The Antigen Season 3
Episode 1: Script
FINAL

[baby coughs]

KARI:
Halfway through 2012, five infants in the United Kingdom had died from pertussis - or whooping cough – that year. Whooping cough isn't just your common cold or tickle in the back of your throat. It can be an extremely contagious respiratory infection that is a particularly dangerous threat for infants. An occasional cough can turn into a consistent cough that can limit a baby's ability to breathe. And pertussis can lead to pneumonia, brain disease, or even death.

Infection rates were seven times higher than in the previous outbreak in 2008, so health officials in the United Kingdom raised alarm. By the end of the year, there were more than 9,000 confirmed cases pertussis and at least ten infants had died from the outbreak. Officials took action to diminish the likelihood of this happening again using a key tool: *vaccines*.

[music cue]

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 my role at Pfizer, I provide technical and scientific support from a physician's and public health perspective for some of the vaccine candidates under development, including some work in maternal immunizations.

In this special 3-part mini-series, we're diving into maternal immunization. As you may remember from season 1, we touched on how vaccines can help us lead healthier lives from the moment we're born. This time around we're diving deeper. We'll explore the history of maternal immunization, the importance of protecting pregnant people and their unborn children, the unique challenges that come with vaccinating pregnant people, and the new and exciting innovations coming down the pike.

The causes of the 2012 pertussis outbreak in the United Kingdom were unclear, but what was maybe even more important than the cause was the solution. Infants are not eligible to receive a pertussis vaccine until they are two months old, and at that point it could be too late, but there is a way to help protect newborns. The response to the 2012 outbreak in the United Kingdom is an example of that protection. The United Kingdom introduced a vaccination program for pregnant women. Immunization of mothers can help protect babies from pertussis. The program was successful. More than 70% of pregnant people got vaccinated against pertussis in the UK during that outbreak. That, in turn, protected newborn babies. In 2012, fourteen babies younger than three months of age died from pertussis. But between the years of 2013 and 2016, 18 babies younger than three months of age died of pertussis in the UK. And of those 18, 16 were born to mothers who had not been vaccinated against pertussis. In 2017, there were no deaths from pertussis among that age group.

Vaccination rates looked very different in the U.S., where less than 5% of pregnant people got vaccinated for pertussis during that same timeframe.

With *all* the stress of becoming a parent for the first time – the check-ups, the vitamins, deciding on which baby gear is best, and all the things to remember and learn – perhaps it isn't surprising that if there isn't an outbreak, a pregnant woman might not see the need to get vaccinated.

But the thing is, preventing an outbreak is just one reason why one should get vaccinated. Especially if one's pregnant. To understand why this is so important, let's start with the basics: what is maternal immunization?

> **BEATE:** So maternal immunization really is more or less defined as vaccines that are given to women in pregnancy.

KARI:
That's Professor Beate Kampmann. She's a pediatric infectious disease specialist and the Director of the Vaccine Centre at the London School of Hygiene and Tropical Medicine.

> **BEATE:** Every woman who's pregnant or every person who's pregnant gives protection to the fetus and the newborn baby through transplacental antibody. And that happens in a natural process. And all we're doing is by enhancing that protection and make it more specific by giving vaccines against specific illnesses that can either make the mother or the newborn baby very ill.

KARI:
Professor Kampmann got into this field after seeing firsthand how infectious diseases affect children.

> **BEATE:** I started work as a clinical doctor in pediatrics and I spent so many nights looking after babies with severe infections, be they born prematurely or, you know, the majority of children in hospital is under five years of age and a lot of them have infectious diseases. And I was always passionate about trying to understand why babies get infected and what's going on with their immune system, that they can fight off infections some better than others. And the younger, the baby is the more tricky it is, of course.

KARI:

She said she's motivated by the fact that some of these infections are preventable.

> **BEATE:** We know that vaccines have made an enormous contribution to lowering the mortality and morbidity in children under the age of five. And that is largely due to vaccinations that we've introduced through the expanded program of immunization. So, you know, to understand why this might be not so effective in young babies or what we could do more to make them more protect against infections, to which they're particularly susceptible has been a passion of mine, for a long time.

KARI:
According to the WHO, in 2020, 47% of all under-5 deaths occurred in the newborn period, that is the first 28 days of life. That's up from 40% in 1990. By vaccinating pregnant individuals, we are providing protection against certain potentially harmful diseases in those first 28 days of the baby's life.

