

# An Increase in *Streptococcus pneumoniae* Serotype 12F

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

[Sarah Gregory] I'm talking today with Dr. Cynthia Whitney, a medical epidemiologist at CDC, about pneumonia vaccines and *Streptococcus pneumoniae* serotype 12F. Welcome, Dr. Whitney.

[Cynthia Whitney] Hello, it's great to be here.

[Sarah Gregory] After the PCV vaccine was introduced in Israel in 2009, there was apparently an increase in *Streptococcus pneumoniae* serotype 12F. Would tell us about this?

[Cynthia Whitney] Sure. First let me tell you a little about pneumococcal conjugate vaccines and pneumococcal disease. *Streptococcus pneumoniae* is a bacteria that is also known as pneumococcus. This bacteria typically just lives happily in our noses and throats and doesn't bother us. Occasionally, if a person catches a virus or their health is off in some other way, pneumococcus can grow and spread and cause disease. The main diseases pneumococcus causes are mild infections, like ear and sinus infections, but pneumococcus can also cause severe illnesses like pneumonia and meningitis. When you add up all these infections, pneumococcal disease is a leading cause of infections and deaths around the world, especially in infants and the elderly. Pneumococcal conjugate vaccines are relatively new type of vaccine that has been shown to be highly effective at preventing disease and in stopping people from acquiring the bacteria in their noses and throats. Pneumococcal conjugate vaccines are now used in infant vaccination programs in most countries around the world. The U.S. and a small number of other countries also use them in some adults. Pneumococcal conjugate vaccines are very specific for preventing certain strains. The vaccine used in Israel and the one we use in the United States protects against 13 different serotypes, and these cause most disease, but there are more than 90 serotypes all together. The manuscript we are discussing here talks about how surveillance for pneumococcal infections in Israel found that the new vaccine program was preventing a lot of disease, but they also detected an increase in one of the strains that the vaccine doesn't cover—serotype 12F.

[Sarah Gregory] What did this surveillance study look for?

[Cynthia Whitney] The surveillance system in Israel was set up by working with all the hospitals in the country—26 of them—to get them to report every time a patient was treated there who had invasive pneumococcal disease. In addition, one large outpatient medical system also contributed cases. Let me explain what invasive disease is. Invasive disease is a set of illnesses in which pneumococcus is grown from a specimen of blood or spinal fluid collected from a person who is ill. Usually the patients have severe illnesses, like pneumonia, sepsis, or meningitis. The authors of this report were able to look at how the amount of invasive disease changed after a new pneumococcal conjugate vaccine program began in Israel. The authors did this by analyzing information from case reports over time and by doing tests on the particular pneumococci causing these infections to see what serotypes they were. In addition, they did special DNA fingerprinting of the pneumococcal serotype 12F strains to see if the strains were related to each other genetically or to other serotype 12F strains around the globe.

[Sarah Gregory] And what were the results?

[Cynthia Whitney] Overall, the surveillance program identified over 4500 episodes of invasive pneumococcal infections in Israel between the middle of 2009 and the middle of 2016. Of these, about 10 percent were serotype 12F. The authors found that rates of pneumococcal disease did drop after the new vaccine program began. Overall, disease rates dropped by about a third, and rates among the youngest kids, the target age group for the vaccine, dropped by about 50 percent. The drop in rates was especially large in young children but rates also dropped among older adults because the children were no longer spreading the bacterial serotypes targeted by the conjugate vaccine. Disease caused by the vaccine strains in particular dropped a lot—by about 80 to 90 percent overall. While overall the vaccine program benefits were great, the investigators did detect a small but significant increase in disease caused by nonvaccine serotypes, especially serotype 12F. This 12F strain is interesting because it seems to be a strain that has been seen in Israel but not yet in other places. Also, the strain was moderately resistant to penicillin. And serotype 12F is now the most common serotype causing disease in Israel.

[Sarah Gregory] What was the study population? Age breakdown, gender, nationality?

[Cynthia Whitney] The study population was the entire population of Israel. Israel has over eight million people, about three quarters of which are the Jewish ethnicity. Cases were captured from all 26 Israeli hospitals and one large outpatient health maintenance organization. The authors estimate that 99 percent of invasive pneumococcal disease cases would be captured by the institutions they worked with.

[Sarah Gregory] Have there been outbreaks of 12F in other countries?

[Cynthia Whitney] Yes. 12F is a strain that, in the past, has not been among the most common causes of pneumococcal disease, but when you look at what serotypes cause outbreaks, 12F is among the top serotypes doing that. There have been outbreaks in jails, homeless populations, daycare centers, and communities of different indigenous persons. It's a little difficult to tell from the report from Israel if the increase in 12F is related to what we would typically think of as an outbreak—which in my mind is an increase in cases in a narrowly defined setting. I think it may be more of a general increase across the country, but the authors don't provide information in the paper about the distribution across Israel.

[Sarah Gregory] Why did this happen? Why did 12F strains increase while strains covered by PCV 7 and PCV 13 vaccines go down?

