MANICA_BALASEGARAM(2)

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SPEAKERS
Manica Balasegaram, Maggie Fox

Maggie Fox 00:01
Hello and welcome to One World, One Health with the latest ideas to improve the health of our planet and its people. I'm Maggie Fox. Planet Earth faces many challenges—pollution, climate change, and new and reemerging infectious diseases. And they're all linked. This podcast is brought to you by the One Health Trust with bite-sized insights into ways to help.

Antibiotics are such important drugs; we need them to treat infections from pneumonia to sepsis to sexually transmitted diseases, such as gonorrhea. That antibiotics are losing out to the quick evolution and mutation of bacteria. And in part because they're not especially profitable drugs, pharmaceutical companies are not racing to make them. The result is that drug resistant superbugs are winning the race.

Dr. Manica Balasegaram is Executive Director of the Global Antibiotic Research and Development Partnership. He's chatting with us about why we need more antibiotics and just what kind of new antibiotics we need. Manica, thanks so much for joining us.

Manica Balasegaram 01:07
It's a pleasure to be here. And thank you for inviting me.

Maggie Fox 01:11
Can you please quickly tell us about the problem of antimicrobial resistance? How many people die every year from these infections and what other problems do these kinds of infections cause?

Manica Balasegaram 01:21
------ infection to begin with humanity since time immemorial, and all microbes whether they're bacteria, viruses, parasites, and develop resistance against the drugs—the antibiotics that we have developed against them. Essentially, what antimicrobial resistance is, is the ability of a microbe to evolve or develop or acquire a mechanism that allows it to survive an assault of an external source like a drug.

So, looking at it from their point of view, it's their ability to survive in a hostile environment, including drugs that humans have developed to ------. So, it's something that we should just see as a normal course of evolution. Now, why it is important for us, while unfortunately, we are developing these drugs

because sometimes, these microbes can cause infections, and it can cause people to get extremely sick. Disability can follow or even death.

Maggie Fox 02:14
So how can having new antibiotics help in fighting these changing germs?

Manica Balasegaram 02:20
Well, we just have to remember (that) people call it an arms race. But I just see that as a process of evolution ------. But we have to be cognizant that drugs that we have developed over the decades can lose their utility, not to all bacteria, and so on, but maybe to some, and that we, therefore, have to start getting ahead of the curve and developing new therapeutics, new treatments, new approaches to either prevent infections or to treat infections, particularly the ones where resistance is emerging, or has emerged, and particularly has been established.

Maggie Fox 02:51
How close are we—the whole world—to running out (completely running out) of useful antibiotics?

Manica Balasegaram 02:58
I think that's not an easy question to answer kind of overall, maybe it's often easier to break that down into because you gotta remember that lots of different bugs out there that cause lots of different types of infections. But I think we are in a situation where certain infections, and particularly caught by certain, let's say bacteria. We're in a situation where we have less therapeutic options, often going towards what we would call kind of last line of defense.

And that is, of course, a worrying situation. And we think we've got it (but) we've got to remember that if we want to be ahead of the curve, we have to be extremely proactive. We are kind of behind the curve in several different areas. What are called gram-negative bacteria that cause infections that can be whether they're lung infection, ------ abdominal infection, that can cause significant sickness, and that the other infections like gonorrhea, for instance, that can cause significant morbidity and sickness.

And yeah, we know that this particular bug is very smart and continuously evolving against all the classes of antibiotics we're throwing at it. We kind of know what we're using a type of antibiotic, then it's kind of you know, it's almost the last line. ------. We're now seeing resistance emerging and becoming established here.

There was a recent report, even from last week, from WHO highlighting this problem. So, we are behind the curve here. And we have to move back. And that requires much more effort, more teams working on this, and more and more resources.

Maggie Fox 04:22
And you've hit on this a little bit. But can you help explain why the world not only needs new antibiotics in general, but entire new classes of antibiotics?

Manica Balasegaram 04:32

Yeah, because we can, of course, churn out lots of different antibiotics of the same class. But looking at different classes and mechanisms of action in particular means that we can have more heterogeneity of approaches. And that means that we can protect ourselves from emergence of resistance in the future, and you will never 100% protect yourself. What you can do is slow it down or be ahead of the curve.

And that's what we need to be, that's why we need to do this so that there needs to be more novelty. This requires more basic science in the areas of different ways of how we can affect the lifecycle of bacteria and how we can essentially find targets. And we need to have different approaches to identify. We can identify potential drugs or alternative approaches that can work. And then we need to have the resources to test that. And this is a long-drawn-out process.

