Sawbones 341: How Horseshoe Crabs (Probably) Saved Your Life

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Intro (Clint McElroy): 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 am your cohost, Justin McElroy.

Sydnee: And I'm Sydnee McElroy. Justin, you know how my dad likes to send me news articles a lot?

Justin: All dads like to send things. Of a certain age, all dads like to send things. My dad sends me new movie trailers and announcements that celebrities have died. Those are the two things that I get from my dad.

Sydnee: [laughs] Well, dads love to tell you when—

Justin: Anybody has died.

Sydnee: When anybody has died.

Justin: Especially celebrities, yes.

Sydnee: That's a big dad thing. And I will say that along those lines, usually the news stories that my dad sends me are not necessarily cheerful ones.

Justin: Mm hmm. Mm hmm. Bit of a morbid streak on ol' Tommy Smirl.

Sydnee: [laughs] These are the things he usually likes to tell me about. And so, when I got an email this past week from my dad with a news article in it, I was like, "Dad, things are pretty heavy. I don't know if I can handle this."

Justin: Yeah.

Sydnee: "What have you brought me?"

Justin: Yeah, "What fresh Hell have you delivered to my doorstep?"

Sydnee: [laughs] But what was inside was so— was a nice little story. A nice little thing about the world and about medicine that I didn't know. It was a pleasant little… mostly pleasant little story. And it made for a really good episode. And so, I thought it would be something that I could then share from my dad to me to all of you.

Justin: So this one's suggested by Tommy Smirl.

Sydnee: By Tommy Smirl. Which I would be remiss if I didn't tell everybody about his podcast here.

Justin: Yeah.

Sydnee: Which is Court Appointed. Which he does with my uncle Michael Meadows, who is a lawyer, and it's sort of Sawbones-like, except for law.

Justin: Yeah.

Sydnee: So, check that out.

Justin: Yeah. Sydnee and I have both been on episodes and, uh, every week they do a new one about law. It's like Sawbones, but law.

Sydnee: Yeah.

Justin: Lawbones.

Sydnee: [laughs] They should have called it that.

Justin: That title, they should have called it Lawbones.

Sydnee: They should have called it that. I don't know why they didn't.

Justin: Everybody would have really known what that meant.

Sydnee: [laughs]

Justin: Just from reading it.

Sydnee: The article that my dad sent me is about horseshoe crabs.

Justin: Didn't see that one coming, did you, listener?

Sydnee: No, I didn't, and I have to say when— I think the subject line was, "Did you know this?" [laughs]

Justin: I did not.

Sydnee: And then I opened it and it was an article about horseshoe crabs, and I was like, "Dad, what? What is this?" And the reason that there are stories circulated about horseshoe crabs, and we'll get to it, is that there is a connection between the horseshoe crab and the COVID vaccines that are in development.

Justin: I couldn't fathom it.

Sydnee: That is where this eventually is headed.

Justin: Okay.

Sydnee: Now, it takes us a while to get there. [laughs] So, first of all here's what you need to know about horseshoe crabs. They're not crabs.

Justin: That's a really wild start. Of all the places I thought you would start, that's not— are they horseshoes? We should get to clear this up.

Sydnee: They're neither. They're, actually, they're arthropods. They're not crustaceans, they're arthropods, which are— so they're more closely related to spiders than they are crabs. My sibling Teylor referred to them— when I was learning about all this, I was so fascinated I was sharing these facts with people, and Teylor said, "Oh yeah, those are tactical spiders." Because they wear tanks. They're spiders in tanks.

Justin: [laughs]

Sydnee: And if you haven't seen one, if you're sitting there thinking, "Have I seen one of these things? I'm not sure, maybe." Google it up real quick. Just google it up and look at a horseshoe crab while you're listening. They do kind of look like spiders in tanks. They do look like tactical spiders, I would say. And make sure you look at the, like, flip 'em over, too. Look at both sides.

Justin: Yeah. I don't know how you do that with a glossy jpeg.

Sydnee: [laughs] Well, there are pictures of both sides.

Justin: Flip your monitor upside-down.

Sydnee: Just google both sides of—

Justin: Both sides of horseshoe crab. That's where you get the detractors and the people who are saying nice stuff about them. Fair and balanced horseshoe crab coverage.

Sydnee: [laughs] They're wild looking. They're cool looking. It's one of those things where I know I had seen them, but then in my head, when I heard the word horseshoe crab, that image did not appear. So, I don't know that I had connected that that's what this thing was. So, they have been around for, like, half a billion years. Almost half a billion years.

