Effect of PCV on Pneumococcal Meningitis

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hi everyone, I'm Sarah Gregory, and today I'm talking with Dr. Shamez Ladhani, who is calling in from London. He's a pediatric infectious diseases specialist and the clinical lead for vaccine-preventable diseases at Public Health England. We'll be discussing his article about the introduction of pneumococcal vaccines in the UK. Welcome, Dr. Ladhani.

[Shamez Ladhani] Hi, Sarah.

[Sarah Gregory] So, let's start with some basics here. What is invasive pneumococcal disease? Is it what people call "pneumonia?"

[Shamez Ladhani] Sarah, pneumococcal disease is a term that's used to describe infections caused by this particular bacterium called *Streptococcus pneumoniae*, or the pneumococcus. And the reason it's called pneumococcus is because…identified as the cause of pneumonia more than a hundred years ago. But we know that this organism actually causes a whole range of infections across the life course. So, it is commonly carried in the nose and the throat of young children, and doesn't really cause much of an infection in the majority of them. Occasionally, however, they do get local infections of the ear and the throat, but these are usually self-limiting and get cured with oral antibiotics. The pneumococcal disease that we worry about most is actually the more invasive infection, which is pneumonia and septicemia, and the worst of them of all is pneumococcal meningitis, which is associated with a lot of morbidity and mortality across the world.

[Sarah Gregory] So, this is the same thing as pneumococcal meningitis, right?

[Shamez Ladhani] Yes. So, meningitis is an infection of the lining of the brain. And meningitis can be caused by a whole range of bacteria and viruses. And pneumococcus is one of the most important causes of bacterial meningitis, and it is one of the nastiest causes of bacterial meningitis because it's associated with a very high case fatality rate. On top of that, up to a third of those who develop pneumococcal meningitis and survive the infection end up with very serious long-term complications, ranging from deafness to blindness to epilepsy and developmental delay.

[Sarah Gregory] There are other causes of meningitis though, too, right?

[Shamez Ladhani] Yes, so, the term meningitis literally means an inflammation of the lining of the brain and there's a whole range of causes. It can be infectious or noninfectious, and of the infectious causes, it tends to be bacteria or viruses. And the distinction is that viral meningitis usually is self-limiting and doesn't cause any long-term problems, but bacterial meningitis, while rare, is associated with a lot of morbidity and mortality.

[Sarah Gregory] Your article notes that there are different pneumococcal serotypes. So, tell us what a serotype is.

[Shamez Ladhani] So, the pneumococcus is, is very, very common in carriage in young children. And they're not all the same. They all differ in terms of the genetics of the bacteria and also the outer sugar coating of this bacteria, because it is this outer sugar coating that gives them very characteristic features. And different sugar coatings are known as serotypes. So, different

serotypes have got different sugar coatings, and they behave like different strains of the bacteria. But the pneumococcus is one of those that has almost a hundred different serotypes. And that's important because the vaccines that we have at the moment only target some of the serotypes and not all the serotypes. So, even the best vaccines that we have against pneumococcal disease will only protect against a proportion of the pneumococcal bacteria that are carried by children and other age groups.

[Sarah Gregory] Okay, are the same serotypes then found everywhere, or do they kind of cluster in one place?

[Shamez Ladhani] No, so, different regions of the world have different distributions of these serotypes. What we do know is that some serotypes are much more invasive and severe, and others are not so much. Some serotypes cause particular infections such as meningitis or septicemia or pneumonia and then there are other serotypes that just sit at the back of the throat and are not very good at causing invasive disease. So, each serotype behaves very differently. And different countries have different distributions of their…of these serotypes. But the more invasive and severe serotypes tend to be found across most parts of the world. So, the vaccines that have been developed have targeted those major serotypes, which are essentially found in the majority of countries across the world.

[Sarah Gregory] Okay, so, speaking of vaccines, could you briefly remind us how vaccines actually work?

[Shamez Ladhani] The pneumococcal vaccines have been around for more than three decades. The original vaccines literally took the sugar capsule of these bacteria and injected it into people, and they would develop antibodies against the sugar capsule. And that vaccine worked and protected adults against pneumonia and invasive disease due to the serotypes in that vaccine.

