Bird Flu:
Is It the Next Global Pandemic?

PODCAST 42

00:09
Dr. Jane Caldwell
Hi, this is Jane Caldwell. Welcome to the *On Medical Grounds* podcast, your source for engaging, relevant, evidence-based medical information. Today *On Medical Grounds*, we will be speaking with Dr. Matt Binnicker. Dr. Binnicker is the Director of Clinical Virology at Mayo Clinic in Rochester, Minnesota and the Chief Scientific Officer for Mayo Collaborative Services. He is a professor of laboratory medicine and pathology and is a past president of the Pan American Society for Clinical Virology. Dr. Binnicker's laboratory was one of the first in the United States to develop a molecular test to diagnose COVID-19. His research focuses on the development of novel, rapid methods to diagnose viral infections.

Hello, Dr. Binnicker. Thank you for joining us.

Dr. Matt Binnicker
Thanks, Jane. Glad to be here.

01:12
Dr. Jane Caldwell
Highly pathogenic avian influenza viruses have been detected in wild aquatic birds, commercial poultry, and backyard flocks beginning around January 2022 in the U.S. To date, over 100,700,000 birds have been affected. Recently, cases of bird flu have been detected in 171 dairy herds, and there have been 13 reported human cases in the U.S. There have also been human cases reported overseas.

We have a lot to unpack in our discussion today concerning bird flu and its recent jump into livestock and humans. So I'll begin by asking, do you think that bird flu, H5N1, has been in dairy cattle for a long time and we just didn't think to test for it? Or is this a recent occurrence due to a mutation in the bird flu virus?

Dr. Matt Binnicker
Well, Jane, it's an important question. First of all, I want to thank you for having me on. This is a very timely and important topic. And I'd start out by saying that we've known about avian influenza or bird flu for more than two decades. It's caused intermittent outbreaks mainly in migratory birds and the bird population, non-migratory birds and poultry facilities.

But as you mentioned, over the last two to three years, we've seen the largest outbreak among migratory birds, backyard bird flocks, and poultry in recorded history. With regards to dairy cattle and its detection in dairy cattle, it's really hard to know for sure whether avian influenza has infected dairy cattle in the past or not, because we haven't routinely tested for avian influenza in dairy cattle. But my best guess is that

this is more of a recent occurrence, the infection of avian influenza into dairy cattle. And that is probably due to this virus gaining some functionality, undergoing some mutations because of its extremely broad spread among bird, poultry and then crossing over into certain mammalian species before it infected dairy cattle, and those mutations have probably allowed this virus to better infect and be spread among certain mammalian species like cows. So again, hard to know for sure but I think it's more of a recent occurrence that we've started to see these infections arise in dairy cattle.

03:57

Dr. Jane Caldwell

So let's get totally molecular. Could you describe to our listeners the morphology of the influenza virus and explain how it's able to rapidly mutate?

Dr. Matt Binnicker

Absolutely. So influenza viruses are what we call RNA viruses. And I think through the COVID-19 pandemic, many in the public learned a little bit about RNA viruses because SARS-CoV-2 that causes COVID-19 is also an RNA virus. And basically what that means is influenza, SARS-CoV-2, they have a genome that's made of RNA. The other type of genome is DNA.

Now, what does having an RNA genome mean? It means that the viruses that have an RNA genome are more prone to undergoing mutations as the virus replicates. And influenza uses an enzyme. And to get technical, it's called an RNA-dependent RNA polymerase. And that's the protein in the virus that makes new copies of its RNA genome. And I like to describe that enzyme as like a young child who's just learning how to write. They can write out a sentence or a paragraph and you can make sense of what they've written, but there's gonna be spelling errors. There might be some words that are missing that should be there. And that's kind of what the influenza virus does when it replicates, is it will replicate its genome, but there may be errors in the amino acids that make up that RNA genome. And in lot of situations that doesn't change the way that the virus functions. It doesn't change how it infects cells or causes disease. But in some situations, those changes can be significant in allowing the virus to be spread more efficiently maybe causing worse disease. So again, that RNA genome makes the virus more prone to mutations. And then the last thing I'd mention is that influenza virus has what we call a segmented genome, meaning its genome is broken up into different parts. And that can lead to an event called genetic mixing. If a cell becomes infected with two different influenza viruses they can actually mix their genetic components and that may even lead to the emergence of a brand new virus that expresses new proteins and that can result in an epidemic or pandemic.

06:47

Dr. Jane Caldwell

I know that pigs are able to be infected by both bird and human influenza strains. Could that mixing occur in a pig?

Dr. Matt Binnicker

It certainly can. It is interesting you brought up infection in pigs, as that possibility with this avian influenza virus that's circulating has a lot of scientists, researchers, and public health officials quite worried. And that's because pigs have been referred to as the evolutionary playground for influenza.

