TPWKY - Special Episode - Lina Zeldovich

EW: Hi, I am Erin Welsh and this is, this podcast Will Kill You. Welcome to the latest episode in the TPWKY Book Club series. In these episodes, I bring on authors of popular science and medicine books and chat with them about their work, what inspires them, and how their book can change the way we understand the world around us. I've gotten to have some incredible conversations so far this season, and we've got even more great authors and books lined up for the rest of the year, so stay tuned. If you'd like to check out what books we'll be featuring on future episodes as well as get the full list of books we've covered in the past, head over to our website. This podcast will kill you.com. Under the extras tab, click on bookshop to go to our bookshop.org affiliate page, which has the list for books featured in these episodes. As well as other podcast related lists, I'll be adding more books throughout the rest of this season, so check in regularly if you'd like to read along. As always, we love hearing from you all about the books you've enjoyed, any books you'd like to hear, featured suggestions for episode topics, anything you'd like to share. The best way to get in touch is by filling out the contact us form on our website. Two last things and that is to please rate, review, and subscribe. It really does help us out. And also you can now find full video versions of most of our new episodes on YouTube. Make sure you're subscribed to Exactly Right Media's YouTube channel, so you never miss a new episode drop.

Alright, now let's get into the book of the week. Antimicrobial resistance is not a new problem. The first penicillin resistant bacteria appeared just a heartbeat after the widespread introduction of the antibiotic in the early 1940s, but it is a growing and deadly one. The WHO estimates that in 2019, antimicrobial resistance directly led to 1.27 million deaths and contributed to 4.95 million deaths around the globe. Nearly 5 million deaths due in part to antimicrobial resistance. That's more death than HIV, tuberculosis and malaria combined. What's more is that these numbers are expected to grow in the coming years. Our standard approach to combating these superbugs has primarily consisted of developing new antibiotics, a strategy that buys us much needed time, but is ultimately no match for the rapid evolution of resistance. To have any hope of curbing infections and deaths due to antimicrobial resistance, we need to think outside of the antibiotic box. Fortunately, some researchers have been doing exactly that for over a century. In this week's episode, I am joined by journalist and author Lina Zeldovich to discuss her book, the Living Medicine: How a Forgotten Cure May Rescue Us When Antibiotics Fail. That Forgotten Cure refers to phage therapy, the use of bacteria, specific viruses called bacteria

phages to treat antibiotic resistant infections. Many of us, such as those of us here in North America or Western Europe, may have learned about phage therapy in school only as a blip in the history of medicine, if we learned about it at all. Soon overshadowed by the development of antibiotics, or maybe you learned about it in our antibiotic resistance episode from years back, which featured Stephanie Strathdee sharing her and her husband, Tom Patterson's story. But in other parts of the world, phage therapy never faded from memory. Rather, it remained a leading treatment for bacterial infections and a central focus of medical research. Why it fell out of favor in some countries and lingered in others, gives us insight into how external events and cultural differences can shape scientific developments. As we're fond of saying on this podcast, science doesn't happen in a vacuum. In The Living Medicine, Zeldovich takes readers through the history of phage therapy where we get to meet the visionary researchers that championed this treatment, discover how phages are found and administered, and learn of the profound promise they hold for the global problem of antimicrobial resistance today. This book will have you marveling at this forgotten cure and grateful for those who did not let it slip into permanent obscurity. I have always been such a fan of phage therapy, and it was a joy to chat with Lina and learn more about its history and current developments in the field. I'm so excited to share this conversation with you all. So let's just take a quick break and get into it.

EW: Lena, thank you so much for taking the time to chat with me today.

LZ: Thank you for having me. I'm very excited to talk about all things phages.

EW: Let's start at the very beginning. What are bacteria phages, and what is phage therapy like? What does it mean if someone is receiving phage therapy?

LZ: So phages are viruses, and this is where it really gets interesting because we tend to think of viruses as some really bad things that make us sick. So phages are different. Phages don't have the right biological equipment to icic humans. They can only attack bacteria, and that's why they call bacteria fe. They, they prey on bacteria out there in nature and they've been doing this for millions of years, kind of evolving alongside each other. Typically it's like one phage per one bacteria. They're very picky at, you know, what they eat and that makes bacteriophages our friends. So basically an enemy of my enemy is my friend. So we can use this amazing creatures as alternatives to antibiotics when antibiotics don't work. And there are different ways of administering, you know, phage therapy, but basically you either drink them for intestinal diseases or you put them on skin or wounds. Um, and there are some trials out there that inject bacteria phages into the bladder for people who are dealing with, uh, recurring

UTIs. You can also administer them intravenously nowadays, but it's more complicated because those formulations must be cleaned from all sorts of things that may, uh, trigger your immune system to go haywire.

