

Impact of Avian Influenza on U.S. Poultry Trade Relations—2002

H5 or H7 Low Pathogenic Avian Influenza

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ABSTRACT: Avian influenza (AI) viruses are Type A influenza viruses of the *Orthomyxoviridae* family. There are 15 subtypes of the virus widespread in migratory waterfowl throughout the world. It has become increasingly evident that some low pathogenic avian influenza (LPAI) H5 or H7 viruses have the capacity to mutate into the more virulent strains that cause extensive economic losses and high mortality. Recent AI disease outbreaks in several countries have increased attention and concern over low pathogenic H5 and H7 AI viruses. This heightened international concern increases the risk of unnecessary trade bans. For the US poultry industry, avian influenza continues to be a challenge to the flow of trade. On one hand, there is the increased focus of world attention on the H5 and H7 low pathogenic AI virus and the possibility of mutation. On the other hand, there are the factors contributing to our finding of infected flocks. Among these, perhaps the most important is the ever-present reservoir of virus in the migratory waterfowl population. With the discovery of exposed flocks comes the threat of trade bans.

KEYWORDS: avian influenza; Type A influenza viruses; poultry disease; trade bans; mutation

INTRODUCTION

Type A influenza viruses of the *Orthomyxoviridae* family, widespread in migratory waterfowl throughout the world,^{1,2} can be subtyped by the “H” or hemagglutinin on the surface. Of the 15 subtypes, H5 and H7 have shown an ability to mutate from low pathogenic viruses to highly pathogenic forms that cause high mortality and significant economic losses. Owing to increased international concerns over the possibility of mutation, U.S. poultry trade export restrictions have resulted from H5 or H7 low pathogenic avian influenza (AI) cases frequently in 2002. The U.S. has adopted several programs to reassure trading partners that the risk of transmission of low pathogenic AI through poultry products has been negated.

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PATHOGENICITY CHARACTERISTICS OF THE VIRUS

Avian influenza viruses are classified as one or the other of two distinct pathotypes: low pathogenic or highly pathogenic. The current Office International des Epizooties (OIE)³ Avian Influenza chapter has specific criteria for designating an AI isolate as highly pathogenic strain and thus a List A virus. Requirements are:

Any influenza virus that is lethal for six, seven, or eight of eight 4- to 6-week-old susceptible chickens within 10 days following intravenous inoculation with 0.2 mL of a 1:10 dilution of bacteria-free, infectious allantoic fluid.

For all H5 and H7 viruses of low pathogenicity, if growth is observed in cell culture without trypsin, the amino acid sequence of the connecting peptide of the hemagglutinin must be determined. If the sequence is similar to that observed for other HPAI isolates, the isolate being tested will be considered to be highly pathogenic.

Subtype H5 or H7 AI isolates that do not meet these criteria are considered low pathogenic. Losses from highly pathogenic strains are much more devastating than those from low pathogenic viruses. It was not until the ability of LPAI to become highly pathogenic was recognized that LPAI infections became an issue.

The OIE is currently considering a proposal to change the definition of avian influenza viruses of concern. Unlike the current OIE definition of avian influenza, the proposed OIE revision does not differentiate between low and highly pathogenic H5 and H7 isolates with regards to reporting to OIE. In the future, all H5 and H7 AI isolates would be treated as notifiable disease viruses. If this revision is adopted, it is reasonable to expect that additional trade requirements and restrictions will be developed and imposed by U.S. poultry trading partners even though the virus will not have changed.

MUTATIONS

With advances in diagnostics, recent outbreaks of low pathogenic avian influenza that mutated to the highly pathogenic form have been documented and studied extensively in several countries. Examples of mutation to a more pathogenic form were first found in the Pennsylvania outbreak of 1983–1984 and in other significant avian outbreaks of recent years: Mexico (1993), Australia (1994), Pakistan (1994), Italy (1999–2001), and Chile (2002). The actual molecular site and type of mutation can be identified, and shifts towards high pathogenicity can be followed through gene sequencing of the cleavage sites.

Mutation in Mexico

After H5 avian influenza was recognized in Mexico in 1993, flocks in 11 states were found to be serologically positive for the H5 virus. In just over a year, chickens were dying from infection with the highly pathogenic H5 virus. Horimoto *et al.*⁴ found the presence of multiple basic amino acids at the HA cleavage site, which confers greater cleavability. Greater cleavability allows for systemic replication beyond the respiratory and gastrointestinal tracts.

