Sawbones 318: Hydroxychloroquine

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[theme music plays]

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

Sydnee: And I'm Sydnee McElroy.

Justin: Uh, Syd, y'know, it seems really unfair, in this day and age… lots is unfair about this situation we find ourselves in. The unpleasantness, as I have called it repeatedly.

Sydnee: Yes.

Justin: It isn't catching on, but that's okay. I'm patient. I've got nothing to do but wait.

Sydnee: That's a bit of an understatement, but…

Justin: Yeah, it is.

Sydnee: Carry on.

Justin: It is. That's fair. The very unpleasantness? Super unpleasant? I'll work on it. Um…

Sydnee: I don't know. A lot of people are calling it the dystopian—the sickness.

Justin: The sickness is like, very…

Sydnee: It's quite dystopian. Yeah. It's hard.

Justin: Charlie just says 'the virus,' which is like… accurate.

Sydnee: Yes.

Justin: But lacks some amount of pageantry. Um, no, it seems unfair, because I feel like I have to educate myself about something new every few days. I used to be able to go months without learning anything, and it was perfect. I'm 39 years old. I get it. Y'know what I mean? Like, as far as the whole… thing. Life and stuff. I get it.

Sydnee: Right. Uh-huh.

Justin: Now I have to find myself educating myself constantly.

Sydnee: Yes. Welcome to what it's like to be a doctor.

Justin: Yeah. I don't get paid enough to learn new things constantly. I'm—now I'm constantly like, "Now, what is that? Is that an effective… is that good for the… what does this chart mean?" I'm like, looking at charts. On the toilet.

Sydnee: See, this is not new to me. There's a lot of rhetoric in medical school. They try to sell us on this idea of being a lifelong learner. Which sounds very exciting, until you realize like, oh man, they really do mean lifelong, and everything keeps changing, and everything's new, and then… what we thought we knew, we didn't. And we didn't know, we do now, but then it's wrong.

Justin: Here's the new thing that I'm—

Sydnee: That's medi—that's science, man.

Justin: That I feel like I need to learn more about.

Sydnee: It keep evolving.

Justin: We have mentioned it briefly, but I think—okay. Tell me if I'm saying it right. It's the… chloroquinine?

Sydnee: Nope.

Justin: See? I didn't even get close.

Sydnee: Hydroxychloroquine.

Justin: Hydroxychloroquine.

Sydnee: Also, the brand name is Plaquenil, so you may have seen Plaquenil as the…

Justin: Plaquenil. I've heard from some, uh, angles, that there—it's a miracle drug for COVID, that everybody should just be taking. I've heard of people taking it and um, well, *dying* from it. From taking it.

Sydnee: Sure.

Justin: Y'know, a little bit of everything in between. So I thought, maybe – and I asked you to do this a few days ago, that it would be helpful to like, have an episode… there's so much misinformation out there. Have an episode to kind of like, build that base level of education about this, so we're all a little bit more discerning when we, y'know, get into these discussions about this, and watch the news, and et cetera, et cetera.

Sydnee: I think it's a good thing to talk about. One, because it's an interesting drug. It's an interesting medication that is—

Justin: Well, they're all interesting to me, Syd. Don't get me started on these *fascinating* pills.

Sydnee: It's got an interesting history that we can get into, first. And then, I think it leads us into a discussion that is relevant to the time, but it's also—it's kind of at the heart of our show, which is… we are living in a time right now where the lessons of Sawbones, the lessons of medical history, are so relevant. And so important to keep in mind. Because the—the soil is rich for snake oil these days. And I'm not saying…

Justin: Ooh. There's probably to get a way to get a rhyming couplet out of that, if you work on it a little bit.

Sydnee: I'll work on—I'll keep—I'll keep work shopping it. I'm not saying that hydroxychloroquine is necessarily snake oil. But, I am saying that we live in a moment where you're going to start to understand and empathize with all those people of the past who did things that seemed totally outrageous by our modern standards. You're gonna start to understand where they may have been coming from, and I think that's an important lesson to keep in mind as we move forward.

Justin: Ugh, empathy! That's the wor—you tricked me! You said I could have a refreshing Coke Zero if we did the podcast. You never mentioned anything about empathy!

Sydnee: You gotta have empathy, too. Sorry. So, first of all, what is this medicine? Why is everybody so excited? What do we use it? Obviously, it had a whole life before COVID. What was it?

Justin: I know from listening to you. I know it was originally an anti-malarial drug.

Sydnee: That's right. We're gonna kind of take it—hydroxychloroquine is like, the story of chloroquine, which is really the story of quinine, which is really the story of malaria. Which we've done a whole podcast on, so I'm not gonna belabor malaria. I mean, I think it's a fascinating topic, and you could do episodes upon episodes about it, but… we've covered that before. So, I'm

just gonna focus on the parts of it that are relevant to this specific medication.

