Sawbones 387: The Malaria Vaccine

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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 am your cohost, Justin McElroy.

Sydnee: And I'm Sydnee McElroy.

Justin: And a special extra triple welcome to you this week for the Maximum Fun Block Party.

Sydnee: That's right!

Justin: If you don't know, if you haven't heard, this is your first interaction, this week on Maximum Fun, our podcast network, everybody's putting out shows that are gonna be a perfect place to start listening to, uh, a Max Fun program.

So if you've never listened before and you want an episode that's not gonna anticipate anything of you, that does not expect you to know anything about the show, this is the week to listen to it. And that's what we're doing with *Sawbones*, too.

Sydnee: We started off strong by saying who we are.

Justin: Yes.

Sydnee: So, there's one hurdle.

Justin: Huge.

Sydnee: Overcome.

Justin: We're really married.

Sydnee: Yes. I'm— I'm really a doctor.

Justin: I'm— yes.

Sydnee: I'm a family do— I'm a doctor of medicine. A family one.

Justin: We used to do a podcast about *Two and a Half Men* and then we did one about television, and now we do one about medicine, and we've been doing it since 2013. It used to be a lot of just old medicine, the ways people have tried to treat people over the years with different weird stuff, and it's evolved recently as, well, unprecedented times, as the press releases like to say.

Sydnee: His— history is happening.

Justin: History is happening all around us and has been for quite some time. So we'll, uh— we talk about those sorts of things. We'll talk about, uh, sometimes there's wellness trends, things like eating—

Sydnee: Thank you, TikTok and Gwyneth Paltrow.

Justin: —dirt, or sunning your... your perineum.

Sydnee: Hmm!

Justin: The taint— taint— what?

Sydnee: That was good. You used the right word there.

Justin: Yes, I did use the right word, Sydnee. I'm very proud of myself. Um, so this week we are talking about— this is sort of a— a blend of history and the modern, so it's a surv— a little bit of everything that *Sawbones* is doing right now.

Sydnee: Well, Justin, there's so much that— we have been watching science happen in real time in the last... it was like— I've been saying in the last year, and then I started saying in the last year and a half, and now I'm saying going on two years. [laughs] Which is accurate, but also... hard.

Justin: Yeah.

Sydnee: Difficult. Uh, and watching science in real time, and history happening, and all of this unfolding, has been hard... and stressful.

Justin: Yes.

Sydnee: But here's some science unfolding in real time that's good! That has, like, a happy note. Like, fun, rewarding science in real time.

Justin: Yes!

Sydnee: How about that?

Justin: Yes!

Sydnee: We need— we need a *good* story.

Justin: [singing] We need some happy science. Right this very minute.

Sydnee: That's right.

Justin: [singing] Beakers in the window. [beat] Um... [whispering] What's another science thing?

Sydnee: Flasks? Test tubes?

Justin: [whispering] What's the little— what's the little...

Sydnee: Bunsen burner?

Justin: No, no, no, no, no.

Sydnee: Microscope?

Justin: No, it's, like, a little—

Sydnee: Electron microscope.

Justin: [very quietly] No, just listen! It's a little... [unintelligible]

[normal volume, singing] Chemicals in the pipette, yes, we need some happy science!

Sydnee: Ohh.

Justin: [singing] Right this very minute.

Sydnee: I love pipettes.

Justin: [singing] We need some happy science now!

Sydnee: I like micro-pipettes.

Justin: Micro-pipettes! That sounds like something we'd see advertised to us on Nick Jr.

"Micro-pipettes are the cutest pets! But they hide a secret: they're actually USB drives! Full of [holding back laughter] all of Wikipedia." [laughs quietly]

Sydnee: [laughs] Okay—

Justin: That'd be cool. It'd be a cool gift for kids.

Sydnee: [amused] Why would you put Wikipedia on a USB drive?

Justin: So kids could learn something.

Sydnee: It's already— it's in the net.

Justin: It's an educational tool.

Sydnee: [loudly] It's in the net!

Justin: But it's educational tool now.

Sydnee: Oh.

Justin: Micro-pipettes are an educational tool with— filled with tiny pipes.

Sydnee: It's like Encarta.

Justin: Hmm.

Sydnee: It's just like Encarta.

Justin: It's just like Encarta.

Sydnee: [laughs] Back to— back to science in real time. We have had a, uh— we've had some big vaccines come out this year.

Justin: Mm-hmm.

Sydnee: And there were some of us who believed when these big vaccines came out that there would be, like, celebrations. Like, people sobbing in, like, joy, and just, like, running to the pharmacies like, "Give me my vaccines!"

Justin: [laughs]

Sydnee: And, like, it would be a new era for, like, vaccine love. You know?

Justin: And?

Sydnee: 'Cause most people are already pro-vax. This is a really important point we make on this show.

