Sawbones 218: Antibiotics

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

[theme music plays]

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

Sydnee: And I'm Sydnee McElroy.

Justin: Well Sydnee, it's cold and flu season.

Sydnee: Yes it is, Justin. Did you get your flu shot?

Justin: You know I did!

Sydnee: Good. Because no matter what— we're not gonna talk about the flu, because we've talked about the flu before. I just wanna briefly say: no matter what you've heard on the news about how effective or ineffective the flu shot may be, you still should get your flu shot. We still recommend it. Even if there's a chance it's not going to protect you, there's a chance it will.

And also, we have reason to believe that because of some cross-reactivity, even if it's the wrong strain you may have a less severe version of the flu if you get it. So, as someone who has had their flu shot and then still got the flu, I will still strongly recommend to you, get your flu shot.

Justin: Get your flu shot. But it's not just cold, it's not just flu. There's a lot of bugs this time of year.

Sydnee: That's right. This is the time of year where everybody gets, you know, the sniffles.

Justin: And they come into your office and they say, "Sydnee, make me feel better."

Sydnee: It's true. It's very frustrating to have upper respiratory infections, meaning, like, the stuff that makes you have a runny nose and a sore throat and cough and congestion, and that kinda stuff. Even, like, sinus infections are kind of in this same arena, because most of them are caused by viruses, and there's not much we can do to expedite your healing from a viral infection in this case. There are other viruses, maybe, but for this case, it's usually just time and fluids and rest, and you'll get better.

Justin: No magic pill for that.

Sydnee: But one thing that generally will not help unless you do happen to have a bacterial infection are antibiotics.

Justin: And you get a lot of people asking you for those, I know.

Sydnee: It's a common problem because, you know, sometimes you have an infection and then your doctor tells you you need antibiotics, and then other times your doctor might tell you you don't And so it can be hard to understand why sometimes it seems like we're withholding something, right? Like, "Well this treatment has helped me before, why won't you give it to me again?"

But the truth is, if you have a viral infection, which you most likely do, antibiotics aren't going to help you at all, they do have side effects, and every time we misuse antibiotics, and we're gonna talk about this a little more, we run the risk of building up more resistance to these antibiotics. So, I think it's a good time of year to talk about antibiotics.

Justin: Let's do it.

Sydnee: So, thank you to Samantha and Ian and Austin and Jessie and Sydney and Matthew and Cecelia and Alison and Sage and Megan and I think a lot more people have suggested this over time. It got overwhelming. [laughs]

Justin: [laughs]

Sydnee: I don't know why we haven't covered this yet. This is a big topic in medicine, right?

Justin: Right.

Sydnee: Antibiotics. The story doesn't really formally begin until the 1900s. That's, like, the origins of what we think of today as antibiotics. But we have been trying to treat infections, even when we didn't know what they were, for a really long time. Which is the truth for everything, right? We don't know what this is, but we're gonna put some stuff on it and see what happens.

Justin: Some honey, some frog legs…

Sydnee: Well, honey— you use honey, but honey's not a bad idea in this case.

Justin: Nice. Crushed it, got it in one. Take that, old-timey doctors.

Sydnee: And that was one of the mainstays of early, uh, what we now understand is an infection, meaning some sort of bacteria's growing on something, somewhere that it shouldn't. Honey was one of the most common treatments, and that probably was in some cases somewhat effective. It doesn't treat all infections, but it probably did help sometimes, especially with skin issues. The ancient Egyptians would actually rub bread mold on wounds that looked like they were not healing properly, now we would recognize as infection.

Justin: That's weird.

Sydnee: Yes.

Justin: That's really, really weird.

Sydnee: Cause as we will get into, that may have been—

Justin: You think that would have worked?

Sydnee: Maybe. I don't know what bread mold it was, but…

Justin: Maybe some bread mold.

Sydnee: Maybe. Let me say this. I don't know if it worked or not, but using mold to treat infections was practiced throughout history in Egypt, in Greece, in Rome, in China and in Serbia.

Justin: Wow.

Sydnee: So… now, we have said this on the show before, just because a lot of people did it, doesn't mean it worked. [laughs] But—

Justin: It is counter-intuitive enough, though, that it makes you wonder. Like…

Sydnee: Did they see some effect?

Justin: Or do they understand on some deeper level? Sydnee, do you believe that there are some medicines that we know instinctively work?

