

SARS-CoV 2 in Children and Teenagers

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

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Isabella Eckerle, head of the Center for Emerging Viral Diseases at the University of Geneva. We'll be discussing what we now know about COVID-19 in children and teens.

Welcome Dr. Eckerle.

[Isabella Eckerle] Hi! Welcome.

[Sarah Gregory] At the beginning of this pandemic, it was thought that children weren't really a concern for getting and spreading COVID-19. That belief lingered even though new science is saying otherwise. I've seen masked parents with children who are not masked. Why was it initially believed that COVID-19 wasn't spread by children?

[Isabella Eckerle] So, the first data that hinted into that direction were mainly household studies. So, quite early in the beginning of the pandemic there were some studies conducted that looked at index patients who brought infection into household, and it was found that in many cases that the index cases were adults but only very few households where actually the child was an index case. So this was leading to the theory that children spread it less, and it was also seen that apparently the seroprevalence in children is lower, so there is also the thinking that children get it less. So basically, if there are less children who get it, then there are also less children who spread it. On the other hand, we have to keep in mind that most of these data were collected during some kind of lockdown with school closures in place or some precautions or maybe parents being scared. So, maybe they do not represent completely the real-life scenario like we had it before the pandemic started or like we have it now when in many places the measures are...are being lifted.

[Sarah Gregory] Oh, okay. Just real quickly, would you explain to our listeners what an index patient is?

[Isabella Eckerle] Ah, yes. So it means that you...you take, for example, a hospitalized patient that has tested positive and then this is your index patient. So, this is the first patient that you investigate, so you know he or she is positive for SARS-CoV-2. And then you go into the household of that person and you see if other people are sick as well.

[Sarah Gregory] I see, okay. Going back now, so if a child does have COVID-19, actually the infection, do they tend to be more asymptomatic than adults?

[Isabella Eckerle] So, at the moment we cannot really say what percentage of children is asymptomatic because we just don't have the studies yet, and most studies that were done, especially in the beginning, were somehow focusing on symptomatic children or adults. And this is just the reason because these are the people that are seen in the health system. So, if you want to set up a study where you look at asymptomatic infection, you have to look in the community. And these studies are ongoing at the moment, but there are not a lot of results. So basically, what we can say is that usually children get less sick and many of them that we see in the health system that come for testing have something that is like a common cold or upper respiratory tract infection or a mild fever—so all symptoms that are first of all quite common in children, and that

are not necessarily a reason to go to the hospital. So, I think it's a bit more now because people are scared, but we also have to keep in mind that there is a fine line between symptoms, between asymptomatic. Sometimes children can also not express some kind of discomfort. So, we really don't know how many of them are actually asymptotically infected. But what we can say is that children are most of the time, they are just mild cases.

[Sarah Gregory] You did a study analyzing children with COVID-19. First of all, what percentage of children versus adults do you think have the disease now?

[Isabella Eckerle] So, what we...so, when we think about disease and about symptomatic patients, I can give you some numbers from...from our hospital, what we saw. So, in the study that we published in *EID*, we looked at pediatric patients and that was up to the end of March. So during that time, we had around 3,000 confirmed cases in Geneva and we had screened more than 600 children, and we had found only 23 of them that were positive. So, in the children that came to the hospital but even in the overall population of people that were sick with COVID-19, children are really just a very small percentage. Now, when we not speak about the disease but about infected, as I said, it's very hard to say at the moment because asymptotically infected people don't turn up in the hospital. So you have to go out in the community and do random testing to really find the infections. And...and this we don't know at the moment, but we can definitely say that at least for the disease, children are much less represented in this pandemic than adults.

[Sarah Gregory] Okay. So, what was the age span of the children you looked at in the hospital?

[Isabella Eckerle] So, we looked at all children that were tested positive for SARS-CoV-2 below the age of 16 years. And so we ended up with a...median age of 12 years, but with quite a huge range. So the smallest child was 7 days old and the oldest child that we included was 15.9 years.

[Sarah Gregory] And when you began your study, what were you looking for?

[Isabella Eckerle] So, we were interested in the specimens that we had received as part of our routine diagnostic care, and we were wondering if the children at the time when they got diagnosed would be able to spread the virus. Now, by the study that we did, we cannot directly comment on transmission but we looked for infected virus. So, this can give us at least indirectly a hint if the children have infectious virus, and then this could also mean that they could spread this infectious virus.

