Science Will Win
Season 3, Episode 1
Script

[INTRO OPENING]

Imagine this: It's a humid Tuesday evening. You're hurrying down a crowded sidewalk to catch your train home from the office. The low sun is almost dizzying. Your mind is consumed with thoughts of your latest work projects, making it home on time to take the dog out, and the sweaty shirt sticking to your back underneath your blazer.

But then–

Your foot catches on a curb and you fall onto the sidewalk. You throw out your hands just in time to catch yourself, but a sharp pain mingles with the burn of the asphalt. You blink away the shock to find that you landed palm-down on a shard of broken glass. The jagged edge sliced into the heel of your left hand.

You scramble to your feet. The cut isn't bleeding much, so you dig some napkins out of your bag to cover it up and focus on squeezing through the crowd to make your train. Luckily the journey home is relatively short.

At home, you bundle your palm in gauze and try to ignore the momentary twinges of pain.

But after a couple days of using your phone one-handed, you start to feel strange. Is it just the summer heat, or are you starting to get feverish? When you unwrap the cut on your hand, you find it swollen. It's throbbing and hot to the touch.

Is this an infection?

You were hoping it would clear up on its own – after all, it's just a small cut – but you're feeling warmer, clammier. Two more days go by before you make it to the doctor.

The exam room is filled with a sharp, familiar medical smell: a mixture of latex, rubbing alcohol and nose-burning, heavy duty floor cleaner.

Finally, the doctor comes in. You wince as she unwraps your bandage and swabs a fluid sample from your tender wound. She tells you the test will take up to three days to come back. The wound is certainly infected – but they're going to grow bacteria from the sample in a lab to see what the infection is.

Though the doctor sternly reminds you to wash and tend to your wounds more thoroughly in the future, and not to delay coming to the doctor next time, she also assures you that most infections are very treatable.

You aren't particularly worried. After all… it's just a small cut. You take some medicine for your fever and go home.

The next day, you wake up with chills. Anxiety starts to seep in.

It's a balmy Sunday, but you feel feverish enough to stay in bed with a fan pointed directly at your face. Dozing off.

You're jolted awake by the harsh buzzing of the phone on your nightstand. When you hear the doctor's voice on the phone, she sounds urgent. She wants you to come back in right away.

Back on the cold table of the exam room, your doctor tells you that your infection is caused by MRSA. The name rings a bell – maybe from something you saw on TV – but you aren't sure exactly what it is. The word still makes you nauseous.

The doctor starts rattling off an explanation: MRSA is a type of staph infection. It's difficult to treat since it can be resistant to many antibiotics. There are only a small handful of medicines that can treat it.

The bacteria infected the cut on your hand, and now it's likely in your bloodstream.

In the weeks that ensue, you're back and forth from the doctors office, struggling with worsening symptoms. A rash creeps across your hand. Your head is pounding and aching constantly.

One antibiotic after another proves ineffective. And now, you find yourself in the ER with an I.V. of the strongest antibiotic and a narrowing pool of treatment options.

All from a small cut.

This is an example of a so-called "superbug" and they're becoming increasingly common. Today, even healthy people are getting sick from bacteria that have evolved to survive our strongest tools: antibiotics. If we continue along this path, these superbugs are only going to get harder to manage.

But doctors and researchers are helping to change our course by leaning on the latest tools – even artificial intelligence and machine learning – to understand the problem and find new treatments.

[THEME MUSIC]

Jeremiah:
This is season three of Science Will Win. And I'll be your host, Jeremiah Owyang. I'm an entrepreneur, investor, and tech industry analyst. I'm passionate about emerging technologies and the way they can shape our world.

In past seasons we covered the science behind gene therapy and oncology, but this season we're talking Artificial Intelligence (or "AI") specifically how AI can help the scientific community overcome one of the greatest challenges facing humanity: antimicrobial resistance, or AMR for short.

You might know it as antibiotic resistance or drug resistance. At its core, what we're talking about is the way bacteria evolve to outsmart antibiotics. This makes certain antibiotics – the ones we've been using against certain bacteria for decades – ineffective.