Justin: That's so many.

Sydnee: Like, before dinosaurs, there were horseshoe crabs, and they're still here. So, I guess they won. In that sense.

Justin: I tell you what's weird to think about, is like, in the existence of this animal we are but a blip. We are a blink in the eye of this animal. And we show up and we're like, "You're crabs." [laughs] Like, "Um… no we're not, but we'll be here long after you're gone and we've been here a while, so you go ahead and call us whatever you like there, you sad little organism."

Sydnee: We call them, one phrase I found a lot was 'walking fossils'. Which is kinda mean.

Justin: Kinda mean.

Sydnee: Like, they're still here.

Justin: They ain't crabs.

Sydnee: There are fossils that aren't walking, those are fossils.

Justin: No. Like, my dad is walking fossil.

Sydnee: [laughs] These are arthropods.

Justin: These are arthropods.

Sydnee: There are currently four species of them in various parts of the world, but we're gonna focus mainly on ones that live along the Atlantic coast of the US, as well as in the Gulf of Mexico, called the limulus polyphemus.

Justin: Mm. Tripped off the tongue.

Sydnee: Yeah. I kinda like it. So, why are we gonna talk about these limulus organisms? Well—

Justin: What's limulus?

Sydnee: That's the— limulus polyphemus, that's the name, the scientific name.

Justin: Okay.

Sydnee: Of the horseshoe crab.

Justin: Okay.

Sydnee: Which is not a crab. Or a horseshoe.

Justin: [laughs]

Sydnee: You can call them tactical spiders if you prefer.

Justin: Yeah. It's actually more accurate. [laughs]

Sydnee: It is. So, like I alluded to, they play a really important role in the development of a lot of drugs and vaccines, and will do so, eventually, when the time comes, in the COVID vaccine, because the blood of the limulus of the horseshoe crab, is very important in this development. Now, before I tell you why, I need you to know that the blood of the horseshoe crab is blue.

Justin: Okay, cool. Like Spock.

Sydnee: And you can see— [laughs] It's a light blue. It contains— and it's because, you know we have hemoglobin? That carries oxygen in our bodies.

Justin: Yes, I do.

Sydnee: They have hemocyanin, which contains copper. That's what the '-cyanin' indicates, that there's copper in there, and it makes it blue.

Justin: Okay.

Sydnee: So, their blood is blue.

Justin: That's cool.

Sydnee: It's a really light blue. When I was watching videos of them, like, taking blood from horseshoe crabs, it looks sort of like— you know the Smurf ice cream you can get at Kings Island?

Justin: Yes, I do.

Sydnee: When it's melted. Like that.

Justin: Okay. Like melted Smurf ice cream.

Sydnee: Right, It's like light blue.

Justin: Light blue.

Sydnee: Yeah. Other than being blue, because that's not really the helpful part, it's just…

Justin: It's cool.

Sydnee: It's just wild. Other than being blue, the blood has a factor in it that makes it very useful in checking for the safety of a vaccine or a drug that we're gonna inject in a human.

Justin: Okay.

Sydnee: Okay? So let's go back to talk about how did we figure this out, what doctor—

Justin: Yes, that is where I am at, currently.

Sydnee: Yes. I know, this is like, who in the world, right? How did we— okay.

Justin: Probably the same guy that looked at a horse and was like, "I'm gonna make glue out of that."

Sydnee: [laughs] Doctor Frederick Bang discovered it.

Justin: Okay.

Sydnee: Good name. Fred Bang. Dr. Bang attended Johns Hopkins School of Medicine got back in like the 30s. He went on to focus on medical research, largely. He got his MD and then decided, like, he wanted to do the research end of things more so than the direct patient care end of things. He specialized in some specific areas of, like, parasitology, virology, pathology, and he had a very specific interest in studying marine life and the way that you could apply things that we learn from marine life to medical science.

That was his, like— from descriptions, he sounds like a cool dude. From descriptions, he was a very creative kind of out-of-the box thinker and looked at, like, the whole big picture and was able to find, as we'll see, find answers to, like, medical problems from humans in the marine world, by studying the marine world. He also worked in public health and studied things like tropical diseases, like malaria and that kinda thing.