And as I said, we're behind the curve. So, there'll be no miracles that can just appear overnight. This kind of intergenerational, continued toleration of a kind of effort that is required. The reason why a lot of people look at conventional approaches (is) because you often know that you're on safer ground, you often know much more about the approach you're taking, chances ------ success could be high.

If you take a very novel approach, they have a lot more uncertainty. And this is likely to fail. Then you add on to the mix ------ all of this is not really seen as something that is very commercially lucrative enterprise. That creates a lot more risk around this whole venture. Whether you're doing it as a nonprofit, or for-profit approach, you still have the same scientific challenges to face.

Maggie Fox 06:00
So, you've spoken about the need to not only develop new antibiotics, but to find the right infections to go after. Can you talk about that a little bit?

Manica Balasegaram 06:09
------ you have developed therapeutics or brands that can target your bacteria or bacteria that you want to target, but------ people with types of infections. So, you have to also demonstrate that it will work in these infection types. And the human body is complex. So, you have to ask questions like if what you're developing actually able to go and penetrate into the lungs and be effective when you have been practicing ---- -- , for example, right!

So yeah, one has to look at it from that perspective that there are many different angles that want us to cover in the kind of scientific and development process as well. But we also have to look at the ------. And a good example of that is that we need to ensure that we do research and understand that we are developing tools that can be used once it's in adults, but also in children and, particularly, newborn babies, ------.

Seeking that kind of integrated approaches is extremely key but that doesn't always happen all the time. A very good example is that it's well known that pediatric drug development that drugs that developed for instance, for children and newborns, lags behind. There's multiple reasons why that happens. But particularly in the case of antibiotics and infections where we know that children are a high impacted population, and they are very vulnerable, particularly very young children and newborns.

It's extremely important that we prioritize certain populations when we talk about the research process. So, and by the way, it's important to understand that certain approaches may not work in children, or you may find that they are toxic in children. So, these are all things we have to take into account when we're trying to identify the right type of treatments for the future.

Maggie Fox 07:42
So, tell us a bit more about what you're doing at the Global Antibiotic Research and Development Partnership.

Manica Balasegaram 07:50
So, we're a nonprofit organization. Our focus is on global health. So not just the needs of rich countries, but also the needs of low- and middle-income countries. And our focus is where we think the biggest problems (are), what are the biggest problems, and where are we seeing these problems. And what can we do to help.

So, we have developed a strategy around focusing on sepsis, including hospital-associated infections that can lead to sepsis, and also looking at our children and newborns. And within that, we're focusing on the WHO ------ gram-negative infection. We also have a program on sexually transmitted infections, or STI is, which is primarily, for the moment, focused on gonorrhea as well. And this is something that we were requested to do by the World Health Organization.

So, we're a public-private partnership. We work with both the public and private sector. We're largely funded by (the) government. And when we work with the private sector, we find partnerships with them that bring us into kind of a project where we will support the research and development but also looking at access, including for high burden low- and middle-income countries. So, areas where we are partners may not have a primary interest to go into at the outset.

And through this, we have a range of different projects in our portfolio. Some of them are new drugs, for instance, in phase 3. Some are drugs that have been recently brought to the market. But we are partnering with companies to help to expand the access to them. And some projects are really seeing how we can better use old existing generic drugs potentially in combination.

Maggie Fox 09:15
So, what's in the antibiotic pipeline right now? Are there some new drugs coming up?

Manica Balasegaram 09:19
It depends where you're looking. There's a preclinical and clinical pipeline, and I can simplify it that way. There's a lot of work done in both areas ------. So many of these candidates on the list will never make it even if they are very promising and are novel in thought. The answer is that we have to increase the number of candidates in both preclinical ------clinical pipeline if we want to have success and long-term success.

And the output is not just to develop one new drug that's going to save us all forever. As I've said before, that isn't going to happen for the reasons that I mentioned. So, we need to have a dynamic

process where we can continue to evolve to look at the priorities and we need to have a process where and financing, in particular, and incentives that will allow us to ensure that there is a sufficiently robust pipeline, both preclinical and clinical.

Now this requires more work in basic research. It requires more work in discovery. And it requires more financing in both preclinical and clinical development. But one thing I would like to say, which is extremely important for me is that the innovation is all great but if these drugs never reach the patients around the world who really need it the most then it is all for nothing. Okay, so you know, I would say the utility is significantly diminished.

So, we have to also find ways of how we can successfully introduce these drugs to the people who need it the most while also ensuring that these drugs are not overused and that in its own right is another significant challenge that we have to ------ process.

Maggie Fox 10:56
Manica, thanks so much for joining us.

Manica Balasegaram 10:59
An absolute pleasure. Thank you very much.

Maggie Fox 11:02
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