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INFLUENCE OF DIRECT CONTACT WITH POULTRY ON ACQUISITION OF AVIAN INFLUENZA (H5N1): A LITERATURE REVIEW

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INTRODUCTION

Avian influenza, otherwise known as the disease associated with H5N1 virus, has been a public health concern for many years. Especially in the past decade, researchers have struggled to find effective treatments for this disease because of the severe symptoms it causes. In 1997, it was found that this virus infected both birds and humans, and the first documented case of transmission from birds to humans occurred. In 1999 in Hong Kong, further cases were documented in which poultry was responsible for transmitted the disease to humans, and it was established that poultry was the main mode of transmission of the disease. In 2003, human-to-human contact was correlated with transmission of the disease, but poultry remained the main source of transmission. Documented cases occurred in China and the Netherlands, and the U.S. was alerted to the disease and the potential for it to spread. In the years since then, epidemiologists in the U.S. have deemed avian influenza as a serious potential threat and have employed preventive health measures to combat the disease.

Avian influenza is caused by type A strains of the influenza virus and is spread by birds (World Health Organization, 2008). It occurs worldwide, and causes extreme symptoms in humans. It is also highly contagious and is caused by direct contact. The incubation period is around two to three days. Diarrhea, vomiting, and other gastrointestinal symptoms will present, and in some patients abdominal pain occurs also. Bleeding from the nose and gums has also been reported, and chest pain is one of the more serious of symptoms. Watery diarrhea without blood is the main symptoms that distinguishes H5N1 from seasonal influenza. Symptoms have been known to vary from patient to patient and some present with respiratory symptoms. Two documented cases from South Vietnam had encephalitis but no respiratory symptoms. Another case from Thailand presented with vomiting and diarrhea but no respiratory symptoms. All three of these cases were associated with direct contact with poultry.

When respiratory symptoms do present, they tend to occur early on in the disease and occur in the lower portion of the respiratory tract. Patients present with difficulty breathing (dyspnea) and difficulty speaking. The voice often becomes hoarse. Crackling upon inhalation is a common sign that the disease is developing in a human. In the middle of the course of the disease the patient begins having productive cough and bloody sputum is present. These types of symptoms were reported in recent cases of the disease in Turkey, and during the Hong Kong outbreak of 2003, severely ill patients developed pneumonia (inflammation of the lung tissue).

Once symptoms develop, clinical deterioration is rapid (WHO, 2008). Most patients with this infection have been reported to develop acute respiratory distress

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within thirteen days, and leukopenia, thrombocytopenia, and disseminated intravascular coagulation (DIC) occurs. In a sense, deterioration of the immune system occurs.

There is some evidence to suggest that antivirals are effective at treating symptoms but to date there is no cure. Oseltamivir (Tamiflu) is effective to some extent in reducing viral replication and improves prospects of survival. It slows progression of the disease but does not halt it. It is currently recommended that oseltamivir be prescribed within forty-eight hours of onset of symptoms and is still the drug of choice for avian influenza. There is significant mortality associated with H5N1 and for this reason the antiviral drug should be administered early in the course of the disease. The dose for children and adults over the age of thirteen is 150mg per day.

Because of the seriousness of the symptoms of this disease, avian influenza has become a national health concern. This paper will attempt to describe the link between direct contact with poultry and acquisition of the disease, and will describe direct contact with poultry as a significant risk factor in acquisition of symptoms.

REVIEW OF STUDIES

Su et al. (2007) studied the correlation between having the H5N1 virus and exposure (direct contact) to poultry. The study was a case-control study in that it started with individuals who already had the disease, and then looked at their exposure levels. This data was compared to a control group who did not have the disease, and then exposure level of this group was recorded. The sample size of the study varied because the authors looked at several populations, and actually compiled the results of several sub-studies, but the study which was talked about in greatest depth showed a sample size of twenty-two. This is a relatively small sample size, but because of the fact that this disease is still relatively rare, this is to be expected. To control for confounders, the authors noted that age ranges varied in the subjects examined and age ranges also varied in the control group. In order for this study to have more power, the age ranges should match more exactly, but again, because of the fact this disease is so rare, it would have been difficult to get an exact match between the experimental group and the control group.

Overall, the study showed that there is a link between direct contact with poultry and acquisition of the H5N1 virus. It was well done in that it combined results of several smaller studies, and gave an overall picture of the disease. It also implied that the virus can be spread by direct contact between humans, but did not give data on this matter to any great extent. A weakness of the study is that it had a very small sample size and did not have much data on the controls. Also, it did not give much data on the animals which the individuals were exposed to. It stated that the birds had been infected with H5N1, and that subjects came into contact with them before the meat had been fully cooked, but did not give any more data on the birds than this. This authors also made a point to state that the disease can be treated if diagnosed early in the course and that the virus is susceptible to treatment by Tamiflu and Relenza, both antivirals. They state that avian influenza could become a growing problem and a pandemic in the world if infection in humans is not controlled. They emphasize that individuals infected with the virus have a history of exposure to poultry infected with H5N1.