This season, we'll hear from researchers, doctors, patients, patient advocates, computer scientists, and AI experts. All of them are on the cutting edge of the fight against antimicrobial resistance.

The story you heard at the beginning of the episode is a hypothetical scenario, grounded in truth. We see stories like this playing out today, and the data show that they will become even more common.

[MUSIC]

This season is all about how artificial intelligence is helping us tackle antimicrobial resistance. But to understand *why* AI is helpful and what it can actually do, we first have to understand the problem at hand.

So, let's take a step back.

You're probably familiar with antibiotics. You might be prescribed them when you're sick with a bacterial infection, and then, well, they kill the infection inside of you. But antibiotics as we know them today are a relatively new tool. You might have even heard the story of the discovery of penicillin – a sort of magical accident.

It's 1928. Alexander Fleming, a physician and microbiologist in the United Kingdom, starts culturing Staphylococcus bacteria in a petri dish.

He goes away on vacation, and comes back to find that the dish has been contaminated with some kind of mold.

This could have meant his experiment's a bust. But he notices something: where the mold is growing, the bacteria… is not. It turns out, the mold produced a chemical that kills bacteria.

Fleming would call that chemical: penicillin.

> Jay Purdy:
> How do antibiotics work when you really get down to it, what do they do? It's really pretty simple. An antibiotic will inhibit the bacteria from surviving. And there's different ways to do that.

Jeremiah:
That's Jay Purdy.

Jay:
I'm the Vice President and Therapeutic Area Lead in Global Medical Affairs here at Pfizer for antibacterial and antifungal programs.

Jeremiah:
Jay has a keen understanding of the problem because before he started working at Pfizer, he was a practicing physician.

Jay:
The important, uh, issue for me has always been taking care of patients. And I found as an infectious disease physician, um, some of my patients died because I didn't have effective antibiotics. And that, that bothers me. It bothers all physicians when you don't have the tools that you need to save lives. And so, when I had the opportunity to join pharma, I decided to take it because I was at University of Chicago and we have a motto. We changed the world, one life at a time, one patient at a time. And that's a great motto. And physicians that do that, I have a great deal of respect for. But within the pharma world, if we choose the right drug, we develop it correctly and get it to the patients in need, we can really make a difference. And that's what I love about my job.

Jeremiah:
As Jay explained, “antibiotics” work against bacteria. These medicines target a variety of bacteria in different ways.

Jay:
You can inhibit an important molecular pathway within that bacteria so that they just can't survive anymore. It's unable to reproduce and move forward. Or you can produce an antibiotic that actually kills the bacteria. And there's some really innovative ways to do that. Some of them literally the molecule itself goes onto the surface of the bacteria and punches holes in the surface of the bacteria and they just basically bleed out. Sometimes these antibiotics come in and bind a, a protein that keeps it from working and, and therefore kills the bacteria.

Jeremiah:
Penicillin, for example, works by inhibiting the production of a substance that makes up the cell walls of some bacteria. The cell walls weaken and *explode*. Then, our immune systems clean up what’s left.

Penicillin is still among the most widely used antibiotics out there, but what you might not know is that Alexander Fleming himself never actually turned his discovery into a reliable medicine.

Fleming, and several other chemists he recruited for help, tried for years to isolate penicillin from the mold that produced it.

Eventually, they all gave up.

But the promise of a drug that could kill bacteria, vanquish infection… it was alluring, and badly needed. And so in the following years, a handful of other scientists gave it a try.

Two in the UK, named Howard Florey and Ernst Chain, were able to isolate penicillin. But they had another problem: they couldn't make enough of it fast enough.

That's where Pfizer comes in, specifically Charles Pfizer & Company. In the early 1940s, they were a small chemical company making citric acid. The U.S. was facing down the threat of World War II, and all of the potential sickness and infection. And Pfizer provided the breakthrough that penicillin needed.

