Sawbones 444: Grapefruits

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Clint: *Sawbones* is a show about medical history, and nothing the hosts say should be taken as medical advice or opinion. It's for fun. Can't you just have fun for an hour and not try to diagnose your mystery boil? We think you've earned it. Just sit back, relax, and enjoy a moment of distraction from that weird growth. You're worth it.

[theme music plays]

Justin: Hello everybody, and welcome to *Sawbones*: a marital tour of misguided medicine. I'm your cohost, Justin McElroy.

Sydnee: And I'm Sydnee McElroy.

Justin: And I'm so excited to be with you today, Syd. I'm excited to be with you every day.

Sydnee: Aww. Well, I'm—thank you.

Justin: I feel bad for our listeners. They only get a half hour with you. Or, you know, an hour if they're listening to *Still Buffering* and *Sawbones*. Or I guess if they're one of your clients that you work with, they could see you there...at Harmony House, I guess.

Sydnee: That's true. These are—

Justin: Or at the store. They could run into you at the store.

Sydnee: Yeah, that's true. Would you like to name some other place where [laughs quietly]—

Justin: I don't wanna further dox—

Sydnee: —people may talk with me?

Justin: —I don't want to further dox you, no.

Sydnee: I was gonna say. [laughs quietly]

Justin: [laughs quietly]

Sydnee: Do you wanna name, like, where our dentist is, and where I get my hair done while we're at it?

Justin: Our dentist just retired. Shout out to Judy. Um...

Sydnee: She's fine. She just retired.

Justin: I think I said she retired! [laughs]

Sydnee: Well, the way you said "shout out." [laughs]

Justin: Shout out? That's not like "In memoriam!"

Sydnee: I don't know. There was something weird about it. By the way, I didn't know. I was messing with the soundboard before we started. Is that right?

Justin: Oh, that's good to hear.

Sydnee: They're all up.

Justin: No, it's not right! Hold on. [sighs]

Sydnee: Okay.

Justin: Um, is that better? Okay, that seems good.

Sydnee: I don't know!

Justin: No, it's fine. Yeah. Okay.

Sydnee: I mean, I'm just in the room. I can't hear anything! I'm just talking. Um...Justin. [laughs quietly]

Justin: Sydnee!

Sydnee: Uh, we—

Justin: Can't get the heater to turn off! Please turn off!

Sydnee: No, I'm cold. We got an email from...it is loud, though. We got an email from one of our listeners, Isabelle—thank you, Isabelle—asking about grapefruits.

Justin: Oh, okay.

Sydnee: And I realized we have definitely referenced grapefruits, I believe in, like, a weird medical questions episode. But we've never done a whole thing on grapefruit, grapefruit juice, and its interaction with medicine specifically. That medical part of the grapefruit. And I also realized that in terms of the history, like, when did we, how did we, why do we know that grapefruit juice interacts with medicines? And that question really intrigued me. I mean, think about it. There's lots of foods and juices.

Justin: There's lots of juices.

Sydnee: How did we figure out specifically that grapefruit juice was a problem?

Justin: You ever had a hotel continental breakfast and they had, like, a wide array of juices? And in that context, even though you don't drink juice ever, in that context when they have the little glasses you're like, "God, that'd be good. God that little glass of grape juice right now, that'd go down so smooth."

Sydnee: Not me. I've never been a big juice drinker, and then as I've gotten older I've developed acid reflux, so I definitely stay away from fruit juices.

Justin: Right, right.

Sydnee: I prefer my fruits in their original, like, fruit form, personally. As opposed to—

Justin: You like all the fiber and the gunk.

Sydnee: Yeah. I like to bite into an apple. I don't want to drink its juice. Well, I mean, I am drinking its juice. But, like, in the—I'm gonna eat its flesh and drink its juice all at once. I like fruit that way. But that's fine. If you're into juice, I'm not... [laughs] I'm not gonna give you a hard time.

Justin: There's no shame if you're into juice.

Sydnee: But if you are into grapefruit juice—

Justin: Which was the name of Randy Moss's juice chain that he opened at the Charleston Town Center. Into Juice.

Sydnee: I don't think it was that.

Justin: It was Inta Juice.

Sydnee: Oh, Inta Juice. I thought you meant there's no shame if you're into juice.

Justin: No. It's just Inta Juice. Maybe the full—[wheezes] the full, unabbreviated title is "There's no shame if you're into juice." But no, it's just Inta Juice.

Sydnee: But I will say that if you are into grapefruit juice, there are some things you should know.

Justin: Okay?

Sydnee: Uh...

Justin: It's bitter.

Sydnee: Yes.

Justin: Not very good to drink. Is that part of your work?

Sydnee: Well, I feel like we should put the disclaimer out there, because this is—Justin and I don't have a lot of the same food preferences, but we agree on two things. We don't like olives...

Justin: Ugh.

Sydnee: ...and this is no—again, no shade if you do. That's great. More olives for you, 'cause we're not eatin' 'em.

Justin: That's right, that's right.

Sydnee: And we don't like grapefruit.

Justin: Sorry, guys. I've tried. I've tried. Grapefruit is one that I've, like, tried many times.