Justin: It's not even pro-va— pro-vax, I would like— I think is— and now, I know we have a pin that says "pro-vax." I think we should strike it from the record. I don't think you should be— I think there should be anti—

Sydnee: Well, there's not two sides to this.

Justin: No, there's not two sides.

Sydnee: There are "Vaccines are safe and effective and you should get them," and then there are people who are wrong, and those are the two sides. Some things don't have two sides. Um, but I thought that it would really help us fight some of the misinformation. Didn't happen exactly... like I thought.

Justin: Not just like that, I don't feel like.

Sydnee: Not exactly like that. But here is a vaccine that just came out. Last week's episode we referenced that there was a malaria vaccine in the works. *Two days* after that episode airs...

Justin: Yeah. Yeah.

Sydnee: ... a vaccine—

Justin: All of a sudden. Just like that.

Sydnee: —is approved for malaria. Well, the World Health Organization, the WHO, officially endorsed and recommended this new vaccine for malaria. The first one to be used widely. Not the first one to be studied. Many, many, many attempts have been made at a malaria vaccine, but the first one that has been approved, recommended, and hopefully will be widely dispersed.

Justin: That's thrilling.

Sydnee: And that was on October 6th. It was, uh, from GlaxoSmithKline Biologicals. They released the vaccine, RTS,S/AS01.

Justin: [through laughter] Gotta spice that up—[wheezes] [through laughter] science, gotta spice it up!

Sydnee: They already did. Already did, don't worry.

Justin: Oh, okay.

Sydnee: I got a name for you.

Justin: Sydnee...

Sydnee: Do you see it?

Justin: No— Sydnee...

Sydnee: Are you already looking at it? It's right there.

Justin: [simultaneously] Sydnee, this is not good!

Sydnee: It's— it's r— I didn't make it up. This is really the name.

Justin: I know.

Sydnee: This is really the name.

Justin: [groans]

Sydnee: Mos— Mosquirix. Mosquirix.

Justin: Mosquirix.

Sydnee: It's like mosquito, but then...

Justin: It sounds like a pesticide.

Sydnee: ... rix.

Justin: Mosquirix.

Sydnee: Mosquirix. Because... as you may or may not know, malaria is spread by mosquitoes. We— by the way, I should mention, um, especially if you're new to the show, we have done an entire episode about malaria before, which is why I will not get into the details, because there's a whole episode about malaria that you can listen to and enjoy, and, I mean, malaria, if you live in the US, you are not as aware of what a huge problem malaria is worldwide.

Justin: You're not awaria of malaria.

Sydnee: [muffled groan] That... okay.

Justin: Yeah.

Sydnee: Sure. Anyway. This is— so, Mosquirix. [laughs quietly]

Justin: [wheezes] It's not gettin' better.

Sydnee: I don't know. I think RTS,S is better. But it is the first—

Justin: Weirdly, yeah.

Sydnee: —vaccine to make it out of all the testing and into common use. Uh, there— there actually, just for a little bit of context, this vaccine, the first data that showed that this could be effective was published back in 2015.

Justin: Hmm.

Sydnee: And, uh, it was sufficient enough—

Justin: What's the lag?

Sydnee: —for, at that time, the European Medicines Agency recommended it, in July of that year. And said, like, "Yeah. This looks good. Cool. We— yeah, this— this works."

Um, but a few months after that in, like, October of that year, the World Health Organization said, "You know, I think we need a pilot study to see if, like, implementation is possible."

And we'll kind of get into that. That was always one of the big questions about a vaccine like this. Not just could you make it, but then could you get it to people effectively.

Um, so they did finally start. They recruited. They have to— you know, a study of that size and— and in humans, it takes a while. You can't just do it. It takes a while to create. And so, it wasn't actually begun until 2019, and they did this gigantic pilot study in Ghana, Malawi, and Kenya. It was planned to continue until 2023, but they have decided they have enough data. They don't— they can continue the study, but in the meantime they already have enough data to say this is— this works. This is good. And that's what we just had announced.

The story of the malaria vaccine, though, dates back to the 1960's. Because, as I said, malaria is a huge problem worldwide. There— you know, even though in the US we are not as aware of it, there are about 229 million cases of malaria worldwide each year.

Justin: [hisses] Gosh. That's staggering.

Sydnee: Lots of malaria.

Justin: Lots of malaria. Big problem.

Sydnee: Yes. Uh, and the— and about 410,000 people or so die each year from malaria. Now, those numbers have gone down since they started work on vaccines, but there's still— obviously that's a lot of people that die each year from malaria. And, um, most upsettingly, I think, for a lot of people, about two thirds of those are children under five.

Justin: Oh my gosh. Ugh.

Sydnee: So you can see why— when you hear those numbers, the question that I had was, "Why haven't we come up with a vaccine earlier?" Um, because a lot of the vaccines that we have in common use in most parts of the world, and including here in the US, are aimed at childhood diseases, right?

