The Antigen Season 3
Episode 3: Script
FINAL

COLD OPEN:

DR. BILL GRUBER:

I was due to come on duty in a pediatric intensive care setting where it was in the middle of the RSV season. And there were anywhere between 40,000 to 120,000 children hospitalized each winter in the United States for RSV. So I was working in the ICU and I had, uh, six children simultaneously that were on ventilators. And this was at a time when there was a thought that a drug might be able to help these children that could be aerosolized, so passed in the air through their intratracheal tubes to try to protect them and get them off the ventilator sooner and allow them to recover.

And I had been helping individuals develop and try to figure out, you know, was this really going to work for babies or not? And I came into the intensive care unit and all six of these children were in danger of getting much worse and risking death because it turns out that the drug has delivered through the ventilator is very insoluble and it was causing the ventilator not to work properly. And this was not really known up to that point in terms of that being a major issue. And so I quickly had to make sure that we fixed that problem. And fortunately all those babies, you know, did better. But it came to me at the moment, you know, trying to treat babies for this disease is not the answer we need to protect and prevent the disease from happening in the first place.

KARI
This is The Antigen and I'm your host Kari Yacisin. I'm an infectious disease physician and a lead in U.S. Medical Affairs for pipeline vaccines at Pfizer.

In this special 3-part mini-series, we're diving into maternal immunization.

So far, we've covered how these vaccinations work, their impact, and the barriers and challenges of expanding maternal immunization.

In this final episode, we'll dig into how maternal vaccinations come to be and explore some exciting innovations and research.

[music cue]

KARI
Vaccines ideally provide protection so that otherwise vulnerable infants are shielded against dangerous diseases and help avoid the serious implications of any baby needing a ventilator. Dr. Bill Gruber, who you heard from at the top of the episode, has spent much of his career working towards that goal of developing vaccines to help prevent serious infectious diseases. So how are maternal immunizations developed? Well, they go through the same process as vaccines in general, with an added step of ensuring that they are safe for pregnant people. This process involves a lot of different people and different organizations.

DR. BILL GRUBER:
I guess it's shop worn when people talk about things, taking a village, but this really does take a village or an army, whatever metaphor that you want to use of diverse talent.

KARI
Bill is the Senior Vice President of Pfizer Clinical Research and Development, and is responsible for global clinical development of vaccines. He is a pediatrician and vaccinologist, an expert in vaccines. In fact, in 2021, he received the Pediatric Infectious Disease Society, Stanley A. Plotkin Lecture and Vaccinology Award, an award that recognizes an individual who has made significant contributions to vaccinology that have impacted the lives of children. I have worked with Bill and respect him and his work.

DR. BILL GRUBER:
You need the talent that basically identifies the importance of the pathogen. So people working on the front lines that identify, okay, there's something out here that requires we should work to try to prevent it's a cause of serious disease. Then the work that's done by academics and, and others in, uh, government and industry to identify, okay, so what's what should be the target? You know, how do we attack this particular pathogen? And what's important that would be its Achilles heel, that if we could find a way in the case of antibody to attack this particular part of the virus is likely to prevent it from causing disease. And then, you know, one goes from there to exploiting, whatever technology is developed that identifies the target to make a vaccine. And that often begins with academic work and then in partnership with government and industry, uh, that work is extended, not only to the science, but then how do we make it how do we study it to make sure that it is truly safe and can be effective?

KARI
Finding a potential vaccine to make is just the beginning. After identifying a target to make a vaccine, that potential vaccine then needs to undergo preclinical testing. This means testing the vaccine in the laboratory. This preclinical testing is done to assess the safety of that potential vaccine and assess if it triggers an immune response. The researchers might change that potential vaccine to make it work better, but once they're confident that the potential vaccine is expected to be tolerable and to work, they can then start clinical trials. That is study that potential vaccine in actual humans, starting with adults.