Sydnee: I like bitter. I drink IPAs. I like the bitter flavor profile. You'd think I would like grapefruit. Just don't like it. Don't like it. Anyway—and boy, my mom was of the generation where grapefruit was huge, you know? A half a grapefruit for breakfast in the morning was like...

Justin: It was a thing.

Sydnee: The thing.

Justin: I remember that being a big `80s thing. My mom did it too.

Sydnee: I learned about grapefruit a lot more in medical school in the context of the way that it can interfere with certain medications, and you may know this because you may have been told at some point by a doctor or pharmacist or somebody prescribing you a medication that "Hey, FYI, don't drink grapefruit juice while you're taking this."

And if you're like me you're like, "No worries there."

Justin: I, uh—yeah. I remember I found out about it from you, because I was, I don't know, I was into some health thing, and I had read that grapefruit juice would, like, help with, I don't know...I don't know what it is. You probably know. Metabolism or something.

And, um, you told me not—that I should be careful with it, 'cause it could mess up my brain pills. And it's like, I don't like grapefruit juice anyway, and I'm gonna be sad about eating grapefruit juice. And also my brain pills won't work, so I'll be even sadder about this grapefruit juice. I could get pretty despondent about the grapefruit juice. I don't know!

Sydnee: It's actually the other way around.

Justin: Oh. So I'd get, like...

Sydnee: It'd be too high.

Justin: Too anxious about the grapefruit juice.

Sydnee: So, this is the thing. When I learned about grapefruit juice, I—you learn about lots of interactions and once-offs and things that can happen in medicine. And then as you start practicing, sometimes you learn that, like, that almost never happens. Like [laughs] 99% of the time, the patient's gonna do that thing, and everything will be fine, and it's pretty rare.

Grapefruit was one of the things that I thought was, like, this esoteric kind of board question fact. And then I had an actual—I knew someone, it actually wasn't my patient, but I knew someone who actually had this problem and was discussing with me. They were on Wellbutrin, they were taking their Wellbutrin, and all of a sudden, they just started having these weird symptoms. Like, they were tired and, like, out of it, and dizzy, and they didn't know what was going on, and we were going through all these different things. They were just kind of talking to me. Like, "You're a doctor, you know things."

And I finally—and finally they said "The only thing I've been doing different is I started drinking a glass of grapefruit juice every morning because I read a book that said I should."

And I was like, "Oh my gosh! I know it!"

Justin: It's like a board question that they laid it out like that.

Sydnee: Mm-hmm.

Justin: It's like a very easy *House* mystery. [wheeze]

Sydnee: It was. And so they stopped it, and a couple days later...one to three days is usually how long it takes...doing better. So, anyway.

Justin: I bet they were relieved to have an excuse to not drink grapefruit juice anymore.

Sydnee: It's great when you can solve something like that. I had somebody who was worried 'cause their armpits had turned brown, and it was their deodorant. I told 'em to change deodorants and tell me what happened, and it changed.

Justin: Hm!

Sydnee: Yeah. It's always very exciting when these things are easy to solve. So, what's the deal? We take medications, but obviously they don't stay in our bodies forever, right?

Justin: Right.

Sydnee: That's why you take a pill daily, twice a day, three times a day, whatever. Like, different—you take them in different dosing intervals. Some are weekly, monthly.

Justin: Your body starts processing them, and...

Sydnee: You break 'em down. Otherwise you would just continue to add to that medication to your body and, I mean, eventually it would be toxic. So something in your body is breaking them down. One of the enzymes responsible for breaking down medications, a lot of medications, a lot of different drugs that can be prescribed, is called CYP3A4.

Justin: Mmm, classic.

Sydnee: And that is—it's part of the cytochrome P450 family of proteins.

Justin: Choice.

Sydnee: These are enzymes that will oxidize foreign molecules. They live in your liver and in your intestine. And collectively the P450 family metabolizes 60% of all of prescribed drugs.

Justin: Wow.

Sydnee: And specifically this one, CYP3A4. C-Y-P-3-A-4. I'm gonna say CYP3A4 for simplicity.

Justin: Yeah, good. It's like a cool nickname.

Sydnee: CYP3A4 is responsible for half of that. So...it's the—it's the one. It's the reason that you have to keep taking pills, and also that stuff doesn't just accumulate in your body forever.

Justin: What if we could take a pill that would get rid of those? Wouldn't that be nice. You'd just have to take one pill and never think about it again.

Sydnee: Well, you're kind of bumping up against what happens. [laughs]

Justin: Uh-oh!

Sydnee: By the way, enzymes, in case—I realized I was talking about enzymes. Do you know what enzymes are?

[pause]

Do you have an idea, a concept of what an enzyme is?

Justin: Honey? Look at me in the eyes. Not—

Sydnee: [laughs]

Justin: [laughs] Not a single inkling of what an enzyme is. I could guess for a hundred years and not get anywhere close.

Sydnee: It is something in your body, usually a protein—typically these are proteins—and they catalyze reactions. They make things happen faster. They make—there are tons of chemical reactions constantly happening in your body all the time, right? That's what keeps you alive. All of these reactions shifting back and forth. If they all reached equilibrium at once, you...you'd die.

Justin: Okay, so good. So we're—we're...