As you may remember, or if you haven't listened to the episode before, I'm gonna tell ya. Malaria used to be a scourge throughout the world. We now kind of associate it with largely tropical parts of the planet, where it is still a huge problem, of course. But it used to be a problem everywhere. It was a problem in the United States. It was a problem throughout Europe.

Justin: It seems like a very common, uh… it almost got like… I don't know if a trope can exist in the real world. But uh, adventures and expeditions being undone by malaria is so common that it almost seems to be like, "Oh great, yeah. I know. Malaria. I get it. It happens every single time."

Sydnee: It—malaria has been—and all throughout history. I mean, the ancient Greeks talked about malaria. Shakespeare wrote about malaria. They weren't calling it malaria. You'd see it, um, referred by different terms for fever, really. Because that's the hallmark of malaria, are these like, fevers that appear at pretty standard intervals.

And they're intense fevers, and then they go away, and you could see these fevers come and go, and… it was very scary, 'cause at the time, we had no idea where it came from, why it happened, what to do about it… we didn't know that it was being carried by mosquitos. We didn't know that it was a parasite. We didn't know any of that.

So, until the 1600s, our treatments for malaria were like, our treatments for… everything else. Specifically, everything else that caused a fever.

Justin: Just guesses.

Sydnee: We just guessed, and we did a lot of things that were ineffective. We did a lot of things that were messy, and we did a lot of things that were deadly. But malaria could be deadly as well, so… if you had the tertian fever, then you do what you gotta do. So, we did a lot of bloodletting. We gave a lot of laxatives.

Justin: Sure. Get it out. Whatever's in there, get it out.

Sydnee: Something to make you puke. We did—and then, of course, we did a lot of like… spells and chants and prayers and those sorts of things. Mystical thinking to try to fight malaria. As well as, like, gross things, like poultices and tinctures of smelly things.

But, it was really the Spanish conquerors returning from the Andes that took a treatment that had been discovered there by people who were native to that region, who found the bark of a certain tree was very effective in treating fevers and what they would call 'the shivers,' which are probably like, chills. Rigors. So, it was very effective in treating malaria, even if you didn't know you were treating malaria. So, and that was the bark from the cinchona tree.

And uh, they were using this bark, and there's… we get into it in the episode. There's some theories as to how exactly they figured out this particular bark. Like, supposedly, somebody fell in—who was sick, fell in the water, and drank the water, and it was bitter, because the trees were growing in that water. But then they got better, and the bitter bark from the trees…

Justin: The bitter bark made them better.

Sydnee: [laughs]

Justin: The bitter bark made them a bit better.

Sydnee: I mean, very better.

Justin: I bet the bitter bark made them a bit better.

Sydnee: I don't have—I can't.

Justin: I don't think I have any more.

Sydnee: I don't have any more. Anyway, so, they had figured out that this cinchona tree was important. These Spanish conquerors found this knowledge and took it back to Europe, and told everybody about it, and everybody got very excited about the bark from this tree. It would be—

Justin: The bitter bark.

Sydnee: The bitter bark that made it better. It would be many years before they figured out that it was quinine in the bark that had this effect. That that as the active compound that did this. And it was many, many more years before they could actually isolate quinine itself. That wasn't even until like, the 1950s. But we're getting a little ahead of ourselves.

And uh, even when we did, we knew that it wasn't a perfect medicine. We knew that the bark itself, if you took it in the wrong doses, if you took like, the extract of the bark, as it was administered previously… or, quinine itself, when we eventually had it, there were a whole host of side effects, and it had a very narrow therapeutic window. Meaning, just a little too much, and you can get really sick. But not enough, and it doesn't work.

And so, some drugs are very forgiving.

Justin: Right.

Sydnee: Quinine is not. So, if you took too much of it, you'd get dizzy, you'd get ringing in your ears, you could have vision changes, your heart could beat really fast and irregularly…

Justin: Would it still work?

Sydnee: Yeah. It would work, but I mean…

Justin: Unpleasant.

Sydnee: You might have a seizure, or you could go blind. You could die. So…

Justin: That’s one of the worst ones you've said so far.

Sydnee: Yes.

Justin: Absolutely.

Sydnee: So uh, it’s interesting. Because we eventually, like I said, pieced together that it was this quinine in the bark that was responsible for all of these… all the therapeutic effects, people started trying to synthesize quinine. Like, well, can I just make that molecule?

Justin: Right.