DR. BILL GRUBER:
And of course that's done first in small numbers of individuals and then in hundreds and ultimately thousands and tens of thousands. And then even after licensure, we study the vaccine in millions and tens of millions of individuals by monitoring what the, the safety of the vaccine in those populations.

KARI
This is where that extra-safety component comes into play. Pregnant people and fetuses can be particularly vulnerable to certain health conditions so maternal immunizations require another level of scrutiny.

DR. BILL GRUBER:

So we begin very judiciously with small numbers of individuals first, and non-pregnant individuals to assure ourselves about the safety profile and that the vaccine will produce the right sort of immune response.

KARI
If the vaccines are deemed safe, the process continues by introducing the vaccine to trial participants who are pregnant.

DR. BILL GRUBER:

And then we very carefully move into the pregnant woman, monitor them very closely during the conduct of the trial, both in terms of assuring safety, but also ensuring that we're getting the right sort of antibody and that that antibody is passing to the newborn. And even after the newborn is born, we follow that child for a number of months after the delivery to make sure that there are no long term effects that would suggest that the vaccine could not move forward and, and be approved and used.

KARI

There's a lot of careful, close monitoring in clinical trials. Vaccine research and development teams want to ensure that reactions to vaccines are minimal. Common reactions include injection site soreness, redness, and swelling. Some patients also have fever, chills, headache, fatigue, or muscles aches. Development teams are particularly careful given the fact the patients receiving these inoculations are pregnant.

DR. BILL GRUBER:

And we take all of that information together to decide is the risk versus the benefit of the vaccine favoring the potential benefit of this vaccine for protecting against disease. And then of course, it's not just our judgment or the investigators that conduct the trials, it's the judgment of regulatory bodies and recommending bodies to judge that safety independently to determine, yes, this is something that we think on balance really serves to benefit the newborn and oftentimes the mother as well.

KARI
Of course, this work could not be done without participants. They have a key role to play when it comes to clinical trials, and ultimately, developing safe and effective vaccines.

DR. BILL GRUBER:

They're the critical ingredient, these people are real heroes, right? They're the individuals that basically are involved in actually receiving a vaccine before it's absolutely known whether it's going to work. And the safety is assured. And, um, you know, particularly those individuals that are enrolled in the very earliest phases before the vaccine has ever been given to any human being, they're tremendous heroes. Then they can continue to be heroes in the community setting and for their own health.

KARI
This work takes a lot of time, brain power, and patience, so it's gratifying to see progress.

For decades, Dr. Gruber has been working on vaccine development for two pathogens that cause serious disease in infants: Group B streptococcus, or Group B strep for short, and respiratory syncytial virus, or RSV.

DR. BILL GRUBER:

Yeah. So these are two pathogens. I've been interested in my entire professional life, and I have the good fortune of having been trained by individuals that were experts in understanding each of those diseases. So let me start with group B strep.

KARI

Group B strep is the most common cause of life-threatening bacterial infection in newborns. According to the World Health Organization, Group B Strep causes around 150,000 preventable stillbirths and deaths each year.

DR. BILL GRUBER:

The bacteria is a normal colonizer within the vaginal tract of women, and about 25% of women are actually colonized routinely and have no particular problems typically themselves with the bacteria. But what happens is if the mother does not have sufficient antibody, that bacteria can pass to the infant when the child passes through the birth canal and is born, or can be picked up in the nursery setting and produces disease either in the first seven days, which we call early onset disease or disease beyond seven days, which we call late onset, but that can manifest again as serious bacterial infection, where bacteria in the bloodstream or meningitis or complications of bone or joint infection in the newborn.

KARI

Given how dangerous this disease can be for infants, there's a strong drive to develop a vaccine.

DR. BILL GRUBER:

There's been great interest for decades, in trying to identify a way to protect children and we and others have identified that the best way to do this is by immunizing the mother, giving those mothers that basically don't have that antibody to protect their babies, a boost in that antibody response that passes to the infant and protects them.

KARI

Vaccines to prevent Group B Strep are in development.

[music fades]

KARI

Dr. Gruber has also been working to target another prominent disease: respiratory syncytial virus, or RSV.