Sydnee: So anyway, they catalyze reactions. And—

Justin: We're hot on reactions. We like reactions. We stan.

Sydnee: And lots of things are involved in chemical reactions. There are lots of co-factors and things that are in there. But the thing that characterizes an enzyme is that it will be used over and over again and is not destroyed. So it's like—it's just something that lives in there, and its job is to be like "Oh, look! There's something to break down. I'm here, doot-doo-doo!" And then it breaks it down.

Justin: So I'm kind of an enz—I'm like an enzyme of the podcasting world. You bring me on the world, I sparkle instantly, glitter shoots out my fingertips, and the whole show is... calidicized.

Sydnee: Catalyzed, mm-hmm.

Justin: If I may, catali—catalyzed. Cata—catalyzed?

Sydnee: Catalyzed, mm-hmm.

Justin: Catalyzed. And I can't be destroyed. [laughs quietly] I can—I can, uh...uh...I'm—I'm—I'm an enzyme.

Sydnee: That's a heck of a thing to claim.

Justin: [simultaneously] Podcasting enzyme.

Sydnee: "I can't be destroyed." So this enzyme—

Justin: [unintelligible]

Sydnee: [laughs] —breaks down—that's its job. It's to catalyze and break down a lot of drugs, okay? For the most part. Um, the thing is, so there are stuff that is broken down, that is metabolized by this enzyme. But there's also stuff that can change the activity of the enzyme, kind of like you said. What if something could stop it? What if something could stop it? So if you put something in the body—

Justin: My internet—my internet drops, for example, and I can't be on the podcast anymore.

Sydnee: Yes.

Justin: So the enzyme of me is gone.

Sydnee: There we go. This is gonna be a rough—to just continue this—

Justin: I actually think—

Sydnee: [simultaneously] We'll see if we can get there.

Justin: It felt like I was closing the book on it right there. It felt like a nice closure point.

Sydnee: So if you put something in the body that will block CYP3A4, [it's not going to...break down the drugs.

Justin: Okay, good.

Sydnee: So they'll just stay in there.

Justin: Bad, I'm guessing.

Sydnee: And if you keep taking them, instead of, you know, you take something, the amount of it in your bloodstream peaks and then starts dropping off as its broken down, right? Well, if it's not broken down and then you put more on top of it, and then you put more on top of it, and then you put more on top of it...you see where I'm going. You can get sick. Okay? So there's stuff that you can put in your body that will either block that enzyme, or there are other things that will turn it up and make it work faster and more. So instead of you building up—

Justin: [simultaneously] Caffeine.

Sydnee: —really high levels...[laughs quietly] No, no, no. Really high levels—

Justin: For me.

Sydnee: —of the drug...you would actually decrease the amount of drug in your body that's working, because it's breaking it down so much faster.

Justin: Okay. You're burning through it.

Sydnee: Yes. There are a lot of things that inhibit this enzyme. There are a lot of things that activate this enzyme. And this is at the root of a lot of, like—when we start talking about how two drugs can interact, this isn't the only thing that can cause that, but this is at the root of some of those interactions.

If I tell you like, "Oh, since you're on this medication it wouldn't be safe to start this one." This might be why, because of the way those two drugs interact with this system. If one of them is broken down by that and the other inhibits or activates the enzyme that does it, you can see how all that

would—does that make sense? I know there's a lot of different substances at play here that are doing different things that all interact with each other.

Um, this is also at the root of things we worry about outside of drugs. 'Cause, like, if we're talking about prescription drugs, ideally the same person, or at least people who are communicating with each other, would be prescribing all the medicines you're on, right? So nobody would be prescribing you something without knowing other things that you're taking. And so they would be able to, you know, account for this, and not make those mistakes.

Justin: But they may not know if it's something that's just random out in the world.

Sydnee: A food, a supplement. This is why it's so important.

Justin: A juice, perhaps!

Sydnee: A juice. This is why it's so important to tell your provider if you're taking, like, herbs or supplements or anything like that. Over-the-counter meds. Um, or if you have a major change in, like, your dietary habits. Because...it might interact with the medicine you're on.

Justin: Doctors do not have time for me to sit there and be like, "So, I hit up Teriyaki Express and got my won tons."

Sydnee: I don't mean everything. [laughs]

Justin: [laughs] Anyway, where's that bring me? Okay, Tuesday at 3 PM. I actually don't need to be like, "Yeah. And it was like, I went to the sneaky trip to the Long John Silvers and got some crunchies and chicken tenders." I don't need that. I don't need the judgment.

Sydnee: So, here's the thing. What we have covered here are that there are a huge list of drugs and supplements and foods that can inhibit CYP3A4. There is a huge list. And when I say huge—I shouldn't say huge. It's not something I can list on the show. That would be the whole show. If I listed all of these. There's three different lists.

Justin: [simultaneously] That sounds huge.

Sydnee: There's a list of blockers, there's a list of activators, and then there's the list of drugs that are broken down by CYP3A4 so the blockers and the activators will have an impact on, right?

Justin: Yeah.

Sydnee: All of these lists are available easily online. If you Google, like, what inhibits this. What does grapefruit interact with? These are easily—and if you're not sure, this is always why when it comes to prescription medicines or any sort of other supplements, whatever, that you're putting in your body, talk to your provider—

Justin: To WebMD and...