Sydnee: Medicines that we know instinctively work?

Justin: Like, that we instinctively know sometimes what could help us. Do you think that instinct could drive it? Like…

Sydnee: It's an interesting question. We're so far removed from that now in modern society, it would be hard for me to make a guess. I mean, there are certainly things we're programmed to know are bad for us.

Justin: Right.

Sydnee: You know, there are things that we naturally avoid, instinctually avoid, because they are toxic.

Justin: Ah.

Sydnee: It's an interesting question, but I mean, there's some— our whole podcast would lead you to believe otherwise.

Justin: Yeah.

Sydnee: [laughs]

Justin: Evidence to the contrary. This does seem like kind of an outlier.

Sydnee: The ancient Egyptians also accidentally ingested an antibiotic called tetracycline, which is still in use today, regularly.

Justin: How?

Sydnee: Well, they would brew this kind of beer. It was sort of a chunky… bread… beer thing. It was a mixture that they drank a lot. About 3% alcohol and it was like this fermented bread, porridgey, beer stuff.

Justin: Sounds good.

Sydnee: [laughs] Because of naturally occurring bacteria in their soil and in the things they grew and all this, the beer would contain high levels of tetracycline as kind of an extra product that was created in the process. And this was long before we actually isolated tetracycline and figured out that it was an antibiotic and used it to treat infections.

The thing is, though, beer was elevated to— it was not just a drink. It was not just something you would imbibe. And it was not just used for fun times. It was not, you know, a lot of people drank beer and you would think, "Oh, cause they were all getting intoxicated and it was fun." No. Beer was thought to be a healthy a drink. This beverage was thought to be, um, I don't wanna say magical, but somewhat magical and spiritual and important to the body, important to the culture and their existence.

Justin: You still believe that to this day, yeah?

Sydnee: No, I'm not saying that.

Justin: No?

Sydnee: I just, I am a fan of beer.

Justin: And its magical properties.

Sydnee: I'm not gonna say beer has magical properties. I'm looking forward…

Justin: [laughs]

Sydnee: … to a time when I can drink it again at the end of this pregnancy. [laughs] I know it is not magical.

Justin: I'm kinda jealous of you, because like, I've never denied myself something I love that much for ten months. So, like, I'm jealous of you that you're getting this great experience. Because it's gonna be so good afterwards. And I won't understand that, you know?

Sydnee: [laughs] This is the point where I urge everyone to drink responsibly.

Justin: Do you feel bad for me because I won't experience that great taste of ten months without beer and then beer?

Sydnee: No. I don't.

Justin: Okay.

Sydnee: I don't at all. I don't feel bad for you in any regards to this pregnancy.

Justin: Fair.

Sydnee: [laughs]

Justin: I'll take it.

Sydnee: Anyway, so beer was used medicinally for all kinds of different things. Stomach ailments, coughs, constipation. There's a prescription that you can find for a beer enema that people would take. And we have figured all this out—

Justin: Please, just do Natty Light. If it's going up your butt anyway.

Sydnee: [laughs]

Justin: That or The Beast.

Sydnee: Don't waste something good.

Justin: Yeah, don't make it a good beer.

Sydnee: But we know this, by the way, because we studied bones and found tetracycline deposits in the bones of ancient Egyptians.

Justin: Guess the beer wasn't that great. Cause they died.

Sydnee: [laughs] Well, I mean. We'll cover mortality at some other point.

Justin: Okay.

Sydnee: Traditional Chinese medicine relied on a number of different herbal medications for what would have been, like, again, things that we now know to be infectious. Because people look for certain signs, like,

"Well, that's hot and red and swollen and there's pus coming out, so we treat it with these things." Now we would say, "Ah, that's infected." And some of these things have been found to have natural antimicrobial activity, meaning that you put their herb in a petri dish with some bacteria and the bacteria won't grow there. That doesn't always mean that it'll work in the human body the same way, but we have observed that.

In addition, it should be noted that traditional Chinese medicine brought us Artemisinin, which is a plant-based medicine that has been used for thousands of years for all kinds of different ailments, but is very effective against malaria. Now, when it comes to the Middle Ages, typically on this show you start making fun of people.