[Cynthia Whitney] The authors speculate that use of pneumococcal conjugate vaccine may have allowed this 12F strain to spread and become a more common cause of disease. We know that pneumococcal conjugate vaccines are very good at preventing the strains that the vaccine targets from settling in people's noses and throats, and this has been one of the reasons vaccines of this design have been so effective. If people don't pick up the vaccine serotype strains in the first place, they can't get sick from them and they can't give them to others who might get sick, as well. But, we've learned that taking these vaccine serotype strains out of circulation allows pneumococcal strains that are not in the vaccine to reproduce and spread more easily than they did in the past when they had to compete with the vaccine serotype strains. After the 7-valent conjugate vaccine came out, we saw an increase in serotype 19a, which is a nonvaccine type. It became quite common in the U.S. So the upswing in serotype 12F disease might be a side effect

of PCV use in Israel. On the other hand, it maybe it's just a trend that's unrelated to vaccine. We see this as well—a type might go up for a few years and then go down again.

[Sarah Gregory] The 12F strains also seem to be penicillin resistant. Why would this be?

[Cynthia Whitney] Some pneumococcal strains become resistant and others don't and there might be a few different reasons why this is. We often see resistant strains develop in children, who tend to have a lot of pneumococcus in their throats and who also take antibiotics more often than adults do. One theory is that certain pneumococci develop resistance to antibiotics while they are hanging out in the nose and throat of someone who is taking antibiotics. Susceptible strains in the throat that are exposed to antibiotics either will die off or they need to develop resistance to survive. The antibiotics in this case are providing what scientists call 'selective pressure'—a force that encourages an organism to adapt. A pneumococcal strain that was susceptible to antibiotics might borrow genes from a resistant bacteria that's close to it in the throat and then it can become resistant. This other bacteria is often another type of strep, like strep mitis, not typically pneumococcus. Another theory of why a resistant bacteria becomes more common is that a pneumococcal strain might already be resistant but it's present in low numbers, and if you kill off the other susceptible bugs in the throat, this makes room for the resistant strain to reproduce. In the current situation in Israel, the 12F strain seems to have been found years ago and now is just reproducing more and causing more disease. Whether the resistance genes might be helping the 12F to grow and spread in spite of antibiotic use is unclear. It may be that the conjugate vaccine use has taken so many pneumococcal strains out of circulation that the 12F strains just have more room to grow.

[Sarah Gregory] So what does this mean for public health? Is this a serious concern we should be monitoring?

[Cynthia Whitney] I would call it more of a moderate concern than a serious concern, as the amount of 12F disease in Israel look like it might be leveling off a bit and even with the reported levels of resistance, infections caused by serotype 12F should still be treatable with most antibiotics. But it's a situation that's definitely worth watching, as this strain could spread to other populations where it could cause even more problems or it could become even more resistant to antibiotics. People outside Israel should be tracking pneumococcal disease to see if 12F is popping up, and vaccine manufacturers should think about whether developing a vaccine that targets serotype 12F would be a good idea. Everyone should use antibiotics carefully, and only when they are really needed, to avoid giving resistant strains like 12F a survival advantage over susceptible strains.

[Sarah Gregory] Will there be a vaccine for this serotype in the near future?

[Cynthia Whitney] Several manufacturers are working on new pneumococcal conjugate vaccines with a range of serotypes. I've not heard any of them announce publicly that they are working on a vaccine that targets serotype 12F, although given 12F's prevalence, I wouldn't be surprised if a 12F antigen is being developed. I don't expect a new vaccine targeting the 12F antigen to be available in the next two to three years.

[Sarah Gregory] Are there any basic ways people can avoid getting any kind of pneumonia?

[Cynthia Whitney] Yes. There are several ways to protect yourself from pneumonia. First, do what you can to stay healthy. For example, don't smoke cigarettes or anything else for that

matter. Inhaling smoke damages the lungs' ability to fight off bacteria and viruses. Next, either stay away from people with coughs or get them to properly cover their mouth and nose with a tissue or their sleeve when coughing, and wash your hands to get rid of germs a few times a day. Last, but not least, get vaccinated against diseases that cause lung infections, such as pneumococcal disease and influenza. For children, vaccines against pertussis and Haemophilus influenza type b can also prevent pneumonia. For those of you who still haven't gotten your flu vaccine yet this season, it's not too late. You should still go get one.

[Sarah Gregory] Since you're not one of the authors on this paper, would you tell us a little bit about yourself, and what your interest in pneumonia is, and what you do at CDC?

[Cynthia Whitney] I'm a physician and an epidemiologist and Chief of the Respiratory Diseases Branch in the Division of Bacterial Diseases, in CDC's National Center for Immunization and Respiratory Diseases. I've worked on pneumonia, meningitis, antibiotic-resistant infections, and other issues since coming to CDC in 1993. I've worked on many outbreak investigations as well, ranging from Ebola to SARS to pandemic flu. One of the most interesting things I've been able to do during my career has been measuring the effect of pneumococcal conjugate vaccines when they first came out in the U.S. in 2000. It's been fun to follow the trends since then and to see how the results we are seeing might match or differ from those in other countries. We have not seen serotype 12F strains go up as much as they are reporting from Israel in this manuscript. Right now, in addition to working on pneumococcal disease, I'm spending a lot of my time on another type of pneumonia called Legionnaires' disease. The number of cases and outbreaks of Legionnaires' disease are increasing rapidly. I'm working with a team of scientists who are figuring out how to more quickly identify and respond to cases and outbreaks and to figure out how to best prevent them in the first place.

[Sarah Gregory] Thank you, Dr. Whitney, for taking the time out of your very busy day to talk to me. I've been talking with Dr. Cynthia Whitney about the March 2018 article, Emergence of *Streptococcus pneumoniae* Serotype 12F after Sequential Introduction of 7- and 13-Valent Vaccines, Israel. Listeners can read the article online at [cdc.gov/eid](http://cdc.gov/eid).

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

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