A Collaborative Research Project Funded by:

DFID Department for International Development

Implemented by:

Royal Veterinary College University of London

Pro-Poor HPAI Risk Reduction in the Mekong Region

HPAI Research Brief | No. 15 - Year: 2009

HPAI/H5N1 Transmission Risks: Pathways from Poultry to Humans

Maria D. Van Kerkhove

Key Findings

- To date, the occurrence of human cases of HPAI/H5N1 has been very rare.
- The full extent of asymptomatic or subclinical infection with HPAI/H5N1 is unknown.
- Several epidemiological data gaps limit our understanding of risk factors for human infection.

Highly pathogenic avian influenza, subtype H5N1 (HPAI/H5N1) first crossed the species barrier in 1997 when an outbreak of 18 human cases resulting in six deaths was identified in Hong Kong. In late 2003, H5N1 crossed the species barrier a second time infecting a family from Hong Kong that had recently travelled to Fujian Province in China. Since 2003, H5N1 has been confirmed in domestic poultry and/or wild birds in 61 countries throughout Asia, Africa and Europe.

HPAI/H5N1 in Humans

As of 30 March 2009, HPAI/H5N1 has infected 413 individuals in 15 countries. The number of human cases is not evenly distributed throughout the world and the age/gender distribution varies by country. By far, the largest number of human cases reported has been from Indonesia and Viet Nam each having reported more than 100 cases. No human cases have yet been reported in Western Europe or the Americas. Although the apparent case fatality rate (CFR) of HPAI/H5N1 is high (>60%), this may be an overestimate of the true CFR since relatively few seroprevalence

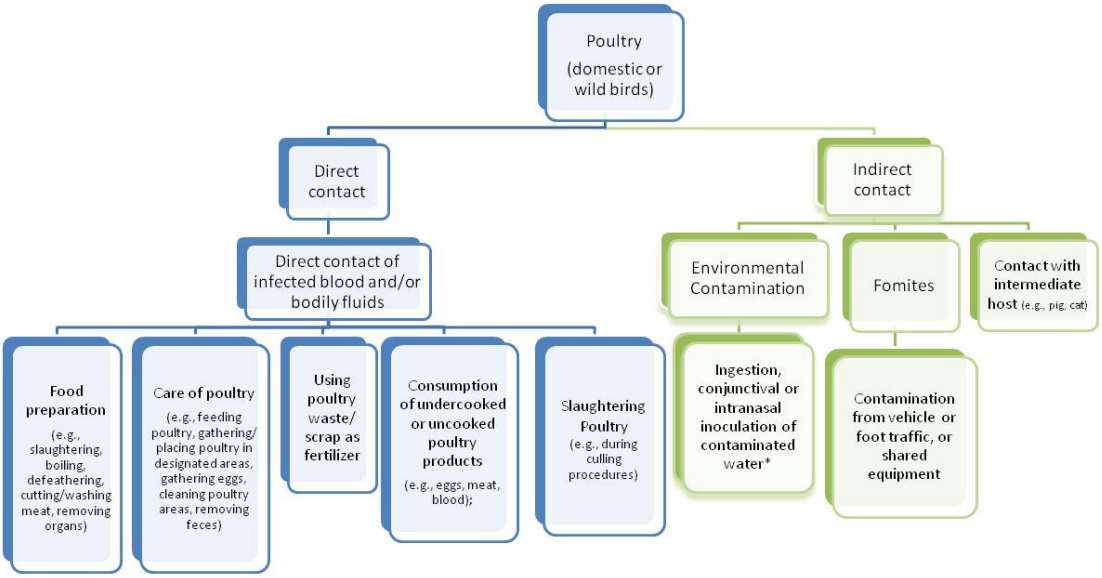
studies have been carried out in humans to determine the number of subclinical or asymptomatic cases in countries affected by H5N1 outbreaks in domestic or wild poultry populations.

Transmission of HPAI/H5N1 from Poultry to Humans

Several epidemiologic studies have evaluated the risk of transmission of HPAI from poultry-to-humans. These studies have identified several risk factors that may be associated with infection including close direct contact with poultry and indirect transmission via the environment. However, despite frequent and widespread contact with poultry, transmission of HPAI/H5N1 from poultry to humans is very rare.

An illustration of suspected pathways of poultry-to-human infection of HPAI, particularly subtype H5N1, is shown in Figure 1. Direct routes may include contact with aerosolized virus, infected blood or bodily fluids via food preparation practices (e.g., slaughtering, boiling, defeathering, cutting meat, cleaning meat, removing and/or cleaning internal organs of poultry); consuming uncooked poultry products (e.g., raw duck blood) or through the care of poultry (either commercially or domestically). Little is understood about H5N1 transmission via indirect routes, though recent studies have suggested an association between exposure to a contaminated environment (e.g., water; cleaning poultry cages or their designated areas; using poultry feces for fertilizer) and infection either through ingestion, conjuctival or intranasal inoculation of contaminated water, soil or via fomites on shared equipment or vehicles transporting products between farms. Other pathways may exist but are currently unknown.

