Neglected Hosts of Small Ruminant Morbillivirus

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

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking with Dr. Claudia Schulz, a postdoctoral researcher at the University of Veterinary Medicine in Hannover, Germany. We'll be discussing our article about the role of pigs and wild boars as hosts of small ruminant morbillivirus. Welcome, Dr. Schulz.

[Claudia Schulz] Hi. Thank you for the invitation.

[Sarah Gregory] So, talk to us about small ruminant morbillivirus. What is it? And measles is a morbillivirus, right?

[Claudia Schulz] Yeah, that's right. Small ruminant morbillivirus was actually formerly called peste des petits, you know. And the taxonomy's changed two years ago…no, three years ago. So, in the rest of the talk I will rather refer to PPRV, which is the short abbreviation, and easier to say it than SRMV.

[Sarah Gregory] Okay.

[Claudia Schulz] And, yeah, it's just good to know. And it's a virus that causes one of the most contagious and highly infectious respiratory diseases in small ruminants. It's a single-stranded, negative-sense, RNA virus, from in the family Paramyxoviridae, and the genus *Morbillivirus*. And that's where measles comes in, because measles is also a morbillivirus. And actually the genus *Morbillivirus* includes various other important contagious viruses of humans and animals.

Yeah, the human measles virus, or measles morbillivirus, is how it's called now, is a type species of this genus and an exclusive human pathogen, which means that there's not really an extrahuman sustainable reservoir. In contrast, there are lots of different, let's say, animal morbilliviruses. This includes small ruminant morbilivirus; and then rinderpest virus (some of you probably know that it was eradicated, but it's still in the list); and then we have the canine morbillivirus, which will cause canine distemper virus; and porcine morbillivirus; and lots of, well, different cetacean morbilliviruses, which, of course, affect cetaceans.

Yeah, just a short excourse to measles. Clinical science, maybe, I think, yeah, it's quite known, but it causes high fever, respiratory distress, inflamed eyes, and rash. And severe measles complications may include encephalitis; blindness; diarrhea, which leads to dehydration. And, yeah, just a few numbers: in 2016, an estimated seven million people were affected, and around one percent died, and mostly children are affected. But there is a vaccine and the WHO targets to eliminate that virus under a global action plan, in five WHO regions. I think it's quite helpful to know about measles because there are other morbilliviruses, they often, you know, cause similar clinical signs in animals, so, yeah, I think it's a good background.

And, yeah, so what is actually also very important and interesting is that measles virus is a close relative of rinderpest virus. So, how did that happen? And it was thought, like, phylogenetically, the ancestor of rinderpest virus, which causes the cattle plague, or *caused* the cattle plague, probably jumped to humans, well, depending on the study, in the 11th or 12th century or in the 18th century, that's a more modern study…

[Sarah Gregory] It's like—that's a huge difference!

[Claudia Schulz] Yes. It depends for you which program and which strains you have, I mean, or use, because, yeah, maybe it's quite a more older now, the 11th to 12th century. Then it's probably also interesting to know when the ancestor of PPR and rinderpest and measles virus, yeah, separates, so it's about the early 17th century. And now we come earlier, back to the present time, and for PPR, there are four lineages. So, it's the same serotype, but divided in lineages, and they diverged from a common ancestor in the late 19th, early 20th century. And, indeed, in 1942, the first PPRV was identified in Côte d'Ivoire. So, that's a little bit different story, background about that.

[Sarah Gregory] Okay.

[Claudia Schulz] And yeah, so in cattle, about 100 percent mortality was caused by this rinderpest virus, and this had devastating effects on economy and profound influence on public health in affected countries, including Africa, Asia, and also Europe. And it took a… really a long time, over five decades of effort, to eradicate that virus. And finally, it was declared…the world was declared free of that virus in 2011. And, of course, the rinderpest vaccine was prohibited, and this is very important in the history of PPR, no? Because, since they are very closely related, there is a cross-reactivity, serologically, between morbilliviruses and the vaccines of RPV or rinderpest also protected small ruminants against the deadly small ruminant plague, PPR. So, you can imagine since that was prohibited, that vaccine, this virus could freely spread over… in large parts over Africa and in Asia.

And yeah, so as I said, there are four lineages. And the lineage one and two are endemic in Western Africa, lineage three circulates in Eastern Africa, and then there's this lineage four, which, yeah, maybe you should keep in mind because it's considered to be a more dominant lineage, let's say. And it started in Asia and spread now also to many African regions.