But polysaccharide vaccines, or sugar-coated vaccines, or sugar-based vaccines do not work in young children because their immune system doesn't recognize the sugar capsule. So, it was really very innovative when conjugate vaccines were developed, where they took the sugar capsule and connected it to a protein, and any protein would do, and then the immune system of young babies could actually see both the sugar and the protein, and that's the basis of the conjugate vaccines which has completely revolutionized the way we prevent invasive bacterial infections in children and adults. And what is very unique about these conjugate vaccines is that, not only do they protect the children against disease, but it stops them carrying the bacteria. And so, then they do not transmit it to other children and adults. So, what ends up as a childhood vaccine ends up providing population protection. So, eighty percent of the reduction in pneumococcal disease that we see with these conjugate vaccines comes from prevention in *adults* who have the biggest burden of disease, because the children are just not transmitting these strains to the adults.

[Sarah Gregory] Okay, so, the U.K. began using the PCV7 vaccine in 2006. Really, what effect did it have on…on new meningitis cases?

[Shamez Ladhani] So, the UK was quite unique in that it was almost six years behind the U.S. in introducing the 7-valent vaccine. The U.S. introduced PCV7 in 2000, and the U.K. only began vaccinating children in 2006, and by then we had very good information about how effective this vaccine...And essentially within four years, we virtually eliminated those seven major serotypes

that the vaccine protects against, not only in disease, but also in carriage. So, the unique thing about this vaccine, as I said, is that it directly protects children against all pneumococcal disease by these seven serotypes, but because these children also don't *carry* these serotypes, all the children and adults were also protected. So, 80 percent of the benefits of the vaccination program were seen in the adults who did not get disease due to this particularly nasty serotype.

[Sarah Gregory] Okay, but then the U.K. started using a different one in—a different vaccine—called PCV13 in 2010. And you made this change because…?

[Shamez Ladhani] So, one of the things that became very clear with these vaccines is that we do know that children under two years of age, up to half of them carry the pneumococcus at the back of their nose and throat. When you vaccinate them with a conjugate vaccine, such as PCV7, the elimination of carriage of those seven serotypes is immediately replaced by new serotypes. So, up—even now, 50 percent of children will continue to carry the pneumococcus, but the serotypes will be different, because they no longer carry the pneumococcal vaccine serotypes, they carry new serotypes.

So, by 2010 what we had seen is complete replacement of this pneumococci in carriage in the children with new serotypes that hadn't been around before. And these new serotypes were causing even more disease in children and in adults, and what we found is that actually, unlike all other forms of pneumococcal disease, these new serotypes had a particular predilection for meningitis, and so, when we looked at the overall impact of the PCV7, by 2010, all the meningitis cases that were reduced because of the vaccine serotypes had been replaced by new serotypes that weren't covered by the vaccine. So, when a new vaccine was licensed in 2010 that provided protection against six new serotypes in addition to the seven, we immediately shifted to the new vaccine to provide added protection to the children.

[Sarah Gregory] So, people that were vaccinated with the 2006 one or…like in the 90s, I don't know, vaccinated with something else? Yeah, should they go back and get…should they now go back and get this PCV13 one, even though they're adults now?

[Shamez Ladhani] So, the advantage of the conjugate vaccine is that it provides population protection. So, if you have a country that has a very good childhood immunization program, such as the U.K. or the United States, giving PCV13 to the children will mean that they will no longer carry those serotypes in the vaccine, and therefore they will not transmit it to the adults, or the older adults. They are automatically protected by the childhood immunization program.

[Sarah Gregory] Herd immunity?

[Shamez Ladhani] Exactly.

[Sarah Gregory] Okay. So, did this change produce any unexpected, or even expected, effects?

[Shamez Ladhani] So, what was quite unusual in what we found is that the vaccine seemed to have a very differential effect depending on the clinical disease that we were seeing. So, we've always reported very good reductions in vaccine-type pneumococcal disease with both vaccines. We also noted huge reductions in children more than adults, because they are directly benefiting from the program. What was unexpected when we did the formal analysis is that the replacement in meningitis happened very quickly with PCV7, and that tells us that the replacing serotypes that came in after PCV7 was established actually were particularly (??)cause meningitis more

than other presentation. So, we saw very little reduction in meningitis incidence with the PCV7. But when PCV13 came in, what we found is that we had an almost 50 percent reduction in pneumococcal meningitis cases across the population. And that's because the vaccine was targeting those very serotypes that were causing a large burden of meningitis after PCV7 came in, and the new serotypes that are replacing PCV13 actually do not seem to be able to cause as much meningitis.

