

Farmer Infected With Avian-Like Swine Influenza

[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. Kristien Van Reeth. She's a professor of virology at Ghent University in Belgium. We'll be discussing a case of avian-like swine influenza in a pig farmer in the Netherlands.

Welcome, Dr. Van Reeth.

[Kristien Van Reeth] Thank you, Sarah. I'm really happy to talk to you today.

[Sarah Gregory] Well, good. We're happy to talk to you. So to start, what is avian-like swine influenza? I know we have avian flu and swine flu. Is this a mutant combination? Does it affect birds, pigs, people...?

[Kristien Van Reeth] This virus originally comes from birds (from wild ducks) but it has crossed the species barrier to swine. It has become completely adapted to swine and has done so by mutation. But up until now it is still a mystery what sort of mutations have been responsible for the adaptation of a bird flu virus to pigs. This virus belongs to the subtype or subcategory H1N1, and we also have H1N1 in birds of course, but also in people. But the virus in the human population is a different H1N1 as compared to this swine virus, and interspecies transmission (so, transmission between species) is very rare. Swine H1N1 virus has only very rarely infected humans. So they mainly affect pigs.

[Sarah Gregory] Does it have anything to do with the H1N1 pandemic of 2009? Or the swine flu outbreak the year before?

[Kristien Van Reeth] Well, those two viruses (the pandemic virus and the avian-like swine virus) have just a few things in common. The pandemic virus is also a virus of swine origin, and the pandemic virus is a reassortant (in other words, it's a hybrid or a combination virus) and it has part of its genetic material (2 out of 8 genes) from the avian-like swine part. But the remaining genes come from another swine part that is widespread in North America, and these genes also include the one for the hemagglutinin. And the hemagglutinin (or H1, in this case) is by far the most important protein. It is so important because it is the target for protective antibodies. So, both viruses are H1, but the H1's have a very different origin and they are also antigenically very different.

And another important difference is that the pandemic virus is widespread in both pigs and people. Avian-like swine influenza is only present in the swine population. The pandemic virus is actually really unique because it is the single known example of a swine origin virus that has acquired the capacity to spread readily among people. And up until now, we don't know which mutations or which genetic changes are responsible for this very special trait.

[Sarah Gregory] Okay. So this did jump from a pig to a farmer. So how does it do that?

[Kristien Van Reeth] You're talking again about the avian-like swine flu virus right?

[Sarah Gregory] Yes.

[Kristien Van Reeth] Okay. So, swine influenza viruses can spread through respiratory droplets that contain infectious virus and that spread through the air, and they can then land in the airways

of humans and infect them. Another possibility is that humans touch a surface with virus on it and they then touch their mouth or nose. So swine flu virus (and actually all influenza viruses) spread in a similar way as the novel coronavirus.

[Sarah Gregory] This avian-swine flu, is it mainly an issue on farms?

[Kristien Van Reeth] It is an issue. There, people are in close contact with infected pigs. So, yes, it is mainly an issue on swine farms and also on large agricultural fairs that house pigs.

[Sarah Gregory] Once a pig has spread it to a person, can then that person spread it to another person?

[Kristien Van Reeth] That's a very important question. And this is what we call human-to-human transmission. And that is considered a very rare event. It is already very difficult for the virus to jump from a pig to a human, and usually it stops there. This is what virologists call a dead-end infection. And, so there is no further spread in the human population. And if it does occur, it is usually very, very limited. So, just one or a few other humans. And as I said, the 2009 pandemic virus is the single known swine origin virus that's really had the capacity to spread from pigs to humans and then further in the human population.

[Sarah Gregory] So your study is about a farmer who had avian-swine flu in the Netherlands in 2019. Tell us what happened.

