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## 2. Avian influenza and the viruses that cause it

Avian influenza is caused by influenza viruses that are common in wild birds and occasionally infect poultry. When poultry are infected, they may have no disease, mild disease or very severe disease. Chickens, quail and turkeys are especially susceptible, while ducks more commonly show no disease but act as a reservoir for the virus. Other poultry species, including guinea fowl and pheasants, and also ostriches, can become affected. While wild birds are generally not affected by the AI viruses that they carry, they can occasionally suffer disease. This has been observed as a result of infection with the H5N1 virus in Asia and parts of Europe and may be a result of the virus's first becoming highly virulent in domestic birds.

Influenza viruses have two main surface antigens: haemagglutinin (H) and neuraminidase (N). There are many H and N subtypes, but highly pathogenic avian influenza viruses have historically been H5 and H7. In addition, H9AI viruses are widespread around the world and known to cause sufficient morbidity to warrant their monitoring to see if they develop into more virulent forms. The avian influenza virus currently causing the major epidemic in Asia is H5N1, with some occurrences of H5N2 being reported as well. The viruses that have caused disease in Pakistan in recent years are H7N3 and H9N2, but H5N1 has also become a problem of great concern there. AI viruses are also classified by pathotype – highly pathogenic (HPAI) and low pathogenic (LPAI) – a biological characteristic of the virus's virulence in chickens. Currently, the pathotype definition has been expanded to include the genetic sequence coding for basic amino acids in the cleavage site of the H protein. All AI viruses that have these sequences at the critical site are considered notifiable, and the viruses are denoted as HPNAI (highly pathogenic notifiable avian influenza) and LPNAI.

The known evolution of H5N1 viruses in Asia began in 1996 in southern China with the identification of an HPAI virus (Goose/GD/96) that was fatal to geese in Guangdong province. In 1997, the Hong Kong Special Administrative Region experienced the first major outbreak of H5N1; it was associated with seven human deaths, alerting the international community for the first time of the potential threat caused by this new strain of this virus as a true zoonosis. Though exact dates and figures remain unknown, retrospective analysis reveals that in mid-2003 the H5N1 virus strain of AI expanded its territorial enclave elsewhere in China. Within months – late 2003 to early 2004 – numerous countries in Asia reported its occurrence, and by late 2007 the disease was reported in over 60 countries. Though many or most countries have been able to limit its spread or occurrence in poultry, the virus has become endemic in several key countries – a worrisome reality because of three main factors: (1) high poultry density and duck-rearing practices, (2) wildlife habitats for possible maintenance in long-term or continuous virus circulation within the wild bird population and (3) unregulated trade.

In mid-2005, following a major outbreak in wild birds in Lake Qinghai located in western China, H5N1 outbreaks were detected in the Russian Federation, Kazakhstan and Mongolia. The disease was then reported in Romania, Turkey and Croatia in October 2005, confirming the westward spread of the virus and the potential threat to other countries and continents still free of the disease. The epidemic eventually reached Africa, where it was first reported in Nigeria in February 2006.

The emergence of the H5N1 strain in Asia and its subsequent spread to other continents is a result of, among other factors, years of rapid development of unregulated poultry production to meet the increased demand for animal protein. Highly concentrated domestic poultry production in densely human-populated regions and a rapid evolution of animal and farming production systems have provided the ideal conditions for the emergence of new virulent strains of avian influenza. Although there are numerous commercial-level poultry operations in countries affected by the recent H5N1 HPAI strain, the majority of such operations are still “backyard” activities where surveillance and biosecurity are minimal and farmers have little knowledge of the potential linkages between their husbandry activities and disease spread or associated human health risks. The exchange between commercial poultry species and backyard farms is often very active, allowing for the transmission of this virus between these two not-so-separate sectors. Furthermore, farmers who depend on their fowl for subsistence are reluctant to destroy their flocks or to inform the authorities about sick birds, preferring to attempt to sell them or eat them, thus contributing to the subsequent spread of the disease.

The transboundary trade in poultry and poultry products, both legal and informal (traditional), is likely to have contributed to the spread of HPAI viruses. Long land borders exist between many of the infected and at-risk countries, and the smuggling of poultry and poultry products across many of these borders is acknowledged, as is the practice of intercommunity gamecock fights.

## 2.1 CLINICAL SIGNS

The clinical signs of AI infection are variable and influenced greatly by the virulence of the viruses involved, the species infected, age, concurrent viral or bacterial disease and the environment. The virulence exhibited in chickens can vary during an outbreak.

### Infection with non-pathogenic viruses

- There are no clinical signs in infected birds, so evidence of exposure is determined by serological conversion.
- Some of these viruses have the potential to become virulent through genetic mutation.

### Infection with low or mild virulent viruses

- Clinical signs in chickens and turkeys range from inapparent to mild or severe respiratory disease and can be confused with infectious laryngotracheitis and other respiratory tract infections.
- Mortality ranges from 3 percent in caged hens (layers) to 15 percent in meat chickens (broilers).

- Egg production in layers can sometimes drop to 45 percent of the expected egg yield of a large flock, returning to normal levels of production in 2–4 weeks.
- Mutation to virulence has been demonstrated in outbreaks.

