**Global Perspectives, Barriers, and Solutions**

I have had the privilege of traveling to several different countries in Africa and to be able to visit some of these clinics where I have seen mothers who have woken up at the crack of dawn and have walked the equivalent of seven or eight miles, holding one, sometimes two children to get to the clinic on vaccine day because they know that that vaccine is going to protect their child. So I think they tend to see vaccines as something that is really going to save their children and they are very grateful and appreciative of vaccines.

This is The Antigen. I'm your host, Yasmeen Agosti.

For this episode of The Antigen, we're going global--talking about vaccine perspectives and challenges and progress around the world. As Martha Rebour, Executive Director of the United Nation's Shot at Life Campaign, highlighted at the top of the show, the impact of vaccines on global health has been substantial. The Centers for Disease Control or CDC estimates that between 2011 – 2020, vaccines will have prevented more than 23 million deaths in low income countries. Vaccines come only second to clean water as the most effective public health intervention we have. Global health is a BIG topic, and vaccines are just part of a much larger effort to improve the health of people around the world. This episode will only scratch the surface!

In many low and middle income countries, infectious disease is a much bigger problem than we see here in high income countries. Not just the number of people who get sick, but how sick they get, how likely they are to die and if they do survive, the long-lasting impact on their family and their futures. In the context of weak or fragile health systems, the role of prevention through vaccines becomes even more important because the safety net just isn't there. For many people, vaccines are the safety net.

Dr. Seth Berkley, the CEO of the Global Alliance for Vaccines and Immunization or GAVI, explains how getting sick relates to poverty.

If a child is constantly sick, what begins to happen are the following things. First of all, their nutrition status may go down if they were, you know, not very well nourished. If they're, if they're constantly sick, then they could tip into malnutrition. The family has to often pay out of pocket for healthcare for those illnesses that occur. Even special foods. If the child is sick, somebody has to stay home with that child. And that might be the parent, or it might be a sibling who might have to stay home from school and themselves not get educated. So, the combination of all of those effects means that the illness is a big drain to the family and allowing, um, that family to tilt towards poverty. And it's estimated that 100 million people get tipped into poverty, due to ill health and, and health related

expenditures. So, what we're trying to do is basically keep children and families healthy so that they could live up to their full potential as the next generation.

Vaccines are not always easy to come by. According to the World Health Organization or WHO, more than 19 million infants didn't receive any routine vaccinations in 2018. Why? Well, there are a number of reasons or really barriers that need to be overcome: Geography, conflict or vio-lence, fragile health care systems, these are just a few examples.

Martha Rebour, describes one example from the Democratic Republic of Congo, a country which has struggled through decades of conflict.

Something that's not well known right now is there more children have died in the DRC, the Dem-ocratic Republic of Congo, of measles, then Ebola. So, Ebola always gets a lot of press and at-tention, but in fact more children have died of measles. And the challenges faced by healthcare workers are incredible because I think in the past there was very much an understanding that clinics and health care workers are sort of off limits during any conflict. And it used to even be, there would be a, a pause in conflict and warfare for maybe a day so that children could get vac-cinated. And I just don't think there's that understanding anymore. And so there, there's a real barrier. If you live in a conflict area, you can imagine as a mother, sometimes you don't even necessarily want to go outside of your house or outside of your village and walk for a ways be-cause you don't know that you'll be safe.

Unfortunately, this is not a unique situation. Janti Soeritpo, President and CEO of Save the Chil-dren U.S., explains further.

You know, currently there's about four, there's over 400 million children actually living in areas impacted by conflict, right? We often forget, uh, how many children are actually living in those areas. And, and it's also protracted conflict, right? So, it's going on for years and years and years. Um, countries like Nigeria, Somalia, areas of Ethiopia, Congo, Syria, obviously, uh, as we speak.

And what you see is even if we get access to those places, it's often very unpredictable when violence erupts. So that means that our people in healthcare clinics sometimes need to stop their program and essentially run for cover. We can't get the supplies because they're essentially, the infrastructure is broken down and the supply chain is, uh, is broken. It means that people can't travel to the clinic because it's unsafe to go out. So, there's lots of ways in which even, you know, basic services get disturbed because of the presence of conflict.

So, clearly conflict makes it really difficult for people to reach vaccines and for vaccines to reach people.

It doesn’t just restrict people to their homes out of fear for their physical safety. It can also push them out of their homes and away from community resources, including health care. In the Con-go alone, 4.5 million people have been internally displaced by conflict and violence.

Natural disasters also displace people--either within their own country, into neighboring countries or far beyond into other continents. It’s not always possible to bring medical records with you when you are fleeing a bad situation. This creates a unique challenge for a group of people who are even more vulnerable to infectious diseases.

