. And then the pituitary releases hormones into the bloodstream that go and talk to your adrenals. And your adrenals gland sits right above your kidneys in your lower back. And the adrenals release as the name suggests adrenaline, also called epinephrine, and also a molecule called cortisol, which is involved in the kind of longer term stress response as some healthy effects to the immune system. Okay, so the hypothalamus pituitary adrenal axis. I know that's a mouthful, you don't need to remember the names. The hypothalamus pituitary adrenal axis maintains your physiological balance of what you perceive as stressful and what you don't perceive as stressful. People who drink regularly, so this again could be just one or two drinks per night, or it could be somebody that drinks just on Fridays or just on Saturdays or maybe just on the weekend, two to four drinks. Well, those people experience changes in their hypothalamus pituitary adrenal axis that result in more cortisol, more of this so-called stress hormone being released at baseline when they are not drinking. This is really important. People who drink a bit, and when I say a bit, I don't mean one or two steps, or even a glass of wine every once in a while. I mean, again, people that are maybe having one drink a night with dinner and maybe on the weekend a few more. Again, I offer a bunch of different patterns to explain how it could also be two or three drinks on Friday or six drinks only on Saturday. Well, all of those groups experience increases in cortisol release from their adrenal glands when they are not drinking. And as a consequence, they feel more stressed and more anxiety when they aren't drinking. This is a seldom talked about effective alcohol because so often we hear about the immediate effects of alcohol. We've been talking about some of those effects, effects like reducing the amount of stress. I mean, how many times have we heard somebody say, oh, I need a drink and then they have a drink and they'll calm down. Now they can shake off the thoughts about the day's work. They can start to think about things in a maybe more grounded or rational way, or at least they believe that, or they can somehow just relax themselves. Well, while that very well may be true, that it can relax them when they are not drinking, that level of cortisol that's released at baseline has increased substantially. Again, this relates to a defined neural circuit between brain and body, and it has to do with the ratio of cortisol to some of the other hormones involved in the stress response. We'll provide a reference to the study that describes how all of this works for those of you that really want to delve into it. But let's go back to this issue of those who are prone to alcoholism versus those who are not. Remember, there are people who have genetic variants that, meaning genes that they inherited from their parents, that make it more likely that they will become alcoholics. But there are also people who drink often, who start to experience this increase in alertness, the longer they drink across the night. Part of that effect, we think, is because of changes in this hypothalamic pituitary adrenal axis. So, alcohol is kind of a double hit in this sense. It's causing changes in our brain circuitry and neurochemistry that, at the time in which we're inebriated, are detrimental. And it's causing changes in neural circuitry that persist long past the time in which we're experiencing the feeling of being tipsy or drunk. Now, again, I don't want to demonize alcohol. I'm not saying, oh, you know, if you have a glass of wine now and again, or you drink a beer now and again, or even have, you know, a mixed drink now and again, or a shot that that's necessarily terrible for you. I certainly do not want that to be the message. What I'm saying is that if people are ingesting alcohol chronically, even if it's not every night, there are well recognized changes in neural circuits. There are well recognized changes in neurochemistry within the brain. And there are well recognized changes in the brain to body stress system that generally point in three directions. Increased stress when people are not drinking. Diminished mood and feelings of well-being when people are not drinking. And as you'll soon learn, changes in the neural circuitry that cause people to want to drink even more in order to get just back to baseline, or the place that they were in terms of their stress modulation and in terms of their feelings of mood before they ever started drinking in the first place. So again, I don't want to demonize alcohol, but I do want to emphasize that there are long term plastic changes, meaning changes in neural circuitry and hormone circuitry that across a period of several months and certainly across a period of years of the sorts of drinking patterns I described, which I think for most people are going to sound like pretty typical. I mean, nothing that I described so far was about drinking a case a night or about binging on alcohol and the way that we often hear about it in the news. These are pretty common patterns of alcohol consumption. I mean, all you have to do is board a transatlantic flight or actually go to an airport on a Sunday afternoon and a sunny area of the US. And you know, people are having three, four, five, six beers, et cetera. Again, personal choice is personal choice. I'm not telling you what to do, but it's very clear that those sorts of drinking patterns are changing neural circuitry and they're changing hormone circuitry. And I'd love to be able to tell you that they're changing them for the better, but they simply are not. They're actually changing them for the worst and worse is defined as making people less resilient to stress higher levels of baseline stress and lower mood overall. Before we continue with today's discussion, I'd like to just briefly acknowledge our sponsor athletic greens now called AG one athletic greens, AKA, one is an all in one vitamin mineral probiotic drink that also has adaptogens and digestive enzymes. I've been taking athletic greens since way back in 2012. So I'm delighted that they're sponsoring the podcast reason I started taking athletic greens and the reason I still drink athletic greens twice a day is that it supplies total foundational coverage of my vitamin mineral needs. And it supplies important nutrients that I need to support my gut microbiome, the gut microbiome as many of you know supports the immune system. It also supports the so called gut brain access, which is vital for mood for energy levels for regular focus and many other features of our mental health and physical health that impact our daily performance and high performance in any endeavors we might be involved in. If you'd like to try athletic greens, you can go to athletic greens dot com slash Huberman and claim a special offer they're giving away five free travel packs plus a year supply of vitamin D three K to with every order and of course vitamin D three K to vital for all sorts of things like hormone health and metabolic health and K to for cardiovascular health and calcium regulation again, you can go to athletic greens dot com slash Huberman to claim that special offer. Now I've been talking a little bit about genetic predisposition, but there are a couple of important points I'd like to make about that. First of all, what sorts of genes are involved in setting someone down the path of alcoholism or not. Well, it should come as no surprise that the genes that chronic alcohol usage modifies they tend to fall primarily in the pathways related to genetic control over serotonin receptors, GABA receptors, remember that top down inhibition and the involvement of GABA and no surprise the HPA the hypothalamic pituitary axis all of those of course combined with environment they combine with patterns of abuse right we know that if you're in a social setting where a lot of people are drinking the likelihood that you're going to drink is much higher. Social pressures trauma right some people will use alcohol to self medicate to try and turn off their thinking or to deal with trauma etc so they combine with the environment but the genes that are in the serotonin synthesis and receptor synthesis pathway GABA and HPA access combined with environmental pressures to give rise to alcohol use disorders. There's a fairly coherent picture that we have here right this is not a case where for instance people that have a lot of the enzyme from a tablizing alcohol which we'll talk about a minute alcohol dehydrogenase. It's not like they are necessarily the people that become alcoholics whereas certainly in certain cultures certain Asian cultures in particular. There are gene differences that lead them to have low levels of alcohol dehydrogenase there actually people have so little alcohol dehydrogenase that when they ingest alcohol they get very red and they just feel sick so if you're somebody has a sip of alcohol and you just feel horrible it makes you feel nauseous chances are you have. Gene variants that create a situation where you're not making very much alcohol dehydrogenase you just simply can't metabolize alcohol so you just get a rapid build up of the toxic effects of alcohol the seat of aldehyde you're not converting it into those empty calories. But in cultures where you have a lot of genetic variants and genes expressed in people where they have a lot of alcohol dehydrogenase sure they can drink more and they're converting more of that alcohol from its toxic form to a non-toxic form and yes of course you will observe more alcoholism in those communities because they're drinking more but I do want to emphasize that the environmental factors are playing a strong role there too because if you can drink more you're likely to drink more if you're somebody that feels sick immediately from drinking it's likely that you're drinking. It's likely that you're not going to engage in alcohol consumption especially if these things are genetically related and of course genes and culture and location in the world tend to run together. So do you have the gene for alcoholism? Well there isn't one single gene chances are if you have an immediate relative whose a chronic abuser of