EW: Yeah, I mean it seems like it can be quite a complicated process to, from finding the right phages to purifying them to then administering them. And I was wondering if you could just walk me through, you know, how people go through this process. How, where, where do you find phages?

LZ: So phages, you can find phages everywhere. There are out there in soil, in water, in the air, in sewage, on rotten fruit. Just, you know, basically everywhere in on this planet where there is bacteria, there are phages that are preying on it. And like I said, they've been doing this for millions of years before humans came along. And the way scientists find these phages is they go out there and they take samples of everything. They come back to the lab and they, you know, use these, uh, samples to isolate phages and, you know, test them on what bacteria pages that you just found will work and that's how they know that they've got a phage for, let's say, you know, this, uh, you know, strain of color or this strain of dysentery or this strain of something else.

EW: Then once you have that phage that works for whatever bacterium you're trying to attack, what's the next step? Like, how do you grow these phages? And then what is the purification process like? Or maybe why is the purification process so important?

LZ: The way it works is that first you grow your bacteria. Which is very easy. Most, um, most bacteria is fairly easy to grow. You just put a bunch of, like meat scraps. You cook, uh, basically a bullion, and you see this bullion with bacteria and they just love it. They, they, they, they so happy there. They procreate, they grow. And once you have enough there, um, you inoculate the brew with phages and phages set to work, and they attack this new bacteria. The way they work is that they get into bacterial cells. They multiply inside the, the burst bacterial cell open. And once you have almost no bacteria there, you know, you have a lot of phages, and that's when the purification step comes in. And again, if you're just putting phages on your skin or drinking them, you can actually skip that step. Historically, it worked just fine. What gets tricky is that if you wanna give it somebody intravenously. You don't want all these bacterial debris in there because your immune system is going to react to that. You know, bacterial debris and toxins and whatnot. And it may go into shock and you know, purifying well, it sounds kind of simple, but it's not 'cause you need ultra sophisticated equipment. Basically you need special centrifuges that spin very fast and they like managed to like separate phages from everything else and

that's how you get your clean phages. Again, I said it sounds very simple, but the right equipment for that. 'cause we are dealing with like super tiny structures that only became available fairly recently.

EW: I'm trying to imagine the timeline for this and, and I know that it can be very different depending on, in the us you know, right now I think we're still at that case by case basis. How do we approach this from a non case by case basis, and what does that timeline look like? Like do we have to be reactionary or can we be proactive?

LZ: So I think we still approach this on a per case basis. If, if a team of doctors wants to treat a patient that is who's not responding to antibiotics, they would have to go to the FDA and file this investigational new drug application, in this case, phages, and they would receive an approval from the FDA and they would proceed.

EW: It's such an incredibly, like an obvious solution to what is growing, to be an, in an increasingly, uh, huge problem, you know, antibiotic resistance. And I wanna kind of get into the differences between phages and antibiotics in terms of, you know, in, in an ideal world where phage therapy does not have to be approved case by case and it's more of a routine thing, would there still be cases where antibiotics would be used over phages?

LZ: Probably, I think at least at this point it looks like antibiotics would still be our like first line of defense. Hmm. And that's because it's just so easy to use them. As I mentioned with phages, you need to know what particular infectious organism. Uh, you are infected with, and then you would have to go and find a phage for this particular infectious organism. Uh, and maybe you would need more than one. So if you have it in your library, that may take hours to days, and if you don't, then it would take days and weeks sometimes. So if you are an antibiotic. Work. In the meantime, you're golden. You don't need anything. Mm-hmm.

EW: Mm-hmm.

LZ: However, if your antibiotics don't work anymore, that's when you will need a phage or multiple phages. I think antibiotics are still going to be our first line of defense for a while. The interesting thing about antibiotics and s and how, like, you know, the pros and cons, you know, antibiotics are static molecules that we synthesize where chemical reaction or some other means, um, and they're static, they don't evolve.

EW: Mm.

LZ: And bacteria are amazing at various. Mechanisms of resistance that they just evolve. Mm-hmm. You know, from one day to the next. All sorts of tricks. You know, some of them develop these pumps, they spit antibiotics out once they enter bacterial cells. Others have these molecular scissors, you know, enzymes that literally shred antibiotic molecules to bits. You know, some bacteria have very slippery auto coats if you'd like. So antibiotics can stick to. And some manage even surround themselves, kinda like in a protective ink that also destroys antibiotic molecules. So when we run into this kind of issues, that's when we need phages because phages evolve alongside antibiotics for a long, long time. So even if a bacteria develops, uh, resistant to a phage, the phage will eventually evolve to attack it better and it. Doesn't necessarily have to take a long time to evolve because you know, at that, at the, at the level of this microorganism, it can happen very fast.