Sydnee: I figured out the active part. Instead of having to like, go harvest it from trees, can I just make that in a lab? The first person who tried to synthesize it was William Henry Perkin, and he failed in making quinine, but he succeeded in making a beautiful, purple dye known as Perkin’s mauve.

Justin: Well, that’s great!

Sydnee: He started like, a whole business with this dye.

Justin: I'm done with trying to help people.

Sydnee: [laughs] He made a living off of this beautiful…

Justin: Look at this beautiful dye I made.

Sydnee: … purple… yeah.

Justin: I'm done wasting my time with medicine. Beautiful, beautiful dye.

Sydnee: It’s interesting, ‘cause this theme kind of continues for a while with malaria treatments. So, Paul Ehrlich also had an idea as to a synthetic treatment for malaria. But his was methylene blue, which didn’t have the same side effects as quinine, was not as consistent in treating malaria as

quinine was, but also would turn you blue if you took enough for it to be effective.

Justin: That's huge. I mean, that's huge. Who doesn't want to walk on the wild side a little bit? A little variety.

Sydnee: So that's—I mean, most people considered that somewhat of a… of a drawback.

Justin: Yes.

Sydnee: So then, scientists at Bayer, specifically, Wilhelm Röhl, decided that we needed a different medicine, 'cause that one guy just made purple dye. That didn't help anybody. [laughs]

Justin: The other guy—

Sydnee: Quinine is still making, y'know, people have seizures.

Justin: That guy made human dye. Blue, human dye.

Sydnee: That guy turned people blue. [laughing] There's gotta be something better. So he made quinacrine, which was also called mepacrine or Atabrine, uh, and it worked… well enough that it was actually, like, one of the predominant medicines that was used during World War II.

Justin: Hm.

Sydnee: By this point. This was like, the preferred malaria medication during World War II. However, it still did have a lot of side effects; some of them, similar to quinine. It could cause seizures, it could cause ringing in the ears. Some news ones. It could cause psychosis.

Justin: Hm.

Sydnee: Which is still a problem today with some malaria medications.

Justin: Sure, yeah.

Sydnee: Uh, but it also, unfortunately, could turn you a color. This one, yellow, though.

Justin: What?!

Sydnee: So I guess you have a choice. [laughs]

Justin: What is going on?!

Sydnee: It took us a long time to figure out how to treat people for malaria without…

Justin: Yeah, but like, the whole—

Sydnee: Like, Easter egg dyeing them at the same time.

Justin: Yeah, but like, most medicines don't have all these like, Hogwarts level side effects. Like, it's like Willy Wonka's Candy Factory in here. You're just popping malarial pills and turning every color of the rainbow. It's like a Skittles ad in this episode!

Sydnee: It took us a while to figure out mala—malaria is tough—it was tough to…

Justin: I don't care! Why were the pills turning people so many different colors?! [laughing] It's a wild side effect to be so consistent!

Sydnee: Uh… I mean, eventually, we figured out how to make a malaria medication that *didn't* turn people colors.

Justin: That's great. That's very good. I'm looking forward—I mean, yeah, I assumed, but…

Sydnee: From some of the—and I'm gonna—I wanna—at the end of—I have the name of a couple articles I read. 'Cause some were very interesting about this. But it seems like—

Justin: Others, not so.

Sydnee: [laughs] No. No, but I—I—there were a couple articles in particular that I got a lot of this information from. And one in particular pointed out that there was a lot of overlap between like, early pharmaceutical companies and industrial dye companies.

Justin: Hm.

Sydnee: Which is just fascinating. I mean, I guess, like, if you're a chemist, you can probably make a lot of different things.

Justin: Sure.

Sydnee: Y'know. I mean, you will apply your skills to whatever you are… y'know, hired to do. But you probably can do—anyway. That's fascinating, to me, that people make these things. All you chemists out there, you cool chemists.

I'm done.

Justin: Okay.

Sydnee: Sorry.

Justin: [snorts]

Sydnee: Anyway, so… [laughs] Even prior—

Justin: I didn't want to interrupt you when you were on a roll.

Sydnee: About how cool chemists are. Anyway, even prior to World War II-

Justin: ‘Cause you know there’s some—every episode when we compliment any group of people, we always get tweets that are like, “Thank you. Finally.” Had a cat who worked in a lab… I think two weeks ago, we were talking about how helpful, uh, lab technicians are. And they were like, “Finally. They mentioned us for two seconds, but at least we got in there.” Like, I'm sorry. Y'all are great. Everyone’s great. Chemists… love it.

Sydnee: Trying to give everybody their due… yes. Pharmacists, who wrote some of these articles. Thank you.

Justin: People who work in the industrial dye industry. Like, what’s up. Crushing it, I bet.