alcohol or several relatives who are chronic abusers of alcohol well that's going to predispose you to be an alcoholic. But since you don't know which genes you express unless you do genetic testing and those things are available but most people aren't doing that this assay if you will it's not an assay as we say an assay is a test that you run in the lab to determine something and it's not one that I recommend that you go drink in order to do but if you've noticed that you or somebody else is somebody who can drink a lot throughout the night and have increased energy and just drink and drink a drink. And especially if there's blackout episodes not remembering things the next day despite being alert throughout the entire night and so on well then I would be very concerned that you might actually have a genetic variant predisposing you to alcoholism. The other thing that predisposes people to abuse of alcohol is age people who start drinking at younger ages are greatly predisposed to developing alcohol dependence regardless of your family history of alcoholism. So I'm going to repeat that people who start drinking younger are at great risk for developing alcoholism even if they don't have alcoholism in their family. Now of course you don't have to be an epidemiologist understand that if you grew up in a family of drinkers and alcohol is everywhere and especially if there's peer pressure or lack of oversight then there's going to be a higher tendency or a higher probability I should say that you will start drinking at a younger age. However, even people that grow up nowhere near their relatives if they start drinking at a young age so for instance at 13 or younger or 14 or 15 there's a much higher probability that they're going to develop a long lasting dependence on alcohol. People who take their first sip of alcohol later 15, 16 or one would hope even later I can say one would hope because I'm now that you know age in generation where you you know you think about all the things that young people do and you go oh gosh if they own alcoholism. So if they only would wait or if they only would abstain you know this is what happens I don't know there's some neural circuit for that that I can't explain yet but people who for instance drink only once they reach legal age of drinking which in the US I believe in every state is 21 years old. If they take their first drink at 21 the probability that they'll go on to develop full blown alcohol dependence or alcohol use disorder as it's called a UD is very low. Now a subset of them will because they have such a strong genetic predisposition or maybe life circumstances create a pattern in which they become a chronic drinker but I found this very interesting genes matter but also the age in which somebody starts drinking really matters. Now whether or not that's because there are changes in neural circuitry as a consequence of that drinking that make people want to seek out more and more alcohol or whether or not there's some other effect maybe it's a change in hormones etc. That predisposes those young drinkers to become chronic drinkers or even full blown alcohol certainly developing alcohol use disorder there's definition for that we can talk about it involves the amount of drinking over a certain period of time etc. So it's very clear that drinking early in life creates a propensity for the development of alcohol use disorder later in life. And while there is a genetic component to developing alcohol use disorder I find it very interesting that if people who have those gene variants delay their onset of drinking will then the probability that they'll develop full blown alcohol use disorder drops as well. So again it's genes and environments not any other or and there's no single gene for alcoholism. Well I promise you I will also talk about some of the documented positive effects of alcohol although they are very few and far between they do exist. But before I do that I would be remiss if I didn't emphasize some more of the terrible things that alcohol does in the way that it does it. And for those of you that enjoy alcohol I again I really like to say I feel guilty about telling you this because I know how much some people enjoy a good drink every once in a while and I say a good drink because some people do like the taste of alcohol. I suppose I lucked out and then I don't really like the taste of alcohol and that just puts me to sleep but I know that people do enjoy it. And I do want to point out that there is zero evidence that you know provided somebody is of drinking age or certainly not in the stage of brain development that having one drink or two drinks every now and again meaning every three or four weeks or once a month that is not going to cause major health concerns or major health issues for most people. I suppose if you have zero or very little alcohol dehydrogenase it might make you feel sick but then you're probably not the kind of person that's going to be drinking at all. So again if you enjoy alcohol drinks I'm not trying to take them away from you by any means but you should know what drinking does if you're consuming it in this kind of typical chronic pattern as we can now refer to it which is that one or two a night or a few stacked up on Friday and maybe three or four weeks. Today and maybe three or four on Saturday this kind of pattern of drinking which is quite common and one of the more serious effects that we should think about is the impact on the so called gut brain access or for today's discussion the gut liver brain access. I don't think the gut liver brain access has ever been discussed on this podcast maybe any podcast although the moment I say that I'm going to the gut liver brain access people are going to come after me with I suppose gut liver brain and brains in any event. You have a gut that gut runs from your throat down to the end of your intestine your gut and your brain communicate by way of nerve cells neurons and nerve connections the vagus nerve in particular and by way of chemical signaling. Your gut also communicates by way of chemical signaling and believe it or not by way of neural signaling to your liver and as we talked about earlier the liver is the first site in which alcohol is broken down and metabolized into its component parts. The liver is also communicating with the brain through chemical signaling and neural signaling so we have the gut liver brain access and what you find is that people who ingest alcohol at any amount are inducing a disruption in the so called gut microbiome the trillions of little micro bacteria that take resident in your gut and that live inside you all the time and that help support your immune system and that literally signal by way of electrical signals. In chemical signals to your brain to increase the release of things like serotonin and dopamine and regulate your mood generally in positive ways what alcohol really disrupts those bacteria this should come as no surprise I mean earlier we talked about this and it's well known if you want to sterilize something you want to kill the bacteria you pour alcohol on it I can remember scraping my myself or cutting myself I was always the injury myself when I was a kid and you know the moment they take out the peroxide like oh boy here it comes but if there's no peroxide. You've got a wound there and you need to clean it out yeah they they'll use alcohol which I do not recommend by the way that's one of the harshest ways to clean a wound but for centuries thousands of years really alcohol has been used in order to clean things and kill bacteria. So alcohol kills bacteria and it is indiscriminate with respect to which bacteria it kills so when we ingest alcohol it goes into our gut it kills a lot of the healthy gut microbiota. At the same time the metabolism of alcohol in the liver which you now understand that pathway involving NAD a seat a laldehyde and acetate that pathway is pro inflammatory so it's increasing the release of inflammatory cytokines things like IL-6 etc. turmericicosis factor alpha if you'd like to learn more about the immune system we did an episode all about the immune system you can find at ubermanlab.com I'll teach you all the basics of what our cytokines what our mast cells etc. In any event all these pro inflammatory molecules those are being released you've now got disruption of the gut microbiota as a consequence the lining of the gut is disrupted and you develop at least transiently leaky gut. That is bacteria that exist in the gut which are bad bacteria can now pass out of the gut into the bloodstream so you've got a two hit kind of model here in biology we talk about two hit models that is kind of a one plus one equals four and it's generally when you hear two hit it's not a good thing so you've got bad bacteria from partially broken down food moving out of the gut the good bacteria in the gut have been killed you might say why isn't the alcohol kill the bad bacteria in the gut well the bad bacteria that are from partially digested food oftentimes escape the gut before the alcohol can disrupt them and so now you've got leaks in the gut wall you've got the release of this bad bacteria you've got inflammatory cytokines and other things being released from the liver and they are able to get into the brain through through what's called a neuro immune signaling and what's really bizarre in terms of the way that this manifests in the brain I mean it's not the way I would have done it but then again as I always say I wasn't consulted at the design phase and anyone who says they did you should be very skeptical of them. The net effect of this is actually to disrupt the neural circuits that control regulation of alcohol intake and the net effect of that is increased alcohol consumption so this is just terrible right I mean to your take in something that disrupts two systems the gut microbiota and it disrupts in two ways it's killing the good gut microbiota and it's allowing the bad. The bad bacteria to move from the gut into the bloodstream you've also got pro inflammatory cytokines coming from the liver and those converge or arrive in the brain and create a system in which the neural circuits cause more drinking that's a bad