Avian Influenza is a respiratory and/or systemic disease of poultry with the potential to cause rapid and severe illness, as well as high mortality, and which has major economic implications.

There are two main categories of avian influenza A viruses: Low Pathogenicity Avian Influenza (LPAI) and Highly Pathogenic Avian Influenza (HPAI). Various LPAI strains are known to be carried by wild waterfowl and shorebirds, which are typically asymptomatic. When the virus is transmitted to naive, domestic poultry, especially chickens and turkeys, some LPAI strains can mutate to the HPAI form and cause more serious clinical signs and high mortality. General avian influenza is often referred to as "bird flu" by the general public. Another name for HPAI is "fowl plague".

The HPAI strains can spread very quickly, are highly contagious, and can result in poultry quarantine areas and international trade bans for the U.S., especially if commercial poultry flocks become infected. For example, the U.S. HPAI outbreak that occurred from December 11, 2014 to June 16, 2015, was the country's largest and most significant animal health emergency ever recorded. The outbreak began in captive wild birds and backyard flocks in the northwestern U.S. and spread to commercial premises in 21 states. The commercial turkey industry in Minnesota and egg-laying chicken companies in Iowa were most affected; 7.4 million turkeys and 43 million layers died from the disease or were depopulated to contain the disease. Direct cost estimates related to disease response activities of poultry depopulation, disposal, virus elimination, testing, and indemnity payments were close to $1 billion; making this HPAI outbreak the most expensive U.S. animal health emergency documented. The indirect cost of the economic loss to the commercial industry was estimated at $3.3 billion or more.

Etiology

Avian influenza viruses belong to the Orthomyxoviridae family of RNA viruses. Influenza A viruses are typically classified based on proteins on the surface of the virus, called hemagglutinin (HA) and neuraminidase (NA). There are currently 16 HA subtypes and 9 NA subtypes known to infect avian species, with 144 possible HA/NA combinations that could affect birds. The H5 and H7 subtypes are of greatest concern because they can mutate to the HPAI form, which can cause mortality up to 100% within 24 to 48 hours in susceptible birds. All other avian influenza strains are classified as LPAI strains, which generally have milder clinical signs such as respiratory disease, conjunctivitis, and reduced egg production.

There are rare reports of limited human infection with H5 and H7 avian influenza subtypes in Asia, Africa, and Europe, in which people with direct contact with infected poultry developed respiratory illness and fever, some of which resulted in hospitalization and deaths. Other mammals can also become infected with avian influenza viruses including pigs, cats, dogs, seals, tigers, and leopards. Pigs are proposed to be a "mixing" vessel for co-infection with bird and mammal influenza viruses, with the potential to develop a new reasserted strain that could infect people.

Susceptibility of the agent

Avian influenza viruses are RNA viruses with a lipid envelope which is susceptible to inactivation by most common disinfectants. The U.S. Environmental Protection Agency has a published list of disinfectants with labeled claims to be effective against Avian Influenza:

The unprotected virus is fairly fragile in the environment. However, organic matter, low temperature, and high humidity can increase its ability to survive outside a host. For disinfection of poultry premises, it is important to first remove the organic material (i.e. manure, dirt, egg material, nasal secretions, etc.) by scraping, followed by cleaning with water...
and soap/detergent. The virus can survive in organic material, making disinfectants ineffective. Apply the disinfectant according to the product label directions.

Heat and natural sunlight can aid in inactivation of avian influenza viruses if most of the organic material has been removed. Temperatures between 38 and 49 °C (100 and 120 °F), held consistent for a total of 7 days, can be used as a heat treatment to disinfect a poultry house.

Infected carcasses, manure, litter, and eggs should be disposed of properly. Some disposal options include composting, incineration, burial, and transportation to landfill, but disposal must be conducted in accordance with local environmental and state/federal Department of Agriculture regulations to ensure that the virus does not continue to spread or contaminate the environment.

Avian influenza cannot be transmitted through properly cooked poultry meat and egg products.