Sydnee: No. [laughs quietly] Talk to your provider about all these things so that you aren't in a situation where you're getting sick and you don't know why and it's easily fixable by just stopping one of the things that you're taking. Um, so that's—it's all available. I'm not gonna read every single medicine. There's tons of them, okay? And this isn't the only sort of reason why you might have an interaction. For instance...so, grapefruit juice can block this enzyme, which will increase the blood levels of medicines you take that are broken down by the enzyme. Well, grapefruit juice also can interact with certain proteins called drug transporters, which you can imagine what they do.

Justin: Transport drugs!

Sydnee: They transport drugs, specifically into your cells so that you use them. Well, if it interferes with them, it may actually decrease the effect of the medicine in your body. [laughs quietly]

Justin: Dang! I can't catch a break!

Sydnee: So grapefruit juice is gonna increase the effect of some medicines, and decrease the effect of other medicines. We know what ones, though. So

it's really easy to ask the question, is grapefruit—can I have grapefruit? Does grapefruit interfere with anything I'm taking?

Justin: We're talking a lot about grapefruit juice, but do we also mean just straight grapefruit, or...

Sydnee: Yeah, I mean, it's just grapefruit.

Justin: Yeah.

Sydnee: Yeah, grapefruit. Um—

Justin: I know there's the same thing. I just meant, like, I didn't know—I guess now that—I feel a little silly. [crosstalk]

Sydnee: [laughs] You just need to be carefable—carefable.

Justin: One more time? [snorts]

Sydnee: [laughs quietly] About the ingestion of grapefruit.

Justin: I always am! I knew that instinctively. My body was saying, like, "This isn't good for you, Justin."

Sydnee: Be carefable.

Justin: Be carefable with this bitter juice.

Sydnee: And on top of all that, it's different in different people depending on how much enzyme you have. So for some people a little grape juice wouldn't hurt them, but a lot would. Some people can tolerate more.

Justin: Grapefruit juice.

Sydnee: Yeah, grapefruit juice.

Justin: You said grape juice. I didn't know—do we need to need to be careful about—

Sydnee: Oh, sorry. Grapefruit juice. No, not grapes. Grapefruit.

Justin: Okay.

Sydnee: We're all over the place here. Um, your age, what other, you know, again, medicines you take, what comorbidities you might have. All of that comes into play. And in some cases it can take a very small amount, a very small amount of grapefruit juice can throw off the medicines you're taking. So it can have a huge impact. Um, how did we figure this out? So that's the story.

Justin: [simultaneously] I don't know!

Sydnee: That's why we tell you. That's what you need to know about. If you're on meds and you've never bothered to ask or to look it up, or if you have concerns, please ask about the medicines you may be on. Um, but how do we figure this all out? I want to tell you that. But first, we gotta go to the billing department.

Justin: Let's go!

[ad break]

Justin: So, Syd, how did we start to unravel this grapefruit mystery.

Sydnee: Okay. I found a great article from Atlas Obscura that interviewed the guy who figured this out, and I thought that was a great source. It's by Dan Nosowitz from 2020. And it's a great article just about how weird grapefruit is, 'cause grapefruit's weird, right?

Justin: Mm-hmm.

Sydnee: Justin, why is it called grapefruit?

Justin: That's a great question that I have no idea.

Sydnee: Yeah, I thought that was a great place to start. So, okay. First of all, it's part of the citrus family, right?

Justin: Yes, it's in the orange, lemon lime...

Sydnee: Did you know there were probably originally three, like, primary citrus that all citrus have derived—been derived from?

Justin: No, I didn't know that Sydnee.

Sydnee: There was probably a citron, a pomelo, and a mandarin, and all other citrus fruits are just mixtures of various varieties of that. Right? Grapefruit is a pomelo, and a sweet orange. A sweet orange is a mixture of a pomelo and a mandarin, so work all that out. [laughs]

Justin: Okay.

Sydnee: Um, it was probably originally found in Barbados back in, like, the 1600's. It wasn't called grapefruit until the 1830's is the first mention of it as a grapefruit. Before that it was called the shaddock, the golden orange, or the forbidden fruit.

Justin: Oh my!

Sydnee: The forbidden fruit!

Justin: It's weird that we cultivated this. You know, we've used—for... [sighs] ages we've used genetic engineering to make our fruit more delicious, and make our fruit sweeter and more scrumptious to us. Like, we've genetically modified it to do that. It's weird that we kept chasing after this grapefruit thing, just thinking that it would get better eventually. Like, it's weird that we didn't say like, "Let's give up on grapefruit. It's not working. It still tastes bad. There's other fruits." Like, "Hey, everybody. We had a good run. Let's go home."

Sydnee: There are a lot of people who like grapefruit. It's a complex flavor profile.

Justin: They've learned to, for sure.

Sydnee: It's not just sweet, and then there are a lot of citrus fruits that are sweet and tart, of course. It's not just sweet and sour. There's bitter.

Justin: Yeah.

Sydnee: So it's all of that in there.

Justin: Yeah.

Sydnee: But there are people who like that, you know? So, like, it's not wild to think people would cultivate it, 'cause some people probably enjoy it. In fact I know people enjoy it. My mom very much loves grapefruit.