situation and this is why people who drink regularly even if it's not a ton of alcohol again of this sorts of patterns of drinking I talked about before and certainly for those that are chronic heavy drinkers what you end up with is the brain. What you end up with is a situation in which you have inflammation in multiple places in the brain embody and the desire to drink even more into further exacerbate that inflammation and the gut leakiness so this is basically a terrible scenario for the gut liver brain access and it's especially prevalent in so called alcohol use disorder again people they're ingesting somewhere between 12 and 24 drinks per week for those of you that are interested in learning more about the gut liver brain access and in particular alcohol use disorder I'll provide a link in the show no captions. There's a wonderful review on this that details that but on the positive side it points to the possibility that at least some again at least some of the negative effects of alcohol consumption whether or not you're somebody who's currently ingesting alcohol or who used ingest alcohol is trying to so called repair these systems of the brain and body whether whether not replenishing the gut microbiota is going to be beneficial and we know that there are ways to do that and we know that there's at least some promise for the ability for the system to repair itself how does one do that I've talked before about this on the podcast but studies done by colleagues of mine at Stanford Justin Saunemberg who's been on this podcast as a guest an amazing episode all about the gut microbiome and his collaborator Chris Garner also at Stanford School of Medicine have explored not alcoholism but what are ways to improve the gut microbiota in particular to reduce the production of inflammatory cytokines and to adjust what's called the inflammatory you've heard of the genome and the proteome etc well the inflammatory is the total array or at least the near total array of genes and proteins that control inflammation how can you reduce inflammation and make that inflammatory healthier well they've shown that two to four servings of fermented foods per day and here I'm not referring to fermented alcohol in time at low sugar fermented foods of things like kimchi sourcrout not to for the for those of you that like Japanese food there are others I know things like key for things like yogurt have a lot of active bacteria again low sugar varieties of all these things those are terrific at reducing inflammatory markers and at improving the gut microbiome one could imagine that either inoculating oneself from some of the effects of alcohol although I prefer that people just not drink alcohol chronically frankly or if somebody's trying to repair their gut microbiome because they ingested a lot of alcohol or because they had a lot of these inflammatory cytokines for many years or even a short period of time regular ingestion of two to four servings of these fermented foods can be quite beneficial want to make it clear that has not been examined specifically in the context of alcohol use disorder but because a huge component of the negative effects of alcohol use disorder are based in this gut liver brain access and disruption the gut microbiome in the inflammatory cytokines it stands to reason that things that are well established to improve inflammation status in other words reduce inflammation such as ingesting two to four servings of low sugar fermented foods per day make sense in terms of trying to repair or replenish the system one could also imagine taking probiotics or prebiotics certainly that would work as well although I've sort of favored the discussion around fermented foods and replenishment of the gut microbiome mostly be able to do that. So mostly because there are more studies that have examined that in humans and because of the direct relationship that's been established between doing that and reducing negative markers within the inflammatory and I should mention along the lines of repair and recovery I put out a question on Twitter the other day I said what do you want to know about alcohol more than a thousand questions take some more of those questions a little later in the episode but one of the things I noticed is that many of the questions hundreds in fact related to the question of well if I drank a lot previously am I doomed can I reverse the negative effects or I'm trying to drink last and I'm trying to improve my health as I as I do that what should I do well certainly focusing a bit on the gut microbiome ought to be useful the other thing I should mention is as people wean themselves off alcohol even if they're not full blown alcoholics or have alcohol use disorder they should understand that that increase in cortisol that we talked about earlier that leads to lower stress threshold and greater feelings of anxiety and stress that's going to be present and it's going to take some time to dissipate so for some people it might even just be helpful to realize that as you try and wean yourself off alcohol or maybe even go cold turkey that increased anxiety and feelings of stress should be expected and in that case I would point you to an episode that we did on master stress you can find that again at Hubertman lab.com it's got a ton of behavioral nutritional supplementation based exercise based I suppose exercise as behavioral but a lot of tools you can navigate to those easily because we have time stamps you can go right to the topic of interest those tools are going to be very useful in trying to clamp or control your stress and the point here is just that some increase in stress should be expected and it should be expected because of that increase in cortisol that occurs with even low level consumption yet chronic alcohol consumption. Now I'd like to talk about a fairly common phenomenon which is post alcohol consumption malaise also referred to as hangover. Hangover is a constellation of effects ranging from headache to nausea to what sometimes called anxiety which is anxiety that follows a day of drinking. Hangs I think we can understand physiologically if we think about that process of alcohol intake increasing the amount of cortisol and the ratio of cortisol to some other stress hormones that well explains why some people wake up the day after or even the day the day after a night drinking and feel anxious and not well and stressed for reasons they don't understand. So if you're somebody who experiences hang anxiety then again I refer you to the master stress episode that we put out some time ago and you can find that you've been lab dot com tools to deal with anxiety tools to deal with stress ranging again from behavioral to nutritional supplement based etc. That of course is not justification for going out and drinking so much that you get anxiety induced hangover but for those of you that are experiencing post alcohol consumption anxiety as it were that could be a useful resource because I certainly don't want anyone experiencing uncomfortable amounts of anxiety and there are great tools and resources for that. Now the other aspects of hangover such as the stomach ache or headache or feelings of malaise or fogginess those can be related to a number of different things and probably are related to a number of different things. First of all the sleep that one gets after even just one yes even just one glass of wine or a beer is not the same sleep that you get when you don't have alcohol circulating in your system and not trying to be a downer here but this was discussed in the human lab podcast episode where I had Dr. Matthew Walker from UC Berkeley on and of course Dr. Walker is a world expert in sleep runs one of the preeminent laboratory studying sleep and its effects wrote the incredible book why we sleep. And so on Dr. Walker told me and certainly supported by lots and lots of quality peer reviewed studies in animals and in humans that when alcohol is present in the brain and blood stream that the architecture sleep is disrupted slow wave sleep deep sleep and rapid I move in sleep ball of which are essential for getting a restorative night sleep or all disrupted. So for those of you that are drinking a glass or two of wine or having a hard liquor drink or a beer in order to fall asleep the sleep you're getting is simply not high quality sleep or certainly not as high quality as the sleep you be getting if you did not have alcohol in your system. Of course when we're talking about hangover we're talking generally about the consumption of more than just one or two drinks of course for some people one or two drinks is probably sufficient to induce hangover but for most people it's going to be having three or four exceeding their typical limit as it's called again not the legal limit that's a whole other business but when one ingest too much alcohol for them. One of the reasons they feel terrible the next day is because their sleep isn't really good sleep in fact it's not even sleep it's often considered pseudo sleep really that's what it's called in the sleep science field because people are in kind of a low level hypnotic kind of trans it's not real sleep their multiple ballots of waking up they may not even realize they're waking up multiple times. Okay so there's the sleep induced effects then there are the disrupted gut microbiome effects some of which we talked about earlier so now you understand the mechanism of alcohol destroying good healthy gut microbiota which then leads to leaky gut and things of that sort but one could imagine again could imagine and there's some evidence starting to support this that again ingesting low sugar fermented foods or maybe in prebiotic or probiotic to support the gut microbiome might assist in some of the gut related malaise associated with hangover in other words get those gut microbiota healthy again as quickly as possible or maybe even before you drink have those got microbiota healthy I would hope that you do that I think everybody should be doing something to support their gut microbiome whether or not the ingestion of low sugar fermented foods daily or at least on a regular basis or ingestion of probiotic or prebiotic the gut microbiome is so important for