Sydnee: Sure.

Justin: Unless you are doing bad things to the environment. I don't know. I don’t pay close enough attention. I don’t love that.

Sydnee: Then that’s not so great. That definitely happened, probably.

Justin: Want to cover all my bases.

Sydnee: Well, I assume. I don't know.

Justin: I don't know.

Sydnee: Probably…? Anyway. So, chloroquine had actually been in the works at Bayer, even prior to World War II. So, even as they were giving people this quinacrine that turned them yellow, they had chloroquine. Now, they initially thought – and this was like, a big mistake that they would realize later. They thought it was too toxic to give to humans, and so, they had just kind of shelved it and hadn’t even considered it.

Justin: Mmm.

Sydnee: But, in light of all these other medications that, y'know, did a lot of things that people would prefer they didn't… they went back and took a second look at it after World War II, and went, "Well, y'know what? Actually, this was actually a pretty decent medicine." There were some side effects, but it didn't change you blue or yellow or any other color. So, that was nice.

Justin: Yeah. Nice.

Sydnee: Um, and a lot of the other side effects it had were similar to these same meds, and somewhat less so. So why did we not give it a chance?

So, over the next couple decades, it became very popular as an alternative to these other medications that, y'know, turned you blue and whatnot. And uh, and eventually, they added… if you know chemistry, all they had to do was tack on a hydroxyl group to one of the rings to make it hydroxychloroquine.

Justin: Sure, yeah.

Sydnee: Chloroquine, hydroxychloroquine.

Justin: Yeah, for sure.

Sydnee: Anyway, that doesn't really matter. The point is, what that did was make it even better tolerated.

Justin: Okay.

Sydnee: That was basically the idea, there. So, now we have this great malaria medication. Hydroxychloroquine. That I… did I take that or chloroquine? I've taken this before.

Justin: Hmm.

Sydnee: Uh, 'cause you can—I mean, we still use this medication today. It's an option, not all over the world, because it depends on if there's resistance in the malaria of that region.

Justin: Hm, okay.

Sydnee: Because malaria has gotten smarter through the years, and is resistant to some of these early medications; specifically, chloroquine, hydroxychloroquine in some parts of the world. But I believe, when I went down to central America, I was able to take it. But anyway.

So, we still use it today. Still a worthwhile medication. It's interesting in that, if you want to know the mechanism of action…

Justin: And I do.

Sydnee: Of course. Uh, we don't know exactly how it works.

Justin: Fun!

Sydnee: We have some ideas as to what it does, uh, inside the malaria parasite. But we're not entirely certain. We have some theories, and like, there's some things we're pretty sure that it definitely is doing. But as to every—all the little teeny, tiny molecular reasons as to why it does what it does, it's not completely understood.

Justin: Hm.

Sydnee: But, we have this medication. It works for malaria. And back then, when we get a new medicine, and it does something…

Justin: We use it for everything.

Sydnee: We try it for everything else.

Justin: I want to hear all about that.

Sydnee: Well, I'm gonna tell you about that, Justin. But first, let's go to the billing department.

Justin: Let's go!

[theme music plays]

[advertisements]

Justin: Syd, we got this great new drug. I want to pitch you on it. It does something. And doesn't change you a color, and I want to put it in production for… everything. I just want to take it—take—put it through its paces. Let's get tryin' it.

Sydnee: So let's do it. So, we've got chloroquine, hydroxychloroquine now, this is great. We're using it for malaria so that we don't have to either go harvest tree bark every time we want to treat malaria, or turn someone yellow or blue. And that's great. So why don't we try it for other things, and see what else… what else it's got up its sleeve, so to speak?

And this was common practice, if you looked back to like, the late 1800s and early 1900s, when you find a new, effective medication. Similar to we've always done, right? With medical practices. Like, bloodletting. We used it for everything. Mercury. We used it for everything. 'Cause it's what we had, and anything that did anything was better than… nothing. Or at least, so we thought. That's not always true.

So…

Justin: Do we still do that? Is that how we found out stuff like… wellbutrin helps you quit smoking, that kind of stuff?

Sydnee: Uh, no, not exactly like that. We have reasons why we would try something for a new application. Like, we would see properties in the medication that might make it useful for a different condition.

Justin: We understand that neurochemistry a lot better, too, these days.

Sydnee: Precisely. The mechanism of action and that is so much more well understood; especially, a drug that's developed, as opposed to kind of going back the other direction and taking a drug… we don't know why this worked, we just made this thing, and it seemed to work, as opposed to, this was designed to do this.

