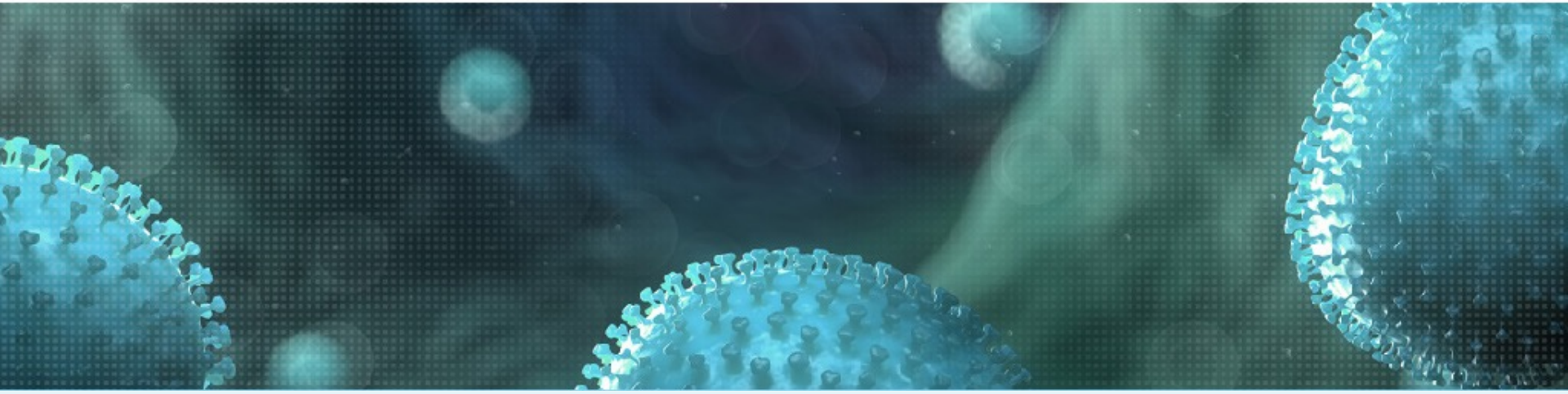
Erasmus MC

NIC NATIONAAL INFLUENZA CENTRUM

Viroscience lab

WHERE SKILLS MEET TO STUDY & PROTECT



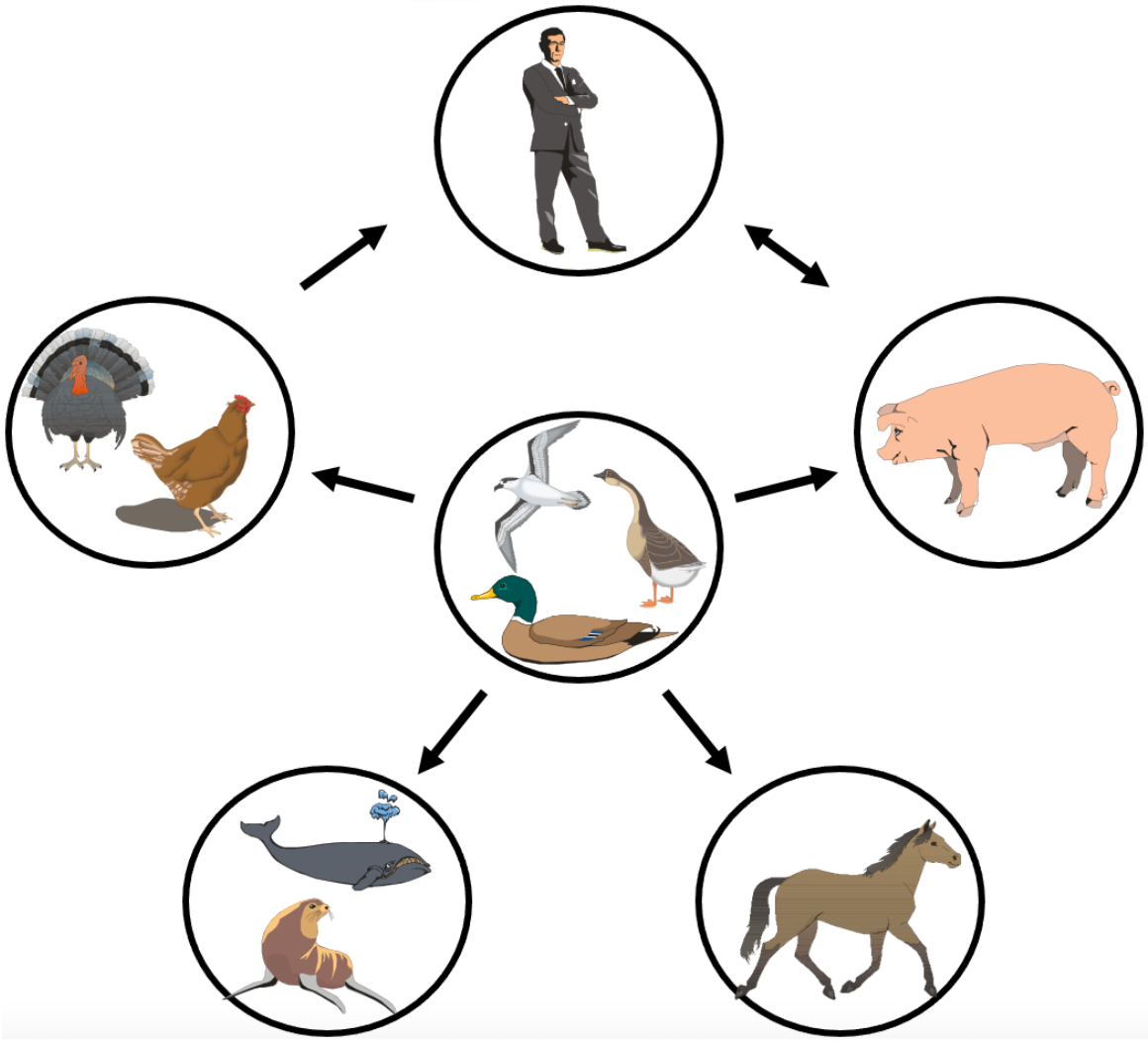
Influenza A/H5 virus evolution and ecology