you to do that. So that's why I'm so important for so many different things in terms of hangover and head ache we know that that's caused by vasoconstriction the constriction of blood vessels that tends to occur as a rebound after night of drinking alcohol can act as a vasodilator it can dilate the blood vessels part of that is associated with the increase in so called parasympathetic tone we have an autonomic nervous system it's got a sympathetic component these are neurons that make us more alert and if they're very active they make a lot of the same thing. They're very active they make us very stressed there's also the parasympathetic aspect of the autonomic nervous system this is all just fancy geek speak for the parts of your brain embody the nerve cells that make you very relaxed when you're very relaxed there tends to be vasodilation it allows for more movement of blood and other things through the blood stream and alcohol tends to induce some vasodilation at least in some of the capillary beds and then when the alcohol wears off there's a vasoconstriction and people get brutal headaches that's why some people will take aspirin or Tylenol or advill or things like that this sort of non steroid anti-inflammatories I should mention there is a lot of literature coming out that some of these non steroid anti-inflammatory drugs are not good for us for a number of different reasons the way they impact the liver the way they impact the immune system and no surprise the way they impact the gut microbiome so I'm not one to tell you what medications to take or not take but you certainly would want to do a quick web search of effects of non steroid anti-inflammatories and aspirin before you start taking those or stop taking those for that matter generally they will alleviate headache but they can often have other issues including liver issues and keep in mind the night after drinking your liver is already taken a beating because of the knee to the liver to convert alcohol from a sea of aldehyde into acetate which is now a pathway that you well understand so I'm not certain and in fact I believe it's not the greatest idea to burden your liver further through the use of things that are going to cause it to have to work harder and metabolize things if the goal is simply to alleviate a headache there's a lot of kind of lower old school lore about how to relieve a hangover we already talked about how eating food won't do that but eating food will prevent the rapid absorption of even more alcohol into the bloodstream there's the lore that one should simply ingest more alcohol what terrible advice that is that's just going to delay and even worse hangover however I'd be remiss if I didn't say that the reason that that myth came to be or that I should say that truth came to be because indeed ingesting more alcohol will alleviate a hangover but then a worse hangover will show up the reason that came to be is because ingestion more alcohol will cause those constricted vessels that are giving the headache to dilate again but of course ingesting more alcohol to relieve a hangover simply a bad idea just don't do it I think this is called the hair of the dog approach maybe someone can put in the show note captions on youtube why it's called the hair of the dog I can come up with a few ideas but they're not it they're going to be very good ones and some of them would probably even be outright ridiculous so do not ingest more alcohol simply to try and recover from a hangover I know many people have tried that one before but that's a terrible idea now one thing that you'll also hear out there is that deliberate cold exposure for instance taking a cold shower might relieve hangover I find this one particularly interesting because we've done episodes on the benefits of deliberate cold exposure we have an entire episode about that you can find it again hubermanlab.com there are direct links to some of the tools related to deliberate cold exposure and we have an entire newsletter on deliberate cold exposure protocols you can find on hubermanlab.com go to our neural network newsletter so these those of you that are interested in ice baths and cold showers and ways to leverage those you can find that there what you won't find there is a description of how to use deliberate cold exposure for sake of treating hangover but here I went into the literature and I found something kind of interesting there is some evidence that increasing levels of epinephrine in the bloodstream can actually help with alcohol clearance that was very surprising to me and I want to point out this is not a large and robust literature but there's some evidence pointing to the fact that when levels of epinephrine adrenaline are raised in the brain and bloodstream that some of the components of alcohol metabolism can be accelerated and some of the inebriating effects of alcohol can be reduced so maybe this old school lore of taking a cold shower actually has something to it so in thinking about the use of deliberate cold exposure in order to reduce the effects of hangover or to more rapidly clear alcohol from the brain and bloodstream I want to be very clear and I want to emphasize your safety the way to do that is to understand that alcohol lowers corbati temperature okay it can make people slightly hypothermic it's going to drop corbati temperature so if you were inebriated and you went and got into a body of water right a pool or a lake or something first of all that's extremely dangerous to do while you're inebriated people drown all the time people drown they die as a consequence of doing that so please don't do that but also if it's very cold water your corbati temperature is going to drop even further now if you've heard the episodes that have done on deliberate cold exposure previously I've talked about how normally when people are not ingesting alcohol they get into an ice bath or a cold shower and their body temperature initially dips but then it rebounds and increases that's a process that's going to occur when people do not have alcohol in their system when you have alcohol in your system one of the reasons that you become hypothermic is because there's a disruption in those hypothalamic brain areas in particular the brain area called the medial preoptic area that regulates corbati temperature so it's not so much that alcohol makes you cold it's that alcohol disrupts the central command centers of the brain that control temperature regulation and that leads you to be slightly hypothermic so if you then go get into a very cold lake or you get into even a cold shower or an ice bath there's the possibility of you going very very far down the ladder into very hypothermic territory and that can be very dangerous now in terms of dealing with hangover when the alcohol has been largely cleared from your system well that's where some of this kind of old lore combines with some of the modern science and says well if you can spike adrenaline and certainly getting into an ice bath or getting into a cold shower or any kind of cold body of water provided you can do that safely that will sharply increase your adrenaline and I should say you're dopamine that's been shown and we've talked about this on the podcast before you get these long extended increases several hours of increases in dopamine from deliberate cold exposure it's well documented in humans by the way so one could imagine using deliberate cold exposure as a way to accelerate the recovery from hangover provided that's done safely I think there's no reason to not explore that and if you're wonder what safely is and what temperatures to use please check out the episode on deliberate cold exposure cold showers therefore might actually be one way to at least partially relieve hangover certainly the science from various places in the literature converge to say that but again be careful please be careful not to get into cold water when you are inebriated it's absolutely dangerous for all the obvious reasons and it's dangerous also for the non obvious reasons not the least of which is the dramatic decreases in corbati temperature that can make you dangerously hypothermic now how would you go about using deliberate cold exposure to accelerate recovery from hangover well there I would look to the kind of standard protocols of you know one to three minutes or maybe even six minutes if you can tolerate or if you're really cold adapted you do seven or 10 minutes in a cold shower although that could be a lot most people are going to experience a sharp increase in epinephrine and adrenaline and a long lasting increase in dopamine from one to three minutes of deliberate cold exposure ideally done immersion up to the neck again do this safely please please please or a cold shower where you're getting under the showers much as possible how cold well that's going to vary person to person I suggest making it as cold as is uncomfortable such that you really want to get out but you know you can stay in safely without for instance giving yourself a heart attack because if the water is really really cold of course you give yourself a heart attack most showers won't go that cold although probably some will again please use caution spike your adrenaline spike your dopamine with deliberate cold exposure safely other components of hangover that could be good targets for trying to alleviate hangover and here I hope you are getting the picture because it is accurate to say that hangover is a multi faceted phenomenon it's not like one molecule and one receptor it's a bunch of things happening in the brain and body but is the dehydration associated with alcohol alcohol is a diuretic for multiple reasons it causes people to excrete not only water but also sodium sodium is an electrolyte critical for the function of neurons so making sure that you have enough sodium potassium and magnesium so called electrolytes is going to be important for proper brain function body organ function even for people that just had one or two drinks the night before it's likely that your electrolyte balance and your fluid balance is going to be disrupting that's because alcohol also disrupts the so called vasopressin pathway I talked a lot about vasopressin in