

Avian Influenza A (H5N1)

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[Ted Pistorius] Welcome to this CDC podcast. I'm your host, Ted Pistorius. Today, I'm talking with Dr. Tim Uyeki of the Epidemiology and Prevention Branch in the Influenza Division. We're discussing an article about avian influenza A, or H5N1, that appears in the May 2009 issue of *Emerging Infectious Diseases*. Welcome to the show, Tim.

[Tim Uyeki] Thanks for inviting me.

[Ted Pistorius] Tell us about H5N1.

[Tim Uyeki] H5N1 is a subtype of influenza A virus. There are many subtypes of influenza A viruses, and most of these subtypes are found in birds. This subtype, H5N1, occurs mostly in birds, it's very contagious, and it can kill them. Especially, what we're talking here is a subtype that's really referred to as highly pathogenic avian influenza A H5N1 virus. This highly pathogenic H5N1 virus does not usually infect people, although some rare sporadic infections with H5N1 viruses have occurred in humans. And most of these cases have resulted from people who had direct or close contact with sick or dead poultry that were infected with this virus.

One of the features of influenza A viruses is that they are dynamic; they are constantly changing and evolving. And over time, they might develop the ability to adapt to infect and spread more easily among people. To date, there have been more than 400 cases of H5N1 virus infections in people that have been reported in 15 countries since late 2003, and approximately 60 percent of those individuals have died. More than 60 countries in the world have reported detecting H5N1 virus among birds, mostly in poultry, and this has occurred in many regions of the world, including Asia, the Middle East, Europe, and West Africa. To date, this highly pathogenic H5N1 virus has never been detected in North or South America in a wild bird, domestic poultry, or in a human.

[Ted Pistorius] Then why is H5N1 of interest?

[Tim Uyeki] For people worldwide, chickens and ducks are an important source of food, an important source of protein, and an important source of income. This highly pathogenic H5N1 virus, when it does infect—when H5N1 virus infects domestic poultry, generally there is close to 100 percent mortality. It's not always 100 percent, but it can be, and this can occur very quickly in 24 to 48 hours. And therefore this is a big threat to agriculture, as well as to public health. So in order to control the spread of the virus among birds, often many domestic poultry are killed in an area to contain the spread. This can potentially have a huge economic impact upon the country and really affect agriculture, and of course we're very concerned about public health. And the reason why we're very concerned is that, although this virus appears to be a rare cause of infection in humans, it is evolving and it is possible that this virus could cause the next influenza pandemic among people. We do see this virus causing very severe disease and high mortality among humans. Right now, most people in the world have never been exposed to

highly pathogenic H5N1 virus, and therefore most people in the world remain susceptible to the virus. And therefore, if this virus acquires the ability to infect people and spread from person-to-person in a sustained manner, it will cause an influenza pandemic in people. Right now, that has not happened; we hope it never happens, but we need to be prepared for this.

[Ted Pectorius] So tell us about the article.

[Tim Uyeki] Since 2004, Thailand has experienced outbreaks of H5N1 virus among poultry, and those have resulted in 25 human cases and 17 deaths. Most of those cases had severe disease, but the frequency of asymptomatic infection or clinically mild disease from H5N1 virus infection is unknown. And therefore, in 2005, Thai scientists conducted a study to learn more about the frequency of less severe H5N1 virus infections. Nine hundred and one study participants were enrolled from four rural villages in Thailand that had experienced poultry outbreaks of H5N1 and where at least one human case of H5N1 was confirmed. During this study, Thai scientists interviewed villagers and asked them about their exposures to sick or dead poultry or to a person who is sick from H5N1 virus. They also were interviewed about other activities, their underlying medical history, and a blood specimen was collected from them that was tested for antibodies to H5N1 virus. So the objective of this study was to determine if study participants who had been exposed to H5N1 virus-infected poultry developed an immune response, which would be detected by the presence of antibodies to H5N1 virus in their serum. So we wanted to see if there was any evidence that these individuals had antibodies to H5N1 virus. That would suggest that they had had either asymptomatic infection or had experienced clinically mild disease, but had never been identified as a severely ill H5N1 case in 2004.

[Ted Pectorius] That sounds really interesting. What did you learn?

[Tim Uyeki] We found that people in these villages who participated in the study had a lot of exposure to backyard poultry, including ducks and chickens. Nearly 70 percent of the participants reported direct physical touching or very close contact with backyard poultry. About 25 percent reported direct or close contact with sick or dead chickens, and seven percent reported close contact with an H5N1 patient while that patient was sick. Overall, of the 901 study participants from the four villages, all tested negative for H5N1 virus neutralizing antibodies. Therefore we found no serologic evidence of asymptomatic or clinically mild illness with H5N1 virus infections. Our findings suggest that, although people reported an increased risk of exposures to potential H5N1 virus-infected poultry or to people who were confirmed as H5N1 cases, all of the study participants had no evidence of H5N1 antibodies or no evidence of infection with H5N1 virus. However, it should be noted that there were some limitations to this study. The study was conducted in 2005, and that's when serum was collected from these individuals, but the exposures to H5N1 virus occurred in 2004. It's possible that some people could have developed antibody levels in 2004. In other words, they were infected in 2004, but by the time that they were sampled in 2005 and tested, their levels of antibodies could have declined.

[Ted Pectorius] Knowing this, is there anything people should do to protect themselves from H5N1?