Anyway, so he wanted to look at the circulatory systems of marine animals, because in some marine creatures, like horseshoe crabs, you can actually study their circulatory system while they're still alive. Which is, like, harder to do in us, for instance. Especially back then. Like, nowadays we can inject dye and take pictures of you and things like that and we can learn some things, but to investigate an entire circulatory system while an animal was still alive was still hard to do. And so, he was doing this in horseshoe crabs as a way to try to understand how our circulatory system works. It's good to know that theirs are a little different. So, in humans, ours is fairly closed, right? So, we have little capillaries, tiny little blood vessels, we have veins, we have arteries, and the blood goes through all those things.

Justin: Gooshes around.

Sydnee: And doesn't just, like, collect in big, giant, open spaces in our body. Intentionally, anyway.

Justin: Yeah.

Sydnee: Well, in horseshoe crabs it's different. So, the blood goes from these vessels into, like, these big what are called sinuses, where it can have direct contact with different tissues within the horseshoe crab. Now,

the reason that this is important to know is that if a bacteria invader gets in us, us humans, it has to go through, like all these little blood vessels, right?

Justin: Right.

Sydnee: Probably like a capillary first. Before it's going to get anywhere to do any damage. And what do we have in our blood?

Justin: … hemoglobin.

Sydnee: Well, that, and white blood cells.

Justin: Ah, yes.

Sydnee: We have an army to protect us. So, hopefully, because that's the way invaders enter our body, we can stop them. Obviously, we don't always, we get infections, but like, that's why it works that way. In horseshoe crabs, because they have a more open, only a partially-closed, partially-closed, circulatory system, if one of those little invaders gets in it can get into one of those big pooled areas of blood directly in contact with a tissue really easily. So, that's bad, right?

Justin: Right.

Sydnee: And they have these big shells to protect them, but all you need is a teeny, teeny little crack for a bacteria to get in and it can instantly have access to the whole horseshoe crab. Bad for the crab.

Justin: Very vulnerable.

Sydnee: Very vulnerable. So, they rely on a different kind of mechanism to defend them from invaders. And this is where Bang comes in. Dr. Bang. He noticed that in a particular crab that had died, all of its blue blood had clotted into, like, a jelly mass.

Justin: Okay.

Sydnee: Big, blue jell-o.

Justin: Got it.

Sydnee: Okay? And he examined the crab and he found that it had been infected with a strain of vibrio bacteria, which is in the cholera genus. Related to cholera.

Justin: Alright.

Sydnee: So, this crab had been infected with this bacteria and all of its blood had clotted. And he found that that wasn't usually what happened when crabs died, and that didn't happen with every bacteria, and that didn't even with— he was still trying to figure out, like, why in this particular crab? What triggered this in this— you know what I mean?

Justin: Yeah. So, something weird about the bug that it had gotten triggered this response.

Sydnee: Right, triggered this response. And so, what he was eventually able to deduce is that it seemed like it only happened with gram-negative bacteria. Which, the important thing to know here is that we use a stain called a gram stain that turns some things pink and some things purple and it helps us figure out what kind of germ it is. That's all you really need to know. These are lab definitions. So, he figured out that gram-negative bacteria are the problem, right?

Justin: Okay.

Sydnee: And even when he would, like, heat kill gram-negative bacteria and then introduce them to the crab blood, it still clotted.

Justin: Huh.

Sydnee: So even dead gram-negative bacteria were causing this.

Justin: Weird.

Sydnee: Which he really didn't understand.

Justin: So, it had something to do with something that's in the blood, more than something that's in the— something that it's doing.

Sydnee: Well, it's definitely the bacteria, but it's not just the bacteria.

Justin: Got it.

Sydnee: This is where Dr. Jack Levin comes in. And this is one of these, like, happy coincidences. So, Dr. Bang needs somebody— he's doing these investigations and he needs some help and so he talks to somebody, one of these colleagues that he's working with and he's like, "I need another person to help me with all this work, I think I'm onto something but this is—"

Justin: And this guy's like, "You gotta get Jack."

Sydnee: [laughs] He's like, "Well, you need a hematologist; you need somebody who understands blood. I know this other guy, Dr. Jack Levin, he's a hematologist. Why don't you get him to work with you?" Well it just so happens that Dr. Jack Levin had been investigating something called endotoxin, which is a toxin produced—

Justin: I thought you were about to say he owned a bunch of horseshoe crabs. That would have been quite a thing.