the way that it interacts with and controls different aspects of water retention and water release from the body in the form of urine in the episode on salt so you again I'm referring to Huberman lab calm as the site where you can find that episode on salt balance and waste to restore electrolyte balance having your electrolytes at the proper levels before you drink as ideal some people will say for every glass of alcohol that you drink you should drink one glass of water I would say better would be two glasses of water given the dehydrating effects of alcohol and even better would be water with electrolytes that certainly would set you up for a better day the next day and if you don't manage to do that I suppose it's kind of geeky walking around with electrolyte packets out at the bar or what not although you know geeky my book is a good thing the next day you could take some electrolytes upon waking maybe even some before you go to sleep at the night of drinking so hangovers made worse by disturbed sleep made worse by disrupted got my bio made worse by disrupted electrolytes made worse by the depletion of epinephrine and dopamine that's why replenishing the microbiome with fermented foods low sugar for menta foods that is that's why using safe deliberate cold exposure for spiking adrenaline and for increasing dopamine and that's why consuming electrolytes are all going to be beneficial the folks over at examine dot com a website that I really like because it just has so much useful information have assembled a list of things that have been proposed purported to improve or I should say to remove the effects of hangover and as they point out and I would like to point out over there isn't a lot of quality science to support the idea that any one compound can eliminate hangover and that's probably because hangover again arises from multiple organs and tissues and systems in both the brain and body nonetheless they have a terrific list over there of things everything from Japanese pear fruit juice has been proposed to do this to some other really esoteric things even things like you know him buying frankly when I look at the literature there and elsewhere one simply cannot find the magic substance the one herb the one potion that can wipe away hangover getting rid of hangover is going to be best solved by doing a collection of a small number of very powerful things which I've already listed off a few however there are some additional things that one can do for relieving hangover and one of them is to be very thoughtful about what sorts of alcohol one consumes so I find this interesting there have actually been studies of which types of alcohol lead to the greatest hangover hangovers there's actually a lot of legend and lore about this as well some people have said for instance that drinks that have a high sugar content lead to greater hangovers turns out that's not the case or at least that's not with the science points to if you look at the expected hangover severity what you find is that at the bottom end of the scale there's a drink that I'm not going to tell you for the moment but what you find is that near it is for instance beer the consumption of beer provided it is not over consumption right it's not far beyond the tolerance of the individual says one or two beers is less likely to cause a hangover then say whiskey and a glass of whiskey or I should not it's much whiskey is beer of course but the glass of whiskey for instance is more likely to cause hangover then gin is it turns out again this is what's fallen out of the data and yet a glass of rum or red wine is more likely to cause a hangover than any of the other things I've mentioned so far at the top top top of the list of drinks that induce hangover is brandy and one could then say well doesn't brandy have a lot of sugar maybe it's the sugar that's causing hangovers and this is something that's been again discussed over and over that people say oh it's the high sugar drinks that cause hangover turns out however that when one looks at drinks I'll call it drinks and sugar content and hangover at the very bottom of the list is gosh this makes me cringe just to think about is ethanol diluted in orange juice can't believe people actually drink this but ethanol diluted in orange juice so this is not vodka in orange juice okay vodka was third on the list from the bottom of drinks that induce hangover again this is within amounts that are comfortable for the person to drink that they have enough experience with or that they have the body weight to tolerate without getting very very drunk so the point is that if it were sugar that's causing hangover well then the ethanol diluted in orange juice would probably be at the top of the list in terms of inducing hangover but it's not it's at the bottom of the list and brandy is at the top of the list so what you find is that what scales from ethanol diluted in orange juice to beer to vodka to gin here I'm ascending the hierarchy of things that cause hangover gin white wine whiskey rum red wine and then brandy at the peak it's sort of the world heavyweight champion of hangover inducing drinks well what's increasing our congeners within those drinks congeners are things like nitrites and other substances that give alcohol it's distinctive flavor and that also lead to some of the inebriating effects of alcohol now then you ask okay well what is it that these congeners are doing and what are these nitrites doing and guess what while they do have effects on the brain and on other tissues their main effects are to disrupt the gut microbiome so what this points to again is that having a healthy gut microbiome and perhaps ensuring that you bolster your gut microbiome the day after drinking is going to be especially important for warding off hangover at least reducing the effects of hangover or the symptoms of hangover or both I would love to see a study on this I could imagine designing the study myself although this isn't really the sorts of things my laboratory does but you imagine some people getting probiotic and prebiotic some regularly some just after drinking or low sugar fermented foods and see what the effects are in terms of subjective effects of hangover but also some physiological measures I think the way to think about hangover overall is that again it represents a multi-faceted multi organ multi tissue phenomenon and the best way to deal with it is as a multi cell multi tissue multi chemical phenomenon and before I listed off some of the things that one could do in order to adjust hangover again the one that comes out at the top of that list I believe it's based on my read of the data is to support the gut microbiome and certainly not to ingest more alcohol and I suppose if we were to get really honest with one another and ask what's the best way to avoid a hangover it would be to not drink in the first place so we've covered the major effects of alcohol that lead to this state that we call drunkenness or inebriation again there's a range there you can be tipsy people can be blackout drunk people can be passed out drunk we've also talked about hangover and the fact that it's a multi faceted phenomenon and recovery from hangover involves a multi faceted approach next I want to talk about tolerance tolerance alcohol is a very interesting phenomenon it has roots mainly in the brain and in brain systems there's not time in the world let alone within this podcast to get into all the aspects of tolerance there are more than ten different types of tolerance there's functional tolerance chronic tolerance rapid tolerance there's metabolic tolerance there's psychological tolerance let's keep it simple for sake of today's discussion and for those of you that are interested in learning about all the different types of tolerance and aspects of tolerance there's an excellent review we will provide a link to this this was published in 2021 so it's pretty recent in the journal pharmacology about chemistry and behavior insanely or not so insanely that was the first journal I ever published in so I have a particular affection for that journal nonetheless it is called tolerance to alcohol a critical yet understudied factor in alcohol addiction and while this paper does include alcohol addiction in the title it's not just about alcohol addiction here's the basic summary of what tolerance is first of all tolerance refers to the reduced effects of alcohol with repeated exposure and it is caused mainly by changes in neurotransmitter systems in the brain that are the direct consequence of the toxicity of alcohol that aldehyde molecule that we talked about before there's enormous number of chemicals that change with repeated exposure to acetyl aldehyde everything from GABA to dopamine to serotonin second messenger systems a denocene and on and on rather than going to each of those in detail I just want to talk about the contour of the reinforcing and the tolerance inducing effects of alcohol what do I mean by that so here we are back to our old friend meaning the molecule that comes up over and over again in these podcast episodes which is dopamine whether or not somebody has a predisposition alcoholism or not whether or not their experience drinker or not when people initially start drinking there are increases in dopamine or what we call dopaminergic transmission dopamine is involved in motivation craving it creates a sense of well-being and increases energy typically only at the beginning of alcohol exposure that occurs in most people as a sharp spike as a increase again if somebody does not have alcohol dehydrogenase or has very low levels of the enzyme that convert that acetyl aldehyde in acetate and metabolize alcohol in other words they will feel sick and lousy in a way that will override any recognition of the dopamine release that the people that are listening to this and just think alcohol just makes me feel sick I don't like it okay that's a specific subcategory of people but most people experience some sort of mild euphoria that's why so many people drink right it the current estimates are that in most countries and certainly in the US as many as 80% of the adult legal drinking age population drinks alcohol and that number could