We also notice things in clinical trials. Like, I—we did it to see if it would have this effect on humans, but as we were doing the study, we observed this other effect it had. And so, that's where you find some of these kind of—like you said, like with wellbutrin also being used for smoking cessation, that's where you see that. In the study, they found that a lot of people quit smoking.

Justin: I'm overwhelmed that I'm married to such a smart person. Sometimes it just hits me. I love you so much.

Sydnee: Well, thank you.

Justin: Sorry. Go ahead. Continue.

Sydnee: I love you, too.

Justin: Well, thanks. I didn't mean to interrupt. Please, go on. So, we've figured out… we want to try it for everything, is the point.

Sydnee: Okay. So, at that point, when you talk about things like lupus, or rheumatoid arthritis, we didn't really have great medications at that point in history for these conditions. And so, these medicines, hydroxychloroquine, it was tried for those conditions, and… they saw a response. And it turned out—y'know, it's always interesting. If you look back, you'll see that, like, well, we tried it for this, and we thought it worked. And half the time, we were like, no, that actually… we just… it didn't work. We just hoped it did.

It did. I mean, there definitely were effects. And to this day, it remains an important treatment for these conditions. There, of course, are a lot of other options as well. But it still is used as Plaquenil. Hydroxychloroquine. Either way. Whichever you want to call it.

We know, again, why does it do this? Why is it so effective for these conditions?

Justin: We don't know.

Sydnee: We're still not entirely sure. We know it has something to do with the inflammatory response. It has a way of suppressing the inflammatory response that is so central to lupus and rheumatoid arthritis and other, y'know, autoimmune conditions.

And so, but as to the exact mechanism of action… we still don't know. Which is important to know that, if anybody tries to tell you they know exactly what it's doing, hopefully, in patients with coronavirus… we have no idea. I mean, we don't know. Again, it plays into this idea. We know that it has some effect on the inflammatory pathway. There are a lot of different things we've observed that it could be. I could get into the biochemistry of what it could be doing. But again, it's still—we're still guessing, somewhat.

Justin: Mm-hmm.

Sydnee: So it became very popular. And occasionally, we would find that, because it was so popular, doses of hydroxychloroquine throughout time have been pushed too far. And so, we know the dangers of this medicine, because we've seen, y'know, patients have these side effects.

Justin: Right.

Sydnee: It can cause retinal toxicity, resulting in vision loss. Again, that's usually chronic use. But it can do that. There are also irregular heartbeats, arrhythmias, that are associated with hydroxychloroquine. And we know, because we've been using it for a long time.

For rheumatoid arthritis specifically, the real breakthrough for hydroxychloroquine was actually when we found newer meds. Other meds, methotrexate and sulfasalazine, that we could combine with it. And we could see a huge effect from that, so, it's used in a lot of combos and things now.

And over time, we've seen some other positive things from hydroxychloroquine, like… in rheumatoid arthritis patients who were on it, they had fewer, uh, cardiovascular events. Like, heart attacks. Things like that. And they had a lower rate of developing diabetes. Why?

Justin: I was about to ask you why, and I bet the answer is, we don't know.

Sydnee: [laughs] Again, it probably has something to do with all these inflammatory pathways that it's interrupting.

Justin: Is that common? To not understand the mechanism of a medicine?

Sydnee: Mmm… I don't want to say—I mean, it certainly happens. This is not the only medicine that we're not sure exactly how it works.

Justin: Hm. Wow.

Sydnee: It is not alone.

Justin: That's wild.

Sydnee: Again, more and more, we're designing medications, right?

Justin: Hopefully know why those work.

Sydnee: [laughs] So, yes. We're more likely to understand exactly how they work if we… but there are a lot of medicines that have been around, and worked well for quite a long time, and… we don't want to stop using them, 'cause they work. We know they work. We've put 'em through their paces. But what… y'know, sometimes it was luck that led us to them in the first place. Really, scientific luck.

Justin: I don't think it—

Sydnee: Somebody with a brain picked it. [laughs]

Justin: I don't think it got falling into a lake is scientific luck, to be fair.

Sydnee: No, but the synthesis of—

Justin: Unless he was doing some like, astronomy or something. He just wasn't looking where he was going.

Sydnee: The synthesis of chloroquine and hydroxychloroquine and all that, that's scientific luck. Y'know.

Justin: Got it.

Sydnee: Somebody knew what they were doing when they made these molecules. Maybe they didn't exactly understand why, but… uh, for lupus, it's still a good choice. It can reduce the number of flares of lupus. It can reduce the severity of flares. It has a lot of, um… suffice to say, it has a lot of positive effects in lupus patients, and it's a good—there are other medications, too, but it is a good choice, um, for a lot of patients with lupus.