DR. BILL GRUBER:

So respiratory syncytial virus is a virus and you may wonder, gosh, that's a strange sounding name, respiratory syncytial virus. What in the world does that mean? This is really based on a feature of what one sees when this virus grows in tissue and you can examine this under the microscope. And syncytial is just sort of a fancy name for the ability of, of cells to essentially lose the integrity of their membranes, that join cell to cell and become giant cells. And this was described when the virus was first identified as a cause of disease in the 1950s, the virus had been causing disease for ever before that, but this was when people were first had the techniques to identify the virus as a specific cause.

KARI

You may be familiar with RSV, it's been in the news recently. The CDC has said there are more cases this time of year than are typical in many parts of the U.S. Most children get RSV sometime before the age of 2, but experts are speculating that more kids are getting the virus this year, and getting severe cases, because they were not exposed as they would've been because of the Covid-19 pandemic. This is most likely due to social distancing and mask wearing over the past two years. And infants are at highest risk of needing hospitalization during the first season they are exposed to the virus.

So what *is* RSV?

DR. BILL GRUBER:

The disease that's caused in young infants is one focused on the respiratory tract in which the virus typically first gains access to the upper airways, the nose and the trachea, but then descends down into the lower respiratory tract. And it has a predilection for wanting to attack the tiniest airways, called the bronchials, just before you get to the little air sacks of the lung or the alveolar line, and this causes damage to that epithelial lining and constriction or loss of the airway diameter. This is a real problem because you obviously need to be in a position where the airways are open so that you can adequately exchange air, but particularly if it affects the small airways, the amount of airway resistance that's associated with narrowing is something that works as a function of the fourth power, meaning that if you have a 50% reduction in airway size, you have about a 16-fold increase in airway resistance.

KARI

Why is this particularly dangerous for an infant? It's because of the way a baby's chest and lungs develop.

DR. BILL GRUBER:

Well, a baby and those of you that have had young babies will know this, that when the baby's first born, the chest is very compliant, meaning that there's not a lot of bony structure, much of it is cartilage and relatively soft. So when the baby has obstruction in the airway in terms of trying to breathe, and as it tries to expand the chest cavity, in fact, just the opposite happens when the air,

when the lungs cannot expand the chest actually collapses so that you actually can see something that we call sternal retractions, which just is a fancy term for saying that when you look at the breast bone that it collapses in. And that's when, you know, when a child has bronchiolitis that they're in severe trouble because it means they're not expanding their lungs.

They're not getting appropriately oxygenated. And this is the reason why respiratory syncytial virus has become such an important target for a vaccine. We know that when babies get in trouble in the United States, anywhere between 40 and 120,000 in an average year, about 58,000 of them are hospitalized in the United States each year and worldwide, particularly where there's lack of sophistication to support respiratory disease in children, unfortunately, a number of those children die. And so hence since the 1950s, when the virus was first discovered, there's been an intense effort to try to figure out how can we protect these babies and reduce the potential for them to be hospitalized or die due to this disease.

KARI
Multiple companies, including Pfizer, are working on vaccines to address RSV. News outlets like CBS, CNN, NBC, and the Wall Street Journal have reported that some RSV vaccine candidates are nearing review by the FDA.

RSV candidate vaccines, including those from maternal immunization, are going through the steps required to get from development, and if regulatory approved, to being licensed for use.

[music cue]

KARI
While progress in terms of vaccine development could have a significant impact, it’s also important to address inequities with existing vaccines and within the development process itself.