EW: Let's take a quick break and when we get back there's still so much to discuss.

EW: Welcome back everyone. I've been chatting with Lina Zeldovich about her book The Living Medicine: How a Forgotten Cure May Rescue Us When Antibiotics Fail. Let's get back into things. Not only do phages evolve with or in response to bacteria, they are, as you describe in your book, an infectious cure. So someone receiving phage therapy can spread those phages to another individual as well, which is really just remarkable.

LZ: It's, I mean it, for me, it was also a total eyeopener, right? Because we tend to think of diseases as contagious, right? Mm-hmm.

EW: Mm-hmm.

LZ: Well, so phages can be contagious too. And I think we'll get into history in the phage therapy, uh, in a little bit. But the first person who realized that, you know, phages as cure can be contagious, was one of the early pH therapy adopters, Felix d'Hérelle. Who's trying to stop an outbreak of salmonella in France, in chickens in France. Mm. And he realized that as soon as one chicken. Would get, um, a bacteria pH against the salmonella, the entire coup would recover because they all pack at each other's pieces. So it would just spread through all of 'em and suddenly they would be not sick anymore.

EW: That's amazing. I mean, also talk about like, then you just have to get one chicken, uh, chicken cure and then you're done. That's it. Yeah. Uh, that's so

cool. I would love to get into the history now of bacteria phage therapy and I think it is. It's surprising to a lot of people who are used to using antibiotics and used to having antibiotics be the frontline of, um, you know, bacterial infections to realize that not only phage therapy exists, but that it actually predates the discovery of antibiotics. And so can you take me through sort of the almost simultaneous, I guess, discoveries of bacteriophages?

LZ: So the year is 1917 and two things are happening almost at the same time in two different parts of the planet. There is Felix d'Hérelle in Paris working at the Pastoral Institute, which is like the holy grail of science, medical science at the time. Um, and he is both neuro biologist and, and a medical doctor, which was very common at the time. And so he's dealing with patients who have DYS theory and. Again, this is before antibiotics. You got DYS three, you might be dead, and you know, very shortly. And so, you know, people are dying. But one of his patients recovers and he figures this has to be something in his stomach that helped them recover. So he start looking at to, uh, this person's stool sample. And he realizes that there is no dysentery bacteria in there anymore. So he's like, Hmm, something's killing it.

EW: Hmm.

LZ: So let's try this. He takes like these two samples and inoculates other dysentery bacteria samples, you know, with with it. And lo and behold, dysentery bacteria. Dies there too. And then the next one. And the next one. But he can't see what it is because phages are much smaller than bacteria. Mm. And at the time, they could see bacteria under the microscope but not phages. In fact, that took an electronic microscope of 1930s to actually see any virus. So he goes, well, I think I discovered a parasite of microbes that is so small that we can't see it. It's invisible, but I know it's there. And he publishes a paper in it at the same time out there in the country of Georgia, in Pel, which by the way is a beautiful city and at the time was called the Paris of the East. Really interesting dichotomy. Yeah. There is another scientist, a Georgian scientist, uh, George Eliava, who is a little bit younger, not as experienced, but just came back home from the front lights of World War I, which just ended, um, where he tended to, you know, seek soldiers who had, you know, cholera and dysentery and whatnot. And he is looking into. Presence of cholera in the city water in, in, in the river where everybody gets the water from. And, you know, lo and behold, cholera is there and you know, he sees it and that's not good news. He's looking at it through his microscope and something interferes like he has to go somewhere. He's, he lacks his lab and comes back to it like a day or two later, and he's looking at the same samples of water and there's no color there anymore. Which doesn't make any sense. Cholera doesn't die that quickly, so he

goes back to the river, brings back water, repeats the same experience, same result after a few hours. No cholera does it again. Same result. He knows he's onto something, but he can't figure out what is he onto. Mm-hmm. Uh, fast forward a few more months, he has to go to Paris to study at the Pastor's Institute, how to, you know, make vaccines and, and other medicines. 'cause that's, again, at the time where that's where everybody went to study. He goes to Paris and he walks into this really heated debate. So Dells. Scientific, the scientific role did not welcome d'Hérelle's finding, ah, peacefully. Uh, because it really, to them it didn't make sense. You know, you're talking about invisible destroyers that, you know, destroyed isn't theory. No. It also doesn't fit into the established immunity theory, uh, you know, at the time. So basically at that moment, d'Hérelle is a laughing stock.

EW: Hmm.