Yep, so since 2008…no, now I'm sitting in Europe, so we'll focus a little bit on Europe, because it was also the background of the study we did. Since 2008, actually, there were repeated outbreaks in countries in Northern Africa, like Morocco, Algeria, and Tunisia, but also in Asia, which borders Europe, and, yep, so it was Turkey, for example. And this now poses other risk to Europe, because, of course, it's a neighbor. And this was emphasized by a recent outbreak in Bulgaria, in June 2008, near the Turkish border. So, it's quite…quite new.

[Sarah Gregory] So, your study is about these neglected hosts of small ruminant morbillivirus. So, tell us a little bit more about that, beginning with what are the usual animals that carry it.

[Claudia Schulz] Yeah, well, the susceptibility of infection and disease differs considerably between ruminant species. And even-toed ungulates are, yeah, susceptible. And the most susceptible species are small ruminants, or, particularly, goats. And they show severe, highly infectious respiratory disease. So, in goats, the morbidity and mortality is up to 100 percent, a little bit similar to cattle…to the cattle plague, the rinderpest virus. Sheep, interestingly, they can also succumb to disease. But often, actually, they also show subclinical infection, which is important due to the spread, or silent spread, of the virus in different countries.

And yeah, just a little bit more about the clinical science in severely affected animals. The incubation period is about three to 10 days, and they show high fever, necrotizing erosive

stomatitis, mucopurulent nasal and ocular discharge, bronchopneumonia, and yep, severe diarrhea. And the clinical signs, they get more and more severe, and death is around the second week. There are different forms, like peracute, which the animals die very quickly; there are also acute and subacute forms.

And for morbillivirus, it's known that they cause immunosuppression. So, what is very important, together with these viruses, is that concurrent pathogens, which are already in the host, they were already infected with this pathogen, or maybe during the morbillivirus infection, they can also infect themselves with another, secondary pathogen. And these animals actually can even show more severe results and can result in severe respiratory disease complexes. And if they survive that, the goats, their reconvalescence times lasts several weeks, actually, because it's very severe disease.

And yeah, it's spread by excretions or secretions, after…oronasal or occular secretions, but can also be spread by feces and urine. And yeah, so, in general, it can be spread to other even-toed ungulates, which belong to the order Artiodactyla and this is particularly during the febrile phase of the disease. So, of course, the contact animal also infects itself by aresol, through direct contact. And oral route is rather unlikely; but, on the other hand, I mean, the oral and the respiratory tracts are connected somehow, because it's not a closed system.

Yeah, the virus itself is quite instable and it doesn't survive for such a long time. For example, foot-and-mouth disease virus is very resistant; this is not the case with morbilliviruses. And so, fomites are not that relevant, but, of course, can't be excluded in transmission. Yeah, what is interesting, particularly in the view of importance is that, if there are common grazing grounds or the animals gather near water holes, they…that's where the transmission occurs between species of the same…or animals between the same species or between different species.

And, yeah, what is also an important factor is in the transmission is that, of course, these animals are quite small, in contrast to cattle, for example. So, the movement, mobility of this animal is quite easy, concerning trade, but also in transhumance. And this, on the other hand, for example, with sheep there's an impact, for example, if they spread the virus silently to other contact animals on the way, whereever they're going, across borders, also.

And so, I think we…just a little bit to the question "Who gets the virus?" I mean, I've already said that it's a virus of even-toed ungulates, and according to the current PPR technical disease card of the World Organization of Animal Health, which is the OIE, cattle or other ruminants, particularly cattle and pigs, develop inapparent infections and do not transmit the disease, so they're dead end hosts. Then, yeah, in cattle and buffaloes, there actually have been fatalities reported. And there's also, in a more recent study of cattle, that they isolated some virus from the blood, yeah, then which might also play a role in the transmission over further distances are dromendaries. So there have been, recently, reports, that yeah, that questioned if they…if PPR might be an emerging disease in these dromendaries. On the other hand, there are no reports of other transmission between cattle and goats or dromendaries and goats. And, of course, if you have a dromendary which is maybe infected with other pathogens, it's difficult to judge about the role of these hosts. But then, yep, they go very large distances, between different countries, so I think that's important, quite.

[Sarah Gregory] So, your article mentions that eradication of this virus is targeted for 2030 by WHO. Is this going to happen?

[Claudia Schulz] In general, I think we should come back a little bit to this rinderpest and smallpox eradication. There were several drawbacks of these studies and I think this helps to judge whether, yeah, eradication will be possible or not. The experience of the eradication of rinderpest virus or smallpox virus was actually that the force of the international community, the joint forces internationally, but also on the local level, are important to eradicate these diseases. But not only during the eradication phase, it's important to have enough money and collaboration and so on. But also after the eradication, it's important to…for it to go on with surveillance of these viruses, because maybe you've missed some endemic host here. And then just…for example, for rinderpest, a mass resurgence was reported in 1980, so it took another 16 years to get rid of that virus, but, in general, it took over five decades, which is a long time. For smallpox, it was a little bit similar. But the intensified eradication program started in 1967, but it only took 13 years until the world was declared free in 1980 from that virus. So, that's just a little bit of a background.