CEIRR
CENTERS OF EXCELLENCE FOR INFLUENZA RESEARCH AND RESPONSE
WWW.CEIRR-NETWORK.ORG

Ron A.M. Fouchier, PhD
Professor, Molecular Virology

Pandemic and Disaster Preparedness Center
PDPC

Influenza A virus
- Host range (simplified) -



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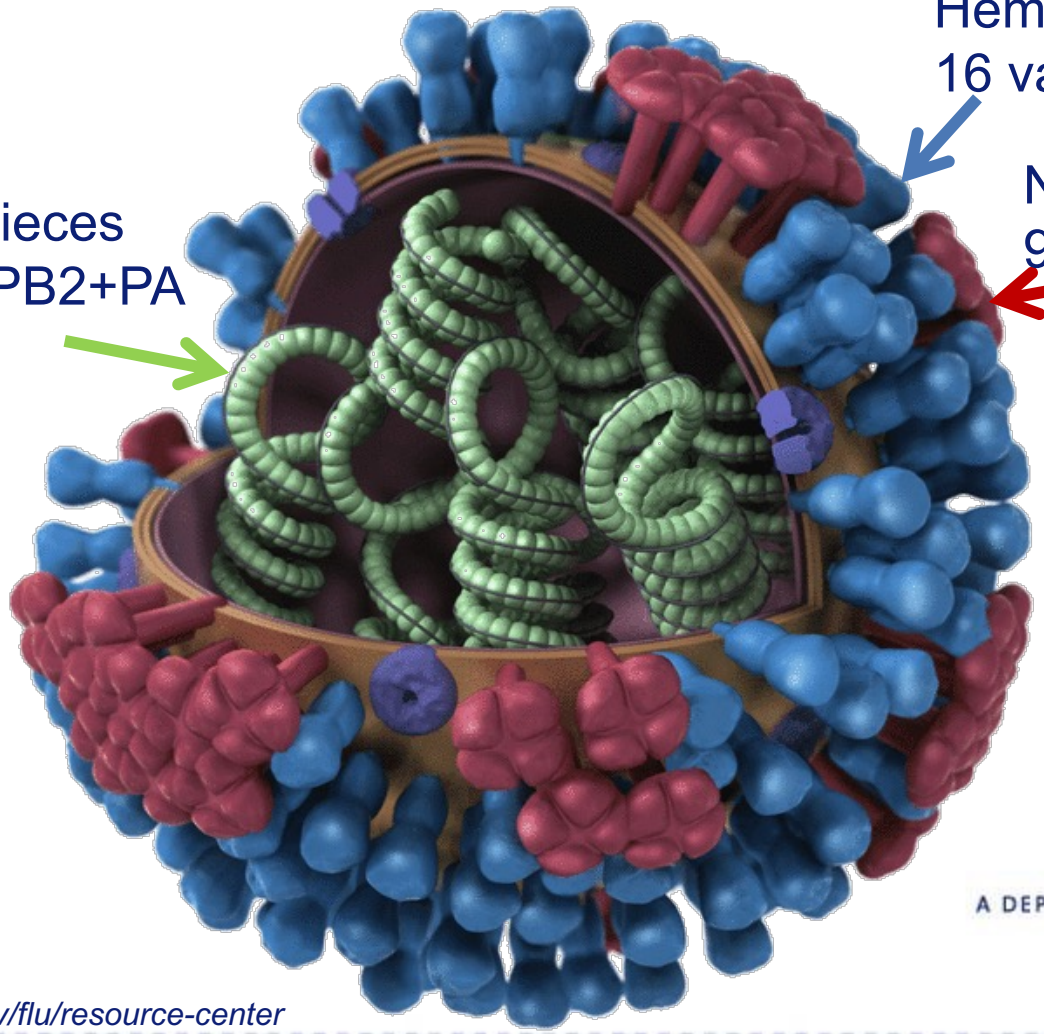
Influenza A virus
- Structure and (antigenic) subtypes -