Justin: Yeah. Not the people, although, I mean, holistically speaking, yes. But the Middle Ages is normally where if we are building up a head of steam treating something, we all take a collective dump. I mean, I can't think of a nicer way to say it than that, but we usually take a dump during the Middle Ages. [laughs]

Sydnee: Now, I have to tell you that there is something that came out of the Middle Ages when it comes to fighting infection that actually is useful.

Justin: Excalibur.

Sydnee: [laughs]

Justin: That's the only good thing about the Middle Ages, that one.

Sydnee: No, it was not a sword.

Justin: The magical sword, Excalibur.

Sydnee: It was not, no. It was not a sword. So, I wanna tell you about—and this was something, I think, we independently had a lot of listeners, when this came out in the news, tell us we should talk about. And we haven't covered it before, so here you go. Bald's eye salve. This is a recipe for a medicine…

Justin: Okay.

Sydnee: Eye salve, it's a salve for your eyes.

Justin: Eye salve. Is this a brand?

Sydnee: Well, it's from a guy, Bald, who made it.

Justin: Oh, okay. It's weird to think of brands in the Middle Ages.

Sydnee: Its from his book, Bald's Leechbook, which is a medical text from the 10th century in England.

Justin: [laughs] Mm hmm.

Sydnee: Which was a collection of a lot of recipes from the day, you know, for different ailments. So, this was used for styes, which were known at the time as "wens". So, a stye, you know what a stye is on your eye? It's a little infected area on your eye lid. You know what I'm talking about?

Justin: Mm hmm. Yeah.

Sydnee: Okay. So, this is a salve you would put on your eye. It contained wine, garlic, some sort of allium species like a leek or an onion, and ox gall. And so, you mix all this together, you have to put them in a brass vessel for nine days, well, nine nights I should say, and then at the end of that, you use it.

So, a team of researchers in 2015 took this recipe and reproduced it exactly, including the nine nights in a brass vessel and all that. And then used it in petri dishes as well as in some tissue from chronic mouse wounds that had staph bacteria, specifically MRSA staph bacteria, which is the kind that is very resistant. Methicillin-Resistant Staph Aureus. So that's— a lot of people get scared when they hear that. You think, "It's called the Superbug," right? So, very resistant bacteria. So, they tried it against all this stuff, and it seemed to work.

Now, this was not in a human body, or even in a live mouse body, I should say. It was in tissue from, so what would this do in the human body? I don't know, I can't tell you. But, at least in petri dishes and in tissue cultures, it worked to kill the bacteria. They even kind of put it up head to head against Vancomycin, an antibiotic that we commonly use for MRSA infections, and they said it worked just as well, if not better.

Justin: Why?

Sydnee: It's interesting. The theory is that it has to do with the allium, the leek or the onion. There are compounds in there that we know are antimicrobial, and so— but they don't, but this doesn't work on its own. You have to follow the directions. [laughs] You have to mix these ingredients, and you have to leave them for nine nights. It doesn't— they tried variations of it, and it didn't work unless you followed that recipe exactly.

Justin: That's so strange.

Sydnee: It's very strange. There was also some theories that because there was copper in the pot, and copper is known to be antimicrobial— we've referenced this before, copper inhibits the growth of bacteria— that maybe it was something synergistic between the allium and the copper. Anyway, the point is, it worked. And then it began to call into question all of these old recipes from, I mean, the Middle Ages or any time in history.

Justin: This is undermining the very premise of our show!

Sydnee: [laughs]

Justin: This is infuriating.

Sydnee: Now, I will say this—

Justin: How am I supposed to sit in judgement from my perch? My modern perch? And judge my ancestors?

Sydnee: To be fair, they were not the first researchers to have tried this. In 2005, a team of researchers did it and they could not reproduce the— they could not make this happen.

Justin: Hmm.

Sydnee: I shouldn't say reproduce, because they did it first. But they could not get these same results.

Justin: Maybe they didn't leave it for nine whole nights or something.

Sydnee: [laughs] Well, and they also called that into question, actually, in the 2015 study. I don't think they did it exactly right. So, it's hard to say. I think it is definitely worth investigating and repeating, because, as we're going to get into towards the end of the show, antibiotics, if you

don’t use them right, don’t work forever. So, it’s always good to look for alternative methods that work to treat infections.

Justin: It’s so sad that you have to add that coda.

Sydnee: That work. [laughs]

Justin: That work!