[Kristien Van Reeth] Yes. Back in September 2019, the farmer and part of his pigs simultaneously had influenza-like symptoms. Only the younger pigs were affected. So, the 14-week-old fattening pigs and also the gilts (these are the young female pigs that have not yet had piglets) and the older animals (the sows), they were not sick. So, we as a diagnostic virology lab, we got samples from the farmer and from the sick pigs, and also from an animal caretaker of the farm because he had been sick 2 days before the farmer. The samples had been collected 1 week (or 6 days) after the onset of disease, and we could isolate virus from the sample of the farmer and the pigs, but not from the sample of the animal caretaker. So, it is possible that the animal caretaker had also been infected but that the samples had been collected too late because influenza virus is only shed in respiratory droplets during a very short timeframe. And we had then analyzed the viruses better, and this has been done in collaboration with our colleagues from the Friedrich-Loeffler-Institut in Germany.

[Sarah Gregory] Was anyone else affected? It was just the one farmer?

[Kristien Van Reeth] We suppose (or at least it is possible) that the animal caretaker had also been infected. But there haven't been any symptoms in close contacts or family members of the farmer and the animal caretaker. And apart from them, there's also a stable hand working on the farm (a younger boy, 16 years old). He's visiting the farm only once a week, and he didn't show any symptoms. So it's most likely that there hasn't been any further spread to other humans.

[Sarah Gregory] Were the symptoms different in the pigs and the farmer?

[Kristien Van Reeth] They were actually very similar. So, both the pigs and the farmer had fever, lethargy, lack of appetite, breathing difficulties, and a cough. It is true that the symptoms of influenza in humans and swine are very similar, and usually there is not much mortality. Healthy people will not die from an infection with human flu or swine flu. And it's also important to

mention that many infections remain mild and especially in the pigs, many infections are even without symptoms.

[Sarah Gregory] Were the pigs or the farmer vaccinated?

[Kristien Van Reeth] The farmer and the animal caretaker had not been vaccinated recently, and the pigs, only part of the pigs had been vaccinated. So the sows, the reproductive animals, the older animals, they had been vaccinated and they did not show symptoms. The symptoms were in the younger animals who had not been vaccinated. It's common policy to vaccinate only the sows on a swine farm as these are the most valuable animals, and in veterinary medicine vaccination is also an economic issue.

[Sarah Gregory] Would seasonal influenza vaccine protect against this type of flu?

[Kristien Van Reeth] Most likely not. Because the H1N1 influenza virus in the seasonal vaccine is a human virus and it is just too different from this avian-like swine influenza virus. The human vaccines are meant and designed to protect against the human influenza viruses. And they are not expected to protect against swine influenza virus. But then again, as a researcher, you can never say never because the immune response to influenza is extremely complex. The response to vaccination is also affected by what we call preexisting immunity. Many humans have undergone several infections with different sorts of influenza viruses before they get their first flu shot. And it is known that this can enhance and broaden the immune response upon vaccination. So, the short answer is that the human influenza vaccine does not protect against swine flu, but there may be a very tiny little bit of cross-protection.

[Sarah Gregory] What was the purpose of this study?

[Kristien Van Reeth] I have to stress that this was not an experimental study that was designed by ourselves. It was more an experiment of nature. It is actually part of surveillance for swine influenza viruses—so, a monitoring system for swine influenza viruses. Swine flu researchers worldwide, they want to get a better picture of the influenza viruses that are out there on swine farms and the viruses that jump from swine to people. And this should actually allow us to identify the swine viruses with the highest public health risk. And we also share all data and also the viruses themselves with the World Health Organization. And based on our data and their own analyses, WHO will actually select what they call 'candidate vaccine strains'. So they will prepare very small virus stocks from some of the swine viruses that have transmitted to humans. So, they want to be prepared in case these viruses should cause a pandemic. Then they can very rapidly start vaccine production and we wouldn't have to start from scratch, like is now the case with the novel coronavirus.

[Sarah Gregory] I see, okay. So, this strain was part of a Eurasian clade. Where and when did it emerge, and how did it get to the Netherlands?

[Kristien Van Reeth] So, this virus was first discovered in pigs in Belgium in 1979 by my major professor, Professor Pensaert. And soon thereafter, the virus was also reported in the neighboring countries in Germany, the Netherlands, France. And it has become very widespread all over continental Europe, and it has remained the dominant strain in swine on the European mainland up until now. A similar virus was also introduced in the Asian swine population at a later time point (around 1993), and it is also widely circulating in pigs in China. So, this virus is widespread in most parts of Europe and in China and some other parts of Asia, but I have to

stress that you in North America have other swine H1N1 lineages. You don't have the avian-like swine H1N1 virus.