So because of conflict, because of drought, uh, there is a lot of people around the world who have to be on the move and without careful record keeping when they come into country some-times UNICEF or whoever's meeting at the border, they don't know if they've been vaccinated and, and there isn't always a UNICEF office going to be at every border. So, I think people who are refugees are also, are at great risk of not getting a full course of vaccines.

Even in the absence of conflict or disaster, it can be just plain hard to get vaccines to people in hard to reach places.

There's also a new phenomenon that we, we talk a lot about the last mile. So the children that live very far away from any kind of infrastructure of roads and you know, it could be a terrain that's very difficult.

It’s easy to imagine what this what this might look like - an isolated mountain village or a sub-Saharan community far from a main road. But surprisingly, there are also urban areas in which access can be just as challenging.

A more recent phenomenon is children who live in urban slums and these are not always in the world's poorest countries. These are in what we call middle-income countries. So they might live in a favela in, you know, a major city in Brazil and there isn't regular health care being given and there isn't infrastructure and there isn't clean water. And so, while we may look at the overall country's statistics and look like there's a pretty good percentage coverage, I think if when we've learned now with our access to data, which has been so powerful, is when we zero in on certain neighborhoods, there's extremely low vaccination rates.

This might sound familiar to you from Episode 1 - recent measles outbreaks in the U.S. were caused in part by pockets of low vaccination rates, which were otherwise hidden by a high na-tional immunization rate.

It’s easy to feel overwhelmed by the global picture when you’re only looking at the challenges to vaccination. Thankfully, there are a lot of governments and organization focusing on solutions While

you can't solve everything at the same time, you can prioritize. Martha Rebour explains how Shot at Life's chose to approach improving global access to important pediatric vaccines.

So, the first two diseases, um, were chosen, polio and measles, because those are two diseas-es that we could see eliminated in our lifetime. They cannot be carried by animals. And as we all know, polio is very close to being eliminated. So, we thought it was important that we joined the efforts to eradicate polio.

Global polio incidence has been reduced by 99.9% since the Global Polio Eradication Initiative was founded in 1988. Just this year, after decades of coordinated efforts, the second of three polio strains was eliminated – an important public health achievement. But the job isn't done just yet.

The disease is still endemic in three countries – Afghanistan, Nigeria and Pakistan – countries struggling with conflict and access to vaccines. And until we are able to stop transmission of the polio virus in these three countries, all countries remain at risk of importing cases into their own populations.

This sobering fact provides an important guide post to the world community. Serious infections cannot be eliminated simply by having invented a good vaccine. That vaccine needs to reach people.

Measles is not as far along as polio. And we know, unfortunately this year there have been some really devastating outbreaks, not only in the US, but around the world, but it is a disease that could be eliminated. And that, again, as I said, is devastating if you are in an area where you do not have access to clean water and hygiene and many children pass away from measles and have terrible complications like blindness and cephalitis. So those are two diseases were chosen for the fact that we could be part of sort of history in the making of eliminating them and really joining the efforts.

So in addition to polio and measles, Shot at Life chose pneumonia and diarrhea since they are two of the leading killers of children around the world. Together, they cause one in every four deaths globally in children under the age of 5.

"Under 5 mortality" is a term you hear often in global health. As the term implies, it's a measure of how likely you are to die between the time you are born and the time you turn five years old. It's not just an indicator of how healthy children are in a certain country are, but also a reflection of how healthy a country is - socially, economically and environmentally.

Today, 5 million children per year die before their fifth birthday of completely preventable

causes. Now, some of these are related to basic hygiene but a lot of them are also related to preventable diseases, which is where immunization and vaccination really comes in.

To give you a sense of what these numbers look like, let's compare the under 5 mortality rate in the US to some other countries. Here in the US, the rate is 6.6 per 1000 live births. So out of every 1000 live births, 6.6 children die before their fifth birthday. In Angola, that number is 81.1, in Brazil 14.8, Kenya 45.6, and India 39.4. These rates can be found on the UNICEF website.

So in an ideal world, you have no under five deaths that are preventable. Of course, there will be some deaths that are unavoidable and, um, cannot be prevented. And, and this has been a goal for development for years. And, and one of the things that we use in Gavi as a way to measure, um, how much a country has improved over time and what's remarkable if you look at the coun-tries that Gavi has worked, we've seen a 50% reduction in child mortality over the, about 20 years that Gavi has been in existence. Now, of course not all of that is attributable to vaccine preventable interventions, but we've seen an actual 70% reduction in actual vaccine preventable disease deaths. So, um, we can say that a lot of that is attributable to the work that has been done.