Sydnee: I don’t wanna just say alternatives, because there are lots of alternatives.

Justin: Right.

Sydnee: You can put anything on a wound. You just shouldn’t. So, while all of these principles that we’ve kinda talked about, all of these things that have been gleaned throughout history, people using bread molds and honeys and these salves that seem to actually work, there were a lot of efforts— all these principles between that and then getting to, like, modern day antibiotics like Penicillin, you’d think there was a direct line.

But of course, we take a detour into using things like heavy metals for a good bit of history at this point. Mercury and arsenic are, like, how we mainly treat infections. Especially things like syphilis, which we’ve talked about before. Things that were very caustic and painful, and not necessarily the most effective. And we really don’t get back into the story of the stuff that actually worked well and didn’t harm people so much until we discovered microbes. So, we’ve talked about this before, we figured out that there were what were first called animalcules.

Justin: That’s a cooler name.

Sydnee: It is kind of a cool name. Germs, bugs, bacteria, microbes, things that cause infection. We figured out the germ theory of disease, that that’s why people get sick, that’s why infections happen. And then we start trying to figure out, “Okay, now we know why this is happening, we have a name for it, we have a target for it.” And the person who really spearheaded that was Paul Ehrlich. He was one of the first to use, like, a systematic approach to figuring out— his idea was that there is a silver bullet. You need to target the bacteria, target the germ, and then we can treat the infection, you know, kill the bug, treat the infection, save the person.

Justin: Hey, what's a germ?

Sydnee: What?

Justin: Like, what's a germ?

Sydnee: Like, something that causes disease?

Justin: Like, could a— is a bacteria a germ?

Sydnee: Mm hmm.

Justin: Is a virus a germ?

Sydnee: Yeah.

Justin: So, germ is a blanket term.

Sydnee: Yeah. Germ we don't really use, like, medically speaking. I don't often say "germ" in, like, you know, an actual jargon context.

Justin: Charlie asked me this morning why she was sick and I told her— she came to the right place— and I told her it was a cold germ. And then she said, "What's a germ?" and I was like "Uh… watch your YouTube, sweetie."

Sydnee: [laughs] No, I mean, when we talk about the germ theory of disease, the idea is that there is an infectious agent that we can look at that is an actual thing, that we can isolate that is causing disease. As opposed to, like, the miasma theory or an imbalance of humors or something else like that.

Justin: Got it. Okay, sorry to break the flow.

Sydnee: So, Ehrlich wanted to find an effective and not so toxic treatment for syphilis. That was his big goal. He tried out lots of different substances on rabbits with syphilis, and the 6^{th} compound of the 600^{th} series worked. It was compound 606, later known as Salvarsan, or Neosalvarsan, which was a less toxic form, and it was the big syphilis treatment for a while, until we get to the 1940s. And I know this sounds like an offshoot because we're still not getting into the real antibiotics that we use, but the principles he used to develop this is what would lead to

everything that is about to happen in antibiotic history. So, he deserves that credit.

Justin: What's about to happen?

Sydnee: Well, I'm gonna tell ya, but first let's head to the billing department.

Justin: Let's go.

[ad break]

Justin: Well Syd, you were gonna— we were get into what doors were opened in terms of antibiotic research at this point.

Sydnee: So, with this concept that we now have something to target, researchers got busy trying to find a way to, you know, actually kill these bacterial invaders.

Justin: Mm hmm.

Sydnee: We usually think of Penicillin as the first antibiotic, and I'm gonna tell you about Penicillin, but it's fair to mentioned that sulfa drugs, Sulfamethoxazole very commonly used now in combination with Trimethoprim, which is something called Bactrim, which a lot of people have heard of, were actually the first to come along. Not that one, but sulfa drugs in general. There was something that was— the brand name was Prontosil, the generic name, if—

Justin: You can do it. I believe in you.

Sydnee: If anyone is interested, [laughs] sulfano-mido-chrys-oidine.

Justin: Sulfamidochrysoidine. Of course.

Sydnee: Mm hmm. Right.

Justin: Easy.

Sydnee: [laughs] It was synthesized by Bayer chemists and marketed in the 30s. So, it actually predates Penicillin. But the problem was the active part of the drug, sulfanilamide, was a dye that had been in use for a while. It's interesting, a lot of people observed that dyes would cling to certain things in petri dishes and so it was a way to— "Oh, well, it targets

that because it only attaches to that." And actually, "Oh, we accidentally killed this cell with this dye. Hey! We killed this cell with this dye."