Justin: Right, yeah.

Sydnee: Like, so many of the vaccines that we've created, and we talk about this a lot on the show, were because the first five years, and even— you could even narrow it down to the first two years of human life for a long time were scary.

Justin: Yeah.

Sydnee: Because there were so many childhood diseases that could, you know, result in mortality in that age group, that, you know, you make it out of birth, that's one success, 'cause that was— you know, that was a terrifying condition for most of human history.

So you get— you— both the pregnant person and the baby make it out alive, and then those next two years are just...

Justin: Terrifying.

Sydnee: ... cross your fingers and hope. Um, and then vaccines came, and we didn't have to feel that way. So... why have we not had a vaccine against malaria? Well, there are a lot of barriers for us to overcome for this specific, uh— this specific illness that aren't quite there for other diseases that we have conquered with vaccines, so to speak.

Justin: Okay.

Sydnee: Although— I say "conquered with vaccines," but then I think, like, did we conquer measles? Because then people don't get it— get the vaccine, and we get measles. [sighs heavily] But we could've.

Um, malaria, first of all, is caused by a parasite. So a lot of the vaccines, all the vaccines we're familiar with, are caused by viruses or bacteria. This is caused by a parasite. So it's totally— this is very different, in that

sense. It's a lot more complex of an organism, so that makes a vaccine more challenging to create.

The parasite— and again, we have a whole episode going into all of the life cycle of malaria and how it causes disease, but to kind of sum up, the parasite is called Plasmodium. There are a lot of different types of Plas— well, there are five. Is five a lot?

Justin: It's not a lot. I mean—

Sydnee: [laughs] It's not a lot.

Justin: —compared to what?!

Sydnee: I don't—[laughs quietly] there are five different types of Plasmodium, but the one that is most deadly and causes the most of the disease burden is called Plasmodium falci-*par*-um— fal-*ci*-parum. I don't know. I say fal-*ci*-parum, falci-*par*-um, either way. It's—

Justin: I think the intent carries over.

Sydnee: It's carried by mosquitoes, specifically the Anopheles mosquito. Um, and it can be passed to a human when the mosquito bites you, right?

Justin: Mm-hmm.

Sydnee: Um, as I said, there's a huge disease burden worldwide. The need for a vaccine is clear. We do have effective treatments for malaria. We talked about that on the episode. There are ways that we can address malaria. They're obviously not 100% curative, or we wouldn't have anybody die of malaria. Uh, and we have other methods of prevention, most famously, you've probably heard of mosquito nets.

Justin: Mm-hmm.

Sydnee: In many places in the world, uh, where you have mosquitoes that carry, um, malaria, it is useful to sleep at night under a mosquito net. In some of my travels, I have slept under mosquito nets.

Justin: Yes.

Sydnee: They're nice. They— you know, honey, they keep out the mosquitoes? They also keep out the lizards.

Justin: Oh! Double— double duty.

Sydnee: I would wake up at night and sometimes see a lizard hanging on my mosquito net, on the outside.

Justin: Doesn't seem fair. He didn't mean you any harm.

Sydnee: Well, no. I mean, not, like, in a bad way. He's just sort of hanging out there.

Justin: He just wants to crawl all over you.

Sydnee: I don't want him to crawl on me.

Justin: Well—

Sydnee: I was thankful for the mosquito net. [laughs] Because the lizard was outside the net. And I could, like— that was a perfect viewing for me. I could see them through the net? But he didn't crawl on me.

Justin: I gotcha.

Sydnee: Um, so we did have other methods of prevention, but again, this is not enough to save all those lives. Why has it taken so long? Well, first of all, as I already said, it's complicated. Not as straightforward as a virus or a bacteria.

Um, the other reason, though, that you'll often find cited, is what's called the lack of a traditional market.

Justin: Ahh, yes. Yes, I can— I can parse that out pretty easily.

Sydnee: This is something that we, uh— we address periodically on *Sawbones* as well. Uh, medical history, as many times as it's full of just some wacky, wild stories that we like to share with you [laughs quietly] is also, unfortunately, also full of, uh, lots of times where marginalized people have been neglected or abused by the medical systems we have in place.

Here's one.

Justin: This is one just like that.

Sydnee: This is one. What do you think it means, Justin, when I say there's a lack of a traditional market?

Justin: Well, Syd, what I would say is that they can't make as much money off of—[wheezes] can't make as much money off of it.

Sydnee: If you look at the parts of the world where malaria is common, in parts of Africa and sub-Saharan Africa and parts of, um, Central and South America, if you look at these specific areas, you have a lot of, um,

people living in poverty. You have a lot of people who are, uh, Black people, who are people of color, and who are not necessarily, um, as able to pay, and communities and governments that aren't able to pay for vaccines and medications the way that a richer country or a whiter country may be able to.