Sydnee: [laughs] No. He was investigating endotoxin, which is produced by gram-negative bacteria. And he thought— and by the way, just to give you a point of reference, endotoxins in human bodies can wreak a lot of havoc. They cause a lot of what we think of as sepsis and septic shock, come from these endotoxins released by gram-negative bacteria. They can make your blood pressure drop really low, they can give you really high fever, they can make you really sick. So, he's investigating endotoxins. He happens to get contacted by Dr. Bang to say, "Will you come help me understand what is happening in these clotted, you know, crabs?" So to speak. And Dr. Levin says, "Oh my gosh. It's an endotoxin. It must be an endotoxin, because even if you kill the bacteria, the endotoxin's still there."

Justin: So…

Sydnee: So, he'd been investigating an endotoxin in humans and rabbits, the two minds come together and they say, "Okay. There is something in the crab blood that when it comes in contact with an endotoxin from a gram-negative bacteria, that makes it clot." Right?

Justin: Right, okay.

Sydnee: So, they're very excited. [laughs]

Justin: I'm excited.

Sydnee: Are you excited?

Justin: They're excited? I'm excited!

Sydnee: [laughs] So, the crabs— I keep calling them crabs. They're not crabs, I know they're not crabs, but like what else am I gonna call them? They're horseshoe crabs.

Justin: Well yeah, we're all friends here.

Sydnee: [laughs] The limulus.

Justin: The limulus.

Sydnee: The limulus. They have amebocytes, which are like their white blood cells, basically. And they do all this stuff that white blood cells do, they engulf stuff and they repair damage and they carry things around. They're filled with these little granules. And these granules contain something called coagulogen. And what they discovered is that when a bacterial endotoxin is sensed in the environment, then the little amebocytes will change shape and release all of this coagulogen, and they will instantly clot all the blood right around it. Trapping whatever is in it. Including bacteria and their endotoxins. All trapped. It's sorta like, remember in Fringe when they would amber something?

Justin: Yes.

Sydnee: When there was a rift between universes and the only way to stop it is just to, like, throw the amber in and freeze everything there? Trap it forever?

Justin: Yeah.

Sydnee: What?

Justin: No I just, I think that Fringe references are… are ones that everybody's gonna enjoy. And I think that there's probably at least a few people who are like, "Yes. Yes. Yes. More Fringe talk, please. Please talk more about Fringe."

Sydnee: [laughs] I would, I would devote a whole podcast to Fringe if you would let me.

Justin: I know you'd love to talk about Fringe. I have a question, is it able to have this reaction without killing the crab?

Sydnee: It doesn't kill the crab. It's just localized, it's just in that one area.

Justin: It probably doesn't feel good, though. Like, "Aw, some of my blood just went to gummy. Aw no, my blood's gone gummy."

Sydnee: [laughs] Well, if you think about where its— think about this, though. Okay. When a bacteria, when a germ gets in you.

Justin: Mm hmm. It doesn't happen much anymore, but go on. [laughs] I theoretically remember germ exposure.

Sydnee: Let's say that a germ gets in you through your skin. It happens, like, at a point where you've had an abrasion, a cut, something, right? Like, your skin has been disrupted. The layer has been disrupted.

Justin: Yes, yes.

Sydnee: So, the germ gets in there. That is where the reaction would take place in the crab. So, like, there's a little break in the shell, right at that place the bacteria gets in, right there the blood is present, bam. It gets clotted.

Justin: Got it.

Sydnee: So, it makes sense. It actually is good in the sense that not only does it trap the bacteria, but also it clots off the place where the abrasion has taken place.

Justin: Okay.

Sydnee: That's the same thing that happens in our bodies, right?

Justin: Okay, yeah.

Sydnee: That's why you don't— that's why, you know, when you get a cut, you clot, so that it doesn't continue to bleed.

Justin: Okay. Yeah.

Sydnee: So, it makes total sense. It's how the horseshoe crabs defend themselves from bacterial invaders and it's this really cool system that Bang and Levin did all their studies in their lab and figured out.

Justin: It's all cool. My only question is, like, who… why do we care?

Sydnee: [laughs] That's exactly what I'm going to address… after we go to the billing department.

Justin: [sighs] Let's go!

[ad break]

Justin: Okay, that's enough waiting. I waited through that entire great ad, I hope everybody is enjoying that sponsor, and now you're gonna tell me why I care about horseshoe crab blood.

Sydnee: It is so human that your first question is, "But how does this apply to me?" [laughs]

Justin: Yeah…

Sydnee: I adore humanity, that we observe these fascinating things in the natural world around us and our inclination is, "Okay, but how does that help me?"

Justin: I'm not a horseshoe crab, I don't have eons to ponder over this stuff. I gotta get better now.