There—there are no studies that have been done on it, specifically, on pregnant patients. But, it is felt to be, um, a safe medication to take while pregnant. And that's common, when it comes to medicines and pregnancy. As you may imagine, doing a study on pregnant people is not…

Justin: Hugely popular.

Sydnee: Right. I mean, y'know, it's very hard to say, "I want to take a randomized group of pregnant people and give some of them a medication, and others not, and see what happens to them."

Justin: Right.

Sydnee: No.

Justin: Which is why we—a big part of the reason it's so hard for us to say which OTCs are—sorry, over the counter medications are like, safe for pregnant women to take, because nobody wants to be the guinea pig, and fetal guinea pig within said guinea pig, uh, on that particular…

Sydnee: Precisely.

Justin: Experiment.

Sydnee: We don't have the same rigor of evidence for those kinds of things. We have a lot of history, like, anecdotal evidence to say, we know for a very long time, this medicine appears to be safer. But it's hard to have the degree of certainty. But it seems to be safe in these patients.

And the reason I'm telling you all this about it is that, it's a very important medicine for some people. And I think that's key to understanding all of the pieces of this story today. This medicine is, y'know, it's life sustaining, lifesaving, it's quality of life saving. It's important for people with conditions, and we've know this for a long time.

Yes, there are other options for malaria. A lot of people say that. "Well, there are other drugs for malaria." Yes, of course, there are other drugs for malaria. For some lupus patients, though, this medication has changed their lives, and it's a big deal for them to not be able to get access to it.

Justin: Right.

Sydnee: So, that's the point I want you to understand about hydroxychloroquine. It has a place. It's listed as one of the World Health Organization's essential medications. So we should, if we can, keep a steady stock of it for the patients who need it.

Obviously, there are still risks, even now, taking it in the appropriate doses and all that kind of stuff. Um, but… it's still a good medication. So, again, how does it work now against COVID-19? The disease caused by coronavirus.

Justin: Yes. Yes.

Sydnee: Well, we don't really know.

Justin: I should've guessed that, actually.

Sydnee: Again, something with inflammation is a theory, of course. Because we know that works on these other inflammatory conditions, and we have seen that, in these severe cases of COVID, we appear to have what is being called the cytokine storm. This big, inflammatory reaction.

Justin: Right. I've seen a lot about that.

Sydnee: Yes. That causes some of the very severe complications, and the mortality. And so, does it have some impact on that? There's also thought that it can help prevent the uh, virus from entering cells. And so, is it—would it be better… to give it to people as like, a prophylactic? Like, should we be giving it to healthcare workers who are being exposed to the virus on a regular basis? There's been some thought about that.

Again, these are all things that have been observed in labs, and are theoretical. But they're not…

Justin: Proven.

Sydnee: They're not proven in any way, shape, or form. There's been some thought, does it have something to do with zinc? Does it bind zinc? And that's why it does that. And it does bind zinc, but does that have any effect in a human body?

Justin: I don't know!

Sydnee: Nobody knows. Uh, in terms of… studies, there have been… I mean, this is an evolving—when—this is—it is April.

Justin: The 12th.

Sydnee: And we've only been dealing with this on a global scale since December.

Justin: Right.

Sydnee: So, it's impossible for there to be good, solid studies on anything at this point. It's just—there isn't enough time.

Justin: Yeah.

Sydnee: You couldn't have done it. Um, there have been very small studies in China and Italy and France, and now, there are big studies. Or, they're putting together larger studies in the US. But they're still… I mean, in the early stages.

Justin: Right.

Sydnee: To look at the effects, specifically, of hydroxychloroquine, as well as hydroxychloroquine plus azithromycin. Which is an antibiotic that many of you probably know as a Z-Pak.

Justin: Oh, right. Yeah yeah yeah.

Sydnee: You've heard of a Z-Pak?

Justin: Yeah, those are very common.

Sydnee: It's azithromycin. That's what they're talking about. A combination of these two is thought to, perhaps, be more effective. But all of these studies that have been published don't hold up to our typical scientific rigor.

Justin: Right.

Sydnee: And the results are mixed at best. And even when they show some positive results, they're fairly modest. There's a problem with how many patients. They're all fairly small. Some of the studies don't have a control group. Y'know, a group of patients who didn't get the medication,

which is necessary for a decent study. Some of them have not been blinded, which means the doctors know which patients got what.

Justin: Oh, that's not great.

Sydnee: Mm-mm. Some of them have not been randomized appropriately. And uh, one of the main French studies that you may have heard cited, if you've been watching any press conferences recently, um, has actually since been retracted for not meeting appropriate standards.