Justin: This is what— this is— can I have a, like, brief sidebar, two minute sidebar? This is what upsets— one of the things that upsets me so much about the anti-vax people. Is because they wanna... you know, the villain of it is always shifting, because it's fake, right?

So the bad guy is the government, but for a lot of these people, "I can't believe you trust Big Pharma like that! You're just letting Big Pharma do— " it's so irritating to be cast on the side that's, like, pro-Big Pharma. The vaccines don't change the fact that Big Pharma is actually super bad, with hearts as black as night! That does not— they just don't wanna put microchips in you, or poison you with [wheezes] vaccines!

Sydnee: They just wanna sell you s— it's not complicated. They wanna sell you stuff.

Justin: Yes. Don't overthink it!

Sydnee: They want you to buy things and make money. Like, that's—

Justin: They're— yes, it's the evil, dark, black side of capitalism, 100%, no question, yes.

Sydnee: That's the big conspiracy.

Justin: That's the conspiracy.

Sydnee: It isn't a conspiracy.

Justin: The same conspiracy since time immemorial. Golden rule: he who has the gold makes the rules. Like, it's not— it's not any more interesting than that! They're bad! [wheeze-laughs] They're, like, actively bad.

Sydnee: Well, I think for me, this is the way I would advise, if you have someone who's reluctant to get the vaccine or to, um— to trust these sorts of things in their life, uh, the way I parse it is this. I'm a physician. I am part of— I mean, inherently I'm part of the medical system in the United States of America.

Justin: Yeah.

Sydnee: I can't help but be. I am a doctor.

Justin: [singing] All in all your just a... nother brick in the wall!

Sydnee: I know my intentions. I know my motivations. I know why I do the things I do and why I recommend treatment to patients that I recommend. I know that. I know I have— I am following the oath that I took when I started medical school.

Justin: In brightest day, in blackest night—

Sydnee: I— well—

Justin: —no sickness shall escape your sight.

Sydnee: [laughs quietly] And just like there are lots of people like me in the healthcare profession, who maybe the system around us is bad, but we are doing the right thing for people, there are scientists and researchers working for this pharmaceutical companies who are— I mean, whose intentions are good, who are on the side of saving lives, who want to make something with all of their knowledge and expertise that will prevent sickness and death, and that is what they're trying to do. And maybe the company they work for, like many companies that many people work for, sucks. [laughs]

Justin: Yeah.

Sydnee: But they're good, honest people who are doing good, honest science. And I think that's what you have to remember, is it's not this faceless entity. There are people there. And, like, you can still be mad at Big Pharma for overcharging for drugs, which they do, and trust that the scientists who sat in a lab and helped figure this out— the whole team of scientists, it's never just one—

Justin: Right.

Sydnee: —were doing the right thing, and that the product is sound.

Justin: Yes.

Sydnee: Like, those two things can both be true.

Justin: Yes.

Sydnee: And that is the— that is— that is the case with the— but we're talking about the malaria vaccine.

Justin: I— listen.

Sydnee: You keep getting me off track on the COVID vaccine.

Justin: Okay, well.

Sydnee: So, not many developers were pouncing on the opportunity for this, right?

Justin: Right.

Sydnee: Even if scientists wanted to, and a lot of doctors wanted to, and a lot of, like, activists, and a lot of well-intentioned people wanted this, and governments were willing to pay for it, you had to convince somebody to make it so that they could, you know... get money.

Justin: Gotcha.

Sydnee: Um, so, Justin, I want to talk about, like, the story of the development of this vaccine, how these barriers were overcome. But before I do that...

Justin: Uh-huh?

Sydnee: We gotta head to the billing department.

Justin: [low voice] Okay, so the billing department is the part of the show— that's our clever name for— and ironic, considering the past five minutes, uh, where we ta— uh, sell you stuff.

Sydnee: It's also the part of the show that confuses all of our listeners who live in countries with, uh, universal healthcare.

[ad break]

Justin: Alright, Syd. No more distractions, I promise. No more of my sparkling... side notes.

Sydnee: Okay. So, first of all, as I mentioned, the first barrier was the parasite itself. Making a vaccine against a parasite. Okay? This is a little trickier. The Plasmodium parasite, uh, has a life cycle, and it changes forms in that life cycle. That's not usually true of viruses and bacteria, you know, like this.

Um, inside the human host, it has two different general stages. So, it gets inside a human, and it's a pre-erythrocyte, or what we usually call the liver stage. It gets to your liver first. Um, and then there's an erythrocyte, which is a blood cell stage, and then it gets into your blood cells. Those are two different, um, forms.