Sydnee: [laughs] Well, when we make something that we intend to put inside a human body, like a drug, like a vaccine, a medicine.

Justin: A pickle.

Sydnee: Huh?

Justin: A pickle.

Sydnee: Okay, we don't use this on pickles, I should say.

Justin: Captain Crunch. Okay.

Sydnee: Or Captain Crunch. This is for, like, medicine. Not for—

Justin: Okay. You could've said medicine.

Sydnee: Yeah

Justin: That would have been more accurate language.

Sydnee: Although, to be fair, if you are gonna make pickles and sell them to humans, you wanna make sure that they don't have, like, infectious bacteria in them either.

Justin: Unless that's what you want and that's— like, hot and spicy and infectious. You ever have those? The little circles.

Sydnee: [laughs] That's a real caveat emptor, there.

Justin: [laughs] I mean, it does what it says on the tin, folks. It says infectious right there on the pickles.

Sydnee: [laughs] So, we wanna make sure-

Justin: And zesty. They slip it in, in the middle. So, it's hot and spicy and infectious and zesty.

Sydnee: And zesty, uh huh. You'd fall for that, because of all the adjectives.

Justin: Look at all these adjectives. It's new, improved.

Sydnee: So, anyway, we wanna make things better and not worse, and so we wanna make sure that—

Justin: [laughs] Usually.

Sydnee: There aren't bacteria in whatever we are putting in your body.

Justin: Right.

Sydnee: Because then they would cause an infection and… that would make things worse. This is also true for all of the equipment that is used for that. So, like, if you think about an IV, like the tubing and all that kind of stuff. We wanna make sure all that stuff is sterile. Right? No bacteria, no germs. Nothing on it, so that we make you better. The way that we have figured this out, prior to this amazing horseshoe crab discovery that

we have just begun to uncover, the way that we used to figure this out was called the rabbit pyrogen test.

And to be fair, this test is still in use today, so when I say "used to figure things out", it is still used to today, although not nearly as often as it used to be used. But back in the early 1900s when we first started making drugs that we could inject in people, first started making these things, and wanted to, like, make sure that they were safe and not contaminated, it was really hard to figure that out. We didn't have a lot of great methods to know, like, I mean germs are really small. [laughs]

Justin: So small.

Sydnee: And you can't see them. And so, how do we figure out if we, you know. It's really easy to accidentally get a germ in there. We have learned this very recently in many ways. No matter how careful you are, sometimes germs get in. So, and they knew at that point to heat things up to kill the bacteria, but even after that sometimes there was something in there, endotoxin, that could make people sick. So, they started doing the rabbit pyrogen test, which was basically we will, once we have made it all up and we think it's all sterile, we'll inject it into a rabbit and see if they get a fever.

Justin: That's not very nice.

Sydnee: Pyrogen, fever-causing.

Justin: Oh, got it.

Sydnee: Yeah. So, a test to cause a fever in a rabbit is what they would do. And if they did, maybe there's a bacteria there, so let's not use this. If the rabbit was fine, great, we can use this. And the test would become standardized, of course, and like, not just as simple as, "Hey, inject this in the bunny and see how the bunny does."

Justin: What's the scale of something like this? Like, are we having to do this, like, for every dose? Once per, like, injection? Like, how are we… I mean, is that, like, a test that's like—

Sydnee: For a batch.

Justin: For a batch, okay. Okay.

Sydnee: Yeah. Yeah. I mean, I don't know, when they first developed the test in 19- whatever, -14 or whatever, I don't know what they were doing. But like, by today's standards it would be, like, a batch.

Justin: Okay.

Sydnee: You wouldn't do this— and again, this test is not done very often today. But I will tell you, it is still used in some very specific cases today. But the problem, you can imagine there are a ton of difficulties with this. First of all, you need a lot of rabbits.

Justin: Yeah.

Sydnee: Lots of them.

Justin: And they're not loving it.

Sydnee: No. Second, you have to test each drug on multiple rabbits. Cause one could be a fluke, so, like, you gotta do it three times.

Justin: Maybe that one rabbit's just sick.

Sydnee: Well, that's the other thing. You gotta make sure the rabbits aren't sick. So, you have to measure their temperatures for like a couple weeks beforehand, and make sure that they're staying normal, and after— I mean, like, it's a whole thing to make sure that this fever is actually caused— if the rabbit gets a fever, is actually caused by whatever you put in the rabbit.

Justin: Right.