be even higher now because in the last couple of years has been a trend towards increase alcohol consumption especially in the wake of the pandemic and during the pandemic topic for another time so there's an increase in dopamine and an increase in serotonin so it's kind of an increase in well-being and increase in mood but it's a very short-lived increase very soon after and actually triggered by that increase is a long and slow reduction in dopamine and serotonin and related molecules and circuits so basically what you're getting is a blip of feel good followed by a long slow arc of feeling not so great which is why typically people will drink again and again across the night the key thing to understand about tolerance is that with tolerance the duration of that long slow reduction in dopamine and serotonin gets even longer in other words the negative effects of alcohol that happen after the initial feeling good extend longer and in fact get more robust however there's also a reduction in the reinforcing properties of alcohol there's a shrinking of the feel good blip that happens when one first ingest alcohol and this has been measured in animals and humans so the first drink that somebody has provided they have enough alcohol dehydrogenase that doesn't make them feel nauseous and sick right away they feel really good and then as it wears off they feel kind of lousy and they want to drink more so they might drink more with each subsequent drink and even drinks on different nights or even different weeks the amount of dopamine that's released is reduced the amount of serotonin that's released is reduced so what you're getting is less and less of the reinforcing properties of alcohol the feel good stuff and more and more of the punishment pain signal aspects of alcohol this is the contour of chemical release in the brain that was referred to by my colleague the incredible doctor on a Lemke who's a medical doctor she wrote the incredible book dopamine nation she was a guest on this podcast on Joe Rogan's podcast on Rich Rolls podcast and several other podcasts world expert in addiction and she talked about this pleasure pain balance that extends beyond alcohol to things like sex and gambling and to other behaviors that can potentially become addictive but certainly includes alcohol so tolerance it seems is a process in which people are ingesting more and more alcohol as an attempt to get that feeling of well being back but what they're really getting is an extended period of punishment of pain and of malaise from the alcohol now you might say well how does that relate to tolerance what turns out what they do behaviorally and when I say they I mean animals do this in humans do this is they start drinking more and more in an attempt to activate those dopamine and serotonin neurons and receptors and as they do that there is an increase in alcohol dehydrogenase so the enzyme that metabolizes alcohol is increased because the body and liver have to contend with all that alcohol so now you've got again the two hit model you're getting less of the feel good chemicals more of the negative chemical release or pattern of subjective feeling I should say and you're metabolizing alcohol more quickly and more readily but it's not taking you to a better place in terms of how you feel that's one of the major underlying reasons for what we call tolerance so if you're somebody who drinks and you notice that the feeling that you are seeking with alcohol is now requiring an additional drink or drinks plural chances are you are disrupting the dopamine and serotonergic systems of your brain and you are doing that in a way that is increasing the pain and punishment signals that follow alcohol ingestion and again that's not just on the night that you're drinking but afterwards as well is that all bad news? Well pretty much but the good news is that if you abstain from drinking for some period of time then of course these systems reset how long you need to abstain will depend on how much you are drinking and how long you are drinking for certainly people who have alcohol use disorder or alcoholics their main goal should be to quit alcohol completely I know there's some debate about this and I don't want to get into that debate because I'm certainly not going to try and direct anyone's recovery their expert counselors and MDs and people who can work with people in fact for some very heavy drinkers and people with serious alcohol use disorder going cold turkey that is stopping drinking completely can actually be medically dangerous so the path to sobriety for certain people looks different than the path to sobriety for other people what I'm referring to here are people that are ingesting again somewhere between on average one to two drinks per night whether or not that's done night to night or whether or not that's condensed to weekend use I know a number of people are going to ask perhaps are screaming is drinking good for me in any way for instance many people have probably heard that respiratory is good for people that red wine is in rich and respiratory I hate to break it to you but the reality is that if indeed respiratory is good for us and there's some debate about this some people say strongly yes some people say no other people say maybe the amount of red wine that one would have to drink in order to get enough rest of our children order for it to be health promoting is so outrageously high that it would surely induce other negative effects that would offset the positive effects of rest of our so I wish I could tell you different again I'm not here to be the bear of bad news but the statement I just made was confirmed by Dr. Davidson Claire when he was a guest on this podcast confirmed by other researchers who work on respiratory and related pathways I wish I could tell you that red wine is good for your health and indeed it might be through some other mechanisms so for instance there have been studies of low to moderate red wine consumption this would be anywhere from one to four glasses per week and I don't mean enormous glasses I mean six ounce glasses of red wine and those cases some of the stress reduction that can be induced by consumption of red wine maybe some of the other micronutrients and components within red wines in particular red wines that come from particular grapes and this gets really nuanced and frankly is not well worked out in the peer reviewed literature certainly not clinical trials at least not that I'm aware of tell me if you're aware of a great clinical trial on this well there may be some positive effects of that very low level of consumption I'm not trying to take away anybody is red wine I'm not trying to take away anybody's anything I would be remiss however if I didn't tell you that rest's fairytrol as the argument for drinking and drinking red wine in particular is just not a good one it's just not supported by the peer reviewed research a few other things about alcohol and health beginning of the episode I referenced a study showing that indeed not just heavy alcohol consumption of 12 to 24 more drinks per week but also light to moderate alcohol consumption of any type wine beer spirits etc does reduce the thickness of the brain it really does reduce cortical thickness in fact and actually scales with the amount of alcohol that people drink and this has been well documented in a number of different studies I can provide a link to several of these one of the more striking ones actually shows that there's almost a dose dependent increase in shrinkage of the gray matter volume and in these white matter tracks these axons these wires that connect different neurons as a function of how much alcohol people drink and that's also what's been seen in this recent study that I referenced at the beginning and that's in the show note captions so again probably the best amount of alcohol to drink would be zero glasses per week or ounces per week for those of you drinking low amounts of alcohol make sure you're doing other things to promote your health and for those of you that are drinking moderate and certainly for those of you that are heavy drinkers please do everything you can to move away from that and to quit entirely but even for the moderate consumers of alcohol you are going to want to be aware of some of the negative health effects and do things to offset those if indeed you're not going to stop drinking or reduce your intake one of the really bad effects of alcohol but that's extremely well documented is the fact that alcohol because of this toxicity of acetyl aldehyde and related pathways can alter DNA methylation it can alter gene expression that can be many things in different tissues but it is associated with a significant increase in cancer risk in particular breast cancer and in particular because breast tissue is present in both males and females but in women it's especially vulnerable to some of the DNA methylation changes well breast cancer and women has a relationship to alcohol intake and alcohol intake has a relationship to breast cancer and women in fact there has been proposed to be anywhere from 4 to 13% increase in risk of breast cancer for every 10 grams of alcohol consumed how much is 10 grams well there we need to think a little bit about the variation in the amount of alcohol and different drinks across the world different countries serve different size drinks and have different concentrations of alcohol and those drinks without going down too much of a rabbit hole and just giving you some good rules of thumb to work with there have been studies of the percentage of alcohol including different drinks and the sizes of different drinks that are served in different countries and here's a kind of a patchwork of those findings in Japan one beer one glass of wine or one shot of liquor as it served there tends to include anywhere from 7 to 8 grams of alcohol in the US one beer which generally is 12 ounces if it's in a bottle one glass of wine or shot of liquor tends to include about 10 to 12 grams of alcohol and in Russia one drink of the very source that I just described typically will have as much as 24 grams of alcohol because of the differences in the concentration of alcohols and