[Sarah Gregory] Okay.

[Shamez Ladhani] So, that was unexpected, because we weren't expecting different effects on different…on the different clinical presentation.

[Sarah Gregory] Okay, so…there's a pneumococcal vaccine for older adults, that, starting at 65 or people that have respiratory problems, like asthma or CPOD…is this…this PCV13, is that one of those?

[Shamez Ladhani] So, what was very unusual at the time is that when PCV13 was licensed, the United States was one of the only countries that recommended giving PCV13 to adults at 65 and over, while other countries refrained from making that recommendation, on the basis of the childhood (??)…on the basis that the childhood immunization program would provide herd immunity over the course of one or two years that would protect all the adults and the older adults. So, we did not recommend Prevnar 13 for our older adults. What we do use in the older adults is a vaccine called the 23-valent polysaccharide vaccine, or PPV23 vaccine. This is a vaccine that just contains the sugar capsule, it doesn't work in children, but it does work in adults, and it helps protect against 23 different serotypes. It's not as effective as the conjugate vaccine, but because we hardly have any PCV13 serotypes, most of the diseases that we see in adults are actually covered by this polysaccharide vaccine.

[Sarah Gregory] Ahh, that's very interesting, cause yes, I know the recommendations here in the States is to have them both now.

[Shamez Ladhani] So, it was, until recently, and my understanding is that has now changed, and the PCV13 is no longer recommended because there isn't much of PCV13…

[Sarah Gregory] Oh!

[Shamez Ladhani] …disease in the U.S. and they are moving to only the polysaccharide vaccine.

[Sarah Gregory] Ahh, that's very new then.

[Shamez Ladhani] That's very new, yes. I think it was last month.

[Sarah Gregory] Oh, *really* very new, yes. Okay, most interesting. Well, I have asthma, so having nothing to do with age, I've had both. So, I guess I'm somewhat covered, eh?

[Shamez Ladhani] Yes, so, I mean, and the big thing is really, you know we do understand how important children are in transmitting this infection to others, and their…to their parents, and their grandparents, especially. And, by protecting children, the benefit that we get across a population is absolutely huge.

[Sarah Gregory] Yes, I can see how that would be. Okay, well, let's leap into your study now, tell us about your study.

[Shamez Ladhani] I am the clinical lead for the surveillance of a number of vaccine-preventable diseases in England, and our job is to make sure that the vaccine program is running smoothly, and that we have enough information to make sure that the program is safe and it's effective, and it's doing what it's supposed to do as we have predicted before bringing the vaccine in. So, I have been working on the pneumococcal vaccine for the last 10 years or so, and I have been involved with this program since PCV13 replaced PCV7 in 2010.

And what we do is we have a national surveillance, where every hospital in England reports invasive infection, such as pneumococcal disease, to Public Health England, and they submit their isolates to us so that we know what serotype is causing the disease. So, we are in a very fortunate position in that we can actually undertake surveillance across the whole country, that's a population of nearly 50 million people, and we get almost 6,000 invasive disease notifications every year, so it's a big number and it's a lot of work. But it is so important to be able to maintain what is essentially a very expensive national immunization program.

And we have been reporting every few years on the impact of PCV7 and PCV13 and how the disease rates have changed over time. What is unique about this one is that we were able to report on the changes that we saw with pneumococcal meningitis. And we're particularly interested in meningitis because it's only responsible for five percent of all invasive pneumococcal disease. It's a small proportion of the invasive disease cases that we monitor, but because it is so severe, with a case fatality of…of nearly 17½ percent, it comes with a lot of burden to the community and…and to society. And we know that up to a third of those who survive the pneumococcal meningitis end up having serious long-term complications. We also know that half of all the pneumococcal meningitis cases occur in children under five years of age, so you can see that these children are going to suffer from the complications for a very long time, once they recover.

So, we wanted to make sure that the vaccine was protecting the population against meningitis as much as it was protecting against other forms of disease. And it's quite unique because not many countries are able to undertake such studies because of the small numbers of cases. And, therefore, looking at trends over time can be difficult if you don't have a consistent surveillance program with very high case ascertainment.

[Sarah Gregory] Do you have any findings that we haven't covered yet from your study?