Sydnee: Also, the rabbits don't necessarily survive this encounter, which is bad. We don't like that. And it can take up to 48 hours for the whole process. So, it takes a long time. It's not a great test. By early 1900s standards…

Justin: Crushing it.

Sydnee: Yes. But by today's standards, we could probably do something better. What Bang and Levin had found was another way of detecting bacterial endotoxin that could contaminate a drug. That's what they've just found, right? Because that's what the horseshoe crab stuff does.

Justin: Yeah.

Sydnee: Well, why don't we just use this in humans?

Justin: Yeah.

Sydnee: Wouldn't that be better?

Justin: Certainly. Certainly, for the rabbits.

Sydnee: Than the rabbit? Yes. So, by the 70s they had produced the limulus amebocyte lysate. And what this means— do you wanna know?

Justin: Mm hmm.

Sydnee: You look like you were about to ask.

Justin: Yeah.

Sydnee: Okay. Lysate is the stuff that comes out of cells when they're broken apart, or lysed. That's when a cell is split, it's lysed. And so, the lysate is the stuff inside, right? So, basically you take some blood from one of these crabs, you spin it in a centrifuge, you separate out the cells, they like, form a little pellet. Those are just the cell parts. Not the plasma part. The cell part. You put these pellets in a solution, you add some sterile water, the water— the cells will, when you put the water in there, they'll try to absorb it all and they'll explode.

Justin: Cool.

Sydnee: They'll suck it all up and explode. And that releases all of this coagulogen stuff, right, into the water. You filter it all until you just get the coagulogen, then you freeze-dry that, and then you've got a powder that you can reconstitute and add to whatever you are testing for the presence of endotoxin.

Justin: Okay. If it congeals, then you got a problem.

Sydnee: And if it doesn't, you don't.

Justin: Okay.

Sydnee: There you go. And it was really simple. All you had to do was like, you put in there, 45 minutes later, you flip the tube upside-down. If it has clotted, you'll have a clot stuck to the top of the tube.

Justin: Easy.

Sydnee: Yeah. So, this test that they developed was way faster and easier and better for the rabbits to use on any number of pharmaceuticals that were being developed, or vaccines that were being developed. And the other part, you're probably wondering, is the horseshoe crabs.

Justin: Yes.

Sydnee: Because this test is a lot easier for humans to do, and the storage, and all these other things…

Justin: But the crabs are like, "Can we get a vote?"

Sydnee: Right. So, here's the truth. You don't have— it is not intrinsic to the process that the horseshoe crab dies. In fact, the attempt is not to kill the horseshoe crab.

Justin: Fantastic.

Sydnee: Just drawing blood from the— they don't draw all the blood out of the horseshoe crab. Just taking blood from the horseshoe crab does not kill the horseshoe crab. Now, because of the whole process, just taking them out of the water and putting them in the thing and putting the catheter in and the whole— and then having to put them back in the water within a certain amount of time. Because of all that, some do die. I mean, it would be a lie to say that they all make it. And the numbers—it's hard to find out. Like, some will say as few as 5% of the horseshoe crabs do not survive the process, some say 30% don't. I'll get into there are some newer methods that have 100% survival rates. But they have better odds than the rabbits.

Justin: Right.

Sydnee: I would say.

Justin: Which are cuter.

Sydnee: … I don't know.

Justin: Okay.

Sydnee: I think that's a matter of opinion.

Justin: Okay.

Sydnee: I have ordered—

Justin: Well, I think I've shared mine.

Sydnee: Because of all this that I've read, I've actually ordered a plush horseshoe crab that should be here tomorrow.

Justin: The kids will love that.

Sydnee: I'm very excited. It's for me.

Justin: I know. But I was trying to be generous.

Sydnee: [laughs] And that's not a joke, I really did. Sorry.

Justin: No— well, of course, you're supposed to run all purchases by me.

Sydnee: [laughs]

Justin: Your husband, for approval. This is our agreement that we put in our vows.

Sydnee: When you see the plush horseshoe crab arrive on the doorstep, that is me.

Justin: Oh yeah, because if you hadn't told me, I would'a seen a plush horseshoe crab show up and be like, "Wha? Who in our household…?"

Sydnee: [laughs] So, the LAL test.

Justin: Lal.

Sydnee: The horseshoe crab test, took off and was soon used in most cases instead of the rabbit pyrogen test. Like I said, there's still a specific few reasons why the rabbit pyrogen test is in use, but for the most part it has fallen out of favor.