Sedyaningsih et al. (2007) conducted an epidemiological study on the connection between exposure to backyard poultry and acquisition of the H5N1 virus. This study was a case-control study in design, because subjects were selected based on whether they had the disease, and then the exposure level to infected poultry was determined. The subjects were individuals in various parts of southeast Asia, and a map of high-risk areas was contructed (highlighting areas in which the disease epidemic was greatest). The study took place between 2005-2006, and the sample size was fifty-four. Of these cases, two-thirds were from rural areas and forty-one of the patients died of the disease. In addition, respiratory sputum samples were collected to confirm infection with H5N1.

The authors also found that the median age of infected individuals was 18.5, and over half the patients were under 20. Six of the patients not only had direct exposure to poultry but also had poultry-related occupations, such as poultry farm working, poultry market working, and shuttlecock feather selecting. Three were poultry farm workers, two were live poultry market workers, and one was a shuttlecock feather selector.

The authors contructed a geographical map of reported cases of H5N1 in Southeast Asia between 2005-2006, and charted the areas in which humans were infected, the areas in which poultry were infected, and the areas in which poultry were not infected. Results showed that, in the areas in which poultry were not infected, no humans were infected. In addition, the areas in which humans were infected were concentrated with outbreaks of poultry infection. Authors concluded that contact with poultry and direct exposure to poultry increases an individual's risk for acquiring the H5N1 (avian influenza) disease.

Overall, the study controlled for confounding variables by comparing the regions which had infected poultry to the regions which did not have reported cases of infected poultry. I think that the study was well done in that it gave a well-detailed map of where the reported cases were, and was precise in describing its methods. It did not have a well-described control group (individuals who did not have the disease), but it did show that a high proportion of infected individuals were indeed exposed to poultry.

Horimoto & Kawaoka (2006) conducted a case-control study in Southeast Asia in which specific subjects were studied who had been infected with the H5N1 virus. The study was case-control because subjects were chosen on the basis of whether they had acquired the disease. For example, an in-depth study was conducted on a three-year-old boy in Hong Kong who had developed a severe form of the disease and later developed Reye's syndrome as a complication. The sample size of the study was 365 individuals, all residing in various parts of Southeast Asia, Europe, Africa, and the U.S. The cases linked to simultaneous outbreaks in birds (avian influenza) were located in Hong Kong, Canada, the Netherlands, and Vietnam. The number of infected cases linked to outbreaks of infection in birds was 202 cases. Therefore, of the 365 cases studied, over fifty-percent were associated with an outbreak of the epidemic in birds, in which there was an outbreak in birds at the same place at the same time. This provides strong evidence for the fact that avian influenza is transmitted by direct contact of birds and humans. In addition, the authors described the symptoms of the disease such as conjunctivitis, pneumonia, liver failure, and respiratory distress. Diarrhea, encephalitis, fever, cough, and multiple-organ dysfunction are also complications. The areas studied

included the U.S., UK, Hong Kong, China, the Netherlands, Egypt, Canada, Vietnam, Thailand, Cambodia, Indonesia, Turkey, Iraq, Azerbaijan, and Djibouti. The authors also found that when the pandemic in birds was eradicated in Hong Kong (by slaughter of all poultry), infected case in humans decreased (2006). This provides further evidence toward the transmission of H5N1 by direct contact of humans and poultry.

The study controlled for confounders by comparing those cases associated with avian outbreak to those cases not associated with avian outbreak. This is adequate control because geographical limitations make it difficult to study individuals of the same demographic group who had been exposed to poultry and did not acquire the disease. That is, the ideal control group would be individuals who did not have the disease and were of the same demographic group. The authors did not do this, but because of the difficulty in obtaining subjects the authors had adequate control. Overall, the study was an excellent study because the data was well-outlined, the sample size was relatively large (compared to other studies) and they were able to provide evidence towards a link between contact with poultry and acquisition of the disease.

Muramoto et al. (2006) conducted a laboratory study at the University of Wisconsin in order to test the molecular feasibility of transmission of the H5N1 virus from poultry to mammals. The authors also wanted to test the replication ability of the virus in mammals, once transmitted from poultry. By studying the replication of H5N1 in mice, the authors could gain evidence as to whether replication of the virus in humans in possible because the mice are serving as a mammalian analog. This study was experimental in design because it was highly-controlled in a laboratory setting and also was a cohort study because the mice examined were chosen based on exposure to the virus and then development of the disease was studied. The sample size in this case was approximately fifty mice. Authors first isolated the H5N1 virus from infected birds (chicken and duck) and then transfected the mice with the virus. They found that the virus did indeed replicate in mice and substantially high titers of the virus were detected on day three of acquistition of the virus. By day six, even higher titers were detected. The authors injected the virus from the birds intranasally at 1,000,000 PFU. Mice were anesthetized with sevoflurane prior to the procedure and virus was detected in lung tissue, brain tissue, and spleen in the days following transfection.