Experience in Italy

From March until mid-December 1999, a low pathogenic H7 virus circulated in the poultry populations in Northern Italy. The virus was characterized and found to meet all the criteria for classification as an LPAI. By mid-December, the virus changed from the original PEIPKGR*GLF to PEIPKGSRVRR*GLF or multiple basic amino acids at the cleavage site known to be a feature of HPAI.⁵ High mortality and great economic losses followed, particularly in the turkey industry.

AI Surveillance in the United States

Over the years, it became increasingly evident that intense surveillance for AI was necessary to protect the nation's flocks. In response, production companies perform agar gel immunodiffusion (AGID) testing on blood taken at processing from most of the flocks slaughtered as an AI screening test. Also, State laboratories investigate any case presenting with signs that may be AI as well as other randomly selected cases. These work-ups may include AGID, enzyme-linked immunosorbent assay (ELISA), virus isolation, and hemagglutination inhibition (HI) testing. For standardization in testing, the National Veterinary Services Laboratories (NVSL) in Ames, Iowa produces the antigen used for almost all AGID testing done in the United States and performs most of the HI testing. If H5 or H7 positives are found at any stage, additional identification by NVSL is made through gene sequencing, intravenous pathogenicity index (IVPI), and growth in cell culture without trypsin. Just the AGID testing alone in the United States accounts for over 1 million tests annually.

Additional surveillance is also part of the National Poultry Improvement Plan (NPIP) which provides a means of certification for AI-clean flocks, which means the flock is free of avian influenza. This category includes breeders of commercial egg-layers and breeders of meat-type turkeys and meat-type chickens.⁶

Migratory waterfowl and other wild aquatic birds are known to be the natural reservoir for AI viruses.¹ Several studies in Texas and Louisiana along the Gulf Coast have shown that up to 10% of the migratory waterfowl returning from wintering grounds in warmer countries to the south are infected with AI.⁷ The major flyways for migratory birds pass over some of the most concentrated areas of poultry-rearing in the United States, and most of these areas do not have a history of AI infections. One notable exception is AI-positive flocks in Minnesota coinciding with the appearance of juvenile migratory and recently infected ducks. When turkeys were raised on the range, these infections were a frequent event. Turkeys are reared inside now, and the incidence of AI has decreased dramatically.¹

DEALING WITH POSITIVE CASES OF LOW PATHOGENIC AVIAN INFLUENZA

Trading bans and concerns over the mutation of LPAI to HPAI have changed the way infected flocks are handled. Recently, there was an outbreak in Virginia. The US government, because of interest and concern among our industry, acknowledged the importance of LPAI and partnered with Virginia to eradicate this disease from

birds in that state. The program took over 4 months to rid the commercial flocks of the Shenandoah Valley of the virus. This action demonstrated the level of importance attributed to low pathogenic AI control in the United States.

Essential parts of any LPAI control program are extensive surveillance and monitoring of all avian species around the infected premises and epidemiologically linked to the infected premises. It is necessary to determine the extent of the infection of this easily disseminated virus so quarantines can be enacted around the entire infected area. Good biosecurity is one of the best defenses in any control/eradication effort.

TRADE RESTRICTIONS

Many countries that receive poultry and poultry products from the United States have placed bans that have significantly affected export markets. Although these low pathogenic AI serotypes have traditionally not had an impact on export trade, the increased awareness and numbers of outbreak events have raised concerns among the international animal health community. There has been and continues to be a significant amount of discussion within the international community on both the economic impact on trade and the regulatory implications.

It is difficult to predetermine which AI finding will generate a ban or what type of ban might follow. The trading partner notifies the United States Department of Agriculture that it is placing the ban and the extent of the area that is banned from exporting poultry products to their country. Bans were enacted on a nationwide basis for an LPAI-positive flock of 4,000 ducks supplying a local market. Bans were put in place on a state with a positive serological finding even though, despite multiple attempts, the virus was never isolated.

Equally as difficult is determining when a ban will end and how to best facilitate the resumption of trade. In 2002, new methods were used to satisfy various concerns raised by trading partners. Negotiations with a number of countries led to agreements to provide immediate notifications of AI disease findings, to provide certifications, to attend arbitration, and to enact regionalization. Other methods to satisfy concerns, such as compartmentalization, which means considering the different poultry industries as separate from each other, were discussed.