> Jay:
> Pfizer developed—it's called "Deep Fermentation"—it's a way to grow up really significant amounts of penicillin, which part to that was very difficult to, to isolate and grow up, um, which became a real need, obviously in World War II, and saved countless lives.

Jeremiah:
Production ramped up enough to treat all the people who needed it. The so-called "wonder drug" was almost too good to be true.

There *was* a catch. Resistance was already brewing.

> Jay:
> Before the first use in a patient, we had already isolated a bacteria that was resistant to penicillin. The bacteria know what they're doing. So they create these molecules, and secrete it into the environment to kill the other bacteria so that they can take over. It's like Martians colonizing the earth, if you'd like to watch those sorts of movies. The first thing they wanna do is kill off the humans so that then they can take over. And it wasn't long before a really significant number of bacteria became resistant. And that's been true of every one of our antibiotics.

Jeremiah:
And unfortunately, the problem of resistance has only gotten worse over time.

> Jay:
> Every time you use an antibiotic, you create pressure on the bacteria to develop resistance. Why is that? Cause you kill off everything that is sensitive to that antibiotic. And the only things that is left are those that are resistant, and those that are resistant now can propagate and move through the community.

Jeremiah:
Just like all life on Earth, bacteria evolve. Every time an organism produces offspring, there's a chance that offspring will have a mutation. Sometimes, those mutations can help the organism survive in the environment.

For us humans, evolution takes *millions* of years to make meaningful changes.

The timeline for bacteria is *wildly* accelerated. Bacteria double in as little as four minutes. They evolve *fast*, and one “predator” they’re evolving to avoid is our antibiotics.

> Jay:
> The problem is once one cell figures out how to do it, once it has that mutation, it'll propagate, it'll make more and more and more of itself where those bacteria that are sensitive to the antibiotic, die. And so you might have one in a billion bacteria in your colon that's resistant to a certain antibacterial, but once you start taking that antibacterial, you kill everything else. The one that that was resistant can just take over. It's like a yard. Um, as long as you've got a thick grass, it's really hard for dandelions and weeds to take over. But you strip that grass off where it's just dirt, and at least in my experience, within just a few days, you're seeing lots of weeds grow up.

Jeremiah:
Scientists knew antibiotic resistance was a possibility from the beginning. But in the decades after World War II, humanity felt nearly invincible in the battle against deadly microbes.

Some even claimed that between antibiotics and vaccines, we’d won. We’d defeated bacteria altogether.

> Jay:
> So in the sixties we were of the opinion that we may have solved the infection crisis. You know, we had the polio vaccine that prevented polio. We had great antibiotics that were, um, saving patients lives, treating invasive infections. And so in 1967, there's this following quote attributed to William H. Stewart, then Surgeon General for the United States of America. And he said “it is time to close the book on infectious diseases, and declare the war won against pestilence.” So we stopped doing the research. Companies felt it just wasn't worthwhile to continue to work in anti-infectives, so we had this research gap where we just stopped. Well, in the meantime, the bacteria, they may not have brains, but on the other hand, they're not stupid. They’ve continued to mutate.

Jeremiah:
All along, bacteria were developing resistances to the medicines we were using. And companies had stopped trying to find new antibiotics. Remember those mechanisms of attack that antibiotics might use? They might bind to proteins inside the bacteria, in order to kill it, for example.

Well, what happens if the bacteria produces a *different* protein? What if the bacteria’s cell wall becomes stronger, stopping the antibiotic molecule from even entering? Those are just a few of the ways that bacteria can evolve to evade or resist all the ways antibiotics work.

To make matters worse, *humans* are doing things that have accelerated antimicrobial resistance. This can happen in a medical setting:

> Jay:

> And there's great studies out there, they're around the world, that really suggest that are really a significant percentage of our antibiotics are being used in patients that really shouldn't be getting antibiotics or shouldn't be getting *that* antibiotic in the first place. And that's the thing we really need to be careful with because, as I said, it drives forward resistance with no benefit.

Jeremiah:
Antibiotic resistance is also a problem in agriculture, right down to the food we grow and eat.