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

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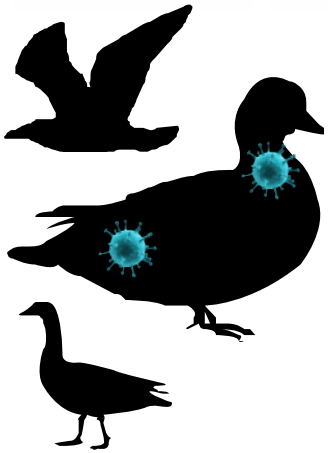
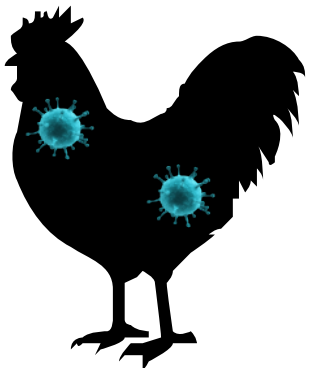
Source: https://www.cdc.gov/flu/resource-center

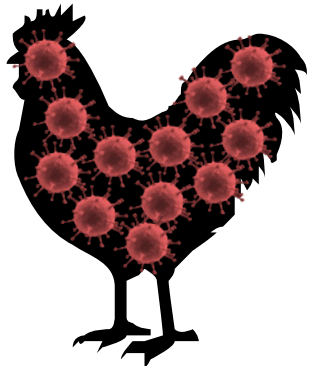
Avian influenza viruses in poultry
- High versus low pathogenicity -



H1-H16

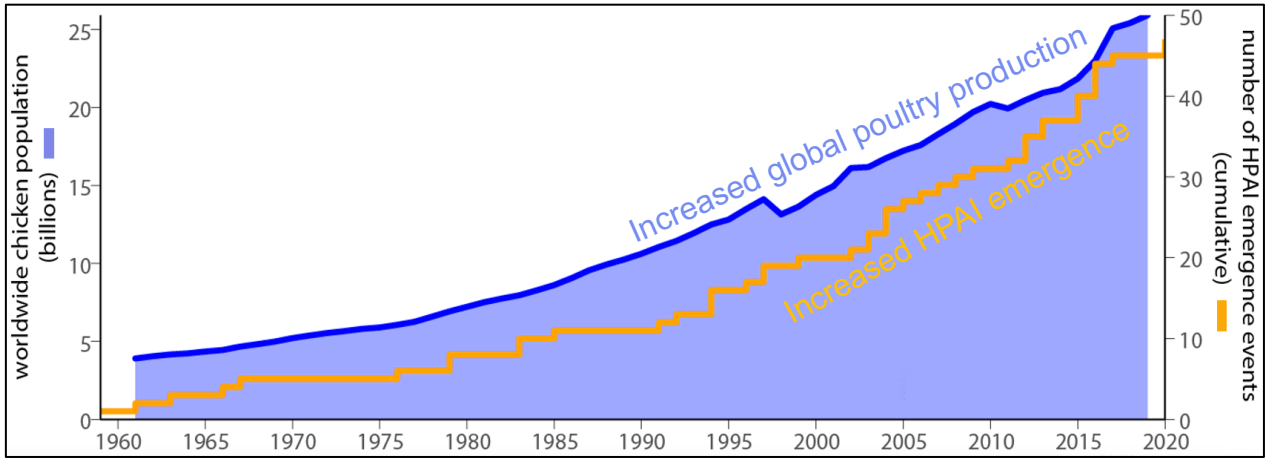


Only H5/H7
Only in poultry



Low pathogenic avian influenza (LPAI)

Highly pathogenic avian influenza (HPAI)



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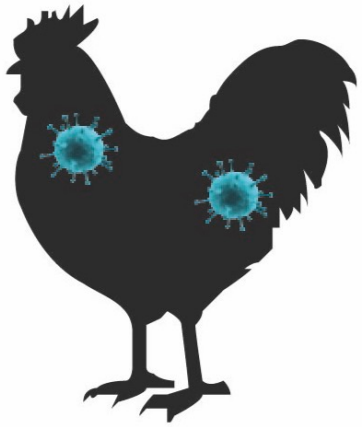
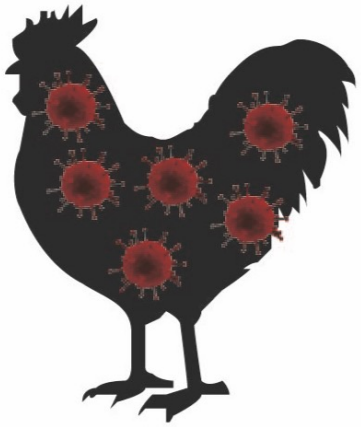
HPAI viruses in poultry
- HA cleavage determines virulence -