Since its inception in 2000, GAVI has helped to vaccinate more than 760 million children in the world's poorest countries – preventing an estimated 13 million deaths. How do they do this? They address two additional barriers to vaccination that I haven't mentioned yet – affordability and fragile health care systems.

The challenges that new and powerful vaccines were not being made available to those living in the poorest countries. Because normally when vaccines come out they start out on being, um, uh, low volume of production and high cost. And of course, what we need in developing countries is, is a, a high volume of production and low cost. And, um, that's problem number one. Problem number two of course, is that in some of the countries we are working, they have fragile or weak health systems. And therefore, what we need to do is help countries have the systems in place to deliver these lifesaving vaccines. So what Gavi brought to the table was a different way of thinking about it. So we would go to the manufacturer and say, well, what if we were to purchase large volumes of that? And in doing that, increased the volume of manufacturing, which drives it from being a, um, the cost of goods goes down because now you're producing very large quanti-ties that has benefits in the primary market for the manufacturer because the cost of the vaccine is less, but it also has a benefit for poor countries because eventually they, as they get wealthier, will be able to afford the vaccine as well. So that's the model.

GAVI doesn't work alone. Overcoming barriers to vaccination is simply too big of a job for any one person, government or organization to solve on their own. It's why they refer to themselves as an The Vaccine Alliance.

And what does that mean? Well, when GAVI was originally set up, the idea was not that this is a separate organization or separate effort, but rather that there were many players in the vaccine space. And if we could bring all of them together and have them work together, that would create the synergies that would be most likely to crack this very difficult problem. And so the Alliance includes not only the UN agencies, WHO, UNICEF, The World Bank, The Gates Foundation, which was a founding partner and obviously is very interested in global health, but it also includes vaccine manufacturers from industrialized countries and vaccine manufacturers from developing country. It includes a civil society. It includes ministers of health from the actual developing coun-tries we are working in. It includes research institutions. And, and by bringing all of those groups together, um, it's, sometimes is difficult to get to decisions, but when we get to a decision, we align the entire community in trying to move that forward. And, and in some senses, I think that's why it's been so successful.

And so just how many people are a part of this Alliance?

So when people say, how many people work at Gavi: is it the 300 people that work at our head-quarters? Is that the 3000 partner people who are specifically working on this? Or is it the esti-mated 168,000 clinics that are actually developing, sorry, that are actually delivering the vac-cine? And, and so, um, you know, this is an important issue. So, it is more than a village and it's not just even those 168,000 clinics, but it's also the people in the community that are encouraging people to step forward and do vaccination.

One of the organizations that GAVI partners with is Save the Children. You heard a little bit from their U.S. President Janti Soeripto earlier. She explains to me how part of their mission is to re-duce under-five mortality, which is where vaccines fit in. She described many of the same issues that we heard about from Shot at Life and GAVI. But what really stood out was her description of what their work looks like on the ground. Even after all the pieces have fallen into place to bring a vaccine to a community – the invention of the vaccine, the funding, the health system strength-ening… nothing can happen without good and simple communication.

We work with a lot of people from the local community so that we really a) speak the right lan-guage, literally. But also really understand the issues for that community because sometimes it's about the availability of the right information, where to go, when to start immunization for children, how to go there and make sure they can get access to it, making sure the access is affordable to them because otherwise people feel that they will not be in a, in a good place to, to go there. But also making sure there are no cultural barriers in the way for people not being able to access it or sometimes it's also sending them simple reminders because people are busy, they're work-ing hard to keep their families alive and healthy. Um, and sometimes if you have to travel for hours to get to a

clinic, uh, that's, that's the, it doesn't always fit in to your schedule, if you don't see the immediate benefits.

The need for good communication and awareness of why vaccines matter is really a universal one. We'll talk more about this in the upcoming episodes.

But what happens when the vaccines that people need don't even exist yet? Lower income countries sometimes deal with life-threatening diseases that aren't even on the public's radar here in the West. Dr. Peter Hotez is trying to tackle this very problem.

He's a pediatrician, professor of pediatrics, and Dean of the National School of Tropical Medicine at Baylor University.