That doesn't mean that they lied or anything. I'm not saying that. But it did not meet… I think it's important to know, before—when researchers decide to do a study, first of all, you're supposed to get it approved. So you like, write up a proposal and send it to a review board to say like, is this fine? Is this okay? Is this okay to do?

And once you do that, then you do an appropriate study, and then you write it all up and send it to journals to be published, and it's reviewed by peers. Like, other members of the scientific community, to look at, how did you go about it? What were your methods? What statistical analysis did you use? What were your conclusions? And does all that make sense? As a scientist, does it make sense?

Justin: Right.

Sydnee: Not, does it say what I want it to say?

Justin: Right.

Sydnee: Does it make science sense? And only then, should it be published. If your peers agree, yes, this makes science sense.

Right now, what's happening is, stuff is being published that is not going through that process.

Justin: Because we're in such a hurry to get it…

Sydnee: Yes. So, you are hearing… and I think, because if you are not in the scientific community, if you're not used to reading studies, it's all coming in at the same volume, y'know? I mean, we heard news reports, before COVID, of "the newest scientific suggests that blah blah blah."

Justin: Right.

Sydnee: "Coffee is good for you, or bad for you, or whatever we decide coffee is today." These are coming in with that same kind of level of certainty. But it's not, in any way, representative of the usual scientific rigor that goes into this process.

Justin: Got it.

Sydnee: So, any study you've heard about hydroxychloroquine, it's… I mean, it really…

Justin: Specific to COVID, you mean.

Sydnee: Yes.

Justin: Right.

Sydnee: We have no idea. We have no idea. Um, a lot of the stuff is working in a lab, and not necessarily in humans. And we've talked about this before. Stuff that works in vivo, or in vitro, in a lab, does not always work in vivo, in humans. If that were true, y'know, we can dump bleach on germs in a lab and kill them. We can't drink bleach, as we have covered in depth on this show.

Justin: Yeah. More than we should have, honestly. Or should've had to.

Sydnee: It's not one to one. And in times like this, of crisis and panic, scientific rigor and ethics will easily be tossed out the window if we're not careful. If you look at the heroic era of medicine, which we have covered on this show many times… at that moment in history, we just—we knew enough science, and enough stuff, to feel like we had a grasp on it.

And so, our theory, when it came to treating people was… look, you've got something that I sort of understand, but not really. But I do know it will kill you. So, anything I do is worthwhile, 'cause you're gonna die anyway. So… now…

Justin: Right. That's the heroic era in a nutshell.

Sydnee: Exactly. So now, let me give you mercury. Now, let me do bloodletting. Now, let me blister your skin to heal your infections. Let's do trepanation. Let's do a lobotomy. All these things were justified, in part, by saying, "Well, it's better than nothing." Right?

Justin: Right, right, right.

Sydnee: You're gonna die anyway.

Justin: Might as well give this a whirl.

Sydnee: Yes. And it's important to know that that's not how science works. That's not how—that's not the level of, um, y'know, professionalism. Those aren't the standards we have held our medical scientists to ever before. We deserve better than that. We deserve more than that.

Hydroxychloroquine may, after appropriate study, show some effect on COVID, but as of now, there's no compelling evidence, really. It's just not there. Again, it'd be great if it was. I hope that one of these medications that are under investigation… will show something.

Justin: That'd be great for everybody. We all win.

Sydnee: Right? I mean, right now, I—my personal greatest hope is on a vaccine.

Justin: Right.

Sydnee: Which is gonna take time, again, 'cause we want it to work and not hurt people. But if one of these other medications turns out to be more effective in treating patients, or preventing infections…

Justin: Yeah, of course.

Sydnee: That would be amazing.

Justin: Forget about it. It'd be huge.

Sydnee: That would be wonderful. I think it's weird to see, if you push back against hydroxychloroquine as a miracle drug, people say, "Well, you just don't want anything to work."

Justin: Who wouldn't want… we all want something to work. [laughs]

Sydnee: Of course I want it to work! [laughs] Of course I would love for it to work! I would love to see studies that showed these things work. They're just not out there, right now. They're still—they're still doing studies. They're still figuring things out. But it's just not out there, yet.

But we do know that it helps people with lupus and rheumatoid arthritis, and some of them need it.

Justin: Right now. For sure. Guaranteed. It definitely works for that.

Sydnee: And when you get it, however people get meds that aren't being prescribed to them… or, when you harass people to prescribe it to you… or, when you are a prescriber who starts giving it out to friends or family or neighbors or whoever…

Justin: Just for the heck of it, just in case…

Sydnee: Just in case, it's irresponsible, and it's reckless, because it hoards the medication and keeps it from people who definitely need it. It also makes it harder for, if we are gonna do these trials, and we are gonna give it

to patients who are already hospitalized, and perhaps, severely ill, it makes it harder to get there!