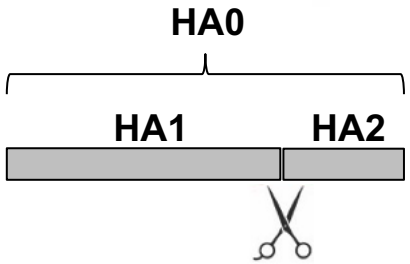
low pathogenic

insertions

in H5/H7



highly pathogenic



AGAGAAACAAGAGGA

R E T R G

monobasic HA cleavage site

HA cleaved by trypsin

tissue-restricted infection

mild symptoms

AGAGAGAGAAGAAGAAAAAAGAGAGGA

R E R R R K K R G

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

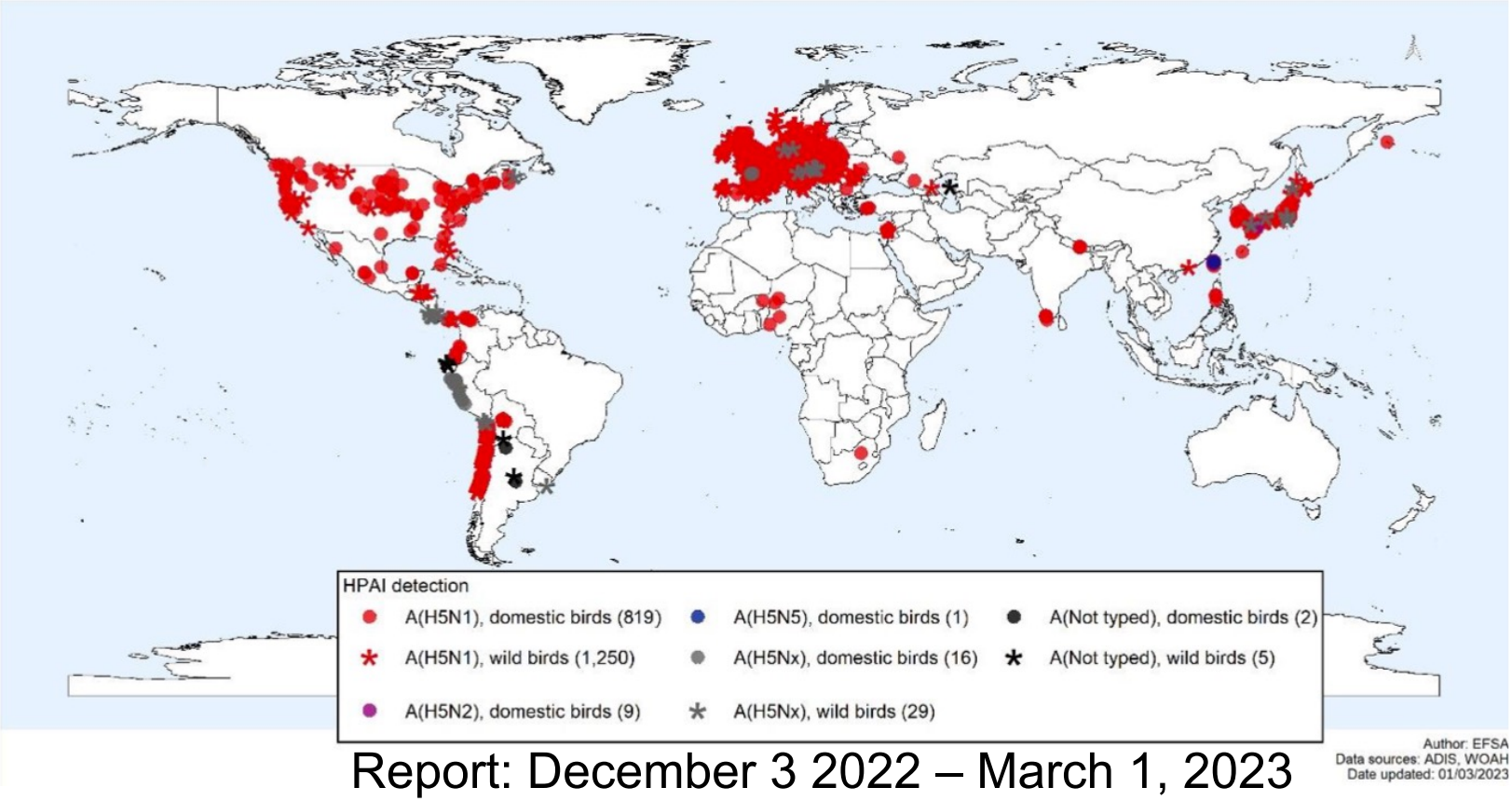
Infection of >30 mammalian species (incl. humans)