[Tim Uyeki] Sure. There have been a number of studies that have shown that the primary risk factor for human infection with H5N1 virus is direct physical contact or close indirect contact, that means really being within about one meter of sick or dead poultry. In other words, people should not touch or not come close to sick or dead poultry. It is true that some poultry, in particular ducks and geese, can be asymptotically infected. In other words, they will be infected but look perfectly healthy and are capable of infecting other birds and also potentially capable of infecting people. But clearly, many birds, particularly chickens, that are infected, show outward signs of disease. They may just initially sit and not move around much, they look depressed, their feathers may be ruffled, they may be lying on their side, they may have swelling in their feet or different parts of their heads. And certainly there are many chickens that are infected that tend to die very quickly within 24 to 48 hours of infection.

So, clearly people should really avoid coming close or physically touching sick or dead poultry. People who work at poultry markets, people who raise chickens and ducks, should definitely protect themselves if their poultry appear ill, and in general, it's always a good idea, even if they don't look ill. Certainly in countries where this virus has infected poultry, individuals should protect themselves by wearing some kind of respiratory protection, some kind of mask, or higher level of respiratory protection, if possible. In addition, it's always good to wash your hands if you've potentially touched poultry or touched surfaces that are contaminated by poultry feces. In live-bird markets, regular cleaning and disinfecting of these markets—certainly disinfecting cages, cleaning cages. What Hong Kong has done is to segregate the types of birds that are sold. In other words, you cannot sell chickens and ducks or turkeys together. You can only sell chickens in one stall, turkeys in the next stall. And the reason for that is that all these different bird species can be infected with different kinds of viruses that can infect each other and potentially create new viruses. So, segregating birds, cleaning up the markets, this will potentially help prevent the spread of H5N1 virus and other avian viruses, and potentially reduce the risk to people who are exposed to these birds. There are really multiple strategies that are needed to prevent and control the spread of H5N1 virus, and this includes vaccinating poultry—some countries have chosen to do this. This includes disinfecting the environment; stamping out poultry that are known to be infected or suspected to be infected. Countries really need to implement very good, active surveillance among poultry and test them regularly, especially countries that are vaccinating poultry because vaccinated birds can be infected but still look well, and they are potentially a threat to transmit the virus to other birds, as well as to people, even though they may look perfectly healthy. So good surveillance is needed, improved biosecurity, compensation of farmers; this is a very complex issue. There's really no single strategy; you really need a comprehensive strategy to prevent the spread of H5N1 virus among birds. Some countries are conducting surveillance in wild birds to try to detect H5N1 virus, but really the focus has been on controlling the spread in domestic poultry.

[Ted Pestorius] It is a complex issue. So what's the public health importance of *this* article?

[Tim Uyeki] Well, the public health importance of this article is that in 2005, this study found no evidence of asymptomatic or clinically mild illness from infection with H5N1 virus in these four villages in Thailand. But this is a snapshot in time, 2005, and Thailand has not experienced many outbreaks of H5N1 among poultry since 2006. However, there are many other countries of the world that have experienced substantial outbreaks of H5N1 among poultry since 2005 and 2006,

and there are some countries of the world in which H5N1 virus is probably endemic among domestic poultry. In other words, outbreaks occur among poultry throughout the year, they're widespread, they particularly occur during the end of the year, beginning of the next year. And during these increases in poultry outbreaks, you see human cases, unfortunately, occurring. So, what I would say is that this study is very interesting, but because this virus continues to change, continues to evolve, these kinds of studies—we call them seroprevalence studies in which we test people's serum for the presence of antibodies to this virus, and we also ask them questions about what kind of exposures they had—these kinds of studies need to be done in a number of countries, and they need to continue to be done over time in order for public health to really assess the risk of H5N1 virus transmitting to humans because this risk can change as the virus evolves. So right now, H5N1 virus infection of people is very rare, but in 2009 we have seen reported cases in Egypt, in China, in Vietnam, and it's likely there have been cases in Indonesia, as well. It's possible that human cases have been missed in some countries. Now, this continues to be a public health threat. We don't know if it's going to cause a pandemic; we need to prepare for this. We don't know that if H5N1 does acquire the ability to cause an influenza pandemic, we do not know how severe that would be. But clearly, what needs to be done right now is to do a better job of controlling H5N1 virus among poultry, worldwide. So we really need to—this is a situation where public health and animal health need to work very closely, and a lot more resources need to be placed upon animal health, such as training more veterinarians, building more animal laboratories, providing training and resources to improve management and detection, prevention, and control of H5N1 virus infections in poultry, worldwide. We also need to do a better job of protecting humans. This is an educational issue to try to change behavior, but there are some strategies that we can do to really decrease the risk of H5N1 virus transmission to people. But it's a very complicated topic. People depend upon birds, particularly poultry, for food and protein worldwide. So, this is an extremely complex issue; there's no single strategy that can really be successful to prevent the spread of this virus among birds. They're really multiple strategies that need to be implemented, and this is a big challenge, but this is really a situation where human health and animal health need to work very closely together.

[Ted Pistorius] This discussion with Dr. Tim Uyeki was prompted by an article in the May 2009 issue of *Emerging Infectious Diseases*. This article, and others on emerging bacterial and viral diseases, can be read online at www.cdc.gov/eid. You can submit your comments on this interview to eideditor@cdc.gov. For *Emerging Infectious Diseases*, I'm Ted Pistorius. Thanks for listening, and have a healthy day.

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