DR. BILL GRUBER:

It's become very apparent that there are certain populations throughout the world, certain races and ethnicities that are at greater risk of complications of infectious diseases. And so when we think about the nature of what we want to do in terms of developing a vaccine that's going to have the broadest possible impact, we think about those populations. And as an example, we know that for instance, populations in low- and middle-income countries, or some people refer to as developing countries throughout the world, that the incidence of group B strep and the impact is much worse in that population, that most of the burden in terms of deaths and hospitalization occurs in those settings. So, therefore, it's incumbent upon us to find out not only how can we study the vaccine in those populations, but how can we get it to them as quickly as possible, once we have a proven, safe and effective vaccine. So we purposefully design our trials to have the broadest sort of distribution of race, ethnicity, ages, particularly if we're dealing, you know, something beyond the newborn period to give us the broadest perspective on something that can be applicable to populations throughout the world. And we take a certain measure of pride that we focus on trying to get that level of diversity. And I think for us, you know, it's a key ingredient to be able to reassure populations that have otherwise felt disenfranchised or felt marginalized, that we're reaching out to them for these sorts of trials, so that they can actually be part of what we learn about the vaccine to make sure that people that look like them are likely to benefit from the vaccine once it's approved.

[music cue]

KARI
I hope you've seen how vaccines can help improve the lives and health of pregnant people and their babies. It's easy to get bogged down in the science and process, but these developments have outcomes that have a real impact on people's lives. Bill spoke to an example of how his work connects to real-life outcomes.

DR. BILL GRUBER:

Vaccines have been the single most important medical intervention for public health. And I've had the good fortune to see the success with other vaccines. I'll mention haemophilus influenza type B, which again is another, it's not a virus, even though it's part of its name influenza. It's a bacteria that used to be a major cause of severe illness in young babies often and young children, less than two years of age in particular and when I was in training, it was common, particularly since I trained in a major urban medical center to have several of these children in the hospital most, all the time that we were treating for this disease.

And of course those that, and particularly develop meningitis, had the potential that they might die, but also they had lifelong disability, if they survived in about a quarter of the time. And that could either be hearing loss or significant mental difficulties or physical difficulties in terms of their motor function, that disease no longer exists in the United States. And in much of the world today due to the development of that vaccine.

KARI

Advances have been made thanks to new technology. For instance, mRNA is just one example of innovation that is driving development to potentially protect against more infectious diseases.

DR. BILL GRUBER:

And there's a real opportunity now based on what we've learned with RSV and, and COVID 19 to have a jumpstart to quickly develop a vaccine that could provide protection. So that's very exciting. I think another thing that's very exciting is the potential for mRNA based vaccines.

[music transition]

KARI
But technological innovations are only one piece of the puzzle. We need the right collaboration between patients, healthcare providers, and researchers to move the science forward.

DR. BILL GRUBER:

The vaccine does no good if it doesn't get into individuals' arms or thighs in the case of young babies. And so that's where industry can really bring a great deal of its expertise to bear, to, you know, solve for those particular problems while solving for the safety and effectiveness of the vaccine. So it really is a partnership from start to finish. And I think all the stakeholders have a vested interest in this entire process in assuring the safety first and foremost, and that the vaccine will work.

[music cue]

KARI
As we outlined in the first part of this mini-series, the potential impact of maternal immunizations are massive. But as Dr. Gruber said, vaccines only work if they are actually received by patients. The barriers that keep that from happening can be sizeable. *And* they *can* be overcome. Just as stakeholders from academic institutions, private companies, NGOs, and governments can work to develop innovations, they can also work together to expand access and acceptance.

There is a lot to feel hopeful about when it comes to the future of maternal immunizations. There's still a lot of work to be done, but the results of that work are potentially life-changing outcomes.

DR. BILL GRUBER:

I'm pleased to have the opportunity to share with you the work that's done to develop a safe and effective vaccines. And in particular, this exciting new advance in the world of maternal immunization to protect against diseases like group B streptococcus and respiratory syncytial virus. And I hope that we'll be in the near future, able to share really good news and both of those areas about vaccines that can be approved and protect children throughout the world.

END CREDITS

KARI
And that wraps up this miniseries on maternal immunization! Thank you so much for listening. Please take a minute to rate, review and follow The Antigen on your favorite podcast app. It helps new listeners to find the show. Special thanks to the maternal immunization team at Pfizer and to the production team at Wonder Media Network.