Genetic mixing ("reassortment") with LPAI viruses

H5N1, H5N2, H5N5, H5N6, H5N8, etc

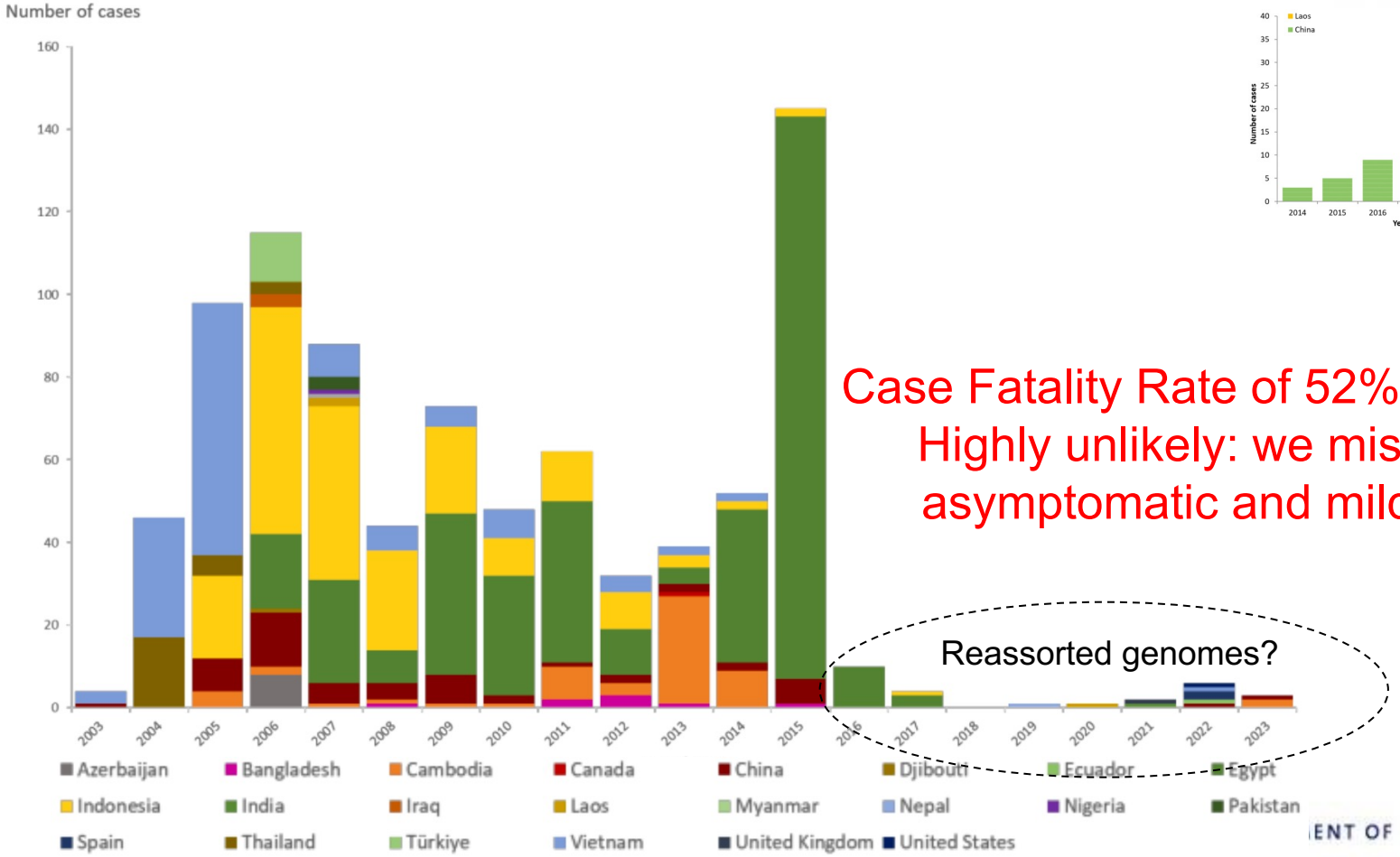
Still causing damage & surprises 25 years later ....

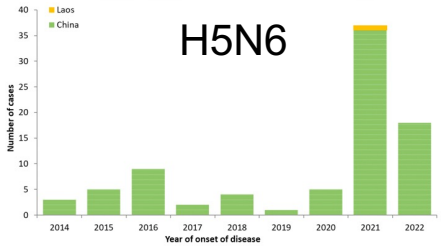
HPAI globally
- Domestic and wild birds -



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!

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Istituto Zooprofilattico Sperimentale delle Venezie
efsa JOURNAL