Justin: Yeah...

Sydnee: Why is it called grapefruit?

Justin: Does it grow in a bunch?

Sydnee: Well, that's what a lot of people thought. For a long time they were like, "Well, it probably was named that 'cause it grows in bunches like grapes. So, grapefruit." No, that's probably not why it was called that. Others have suggested, like, well, maybe it's because it tastes...like a grape?

[pause]

Sydnee: Which is a problem for a couple reasons.

Justin: [wheezes loudly] Let me say the first one. It doesn't.

Sydnee: Yeah, that's the first one.

Justin: At all.

Sydnee: Is that it does not taste like a grape.

Justin: No.

Sydnee: Also, it's kind of weird in that the grape is also a fruit, and so it'd be weird to be like, "Well, that's a grape, and that one tastes—" even if it did taste like a grape.

Justin: Imagine if a grape was a fruit, yeah.

Sydnee: It's a grapefruit.

Justin: Yeah.

Sydnee: Well, grape is a grape...fruit.

Justin: Grape is a grape fruit already, so it's not a good name.

Sydnee: But no, it's not that either. It also doesn't make geographic sense, because the people, when it was first named a grapefruit, the people who would've had access to it would not have also easily had access to grapes, so they wouldn't have had something to compare it to that tasted like grape.

Justin: Hmm.

Sydnee: Hmm.

Justin: Hmm.

Sydnee: Hmm. The plot thickens. It may be because it tastes like something called sea grapes.

Justin: Sea grapes. Now, what are those?

Sydnee: They're not grapes. [laughs]

Justin: God, guys!

Sydnee: They're part of the buckwheat family. They do look like grapes, and they are...sour...and bitter. So maybe grapefruit tasted like sea grapes, and that's why it was called grapefruit.

Justin: Are those still in production? I've never encountered one.

Sydnee: Those don't grow around here. Like, in parts of the Caribbean those grow, yeah.

Justin: Oh, okay.

Sydnee: You won't find those in Huntington, West Virginia. I don't even think you can get 'em at the fancy Kroger.

Justin: Really? Not even at Chacha Kroger?

Sydnee: No, not even at Gucci Kroger. The many names for the...for the—[laughs] you know.

Justin: Every town has a good Kroger and a bad Kroger and an in-between Kroger.

Sydnee: Right?

Justin: It's just a thing.

Sydnee: We have three-we have three levels of Kroger in this town, and the best Kroger is usually either called the fancy Kroger, Gucci Kroger, or my mom calls is the Chacha Kroger, which I don't know where "Chacha—"

Justin: I don't know why, but I started getting into Chacha Kroger. I started calling it that. I like that one more than Gucci Kroger.

Sydnee: I do too. I have a lot of people that I work with that call it the bougie Kroger also.

Justin: The bougie Kroger is judgmental to me. I feel like that's like, "[mockingly] Oh..." You know? It's like, I'm not gonna turn my nose up at it.

Sometimes I want to treat myself to some sushi, maybe, right in front of me at Gucci Kroger. Do you know the funny thing that I noticed, actually? I meant to tell you this, and I should've told you off the podcast. But the lady who does the—one of the ladies. There's a couple different ladies that do the sushi at the Chacha Kroger.

I saw her at Fifth Avenue Kroger, but she was, like, in the back. Like, in the—in the deli section. Like back where—behind the butcher's counter. Like, doing her thing, just not on the split. They've, like, squirreled her away back there. She's still making the sushi at Fifth Avenue Kroger—

Sydnee: Do they have sushi at Fifth Avenue Kroger?

Justin: Yeah, yeah. They have sushi at Fifth Avenue Kroger.

Sydnee: I didn't know that!

Justin: But apparently she's just going there, but they don't have her on the spli—she's an artisan! Put her out there! You know what I mean?

Sydnee: Yeah. No, that's the whole point. You can watch people make sushi, and then you can get the sushi. Which is, I mean, I'm gonna say, like, I know what you're thinking. Kroger? No. It's good. It's good sushi, I'm sorry.

Justin: She knows what she's doing.

Sydnee: I'm sorry, the sushi's good. They've got fancy cheese, and they let you make your own, like, beer pack in, like, a six pack.

Justin: If you got—they got, like, a whole ol—

Sydnee: It's great.

Justin: They got a whole olive bar if you're some sort of olive pervert and you love olives that much.

Sydnee: You're not an olive pervert if you love olives. Anyway, we're talking about Krogers, and we're supposed to be talking about grapefruit. Um, for many years—

Justin: You're welcome for the free promo, by the way, Kroger. Get at us if you feel guilty and you wanna give us some money.

Sydnee: [laughs] Grape—for many years, grapefruit was thought of as a health food. It's a good question why. I mean, it does have, like, vitamin C in it. You know, there are other things that do, too. I'm not saying grapefruit's, outside of all these medication interactions of course we're talking about, grapefruit inherently is not bad for you in any way. Um, there are things in it that are good for you, certainly. Not that it's the only source of these things, but it is a source of vitamin C. To answer, like, why would it be considered medicine...

Justin: I know why.

Sydnee: Why?

Justin: Tastes bad.