Justin: Hey!

Sydnee: So, a lot of people started to notice these things.

Justin: "Good news guys, we don't have to finish the experiment."

Sydnee: "We did it!" [laughs]

Justin: "We did it!" [laughs] "That was so easy."

Sydnee: "We can't see it anymore, but we did it."

Justin: Yeah.

Sydnee: So, but the problem was since sulfanilamide was already widely in use for other things, they couldn't patent it. So, a bunch of different companies started making these kind of things to cure infection, sort of, maybe, with questionable means, really quickly.

Justin: Always a good situation.

Sydnee: Yeah. This is also why when we talk about resistance to certain medications and bacteria not being killed anymore by that drug, sulfa resistance was one of the first to spring up. It's because we were just kinda willy-nilly throwing these sulfa compounds at infections. The first antibiotic that was really formally made and we used and kind of changed the course of human history, I think you have to give to Penicillin. And most people kind of know the story, right?

Justin: Uh… mold was involved.

Sydnee: Yes.

Justin: Louis Pasteur.

Sydnee: Nope.

Justin: Nope.

Sydnee: Okay, well let me tell you.

Justin: Mm… alright.

Sydnee: [laughs] You were so close. You got the mold.

Justin: The mold I knew.

Sydnee: So, Scottish scientist Alexander Fleming. You know that. Fleming, Penicillin.

Justin: Baby, I love you. We've been over this though, you know I don't know any of this stuff.

Sydnee: [laughs]

Justin: It's not a gag. It's not a bit. What were you so angry about? There was something else you were angry at me about yesterday.

Sydnee: Because you didn't know why you couldn't eat before surgery.

Justin: Yeah. You were mad.

Sydnee: [laughs]

Justin: You were mad at me.

Sydnee: Anyway, Fleming was—

Justin: And then I was like, "Uh, okay, well it's your field. What's, uh, what was Mario's original name?" and you were like, "Uh, Jumpman?" and I was like, "Okay, well… I guess we're done talking."

Sydnee: [laughs] Anyway, Fleming worked at St Mary's Hospital, and he went on vacation for two weeks in the fall of 1928, and he left his lab in Paddington—

Justin: Home of Paddington Bear.

Sydnee: [laughs] Hey, you know that. He left it a complete mess.

Justin: [laughs] Don't patronize me, Smirl.

Sydnee: [laughs] And this was not uncommon for him. He was not known to keep his bench clean. His lab bench. His table. The experiment table. It's called a lab bench.

Justin: Yeah.

Sydnee: Just in case you wondered. Anyway, he was not a fastidious scientist, so this was not unusual. And so, he came back from his vacation well-rested in September to find that a petri dish that he had left out with staphylococcus aureus, staph aureus, a bacteria that causes infections, growing on it had become contaminated with a mold known as penicillium notatum.

And he also noticed that in the areas on the dish where the penicillium was growing, the staph bacteria were not. They had actually been lysed and kinda destroyed by the penicillium. Whereas the areas on the petri dish where there was no penicillium, the staph was growing just fine.

Justin: There's a t-shirt in this story somewhere. It's just so wordy. It's like, "Yeah, my room's messy, but I'm trying to discover a new antibiotic, maybe you didn't know. That's how—" and then like, at this point you're at the belly button.

Sydnee: Right.

Justin: You're out of space for more words. [laughs]

Sydnee: This is getting to be a little ridiculous. [laughs]

Justin: [laughs] It's like, a little wordy. It's not, like, bumper sticker material, but there's something in there.

Sydnee: "Aren't we lucky no one told Fleming to clean his room?"

Justin: And then that would be a great conversation starter.

Sydnee: [laughs]

Justin: [laughs] Because that would prompt people to say, "I don't… who is that?"

Sydnee: [laughs] "You know else was messy? Fleming." There.

Justin: Okay, again, you haven't really gotten the nut into there, I think.

Sydnee: Well. [laughs] So, this was not the first time that a petri dish had become infected with a mold or, you know, that this had happened. He was just kinda the first one to stop and look at it go, "Huh. Maybe I

should investigate this a little further." And we had suspected, as I mentioned, throughout history, that mold had something to do with treating infections for a long time, because we'd been sticking moldy bread on infections for, you know, thousands of years. So, this was not a wild idea.