[Shamez Ladhani] So, the findings that I think are very exciting is that children have definitely benefited from the program in terms of all forms of pneumococcal disease, and rates of disease in children remain much, much lower than before the program. So, this vaccine has done amazing; we have over the last 10 years prevented more than 40,000 cases of pneumococcal disease. So it has done its job. What we find difficult to reconcile at the moment is that we've seen a lot of replacement disease in the adults and the older adults at the moment. And the benefits of the program in terms of reducing vaccine-type disease are basically being eroded by disease caused by these new serotypes that have emerged that previously would not have caused a lot of infection.

[Sarah Gregory] Mmm.

[Shamez Ladhani] And the good news about the study that we've done is that these new serotypes do not seem to be causing a lot of meningitis. So, meningitis is benefiting disproportionately, compared to the other forms, which is actually a good thing.

[Sarah Gregory] Dr. Ladhani, how is your study different than other research done on this topic? I think you said yours was more extensive.

[Shamez Ladhani] So, the uniqueness about this study is literally the number of cases, because we have a surveillance program for 50 million. No other country has such a surveillance program to monitor vaccination across a population. Within the United States, which is probably as similar to the U.K., they have regions across the U.S. where they collect information from and, apart from these two countries, there are not many other countries that have such a large population to monitor, and that gives us the advantage of being able to detect small trends very quickly and be able to modify our immunization program to get the most benefits with the current vaccines.

[Sarah Gregory] I already asked you this, but let's go back to…were there any other unexpected findings or effects that you discovered in your study, or doing your study?

[Shamez Ladhani] So, I think one of the most interesting parts of the surveillance is really how unpredictable pneumococcal disease can be, as with any other infectious diseases, they are stochastic and they vary across different parts of the world. And I think what is very unique, when we were doing our analysis, is how different countries have seen such different effects of the same vaccines, for a whole range of reasons.

For example, we have reported very high levels of replacement disease compared to the other countries, and we don't understand why we see more replacement than other countries. What was unique is that different countries have benefited differently from the same vaccination program. This is probably due to a whole range of things, ranging from, for example, the serotypes that were causing disease at the time of vaccination, the serotypes that the children were carrying at the time of vaccination, the exposure to the new serotypes. So, for example, the…the lack of an effect of PCV7 that we saw in the U.K. is not replicated in other countries. In the U.S., for example, there were large reductions in pneumococcal meningitis that were associated with PCV7 and similarly large reductions were seen after PCV13 replaced PCV7. But countries such as Israel and the U.K. have seen that the benefits of PCV7 were rapidly eroded because of replacement disease. Other countries, such as France, saw a rebound in pneumococcal meningitis because of the emergence of new serotypes after PCV7. What is reassuring is that PCV13 seems to be better at controlling pneumococcal meningitis than PCV7 was.

But we still have a big burden of pneumococcal disease, even though it is lower than before. And what we really do need is a universal vaccine against pneumococcal disease that doesn't rely on these serotypes and can just prevent all pneumococcal infections, because that is the only way we will be able to control this disease.

[Sarah Gregory] Okay, so, is that in the works anywhere, or is that just a goal or an idea at this point?

[Shamez Ladhani] It is something that has been in the pipeline for many decades. The pneumococcus is one of the most versatile organisms, which is why it has survived for so long, despite the advent of antibiotics and so many vaccines. There just doesn't seem to be a way of

developing a universal vaccine against pneumococcus. And at the moment all we have is new vaccines in the pipeline that cover more serotypes.

[Sarah Gregory] Ahh.

[Shamez Ladhani] But the idea is that, if you remove the most invasive and aggressive serotypes, then the remaining serotypes really do not have that same level of invasiveness, and you will get less severe disease and you are less likely to have long-term morbidity and mortality. And we do see that; these new serotypes are less fatal, and also they cause less meningitis. And the other thing that we have noted is that these new serotypes are more likely to affect those with underlying serious comorbidities. So, healthy people are less likely to get pneumococcal disease at the moment. So, we are definitely heading in the right direction, and even with replacement disease, the burden of disease is not as great as it was before, in terms of the disease severity. But it is around. And it's going to be around for quite a while, because there isn't any vaccine in the pipeline that looks promising against all pneumococcal infection.

[Sarah Gregory] You've…you mentioned age and said that most people that get this are small children. So, is that the biggest effect on the incidence in the U.K., age?

