OFFLU AVIAN INFLUENZA STATEMENT

10th November 2021

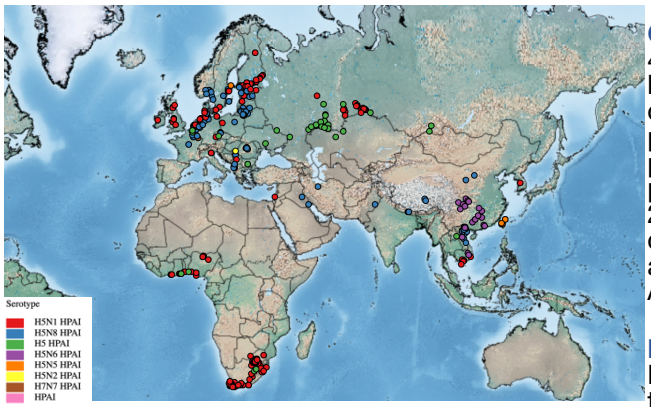

Figure 1: Confirmed Highly Pathogenic Avian influenza events available through OIE WAHIS and FAO EMPRES-i between 1st May 2021 and 10th November 2021. Available here

Global Events

41 countries in Asia(11), Europe(21) and Africa(9) have reported avian influenza in wild birds and domestic poultry to the OIE since 1st May 2021 to present. These have been confirmed as highly pathogenic avian influenza (HPAI) through molecular pathotyping with most viruses falling within HA clade 2.3.4.4b. A broad range of subtypes has been detected (Figure 1) with domestic poultry in Africa affected by H5N1; Europe by H5N1 and H5N8 and in Asia by H5N1, H5N2, H5N6 and H5N8.

Evolution and current picture

H5Nx clades have evolved over recent years leading to subtype diversity, multiple genotypes and also antigenic variability. In 2016, a novel H5 clade 2.3.4.4b emerged and was responsible for waves of H5N8 infections in Europe, Asia and Africa in 2016 and 2017. These were caused by novel reassortant viruses containing internal gene segments from Eurasian low pathogenicity avian influenza (LPAI) viruses and H5N8 viruses which were first found in China in 2013 [1, 2]. Further reassortment with NA genes from Eurasian LPAI viruses gave rise to H5N5 and H5N6 subtypes [3, 4, 8]. Until 2019, the northern hemisphere experienced reoccurring cycles of infection of predominantly H5N8 in wild birds with spill-over events into poultry, with these viruses historically having a relatively stable genotype albeit with internal genes being subject not only to drift but also to reassortment [5].

From mid 2020, H5N8 outbreaks occurred in Iraq, Russia and Kazakhstan caused by new H5 2.3.4.4b variants (“G2”) with closest relatives to 2.3.4.4b viruses detected in Israel and Iraq in 2019 and 2020 respectively. There are indications these are derived from reassortment with Eurasian and North African LPAI however under surveillance makes it difficult to understand the precise origins [6]. These viruses made up most circulating viruses in wild birds and poultry throughout 2021, involving an unprecedented wide range of subtypes (H5N1, H5N3, H5N4, H5N5, H5N6 and H5N8) and wide dispersal throughout Asia, Africa and Europe. This was further complicated by increased reassortment creating an epidemiologically and genetically complex landscape. Two genetically distinct clusters of viruses with changes in known antigenic sites circulated in Japan and South Korea from October 2020 and continued to be detected until spring 2021. They are closely related to separate outbreaks seen in European countries in early (“G1”) and late (“G2”) 2020 respectively. [7, 8, 9].

In Asia, co-circulation of 2.3.4.4h H5N6 viruses with a new incursion of 2.3.4.4b H5N8 occurred in poultry in Vietnam. In China 2.3.4.4h H5N6 viruses have been detected along with 2.3.4.4b H5N6 and H5N8 in poultry and wild birds [10]. Throughout the last 6 months, Vietnam have reported outbreaks of H5N1, H5N6 and H5N8 in domestic poultry and in China there have been reported detections of H5N6 and H5N8 in mixed poultry and wild birds. There have been sporadic reports of human cases of H5N6 in China caused by 2.3.4.4b and 2.3.4.4h clades with approximately half of all human cases (first detected in 2014) detected since June 2021. At least 10 of these have been due to clade 2.3.4.4b viruses that appear to be reassortants with other HPAI and LPAI viruses from poultry. The reason for the upsurge in human cases is still being assessed. Antigenic variation in these strains has been detected. However, the vaccination status of poultry associated with human cases is not known. It is important that authorities keep the composition of poultry vaccine antigens under continuous review and update as required.