And then there's a third— there's a whole other form that it takes in the mosquito, where it goes through sexual reproduction. Those are asexual, that's sexual. It's complicated. It's a complex organism. When you're comparing that to a virus, that just infects a cell and builds copies of itself. This is a whole other thing, right? Um, so what form should we target with a vaccine?

Well, there's lots of opportunities there. Which one is gonna work best? The other thing that's tricky about malaria is that you can get malaria over and over again.

Justin: Oh, you don't have the immunity to it.

Sydnee: Mm-hmm. Unlike many of the other vaccine-preventable illnesses, which we kind of were— that was the whole idea, right? Uh, when we talk about the beginning of vaccines, Edward Jenner noticed— well, and this had been done in many cultures. Again, we have whole episodes on this.

But the whole concept of giving someone cowpox to prevent smallpox was, once you got cowpox and got better, you didn't get smallpox.

Justin: Right.

Sydnee: So something was happening within a natural— you were building some sort of immunity.

Justin: Mmm.

Sydnee: If— with malaria, if— you can get malaria over and over again, which is true. You can get it over and over again. Now, typically when you get it in close proximity, like you get it and then you get it again a month or two later or whatever, it's not quite as bad, right?

The people who get really sick are usually travelers who have never had it before, who don't come from places in the world where it's endemic, or if you have someone who's from a place where it's endemic and they leave for, like, a year and then come back, they're just as vulnerable all over again.

Justin: Phew.

Sydnee: This is also why it's worse in kids: they're getting it for the first time.

Justin: Okay.

Sydnee: Does this all make sense?

Justin: Yeah.

Sydnee: Okay. So, this makes it trickier. This research started in 1967. That was the first time that we see, like, these attempts at, what could we do to make a vaccine against this parasite?

Um, the first researcher, Austrian-Brazilian researcher Ruth Sonntag Nussenzweig, uh, was one of the first ones who tried to make a vaccine by basically taking the sporozoite form of the parasite, this is the form that infects you, that the mosquito has in its salivary glands and then [sucking noise]. Kind of like that, injects into— do you like that noise?

Justin: Charming, yeah.

Sydnee: Injects into you.

Justin: Sonically, just delightful.

Sydnee: [laughs quietly] Um, basically they tried to attenuate it. So, make it so it couldn't be dangerous to you, but it would still stimulate an immune reaction. And there are some vaccines made this way. It's still the virus, but it's been, like, made weak. [laughs]

Justin: Okay.

Sydnee: Okay? So they radiated it. And then, um, injected the sporozoite into mice. And it worked! The mice... didn't get— they didn't get sick. And then they didn't get malaria later.

Justin: Problem solved.

Sydnee: So it seemed like this was something we could do, but there were a lot of barriers. Like, so, do we irradiate mosquitoes? And this was just in mice. It wasn't repeated in humans. And how long will this last? I mean, like, this was just, like, the very early seeds, and this is how scientific research goes, right? You do this early stuff and start to see what works, what doesn't, start to get ideas, but it takes a long time.

Justin: Right.

Sydnee: To figure out what that looks like in a human body. So it wasn't until 2002 that you really see progress made. So look at that huge jump.

Justin: Yeah.

Sydnee: Where other stuff was going on.

Justin: That's wild.

Sydnee: And I'm—

Justin: But again, that's a symptom of, like, the— not having market pressure pushing this thing through.

Sydnee: Yes. You will note that a lot of vaccines were made for diseases that certainly can affect these parts of the world, but also affect places like the United States, or the UK or, you know, other countries that were invested in other vaccines.

So, in 2002, again they sort of go back to this idea of, like, let's radiate [laughs quietly] the mosquitoes, basically, so that these sporozoites that are in them can be radiated, or we can radiate the sporozoites themselves. Either way.

But they tried it again, and they saw that once again, they can trigger an immune reaction, but they don't mature past that liver stage, so they never make you sick, and you're immune to malaria. Um, and they did it in humans then. They actually, like, let mosquitoes, radiated mosquitoes, bite humans.

Justin: Dang.

Sydnee: To give them malaria.

Justin: Sheesh!

Sydnee: But it worked! It seemed to work.

Justin: Okay.

Sydnee: It had really good results. Like, most of the participants did not get sick, and seemed to be immune to malaria, for at least some period of time.

Justin: But still, we're radiating...

Sydnee: Mosquitoes.

Justin: ... mosquitoes. Okay.

Sydnee: So it wasn't cost effective. It was deemed that, like, well, okay, there's some promise here, but this is probably not the best path.

Justin: Would you have to radiate all mosquitoes? For this to be effective?

Sydnee: Well, the idea was if we could irradiate the sporozo— if we could make this form of the sporozoite that is irradiated.

Justin: Okay.

Sydnee: But the way that they tested it was irradiated mosquitoes. [laughs quietly] No—

Justin: Okay, got it.

