

Risk assessment of acquiring Avian Influenza from Poultry Products: Hazard identification

2.1 Avian Influenza viruses

Influenza A viruses are negative-sense, single-stranded RNA viruses classified in the family Orthomyxoviridae, with a size ranging from 80-120nm (Spackman, 2020). Domestic poultry are especially vulnerable due to the intensive nature of poultry farming. The virus can spread rapidly, causing outbreaks in commercial flocks.

2.1.1 Subtypes and pathogenicity

Type A influenza strains are classified by the serological subtypes of the primary viral surface proteins; the hemagglutinin (HA) and neuraminidase (NA) (Hutchinson, 2018). Sixteen HA subtypes and nine NA subtypes can be found in birds, which are the primary reservoir for the virus (CDC, 2022b). AI can be divided into high pathogenicity (HPAI) and low pathogenicity (LPAI) strains based on their ability to cause disease in poultry (Liu et al., 2021). Mutations from LPAI to HPAI are possible and have been described in Australia, the Netherlands, UK and Germany (Byrne et al., 2021). HPAI results in high death rates (up to 100% mortality within 48 hours) in some poultry species such as chickens and turkeys, while LPAI viruses may cause no disease or only mild clinical signs (such as ruffled feathers and a drop in egg production) and may go undetected (Liu et al., 2021). The vast majority of human cases have reported close contact with poultry; there is no reported evidence of sustained human-to-human transmission ("WHO, 2023,"). It's worth noting that LPAI and HPAI refers only to the specific criteria in infected poultry, not the severity of illness with human infections (CDC, 2022c). The clinical illness associated with human infections with AI do not correlate with viral pathogenicity in infected birds.

The primary risk factor for human infection appears to be direct or indirect exposure to infected live or dead poultry or contaminated environments, such as live bird markets. Slaughtering, defeathering, handling carcasses of infected poultry, and preparing poultry for consumption, especially in household settings, are also likely to be risk factors. There is no evidence to suggest that AI viruses can be transmitted to humans through properly handled and cooked poultry or eggs. H5N1 human cases have been linked to consumption of dishes made with raw, contaminated poultry blood (WHO, 2018).

2.1.2 AI virus circulation in poultry populations in the UK in 2021/22 and 2022/23 seasons

The AI strain associated with the current outbreak belongs to the H5N1 clade 2.3.4.4b. Twelve different genotypes of H5N1 have been identified in commercial poultry and wild birds by WGS throughout this current outbreak (UKHSA, 2022).

The first genotype detected in the outbreak was AIV07, however divergence was subsequently detected, and it was reclassified into two separate genotypes: AIV07-B1 and AIV07-B2. The AIV07-B1 genotype contains a HA with high similarity to the H5N1 virus from 2020/21 and was

the primary UK H5N1 genotype detection during 2021/22. However, it later became a minority population and has not been detected in the UK after February 2022. The AIV07-B2 genotype, possesses a HA gene that has diverged from AIV07-B1.

AIV09 is now the most prevalent genotype. It was initially detected in November 2021 and has subsequently been found across the UK in 297 poultry and wild birds. The PB2 segment of this genome has high similarity to H5N3 which circulated through Europe in 2020/21.

Genotypes such as AIV20, AIV55 and AIV08 have only been detected once in commercial farms in February 2022, December 2021, and October 2021 respectively. However, the PB2 segment of genotype AIV08 has high similarity to several LPAI detected in Europe since 2020.

2.1.2.1 Mammalian infections from current strains of HPAI H5N1

There have also been a number of cases of HPAI H5N1 identified in mammals. For example, H5N1 virus was detected in the brains of three red foxes in the Netherlands which presented with neurological signs (Vreman et al., 2022). The H5N1 virus which caused these infections was found to have mutation E627K in PB2. The PB2-E627K mutation has previously been found to increase virus replication, *in vitro*, in mammalian cell lines (Bordes et al., 2023) and pathogenicity, *in vivo*, in mice (Peng et al., 2018). This particular mutation is in the virus polymerase protein, and likely increases virus replication at the lower body temperature of mammals compared to birds (Steel et al., 2009). Another recent example of H5N1 mammalian infection was in a Mink farm in Spain in October 2022. Clinical signs of infection in the minks included neurological manifestations such as ataxia and tremors. The H5N1 virus isolated in this outbreak also had a mutation in PB2 at position 271.

In the UK, 14 animals have been found positive for AI H5N1 since 2021, including Eurasian Otters and Red Foxes (APHA, 2023). When whole genome sequences were obtained from these positive cases, the vast majority showed the PB2-E627K mutation. No other mammalian adaptive mutations have been detected so far in the country.

The dominant circulating H5N1 genotypes in avian species since October 2021, AIV09 and AIV07-B2, do not contain this mutation and despite these mutations for increased mammalian susceptibility appearing, no viruses have been detected with mutations associated to increased tropism of the human receptor for virus entry (Vreman et al., 2022).

Several epidemiological risk factors have been highlighted by Harris et al, as increasing the likelihood of transmission of AI between animal species (Harris et al., 2017). These include close contact with coastal birds or bird faeces (transmission from birds to marine mammals) and close proximity to farms (transmission between pigs and turkeys). The largest epidemiological risk factor for transmission from animal to humans was identified as direct, close and prolonged exposure to infected animals, particularly dead or sick poultry. Age also appears to be a factor in the likelihood of transmission of HPAI H5N1 to humans as infections have most commonly been seen in children and young adults, compared to HPAI H7N9 and H9N2. Despite the results of this paper there is still a significant knowledge gap relating to epidemiological factors associated with cross-species transmission (uncertainty).

2.2 Foods of concern for avian influenza contamination

Of all the documented cases of AI in humans, none have been attributed to the consumption of thoroughly cooked food, including eggs.

Epidemiological evidence suggests that most human infections with AI viruses have occurred following direct or close contact with infected (ill or dying) poultry (CDC, 2022d; Wiwanitkit, 2007).

Transmission of the H5N1 virus to mammals has been observed when domestic cats or tigers and leopards were fed with infected poultry (Keawcharoen et al., 2004; Kuiken et al., 2004). Some human infections are suspected to have occurred following the consumption of fresh duck blood; one news article reported a Vietnamese woman tested positive for the H5N1 strain, following drinking duck blood ("Vietnamese Has Bird Flu After Drinking Duck Blood," 2005). Given this evidence of transmission from poultry products to other mammalian species, including humans, this risk assessment considered the risk to humans of exposure to AI from a variety of poultry products.