Despite clade 2.3.4.4b predominating, some endemic strains of viruses have continued to circulate. Although no longer detected in China, clade 2.3.2.1c caused outbreaks in South East Asia in early 2021. In March 2021 in Laos a human H5N6 case was detected (clade unknown) and in domestic birds H5N6 clade 2.3.4.4h viruses were detected. In South Asia 2.3.2.1a (H5N1) was reported in a crow in India in March 2021 and in poultry in Bangladesh in early 2021. In the Philippines throughout summer 2020 2.3.2.1e (H5N6) viruses continued to circulate in poultry however freedom from HPAI was declared in 2021. There have been sporadic HPAI events reported in India (H5N1), Nepal and Pakistan (H5N8) in April, May and August respectively however to date no genetic information is publicly available.

In Africa there are increasing reports of HPAI events including countries which have never previously detected avian influenza. Sequence data available from African strains in early 2021 are all 2.3.4.4b making up two groups of H5N8 and H5N1 strains similar to European strains detected in 2020 and early 2021. At least four separate 2.3.4.4b incursions have occurred in Nigeria between 2016 and 2019 including one H5N6 incursion relating to European viruses [11]. In Europe since September 2021 there has been an

increase in H5N1 events. Sequence data from recent H5N1 events in September (Russia and the Czech Republic) and October (Italy and the UK), have a similar 2.3.4.4b HA to H5N5 and H5N1 strains found in Europe and Africa in late 2020 early 2021, linking further back to H5N8 circulating in Eurasia. Long branches to the diverse NP/PB1/PB2 segments would likely indicate undersampling or sequencing of wild bird-derived LPAI. Several phylogenetic groups in internal proteins linked by long branches indicate large diversity in wild birds.

Such co-circulation of different H5 lineages in diverse bird populations lends itself to further virus evolution through both drift and reassortment creating an ever-evolving complexity in both virus genetics and spatio-temporal distribution. The constantly changing picture results in significant challenges. Whole genome sequence analyses are important for tracking such evolution and in assessing these emergent events. There are now genetically distinct 2.3.4.4b subclades circulating which are further diversifying and it is difficult to understand their origins. Human infections with 2.3.4.4.b H5 viruses have also occurred in the past year and although we do not understand the precise origins of these outbreaks, the viruses appear genetically similar to strains circulating in wild birds and poultry. There is also an increased need for regular assessment of contemporary viruses against current vaccines used in poultry in different regions using genetic data and though antigenic characterisation using standardised protocols and sera to understand the extent to which antigenic drift leads to reduced vaccine efficacy, by clade. Mitigation strategies based on enhanced farm biosecurity and modifications to production practices are needed when these viruses are carried by wild birds. Enhanced surveillance is needed for early warning and case detection as well as for vaccine antigen matching in places where vaccines are being used or under consideration.

With such a high infection pressure in wild birds and poultry, there will be further antigenic drift, opportunities for reassortment and increasing diversity. OFFLU is closely tracking these events and working with colleagues to survey emergence. Intensive surveillance is providing a high level of detail. It is important that partners continue to engage and that we can increase understanding of vaccination of poultry and ways to make it more effective. . Thank you for continued support to OFFLU to help us understand the ever increasing complexity and risk from H5 HPAI viruses. Colleagues can engage with data through the secretariat: **secretariat@offlu.org**.

Useful Links:

https://www.offlu.org/
https://wahis.oie.int/#/home
https://empres-i.apps.fao.org/
https://www.gisaid.org/
https://www.efsa.europa.eu/en/efsajournal/pub/9979

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