AVIAN INFLUENZA AT THE ANIMAL-HUMAN INTERPHASE IN SOUTH AFRICA

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Introduction

On the 7th of April 2013 the State Veterinary Services, Department of Agriculture, Western Cape Government, reported actively circulating Influenza A virus. The virus was detected through the routine surveillance programme for Avian Influenza in ostriches. Specimens submitted to the Onderstepoort Veterinary Institute were confirmed as H7 positive in 3 ostrich chicks and preliminarily reported as NA1 positive in two chicks although the NA typing was inconclusive. DNA sequencing of the pathogenic marker indicated a low pathogenic genotype. Gastrointestinal symptoms were detected in some ostrich chicks on several farms but no symptoms were detected in older birds and there was no reported increase in deaths. An isolate was subsequently obtained by the Avian influenza laboratory of DELTAMUNE and sent to both the Onderstepoort Veterinary Institute (OVI) and National Institute for Communicable Diseases (NICD) for further investigation. This was done on request of the ostrich industry and the Department of Agriculture, Forestry and Fisheries in order to rule out the possibility of the isolate presenting as the new H7N9 virus from China. The isolate was shown by the NICD to be negative for the new H7N9 strain using a newly established real-time polymerase chain reaction (RT-PCR) assay which targets H7 and N9 gene fragments. The isolate was subsequently independently typed as H7N7 by the Centre for Respiratory Diseases and Meningitis (CRDM), NICD, using conventional RT-PCR and Sanger sequencing and by the University of Pretoria, Poultry research chair, Dr Celia Abolnik, using next generation sequencing.

Control measures

Western Cape Veterinary Services has instituted a 5 km buffer of movement control as well as quarantine of ostrich farms in the region and is conducting surveillance in that zone. The outbreak is confined to two farms within this radius although results from a further five farms are currently outstanding.

Background on Avian Influenza in South Africa

Several avian influenza (AI) outbreaks have been reported in ostriches over the last ten years in South Africa.[1] In the Western Cape the most recent are the highly pathogenic Influenza A H5N2 strain which was detected in 2011 in the Uniondale and Oudtshoorn areas, the low pathogenic (LPAI) H7N1 strain which was detected in the Heidelberg area in 2012 (http://www.elsenburg.com/vetepi/epireport pdf/ November2012.pdf), and most recently the H7N7 strain which was detected in the Oudtshoorn district in 2013. No increase in ostrich deaths was reported in any of these outbreaks. Large scale culling of ostriches followed the 2011 H5N2 outbreak while movement control was implemented during the 2012 H7N1 outbreak. Both outbreaks resulted in a ban on the export of ostrich meat to the European Union which has proved devastating to South Africa's ostrich industry.

Notifiable Avian influenza (NAI), according to the guidelines of the OIE (Animal World Health Organisation), includes detection of the highly pathogenic (HP) Avian Influenza strains of the H5 and H7 types in any birds, and low pathogenic (LP) Avian Influenza in poultry (http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_1.10.4.htm).

For trade purposes with the European Union ostriches are classified as poultry in South Africa and vigorous surveillance for AI is conducted on birds bred for slaughter and export. The Avian Influenza H5 and H7 strains have been detected in wild and migratory birds at a number of localities in South Africa but have so far been typed as low pathogenic (Unpublished data, Zoonoses Research unit, University of Pretoria and CRDM, NICD; Cummings et al 2011[2]). Wild birds appear to be the likely route for the spread of avian influenza across South Africa with aquatic bird reservoirs maintaining AI strains within southern Africa.[3] The highly pathogenic H5N1 strain, which has caused a high mortality rate in birds as well as in humans in several countries in Asia and in Egypt since 2004, has not been detected in South Africa.

Avian Influenza virology pathogenic types

Avian influenza strains are classified as highly pathogenic or low pathogenic based on their ability to kill six week old chicks inoculated intravenously. The HPNAI viruses cause at least 75 percent mortality in four to eight-week-old chicks. The presence of multiple basic amino acids at the cleavage site of the haemagglutinin molecule (HA0) similar to other HPNAI motifs is used as a genetic marker for HPNAI (http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_1.10.4.htm).

The haemagglutinin molecules (HAs) of low-pathogenicity AI (LPAI) viruses do not contain a series of basic amino acids at the protease cleavage site. This site is necessary for infection and is only cleaved by host proteases localized in the respiratory and intestinal organs of birds, resulting in mild localized infections in birds. Haemagglutinin molecules of high-pathogenicity AI (HPAI) viruses possess multiple basic amino acids at the cleavage site which is cleaved by ubiquitous proteases in a wide range of organs, resulting in lethal systemic infection in birds.