the sizes of drinks that are poured in these different countries of course there are other countries in the world those countries are also vitally important but those are the ones that extracted from the studies that I could find what does this mean well what we're talking about is that for every 10 grams of alcohol consumed so that's one beer in the US maybe a little bit more than one beer in Japan or basically a third of a drink in Russia there's a 4 to 13% increase in risk of cancer that's pretty outrageous right and you might think wait how could it be that you know this stuff is even legal well look it's as I described before it's a toxin it's also a toxin that people enjoy the effects of I mean in the US at least they tried prohibition that certainly did lead yes did lead to a reduction in alcohol induced health disorders in particular cirrhosis of the liver it also led to a lot of crime because it became a substance that a lot of people still wanted and that people were willing to break the law in order to provide or I should say to sell and provide but the point is that the more alcohol people drink the greater their increase of cancer in particular breast cancer and that's because of the fact that alcohol has these effects on cells that include changes in gene expression and cancer that is the growth of tumors is a dysregulation in cell cycles right a tumor is a aggregation or the proliferation aggregation is stuff sticking together by the way proliferation is stuff duplicating proliferation aggregation of cells that could be a gliomas gliocels glioma brain tumor right could be lymphoma so within the lymph tissue etc. the mutations that alcohol induces to cause this are wide ranging some of those are starting to start to be understood for those of you that are interested in cell biology I'll just mention that the PD1 pathway again this is super specializing for the aficionados only you don't need to know this the PD1 pathway seems to be up regulated and we knew this from the discussion earlier there's a down regulation in some of the anti-inflammatory molecules that help suppress this proliferation of cancers nowadays there's a lot of interest in the fact that the immune system is constantly combating cancers that exist in us all the time you know little little tumors start growing and our immune system goes and gobbles them up little tumor start growing the immune system senses inflammation sends out these incredible cells these killers B cells and T cells and beats them up cancers proliferate and take hold and cause serious problems when the proliferation of cells exceeds the immune system's ability to gobble up and remove those cells there are other mechanisms of regulating cancers but that's one of the primary one and alcohol hits it again it's a two hit model it increases tumor growth and it decreases the sorts of molecules that suppress and combat tumor growth so again even low to moderate amounts of alcohol can be problematic for sake of cancers in particular breast cancers epidemiologists and health specialists love to try and compare different substances in terms of how bad they are really do they compare substances in terms of how good they are but sometimes they do and what they'll sometimes tell you and what you can find in the literature is that ingesting 10 to 15 grams of alcohol a day so that would be like one beer in the US one glass of wine is the same as smoking 10 cigarettes a day frankly it's hard to make that direct relationship really stick because you know it's a question of you know how long people inhale do they have a predisposition to a lung cancer etc but even if that number is off by plus or minus two cigarettes or even if that number with the equivalent of one glass of wine equals one cigarette per day I think there's general consensus now that nicotine consumed by vaping or by cigarette it's bad for us in terms of lung cancer and other forms of cancer and for some reason I don't know why because this knowledge about alcohol and cancer and these established relationships have been known since the late 1980s the first you know landmark paper on this was published in 1987 I can provide a link to that paper it's actually quite interesting to read well the relationship is there and yet we don't often hear about it right in fact in before researching this episode I'd heard before that alcohol can increase cancer risk but I wasn't aware of just how strong that relationship is because of the serious nature of what we're talking about and because I would hate to be confusing or misleading to anybody I wanted you to emphasize that this statistic that there is a 4 to 13% depending on which study you look at a 4 to 13% increase in the risk of cancer in particular breast cancer for every 10 grams of alcohol consumed that's 10 grams per day so that's one drink per day but I do want to emphasize that if that equates to 7 drinks per week and all those 7 drinks are being consumed on Friday and Saturday it still averages to 10 grams per day and I also want to emphasize that there are things that people can do to at least partially offset some of the negative effects of alcohol as it relates to predisposition to the formation of certain kinds of tumors and cancers I also want to be clear before I say it that doing the things I'm about to tell you is not a guarantee that you're not going to get cancer nor is it a guarantee that alcohol is not going to lead to an increased predisposition for certain kinds of cancers and the two things are consumption of folate and other B vitamins especially B12 you know the consumption of folate and B12 has been shown to decrease cancer risk in people that ingest alcohol but not completely offset it why that is isn't exactly clear it probably has something to do with the relationship between folate and B12 and other B vitamins in gene regulation pathways that can lead to tumor growth at some point soon we will get an expert in cancer biology and in particular in breast cancer biology on the program and we can ask them about this but I realize this is going to raise a number of questions and maybe even cause some of you to go out there and start taking folate and other B vitamins and B12 not incidentally a lot of the reported hangover supplements and treatments have include folate and B12 I don't know if they had the cancer literature in mind when they created those supplements and products I doubt they did alcohol really does disrupt B vitamin pathways both synthesis pathways and utilization pathways so sometimes you'll hear oh you know if you get your B vitamins it helps you recover from from hangover more quickly again the literature doesn't support that but also again there are a lot of studies but more to the point as it relates to alcohol and the formation of tumors and cancers it does appear that decreased folate and other B vitamins like B12 are partially responsible for the effective alcohol and increasing cancer risk and it does appear that consuming adequate amounts of folate in B12 might again might partially really want a bold face and underline and highlight partially offset some of that increased risk there's an additional category that I want to highlight of course and this is vitally important to state even though it's obvious which is that people who are pregnant should absolutely not consume alcohol fetal alcohol syndrome is well known and established it's terrible fetuses experience diminished brain development that's often permanent diminished limb development diminished organ development in the periphery meaning you know the heart the lungs deliver etc ingesting alcohol while pregnant is simply a bad idea and the reason I say this at all is first of all it's important to include in an episode like this but also because we can look at two things first of all we can look at mechanism and then we can also look at some of the lore that still sadly exists out there let's take care of the lore that sadly exists first if you look online you will sometimes be able to find sadly that some people believe that certain kinds of alcohol are not detrimental to fetuses they'll say well champagne is safe for a pregnant mother to drink but beer is not that is absolutely categorically false alcohol is alcohol there is no evidence whatsoever that consuming certain types of alcohol is safer for fetuses than others alcohol is a toxin and the reason fetal alcohol syndrome exists is because the ability of that toxin to disrupt cellular processes remember tumor growth and the way that alcohol can accelerate tumor growth by proliferation of cells the wrong cells the ones you don't want to proliferate well all of embryonic development all of fetal development it's not the growth of a tumor it's obviously the growth of an embryo and it's done in a very orchestrated way I started off-studying brain development that's where I got my beginnings in neurobiology and I still teach embryology to medical students and graduate students the set of coordinated processes that has to take place from conception to birth in order to give rise to a healthy embryo is so so dynamically controlled and so exquisitely precise with checkpoints and recovery mechanisms and redundancy in the genes that are expressed to make sure that if anything goes wrong it's repaired etc alcohol as a mutagen I haven't used that word yet but a substance that can mutate DNA through alterations in DNA methylation and these checkpoints in the cell cycle alcohol as a mutagen is one of the worst things that a developing embryo can be exposed to and again because it's water soluble and fat soluble and gestion of alcohol when people are pregnant passes right to the fetus now I realize that a number of people out there might be thinking oh goodness you know I didn't realize I was pregnant until a certain stage of pregnancy and before I realized I was ingesting alcohol obviously one can't undo what's been done but I want to also emphasize that fetal alcohol syndrome while yes there's a full blown syndrome that manifests as changes in the cranioffatial development that are very obvious and you can look these up you've probably seen these before the pictures before rather has to do with eye spacing forehead size a