The problem was trying to figure out exactly what it is in the mold that's stopping the bacteria from growing. I mean, you can't just grow mold on wounds willy-nilly, that doesn't seem like a smart idea. So, that is what took a long time, was to take that mold and isolate what is the compound in here that will help us treat infections, and how can we do that? Just because something works in a petri dish doesn't always mean it will work in the human body. And even if it will, making that happen, that's a big process. Lots of research goes into that. So, it took a long time. It actually wasn't until 1940, so now we've jumped from 1928 to 1940.

Justin: Wow.

Sydnee: That he was doing this research and he was publishing and another scientist, Dr Howard Florey, who was a professor of pathology at Oxford University, got really excited about it and said, you know, "I think we can help with this." So, him and another biochemist that he worked with, Dr Ernst Chain, started working on this process. How can we make more of this mold and isolate what in it will treat, you know, will kill this staph? So, the problem that— and they were very successful in doing this, except that what they ran into is that it took them 2000 liters of mold culture. So, they had to create 2000 liters of this mold in the lab to isolate enough Penicillin, which was what they called the compound that they found that inhibited the growth of bacteria, to treat a single case of sepsis in a person.

Justin: Mm hmm.

Sydnee: That's a lot of mold.

Justin: A lotta mold.

Sydnee: To treat one person. And they were having trouble overcoming that, cause that, what happened is they had this new thing, they were using it in their lab and it seemed to work really well, and then there was a local case of a guy, Albert Alexander, who was a police constable who had been working in his rose garden when he nicked his face. Probably,

I'm assuming, a thorn or something. And he developed a really horrible cellulitis form that, infection of his skin, an abscess, meaning a big pocket of pus, an infection under there.

He became septic. He was dying. And they were giving him sulfa drugs, which were around at the time, and they weren't working. So, these two scientists, Chain and Florey, were like, "Hey, can we try our new Penicillin? He's gonna die anyway, can we try this? We think this will help." And they did. And it was helping.

Justin: Wow.

Sydnee: And then they ran out.

Justin: … And then what happened?

Sydnee: And then, unfortunately, he passed away.

Justin: Great story, Syd. That's one of your top ten medical anecdotes.

Sydnee: So, they knew it worked!

Justin: Uh huh. Uh huh.

Sydnee: But they had to make more, cause they didn't even have enough in their lab to treat one person.

Justin: I think I speak for all of the audience when I say I didn't think that anecdote was gonna shake out that way. I felt this swelling of hope that you quickly doused with your lack of mold.

Sydnee: [laughs] I'm sorry. They ran out of mold.

Justin: Okay.

Sydnee: Dr Norman Heatley joined their crew and he started growing—

Justin: A lot— can I just take a brief moment to say, a lot of good names in this episode already. Norman Heatley, Howard Florey, Ernst Chain? Don't mind if I do. Just like a lot— Albert Alexander is even good, that's like an Agatha Christie name, that's good stuff. Some good names in this ep.

Sydnee: And all of these people worked together. We always give Fleming all the credit, and he definitely deserves credit for Penicillin, but there are a lot of people helped get us from mold in a petri dish to Penicillin.

Justin: That's always the way with science, right? It's very rare to find—

Sydnee: Yes. It's just, I feel like in history books you always just associate that one name.

Justin: Yeah. I mean Lorenzo made that oil by himself, but other than that, it's about it.

Sydnee: [laughs] I don't think that's how that story goes. So, Heatley joined the crew, and he was growing vats of this mold in, like, bedpans. Like, his lab was just covered with [laughs] all the mold he could grow.

Justin: Tough to get interns.

Sydnee: To try to overcome this, but obviously there had to be something else to fix this, because this was not gonna be reproducible on a mass scale at this point. So, a lab assistant, Mary Hunt, showed up one day with a cantaloupe that she had found covered in a mold, penicillium chrysogenum. And this strain yielded 200 times the amount of Penicillin that the notatum did.

Justin: That's good. That's way more.

