

Historical Prevalence and Distribution of Avian Influenza Virus A(H7N9) among Wild Birds

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

Beginning in February 2013, infections with the zoonotic virus, influenza A, H7N9, have caused serious illness in humans in Shanghai, China. On April 4, the China Animal Disease Control Centre announced that the virus had been detected in samples collected from a pigeon and chickens at a market in Shanghai. On April 17, the virus was detected in a sample from a wild pigeon in Nanjing, Jiangsu Province. Chen et al. concluded that humans were infected by domestic birds; no human-to-human transmission was detected or suspected. The structure of the hemagglutinin, or HA, protein in the virus and the lack of reports of severe disease in poultry indicate that the virus exhibits characteristics of low pathogenicity in birds. Recent phylogenetic analysis indicates that the HA segment of the H7N9 subtype is closely related to a strain that was isolated from domestic ducks in Zhejiang, China, in 2011. The neuraminidase, or NA, gene of the H7N9 subtype is closely related to that of a strain that was isolated from wild bird samples in South Korea in a location adjacent to a domestic bird production facility; additionally, 6 internal genes are closely related to those of an A, H9N2, virus isolated from a brambling sample during 2012 in Beijing, China.

Little information exists on the status of A, H7N9, virus in wild birds to assess their potential as sources of human infection and dissemination of the virus to new areas. Here we report the historic distribution and prevalence of H7N9 subtypes among wild birds preceding this outbreak. This subtype was not known to cause disease in humans until the outbreak during February in China. We also examine the prevalence of individual H7, N9, and H9N2 subtypes in Asia. Finally, we estimate the sample size necessary to detect this low pathogenicity strain of avian influenza virus in wild birds.

Influenza H7N9 subtypes have been identified among wild birds globally by isolation and by using reverse transcription PCR. The H7N9 subtype has been reported among wild birds from Delaware, USA; Alberta Canada; Guatemala; Spain; Egypt; Mongolia; and Taiwan. In these 48 studies, subtype H7N9 has not been detected in wild birds in these locations in Asia: Russia, Japan, South Korea, or China. Furthermore, when subtype H7N9 was detected in Asia, its prevalence was low.

In countries within Asia, less than .1 percent of samples from wild birds tested positive for any H7 subtype, less than .05 percent tested positive for any N9 subtype, and less than .01 percent tested positive for an H7N9 strain, and less than .02 percent tested positive for an H9N2 strain. Assuming an apparent prevalence of .01 percent, we estimate that about 30,000 birds would have to be sampled to detect 1 bird that was H7N9-positive with a .95 percent probability.

Since 1988, the HA- and NA-producing genes of avian influenza subtype H7N9 have been deposited in GenBank 12 times, mainly representing isolates collected from wild bird hosts. In Asia, before this outbreak, an H7N9 strain was sequenced from a wild bird in South Korea that was sampled during 2011 in a migratory bird habitat adjacent to duck farms and also during 2011 in a sample from a mallard duck of unknown status from Japan. In 2008, the other H7N9 strain sequences collected in Asia were from a wild duck that was sampled in South Korea and from a

wild bird sampled in Mongolia. All virus sequences were obtained from ducks and domestic geese, with the exception of a chicken in China and the following from birds in the United States: a turkey in Minnesota, a guinea fowl in Nebraska, and ruddy turnstones sampled in Delaware during 1995 and 2000. Eight of the complete HA and NA genetic sequences are attributed to wild birds, 3 are attributed to domestic birds, and 1 is attributed to a bird that could not be identified as wild or domestic because insufficient information was available.

Variation in the methods used in each study makes a precise calculation of H7N9 subtype prevalence in all wild birds impossible to determine, but given the available data, we conclude that the occurrence of the H7N9 subtype in wild bird populations is rare. We also conclude that sample sizes adequate to detect the virus among wild birds will be in the tens of thousands. Publishing the sample size and genus and species of wild birds tested in China will provide a better estimate of the prevalence among these birds related to this outbreak, especially because wild song birds have been hypothesized to be a possible reservoir. Wild birds are recorded as the predominant source of H7N9 sequences, but this may be an outcome of sampling bias. Because virologists typically focus on highly pathogenic strains in humans and domestic birds, and an H7N9 subtype was not recognized as highly pathogenic, the H7N9 strain was not tested for as frequently in wild birds. The HA/NA subtype concept we used for this analysis is archaic, omitting the contributions of internal protein genes to the biology of a virus; unfortunately, it is the only widespread typing system available for influenza viruses. Subsequently, the best historic prevalence estimate of the circulating internal genes is based on the H9N2 subtype.

I'm Dr. Mike Miller, for *Emerging Infectious Diseases*, and I've been reading an abridged version of *Historic Prevalence and Distribution of Avian Influenza Virus A(H7N9) among Wild Birds*. You can read the entire article online now and in the December 2013 issue of *Emerging Infectious Diseases* at cdc.gov/eid.

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