Sydnee: —you— I mean, obviously if we could irradiate all mosquitoes, that would be great, but that would be a heck of a... this— and we talk about this on the malaria podca— er, on the malaria episode. The, uh— there have been attempts made to, like— what if we could just...

Justin: Kill all mas— mosquitoes?

Sydnee: ... kill all these mosquitoes.

Justin: Listen, the we— nature is a delicate web, friends.

Sydnee: [laughs]

Justin: You don't wanna play in that. Who knows what rung on the ladder that is?

Sydnee: So, based on this idea, researchers thought this might be something to investigate. And you see throughout the early 2000's a lot of different pathways start to be explored for a vaccine, okay? The first is this what we call pre-erythrocytic vaccine. It focuses on the same phase that I just talked about, the sporozoite phase, okay? We can— somehow we can, from the time the sporozoite gets in you to when it infects the liver, you've got, like, an hour. [laughs quietly] So it's, like— it's a tricky window.

Justin: Yeah, right.

Sydnee: But if we can stop you at that point, if we can stop it there, that would be best. But also trigger an immune response so that you're... you know, immune to it moving forward. So that was one thought.

There was the, uh, the erythrocyte stage, which was called the merozoite, but basically this is when it's invading your red blood cells. This is when you can get sick, actually get symptoms from it.

Justin: Okay.

Sydnee: Can we stop it there? Um, like, stop that reproduction part. Could we do that? And then finally there was this transmission blocking pathway where, like, we would create these antibodies in a human that when the mosquito bites you would— they would attack the parasite in the mosquito, which doesn't help you at the time you got bitten, but it would help to reduce transmission by killing the mosquitoes or rendering them not-infective.

Justin: Hm!

Sydnee: So, all of these pathways start being explored, and you see all— I mean, and— I mean, there's over 30, I think, different candidates that have been tried in the last 20 years since then, about 20 years, where they have been, like, taking them through phase one or phase two and then having— stopping, like, seeing, like, "Ehh, that didn't really work very well. Let's take it back to the drawing board."

So, a lot of exploration has been done in all three of those pathways since then. Um, building on that 2002 research, some scientists realized that there was a certain antigen called the circumsporozoite protein, CS protein, uh, that was good at generating protection. So, this was building on this same 1967 research, goes to this 2002 research, and then here, they're building on it further. Um, and what they found is, like, if we could get this protein into people, this would help stimulate an immune response, so your body'll recognize malaria, right?

Justin: Mm-hmm.

Sydnee: But it doesn't generate a strong immune response.

Justin: Hm.

Sydnee: Like, you don't get a big burst of immune... response. Right?

Justin: Okay.

Sydnee: Like you need to generate lifelong protection, or long-term protection at least. So, they combined it with an antigen from Hepatitis B, the surface antigen, which we know is good at stimulating the immune system—

Justin: [simultaneously] Stimulating the immune system, yeah.

Sydnee: —because that's what we use in the Hepatitis B vaccine.

Justin: Yes! Now I have this.

Sydnee: So they combine these two things together, and then through an adjuvant, which— an adjuvant is just something that helps stimulate an immune response.

Justin: Okay.

Sydnee: Okay? They put all this together... into a vaccine, and created the RTS,S... Mosquirix—

Justin: Mosquirix.

Sydnee: —vaccine that we're talking about today. So, uh, it was tested finally. So, it goes through, based on this 2002 research. They're building it slowly. It takes a long time. Um, it was tested in phase three trials, and that's when they start actually— phase three, as you may remember from the last going on two years, is when you actually start giving it to people.

Justin: Mm-hmm.

Sydnee: Um, it was te— well, you can before that. But it's wider, um, studies to actually give to people.

Justin: Great.

Sydnee: So they started doing that in 11 different countries in Africa. It was released in October 2011, the results from that, that showed good results. Um, that it reduced the risk of malaria and severe malaria by 56 and 47% respectively, so, you know. That— again, this is such a serious illness in kids, and we're talking about kids ages 5 to 17 months, that this is— this kind of impact is huge. Is it everything? No. But is it something? Absolutely yes.

Um, what they did find is that, uh, further results were released in 2012 that showed that in infants 6 to 12 weeks, there wasn't a huge response after those first vaccines. What they're trying to do is figure out, like, how many shots are we gonna need to make it something that's effective, right?

Justin: Right.

Sydnee: Like, how early can we give it, and how many shots are needed so that we can protect kids from severe malaria? Um, they kept refining it, and they finally showed in the results that were published that, um, it can reduce clinical malaria by 26% for little kids, up to 36% for kids age 17 months.

Anyway, this was compelling enough data that at that point, um, they decided, like, after all these studies were released, they put all this data

out there, and that's where we get to 2015, when the European Medicine Agency is like, "Yeah, this is enough stuff that we think that this is good," right?

Justin: Mm-hmm.