So, what we did, we took the specimens that we received for our diagnostic testing—so we always have leftover that is stored in...at minus 80 degrees—and then we took part of the sample and inoculated it on saline to see if we can grow the virus. So that means that then in this sample there was infectious virus, and infectious virus is a prerequisite for transmission to another person. And maybe, just as an explanation, so in the diagnostic test that we used, that is a PCR, we cannot say if the virus is still infectious or if this is the replicating virus or if it is just dead RNA. So, the test would turn out positive for both infectious virus and for dead RNA. But that also means that just the positive PCR cannot really inform us about risk of transmission. And we also saw that culturing the virus is quite easy. So, SARS-2 grows really well on saline, and we have a P3 facility in place that you need to do that. So, it was quite easy for us to put these samples on saline and...and generate isolates from them.

[Sarah Gregory] What did you find?

[Isabella Eckerle] So, we found that the cold culture SARS-CoV-2 from half of the specimens—so from 12 of 23 children from which we inoculated the samples on saline—we could actually isolate infectious virus. And we, we saw this infectious virus by, by...identified this infectious virus by change of the saline—so that it would be called cytopathic check. That is very typical when cells get infected, they start to change their morphology and they start to die. And then we also checked for an increase in viral RNA to really prove that the virus is replicating. And then we took all positive isolates and put it in the second passage to make sure that this is really a functioning virus, that it's able to infect cells again and again. And what we also saw that the viral loads of those children where we could get an isolate, they were rather high. So, they had a...a median viral load of 1.7×10^8 copies per mL. And what was also interesting...so, we did not find any relation to age, so, actually the youngest patient in which we could isolate SARS-CoV-2 was a 7-day-old baby. And we also did not see any correlations where most of the children were only mildly sick, they had a upper respiratory tract infection, but we could not correlate fever or cough or any other symptom to the fact if the isolation was successful or not.

[Sarah Gregory] This science continues to evolve since this article was published in *EID*, as does the pandemic. Recently, more than 80 babies in the U.S. were diagnosed with COVID-19. How do you think this science showing that children are also COVID-19 spreaders should impact their interactions?

[Isabella Eckerle] Well, I think first of all it is important to say that we did not directly assess the spread. So, I think you really need epidemiological studies for that. But at least we could show that the biologic prerequisite to spread the virus or to infect others is there by the data that we have. I think the school closures were important in the beginning to get the epidemic under control, and that worked in many regions of the world. But on the other hand, we also saw that if you close schools, you are not doing a favor to children. So, there were increased support, but if you view the children, we know that we cannot close schools forever. It's also a burden for their parents and also that children need to benefit from education and from their peers. So, I think that the key is to keep schools open.

But what we also saw now is that there are outbreaks in schools. So, there were some reports from Israel, from Australia...and this seems to happen when the community transmission goes up as well. So, I think the key for school openings is to not just look at the schools, but to look at the whole community. So basically, you have to keep community transmission low in order to keep schools open. Then there are many precautions that you can take, but I think none of them will be a single solution. I mean, of course as long as children are sick, they should not go to school. They should stay at home until they are well. If a child is tested positive, then contact investigation should be done. But this is only some part of the overall package that you have to deliver.

And, yeah, to keep community transmission low, I mean, it's a big task. It involves all of us, and it includes a lot of other measures like keeping your distance, wearing a mask, making sure that everyone can get tested. And I think at the moment it's a bit of a psychological factor because everyone is tired, everyone is sick of it, and we would all love to go back to normal. But we are still in the midst of a pandemic and we have to find solutions to somehow go on with our lives but still to keep the transmission low.

[Sarah Gregory] Should children wear masks as well as adults given what we know now?

[Isabella Eckerle] So, at the moment it is hard to say. There's no good general consensus which measure should be taken and there are many different varieties of how you open schools, from strict measures to almost no measures across countries. But I think it would be important to put some measures in place, especially if you think of...I mean, the winter season coming where a lot of children will have other respiratory viruses. So it will get even harder to do symptomatic testing because a lot of the children will be sick with the common cold, and then you don't know if it will be SARS-2 or if it will be something else.

So, I think the big task is to put some measures in place to allow children to go to school safely but also not to catch it and not to spread it to others. I mean, some recommendations were, for example, to reduce the class size, to put some mask policy in place maybe during the break, to encourage children to wash their hands. We also see now that especially closed indoor spaces seem to pose risk because there is more and more evidence for also aerosol transmission. So these are all factors that make schools not a very...well, easy place to manage, I would say. But then the good news is also that it seems to be a bit the older age groups—like about the age of 10, 12 years—that are more often positive and that seem to be maybe more of a spreader than the very young children. And I think for those children, it's easy to...well, easy but...it's feasible to educate them how to wear masks, they have a better understanding of how to keep some measures. But then the other thing is also not just to keep these measures in schools, but also to...yeah...to have the same measures when the kids are outside, when they have leisure time activities, and I guess it will be a challenge.

