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From UCMP Children's Hospital of Pittsburgh, welcome to That's Pediatrics. I'm Carolyn Coyne, I'm a scientist in the Division of Pediatric Infectious Diseases.

Brian Martin: And I'm Brian Martin, I'm a Vice-President of Medical Affairs here at Children's.

Carolyn Coyne: And today we have a very special episode with two guests for the very first time on That's Pediatrics history. First we have John Williams, who normally sits as one of the hosts of That's Pediatrics. John is a Professor of Microbiology and Molecular Genetics and is the Division Chief for my division, Pediatric Infectious Diseases. Joining him is Paul Duprex, Paul's a Professor of Microbiology and Molecular Genetics, he's the Director of the Center for Vaccine Research at the University of Pittsburgh. Welcome and thank you for joining us.

So today, we actually have a special episode focused on measles. I feel like I've kinda gone into a bit of time machine but here we are talking about measles and measles outbreak throughout the nation and also in Pittsburgh. So why don't you Paul, you're a basic scientist who studied measles for a long time, why don't you tell us a little bit about measles virus.

Paul Durpex: So, what's interesting about measles is, it is the most infectious human virus on the planet. It's highly, highly transmissible and the problem with a very highly transmissible virus is, if we do not immunize a large number of people, then there will be little pockets of people who are susceptible, who can get that infection and if the virus is imported from somewhere outside of the country, these little pockets can amplify the virus like wildfire. So that's what you need to remember about measles. One thing, highly, highly transmissible alongside a virus which is readily preventable because we have a super vaccine.

Carolyn Coyne: So when you it's the most infectious virus, if there one individual infected with measles, how many other individuals could get measles?

Paul Durpex: So the funny technical term that we use, doesn't really matter but it's interesting to know, is R0 and R naught means how many people from one cases of measles are likely to be infected. Now, this is a bit of a number, which is not an absolute number, but it's a real good way to understand how infectious a virus is or actually a bacterium as well. So, for measles, one person infected with the virus can infect between 12 and 18 people. And that in this part of the world.

Brian Martin: That's considerable.

Paul Durpex: It's highly, highly infectious virus. If you think about something like influenza, much much lower R naught compared to measles. If you think of something like Ebola, big outbreak of Ebola in the world and people are thinking about Ebola coming to America again. Desperately, desperately untransmissible virus, it's really quite hard to catch Ebola. Also, HIV. Not an easy virus to catch. Measles, on the other hand, is so so transmissible that if you get these little pockets of people, who have never been vaccinated, it's very very likely that it spreads from one person to the next to the next to the next to the next to the next, and then you've got 12 or 18 people infected.

Carolyn Coyne: So, what makes it so infectious?

Paul Durpex: So, it's very very infectious because it's evolutionary very very clever. Now clever, viruses aren't clever because virus can't think so what do I mean by clever? Well, it has adapted a wonderful way to get into a person to spread right around the body of that person, catching a ride on the very cells that are supposed to stop it infecting us, so these are cells of the immune system. So the virus is very very lymphotropic. So it infects immune cells really efficiently, it even turns on its own entry receptor so that it allows even more cells to be infected and what it does, and this is another thing to remember about measles, it's very very immunosuppressive. What do we mean by immunosuppressive, just that it really really dampens down the immune system.

So many many kids, not maybe in this part of the world, but in other parts of the world, the developing world, who have bacterial infections, co-infections with bacteria, really can die because of pneumonia. So it goes in, it spreads right around the body and then it has to get out. So how does it get out? Well, it has the ability, in the immune cell, to come into close proximity with a cell in the epithelium. Now, the epithelium is just the cells that enter face in the lungs between the inside of your body and the outside of your body and the outside of your body, of course, is covered in air. So the virus is able to enter the bottom of these epithelial cells and then it hijacks the body so beautifully.

It goes from the bottom of the cells to the top of the cells and what's really nice about the top of those cells is, they're full of beating cilia, so the cilia are whipping around the moving mucus about and the virus does to the top of the cells, where there isn't anything to hold it back. So, because it hasn't come in using those cells, rather it's come in using cells that the immune system spread right around the body and then got to the top of these ciliated cells, it's just whipped out into the air very very efficiently and the other thing about measles is, whenever it's been whipped out into the air so so efficiently, that is before the typical rash, because whenever people think about measles, people think about red spots. But this infectivity is being released into the air before you see the red spots, that's the problem. You can transmit measles before you know you have measles.