Sydnee: So, this definitely helped. Now, they also at some point started radiating it. Which, like, amped it up to 1000 times more Penicillin. So, that was probably the even bigger breakthrough. And so, they finally figured out how to make enough Penicillin to actually be effective, to actually have some clinical impact on people. They took it to American pharmaceutical companies and they began pumping out what was then known as Penicillin just in time for World War II. And you really saw a difference in rates of death from infection if you look at, like, World War I compared to World War II, because in World War II we were able to use Penicillin.

In March 1942, Anne Miller was treated with Penicillin. She was the first civilian. And she was in a hospital in Connecticut, in New Haven. She had had a miscarriage and had developed an infection afterwards, and sepsis,

and was quite, quite sick. And typically at the time, you would expect someone in that position to not survive. And Penicillin saved her life.

Justin: Ah, right.

Sydnee: Yeah. So, there's the happy—

Justin: It's a shame about her name. But other than that, pretty good.

Sydnee: [laughs] There's the happy story you wanted.

Justin: Thank you, Sydnee, I appreciate it.

Sydnee: In 1945, all these people we talked about essentially got a Nobel Prize for the discovery, expect for Heatley. Do you know they left him out?

Justin: Aww, why?

Sydnee: It was just one of those, who knows? They just overlooked it, or his name wasn't on the right paper, or whatever. This was actually, um, I don't know if "righted" is the right word, but many decades later, they recognized him with, like, the first honorary doctorate they'd ever done. To kind of make up for leaving him out of the crew. [laughs] Out of this Ocean's 11 crew that discovered penicillin.

But they won the Nobel Prize and in his speech, in his acceptable speech, Fleming stood up and said, "Listen, this is great and I'm very happy about this," he said something to the effect of, "I didn't know that day in the lab that I had discovered something that was gonna change the course of mankind or save lives," or something very grandiose. But then he turned around and he said, "You should also know, this won't work forever. Bacteria get smarter. They do develop resistance over time. Just because it's killing bacteria now, if we use this too much, if we don't find other ways to treat infections, this won't work for us forever." He warned of this in 1945.

Justin: Wow

Sydnee: Just a few short years after we had discovered and started using Penicillin.

Justin: [laughs] What a buzzkill. Like, couldn't we kick it for a decade?

Sydnee: [laughs]

Justin: I get it.

Sydnee: He was being—

Justin: [laughs] I get how you guys work.

Sydnee: A good scientist!

Justin: No, like, I get it. But like, can we just be— [laughs] Can we just be stoked about Penicillin for a second?

Sydnee: You can for a second.

Justin: [laughs]

Sydnee: And then resistance started building. And, now let me say—

Justin: All I'm saying is it's still a problem in 2018. He could have kicked it for a decade and then dropped that on everybody. Let us just, like, chill out.

Sydnee: [laughs] They were seeing resistance by, like, the late 40s, early 50s. I mean, that's the problem. Like, this stuff happens. Bacteria learn quickly, and they grow— they grow and evolve faster than we do. So…

Justin: God, this is a fun episode. I'm really— this is great—

Sydnee: Sorry!

Justin: No, it's true, it's good! It's good, it's good.

Sydnee: So, from there, all other kinds of antibiotics started hitting the market. If you look at the intervening years, you know, different classes.

Justin: Are they using basically the same, like, idea? Like, I mean, I know biochemistry isn't really your field. But like, is it…

Sydnee: Well, I mean, in terms of how they kill bacteria?

Justin: Yeah.

Sydnee: There are different, there are all kinds of different ways that they attack the bacteria. Cause some are, um, bactericidal, meaning they actually lyse and kill the bacterial cells. Some are bacteriostatic, meaning they'll just stop them from growing. And they target different things within the bacteria, which is why they're used against different infections.

That's why— a lot of times I'll have someone ask me, "Well can't you give me something stronger? I want a stronger antibiotic." And you can't think about antibiotics as stronger and weaker. You have to think about the spectrum of bugs that they kill. There are reasons we use certain antibiotics for a pneumonia versus a skin infection versus a urinary tract infection. It's because we know what kind of bacteria are likely to grow there, and certain antibiotics work better there. Or maybe that antibiotic gets into lung tissue better, or maybe that antibiotic will penetrate the urine better, that kind of thing. So, it's good not to think there's, like, a ladder of antibiotics with the strongest one way up at the top and the weakest one at the bottom, and your doctors picking a weak one cause they don't want you to get better or something. It's better to think of it as like a web of antibiotics that treat different things.