> **BEATE:** I think because we can't really give the vaccines against all of these infections to the babies, because it'll take quite a while for them to generate the immunity that we need for protection. If we give them to the mother, we are literally harnessing a gift of nature to an added advantage.

KARI:
So what do we mean by gift of nature?

> **BEATE:** In every pregnancy, during the pregnancy, especially the later parts of the pregnancy antibody from the mother that she has acquired through exposure in her own history transfers through the umbilical cord and the placenta to the baby. And this is physiologically occurring phenomenon that protects the baby for the first few months in life against all sorts of, you know, changes and infections. And it's really like a shield that has been put around the baby before the baby's immune system has adapted from the way it was in utero, where everything was really protected to the sometimes hostile environment in which the baby finds itself like, you know, being colonized with lots of microbes in the gut, on the skin, et cetera. And by having the antibody of the mom, these obnoxious things can't do any harm to the baby.

KARI:
Pregnancy results in changes in hormones and in the immune system that can cause pregnant people to be more susceptible to certain illnesses – like influenza. If pregnant people get certain infectious diseases, they are also susceptible to getting sicker than those who are not pregnant.

So it's important for pregnant individuals to be vaccinated for their own health. It's also long been known that vaccines for the pregnant person can also protect the newborn.

In 1846, there was a measles outbreak in the Faroe Islands, and they observed that infants born to moms who survived measles during pregnancy seemed to be protected against measles. In 1879, people were immunizing pregnant women with vaccinia, the smallpox vaccine, and observed infants were protected from smallpox. So our understanding of maternal immunization and the protection it can provide to infants started way back in the 1800s.

But it wasn't until 1960 that the United States recommended routine immunization of pregnant women with the influenza vaccine. And in 1961, scientists began giving tetanus toxoid vaccines to pregnant women – and these were shown to be effective in preventing neonatal tetanus – that is tetanus infections that occur within the first 28 days of life.

> **BEATE:** In 1988, the WHO estimated that there were 787,000 newborns who died of neonatal tetanus. And it was observed that women who had been immunized against tetanus sometime in their lives or during the pregnancy didn't have this issue. So the WHO instituted a program of protection by giving tetanus boosters in pregnancy. And now we are having figures of much improved neonatal tetanus cases. We're only down to 25,000 newborns. It's still too many because it is probably entirely preventable, but even between 2000 and 2018, when we have the latest figures, there's been an 88% reduction from the situation before.
>
> And that is really due to the maternal tetanus program. And I think that's one of the main triumphs, but also other infections like flu or pertussis have been shown to be preventable. And those efforts have been primarily been made in the last 20 years or so. So the history of maternal immunization isn't new, it's just there has been added momentum.

KARI:

The introduction of the neonatal tetanus vaccine has significantly decreased infection rates. Vaccines have nearly eradicated some illnesses, like smallpox and polio.

So if we can help prevent certain dangerous infections, what is stopping us from lowering child mortality and morbidity rates from infections even more? In season one of this show, we talked about how a vaccine works. To recap, vaccines introduce the body to a piece of a germ or bacteria so that the body can practice fighting against it. It's like a dress rehearsal.

[music cue]

The body gets all prepared with full hair and makeup and costume and puts on a performance just as if it were the real deal. So when opening night comes around and the body experiences the bacteria or virus in its entirety, the immune system knows exactly how to respond.

There are many different types of vaccines and all of them work a little differently. So I turned to Professor Kampmann for an explanation about those differences and which vaccines are best for pregnant people. The most important factor here is safety for both the pregnant person and the fetus.

> **BEATE:** So the main types of vaccines that we're using for maternal immunization are inactivated vaccines and subunit vaccines apart from the COVID vaccines, which are the mRNA vaccines, this is a relatively new technology where we have less precedent, but we now have millions of dataset that show that they're also safe for use in pregnancy. So for tetanus it's a toxoid for flu, it's an inactivated or subunit vaccine. There are conjugated vaccines as well, being used for using pregnancy, for example, meningococcal vaccine in epidemic outbreak situations. These are all vaccines with a very established safety record for the products. And they're not vaccines that were in any way carry a risk of having pathogen go across the placenta.

KARI:

Let's go over a few definitions. Many of you may already be familiar with an mRNA vaccine because of COVID-19. These mRNA vaccines use a molecule created in a lab to teach our cells how to make a protein that triggers an immune response inside our bodies.