COMMUNICATION PLAN

As part of the negotiations with trading partners for regionalization when an infected flock is found, APHIS has supplied current and timely notifications of all aspects of the disease outbreak. Notifications include the date of the initial finding, the subtype and pathogenicity of the virus, the species and type of poultry, the size of the flock, and the location. Immediately, quarantines are put in place and surveillance testing begins. Follow-up reports to the various countries include any additional positive findings and the depopulation date or the disease management plan.

Certification for Exports

Additional information relative to the disease history of birds whose meat is to be exported is being required. Requirements vary from simple statements to very complicated regionalization schemes with extensive testing. All of the increased record-keeping for the system and increased testing to satisfy the requirements of the certificate have caused the human and economic resources to be redirected.

For some countries, an AI certification system has been devised. A monthly certificate must go from the State veterinarian and the Area Veterinarian in Charge to the Food Safety and Inspection Service (FSIS), Inspector in Charge (IIC) at the plant exporting poultry products. These certificates enable the IIC to sign the detailed veterinary certificate that goes with the exported product.

When any avian influenza is identified by NVSL located in Ames, Iowa, the Federal Area Veterinarian in Charge in the appropriate State and the Avian Influenza Coordinator (AIC) at the Animal and Plant Health Inspection Service headquarters are notified. The health certificate for avian influenza reflects those findings. The State veterinarian and the AVIC sign the certification statement each month. In addition to the "AI-Free" status, the statement has three main categories for positive findings and the resulting actions including extensive testing that must be taken for any positive results.

Testing for Export

Trading partners have the right to protect the health of the poultry flocks in their country in addition to their allowing the flow of trade. Some countries have placed restrictions, and in other instances to maintain the market, we must meet other requirements. For example, the US poultry industry is faced with a requirement to test all poultry and flocks producing poultry products with an extensive 59 sample testing program by hemagglutination inhibition (HI) for H5 and any subtype of avian influenza that has been found in a state over an undefined period of time. This testing must be done in addition to the AGID test. It is difficult to understand the scientific rationale behind the requirement for the HI test on sera from AGID-negative testing. While it is true that the response to the test wanes in time, it is months before the AGID results become negative for a flock. Along with the duplication in testing is large sample size. Is there a need for 95% certainty of finding a 5% infection in the flock? These test results must accompany the product that is shipped.

What the Future Brings

Discussions within the United States with industry, regulatory officials, and other interested parties have led to decisions to develop a national AI H5/H7 program. This program will include periodic testing of all commercial turkey, broiler and layer breeders, and egg-laying birds. Commercial meat birds, chickens, and turkeys will be tested also. In addition, backyard flocks and game fowl will be monitored.

A separate program is being developed to prevent, control, and eradicate H5 and H7 from live bird markets. The National Live Bird Market System Program for Low Pathogenic Avian Influenza has started with trials of bird identification systems to enable inspectors to check for premises identity and test certificates. All birds entering the markets are required to be from test-negative flocks.

CONCLUSIONS

For the US poultry industry, avian influenza continues to be a challenge to the flow of trade. The circumstances around the issue have multiple contributors. On one hand, there is the increased focus of world attention on the H5 and H7 low pathogenic AI virus and the possibility of mutation. On the other hand, there are the factors contributing to our finding of infected flocks. Among these, perhaps the most important is the ever-present reservoir of virus in the migratory waterfowl population. With the discovery of exposed flocks comes the threat of trade bans. There does not appear to be any relief in sight.

UPDATE

APHIS (Animal and Plant Health Inspection Service) has received funding for the live bird market avian influenza program. The program includes monitoring of source flocks, transporters and consolidators, and birds in the markets. Requirements of the program include market closures, downtime, sanitation, and registration. Haulers must have appropriate and working sanitation equipment. Only registered haulers may transport birds to the markets. Federal and state employees will perform monitoring activities to include sample collection and record reviews as well as visual inspections of the premises.

The expanded National poultry Improvement Plan includes “Avian Influenza Clean” commercial flocks through a nationwide monitoring program for layer, turkey, and broiler flocks produced in the United States.

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