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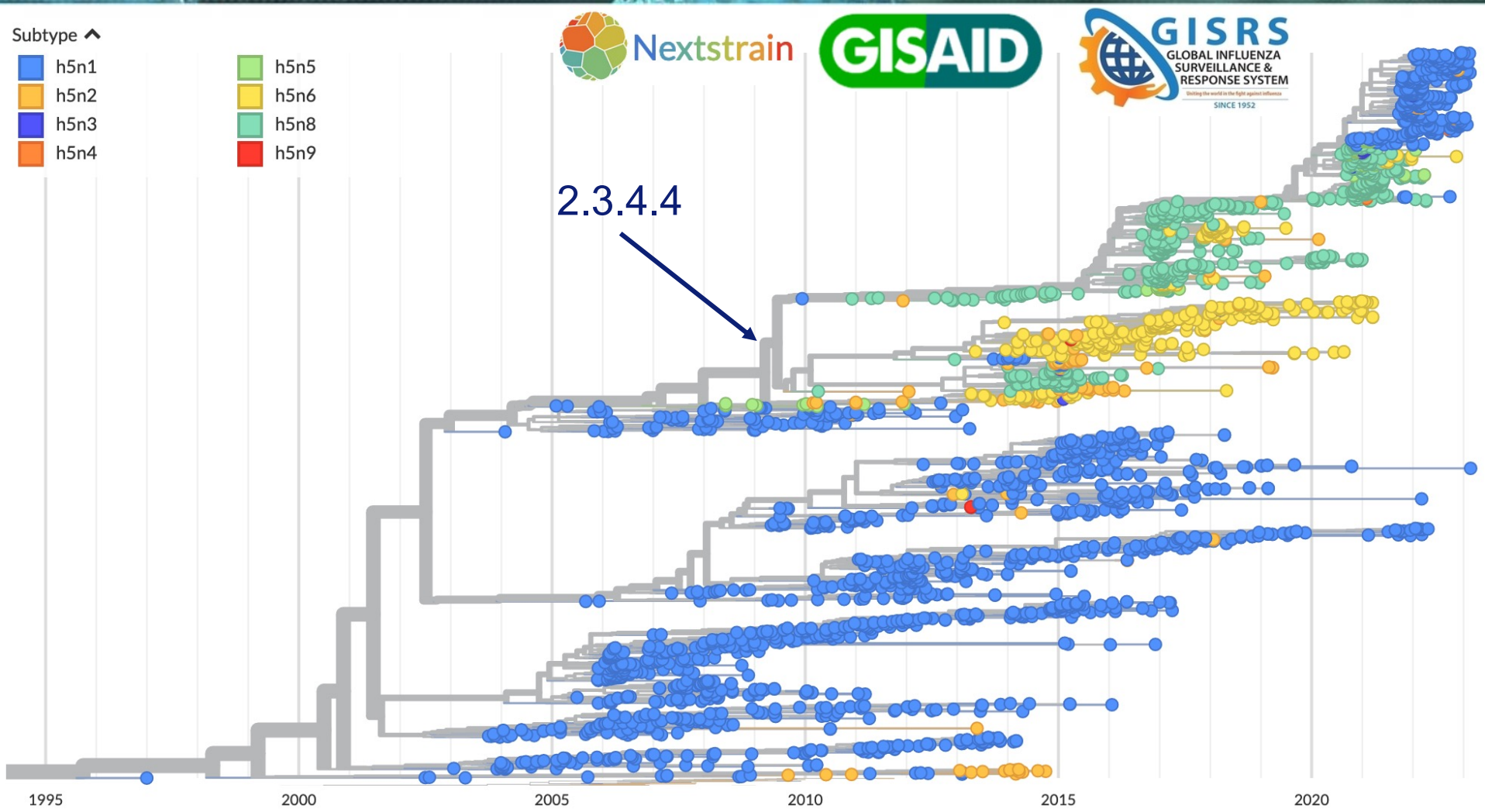
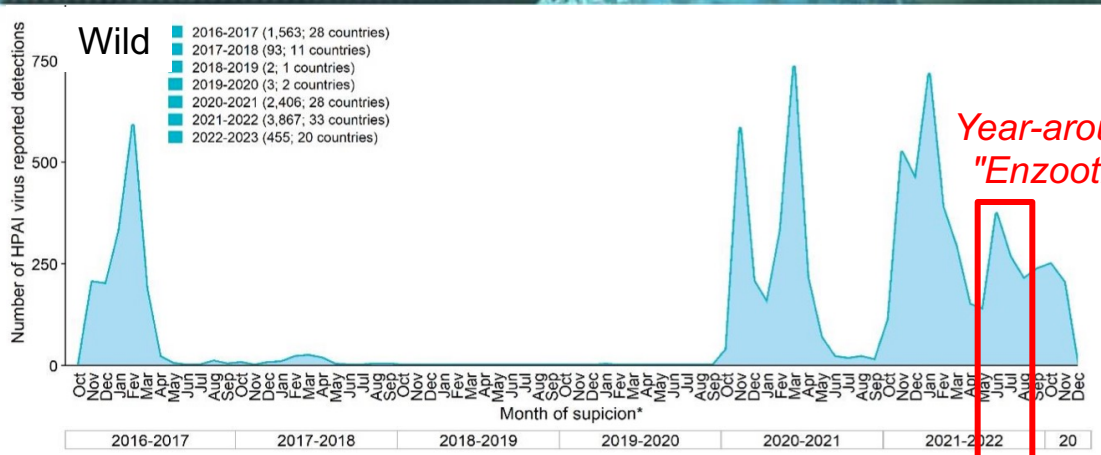
HPAI H5 virus evolution, reassortment
- A/Goose/Guangdong/96 lineage -

