



LAST UPDATED:
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EPII-WIN
DIGEST

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Influenza–avian influenza H5:

Its evolution and associated risk



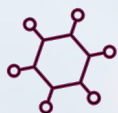
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Summary



Most recent high pathogenic avian influenza (HPAI) global outbreak in birds and mammals from Dec 2022 to present: H5N1 subtype



Wherever these A(H5N1) viruses are circulating in animals, further human cases are not unexpected.

Despite an unprecedented number of outbreaks in wild birds and poultry, **only a few instances of human infections seen.**

In 2023 so far: 4 human cases of H5N1 in 3 different countries.



Stay vigilant

Continue with monitoring efforts

Summary: risk to humans



The risk to the general population for infection with avian influenza viruses is considered low.



The risk of sustained human-to-human transmission is also low and has not been documented.

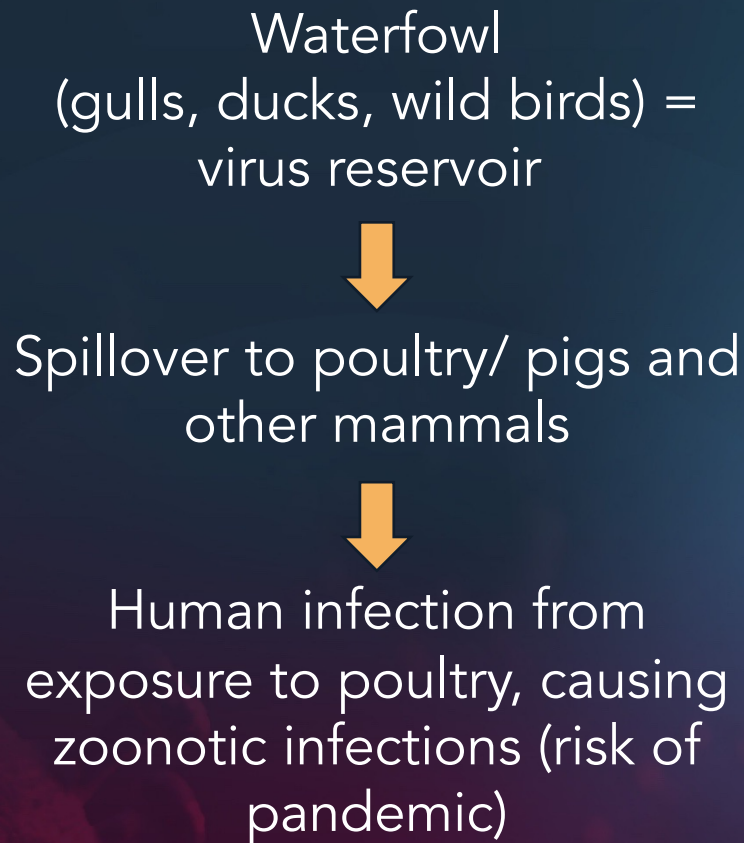


True case fatality rate (CFR) could be lower than reported due to asymptomatic and mild cases which are not detected or reported.