Leishmaniasis is a disease that's, uh, abruptly arisen out of the conflict zones, uh, on the Arabian Peninsula and Syria and Iraq and the former occur in ISIS occupied areas in Yemen. And now it's become a huge problem in Venezuela with the economic downturns there. There's nobody else to develop that vaccine. So we're, so we're taking that on. It's a joint collaboration with the NIH, uh, and a uniform services university where we have a Chagas disease vaccine. And Chagas is, uh, one of the most common causes of heart disease among the poor and Latin America. Six to 7 million people affected. Again, nobody's taking this on. So we're partnering with several, uh, in-stitutions to develop a new therapeutic vaccine for Chagas disease, which we hope will go into the clinic soon. And then we have two parasitic worm vaccines including a vaccine for schisto-somiasis. And we just completed the phase one clinical trial of that. And that's very exciting. And we're looking at conducting larger studies now in Africa as well as Brazil, where the disease en-demic as well as for hookworm infection.

Vaccine development, especially for neglected tropical diseases, could benefit from the same partnership approach used by GAVI. There is historical precedent for this, something Dr. Hotez calls 'vaccine diplomacy.'

Another aspect of what we're looking at is, is how we can partner with countries to develop some of these neglected disease vaccines. So for instance, not many people realize that when Albert Sabin developed the oral polio vaccine, he didn't do it by himself. He had taken his oral polio strains and got permission through back channels from our state department to work with Soviet scientists in the USSR at the height of the cold war to actually make those strains into an actual vaccine. When they were tested on more than 10 million Soviet school children, the vaccine was shown to be safe and effective. And so it led to the licensure of the oral polio vaccine, so two countries putting aside their ideologies for purposes of making a lifesaving technology. And this is something that we're starting to think about for our neglected disease vaccines, not just what we make but how we make them.

And I've labeled this vaccine diplomacy because I think this is go-ing to be an important new frontier in vaccine development.

So clearly collaboration is critical to the global impact of vaccines – whether it be for a new vac-cine in development or for improving access to ones which already exist. The full potential of vaccines, however, cannot be realized without confidence in how and why they matter so much.

Anna Mouser, from The Wellcome Trust, describes a recent study called the Global Monitor, which maps out what global confidence in science and vaccines actually looks like. They did this through a survey of over 140,000 people in more than 140 countries.

So Wellcome carried out a really big piece of research earlier this year called The Wellcome Global Monitor. It gave us a really valuable insight into societal attitudes, not just to vaccines, but also to science in the broad sense. And what we've seen from that is there is a really strong sense globally of the importance of vaccines. And we were very encouraged by that. So 92% of people agree that it's important for children to have vaccines. 92% say that they have had their children vaccinated and this rises in some of the world's poorest countries. So in Ethiopia for in-stance, its actually 100% of people who believe they're important and have had their children vaccinated. I think it's fair to say that attitudes vary more around the perceptions of the safety and effectiveness of vaccines. And for me, it's not unlike the gap that we see between where the scientific consensus on climate changes and where public perceptions of the issue are.

The Global Monitor found that more than three-quarters of the world's population agree that vaccines are safe and effective. But that confidence does dip in certain parts of the world.

So overall, globally, around 84% of people agree that vaccines are effective, but this can fall much lower. For instance, in parts of the world such as Eastern Europe and in France, I'm a country that's benefited from vaccines for many, many years. Around nearly 20% of people dis-agree that vaccines are effective.…and confidence in Western Europe falls as low as 59%.

Vaccines are a part of a much larger mission to improve global health. On their own, they pre-vent between two to three million deaths per year. Ideally, they go hand in hand with other ser-vices and programs you need to provide comprehensive care across the lifespan.

But we are at risk of seeing a reversal of some of the progress that's been achieved. In 2019, the WHO identified vaccine hesitancy as one of the ten biggest threats to global health. The 30% increase in measles cases, globally, indicates we cannot ignore the risk.

So I haven't myself seen it on any of my trips, but we all know the internet knows no boundaries. And so any place where there's the internet, people are going to have access to, um, all kinds of

information. And a lot of it can be false information. So we know that there are places, I know there have been concerns, uh, particularly in Nigeria and some other countries that maybe have, um, a wealthier percentage of the population that's more affluent and more regularly accessing the internet and really looking to the US when they hear that in the US there are these conspira-cies and that there are people choosing not to vaccinate their children. That absolutely has an affect.

We've focused on the impact of vaccines on global health during this episode. But hopefully the word global hasn't led you think of some place far away or unrelated to you. Hopefully, it's high-lighted how interconnected we are.

You know, a disease anywhere is a threat everywhere. As we know we are living in an increas-ingly connected world and a disease can sometimes be just an airplane ride away.

Next time, on The Antigen, we'll look closely at how people think about vaccines. We'll talk about vaccine hesitancy and anti-vaccination sentiments.

The whole controversy about the safety of vaccines and their benefits is really an old story. And, it kind of helps me remember that, that this is not a new problem. It's a persistent problem.

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