**Occurrence**

LPAI occurs regularly in poultry, especially those with exposure to wild waterfowl, aquatic birds, or contact with other infected poultry and contaminated equipment or personnel. Most cases of avian influenza occur during the fall, winter, and spring due to migration of wild birds and the preservation of the virus by colder temperatures.

See the attached table of reported HPAI incidents in the U.S.

**Pathogenesis**

Wild aquatic birds, such as wild ducks, geese, swans, seagulls, and shorebirds, are natural reservoir hosts for avian influenza A viruses. Wild waterfowl can potentially carry LPAI viruses continuously during fall and spring migration over long distances. Younger ducks and geese may succumb to HPAI with signs of depression, inappetence, diarrhea, and death, but adult wild waterfowl are generally resistant and do not show clinical signs. Wild birds can contaminate areas nearby poultry with the virus which can be later transported into the poultry houses. Airborne/wind-related transmission is also possible, which is thought to have contributed to the disease spread in the Midwest U.S. during the 2015 HPAI outbreak. Mechanical transmission of the virus by rodents, small mammals, and songbirds is also possible.

The virus can also be spread via indirect contact and transferred via contaminated shoes, clothing, hands, and equipment used (i.e. bird cages used for holding or transportation, shovels used for handling manure, feeders, waterers, etc.).

Birds infected with avian influenza can spread the virus directly to other birds via respiratory, nasal, ocular, and fecal secretions. Infected carcasses can contain high levels of virus in tissues, so it is important to remove and secure dead carcasses promptly to avoid cannibalism and environmental spread. Some virus transmission may also occur via infected egg shells and internal egg contents. Typically, avian influenza viruses kill the embryo, so transmission to chicks is generally unlikely but may be possible with milder LPAI strains.

The incubation period before birds show clinical signs can vary greatly depending on the virus strain, amount of virus, route of exposure, and species affected. The incubation period can be very rapid (<24 h), especially for susceptible gallinaceous birds. LPAI viruses typically have a longer incubation period (3 to 21 days). During this period, viral particles are incorporated into cells via a receptor mediated endocytosis. Inside the endosome the HA protein must be cleaved for the envelope to fuse with the membrane of the endosome. In LPAI virus the enzymes capable to cleave this protein are present in only a few anatomical sites (respiratory and intestinal epithelium). However, HPAI viruses have a modification in their amino acid sequence that allows the HA protein to be cleaved by ubiquitous enzymes. As a consequence, HPAI viruses can infect (and destroy) a wide variety of cells and systems. After infection antibodies against a variety of the proteins contained in the AI virus are produced. It seems that mostly antibodies targeting the HA are conductive to the development subtype specific immunity. Infection with viruses bearing a different HA protein will be susceptible to develop the disease.

Gallinaceous birds (chickens, turkeys, quail, guineas, partridges, etc.) typically spread the virus for shorter periods of time compared to waterfowl (ducks, geese), which are carriers and may intermittently shed avian influenza for longer periods.

**Clinical manifestations**

LPAI viruses can present with the following clinical signs:

- **Respiratory signs**: coughing, sneezing, gasping; nasal and/or ocular discharge; blue or purple discoloration of combs, wattles, or legs (Figure 1); swelling around the eyes and face (Figure 1)
- **Decreased egg production**: soft or misshapen eggs
- **Red discoloration of the shanks / feet due to subcutaneous ecchymotic hemorrhages** (Figure 2)
- **General/non-specific signs**: depression, ruffled feathers, decreased food and water consumption, watery green diarrhea
- **Possible mortality**, especially if coinfection with other poultry diseases

HPAI viruses may present with these signs:

- **Sudden, acute death which can approach 100% depending on the bird species and strain susceptibility**
- **Neurological signs** such as twisted neck, difficulty or inability to walk
- **See above signs for LPAI**
Necropsy findings

- Poultry that are infected with LPAI may have petechial (pinpoint) and ecchymotic (round or irregular) hemorrhages throughout the body due to rupture of blood vessels. This hemorrhaging is often seen in the trachea, larynx, proventriculus, epicardial fat, and serosal surfaces. LPAI infections can display varying amounts of blood congestion, hemorrhages, and necrosis of internal organs gross lesions. Egg-laying birds may also show shrinkage or involution of the oviduct due to the effects on the reproductive tract.