Influenza viruses are adapted for mammals and some other influenza viruses are adapted for birds and pigs kind of fall somewhere in the middle. They're able to be infected by some viruses, influenza viruses that are more adapted for mammals. They're also able to be infected by influenza viruses that might be more adapted for birds. And that's probably due to pigs having on their cells proteins that we call receptors, and those receptors are actually what the virus binds to. And so the pigs are likely expressing those receptors that a variety of different types of influenza viruses are able to bind to and get into those cells. And as I mentioned earlier, that can lead to, unfortunately, a rare event, but something known as genetic mixing or reassortment, where if a pig is infected with, for example, a human influenza virus and an avian influenza virus at the same time, and those two different viruses happen to infect the same cell inside the pig, as the viruses are replicating, the genetic material, those segments, can reassemble and create a new virus. And that's actually what happened in 2009 when we saw the worldwide swine flu pandemic. And that's actually now been shown to be a virus that had components from bird, human, and swine influenza viruses. So again, pigs are a playground for these viruses coming together and re-assorting and maybe leading to the formation of new viruses that could potentially cause large epidemics or pandemics.

09:23
Dr. Jane Caldwell
You explained that really well. So what would an H5 flu strain need in order to infect humans? Would they need a certain receptor?

Dr. Matt Binnicker
Yeah, so there are a number of things that would need to happen for avian influenza to cause a large outbreak in humans. First is the virus would need to be able to gain the ability to bind efficiently to receptors in the human host and preferably from a viral pathogenesis perspective, be able to bind receptors in the upper and lower respiratory tract because respiratory transmission is probably going to be a requirement to see avian influenza cause a large outbreak in humans. Then the virus is also going to be able to need to replicate inside host cells and leave those infected host cells and go on and infect other cells inside the body.

And then the third requirement is the virus is going to need to be able to be transmitted effectively from one person to another. Again, preferably from the virus perspective through the respiratory route. If we start to see all of those things happen, then that would lead to the higher possibility that we're going to see large numbers of humans infected. To date, the virus just hasn't changed enough to be able to be efficiently transmitted from one person to another.

11:11
Dr. Jane Caldwell
Let's talk about raw milk. There are 30 states which allow the sale of raw, unpasteurized milk to the consumer in some form. In a recent National Institute of Health report, they found that the H5N1 flu virus survived in raw dairy milk, kept under refrigerated conditions for at least five weeks.

Also, when mice consume this infected raw milk, they showed signs of illness, which would suggest that drinking raw milk may pose a risk of transmission to people. Would you care to comment on this report?

Dr. Matt Binnicker
Yes, the presence of avian influenza in milk and dairy products is a really interesting aspect of this most recent outbreak. And not only is it present, but it seemed to be present at very high levels, which raises some concern about potential transmission to individuals who are exposed to raw milk during the milking process or who consume that raw milk or milk products. I think the take-home message from public health officials and infectious disease experts is that drinking raw milk is not recommended. Eating products from using raw milk is not recommended because it can be a source of a number of infectious diseases, not just avian influenza.

So I think there is the possibility that an individual could become infected with avian influenza from drinking contaminated raw milk. And so our recommendation is we are urging the public to only drink milk that's been pasteurized. And if you're consuming any animal product that might contain unpasteurized milk or even meat or eggs, you need to cook that product to a recommended internal temperature and you can get those recommended internal temperatures if you go to the Centers for Disease Control and Prevention website. They list the different types of food products and what the internal temperature should be to inactivate any potential infectious agent and that would include avian influenza.

13:33
Dr. Jane Caldwell
Is your lab developing any rapid molecular tests for the diagnosis of H5 strains in humans?

Dr. Matt Binnicker
So we have been in very close communication with the Centers for Disease Control and a number of diagnostic test manufacturers over the last six to nine months regarding this question, regarding specific testing for avian influenza. The CDC has shared its avian influenza test. They have an FDA approved test.

They've shared it with us and select other clinical testing laboratories in the event that we need to rapidly bring that testing online for patient care. We continue to work closely with the CDC and those diagnostic test manufacturers to make sure that we have H5 or avian influenza tests available to clinical labs as soon as they would be needed at scale. At this point, it's mainly been an outbreak in poultry, backyard bird flocks, and then more recently, dairy cattle. And we've seen, I think the last number was about 13 human cases since April of this year. But we're keeping very close track of the potential for human-to-human transmission because that would mean that we would likely need to bring up specific testing for avian influenza at speed and scale. And I think that we've made the connections with the right groups to be able to do so.

15:14
Dr. Jane Caldwell
I see. Could you briefly outline the process that you use for creating a rapid diagnostic test?

Dr. Matt Binnicker
Sure, so the first thing that we need to do is we look at the genome of the pathogen, in this case avian influenza, and we're looking for a region of the virus that is specific to that virus so that we're not going to be getting positive results if there's another virus present or environmental bacteria. So we want the test to be specific by only looking for a part of the virus's genome that is specific to it. Then we usually have

used over the last 20 years a technology called real-time PCR that again looks for a specific region of a pathogen and then amplifies that region of the genome hundreds of thousands or millions of times during the course of the test and then generates a fluorescent or light signal that the instrument that we use in the lab can detect and basically tell our lab staff there is genetic material in this sample that is avian influenza or it's SARS-CoV-2 causing COVID.