LZ: And at the moment he's out there in the countryside dealing with chicken salmonella. So Eliava walks into Fest and right in the middle of all this and he goes, I've seen that too. And they're like, alright, another one. Uh, but here were the character differences come into place. d'Hérelle was kind of a prickly character. He spoke his mind and. Probably made a fair amount of enemies in his life. And Eliava was exactly the opposite. He was this absolute charmer, like people, he could sweet talk anybody into anything. Um, when I, when I was reading his family's diary, it literally looked, sounded like when he talked about science, it sounded like. Poetry and he spoke fluent French. 'cause he studied in, studied in Geneva. So he went to the institute director, said, can I repeat the experiments? And of course he talked him into it and he repeated the experiments and he showed that basically the same results. And that was kind of like me, like that's, that's where the, things begin to turn a little bit.

EW: And so is that when like the scientific or medical implications of these findings, it was not only like, okay, you know, first there's this ground truthing. Are we seeing what we actually think we're seeing? And then how soon after that was, how can we use this then to help cure infectious disease?

LZ: Yeah. So at fairly soon, um, I think it was 1919, if I am not mistaken, when they first tried phage on. Uh, the very first patient, uh, like a very sick child first, the medics themselves, you know, drank phages and they showed that nothing happened. Um, and then they, um, gave this phages to a very sick child. The child like recovered in 24 hours. Um, I think they were like a few other children. Um, they drank PI theory, phages. And I think the next really big breakthrough was in 1925 when d'Hérelle managed to cure a couple of cases of bubonic plague.

EW: What sort of was the turning point for the medical community then reconsidering phages as a viable thing and as something that is not just, you know, in, in these guys' head where they're just coming and they're talking about nothing and they're like, oh, here comes another one. At what point did that transition happen?

LZ: Um, I think it sort of like slowly happened over like the next maybe few years, like after 1919, but I think if, if the 1925 when d'Hérelle cured bubonic Plague was probably a really, really big turning point because everybody, like immediately paid attention. I mean, there was no cure of them from the Bubonic plague. You got it. You died. I mean, it's almost, it's depopulated. Europe in the Middle Ages.

EW: Right.

LZ: Um, so, and, and d'Hérelle was stationed in some Port city in, in Egypt, and a couple of sailors fell in with chronic plague and he had. Phages that he brought from India where he isolated it from rats. You know, rats can carry the plague but not die from it. Uh, so he, you know, made this new phage concoctions and he treated the sailors with phages and they recovered. And that was just like. Nothing, uh, you know, short of a miracle.

EW: Oh my gosh. I mean, to then go from, you know, laughing stock to cure of bubonic plague. This like very fear disease. That is, that's incredible. And, and then we, we go from that to a whole institute being created for the explicit reason to study phages. Can you tell me a little bit about this institute?

LZ: Uh, so Eliava and d'Hérelle became not just like lifelong friends, but also lifelong collaborators. Um, and, uh, so Eliava had this really grand idea of building a bacteriophage research center and a treatment center in Belize in Georgia. And, uh, at the time he had a fair amount of money because Stalin, who was in Georgia and himself was willing to throw a bunch of money in. To his home state, especially for things like medicine, because healthy populations means. A strong empire and he was building a strong empire. So the plans for the institute were approved. And, you know, there was a, a crazy amount of money given, like, you know, several millions, which God knows how much it would be in today's money. Right. Um, but it was, it was a very. Turbulent time, um, in, in, in history in particular in the history of the Soviet Union. 'cause Stalin was very paranoid about, you know, keeping his grip on the country, uh, keeping his power. And he wasn't tolerating any dissent. And like many brilliant people was known to speak his mind. And eventually that caught out with him. Um, so he was arrested and tortured, like really? Really badly tortured. I, I was

able to find some of the interrogation manuals, and when you looked at it, you could literally see how all this was constructed. Like, you know, people who were interrogating him could even decide what they wanted him to say, right? Like, you know, one day they would want him to say that he was working with the French intelligence, the next day was the British intelligence, but the end result was that he was killed. And, um. The center never materialized in all the glory that it was envisioned, but the, uh, concept of using phages as medicines survived because there was really nothing else at the time. Mm-hmm. And, and it like basically stayed in pel like in a time capsule of sorts. And it was used through all of the years of Soviet power.

EW: This huge loss that the phage therapy field faced, you know, how, how was that immediately felt, and then what were some of the long-term implications of that in, let's say like the, the decade or so that followed Ava's death.