Brian Martin: That's very helpful to hear about that continue of the disease process. Dr. Williams, question for you. Could you please share with our listeners some of

the questions, like I know that the Infectious Disease Department here at Children's has been likely fielding a number of inquiries because measles is, fortunately measles outbreak is a relatively rare event. We have concerns from primary care physicians and from other providers across the care continuum. Could you just share with us some of the questions that are coming in, both from on the provider side and then also on the patient side if any of those a pertinent.

John Williams: Yeah, we've been getting a lot of questions, Brian, both from pediatricians and physicians in the community and other healthcare providers and families. Unfortunately, measles outbreaks are not as rare as you might think and they're becoming more common because of what Paul mentioned about the vaccines. So, measles was declared eradicated in the United States in 2000. Twenty years ago, okay, because we were vaccinating very effectively and, as Paul said, the vaccine works terrifically well. Safe, highly effective. But because of concerns about the vaccine, that have been shown in many large studies to be unfounded, we're in the midst of another outbreak of measles.

So far this year, as of April 26th, we had 704 cases. Only in, not quite five months, that's more than in any year in the United States since 1994 and we're not even halfway through the year. So this is really, we've had recent outbreaks in recent years that people have probably seen and read about but this has been one of the worst. You know, knock on wood, this year there have not yet been any deaths but 10 percent of those patients with measles have had to be put in the hospital. 10 percent. So Paul mentioned, flu, influenza as a comparison. Every year, 10 to 50 million people get flu, only about 1 percent of them end up in the hospital. So the measles, it's really a very severe illness and lots of these kids and adults get sick. So that's one of the questions we've had is, how to treat these patients, how to approach them.

A very common question we get is about vaccines and if people have had their routine vaccines on schedule, then they should be protected. There are some exceptions if, for infants younger than 12 months, they might need an extra dose of vaccine, if they have direct exposure. For adults, who were born between 1957 and 1989, they probably only got one dose of vaccine and they might need a second dose if they have direct exposure. For most of our children, including all of my children, who had their dose at 12 or 15 months and then a dose about four, five years, they're good, they're fully protected.

Carolyn Coyne: You often hear people say, “Well, in the old days, I got measles and it wasn't that big of a deal”. You spoke a little bit about the complications of this and I'm just wondering if you can talk in more detail about that. 10 percent of people might get hospitalized but what are the more severe outcomes that can happen if you get measles.

John Williams: I'll say a few words and then I have a question for Paul about that. Globally, hundreds of thousands of children die of measles every year. It used to be millions. The reason it's not millions anymore is because of the vaccine. Because

the vaccine is safe and highly effective. But when children die, they often die of a secondary pneumonia, as Paul mentioned, the bacterial pneumonia. They can get severe diarrhea and dehydration. So, most of the deaths is in the period when they're acutely sick but I wondered Paul, you mentioned that the measles suppresses the immune system. Is that just short-term of does that go on for a long time.

Paul Durpex: So what goes on for quite some time after the infection and this is what people call the measles' paradox because the paradox is, you get this phenomenal immune suppression, you get all of these secondary infections, especially in the developing world, which leads to the mortality due to measles. But you get this lifelong immune protection. So people who have had measles, that's the one group of people that they say don't need to be vaccinated again. If you've been born before 1957, you most certainly will have had measles, even though you might not know it. If we take some blood, and if we do some tests, neutralization tests, other antibodies and map blood which knock down the virus, they're still doing to be there. So, that's the paradox with measles. You get this profound immune suppression, you get this wonderful lifelong immunity and the problem with the immune suppression is that is leads to many secondary complications.

The other thing which is interesting about measles, and people don't know this is, it's one of the leading causes of blindness in the developing world. It's a real problem for kids longterm and the other thing which is important whenever thinking about other complications of measles is the virus is lymphotropic, infects the immune system, we talked about that already. It's epitheliotropic. It can infects the epithelial cells but it's also neurotropic. So when rare instances, the virus can cause encephalitis and that's what causes most of the hospitalizations in the developed world where we live, are due to these central nervous system complications and then there are other really really rare but absolutely fascinating conditions, known as subacute sclerosing panencephalitis, it's a hugely long name. But essentially what this is and something worth remembering about is, whenever kids get infected, this was the received wisdom. Whenever kids get infected really really young in life, the propensity for this condition, SSPE, was much more likely to occur. What is SSPE? Well, it's the longterm persistence of a human virus in a person.