Sydnee: Well, like I said, the World Health Organization said, "This is really good, but we want to pilot it," because even though this would be a huge impact— it's not everything, but it's something. Even though this would be a huge impact, the delivery of the vaccine was the next big step. They didn't know if you could effectively get these va— if you had the infrastructure to get these vaccines to all the kids who need them in this part of the world.

So that's the great thing about this WHO pilot study. It's unfortunate that we had to delay the vaccine more with the pilot study, except in it they did give the— it was huge, so they did give the vaccine to, you know, tens of— hundreds of thousands of kids.

But, um, what they proved from this pilot study is not only is the vaccine effective, but it's totally feasible. It totally works. They— yes, they can deliver this vaccine to the places they need it, get all the doses to them, um, and reduce, you know, cases and fatalities from malaria.

Um, so, uh, from this pilot study they showed that it's totally feasible to deliver, that they can reach people who are really difficult to reach, typically, with medical care, with, like, sustainable healthcare and continuity of care, and stuff like that. That it is incredibly safe. They've given more than 2.3 million doses of the vaccine.

Justin: Wow, fantastic.

Sydnee: Incredibly safe. Um, that it did not— this was another argument against it, and we hear this again and again sometimes in medicine. Like, "Well, we have this effective intervention that could really reduce mortality from this deadly disease."

And then people go, "Well, won't people be more risky with their behavior?"

Justin: We need— we need a, uh— we need, like, a term for this. Because that exact supposition was made last week, in last week's episode when we were talking about PrEP.

Sydnee: Pre-exposure prophylaxis for HIV, yes. So a lot of people are like, "Well, people will stop using... bed nets. They won't use the bed nets. And the vaccines aren't perfect, right? And so, like, you still want to

use the mosquito nets even if you get the vaccine. But nobody'll do that if they get the vaccine."

Well, no. That wasn't true. It did not in any way negatively impact the use of bed nets, um, getting other childhood vaccinations. The other thing they said is, "Well, but— since the vaccine isn't completely effective, if you get the vaccine and then, like, let's say your kid gets sick, you're gonna assume it's not malaria. You won't take your kid to the hospital, and then they could— maybe they did get malaria and they'll die."

Nope. People still responded to febrile illness, to fever-causing illness, the exact same way they did before. None of this was changed significantly, right? What they showed was not only did the vaccines work, not only are they feasible to get to people, it won't negatively impact behavior, and it really does, in this sort of setting, it does reduce the rate of kids getting hospitalized and, you know, um, dying from malaria.

So all of this was good. It was a significant reduction. It was also cost effective. Of course, if you're a pharmaceutical company— if you're a company, if you're in a business, if you're a capitalist economy, you care about that. So, it was cost effective.

There was this big concern— this was really impactful to me— that— it's a four-shot regimen, okay?

Justin: Okay.

Sydnee: Which I know that— I know a lot of people are like, "That seems like a lot."

Think about if you have had— you've been a kid. You probably don't remember this, but if you've been around kids, if you have kids, kids get a lot of vaccines when they're little, and some of those are three and four shot regimens. You just don't think about it 'cause you just keep bringing them back for their boosters, right?

Justin: Right.

Sydnee: So, it's a four-shot regimen. You give it between 5 and 17 months, and then there's one last dose 18 months later. And there was this big argument that we're like, "Okay. We timed the first three doses with other childhood vaccines, and so we think that won't be a problem. Like, people are already bringing their kids in for these vaccines, and so they'll get 'em. But, like, this last one they're never gonna get, because it's on its own and nobody'll care about it and," whatever.

It wasn't a problem. People still came back and gave their— to make sure their kids got the last vaccine. It shows an understanding of the impact

that these sorts of, like, medical innovations and interventions can have, um, when faced with a deadly disease that can affect children. Which we saw historically with polio, we saw the same impact, right?

When the polio vaccine came out, thousands of parents lined up with their children to allow them to get the vaccine, even early on when it was still experimental. Um, because when you're faced with childhood mortality as the alternative, you do it.

We have not seen that same impact, unfortunately, with the COVID vaccines. But the malaria vaccine has. Um, it's not a done deal. The next step is— there's, uh, Gavi, the Global Vaccine Alliance, which decides if the vaccine is a worthwhile investment.

And so that's the next step. Basically, they have to approve it, and then, um, purchase the vaccine for any country that wants it. So if a country requests it and Gavi approves it, then they can get them the vaccine. That will take about a year. So it's not like, "Bam," snap your fingers, vaccines are out, are everywhere. Um, but this is obviously a gigantic step in that direction.

Um, and in the background it's worth noting, there are other vaccines that are still being developed. 'Cause a lot of people have said, like, this isn't as effective as we wish it was. It is good. But it's not like, for instance, the COVID vaccines, which are, you know, by comparison, *more* effective at reducing serious illness and death.