The process usually takes several months, can take up to a year to develop a new test like this. We've done it a lot faster. More recently with the COVID-19 pandemic, we pulled together a team of about 15 people and developed a COVID test in less than a month, but that's not routine. And so it usually takes quite a bit of time and access to samples from clinical cases. So it can be sometimes a long process to get through.

17:15
Dr. Jane Caldwell
Well, let's move from testing now to vaccinations. Do you think we will also need to have an H5 vaccination for chickens, other livestock, and maybe even humans in the future?

Dr. Matt Binnicker
So I think in the near term, over the course of the next few months, six months, there's more and more of a possibility for widespread use of avian flu vaccination among poultry and livestock, potentially some other animals, mammals that we've seen infected with this strain, because the numbers are so high. And one way to prevent or reduce the chances that the virus changes and gains the potential to efficiently infect and be transmitted among people, is to reduce the infection in birds and animals. So I wouldn't be surprised if we start to see higher rates of vaccination in birds and animals in the near term.

In the event that we begin to see spread among humans, the good news is that there already is a candidate in avian influenza vaccine that's available that the CDC has developed. And that candidate avian influenza vaccine can be shared with vaccine manufacturers to rapidly mass produce that and deploy that. I really hope that we don't get to that point where we need a human avian influenza vaccine that's needed at scale. But again, the good news is that in contrast to the COVID-19 pandemic where there was nothing existing because we didn't even know what the virus was, in this case, we've known about avian influenza for over two decades and there already is a preliminary candidate avian flu vaccine.

19:11
Dr. Jane Caldwell
That's very reassuring. I see that the CDC is funding a five million dollar program to vaccinate livestock workers against seasonal flu to reduce the pandemic risk of H5N1. How does vaccinating them with the seasonal flu help?

Dr. Matt Binnicker
Yeah, vaccinating against seasonal influenza, can generate some immunity that might be cross protective. But I do think that a more specific vaccine that's going to generate a specific antibody, and immune response to H5N1 will ultimately be needed. But there has been some work to show that there can be potentially some cross protection from other seasonal flu vaccines. But again, I really do believe that if this becomes an issue where we're starting to see more broad transmission in the human population, we won't be able to rely on seasonal flu vaccination to protect us against H5N1 and we will need that more specific vaccine.

20:33

Dr. Jane Caldwell

Do you see a role that climate change might be playing in the upsurge of the H5 flu virus?

Dr. Matt Binnicker

Yeah, unfortunately there is increasing amount of evidence and data that climate change is likely fueling the upsurge and spread of avian influenza. To start with, climate change we know has impacted the route of migratory birds, those birds that go from Northern Hemisphere to the Southern Hemisphere and vice versa and the route that they've typically taken. The temperatures, the water temperatures, the weather patterns have changed the route of those migratory birds and that has brought them into contact with other non-migratory birds and animals that they probably haven't come into contact with in the past. So the avian flu viruses that these migratory birds are infected with are now being transmitted to other birds and animals that wouldn't have occurred prior to climate change. There's also emerging evidence that climate change is making it more likely for flu viruses to survive for longer periods of time outside a host and even be spread more efficiently from one host to another. Factors like temperature, the humidity outside, even the strength of the UV light from the sun, all of those factors can influence the spread and survival of respiratory viruses like avian flu.

22:27

Dr. Jane Caldwell

Fascinating. Now as a virologist, does the threat of a new viral pandemic keep you up at night?

Dr. Matt Binnicker

Well, not yet. I haven't lost sleep over avian influenza yet. I definitely do think about what could be the next viral pandemic. I think there's two points that I would make here is since we've known about avian influenza, this is probably the point in history where there's the greatest chance that we could see a large outbreak in humans. Again, because of the scale, the number of infections that have been documented in birds and now a number of different mammalian species. So I think it just has created this environment where the virus has a greater chance of changing and mutating and adapting to humans. So there's that chance. The good news is that we're much better prepared to fight an avian influenza outbreak or pandemic than we were to fight against COVID-19. We didn't know what the virus was that caused COVID-19. We know much more about avian influenza viruses.

We didn't have a candidate vaccine for COVID-19. We have one for avian influenza. We didn't have any antivirals to fight against COVID-19. We actually have antivirals that we use for typical human influenza, and those antivirals have shown to be effective in helping to treat patients with avian influenza. So while it is, you know, concerning, we do have more tools in place to help, but we need to be diligent in continuing to make sure we have tests to make sure that we have the right ways to prevent and treat disease because again the chances of this happening are probably higher than they've ever been in history.

24:43

Dr. Jane Caldwell

Well, Dr. Binnicker, I want to thank you so much for taking time from your busy schedule to speak with us and sharing your knowledge of viral infections.

Dr. Matt Binnicker
Well, Jane, thanks for having me on the program. It was really great to talk about this important topic.

Dr. Jane Caldwell
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