[Shamez Ladhani] Yes. So, for meningitis to occur, the bacteria have to get into the bloodstream, and then they have to cross the very protected blood-brain barrier to enter what is quite a sacred place in terms of the area, the fluid surrounding the brain. And infants have a very immature membrane compared to the adults and therefore are more prone to meningitis. As they get older, the risk of meningitis becomes less and less. So, if you can prevent pneumococcal infection in the first five years of life, then you are disproportionately going to benefit meningitis because these children are less likely to develop meningitis.

[Sarah Gregory] Let me ask you one more time. Were there any other findings that surprised you?

[Shamez Ladhani] One of the other things that surprised me, actually, is that the case fatality rate has not changed. So, we have seen a reduction in disease because of the PCV13, we have seen that the serotypes causing pneumococcal meningitis are now virtually all non-PCV serotypes. So, they are all the new emerging serotypes. But the case fatality, the chances of dying from pneumococcal meningitis, has not gone down, even though the risk of developing the meningitis is lower.

[Sarah Gregory] Ahhh.

[Shamez Ladhani] And what that tells us is that, actually, once you develop the meningitis, then it doesn't seem to matter which serotype caused the meningitis. Your outcome is decided by your response to that infection. And that is a real shame. Because it means that those who get meningitis are still going to come out worse from it, even if the serotypes are different.

[Sarah Gregory] That's, yeah, that's not good, that's not good.

[Shamez Ladhani] So, what we're learning with meningitis is that much of the damage that occurs within the brain and the surrounding area is due to the inflammation and the immune system attacking the bacteria rather than the bacteria themselves. So, actually the serotype or the bug itself is less important, but the way the host tries and destroys the bacteria is very important in determining the long-term outcome.

[Sarah Gregory] In the big picture, how will this research be important to public health?

[Shamez Ladhani] So, one of the things that is important is providing clinicians with (??) information. So, it is important to be able to tell parents about the effectiveness of this vaccine and how it prevents meningitis. For pediatricians, it's important to inform parents of the outcomes of pneumococcal meningitis. For policymakers, pneumococcal meningitis is one of the most expensive diseases, in terms of healthcare costs and it's important to know what contribution meningitis lends to the total burden of disease. And for the vaccine manufacturers, I think it's important for them to know which of these new emerging serotypes are more likely to cause meningitis. And while the numbers of cases might be very low, it is important to consider these serotypes in new vaccines because preventing meningitis has a preferential benefit compared to pneumonia, for example, which is less likely to be fatal.

[Sarah Gregory] Okay, then everyone should get their vaccines, right? These…these pneumococcal vaccines, the PCV ones?

[Shamez Ladhani] The immunization strategy in the U.S. is very different to other countries where there's a nationally-covered program. So, in the U.S., individual protection plays a much bigger role, in which individuals essentially pay for the vaccines that they receive. And when you have individual protection, then every person who gets vaccinated will be protected. In a national immunization program, the priorities are to use the healthcare resources as efficiently as one can to reduce the burden of disease, in terms of healthcare costs. So, in the U.K., for example, because of the large herd immunity effect of the pneumococcal vaccine, it is unlikely that the U.K. would recommend an adult pneumococcal conjugate immunization program because the majority of the infections would be protected through a childhood immunization program, where there is a high vaccine uptake. So, in the U.K. we are very focused on ensuring that 95 percent of all our children, at least, receive their primary immunizations for that reason of maintaining herd immunity.

[Sarah Gregory] What are some of the potential next steps for you, and for policymakers?

[Shamez Ladhani] So, the U.K. is going through a very exciting phase in the pneumococcal immunization program at the moment because it has recently been decided that we will be moving to a 1+1 pneumococcal immunization schedule for children. So, just to give you a bit of background, Sarah, the pneumococcal conjugate vaccines PCV7 and PCV13 were both licensed as a 3+1 schedule, which means you give three doses of the vaccine to infants and then a booster in the second year of life. The U.K. was very unique in 2006, in that it only recommended two infant doses with a booster in the second year of life after doing clinical trials that showed that two doses provided adequate protection to infants until they received their booster. And that was quite a unique move, and in fact, as a result of the U.K. surveillance program, we were able to show that the 2+1 schedule was very, very effective and nearly all countries around the world have moved to a 2+1 schedule with the pneumococcal conjugate vaccines. In the U.S., it is still 3+1, but I think that's one of the very few countries that have maintained that schedule.