So, we're used to DNA viruses lasting for a long time so we're used to DNA viruses hanging around in cold sores but we're not typically used to RNA viruses and that's sort of a technical thing, a little bit of a technical thing but we're not used to viruses like measles hanging around so long in our bodies but what can happen is, the virus, whenever it infects a very young kid, can lie dormant somewhere, typically people say it's central nervous system but that's not been proven and what happens is the virus reactivates whenever the kid is, on average, about eight to ten years after that primary infection. How does that manifest? Well in the first instance, there's the kid is maybe has some of the fine motor, or the teenager has some fine motor skills are lost, but just let's say somebody who is a little bit awkward. But after two years, the virus has

reactivated and spread so excessively in central nervous system that the adolescent is in a coma and there is no cure, no one has survived this condition ever.

Carolyn Coyne: Wow.

Paul Durpex: So you don't want to get measles as a very young kid, in fact, you don't want to get measles at all. That's the worst case scenario but it's still not a nice disease.

John Williams: Well and I think, as Paul mentioned, there used to be millions of cases a year in the U.S. as well as in developing nations because essentially measles is so contagious, as Paul says, that everybody got it. Okay, so about one out of a thousand children would have severe brain involvement that would often lead to severe irreversible damage or death. The kind of things that Paul is talking about and some people might think, well one of a thousand, those are pretty low odds. Okay, there are four million kids a year born in this country, right? So that's thousands and thousands of children, that that used to happen to and still happens in developing nations and it doesn't happen now because of vaccine.

Carolyn Coyne: So what do you tell people right? So I mean, I can imagine there's a lot of people certainly within our own city saying, oh my god, there's four or five cases of measles, what do I do, should my child go to school, what should I look for, should I be re-vaccinated, so what do you tell people who are scared because they seen the news and they see that it's now in Pittsburgh.

John Williams: Well, I think, as a pediatrician, and somebody with kids, what we've been telling people is, number one, get your routine vaccines. If everybody were all their routine vaccines, including the measles vaccine, it wouldn't be an issue, as Paul said, with a lot of population immune, you're okay. Currently, our city, many schools and many people are good about getting vaccines. So, in terms of direct risk of people right now, it's not very high because there are only a few cases and, unless somebody has direct exposure to those cases, or it becomes more widespread, then people are okay. I think there are guidelines, actually from the CDC and posted on our website and that we have circulated to pediatricians about who might consider getting either an extra dose of vaccine or vaccine early.

I think the common question people often have about that, and this touches back to what Paul said before, about whether you're immune or not, should we, in a children's hospital like this, should we ask our doctor to check and see if we're immune or just get a vaccine. The answer is usually just, get a vaccine, it's completely safe to have extra doses so I had individual measles vaccine in the early 1960s before it was combined as the MMR and my parents were great at a lot of things but keeping medical records, it turns out, was not one of them. So later in life, I had to repeatedly keep getting MMR vaccines so I've had four measles vaccines in my life. I'm fine but I know I'm well protected. I'm glad for that.

Paul Durpex: If you think about the vaccine, what I always have to say is, it's always always safer to get the vaccine then it is to get the disease and that's just a matter of trying to understand what the risks are. Nothing in life is without risk. Driving in the car to get the vaccine is way way way more riskier than getting the vaccine and getting the disease is not without risk as well. So that's what we have to try and help people understand and it's difficult right, people don't easily weigh up those risks, people are maybe afraid getting into an airplane but very happy to drive to Giant Eagle and we weight that up as a society.

Brian Martin: We are poor assessors of routine. Humans are routinely poor assessors of risk, no question.

Paul Durpex: And it's really difficult, it's difficult for people and you know, look at us right, we are fortunate, we know what a virus is. We've been train and taught about vaccines and we know what it is. So you have to also have sympathy and understanding for people who are just trying to do the right thing for their kids and then this is where the internet's great but the internet is very very challenging because it's difficult for people to weigh up the evidence whenever all the evidence on Google looks to be the same. So John already mentioned, where do you get your advice? Well, you get your advice from CDC and you get your advice from what's been posted on the UPMC Children's webpage rather than some Hollywood celebrity, who might not really know how to spell virus. That just seems to make sense. So we should understand risk and we also should understand where we should get our information from.

Brian Martin: Can't put it more succinctly than that.

Carolyn Coyne: Talk to your pediatrician if questions.

Brian Martin: No question.

Carolyn Coyne: Well thank you both for joining us. That is informative and educational. Thank you.

Brian Martin: Thank you.

John Williams: Thanks for having us.

Paul Durpex: Thank you.