Justin: Yeah. There's no… I mean, it's a loser. I understand the idea. And it's also, like, you covered it. This is not like, a fun drug that you can kind of like, mess around with a little bit and take, and maybe something good will happen, maybe something won't.

Sydnee: No. It's not benign. As you may have seen, it can cause a change in the rhythm of your heart. A change in the electrical conduction of your heart. Something we call… you'll hear us call it QT prolongation. And what we're actually talking about is not your heart – we're talking about the EKG.

Justin: Oh, okay.

Sydnee: That we look at, that tells us the electrical, like, that we look at to see the beat of your heart. That we read. We're talking about a specific segment of it gets longer. A segment we call the QT segments gets longer, and that can be… when we start to see that on an EKG, it's a warning sign. It's a big red flag to us that, ooh, if this continues to get longer, you're at risk for a deadly arrhythmia that can kill you.

Justin: [sighs] Yeah.

Sydnee: And… azithromycin, the Z-Pak, can also do this. So if you take them both together, unmonitored…

Justin: It's a bad scene.

Sydnee: It's a very bad—somebody's going to get harmed. And someone has already died after taking some sort of… I think it was like… aquarium cleaner?

Justin: Aquarium something, yeah.

Sydnee: That contained chloroquine, as a way of trying to prevent them from getting the virus.

Justin: [sighs heavily]

Sydnee: So you can't just put these ideas out there without appropriate scientific backing. We need to tell people the truth. We need to be transparent. When things work, they need to know when things don't work. They need to know. When there's uncertainty, trying to push people on a medication that is unproven is false hope. And while hope is wonderful, false hope is worse than nothing at all.

Justin: It's—well, and especially like this, when it's hurting people. I mean, we talk a lot on the show about like, if it doesn't hurt you, if it doesn't hurt other people, uh, and y'know, you're not losing money on it, like… go for it. Y'know, like, give it a whirl. Who knows, maybe it'll work for you. But this is like… every time you buy this and hoard it, you're like, keeping it from people that actually need it. It's ridiculous.

Sydnee: And I'm seeing a lot of this. Not just throughout the lay community, but throughout the scientific community, too. A lot of people are scared, and a lot of people are, uh, forgetting the things that they've been taught in school when it comes to the scientific method, and the way we go about things, and the reason that it is—it's frustrating how long, sometimes, it takes to prove that something works or doesn't work.

But that process is there for a reason, and ethics tell us, you can't just throw it out the window because you're trying to be expedient. Because you will harm people.

Justin: Right.

Sydnee: And right now, I would be very cautious. You're gonna see a lot of articles, especially on like, social media and stuff, that will try to tell you that there's this secret wonder drug. And I've seen these protocols. They're not always, um, advertised like they would be to the consumer. I've seen them…

Justin: That look all doctor-y?

Sydnee: Yes. They're trying to sell them to me as a medical professional. And if you listen to this show, you know that, right now, no matter how smart and advanced we think we are, this is a time when snake oil will be rampant. And you just need to… if you talk to your doctor, talk to medical professionals, make sure that the people you're listening to are the people who are actually, y'know, reading the studies, finding the evidence, doing things the appropriate way…

Justin: Yeah.

Sydnee: And not a Facebook post.

Justin: Ahem.

Sydnee: [laughs] Thank you to um, Martin J. Bergman and Derek Lowe for the articles that were fascinating on the subject of hydroxychloroquine and the history, and all these dyes, and turning people different colors. Fascinating.

Justin: Yeah, I hope you bookmarked those bad boys, 'cause I would love to dive in as soon as I get a little free time.

Sydnee: I feel like you're giving me a hard time.

Justin: Thank you so much for listening to our show, Sawbones. We hope you've enjoyed yourself. Hey, if you need a little, uh, reading material, um, right now… maybe hop on over to buy a uh, copy of the Sawbones book. You can go to BookShop.org, and it'll help you find a local bookstore where you can um, shop online and get it sent straight to ya. We don't—nobody pays us to say that, I just think it's a good service.

Um, thank you to the Taxpayers for the use of their song, Medicines, as the intro and outro of our program. And thank you to you for listening. Hope you're staying safe.

Sydnee: Stay home. Wash your hands.

Justin: Stay home. Yep. The whole bit. Uh, we're getting through it, folks. I bet, right now, if you take a moment to think about where you were a month ago, the fact that you have strung together this many consecutive days of this, uh, and are still standing, you would find it very impressive, your past self. So, here we are. We're doing it. We're getting through it. Just keep your chin up and hang in there.

That is gonna do it for us for this week. So, 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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