And they also used some experience, and set up a program, which is, yeah, a little bit similar to that used for foot-and-mouth disease. And it's called the Global Strategy for the Control and Eradication of PPR, which is based on the strategy and progressive control pathway. This is based on three pillars, which includes the control and eradication of PPR disease; the strengthening of veterinary services; and the prevention and control of other important diseases, such as capripox or contagious caprine pleuropneumonia. Now we come to the progressive control pathway. There are actually four points or stages:

- The *assessment* stage, I guess maybe I should laugh about, one to three years. So, the program started in 2015, so now we're up to 2019. So, we're around the assessment and to the control stage, which they…yeah, I think takes about two to five years.
- So, we're in the *control* stage now, which means, yeah, control in identified areas or husbandry assistance, and vaccination has started.
- Yeah, the third stage is the *eradication*, and
- the fourth stage is the *post-eradication* stage.

So, there's still some time to go…to go on.

[Sarah Gregory] Just for the listening audience, for clarification here, is measles part of this eradication plan, or is that a different strain that's going a different path?

[Claudia Schulz] Ah, yeah, it's going a different path, actually. Yeah, this is coordinated by the WHO, while the PPR eradication is coordinated by the OIE, which is the World Organisation for Animal Health for animals, and the Food and Agriculture Organization. So the, now…maybe it should be mentioned that it's the Global Framework of the Progressive Control of Transboundary Animal Diseases that is, like, all of the head of it; it's called GF-TADs, in short. Yeah, so it's different.

Yep, and now I think it's important to mention the challenges there are. So, these animals, they are small and, yeah, they are easy to bring from one place to the other. The animal value is quite

low, and the turnover of that animals is very high, as well—about 30 or 40 of these animals come up each year in country; for cattle, it's 10 percent. And what is also challenging is the vaccination of these animals. It's a huge number of animals who are right around 2.1 billion animals, and over 80 percent of them are at risk at the moment, worldwide. So you can imagine how much vaccine you would need to, yeah, do that. And it costs…will cost about $1.15 billion in five years to do this vaccination. But the good news is that there are very potent vaccines on the market. Also, there are live, attenuated vaccines.

Other challenges are political unrest, which also has an effect on illegal trade, for example. And that virus spreads very quickly between flocks, which can be an advantage or disadvantage, because when it spreads quickly, you have many animals very quickly infected and immune or dead. But, of course, when you have a silent spreader, which is, like, walking along, that can spread the disease quite easily to other flocks that are around. And, yeah, so the role of sustainable reservoirs that don't show clinical signs, that's a real challenge. And it's not clear at the moment which reservoirs really exist, so that part of the research to find out which animal species are relevant. And again, you need a posteradication program to be sure that the virus is eradicated.

So, in summary, yes, I think, in general, the eradication can be feasible, probably around 2030, but of course, there's still some research necessary. So, the positive side, you have good vaccines; effective, sensitive diagnostic methods; and comprehensive international and regional programs to combat the disease. Probably there is no animal with a carrier state, which is also important; and then, there is the mobilization also of regional, and not only of international, authorities and stakeholders.

[Sarah Gregory] So, what brought the possibility of this morbillivirus being in pigs and wild boars to your attention?

[Claudia Schulz] Yeah, the aim of the project I was working on, that's called IUEPP, which means "Improved Understanding the Epidemiology of PPR" and was financed by ANHIWA ERA-Net, and included the investigation of the role of different European animal species that might pose a risk for introduction and spread of PPR in Europe. And, yeah, on the other hand, pigs, or particularly wild boar, are widely distributed in Europe, and important reservoirs for other viruses or, yeah, pathogens, such as African swine fever or FMD or classic swine fever. And, yeah, and suids also belong to the Artiodactyla order, as do ruminants, camelids, and cetaceans, so they should be considered. And of course, there are other animal species that are interesting.

But, yep, with pigs, well…the FLI, where I was working, they have experience with pigs and wild boars, which was quite easy to do that experiment in that…in that facility. And yeah, so but what was also interesting, was that pigs also can be infected with canine distemper virus and also rinderpest virus, and actually it can also be infected with PPR, they're both known. With the Lineage two strains, I did some experimental infections, but they did not transmit the virus, similar to canine distemper, where they don't transmit the virus. But for rinderpest virus, it was possible for pigs to infect cattle by contact. So, in general, morbillivirus may be transmitted between ruminants and suids. And actually, we rather planned to prove they wouldn't transmit the virus, so it was quite surprising and unexpected that they really excreted the infectious virus and transmitted to another pig and goat. So, yeah, this was quite exciting.