LZ: So the decade that followed this was really, was a really difficult decade because we kind like get into World War ii. Mm, right? Mm-hmm. Um, so what happened in late thirties in, in America is that phage therapy in the west basically fell out of favor and for really interesting reasons. For no fault of, you know, phages, uh, it was mostly because it was kind of misused. People didn't necessarily know how to grow phages properly, and even when they did, phages didn't always work. And that happens too sometimes phages don't work for eczema, they don't work for hives, they don't work for allergies, right? Or, or herpes or whatever. But some companies advertise advertised pages for this. Uh, uh, you know, health issues. And of course phages did nothing to those undermining, you know, people's, people's trust and, and, and physicians' trust. And so all the prompted some prominent American physicians to examine medical literature in the late 1930s and they decree that phages aren't really trustworthy enough to use this medicines except maybe for like very specific things like staff. And then shortly after that, western medics learned to mass produce antibiotics, and that was. The end of phages.

EW: Yeah. Penicillin became the answer and then the answer. Yeah. Penicillin became the answer. You know, at the same time though, in the Soviet Union, phages were being used at a larger scale than they had been previously. Can you tell me about some of the prophylactic use of phages during World War II in Stalingrad?

LZ: Yeah, that is like one of my favorite topics because it's just so mind boggling and it's like so unknown, right? Yeah. And the prophylactic phasia, I, I had no idea. I always thought of it as a treatment, not a prophylactic.

EW: Yeah, it's amazing.

LZ: So we're now into 1942 and the Nazis forces a closing and on Stalingrad, like the Soviet strength hold on the. Vulgar River named after Stalin. So there's so many things are like, uh, uh, are tied to this city. You know, like first it bears Stalin's name. Second, it sits on the way to the oil field of the caucus and whoever gets to keep the oil field. The war because you need oil to run all this heavy machinery. And so the battle for stare absolutely brutal. Neither side can afford to lose the city.

EW: Mm.

LZ: And so sometime in summer, the the Moscow hears some rumors about. Cholera cases among the German troops. And at first they, they're very happy to hear that because, okay, well that's that, that's good. And then they realize that, no, it's not good because CA cholera doesn't care, right? Doesn't care about front lines. If it's on that one side to or beyond the other, and they realize they've got this whole city that's been bombed out to Smith. The rains with like sewage broken, you know, water mains broken. Um, they realize it's going to be a disaster. And so they sent a woman there. Uh, her name is Z Oliva and she's one of the leading Soviet biologists, um, or microbiologists at the time on a tiny plane that manages to somehow evade the German bombers and actually land there. And, and, and she comes with this tiny little bag of, of phages. And, and she hears that colors already arrived and she knows that she doesn't have enough phages. So she calls Moscow and says, we need more phages. Mosco loads up all its phage arsenal on a train, and the train goes to Stalin, gra, and it never makes it because it gets bummed out to smooth rains. And she goes, okay. We'll have to grow phages here. We've got vulgar right there. There's gotta be, uh, cholera in there and their phages will be in there. And of course they are. So they, you know, take the samples and they go underground. They go into the basements so that, you know, bombing can destroy them. And in that, in those basements, they grow enough phages to basically. Give for prophylaxis the entire c um, on a daily basis. I think she wrote in her, uh, memoirs that 50,000 people took this bacteria phage daily and it never before happened in history. And it was so profound that you couldn't leave the CD without having a certificate that you took your phages. Um, and even bakeries wouldn't give out bread without that paper.

EW: I mean, it's such an incredible story, and like you said, it's such a profound demonstration of the power of phages, but also it, it does make sense considering the larger historical context, how this discovery did not become

more widely known and did not sort of make. Phages be front and center of biomedical research at the time.

EW: And I wanna kind of talk about that historical context, how this implementation of prophylactic phages didn't happen in a vacuum. There's war as the backdrop. And so can you talk about sort of this, uh, larger context and what that meant for the distribution of this information?

LZ: Yeah, it's a very good point. I mean, yeah, not all secrets were shared and I think, uh, that there, there actually were some medical collaboration during World War ii and there were some European and American scientists who were working with Zeva. But more so on antibiotics than, than than phages. And I think they just didn't think the phages were realistic enough that they were like, like really useful. I don't know why it didn't happen. Part of it could have been just like the general, you know, mistrust. It's just never took off.

EW: Let's take a quick break here. We'll be back before you know it.

EW: Welcome back everyone. I'm here chatting with Lina Zeldovich about her book, the Living Medicine. Let's get into some more questions. There was a, a passage in your book where you talked about sort of these social and cultural and scientific differences between the west and the Soviet Union and how that sort of led to one pursuing antibiotics and the other pursuing phages. In terms of, again, kind of like as we talked about this reactive versus proactive approach to medicine and public health, and I was wondering if you could talk a little bit more about that.