So, the evolution and epidemiology of swine influenza viruses is very, very complex. It is much more complex than the situation with human influenza viruses. And one reason for this complexity and diversity of viruses is that pigs do not travel. There is actually very little movement of live pigs between Europe and other continents, and this is why you in North America don't have this avian-like swine influenza virus.

[Sarah Gregory] I see, okay. So your article describes this strain as being antigenically related to previous isolates. What does that mean?

[Kristien Van Reeth] It means that antibodies against older avian-like swine influenza viruses still react with this virus. So, antibodies against similar viruses from 20 years ago will still bind to the present virus. So it also means that the immunity that is present in the swine population can protect the pigs to some degree against this virus, and this will prevent the virus from causing a real pandemic in pigs.

[Sarah Gregory] Did this virus have any interesting mutations? Why might these mutations be important?

[Kristien Van Reeth] Well, mutations are important if an influenza virus has to adapt to a novel host. And we did compare the virus from the farmer with the virus from his pigs, and we did find several mutations, mainly in the hemagglutinin protein. But this is no surprise. It was to be expected because influenza viruses tend to undergo mutations very, very easily. And for us as virologists, it is easy to pinpoint these mutations. But a much more difficult question is what these mutations really mean. Do they make the virus better adapted to humans? Do they enhance transmission of this virus? And so on. And this question is really difficult to answer, and many of the statements about the importance of mutations are actually mere assumptions because they are based on studies in very artificial systems, in cell cultures in the lab or in the ferret model which is too different from humans. And ideally one should be able to compare the mutated virus and the original virus in large groups of human volunteers, in large groups of the natural host. That would tell us something about the importance of the mutations for the behavior of the virus. But such experiments are just very, very difficult to perform, as you will understand I think.

[Sarah Gregory] So this is an avian-swine flu. How do bird flu and pig flu merge in the first place?

[Kristien Van Reeth] This virus has not undergone a merge. It is a wholly avian virus that has undergone small mutations to adapt to pigs. Another thing that frequently happens with influenza viruses is that they reassort. So, a reassortant is a combination virus between two or more different influenza virus. And this also frequently happens in pigs, and it can only happen when a pig is simultaneously infected with two different influenza viruses (for example, one strain from birds, another strain from pigs). And then those two viruses can swap genes and they will mix and match genes to make a new combination virus, or in virologist terms, a reassortant. Most of the swine viruses are actually reassortants with a mixture of genes from human, avian, and swine influenza viruses. So reassortment happens all the time in pigs because they are so frequently infected and they are considered real mixing vessels for influenza viruses.

[Sarah Gregory] How very unfortunate. Are there any highlights to the study we haven't covered?

[Kristien Van Reeth] I would like to highlight the important role of veterinarians in studies like this. So, the first author on this paper is my Ph.D. student Anna Parys. She is a young veterinarian and she has been the driving force behind this study. And also the veterinarian of the swine farm and the swine farmer, they have been incredibly helpful to us and they have been really essential for this study. So, diagnostic virology labs and research labs can only do a good job if they are in touch with the fields and if they get help from people in the fields. And the vets and swine farmers are really very important here.

[Sarah Gregory] Well, thank you for that. What is done to prevent swine flu? Both among the pigs themselves and the farmers. Are there different approaches in different countries?

[Kristien Van Reeth] Vaccination is the best means of preventing influenza viruses. There is a vaccine for swine flu, but it is not widely used in Europe for different reasons. Only about 20% of the farms are vaccinated, and mainly the reproductive animals (I also told you that this is an economic issue). And the protection by the vaccine is not 100%. The vaccines can never cover all of the circulating strains. And the other way around, there is (as we already said) an influenza vaccine for humans but this is actually not meant to protect against the swine strain.

[Sarah Gregory] So why is this study important to public health? I can see a variety of reasons. Does it have ramifications for countries besides the Netherlands? You mentioned WHO choosing certain strains to get a jump on vaccine production. Anything else?