Avian Influenza strains do not normally kill wild birds, but highly pathogenic avian influenza strains may be highly infectious and pathogenic for poultry. Although Low pathogenic strains do not kill chickens, outbreaks of these strains may be difficult to control because they can spread undetected through populations and have the potential to revert to highly pathogenic phenotypes (reviewed by Alexander, 2007[4]).

Risk to humans in South Africa

Avian influenza subtypes H5, H7 and H9 have the ability to infect humans although human to human transmission is usually limited. Following the 2011 and 2012 H5N2 and H7N1 outbreaks in ostriches the CRDM, in collaboration with the Outbreak Response Unit, NICD, conducted sero-surveys in those high risk persons who were involved in the ostrich AI outbreaks. Screening of sera from 207 persons identified as high risk of exposure to AI types H5N2, as well as 66 sera from veterinarians, ostrich farmers, farmworkers and abattoir workers that were involved in the H7N1 outbreaks of 2011 and 2012, identified 4 people with significant HAI antibody titers greater than 1:40 for Influenza H5N2 or H7N1. These four cases included a veterinarian who was actively involved in postmortem investigations of culled ostriches, a farm worker and two abattoir workers. This survey suggests a low risk of infection for humans involved in the control of AI outbreaks with a seroconversion rate of 1.4% for Influenza A H5N2 and 1.6% for H7N1. Reported symptoms included conjunctivitis and flu-like illness although these were based on retrospective questionnaires completed at the time of specimen collection and could not be directly linked to the outbreak in question.

Pathogenicity of AI strains other than Highly Pathogenic H5N1 for humans

Human infections with Avian Influenza strains H5N2 and H7N1 have previously been detected in other countries. Several outbreaks of low pathogenic avian influenza (LPAI), highly pathogenic avian influenza (HPAI) H7N1 and LPAI H7N3 viruses occurred in poultry in Italy between 1999 and 2003. A serological survey of poultry workers found evidence of anti-H7 antibodies in 3.8% of serum samples collected during 2003 when LPAI H7N3 virus was circulating. Of 185 people tested, only one person showed symptoms of conjunctivitis during the outbreak.[5] A sero-survey conducted following the epizootic caused by H7N7 virus in the Netherlands in 2003 showed that approximately half of the individuals exposed to poultry as well as the household contacts of infected persons had anti-H7 antibodies. Symptoms included conjunctivitis without fever, upper respiratory tract symptoms, or both, and severity ranged from mild to fatal with one death reported.[5-7] Influenza H5N2 infection has been reported in humans in Japan although no symptoms were recorded.[8]

The possibility of human infection as demonstrated in this study emphasizes the need for biosecurity measures during culling procedures or during the handling of infected birds. Different strains and N types of avian influenza apparently have different infection rates in humans.

The emergence of a low pathogenicity H7N9 strain in China at the end of March 2013 resulted in severe pneumonia in 132 human cases by 14 May 2013, including 33 deaths. This outbreak serves as a reminder that the presentation of low pathogenic strains can be unpredictable in human infections. http://www.who.int/influenza/human_animal_interface/influenza_h7n9/Data_Reports/en/index.html.

Biosafety precautions

It is recommended that increased biosecurity precautions be practiced when dealing with Avian Influenza H7, H5 and H9 strains. People involved in the control of outbreaks should wear gloves, goggles and infection control masks (N95) when dealing with birds with suspected infections. Human and animal laboratories dealing with H7, H5 and H9 AI strains should only conduct molecular diagnoses in BSL-2 laboratories following the inactivation of specimens under BSL-3 conditions (BSL-2+). However, virus isolation and amplification of these strains should only occur under BSL-3 conditions because of the potential pathogenicity of these strains in humans. Furthermore, these precautions should mitigate the possibility of virus escape into bird populations and should prevent recombination between human and animal influenza strains in infected humans or in the laboratory.

Conclusion

From the sero-survey conducted in South Africa it is considered that the H5N2 and H7N1 AI strains pose a low risk of human infection and disease. Further investigation of the H7N7 strain is underway. Healthcare workers and animal handlers are encouraged to submit specimens from patients presenting with conjunctivitis, influenza-like illness or severe respiratory infections, who have a history of exposure to avian influenza positive ostriches or sick birds, to the CRDM, NICD, for investigation.

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