About avian influenza

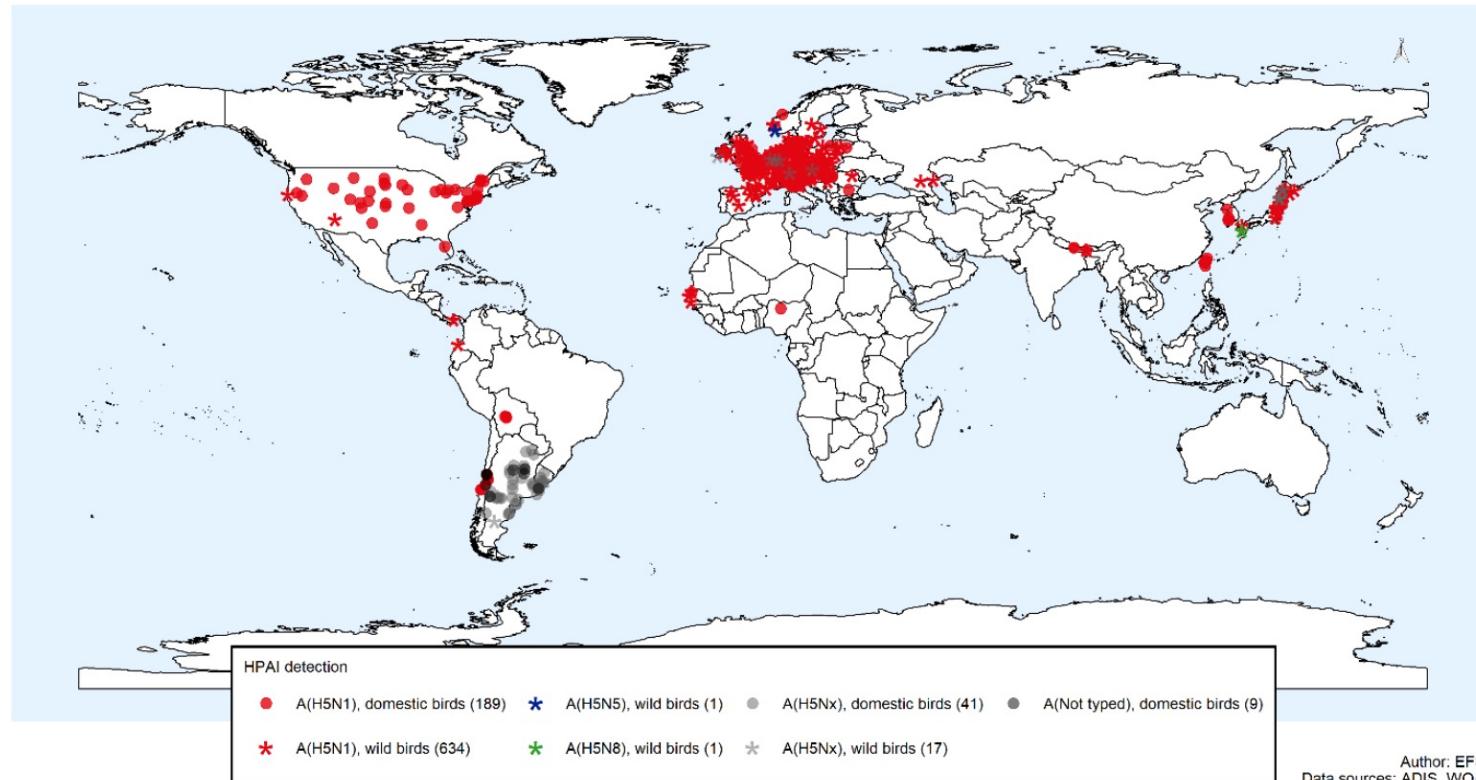
- Avian influenza = type of influenza A virus
 - Classified by combinations of proteins on virus surface: hemagglutinin (HA) and neuraminidase (NA)
 - 16 HA variations x 9 NA variations = 144 known subtypes including H5N1
 - Only influenza A viruses are known to have caused pandemics.
- Low vs high pathogenicity avian influenza viruses (LPAI vs. HPAI) only relevant for infection and disease in birds, not for disease severity in humans.
 - Thus far, only H5/H7 and only in poultry mutate to become HPAI.
 - Increased poultry food production = increased HPAI emergence.

Avian influenza ecology and transmission



Current situation:

Global spread in birds and animals to all continents
(except Oceania and Antarctica), Map 2 March to 28 April 2023



[Source](#)

In 2023:

- Approaching endemic spread in Europe in 2023
- 65 countries/territories (2021= 49 countries)

Human cases of infection with avian influenza viruses

- Human cases and fatalities have been low in last 8 years despite substantial outbreaks in poultry globally.
- 873 reported cases including 458 fatal cases reported to WHO in total over last 25 years.
- Numbers do not accurately give case fatality (CFR) rate as do not include mild, asymptomatic and untested cases which are not detected and reported.
- True CFR likely to be lot lower than 52%.



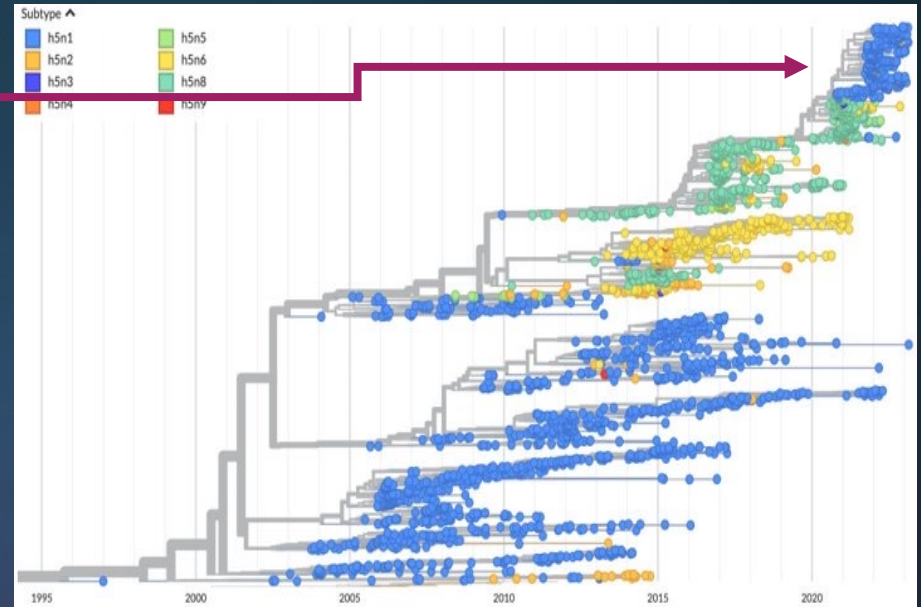
Credit: WHO / Jonathan Perugia

Current situation: Global outbreak from late 2021 - present

- Avian influenza A(H5N1) clade 2.3.4.4b has affected large numbers of wild and domestic birds in areas previously affected and in new areas previously unaffected (e.g. many countries in Central and South America).
- Increased reports of detections of A(H5) viruses in mammals: scavenging or carnivorous wild, domestic, captive and farmed. This raises concern the virus may evolve to be better adapted to mammals.
- Also mass mortality events in mammals. **Studies are needed to confirm whether mammal to mammal transmission has taken place.**
- Mammals have been found with severe neurological and respiratory problems
- It is likely that many mammals are infected by consuming raw infected birds or direct contact with infected birds.