- Birds that die quickly of HPAI may show minimal gross lesion change on necropsy, which might consist of dehydration and congestion (reddening) of viscera and muscles. In HPAI cases in which the birds do not die acutely, the lesions are more severe compared to LPAI. Necrosis of the liver, kidney, spleen, and lungs may be observed with fibrinous exudate in the air sacs, oviduct, pericardial sac, or peritoneum. Due to the vascular damage, edema and hemorrhage can be seen in multiple organs.

Diagnosis

Confirmation of avian influenza via laboratory diagnosis is important because the virus can mimic many other poultry diseases. Diagnostic tests may include:

- Serology Blood Tests, i.e. Agar Gel Immunodiffusion Test (AGID), Enzyme Linked Immunosorbent Assay (ELISA) - used as a screening test
- Antigen Capture Immunoassay Tests (ACIA) i.e. FluDetect - detects antibodies in swab specimens from sick or dead birds
- Real-Time Reverse-Transcriptase Polymerase Chain Reaction (rRT-PCR) – detects the presence of viral RNA from swab samples; tracheal or oropharyngeal swabs are preferred for gallinaceous birds, while cloacal swab samples are the specimen of choice for waterfowl
- Virus isolation (VI) – determines if viable or live avian influenza virus is present by growing virus in embryonated eggs

Relevant differential diagnoses

Newcastle disease, avian paramyxovirus, infectious bronchitis, infectious laryngotracheitis, chlamydia, mycoplasma, avian cholera (pasteurellosis), infectious coryza, acute poisoning (i.e. aflatoxin, insecticides, rodenticides), duck plague (duck viral enteritis)

Coinfection with other diseases commonly occur, especially with LPAI.

Because avian influenza viruses can mimic many other poultry diseases, it is important to get a laboratory diagnosis. The Pennsylvania Animal Diagnostic Laboratory System (PADLS) can accept bird carcasses and swab samples from poultry and conduct testing to rule out cases of avian influenza, free of cost for backyard poultry flocks. There are three veterinary PADLS laboratories across the state: Pennsylvania State University (Penn State) in State College, Pennsylvania Veterinary Laboratory (PVL) in Harrisburg, and University of Pennsylvania – New Bolton Center (U Penn – NBC) located in Kennett Square with a field laboratory also located in Manheim/Lancaster County.

Prevention

There is no effective treatment of avian influenza, therefore efforts are aimed at prevention and disease control. The U.S. Department of Agriculture – Veterinary Services (USDA VS) emphasizes 6 steps to protect backyard poultry against avian influenza and other diseases.

1. Keep your distance
2. Keep it clean
3. Don't haul disease home
4. Don't borrow disease from your neighbor
5. Know the warning signs of infectious bird diseases
6. Report sick birds

Vaccine effectiveness is highly dependent on strain type, and there is no cross-protection across the 16 hemagglutinin subtypes. Vaccination in the U.S. for HPAI strains or LPAI H5/H7 could cause international trade implications, so its use is reserved for special-case scenarios and emergencies. For these reasons, avian influenza vaccination is uncommon, and the focus is on biosecurity disease prevention. Some limited killed, injectable vaccination in commercial chickens and turkeys may occur as a preventative measure, but typically not in response to an outbreak.

Rapid reporting of suspected cases, and follow up testing to rule out avian influenza is critical for control. PA Department of Agriculture has 24/7 emergency hotline (717-772-2852) in which suspected cases should be reported as soon as possible to prevent potential disease spread. If there is no response from PA Department of Agriculture, the USDA – VS hotline can also be called at (866-536-7593).

References and suggested reading


Authors

Gino Lorenzoni
Assistant Professor, Poultry Science and Avian Health
agl20@psu.edu
814-863-7302

Chrislyn Wood Nicholson, DVM MPH
Poultry Specialist / Veterinary Medical Officer
USDA APHIS VS
chrislyn.n.wood@usda.gov

extension.psu.edu

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