[Sarah Gregory] In the big picture, what are the public health implications of children possibly being as infectious as adults?

[Isabella Eckerle] I think the most important point is that we watch closely what happens in schools now. I think we should take all evidence that we have, and we don't have a clear picture what happens with children, but we have to understand that we cannot say children are just of a lesser risk so we don't look at them at all. One idea would be, for example, to do sentinel testing, to pay especially attention to sick teachers, to offer them testing in a maybe more facilitated way so they do not have to go to a testing center. So, there are many different ways that you can do to tackle this problem. And it also means that you have to think of protection of elderly, of grandparents, of teachers with underlying health conditions, maybe also children that have health conditions. And yeah, I have to say it's not easy. It would be much better if we would have proof that children do not play a role. But now I think there is more and more data emerging that there are outbreaks in schools, and so it means that we should include children in, in the testing algorithms and we should also contact...trace their contacts once we have an infected child and put people in quarantine and make sure we do not miss these clusters. So, I think this is really the key message that we really have to pay attention what is happening, and have some strategies in place to anticipate what...what will happen in winter when there will be more spread of respiratory viruses.

[Sarah Gregory] Since this study was published, have you investigated the issue further? Or have you seen more children in your hospital with COVID?

[Isabelle Eckerle] So actually, in the meanwhile, we did see a few children presenting with this new multi-inflammatory syndrome that was recently described as a late complication of SARS-CoV-2 infection. And in the last month, Switzerland has managed to keep the numbers rather low. However, since a few weeks with holidays season and some of the measures were relaxed,

so we see a small rise in cases again. We did another study where we took the data that we generated through our diagnostic testing and there we looked at viral loads across different ages. So, we also included adults in the first five days of symptom onset. And actually here we found a confirmation of this study, but we did not find any differences in the viral load between children and adults. And we also saw that around half of the specimens that we received for our diagnostic testing are in a range that is compatible with the presence of infectious virus shedding. So, it's basically almost the same like the shedding study that we did. However, in this study that I just mentioned, we only looked at the viral load, like we only looked at the number of RNA copies, but we did not assess any infectious virus shedding in the lab.

[Sarah Gregory] Will you be publishing this article in *EID* also?

[Isabella Eckerle] We had uploaded the study as a Medrxiv—as a preprint to Medrxiv—and we had submitted it to a journal already. But it's not published in the journal yet, it's only on Medrxiv.

[Sarah Gregory] Tell us about your job and what you enjoy most about it.

[Isabella Eckerle] So, I am in Geneva at the Center for Emerging Viral Diseases for two years, and this is a joint institution between the university hospital and the university. And I have to say that I am very lucky in this position because I get to work with our diagnostic virology team and I work in close interaction with our infectious disease team, also with pediatric infectious disease doctors, and we also do research. So, I think for me, it's a fantastic combination. I am a medical doctor from my background and then I spent the last 10 years in virology, so I really love to discuss interesting patients in the morning then analyze their samples in our routine lab and later take that sample and analyze it in the research lab. So for me, this is really what I enjoy most—to see that the work that we are doing, it has an impact on the patient, but we can also go beyond to defend the diagnostics and analyze samples further or isolate viruses, and really look at pathogens that make people sick.

[Sarah Gregory] You live in such a beautiful country. What do you do for fun and relaxation?

[Isabella Eckerle] Yes. So, I'm also very lucky to live in Switzerland. And...well, one of my really favorite hobbies is to go hiking and it's nice because we have a lot of mountains around. And also in Geneva, we have Lac Léman—so the Lake Geneva—so in summer, you can go swimming and go to the beach, and you can also do really nice hikes and sit on the lake and eat ice cream. And so, it's a very nice place and I'm very happy to be there.

[Sarah Gregory] Sounds wonderful. Well thank you so much for taking the time to talk with me today, Dr. Eckerle.

[Isabella Eckerle] Yeah, no problem.

[Sarah Gregory] And thanks for joining me out there. You can read the October 2020 article, Culture-Competent SARS-CoV-2 in Nasopharynx of Symptomatic Neonates, Children, and Adolescents, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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