An attenuated vaccine is a live vaccine that uses a weakened form of the germ. It cannot cause the disease but it can elicit an immune response. An example of a live, attenuated vaccine is measles, mumps, and rubella, or varicella – the chickenpox vaccine.

Then there are non-live vaccines – these are made by inactivating or killing the virus or bacteria like the inactivated polio vaccine.

A subunit vaccine takes a specific piece of the germ, like a protein, and only contains that specific antigen. The immune response is targeted to that certain part of the germ. We see this in the pertussis vaccine in DTaP.

Another example is conjugate vaccines – these use the sugar-like substances called polysaccharides on some bacteria, and attach a molecule – or conjugate – to the polysaccharide. The attachment of a conjugate to the polysaccharide in a vaccine can help some immune systems respond to the vaccine.

A toxoid vaccine uses weakened toxins from bacteria. The weakened toxins cannot cause illness but they can cause the immune system to respond. Diphtheria and tetanus toxoids contained in the DTaP vaccine would fall under this category

There's a lot that goes into protecting the human body, especially a pregnant body. Amazingly, a pregnant woman can transfer her protective antibodies to the fetus in utero.

> **BEATE:** Immunoglobulin and the specific type of immunoglobulin called IgG it's a subgroup gets transferred through the placenta to the baby's immune system. And this works by the maternal immunoglobulin being endocytose within, you know, a particular compartment of the placenta, which is called the, syncytiotrophoblasts. And this immunoglobulin IgG is bound to the FC receptor within this endosome. And then when it's exposed to the fetal site it's released, and then it passes into the fetal capillary system. And with that, it passes into the blood system of the baby.

KARI
For those of us who aren't maternal immunization experts, what Professor Kampmann is essentially saying is that antibodies move from the mother to the child through the placenta. Those antibodies then remain circulating in the infant through the first few months of life, protecting them until they are eligible for vaccines themselves. The protection is especially important for infections that can strike very early in life.

So what's the timing around all this – when should pregnant people get vaccinated in order to most likely transfer antibodies to the child before birth?

> **BEATE:**
> There would always be a tendency to want to vaccinate women or persons doing pregnancy at a time when maybe the first trimester is over, because that's a time when there are by nature, more, you know, complications with pregnancy. There's a lot of early pregnancy loss that occurs naturally. So the tendency would be to give any vaccines in pregnancy at the second or third trimester, and we need to think about when is the peak of the antibody, if the aim of the vaccination is to actually primarily protect the infant. So for example, with a vaccine like group B strep, where we are looking towards preventing group B strep infection in the newborn, one would want to have the maximum of antibody going across the placenta and being available to the newborn whilst if we are protecting a mom against COVID herself, then any antibody at any state of the pregnancy would be a very good idea.

KARI:
It's amazing that we have such an available tool to help protect infants against certain serious illnesses. Following the example of the UK's vaccination program, the U.S. has been catching up. In the U.S. the Tdap vaccination coverage for pregnant women in 2017 was 50%.

This all sounds pretty simple, right? Get a few vaccinations and protect oneself and the baby. But of course it isn't that simple and while vaccination rates are on the rise, pushing for widespread maternal vaccination faces challenges, too.

> **BEATE:** I think the access to the vaccines has been quite a barrier sometimes to implementing what is otherwise a very successful intervention. It's absolutely clear that there's still quite a lot of challenges to implementation of maternal immunization, especially for healthcare workers and

researchers. So in the research side, we need to pay absolute attention to making sure that the short term gain remains a long term gain for the newborn babies as well. We have to pay due diligence and make sure we follow up in the longer term and look at the immune system in some more detail. And for healthcare workers, there is an a situation where really trust has to be built, that they can also comfortably communicate about the benefit of the vaccines for pregnant people. That means they have to have access to the data that are generated to show that benefit in a way that they can use them as good, easy communication tools.

But also there is an element of trust that has to be built in the system and we can all help to increase that trust around vaccination in general, which also might be picked up by pregnant women who's prime interest it is to protect their unborn babies. But we are in the same boat here. We also want to protect born and unborn babies.

KARI:
So safe to say there's a lot more that goes into a successful implementation of maternal immunization. Next time, we'll be digging deeper into those challenges and considerations.

DR. MALIK: There are system level barriers, individual provider barriers, and patient attitudes like vaccine hesitancy. All of these are relevant for pregnant patients as well. We've seen this here and overseas as well.

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See you next time!