Sydnee: That's—that's actually a theory, is that it kind of tastes—like, there's always been this thought, if something sort of tastes, like, sharp, or bitter, or acidic, or something that's unpleasant, that that's a medicinal quality, and that maybe it's better for you because you don't like it as much? I don't know. Anyway, it took—and obviously, like, there were the grapefruit diet, you know, back in the 1930's became popularized. And for years grapefruit had this association of, like, this is what you eat if you want to lose weight, specifically that's where—

Justin: I remember that being a big thing.

Sydnee: Like, as a health food generally, but then it really was, like, taken over by the weight loss industry to say, like, grapefruit is what you eat. And if you look at those diets, by the way, they tell you to eat grapefruit, yeah, whatever. They also tell you to eat 500 calories a day, so...

Justin: Yeah. [laughs quietly] Not—not great.

Sydnee: So, like, not good. Would not recommend. And also, it's not the grapefruit there that's doing something, bud.

Justin: If you watch cereal commercials from the ‘80s as much as I do, which is to say every night as I unwind from a bowl of cereal, it's hilarious how many are like, "Part of this complete breakfast." And it's like, a bowl of cereal, and then just this huge half grapefruit. [wheezes] It's like, "Yeah, it's a complete—it's a complete, healthy breakfast."

Sydnee: All that grapefruit. Okay. So, here we think grapefruit is this, you know, health food. At least that was the popular conception. A lot of people are eating it. We're into the ‘80s now, it's actually 1989, so we've gone through the ‘80s. And I feel like the ‘80s were still the heyday of grapefruit. I mean, at least in my house. My mom loved grapefruit. But David Bailey, who was a researcher working in a lab in London, Ontario, in clinical pharmacology, figured out that grapefruit...there's a problem. There's an issue with grapefruit. He's the guy who discovered this.

And it was a hard—when he...I'm gonna describe how he figured this out. But it was hard for him to sell this idea at first, because people weren't—like, the idea that a food would cause problems with drug like this was not well accepted. Obviously we knew drugs could interact with each other. But we didn't yet understand that food could play a role in that too. So this was groundbreaking.

Justin: That's fairly late. I mean, all things considered.

Sydnee: Well, it would be a hard thing to tease out. You know? Especially, like—

Justin: [simultaneously] Just like we were talking about, like—

Sydnee: At this point we're in 1989. Think about how varied the human diet has become. We all have access to so many more foods all times of the year. Like, by the time we have the technology to start understanding all this

stuff, it's the same time where, like, the average person is eating such a wide variety of foods in any given day, it's such a hard thing to tease out.

Justin: Remember when we for a little bit people were eating those, like, freeze-dried—not freeze-dried but, like, big chunks of cereal frozen in nitrous that would make your, like— dragon's breath I think they called it, or something like that. Where you crushed—

Sydnee: Oh, I don't remember that.

Justin: Anyway, I remember seeing those things and it's like—or Dippin' Dots! Dippin' Dots is a good example. Like, maybe would've accounted for that, that would start doing that. It's gotta be something, you know, that's a huge ri—who knows?

Sydnee: No, that's true, that's true. We just did that and started eating it.

Justin: We just did that and started eating it. We didn't even stop to think about it.

Sydnee: It would take us a long time to figure out there was a problem there.

Justin: Yeah!

Sydnee: I love humans.

Justin: And I hate Dippin' Dots.

Sydnee: Every time I say that it sounds like I'm not one. I am a human.

Justin: We're just a cool—we're just a great species.

Sydnee: [laughs]

Justin: [muffled laughter] That only does good stuff.

Sydnee: I am a human.

Justin: I too!

Sydnee: [laughs] Anyway, so he was working—

Justin: I swear on my blood...moving device.

[both laugh]

Justin: Inside my thorax. That I too am of your human species.

Sydnee: Of which I only have one!

Justin: Just the one heart for me, thank you!

Sydnee: Just the one! Not two. Um...anyway, so he was studying different medicines, and he was working on something called Felodipine. That's a blood pressure medicine. And specifically he was, um, working on the connection between that and alcohol, what happens if you drink alcohol while you're on this blood pressure medicine. Okay? So you've got...think about how you would set up that test. You've got two groups of people. They're both taking the medicine, and you want to know how alcohol will affect them. Well, what's the tricky part about that?

Justin: Um, that you gotta give 'em alcohol?

Sydnee: Well, one group's gotta have alcohol and the other group doesn't have to have alcohol, but you gotta make sure that they don't know...if they're getting alcohol or not.

Justin: Hmm. We got a lot of great—we got a lot—

Sydnee: Which, I mean, if you get a buzz or whatever off of it, yeah, you might know then. But in that moment when you're drinking it, you've gotta not know. And alcohol has a taste, right?

Justin: It'd be easier to do today. Every got a lot of great imitation liquors on the market available.

Sydnee: That's true.

Justin: Probably'd be easier to do.

Sydnee: Back in 1989 it was harder, because you've gotta figure out, like, what can we use to hide the booze?

Justin: Grenadine.

[pause]

Sydnee: You think grenadine is str—no. Grenadine's not gonna hide the booze. No.

Justin: No, probably not.