LZ: In America, well, in, in the West, I should say. And, and in America, probably more, you know, more in particular. Um, by the end of 1930s, the trust in FIAs kind of dropped. And I think people that are generally thought of them with suspicions, even the companies that are that manufactured phages in like 1930s. By 1940s, they switched to antibiotics in, in the post-war era synthesizing molecules that worked consistently the same way. It was easy and cheaper than growing. You know, these finicky creatures with, you know, picky appetites whose biology scientists still didn't fully understand and physicians agreed at the time. A large percentage of American doctors were private practitioners, and many worked from their home offices, and they weren't attached to any bacteriological, labor borders or hospitals. They didn't necessarily have, you know, test labs, let alone like complex facilities to synthesize phages there.

EW: Mm-hmm.

LZ: In those settings, the easy, ready to use medications that had a long shelf life and killed a white spectrum of germs. Were bound to win, which is what happened. I mean, they, they offered all of this advantages, reliable, repeatable, stable, no significant side effects. Known at the time. They definitely won over phages in the Soviet Union. However, medicine was a state endeavor. Mm-hmm. So a family couldn't start a company to grow phages or make penicillin, uh, and medical school graduates couldn't open a private practice. Um, everybody was applied by the states and all medicines. Made at research institutions or like large state owned factories, and that made it harder to produce false advertisements, especially when the director's head was on the line. Right? Right. If their products didn't work, or you know, worse made patients secret, they could be declared the enemy of the people and that was. Yeah. Uh, so conse, you know, consequently, Soviet scientists have like a very different medical paradigm. Western medics embrace stability in life, in laws and in, in, in, in drugs. But the Soviet medics, I, they just learn to exist in this ever shifting landscape. You know, if penicillin was mass produced today, it didn't mean that the factory will still be there tomorrow. The raw ingredients could vanish, the inventor could be arrested, so soy medics used whatever they had on a given day they had on antibiotics. Good. Don't have antibiotics. Alright, let's go to the nearest river finds of phages.

EW: Wow. Yeah. That's a fascinating lens to think about, sort of the, the differences in, in what drives innovation and what drives accessibility to equipment, all of that. Yeah. And so when antibiotic resistance started to show up in around the world, which it did, you know, very soon after penicillin was started to be widely used. Yeah. How did phage therapy, how was that used in the Soviet Union to treat resistant infections?

LZ: Yeah, that's, that's a great question. Like, basically if, uh, antibiotics stopped working, there was always a phage. Mm-hmm. I mean, PEL kind of remained a, a center of, um, all sorts phages, but there were other towns in the Soviet Union that, you know, produced, um, some phages and they could treat patients with it. What was really interesting to me when I was, uh, working on this research is that Tbilisi maintain sort of like a global by the Soviet standards, global, uh, library of phages. And not only maintained, but they constantly updated it and they had literally thousands and thousands of them, and by updating, I mean they would continuously. Gather samples, bacterial samples from all over the country and they would like bring this, this new samples to the labs and they would see, you know, is this bacteria evolving resistance to our phs? Oh, oops, it is, okay, time to find a better pH. Mm-hmm Let's go out to the river. That literally like went on for years and years and years and they never stopped and they still do that.

EW: To anticipate the future problems and to be able to, to have that in advance. And I think that's why I keep thinking about phages as being this proactive approach where you can see almost immediately if you're detecting antibiotic resistance, you can find a phage for that. I. As you describe in your book, there's this incredible moment where, uh, the specific meeting where the knowledge of phage therapy is, you know, brought up in this room, in this academic setting and in, in the us and the American scientists have no idea. They, they know what bacteria phages are, but they have no idea what phage therapy is. I was wondering if you could sort of paint me a picture of that, of that story and, and this kind of reawakening of knowledge about phages in the west.

LZ: Sure. So we are now in the early 1990s when the Soviet Union is falling apart. Maybe it's already falling apart, and this Georgian scientist. Comes from TEI to America for a post doctorate fellowship, and he is working in the laboratory of, of fairly well known, uh, infectious disease physician, Glen Morris at the Maryland School of Medicine. And one day, Glen Morris, who was an infectious disease physician, a practicing physician, comes to the lab and he doesn't look like himself. So. The Georgian, his name is Sandra, sees him like that and he asks, you know, what happened? And Glenn says, well, I just lost a patient to an antibiotic resistant infection. I mean this, this man, he battled through new cancer and chemotherapy and recurring new cancer and chemotherapy. And he was in his like forties, so still fairly young. And, and he went through all of this. And then at the end he succumbed to an antibiotic resistant infection because I couldn't find an antibiotic to, to kill this bug that, you know, infected him.