> Jay:
> The other area that that's very concerning is we often use antibiotics in animal husbandry, to help them grow faster or to survive better. And remember, you know, when you have 10,000 cows all getting a certain antibiotic, they're all developing resistance along with humans that get 'em for a short period. Oftentimes in animals, we use it, we give antibiotics for their entire life. Similarly, for plant growth, um, there's times when, uh, antibiotics are used very broadly. Some of the antifungals are used in tulips in Europe to prevent, um, fungal infections of the tulip. The problem is those, that antifungal is often used in humans as well as needed in humans as well. But if you develop resistance in the flowers and the flower's red and they're in your kitchen and you pick up resistant fungal elements on your skin and you get it into your body, suddenly that antifungal doesn't work anymore.

Jeremiah:
Together, the misuse of antibiotics and the misguided belief that we had won the battle against bacteria have put humans in a dangerous position.

> Jay:
> Yeah so our antibiotic development programs are at crisis point, there's no question. It's getting harder to find good antibiotics, um, because there are only a limited number of genes in the bacteria that we can address and they're getting harder to find. It takes more effort, um, sometimes more cost, uh, to find those molecules and develop 'em. The important thing is not to develop another antibiotic in a class that we're already using.

Jeremiah:
Antibiotic "classes" are subcategories that act on similar bacteria in similar ways.

That means if bacteria develop resistance to one kind of antibiotic, they are likely to already be resistant to another antibiotic within that class. The solution is finding brand new classes. That's risky because many potential new classes of antibiotics could be toxic, and they're also expensive to develop.

Today, artificial intelligence has the potential to play a big role in the discovery of new antibiotic classes, possibly making the process more efficient and cost effective.

But those tools are new, and as of now, the last time a new class of antibiotics hit the market was *1987*.

After more than 30 years without a new class of antibiotics, the scientific community has fallen *way* behind. And this resistance crisis can have life-altering or fatal consequences.

In 2015, Mary Lynne Van Poelgeest-Pomfret's husband went in for a routine operation at the local teaching hospital to fix his enlarged prostate. When Lynne walked into the visiting room to see him after his surgery, she found a scene she didn't anticipate.

> Lynne:
> And when I came, literally to see him and visiting, the room he was in was strewn with all sorts of syringes on the floor. I asked, I said, what's going on here. It was mind boggling. Um, you don't expect it. You'd come in expecting to visit someone who's just come down from surgery or whatever, maybe a bit sleepy or whatever, but I didn't expect to find this sort of scene of carnage almost, I would say.

Jeremiah:
During the surgery, the surgeon accidentally perforated the lining of Lynne's husband's bowel. As a result of the accident, Lynne's husband had been infected with two different antibiotic resistant bacteria.

The doctors put Lynne's husband on strong IV antibiotics to fight the infection, but he was, and still is, unable to recover fully.

> Lynne:
> Well, he has lots of abdominal and bowel issues as a result, but it's more a nuisance factor, let's put it this way. But these bacteria, if you like, the silent monsters at the moment and have been for a few years. But yeah, what can you do? I mean, there's no cure.

Jeremiah:
The bacteria in Lynne's husband are going to impact him for the rest of his life, or until researchers find a cure. While the bacteria usually cause mild symptoms, his condition could potentially get worse at any time. And, he's susceptible to other infections.

> Lynne:
> They raise their ugly head each time you have to go to hospital for any intervention at all. You're put in isolation, you go through the whole rigmarole of, of that because yeah, these bacteria are there, and of course they're worried sick.

Jeremiah:
Lynne has worked as a patient advocate for years. In 2011, she became president of the World Federation of Incontinence and Pelvic Problems, or WFIPP. Her work as an advocate prepared her to navigate the medical system on behalf of her husband. But she didn't know much about antimicrobial resistance until her husband's infection.

Now, AMR has become a larger part of Lynne's advocacy work as resistant infections become more common, like in urinary tract infections or UTIs.