Justin: Probably because it sounds like rapid. [laughs] So, people think it's fast.

Sydnee: [laughs] I could get into why, but it would take us— it would be a whole other thing to explain.

Justin: It would be so boring, probably, too, right?

Sydnee: I don't know that it is of particular interest to the— you can research it if you're interested in it, but there are reasons why this test doesn't work for everything. So, the labs that make this stuff have been interviewed now, recently, by various members of the media, to talk about, like, "Hey, so you're gonna test this COVID vaccine."

Justin: "Do we have, hey, do we have enough crabs?"

Sydnee: "Are ya ready?" And so far everybody's been like, "Yeah, it actually doesn't take a lot to…"

Justin: [laughs]

Sydnee: "We're fine." [laughs] So far, everybody seems fine to test the COVID vaccine.

Justin: In the background you see the horseshoe crabs like, "Are you hearing this?"

Sydnee: [laughs] So far it seems like we're going to be okay. They do not seem upset or worried about it, but it has turned the spotlight on this kind of strange little part of, like, medical drug development that I think a lot of us probably aren't familiar with. And you're probably, if you're like me, when you read these kinds of stories, because I— I mean, I have lived in the science world for a long time, and so I am used to the idea of, like… feeling sad and bad about the animals that are used in these.

Justin: Yeah.

Sydnee: I am used to that, um, that ethical quandary. So, for me, when I hear this, I'm like, "Well, I think rabbits are great and I'd rather us not do this if there's something else we could do, please. And I'd rather us not do this to horseshoe crabs if there's something else we could do, please. Isn't there something we could— isn't there a better way?"

Justin: There's got to be a better way.

Sydnee: [laughs] So, there are other tests. There are new tests that have been developed to try to not do these things. In order to make sure that the drugs and vaccines that we're putting in our human bodies are not contaminated. There's one that's called a monocyte activation test, and it looks for the release of certain substances in the presence of contamination, and there's another one that is basically, it's genetic engineering. They just took the gene from the horseshoe crab that does this, plugged it into the DNA of, like, a yeast cell or something, you can grow those in petri dishes, and it makes the coagulogen. So there you go.

Justin: There you go.

Sydnee: You just produce it in your lab. No animals are harmed in that process.

Justin: Didn't need those crabs anyway.

Sydnee: Except like the yeast, I guess, or whatever microorganism. You can use whatever microorganism. And then they've even used things from other animals. Like, it doesn't have to be the horseshoe crab at that point. If you can just find something that clots in the presence of endotoxin, there you go. You just need to add that in there.

So, they have found ways since 2003, they've developed one of these recombinant ones, basically synthetic ones made in a lab, kind of thing. Synthetic in the sense that they're made in a lab, but it is still the real stuff. We're just using different organisms to produce it, which is a cool thing about genetic engineering. Same basic idea. They have made other ones since then. They have been approved for use in Europe. As recently as this past June, like, just a couple months ago, in the US they're still not fully approved for use as, like, equal to the rabbit pyrogen test or the LAL, the limulus amebocyte lysate test.

Reason for that is tough. I'm not sure. I've been trying to— this is the part that I have been trying to untangle, the mystery in all this for me. So, this test seems to work, you would have no reason to think it wouldn't work just as well, right? And Europe has decided it does. In the US, we're still saying, like, "Look, labs can use it," but before they use it, they have to go through a lot of hoops to prove that it's gonna be sufficient, which is

for most of these labs, they're just saying, "Well, we'll stick with the crabs."

Justin: Right.

Sydnee: "We're not gonna do all this, we'll stick with the crabs."

Justin: And the crabs are like, "It actually doesn't sound that bad. You guys should try it, honestly. We'll fill out the forms, if that's the concern."

Sydnee: [laughs] This is where things get really complicated, and when we get into this— and I have said, I try to be really clear on this show about what I'm not an expert in. And when it comes to, like, marine life management and ecosystems and the ecology of this, obviously I am not— I don't have a degree in any of those things. I understand though that there are a lot of different pressures here.

So, harvesting blood from horseshoe crabs to continue to test our drugs and vaccines and keep us safe is maybe the pressure that is keeping them alive, but is also a reason that their populations are declining. They've been somewhat steady in the last few years, but overall, they've declined.

Justin: Okay.

Sydnee: And the reason is that they're used throughout the world, horseshoe crabs, as like, bait and I think in some places as food, and then also for these tests. And so, because of all those reasons they've been threatened before, as like, we could accidentally destroy all the horseshoe crabs on the planet. Which seems, I mean—

Justin: Bad.