FIGURE 1 KNOWN AND SUSPECTED PATHWAYS TO INFECTION FROM POULTRY TO HUMANS



*via swimming/bathing in water frequently used by domestic and/or wild poultry

Table 1 summarizes possible risk factors for infection identified through epidemiologic investigations of human HPAI/H5N1 cases (see full report for citations). The collective results of these studies have shown that transmission of HPAI/H5N1 from poultry-to-humans is currently limited to individuals who may have been contact with the highest potential concentrations of virus shed by poultry. This suggests that there may be threshold of virus concentration needed for effective transmission and that circulating H5N1 strains have not yet mutated to transmit readily from either poultry-to-human or from human-to-human. The mode of transmission can be quite varied throughout different countries ranging from exposure to poultry during a visit to a wet market to preparing infected poultry to swimming or bathing in ponds, which are frequented by poultry.

TABLE 1 POSSIBLE RISK FACTORS FOR HUMAN INFECTION WITH HPAI/H5N1 FROM SEROPREVALENCE STUDIES

Mode of Transmission	Risk factor
Poultry-to-human Transmission	Exposure to poultry at live/wet market
	Work in retail poultry market
	Presence of sick/dead poultry in the household
	Butchering poultry
	Preparing poultry for restaurants
	Presence of sick/dead poultry in the neighborhood
	Direct touching poultry that died unexpectedly
	Preparing/cooking (no specific practices identified) unhealthy poultry
	Feeding poultry
	>10% mortality among poultry within which poultry workers had worked within past 2 months
	Gathering poultry and placing them in cages or designated areas
Human-to-human transmission	None†
Indirect transmission	No water source in the household
	Swimming or bathing in ponds
	Changing bed linens
	Handling money

†No human-to-human risk factors for infection were identified from seroprevalence studies; however possible human-to-human transmission may have occurred in several clusters in other countries (see full report)

It is likely that direct and indirect human-poultry contact patterns differ between countries. It has been shown that there is substantial variation in the frequency of different poultry contact practices amongst populations in rural Cambodia living in close proximity to poultry. Such differences demonstrate that the potential risk of transmission of H5N1 from poultry-to-humans is not uniform across age and gender and therefore may not be uniform within or across countries. The demographic differences in human cases of H5N1 to date between countries may be because contact patterns with poultry differ between countries. However, it is also suggestive that the variation in H5N1 incidence by age may not be due to exposure alone and that there may be differences by age in intrinsic immunologic susceptibility to infection, pre-existing immunity against human influenza A virus and/or clinical presentation of disease.

Conclusions

Several important data gaps remain in the understanding of the epidemiology of H5N1 in humans:

- First, there remains considerable scope for underreporting of human cases and poultry outbreaks and we currently lack sufficient exposure data from the confirmed H5N1 cases around the world to fully evaluate other potential risk factors (e.g., the environment) for infection.
- Second, the influence of genetic and/or immunological factors on transmission is poorly understood. Although there have been several suspected clusters of H5N1 infection (largely among blood relatives) where H5N1 may have been transmitted between humans, the clusters are difficult to interpret because all suspected family members may not have been tested for H5N1.
- Third, improved knowledge is needed on all potential routes of transmission of H5N1 from poultry-to-humans and the prevalence of risky practices in human populations. Studies to date have evaluated what are believed to be the main potential routes through which people can become infected with H5N1, but we currently lack sufficient data from the confirmed H5N1 cases around the world to fully evaluate other potential risk factors for infection such as the role of water and other environmental factors.

In order to fully evaluate the occurrence of human-to-human transmission, a detailed exposure history needs to be collected from *all* suspected cases and their contacts. Direct and indirect exposure to poultry by species should also be standardized across epidemiologic studies to facilitate pooled or meta-analyses.

Collaboration between human and animal health sectors is essential to understand the risk of transmission between domestic poultry and humans. Current exposure estimates remain too general to explain the current pattern or to predict future cases of H5N1 infection in human populations; however the results of the available studies indicate that indirect exposure to poultry through the environment may play a role in transmission. Rapid, systematic and standardized collection of detailed information on poultry contact patterns in suspected human outbreaks of H5N1 would improve our understanding of transmission from poultry to humans. Detailed exposure information detailing direct and indirect contact should be included in all future human outbreak investigations as well as seroprevalence studies.

Acknowledgement: This Research Brief has been extracted from: M.D. Van Kerkhove, HPAI/H5N1 Transmission Risks: Pathways from Poultry to Humans. Working Paper available at http://www.hpai-research.net/working_papers.html

Disclaimer: The views expressed in this paper are solely those of the author and do not reflect an official position of DFID, FAO, RVC or RDRC.