Lynne:
Now what happens so often that somebody might go to the GP, they get one dose of antibiotics, they don't work, so then they get another one and another one. So in the end, the resistance is increasing exponentially in UTIs. So it's a vicious circle. You're giving antibiotics that in the end are non-effective. The cost is enormous because the problem isn't solved. So it's something that we see on a daily basis, and it may sound, oh, you know, it's just a UTI, a bladder infection, whatever. No, that, that's just one example of how we need to tackle this famous silent tsunami of antimicrobial resistance. And of course, in the long run, those UTIs, if not treated, can lead to far more serious issues.

Jeremiah:
The World Health Organization has declared AMR as one of the top 10 global public health threats facing humanity. Antibiotic resistance is on the rise. Without coordinated, effective, global action, annual deaths from AMR could reach *10 million* by 2050.

There is hope our prognosis could improve.

Lynne:
And if we bring all the bits of the jigsaw puzzle together, and make sure that the focus is on AMR and what it means, pool your resources and, and make sure that we all work towards finding as best a solution as we can.

Jeremiah:
We've reached a turning point. After falling so far behind, the scientific community needs to prioritize both the effective use of existing antibiotics *and* discovery of new classes of antibiotics to address the challenges posed by AMR.

Today, Jay Purdy says that means using the most sophisticated technology we have: artificial intelligence.

Jay:
So artificial intelligence is a very important tool, um, that we can use to determine risk factors on how to treat patients, how best to treat 'em, when to escalate to more expensive or more aggressive antibiotics. And so I see that being used more increasingly in the future, to help guide physicians as a tool.

Jeremiah:
Historically, discovering new antibiotics has been a slow process. We need to determine which bacteria are the biggest threats, find molecules that work against them, and turn them into safe and potentially effective treatments. AI can help speed that process up.

Adrian:
Artificial intelligence, I think, can play a role in two ways.

Jeremiah:

That’s Adrian Egli. He’s a professor of medical microbiology at the University of Zurich in Switzerland.

> Adrian:
> Um, the first one is in diagnosis. So, more rapidly finding, um, a pathogen more rapidly finding a resistance mechanism. And the second way would be in drug discovery.

> Adrian:
> So image analysis, data analysis, prediction of resistance, this is all, all applications where artificial intelligence can be used.

Jeremiah:
We’re going to hear a lot more from Adrian this season. We’re going to hear about his work in diagnostics, and the ways artificial intelligence is already assisting researchers to work and learn more quickly than ever.

We’ll hear from experts, from inside and outside Pfizer, about how AI can help us make sense of how AMR is spreading and understand the problem at hand.

And we’ll learn how AI can help identify new antibiotic options from that narrowing pool of possibilities and speed up drug development.

And we’re going to explore how AI can potentially build a better, safer future.

> Adrian:
> Antibiotic resistance is not just a problem between humans, it's also between humans and the environment and animals. And this is tremendously complex. And so having a supportive system like artificial intelligence, um, could really help us to solve these, uh, complex questions we have there.

> Jay:
> Antibiotic resistance impacts every person on the planet. Um, if not today, then in the future, there's no question. And if you're infected with a resistant pathogen, it just worsens your prognosis in every way, and so, if not for our benefit, for our children's benefit, we really need to be worried about antimicrobial resistance

> Lynne:
> And we have to be smart because otherwise the superbugs will, they're smarter than we are, as we know, but we have to be as smart as we possibly can be.

Jeremiah:
Next time on Science Will Win:

We’re going to start piecing together how artificial intelligence can break down the data and help us understand the problem at hand. How exactly are bacteria evolving? Who is most at risk? And *why* is it important for all researchers to have access to clear data?

Marinka Zitnik:
And I think especially with new capabilities of algorithms that, and the breakthroughs we have seen in machine learning literature over the last several years, uh, there are the opportunities that we could not have imagined just a few years ago that now seem within reach.

Jeremiah:
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Special thanks to the responsible AI and anti-infective teams at Pfizer. And thank *you* for listening!