The authors controlled for confounding factors by having control groups in which the mice were not infected with the virus and these mice did not acquire the disease (exact numbers were not given). Authors concluded from the evidence that it is possible for mammals such as mice to acquire the virus from infected birds and that the virus does indeed replicate in mammals. This shows that direct contact with poultry may lead to acquisition of the disease in humans.

Overall, the study was a good study because it had strict control over the subjects (mice in a laboratory setting) and was able to provide microscopic data to show that the virus (H5N1) did indeed replicate, thereby showing that it is possible to transmit the virus directly from birds to mammals. A disadvantage of the study was that it was so highly controlled that one tends to wonder how generalizable this is to the real-world setting (as cases of interest occur outside the laboratory and in humans). But the study did provide evidence for the direct transmission of poultry to humans.

Vahlenkamp et al. (2008) studied the transmission of the H5N1 (avian influenza) virus from birds to humans, and also studied the replication of the virus in cats, knowing that if the virus can be transmitted from birds to cats, the potential for replication in humans also exists. The study was cohort in design, because animals were first infected with the disease (exposure) and then examined on the basis of whether they acquired the disease. The liver tissue of the cats was examined, and in all cats that acquired the disease, gross lesions were found widespread throughout the tissue. A total of nine cats were studied. The study also controlled for confounding factors because a control group in which cats were not infected with the virus was studied. This group did not acquire the disease, and the study was conducted at the Federal Research Institute for Animal Health in Germany.

Authors concluded that cats infected with the H5N1 virus obtained from poultry can develop the disease, and therefore concluded that transmission of the virus from poultry to humans is possible. Authors also discussed the fact that transmission of a similar virus, HPAIV, has already been reported to be transmitted from poultry to humans, thereby providing further evidence that H5N1 may be transmitted from poultry to humans.

The study was well done in the sense that a logical conclusion was made based on the evidence and proper control groups were included. Authors also tested the effectiveness of an H5N1 vaccine on disease control in the cats, and found that non-vaccinated cats had higher rates of development of symptoms of the disease. They found that cats not vaccinated developed symptoms of fever, anorexia, and respiratory distress, and developed these symptoms within two days of inoculation with the virus. Cats were given doses of the virus oculo-nasopharyngeally, and microscopic analysis of the infected tissue was conducted. Researchers found that acute multifocal hepatocellular coagulative necrosis was present, and intralesional influenza virus antigen was also detected.

CONCLUSION

Overall, there is a substantial amount of evidence in the literature to show that direct contact with poultry leads to acquisition of the avian influenza (H5N1) virus. For many years, there was question as to whether the virus could be transmitted from poultry to humans, and now the recent evidence has led scientists to believe that this route of transmission is indeed possible.

The epidemiologic studies discussed in this paper looked at the situation from different angles. Some studies took geographical data and were able to show that regions where outbreak of H5N1 among poultry occurred were regions of higher occurrence of outbreak among humans. Other studies showed that workers who had occupations that involved direct contact with poultry had higher rates of disease of avian influenza. Some of the occupations implicated include poultry farm working, poultry market working, and shuttlecock feather selecting.

The studies also were also a combination of case-control and cohort studies, showing that, even when examined from different viewpoints, data suggest that direct contact with poultry leads to the avian influenza disease. The studies listed were proficient in providing sufficient data to support the theory and were adequate at

controlling for confounding variables. Overall, the studies provided an adequate case to support the notion that direct contact with poultry leads to acquisition of H5N1.

The statement of the problem is essentially the fact that avian influenza is a life-threatening disease which can lead to serious respiratory and cardiac symptoms if not treated. The disease has already caused a significant amount of mortality among humans in various parts of the world (areas specifically studied include parts of Southeast Asia) and will pose a significant threat to the world population in the future. That is, if a cause for acquisition of this disease is not determined by epidemiologists, the disease could become a world-wide pandemic. Because of this threat, scientists have struggled to gather data on the epidemiology and cause of the disease, and narrow down its route of transmission so that the spread of the disease can be controlled. Knowing the source of the problem will lead to the control of the disease.

Because of the data presented in this paper, I believe that contact with poultry is indeed part of the problem, and a prime source of disease transmission. For this reason, individuals and workers at risk should take extra contact precautions when dealing with these animals. In addition, workers in parts of the world at high risk for the disease (such as Southeast Asia) should be educated on symptoms of the disease and ways to prevent its spread. Workers should be encouraged to handle the poultry with caution and to wear gloves when preparing it. The literature supports this opinion because it shows there is a correlation between contact with the poultry and acquisition of the disease. It shows that higher rates of the disease occur where workers are in direct contact with poultry, and animals exposed to the virus obtained from poultry do indeed acquire the disease.

Overall, the literature provided sufficient data to show that direct contact with poultry leads to acquisition of the avian influenza disease.

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