EW: Mm-hmm.

LZ: And Sandra just went, so, and the bacteria phage didn't work either, and Glenn just gave him that stare, like this, this, this, this sta like what? And when I was talking to Sandra and I talked to Sandra so many times for this book was just a moment of reckoning. I was just like. Oh my god, these people really don't know. Like we could treat this in my hometown. You know, he came to America because it was the place to do science right. And. How can this be? And so he basically took it up upon himself, uh, to work for the next 25, 30 years to work with the FDA, to convince him that this was a credible treatment. And if it's done right, it can really say. So many lives.

EW: It, I mean, what a moment of shock on both sides. Like what do you mean phage therapy? What do you mean? What do you mean phage therapy? Like how do you not know what this is? What is this? Right. Yeah. It's it's such a, it's

such a mind blowing moment, I think. And then there were several that was like one turning point. There seemed to be several turning points, this like slow, uh, momentum growing of interest in phage therapy in the west, in the us. And um, can you talk about some of the, these major moments that eventually led to people pursuing this as a legitimate field of research with such potential?

LZ: So initially when Sandra and Glenn tr uh, tried to put together some research proposals, uh, to study Fiji for medical purposes, they wouldn't get any money. And in fact, the entire world would laugh at them just like they laughed back then, you know, at d'Hérelle. Eventually thunder kind of like changed his new path a little bit, and he began to work on phages for food safety. So bacterial contamination is, is a huge problem in, in the food industry as we all know. Like, uh. Almost every week something is being recalled, right? So his company now makes, um, phage sprays that you spray on lettuce, meat, sausages, and whatever that kill very specific foodborne pathogens. And they work very well. So. It is easier to get an approval from FDA for food safety or food products mm-hmm. Than medical products because, you know, medical products are, are, you know, for people who are very sick. Right. So I think, I think it was somewhere in the middle of 2000, the first decade of 2000 was when they get their first approval and then they got, you know, more approval for different type of, uh, you know, phage spray and they now manufacture quite a few. So you could probably count. This as a huge milestone. Even the, even though it doesn't appear as huge, but it is. Mm-hmm. Because it basically proved that Fiji were safe. Mm-hmm. You know, they, they, they didn't cause any harm. And then another big milestone happened a few years down the road, somewhere around 2016 when one particular person picked up an antibiotic resistant bacteria as Abaya while traveling in Egypt with his wife and ended up basically on the brink of death in one of American hospitals. So this is a really unique co, you know, couple. The guy's name is Tom Patterson, and his wife's name is Stephanie Strathdee. And she is a scientist herself and they've tried every antibiotic known to science, and none of them worked. And so she was basically a question of losing her husband or trying something else, and she sat down and did research and she stumbled upon phage therapy. And because she had enough scientific knowledge and she knew enough, you know, people, uh, in the scientific field, she was able to work with scientists who, other scientists who studied phages to create. Uh, certain cocktails that were able to kill this bacteria in her husband. And in fact, it was like a first round of cocktails, second round of cocktails. And at the end they also used, you know, one more antibiotic and that, you know, finally cleared it. And that was the first time the FDA ever approved, uh, an investigational new drug pages for use on humans. And it worked. It worked so spectacular because. There was nothing else to try.

EW: Yeah.

LZ: And that was a really like big pivoting point, which kind of brought pages from scientific obscurity back on the front lines. And since then, a whole bunch of clinical trials are relaunched.

EW: That is one of my favorite stories. Um, the, the Perfect Predator, you know, which is Stephanie's book. And I, it is so, it is so amazing because it is sort of this. This huge moment that I think raised awareness too, not just within the scientific community, but more broadly about this, this possible solution. Mm-hmm. And how that then sort of paved the way, you know, if the public wants it, then maybe we should look more into this. And so that, as you said, has led to such a resurgence and interest. Uh, but there are still some hurdles to overcome, as you mentioned earlier, like FDA approval and also. Incentivizing research into phage therapy. What are some of those challenges? In terms of like the logistical side of things? Incentivizing research, uh, making people even more aware than they are.

LZ: I think the original challenge was that. Years back, the FDA didn't necessarily know how to detest pages. Like the, like, if you think about it, the holy grail of a medicine production is to make sure that medicines don't change, that they're always the same. Mm-hmm. And that's what, that's how they pass through studies. And that's, and, and we know they're gonna work the same way in, in, in just about everybody. Phages are tricky because they change, right? They may change within a person because they multiply, right? So a slightly newer duration of phages may have slightly different genome. They also, again, multiply, which means you give a person a particular dose, but then there's more phages. Mm-hmm. You know more than that dose, and you don't know to what extent they're going to grow. So how do you even decide how much pH to give to near anybody? So there was like a lot of challenges like that. But what the FDA is doing now is that, so they have two centers. There's a Center for Drug Evaluation and then there's a Center for Biologics evaluation and that Center for Biologic evaluation, it regulates products. It's derived from like leaving sources, for example, flu vaccines.