number of other features of the cranioffatial development and of course stuff's going on in the brain too it's along a continuum so it is possible that some of the changes that occur are more minor and thankfully the young brain in particular the early postnatal brain is incredibly plastic there are things that can be done in order to help recover neural circuits that didn't develop well etc but even though it's somewhat obvious or should be obvious I really want to make clear that there's zero evidence whatsoever that certain forms of alcohol are safer for pregnant women to ingest another is absolutely wrong no one who's pregnant should be ingesting alcohol whatsoever and certainly if people feel like they can't avoid alcohol while pregnant they really need to work with somebody to make sure that it just absolutely doesn't happen because it's so detrimental to the developing fetus lastly I want to talk about the effects of alcohol on hormones and I want to distinguish between low amounts of alcohol intake, higher amounts of alcohol intake and again this chronic alcohol intake versus occasional use versus really chronic use meaning alcoholic or alcoholic use disorder where people are drinking an immense amount on an ongoing basis the literature on alcohol and hormones is quite extensive and there are of course many many different types of hormones the hormones that most often get mentioned and talked about on this podcast are the hormones testosterone and estrogen which are present both men and women that in both men and women are important for things like libido libido they're also responsible for sexual development actual development of the genitalia before birth and after birth they're responsible for instance estrogen is important for memory and cognition you never want to drop estrogen to low in men or women because it can disrupt cognition and joint health etc to keep this discussion relatively constrained it's fair to say that alcohol and in particular the toxic metabolites of alcohol increase the conversion of testosterone to estrogen now this occurs in a number of different tissues this is not just occurring in the testes of males this is occurring in lots of different tissues and I'll refer you to an excellent review we'll provide a link in the show note captions this is a paper that was published in the year 2000 but the data are still quite strong the journal is called of all things alcohol there's yes literally a journal called alcohol for the publication of data and reviews on alcohol and its effects and the title of the paper is can alcohol promote a romanticization of androgens to estrogens aromatization is this process of the conversion of testosterone and other antigens to estrogens through things like aromatase enzyme and this is a beautiful review that describes every tissue or near every tissue from the ovary and females to the placenta to the liver to the testes in which alcohol can increase the aromatization of testosterone to estrogen now in females this may be part of the reason why there's an increase in estrogen related cancers breast cancer can be either estrogen related or non estrogen related there are other types of estrogen related cancers outside of breast cancer but it appears that one reason why alcohol increases the risk of breast cancer is because of the seromatization from of testosterone excuse me to estrogen in males accelerated or abnormal conversion of testosterone to estrogen can actually lead to growth of the breast tissue in males so called gynacomastia or other effects of high estrogen or I should say of altered testosterone estrogen ratios because that's really what's important and these can include things like diminished sex drive increase fat storage and a number of other things that I think most people would find to be negative effects I once talked about the fact that drinking alcohol can increase the aromatization of testosterone to estrogen I posted that online and I didn't get attacked but I did get criticized for the fact that it has been shown yes has been shown that small amounts of alcohol ingestion so 5 grams or so of alcohol ingestions would be half a glass of wine or half a glass of beer at least in some studies showed increases in testosterone which was kind of surprising but I should point out other studies have shown that alcohol ingestion causes decreases in testosterone over time so there's always this issue whether not you're looking at study of acute exposure versus chronic exposure you know one dose versus multiple doses and exposure I think it's fair to say based on my read of the literature this review and other reviews that focus more particularly on humans that regular ingestion of alcohol is going to increase estrogen levels whether or not your male or female and it's largely doing that through the aromatization process by increasing the aromatase enzyme yes there's some dose dependence but I think if you're somebody who's trying to optimize your testosterone to estrogen ratio regardless of whether or not your male or female well then most certainly you're going to want to avoid drinking too much alcohol so we've covered a lot of topics and data related to the mechanisms of alcohol hangover tolerance cancer risk etc. I acknowledge that I've mainly talked to you about the negative effects of alcohol I want to acknowledge that many people enjoy alcohol in moderation or even light drinking the occasional drink or the occasional two drinks or maybe even on average one drink per night so seven drinks per week I'm certainly not here to tell you what to do and what not to do I do find it immensely interesting however that first of all alcohol is a known toxin to the cells of the body some of you might immediately say well wait what about hormesis what about this phenomenon where if we regularly ingest a toxin it makes us stronger in other words what doesn't kill us makes us stronger there's you know some reason to believe that might be beneficial in terms of some forms of cellular resilience maybe maybe no sorry it doesn't work that way there are processes of hormesis in which for instance exposing yourself safely to increases adrenaline through you know ice baths or other things that increase adrenaline can raise your so-called stress threshold but here we're talking about cellular stress and damage to cells so my read of the literature and again this is my read and I invite others to you know provide studies or I would prefer actually collections of studies that point in the direction if they exist that alcohol can be beneficial but my read of the literature where I should say my understanding of what I would call the center of mass of the literature on alcohol is that no consumption zero consumption consumption of zero ounces of alcohol is going to be better for your health than low to moderate consumption of alcohol and that low to moderate consumption of alcohol is going to be better for you of course then moderately high to high alcohol consumption on the order of 12 to 24 or more drinks per week I realize that for most people listening to this it's probably low to moderate alcohol consumption that is part of their standard repertoire and I'm not here to give you justification for doing that nor am I going to tell you not to do that I would like you to consider perhaps however the negative effects that we understand and that are documented for instance the negative effects of alcohol and the gut microbiome and the things that you can do to better support your gut microbiome the negative effects on the stress system that HPA access that we talked about earlier in the fact that even low to moderate levels of alcohol consumption can increase our levels of stress when we're not drinking and to think about acquiring some tools and you know getting some proficiency with tools behavioral or otherwise that can help you with stressed modulation that don't involve alcohol consumption again the point here is to illustrate where the problems lie with alcohol consumption but also what I've tried to do is to point you to some resources that can help offset some of those negative effects will they offset all the effects I can't say that for sure but certainly taking measures to offset some of the negative effects of any alcohol consumption that you might be having or doing is going to be beneficial to you and those tools and protocols are going to be health promoting in any case if you're learning from and or enjoying this podcast please subscribe to our YouTube channel that's a terrific zero cost way to support us in addition please subscribe to the podcast on Spotify and on Apple and on both Spotify and Apple you can leave us up to a five star review if you have questions for us about the content covered on the podcast or suggestions of topics you'd like us to cover or guess that you'd like us to host on the Hubertman Lab podcast and we'll include all of that in the comment section on YouTube we do read all the comments please also check out the sponsors mentioned at the beginning of today's podcast and check out momentous supplements our new 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month and it is completely zero cost again just go to Hubertman Lab.com and go to the neural network newsletter I'd also like to point out that the Hubertman Lab podcast has a clips channel so these are brief clips anywhere from three to 10 minutes that encompass single concepts and actionable protocols related to sleep to focus interviews with various guests we talk about things like caffeine when to drink caffeine relative to sleep alcohol when and how and if anyone should ingest it relative to sleep dopamine serotonin mental health physical health and on and on all the things that relate to the topics most of interest to you you can find that easily by going to YouTube look for Hubertman Lab clips in the search area and we'll take you there subscribe and we are constantly updating those with new clips especially useful I believe for people that have missed some of the earlier episodes or you're still working through the back catalog of Hubertman Lab podcasts which admittedly can be rather long and last but certainly not least thank you for your interest in science.