Sydnee: So it was actually—he worked on this on a Saturday night. This is according to this interview from Atlas Obscura. With his wife, Barbara. the two of them sat down to figure out, what can we hide...the alcohol in so that the test subjects won't know if they're drinking alcohol or not?

And so they tried all kinds of different things, and at the very end they thought about—they had a can of grapefruit juice and they thought, "Well, let's try that. Let's see if the grapefruit juice can hide—" 'cause it is such a strong flavor.

Justin: It's very powerful.

Sydnee: Maybe it will hide the alcohol. And it did. So he gave his subjects either alcohol and grapefruit juice, and his control group just got grapefruit juice.

Justin: And...

Sydnee: And...it worked! People didn't know which was which. So first of all, the first goal, it did work. Like, they couldn't tell if they were drinking alcohol or not. There was a little bit of difference in blood pressure. But the strange

thing is that he was taking blood levels of the medication, so looking for how much of the blood pressure medicine is still in their blood after taking the pill and drinking the drink. And what he found is that the levels were four times higher than he would've expected in the patients overall, because all of them were drinking grapefruit juice. [laughs quietly]

Justin: Don't these random...these random things freak you out sometimes? Like, these, like, "Oh, I don't know. I just kind of..."

Sydnee: And so he figures this out and he's like, "Okay. The only thing that's off is the grapefruit juice. That's the only thing that makes sense is the grapefruit juice." Because the alcohol was different. Everything else was accounted for. So could it be grapefruit juice? So he tried it out on himself. [laughs quietly] He drank grapefruit juice and took the Felodipine, the blood pressure medicine himself, and checked it in his own blood, and saw that his levels were very, very high. And he knew that it had to be the grapefruit juice. And it took a while to isolate exactly what it was in the grapefruit juice, right? So we know something in grapefruit juice is messing with the blood levels of this medication. It took them a while to figure out that there is something in grapefruit called...furanocoumarins.

[pause]

Justin: Furanocoumarins.

Sydnee: Mm-hmm. These are the compounds that specifically, um, stop that P450 enzyme, that CYP3A4 that we talked about from working. Like, just really, you know, finishes 'em off.

Justin: And we just happened upon this.

Sydnee: Mm-hmm.

Justin: You know what I mean? It's wild! How much of innovation is just happenstance. Do you know that chocolate chip cookies were an accident? Did you know they were created by accident?

Sydnee: Did somebody spill the chocolate chips and—

Justin: No.

Sydnee: [laughs]

Justin: The woman who owned the Tollhouse Inn broke up a chocolate bar because she thought it would make the cookies chocolate. She thought it would melt in the oven and make 'em chocolatey, and they didn't melt. And she was like, "This is good!"

Sydnee: Better, even!

Justin: Better, even. Dippin' Dots, too! Speaking of, created by accident.

Sydnee: That's unfortunate.

Justin: That's unfortunate. That's a bad accident. Some accidents are good, some accidents are bad!

Sydnee: Regular ice cream is better. So he pu—this was published in *The Lancet* in 1991, and it's funny because the original study is, like, literally there are six men who took Felodipine five mg with water, grapefruit juice, or orange juice. I mean, it's just six people. And then they checked, like, the bioavailability with the grapefruit juice and looked at the levels, and how did it affect the amount of drug and—

Justin: [simultaneously] That's a really small study, right?

Sydnee: Yeah, it's very small. And then they, um...yeah. And, I mean, it was really just, like, six people. But they saw a significant change.

Justin: It would have to be significant, I would think, for that—if you're having that small of a sample size, it seems like you would need it to be pretty impactful for it to register.

Sydnee: Yep. So there was a—yeah. 164 to 469% bioavailability, like, higher levels with the grapefruit juice than with water.

Justin: [whispering] That is wild.

Sydnee: Yeah. 469% in some.

Justin: [quietly] That's wild.

Sydnee: So that shows the range, too. That shows, like, even in these six people, these six test subjects, some of them had a much stronger effect from the same amount of grapefruit juice than others, because it has to do with how much of the enzyme you have in the body and, you know, a lot of other factors play into it. Which is why it's really unpredictable. So you may be thinking, "I take a medicine—" You've probably Googled this by now. [laughs] "Does my medicine interact with grapefruit juice?"

And you may think "Well, sometimes I eat grapefruit. And I don't think I've ever had a problem."

And it may be that the small amount you ingested wasn't enough to interfere with your med in your body. But maybe in somebody else, that would cause a huge effect. And the trickier part are meds, um, that don't always immediately show you that there's an effect. If you have symptoms of toxicity, of high levels, it's easy to know something's going wrong.

But sometimes, like, you won't realize that your blood pressure medicine is way too high or something. And some of these drugs, it really doesn't matter as much. I mean, it always matter—dosing always matters. I'm not saying dosing doesn't matter. But for some drugs, if you got higher levels in your bloodstream, it's probably not gonna do much to you. Like, it's just there. You got more than you need. That's not a huge deal.