Sydnee: Right, bad. That's bad. But at the same time, the thought that like, "Well, let's not do this anymore, let's not bleed them, let's do these other things and leave them alone," a lot of the preservation efforts are only because of that. And so, there's a fear that if they're not necessary for human use anymore…

Justin: We'll just forget about them and…

Sydnee: We won't work so hard to preserve them, and then perhaps they could vanish. Which is, it's crappy. If you're thinking, "Well, that's

crappy, so because they're good to us we'll keep them alive, but as soon as they stop being good for us, we won't keep them alive?" Yeah, it's crappy. I mean, I agree, it's really crappy. I don't know what the answer is.

I know I found at least one place where they're trying to farm them. Where they, like, and that's when I said there's a place that claimed 100% survival rate. There was at least one place where they've been able to, like, let them live in captivity, they feed them, they care for them. They claim that the products that come out of these horseshoe crabs are actually superior, because these crabs are healthier and better-off. They've said that the crabs will actually lay eggs, which that was the big question, would they even reproduce in that kind of scenario. They've said that they can and that 100% of then survive the process because they're so much better cared-for and healthier in the interim. So, would it be possible to do that on a large scale? I don't know.

Justin: I dunno.

Sydnee: I don't know. And then, if this recombinant test gets approved, will anybody wanna do that or will they prefer to just do the recombinant test? I don't know.

Justin: A lot of questions. I suddenly care a great deal about horseshoe crabs, I need to protect them.

Sydnee: Well, yeah. I mean, they've been around since like 450 million years!

Justin: Yeah, we don't wanna mess that up.

Sydnee: We don't wanna mess that streak up. You can— there are videos, if this is your thing, there are lots of videos of them mating—

Justin: [snorts and laughs]

Sydnee: [laughs] On beaches—

Justin: Good news for perverts.

Sydnee: No, along the Atlantic coast. Because they all come out and mate at the same time, so like the—

Justin: Nice.

Sydnee: So, the female will lay her eggs along the beach, she'll like scoot through wet sand and lay eggs. Ton of eggs, lots and lots of eggs. And then the males will come and fertilize them, but like a bunch will come… anyway, you can look and the beaches are just blanketed in horseshoe crabs at a certain time of the year. It's a big event, people come out to see all the horseshoe crabs.

Justin: They want— all the horseshoe crabs doing it, Syd?

Sydnee: Well, it's life. It's… beautiful.

Justin: Beautiful. It is beautiful.

Sydnee: [laughs] Anyway. And I also would say, just on that last note. This is probably a very important industry for very specific parts of the world. This horseshoe crab blood harvesting industry. I know that sounds really horrible, to put it like that. Blood harvesting industry. But I would say that there's also, like, some pressures of, like, "Hey, but we need this business. Like, to survive. These are our jobs. This is our livelihood." So, it's a complicated thing, you know? I wanna save the horseshoe crabs. Obviously, I want us to keep testing our vaccines and medications as rigorously as we always have for contamination. I want people to have jobs. What do we do?

Justin: Meanwhile, rabbits are like, "I dunno, choosing between these two options, which are your only two options that you have, is tough."

Sydnee: [laughs]

Justin: "I don't know, let us know what you figure out. We're gonna go back to the warren."

Sydnee: I would prefer we not do that to bunnies either! I am on board with all these things.

Justin: List the animals you wanna take their blood. Go. [laughs]

Sydnee: [laughs] I believe that science, when applied through a lens of morality, can do all these things. We can achieve all these goals.

Justin: Here's hoping.

Sydnee: But we're not quite there yet, obviously.

Justin: Thank you so much for listening to our podcast Sawbones. If you wanna share the show with people, that's the only way, pretty much, that we grow. And in these times, I feel like it's a really good kind of show to listen to. Just, you know, send them a link. We're on all the platforms. SawbonesShow.com I think is our website, if you wanna start there, wherever. It's all good.

Sydnee: If you see a horseshoe crab, look but don't touch. Leave them be. There's some places where I think it's illegal to pick them up.

Justin: Thanks so much to The Taxpayers for the use of their song "Medicines", which is the intro and outro of our program. And thank to you for listening. We really appreciate you and we hope you're hanging in there.

Sydnee: Thank you Dad for this article.

Justin: Thank you, Tommy Smirl. That is gonna do it for us, but be sure to join us again for next week for Sawbones. But until then, 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]