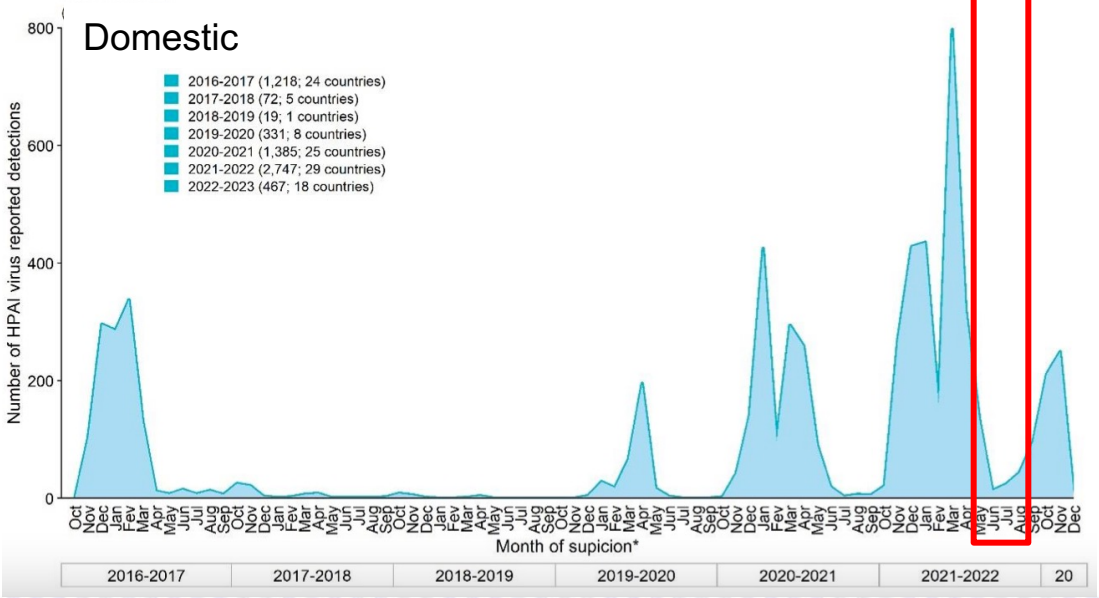


HPAI outbreaks in Europe

- Clade 2.3.4.4b, ongoing problems -



Year-around "Enzootic"



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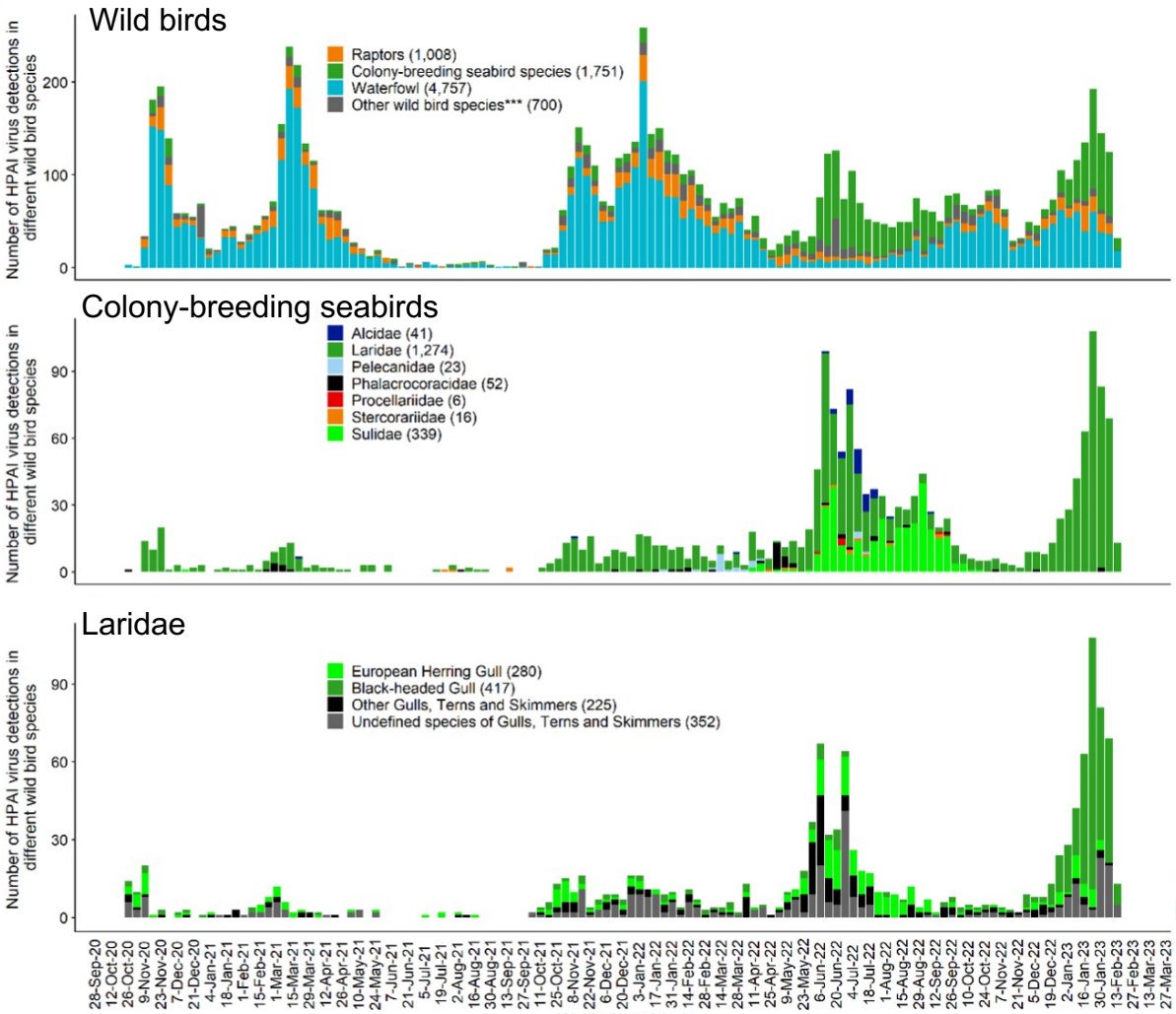
HPAI H5 virus in Europe
- Domestic and wild birds -