What has changed is that, in the last couple of years, we have shown that a 1+1 schedule may be sufficient to sustain the U.K. herd immunity on the basis that even though a single dose in infants isn't very protective, the boosting dose in one year is almost equivalent to a 2+1 or a 3+1 schedule. And because most of the disease reduction in the country is being maintained through herd immunity, you don't particularly need very high levels of protection in infants because they

will be protected through herd immunity. So, the UK has decided that infants will only receive one dose in infancy followed by a booster in the second year of life. Now this has raised a lot of interest internationally as well because it would make a program much more cost-efficient if fewer doses could be given to maintain herd immunity.

[Sarah Gregory] How did *you* become interested in this topic? Tell us about your job and what you do.

[Shamez Ladhani] So, that's a very interesting question, Sarah. I think it started when I took a year off my training to go work in a district hospital in Kenya, and I remember this one particular instance where I was on the wards and a very, very tiny baby came in with severe meningitis and was having intractable seizures. And we worked on her for two or three hours, gave her every medicine that we had over there including antibiotics and after two or three hours she stabilized. And she—she actually recovered from her infection and we had everything under control, and I remember being so excited to save a life. And I walked into the doctor's office, and I said, "Do you know what, we saved a life with—with this kid with meningitis," and one of the professors was sitting there said, "We've saved ten thousand lives because we've just vaccinated the whole city against tetanus." And that really put vaccines into perspective for me.

So, I'm a pediatrician by trade, and I got into vaccines mainly through my work with genomic epidemiology and trying to understand why some vaccines do not protect all children in terms of vaccine failures. And it was only through my work through that, that I realized how important vaccines are in preventing disease. The idea that you can prevent thousands of cases through a vaccination program just fascinated me compared to being in the hospital wards where you help a few children at a time. And in public health there is a definite need for pediatricians to be involved with the childhood immunization program rather than public health specialists, and I found myself in a very unique position of being able to work at a national public health center as a pediatrician and support the childhood immunization program. So, I'm very fortunate in that I can take my clinical skills and bring it to public health to make sure that we have the best available childhood immunization program for the U.K.

I'm currently involved with both the meningococcal immunization program, which is world-leading in terms of the vaccines that we have in our program, and the Hib vaccine program, which has been around for two decades. So, most of my work relates to the prevention of serious bacterial infections in children. And it's amazing to see how well we have done in the last decade.

[Sarah Gregory] I always like to ask a personal question or two, just so listeners can get a feel of who you are as…as just a person. So, what are your hobbies, what do you like to do outside of work and children and infectious diseases?

[Shamez Ladhani] Oh, so, I have two very young daughters who I absolutely adore, so I spend a lot of time with them. My job allows me the flexibility to actually spend quality time with them and do things with them while they're young enough to want to spend time with me, so I'm very lucky. My job is very exciting, I have three employers. So, I work in the hospital where I look after children with infectious diseases; I work in the university where we do clinical trials and we teach; and then I work in Public Health England, where I'm responsible for the national surveillance program for a number of vaccine-preventable diseases. So, I have a real nice combination of jobs that keeps me entertained because I can move from one job to another. But

despite having three employers, my work-life balance is actually very favorable, so I have a very good family life.

[Sarah Gregory] Well, it doesn't sound like you'd have time for a well-balanced family life, but I'm glad to hear you do.

[Shamez Ladhani] You say that, but I'm actually sitting in my office looking at my two girls… kicking each other just outside my office. Then, because they're just getting on each other's nerves, so it's not a holiday being here at work with me at times, but I'm spending time with them and then we're going to go watch a movie after this, so...

[Sarah Gregory] Oh, nice.

[Shamez Ladhani] It genuinely is a good work-life balance.

[Sarah Gregory] I'm glad to hear that. And thank you so much for joining me today, Dr. Ladhani.

And thank you listeners, for joining us. You can read the September 2019 article, Effect of Pneumococcal Conjugate Vaccines on Pneumococcal Meningitis, England and Wales, July 1, 2000–June 30, 2016, online at cdc.gov/eid.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

[Announcer] For the most accurate health information, visit cdc.gov, or call 1-800-CDC-INFO.