Influenza A/H5 virus evolution and ecology

Ron A.M. Fouchier, PhD
Professor, Molecular Virology
Influenza A virus
- Host range (simplified) -
Influenza A virus
- Structure and (antigenic) subtypes -

Hemagglutinin (HA)
16 variants in birds

Neuraminidase (NA)
9 variants in birds

RNP, 8 RNA pieces
RNA+NP+PB1+PB2+PA

Subtypes:
16 x 9 = 144
H3N2, H5N1 etc

H5/H7 Subtypes:
LPAI & HPAI form

Source: https://www.cdc.gov/flu/resource-center
Avian influenza viruses in poultry - High versus low pathogenicity -

Low pathogenic avian influenza (LPAI)  
Highly pathogenic avian influenza (HPAI)

Increased global poultry production  
Increased HPAI emergence
HPAI viruses in poultry
- HA cleavage determines virulence -

low pathogenic
monobasic HA cleavage site
HA cleaved by trypsin
tissue-restricted infection
mild symptoms

highly pathogenic
multibasic HA cleavage site
HA cleaved by furin
systemic infection
fatal disease
H5N1 birdflu
- The A/Goose/Guangdong/96 lineage -

1997: H5N1 birdflu infects, kills humans in Hong Kong
HPAI H5N1 virus from live poultry markets; culling
>2003 spread with wild migratory birds ("spill back")
Spread throughout Asia, Africa, Europe, Americas
Infection of >30 mammalian species (incl. humans)
Genetic mixing ("reassortment") with LPAI viruses
H5N1, H5N2, H5N5, H5N6, H5N8, etc
Still causing damage & surprises 25 years later ....
HPAI globally
- Domestic and wild birds -

Report: December 3 2022 – March 1, 2023
HPAI A/H5N1 virus
- Human cases, global -

Case Fatality Rate of 52% (458/873)?
Highly unlikely: we miss many asymptomatic and mild cases!

Reassorted genomes?
HPAI H5 virus evolution, reassortment - A/Goose/Guangdong/96 lineage -

Subtype
- h5n1
- h5n2
- h5n3
- h5n4
- h5n5
- h5n6
- h5n8
- h5n9

2.3.4.4
HPAI outbreaks in Europe - Clade 2.3.4.4b, ongoing problems -

Year-around "Enzootic"
HPAI H5 virus in Europe
- Domestic and wild birds -

Wild birds

- Raptors (1,008)
- Colony-breeding seabird species (1,751)
- Waterfowl (4,757)
- Other wild bird species*** (700)

Colonel-breeding seabirds

- Alcidae (41)
- Laridae (1,274)
- Pelecanidae (23)
- Phalacrocoracidae (52)
- Procellariidae (6)
- Stercorariidae (16)
- Sulidae (339)

Laridae

- European Herring Gull (280)
- Black-headed Gull (417)
- Other Gulls, Terns and Skimmers (225)
- Undefined species of Gulls, Terns and Skimmers (352)

Week of suspicion*
HPAI H5N1 virus globally
- Mammals -

Mostly carnivores

Infection via feeding

Neurological signs
HPAI H5 outbreaks
- Infection of mammals 2016-2023 -

Domestic pig, wild boar (serology)
Red fox, raccoon dog, coyote,
Otter, badger, polecat, ferret, mink, stone marten
Brown bear, black bear, grizzly bear
Leopard, tiger, bobcat, fisher cat, lynx, mountain lion, cat
Opossum, skunk, raccoon,
Grey seal, harbour seal, sea lion, porpoise, dolphins (3 sp.)

"Adaptive" substitutions (~50% of cases)
PB2 E627K
PB2 D701N
PB2 T271A
.....
NA (mink)

Mammal-mammal transmission ?
Seals (USA), Mink (Spain), Sea Lions (Peru) ?
Avian virus transmission in mammals
- Phenotype/genotype traits; detection -

Based on past pandemics, natural variants, laboratory research

Transcription, Replication
e.g. PB2 E627K

Virus attachment (e.g. Q222L)
Virus stability (e.g. H103Y)

Genetic changes: https://flusurver.bii.a-star.edu.sg
https://gisaid.org
https://www.fludb.org/

Linster et al., Cell. 2014 157(2):329-339
Herfst et al., Cell Host Microbe 2020 28:602-613
Imai et al., Virus Res. 2013 178:15-20
Influenza A/H5 virus evolution and ecology  
- Vigilance, not panic -

- Active (live) and passive (dead) surveillance is crucial
  Wild & domestic animals; birds & mammals; vectors & sentinels
- Early detection and detailed investigation of zoonoses is crucial
- Investigation of unusual events in mammals (pigs, mink, seals, etc)
- To prevent further spread, action required at the animal source (poultry, pigs, mink)
- Sharing virus sequences and viruses is critical for surveillance and research
- Monitor domestic animals, improve biosecurity, investigate management options
  Poultry vaccination? Ensure post implementation surveillance! Exit strategy?
- Monitor wildlife, investigate management options, protect vulnerable species
- Check pandemic preparedness plans, stockpiles, vaccines, drugs, interventions, etc
  "WHAT IF..." scenarios

Kuiken et al., Lancet Infect Dis. 2023 Apr;23(4):398-399
Acknowledgements

Avian influenza overview December 2022 – March 2023

European Food Safety Authority,
European Centre for Disease Prevention and Control,
European Union Reference Laboratory for Avian Influenza,
Cornelia Adlhoch, Alice Fusaro, José L Gonzales, Thijs Kuiken, Stefano Marangon, Grazina Mirinaviciute, Éric Niqueux, Karl Stahl, Christoph Staubach, Calogero Terregino, Alessandro Broglio and Francesca Baldinelli

Other sources:
https://www.who.int/
https://www.woah.org/
https://www.fao.org/
https://www.ofllu.org/