EW: Mm-hmm.

LZ: Which also changed from one season to the next. And so that's where, you know, phages now fall under, and that's, that's the department that regulates it.

EW: Yeah. I mean, it seems like there is a, a promising path forward in terms of getting phage therapy. Just to, to ra some of the standards that we have to not just discard them entirely because of these characteristics that they have. And so

how far away do you think that we are here in the US from phage therapy being like a routine or at least a more widely available option?

LZ: That's a great question, and I've asked that question almost everybody, and you know, the best you get is like, I don't know, five to 10 years or something. It seems that it's moving a little bit faster in Europe, but I don't think we have a lot of options and that's why I think it's it, it has to go a little bit faster because our antibiotics are losing their punch, like way too quickly.

EW: Mm-hmm. You

LZ: know, when I was working on this book, uh, when I first started working on the, on this book, the CDCs 2019 report said that every 15 minutes someone dies from an antibiotic resistant infection. So we talked for almost an hour. Those for people. Mm-hmm. Then CDCs 2022 reports said that it, it's gotten worse. And then newer estimates say that by 2050, antibiotic resistance will kill three people every minute. Yeah. So like you do the math and then United Nations as an. Dream prediction, 10 million deaths annually by 2050. It's like, it's, it's pretty freaky. Yeah. So I think it's like necessity is the mother of adventure. Mm-hmm. So I think necessity will just push us to, to getting this to the finish line sooner rather than later.

EW: Yeah. I, I, I hope so. I mean, I, I would, I would love to see a world in which we have alternatives to antibiotics as part of just building a, a wider toolkit to deal with, right? This growing problem of antibiotic resistance. And I, I wanna close out the interview by asking you what phages mean to you personally.

LZ: I've been fascinated with phages probably since I was a kid. Because I, I was probably, I don't know, maybe six or or seven when I, you stumbled of, upon a phage study in one of the scientific magazines that we had at home. A lot of people in my family was scientists. I, I grew up with all this stuff, just kind of like sitting there and in Russian. The word phage is just three letters, and it's, and it starts with a letter F that looks like a person who is standing with their, uh, arms and their hips, kind of like this very, you know, confident figure that says, don't mess with me. And it was, and the picture of phage itself kind of resembled that. So I started reading that study and there weren't too many familiar words, but I spotted one that I knew. Decent theory, which I was personally acquainted with. Mm-hmm. Because, um, you know, last summer we, uh, the city got a contaminated shipment of grapes and, and so many kids were sick and there were not enough antibiotics. And, you know, eventually my grandfather found some antibiotics somewhere and in a pharmacy, that's what I

took. But the study purported that these phage creatures could be used as an alternative to antibiotics. And that was just so interesting to me that it sort of stuck with me. And, and I also like the phage character as, as a character. Mm-hmm. So I brought my colored pencils and like, you know, color that phage character in different colors. And the whole thing just stuck with me. And it continues to, you know, like some things get lost in your head. And that was one of those.

EW: I, I love that story. What afu? Just like this thing that you came across and something about it just stuck with you. That's wonderful. Well, this, this has been such a fascinating conversation. I've long been a fan of phage therapy and I am just so excited to have read more about it and understand more about the historical context. So thanks again so much for taking the time to chat with me today.

LZ: Oh, thank you for inviting me.

EW: A huge thank you again to Lina Zeldovich for taking the time to chat with me. I didn't know I could love phage therapy even more, but somehow I do. If you enjoyed today's episode and would like to learn more, check out our website. This podcast will kill you.com. Where I'll post a link to where you can find the living medicine, how a forgotten cure may rescue us when antibiotics fail, as well as a link to Lina's website where you can find her other incredible work. And don't forget, you can check out our website for all sorts of other cool things, including but not limited to transcripts, quarantining, and placebo. Read recipes, show notes and references for all of our episodes. Links to merch, our bookshop.org affiliate account, our Goodreads list, a firsthand account form. And Music by Bloodmobile. Speaking of which, thank you to Blood Mobile for providing the music for this episode and all of our episodes. Thank you to Lianna Squillache and Tom Breyfogle for our audio mixing. And thanks to you listeners for listening. I hope you liked this episode and our loving being part of the T-P-W-K-Y book Club and a special thank you as always to our fantastic patrons. We appreciate your support so very much. Well, until next time, keep washing those hands.