But other things, like let's say it has to do with regulating your heart rhythm, that's a huge deal. So this just highlights that I think it's wild how this researcher figured that out. David Bailey is his name, who stumbled upon this making I guess the name of this cocktail, if you mix vodka and grapefruit juice, is a greyhound. [laughs]

Justin: [laughs]

Sydnee: I didn't know that. But anyway, it's a fa—and there's a whole more—if you're interested in that article from Atlas Obscura, like I said, it was from 2020, Dan Nosowitz wrote it, and it's—it tells the whole history of gr—a ton of stuff I didn't talk about. And it interviews him more about his wild, serendipitous discovery that we now know. And I guess in some countries, like, it's really widely—like, on all pill bottles and things, it says "Don't drink grapefruit juice, don't take grapefruit, don't eat grapefruit."

It's something that I think we forget to talk about sometimes in the US. And again, you may be listening and thinking, "My doctor never said." I think that we learn about it along with, like, 50,000 other things that might happen. But I didn't until I researched this episode realize, like, how easily it can happen, how little grapefruit it takes to cause this. Um, I knew the lists were huge.

But, uh, but I think it's a good reminder to let your doctor know, or your provider, if you make major changes in your activities, behaviors, things you put in your body. 'Cause if you're on medicine, it may interfere, and it may be something you want to take a quick look at. There are tons of resources that list the meds that inhibit, the meds that activate, and the meds that are broken down, and other substances too. Obviously not just meds. 'Cause grapefruit juice is not a med.

Justin: Does grapefruit juice have this on the label? It feels like it should, right?

Sydnee: Oh, that's a good question. I don't know if grapefruit juice actually has it on the label.

Justin: Seems like it should. I mean, we don't have any grapefruit juice to test that on.

Sydnee: Um, yeah. I don't know. I don't know if it...I've never had grapefruit juice in the house. [laughs quietly]

Justin: Alright.

Sydnee: [laughs] I don't know if it—I don't like grapefruits. I don't know if it's on the label. I know that, like I said, some medications have it on the bottle. And I've seen some here. But I think that it's something we could all do a better job of, is just reminding people that I am sorry, there are certain medicines that if you're on, you probably just should stay away from grapefruit altogether. I know that's a bummer.

Justin: I know you're gonna miss that delicious bitter juice. Luckily there's lots of other good juices you could try.

Sydnee: Come join us in enjoying lots of other citrus fruits that aren't grapefruit.

Justin: What's your favorite juice, right now?

Sydnee: My favorite juice?

Justin: What's your favorite juice?

Sydnee: I really don't like juice very much.

Justin: Okay.

Sydnee: I mean, I guess if I had to pick it would be...orange? [pause] What's your favorite juice?

Justin: Oh my god. Power rankings, number one is gonna be guava juice. Aww, outrageous. Number two with a bullet: white grape juice. Coming in strong. Number three, bringing up the rear, not gonna count pog juice. That would be cheating.

Sydnee: Oh yeah. Pog...

Justin: Pog juice would be high for me. But I think number three is gonna have to be a cran-apple. That could be cheating too, it's a blend, but still, that's where I'm at.

Sydnee: But orange you can mix with champagne.

Justin: That is also cheating. So, I'm sorry, Sydnee. Your juice opinions are invalid.

Sydnee: You know what? I'll take it. That's fine. [laughs]

Justin: Thank you so much for listening to our show. We hope you have dumped out all your grapefruit juice.

Sydnee: No!

Justin: [wheezes] 'Cause it's poison, basically, is what Sydnee is saying is, it's poison.

Sydnee: No. I'm saying that if you take any prescription medications, or any over-the-counter herbal supplements, anything like that, regularly, just check. Just check.

Justin: On a serious note, um, we love all of our listeners, and we really do care about the people listen to this show, and we love hearing from you and love, you know, your feedback or ideas. All of it. If you like grapefruit, please don't tell me about it. I don't—I love you—

Sydnee: Aww, Justin!

Justin: —I don't want to get a bunch of emails that are like "But I like grapefruit." I understand. I celebrate you.

Sydnee: You have just guaranteed that our inbox is gonna be full of emails titled "But I like grapefruit."

Justin: I'm gonna set up a filter. I'm gonna set up a grapefruit filter.

Sydnee: Hey, and I would like to say, I got a couple of emails from people last week who felt left out and when I talked about how sometimes—that there are a lot of blood tests that are automated that we do, but that some need to be read, actually looked at by humans and not read by a machine, and that I said pathologists do that, and did not acknowledge the fact that

lab techs do that as well. Lab technicians also look at slides. And I did not in any way mean to undermine the contributions of lab techs, or insinuate that they don't do that. Um, sometimes I'm talking fast, and I say one thing and move on. But thank you, lab techs, for all you do, and I'm sorry for how many times we call you from the call room and say "I really need this result! I really need this result!"

And you're sitting there going "They haven't even collected it yet!"

I'm sorry.

Justin: Oh, oh, medical humor. Your—everyone can enjoy these—these—

Sydnee: My lab techs know what I'm talking about.

Justin: Everyone can enjoy these great gags.

Sydnee: They know. They know.

Justin: Thanks to The Taxpayers for the use of their song, "Medicines," as the intro and outro of our program, and thanks to you for listening. That's gonna do it for us. Until next time, my name is Justin McElroy.

Sydnee: I'm Sydnee McElroy.

Justin: And, as always, don't drill a hole in your head.

[theme music plays]

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