Justin: Mm-hmm.

Sydnee: It's not to that level, and we wish it was. It's better, but it's not there. There is an Oxford vaccine that is very similar, but possibly a little more effective— it's been altered in some ways to make it maybe more effective— that is being tested and might go into, um, phase three trials soon.

Uh, they actually used an adjuvant that they used developing the Novavax, which is one of the COVID vaccines that was in development, so.

Um, and then in addition, earlier this year, I think in, like, February of this year, uh, researchers at Yale patented an RNA technique. Uh, the same vaccine approach that we have seen with the COVID vaccines, with the, um, Pfizer and Moderna COVID vaccines. An mRNA, an RNA-based vaccine.

Justin: Mm-hmm.

Sydnee: That could possibly be an avenue. Um, so they have tried to take that approach. Um, so maybe that will come out sometime in the future. This is still early.

But, um, the point is, nobody is saying that, like, this is the vaccine that will end malaria, but it will make a huge dent.

Justin: Sure.

Sydnee: In a very deadly, dangerous disease that impacts—

Justin: If you're— if you're the person whose child, or, you know, self was afflicted by this, like, every single step forward is massive.

Sydnee: And millions of cases a year, millions and millions of cases of malaria a year. And it's not just about those that are fatal. Although it is about that, it's not just that.

Malaria makes you very sick. I've cared personally for people with malaria in parts of the world where it is endemic. You are incredibly ill. You can't work. You can't go to school. You can't take care of your family. You know, you can't do all the things that, as humans, we have to do day-to-day. It takes you out of that while you're sick with it.

Um, and so it's not just about mortality. It's the morbidity burden of malaria on all the people who live in parts of the world where it exists. So if we can decrease *any* of that, that's a huge impact, and totally worth the time and money and effort and... everything that it's taken, over decades, to get us to the point where we can say we have a vaccine against malaria. It's amazing. It's fantastic.

Justin: And I feel like, now, I've played my role in this grand chain.

Sydnee: Oh, you do?

Justin: You know what I mean? I feel like I've done my little part, you know? More than— not as much as— as many, but more than most, I would say, in moving this forward.

Sydnee: I— I don't know—

Justin: By just telling people about it, helping to spread the word. We all have our part to play, and this has been ours. Huh. I guess "hero" feels like a strong word to use, but...

Sydnee: I don't know. I mean—

Justin: It's just a podcast, but was— you know?

Sydnee: Yeah.

Justin: Was it just?

Sydnee: Uh-huh.

Justin: Hm.

Sydnee: Well...

Justin: Something to think about.

Sydnee: Yeah. I'll— I'll think about that later. Um, in the meantime— [laughs quietly] please think about, uh, getting vaccines that may be applicable to *you*.

Justin: Yeah! Hey, why not just go get a vaccine if you haven't gotten the— vaccine against the novel coronavirus? It's a bad one, folks!

Sydnee: Yeah. There—

Justin: The, uh— this virus? I don't know if you've heard about it, but it's a stinker!

Sydnee: There are two great vaccines out there you could get right now.

Justin: Oh yeah. Don't forget that flu shot.

Sydnee: That's right!

Justin: Nobody wants the flu!

Sydnee: You get a vaccine against COVID-19, you get a flu vaccine. Just get 'em.

Justin: Just get 'em!

Sydnee: Just— you know, just get 'em! [laughs quietly]

Justin: Hey, here's a thought. Just get 'em!

Sydnee: And if you know somebody who's hesitant, talk to 'em about it.

Justin: Yeah!

Sydnee: We've done many episodes about vaccines generally, about the COVID-19 vaccines, about the flu vaccine.

Justin: Yeah.

Sydnee: We have so many episodes addressing that. Here at *Sawbones*, we love vaccines and, um, are happy to give you all the information we can, that we are capable of giving you, um, to encourage you to get them.

Justin: Um, thank you so much to The Taxpayers for the use of their song, "Medicines," as the intro and outro of our program.

Hey, if you're a, um, regular listener, first o— new listener: welcome, hope you enjoyed yourself. If you're a regular listener of ours, um, why not go check out some other Max Fun shows? This is the week to do it. If there's one you think you've been interested in checking out. Um, Sydnee does one with her siblings called *Still Buffering* about pop culture. I do one with my brothers, uh, about advice. Our dad and I play dungeons and dragons. Whatever.

Sydnee: Those are called *My Brother, My Brother, and Me* and *The Adventure Zone*.

Justin: Yeah, and *Still Buffering*—

Sydnee: You didn't say the name. Well, you said mine.

Justin: Oh, sorry.

Sydnee: I was— I was returning the favor.

Justin: Ah, thank you. Uh, so go check those out! That is gonna do it for us. Uh, until next week, 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]

[ad plays]