[Kristien Van Reeth] No. So we hoped that studies like this will allow us to identify swine strains with a higher public health risk. And actually this virus is not only present in the Netherlands. It is present all over Europe and also in large parts of Asia. And should it ever gain the capacity to spread in humans, then it can become important worldwide. So, it has ramifications for countries besides the Netherlands, for sure.

[Sarah Gregory] You mentioned that there isn't actually a vaccine for this flu for people yet. So is there anything that farmers or agricultural workers can do to protect themselves?

[Kristien Van Reeth] There are a few simple measures that are similar to the measures we can take to prevent coronavirus infections, apart from vaccinations, such as washing hands frequently, restrict eating in animal areas, maintain proper building ventilation, and so on. But I should add that I'm in favor of vaccination against human seasonal influenza for swine farmers. And this is actually not so much to protect the swine farmer, but by vaccinating humans we can prevent transmission of influenza viruses from humans to pigs. And I want to stress that there is not only virus transmission from swine to humans, but also in the other direction. And interestingly, transmission from humans to swine is much more frequent than the other way around. And by vaccinating the farmer, we can try to limit transmission in this direction and this will help to protect the pigs against influenza viruses and to limit the emergence of novel influenza virus lineages in swine.

[Sarah Gregory] For clarity here, flu in pigs is a different health issue than emerging antimicrobial resistance in farm animals, right?

[Kristien Van Reeth] Flu in pigs has nothing to do with antimicrobial resistance. That's true.

[Sarah Gregory] I know many people wonder this: can you get a swine flu from eating pork?

[Kristien Van Reeth] No. Not at all. Because first of all, the influenza virus does not replicate in the parts of the pig that are meant for human consumption. It is in the lungs and the airway and not in the muscles. And secondly, and even more important, is that viruses cannot survive in properly cooked and roasted meat. Viruses cannot survive very high temperatures, and especially cooking, during a few minutes, it will immediately kill the virus.

[Sarah Gregory] Tell us about your job and how you became interested in this topic?

[Kristien Van Reeth] I graduated as a veterinarian a long time ago (30 years ago), and during my studies I discovered that I did not really like the technical aspect of the veterinary profession. And then in my final year, I did my master's thesis in the Department of Parasitology and I worked on a project to prevent parasitic infections in racing pigeons. And then I discovered that I really had a passion for research in infectious diseases of animals. And when I graduated there was a vacant position at the Department of Virology, so this is where I started and the focus at that time was on viral diseases of swine. And my first project was about porcine respiratory coronavirus and swine influenza virus, and at that time the focus was very much on the treatment and vaccination of animals. So, the project was to help veterinary medicine, but gradually I shifted my focus to human health. So now we are studying the public health importance of swine influenza viruses. And we are also using the pig as a model to test treatments and vaccines for human influenza viruses because humans and pigs are infected by influenza viruses that are just very similar, and also the anatomy and physiology—there are many, many similarities between pigs and humans. We believe that the pig is one of the best influenza models for humans.

[Sarah Gregory] At this time of this podcast, we have just passed the one-year anniversary of the COVID pandemic. I can hear that you're at home, because I hear church bells in the background. What have you done to cheer yourself up during this last year?

[Kristien Van Reeth] Well, this virus has actually (this coronavirus, not an influenza virus) has actually taught me a number of very useful lessons, I think. I have learned to appreciate the ordinary and appreciate everyday life. My life has changed completely because I used to travel a lot, and this has all changed. I learned to enjoy long walks in my own neighborhood, to enjoy cooking at home a delicious takeout meal, the company of just one very close friend. And I actually discovered that a simple life can give you the space to focus on what is really important.

[Sarah Gregory] I so agree with you. I have discovered that I can get so much more done by just being here and living my life at home.

[Kristien Van Reeth] I'm glad to hear that, Sarah.

[Sarah Gregory] Well thank you for taking the time to talk with me today, Dr. Van Reeth.

[Kristien Van Reeth] My pleasure.

[Sarah Gregory] And thanks for joining me out there. You could read the March 2021 article, Human Infection with Eurasian Avian-Like Swine Influenza A(H1N1) Virus, the Netherlands, September 2019, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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