[Sarah Gregory] You want to give us a little of the clinical side of it here?

[Claudia Schulz] Yeah, so the clinical signs in most of the pigs or wild boar were mild to moderate, showed, yeah, according to vitals, and some showed diarrhea, but it was rather short-lived. And also, well, in general, they had higher temperature for several days. And, yeah, they excreted the virus until seroconversion, and afterwards you can still detect RNA in the blood samples, but that's…that's it. And so they were not so clinically affected that they died or it was not so bad. So, if you would see it dead in the field, you would not be able to say "that's PDPPR."

[Sarah Gregory] So, what's the public health significance of these findings?

[Claudia Schulz] In that context, it's important to question, "Are pigs important reservoir hosts?", of course. And to answer that question, I have to introduce some terminology and semantic of host status. So, in *maintenance hosts*, disease persists in their population without external source of reinfection. Hence, in the case of suids, as maintenance hosts, suids could maintain the PPR in their population and spill it back to the virus…spill back the virus to the population of other susceptible animal species, for example, highly susceptible goats. In contrast, *spillover hosts* are dead-end hosts, but they may occasionally play a crucial role in the epidemiology by spilling back the virus to maintenance hosts. This means that suids, in this case, would not be able to maintain the virus in their own population, and require reinfection by external source, such as goats, for example. But, of course, they could play a crucial role, depending on environment and so on. So, it's not easy and, in light of the study results, both theories are possible. And the host status could eventually depend on multiple factors, such as population density, intra- and interspecies interaction, transhumance…animal translocation, and, for example, also anthropogenic factors, such as encroachment of wildlife habitats, agriculture, culture, and so on.

Therefore, I would also like to introduce the basic reproduction number, also called *R-naught*, which is the number of new secondary cases of infection with the host population previously naïve to the pathogen of concern. Since R-naught can potentially be topped up by interspecies transmission from other species, by maintenance hosts, for example, goats, R-naught may change in different environments or due to a change in pathogen traits. And, for example, extinction of a pathogen may appear if the number of individuals is low, even if R-naught is greater than one, means that also, if there are not so many goats around, the pathogen can also be extinct.

Therefore, the epidemiological role of a species, for example, pigs, may not be defined but is rather dynamic considering persistence and transmission efficiency between host population and the respective environment. So, in summary, the role of suids in PPR epidemiology has to be considered in a multihost-pathogen environment interaction system—it's a little bit complicated, but, yep. And…what we also would like to consider is that maybe some animals or pigs, they might be superspreaders, which means that, well, depending maybe also, if they're stressed or concurrent pathogen infections, they might act as an amplifying host. So, they can…if normally the species maybe is a spillover host, depending on the environment, it's…it's possible that one or the other individual excretes more virus, and this can infect another spillover or maintenance host.

[Sarah Gregory] So, tell us a bit about yourself: Where you work, what's your area of expertise, and why you were interested in doing this study in the first place.

[Claudia Schulz] Yeah, so I'm a veterinarian in the background and I studied in Munich and later gained professional experience…expertise in veterinary specialist in virology. In general, actually, I'm interested in the pathogenesis, diagnostic, and control of emerging, notifiable, and vectorborne diseases in wild and domestic animals, and particularly in camelids. But, anyway, also pigs are interesting. And, yeah, so my PhD was about bluetongue virus infection in South American camelids, so it was a vectorborne-based study. And then did another…a postdoc about Schmallenberg virus at the Friedrich Loeffler Institute at the isle of Riems, where the study of PPR was also conducted. And, yeah, after my first postdoc, in the area of Schmallenberg virus, a ANHIWA project came up and, yeah, it was quite interesting to…I really wanted to contribute in that project, which is, of course, very important to find out which reservoirs of PPRV are existing out there, to be able to eradicate that virus. So, at the moment, I'm not working on PPR, but I'm working at the University of Veterinary Medicine, as I have already mentioned, in the field of vectorborne diseases, particularly zoonotic viruses, such as Bunyavirus and tickborne encephalitis virus, which are arthropodborne.

[Sarah Gregory] Thank you so much for taking the time to talk with me today, Dr. Schulz.

Listeners can read the December 2018 article Neglected Hosts of Small Ruminant Morbillivirus online at cdc.gov/eid.

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