And that's what we came up with through the intervening years between then and now, are all these new antibiotics. But, like I said, the problem is bacteria are smart. They're wily. And they keep coming up with new ways to evade these antibiotics. And nowadays we see a lot of different infections, MRSA being one of the big ones that— I see that one in the media the most often. That can cause pretty devastating infections and is very difficult to treat, because only a few antibiotics work against it. There are other ones, klebsiella, enterobacter, acinetobacter, pseudomonas, VRE, there are all these different kinds of infections that now are resistant to lots of antibiotics.

So, in some cases there are still a couple left that will treat them. I have seen cases where there is literally no antibiotic that will treat this infection. Every one we have, and we still do it the same way. We put little antibiotic, like, circle discs in a petri dish of the bacteria and then see where the growth won't happen. And it's the same kind of thing that Fleming accidentally did in his lab. And sometimes, the bacteria grows no matter what disc you put on there. So, the reason I say this is not to be a bummer. You're looking at me like I'm a bummer.

Justin: No I'm not.

Sydnee: I'm not trying to be a bummer. What I'm saying is over-prescribing antibiotics, meaning giving someone an antibiotic that would kill a bacteria when they really have a viral infection, does no one any favors. It's not gonna make you any better any faster. It might give you diarrhea. You might get a yeast infection. And also, maybe next time, that antibiotic won't work quite as well for you. Because what you're doing is, you're selecting for those really strong, resistant bugs that, you know, are living there. So, over-prescribing is a big issue with this.

Self-administration. In the US, it's hard to, like, go buy over the counter antibiotics. But there are a lot of countries where that's not true. You can go buy antibiotics at the pharmacy, just like you would buy Tylenol or something. And that, that's very dangerous, because then you're relying on, you know, everybody to just kind of know when they have an infection that needs an antibiotic. And you can't know that. I mean, sometimes even, you know, as a physician, with all of the years of education and training I have, sometimes I'm having to make educated guesses based on my experience and my knowledge, and do the best I can with that information.

There's no way you can do that on your own, just every time you have a runny nose, think, "Well, I know I need a Zepac," and go buy one over the counter, because that's really dangerous. And then, obviously, there are antibiotics in our environment. They're in our water, in our soil, in our food, in our toothpaste, in our milk.

Justin: The milk I bought today, I had to go to the drugstore so I didn't have a lot of options. The milk I bought today said— I was looking, because I was like, "What about antibiotics?" And I looked on there and it said "tested for antibiotics" and I was like, "Hmm. Well. Okay."

Sydnee: [laughs]

Justin: [laughs] "Okay. That's uh… I mean, it's a start."

Sydnee: "We looked for em!"

Justin: Yeah, "We looked for em." And then they just, like, stare at me blankly. Like, "Oh no, no, no, we tested it for antibiotics."

Sydnee: They're looking at you going, "Do you wanna know? Do you really wanna know?"

Justin: Yeah.

Sydnee: But the important thing to know is that there are still plenty of antibiotics that work, obviously. They're still powerful against most infections, and we're still working to try to come up with new ones and new ways of treating infections. But we should all be better stewards of antibiotics. People in the medical profession, and then all of us as patients, because sometimes I'm the patient, to know that, you know what?

Sometimes you feel so lousy and you think, "Can't you just give me something to make me feel better?" and unfortunately, sometimes the answer is, "No. I can't. There isn't anything that's gonna make you feel better faster." You will get better, but you're just gonna have to wait it out. Go home and rest. Don't go to work, don't go to school, get in bed, get some tissues, watch some Netflix and eat some chicken soup.

Justin: Folks, that's gonna do it for us for this week. Thank you so much for listening. Thanks to The Taxpayers for letting us use their song "Medicines" as the intro and outro of our program. Thanks to the Max Fun network for having us as part of their extended podcasting family. And thank you to you at home, for listening to our program. Hey, if you haven't checked out Court Appointed yet, that's the show that Syd does—sorry, Syd's dad does with Sydnee's uncle Michael.

Sydnee: Who is a real, actual lawyer.

Justin: A real actual lawyer. It's a show about law stuff and I'm gonna be on a new episode that's probably out…

Sydnee: Monday.

Justin: Monday. About net neutrality. So, if you're interested in that topic, or wanna hear me bloviate on a different format, then go check that totally out. So, 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]

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