Evolving virus genetics in bird and mammals: same lineage from 1996, genetically mixed

- Current H5N1 subtype is very different to original (blue at top)
- 2.3.4.4.b clade is now dominant form of H5N1 globally in detections among birds and mammals
- 1997: Hong Kong bird flu outbreak- first evidence influenza from birds could infect and kill humans. Source was originally a goose in Wandong, China from 1996. Virus continued circulating
- 2003: Spread to Hong Kong then numerous virus spreading events with bird migration



- Last 10 years: genetic mixing in birds and animals between LPAI and HPAI from same 1996 lineage has led to new virus subtypes

Assessing the risk of HPAI H5 to human health through TIPRA

TIPRA is the Tool for Influenza Pandemic Risk Assessment.

- **TIPRA scores pandemic risk, with human infection a major score driver**
- Expert driven process to highlight research gaps and a tool to weigh different elements of risk in 3 areas
 - Public Health
 - Animal Health
 - Virology
- Supports a timely and updatable hazard risk assessment
- Documents risk features of the virus
- Identifies knowledge gaps
- Facilitates information sharing



Link to TIPRA: [https://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-\(tipra\)](https://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-(tipra))

Has the risk changed?



- H5 virus was last rated in 2021
 - Low risk for human infection/human cases low then
- TIPRA tool is being used to assess H51 clade 2.3.4.4.b viruses in May 2023
 - Since 2021 prevalence of 2.3.4.4.b H5N1 is now high, and human exposure is at all time high
- Despite genomic changes, key changes for human-to-human transmission likely have not seen
- **Risk to humans is still relatively low;** still mainly a bird virus
- **Vigilance is key**
 - Preparedness and risk assessment needs strong data
 - Current data needs include:
 - Genomics of the virus
 - Population immunity in humans
 - Infection in animals
 - Role of poultry vaccination

What can we do collectively to be prepared?



In outbreaks:

- **Rapid investigation** and action taken at animal source and wherever human cases are detected
- **Active and passive surveillance** in wild and domestic birds and mammals, including humans

For countries and researchers:

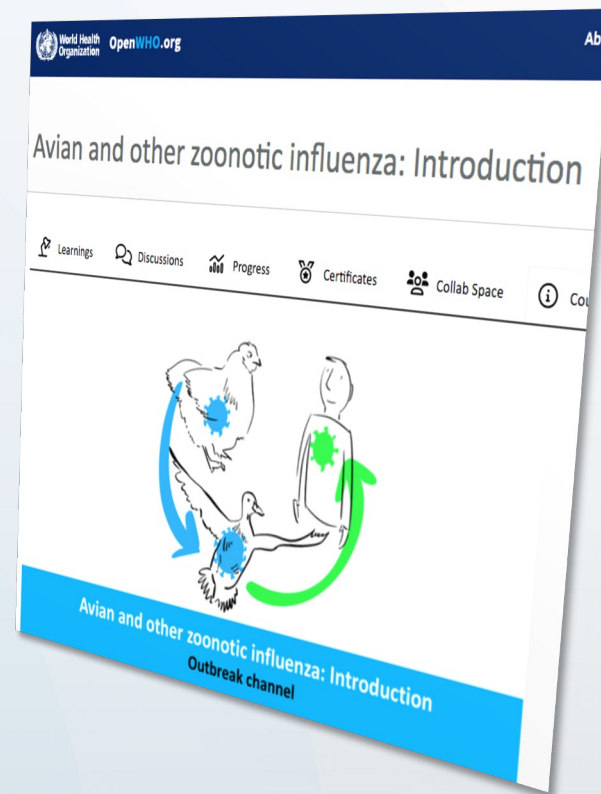
- Update **pandemic plans** and look at preparedness capacities
- **Data sharing** including virus genome sequences, key for research
- Countries with experience in **vaccinating poultry** can share their experiences/best practices

For individuals/all:

- **Open WHO training modules** for influenza preparedness available

Useful links

- TIPRA: [https://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-\(tipra\)](https://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-(tipra))
- WHO Global Influenza Programme page: <https://www.who.int/teams/global-influenza-programme/avian-influenza>
- Open WHO course **Avian and other zoonotic influenza**: <https://openwho.org/courses/avian-and-other-zoonotic-influenza-introduction>
- Full presentations and EPI-WIN webinar recording available: <https://www.who.int/news-room/events/detail/2023/03/29/default-calendar/epi-win-webinar-influenza-avian-influenza-h5-its-evolution-and-associated-risk>





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