### Infection with highly pathogenic viruses

- In peracute cases involving sudden death, as in the 2004–2005 outbreak in Viet Nam, clinical signs may not be seen and mortalities may occur within hours after onset of depression (i.e. despondence, inactivity, lethargy, etc.). Overall mortality rates for peracute/acute cases nearing 100 percent have been reported.
- In acute cases, mortalities occur as early as 24 hours after the first signs of the disease, and frequently within 48 hours. In other cases, more diverse visible signs are seen and mortalities can be delayed for as long as a week.
- Clinical signs in chickens and turkeys include severe respiratory distress with excessively watery eyes and sinusitis; cyanosis of the combs, wattle and shanks; oedema of the head and eyelids; ruffled feathers; diarrhoea and nervous signs.
- Eggs laid after the onset of illness frequently have no shells.
- Some severely affected hens may recover, but they rarely come back into lay.

The disease in turkeys is similar to that in chickens, but it is often complicated by secondary bacterial infections such as those resulting from fowl cholera (*Pasteurella multocida*), turkey coryza (*Haemophilus gallinarum*), or colibacillosis (*Escherichia coli*).



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Figure 1: Oedematous cyanotic comb and wattle of a chicken with highly pathogenic avian influenza



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Figure 2: Oedematous wattles

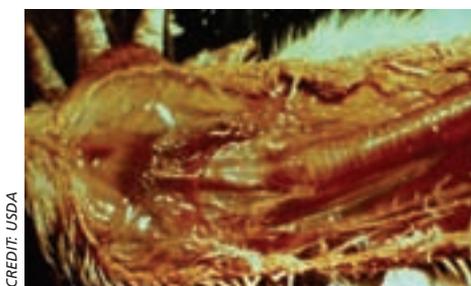
## 2.2 GROSS PATHOLOGY

In many cases, poultry dying from the peracute form of the disease lack visible gross pathological lesions. With acute infections in chickens, there is severe lung congestion, haemorrhage and oedema in dead chickens, while other organs and tissues appear normal. More varied visible lesions are seen in chickens surviving 3–5 days, including congestion and/or cyanosis of the comb and wattles and swollen heads. The changes in the combs and wattles progress to depressed areas of dark red to blue areas of ischaemic necrosis. Internally, the characteristics of acute infections with viruses causing HPAI are haemorrhagic, necrotic, congestive and transudative changes. The oviducts and intestines often have severe haemorrhagic changes.

As the disease progresses, the pancreas, liver, spleen, kidney and lungs can display yellowish necrotic foci. Haemorrhages (petechial and ecchymotic) cover the abdominal fat, serosal surfaces and peritoneum. The peritoneal cavity is frequently filled with yolk from ruptured ova, associated with severe inflammation of the airsacs and peritoneum in birds that survive 7–10 days. Haemorrhages may be present in the proventriculus, particularly at the junction with the ventriculus (gizzard).

In cases resulting from mild pathogenic avian influenza viruses, lesions may be seen in the sinuses, characterized by catarrhal, serofibrinous, mucopurulent or caseous inflammation. The tracheal mucosa may be oedematous with exudates varying from serous to caseous. The air sacs may be thickened and have fibrinous to caseous exudates. Catarrhal to fibrinous peritonitis and egg yolk peritonitis may be seen. Catarrhal to fibrinous enteritis

*Figure 3: Oedematous wattles dissected*



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*Figure 4: Haemorrhage in the mesentery of the small intestine*



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*Figure 5: Large haemorrhages in the fat on the serosal surfaces of the abdominal organs*



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*Figure 6: Haemorrhage in the muscle and the fat around the heart*

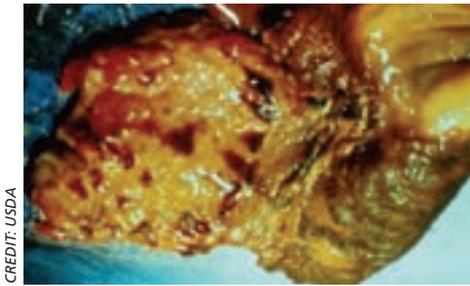


Figure 7: Ecchymotic haemorrhages in the proventriculus

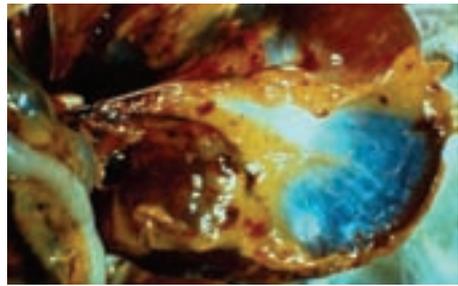


Figure 8: Haemorrhage in the muscle and the fat around the gizzard

may be seen in the caeca and/or intestine, particularly in turkeys. Exudates may be seen in the oviducts of laying birds (Easterday *et al.* 1997). Histopathological lesions seen in the gross changes described here are not definitive for HPAI, although vasculitis in the brain and other organs may be highly suggestive of the disease.

### 2.3 DIFFERENTIAL DIAGNOSIS

The following diseases must be considered in the differential diagnosis of virulent AI:

- Other diseases causing sudden high mortality:
  - Newcastle disease
  - infectious laryngotracheitis
  - duck plague
  - acute poisonings
- Other diseases causing swelling of the combs and wattles:
  - acute fowl cholera and other septicaemic diseases
  - bacterial cellulitis of the comb and wattles

Less severe forms of the disease may be confused with, or complicated by, many other diseases with respiratory or enteric signs. HPAI should be suspected in any disease outbreak in poultry that persists despite the application of preventive and therapeutic measures for other diseases, or when the epidemiological context is highly suggestive of the introduction of the infection.