efsa European Food Safety Authority

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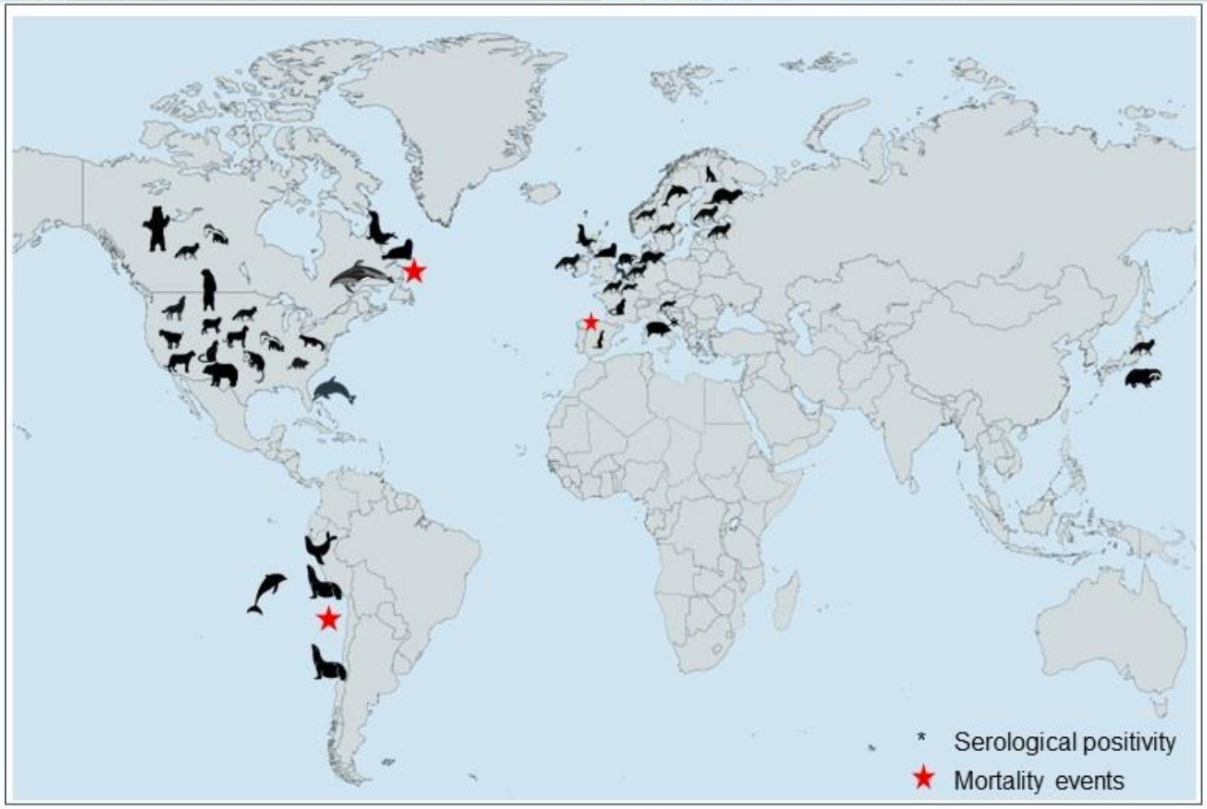
HPAI H5N1 virus globally
- Mammals -



Mostly carnivores

Infection via feeding

Neurological signs

American black bear (Ursus americanus)
American mink (Neogale vison)
Amur leopard (Panthera pardus)
Amur tiger (Panthera tigris)
Bobcat (Lynx rufus)
Bottlenose dolphin (Tursiops truncatus)
Brown bear (Ursus arctos)
Cat (Felis catus)
Common dolphin (Delphinus delphis)
Coyote (Canis latrans)
Domestic pigs (Sus scrofa)
Eurasian otter (Lutra lutra)
European badger (Meles meles)
European polecat (Mustela putorius)
Ferret (Mustela furo)
Fisher cat (Pekania pennanti)
Grey seals (Halichoerus grypus)
Grizzly bear (Ursus arctos horribilis)
Harbour seals (Phoca vitulina)
Lynx (Lynx lynx)
Mountain lion (Puma concolor)
Porpoise (Phocoena phocoena)
Raccoon (Procyon lotor)
Raccoon dog (Nyctereutes procyonoides)
Red foxes (Vulpes vulpes)
South American fur seal (Arctocephalus australis)
South American sea lion (Otaria flavescens)
Striped skunks (Mephitis mephitis)
Virginia opossum (Didelphis virginiana)
White-sided dolphin (Lagenorhynchus acutus)

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)

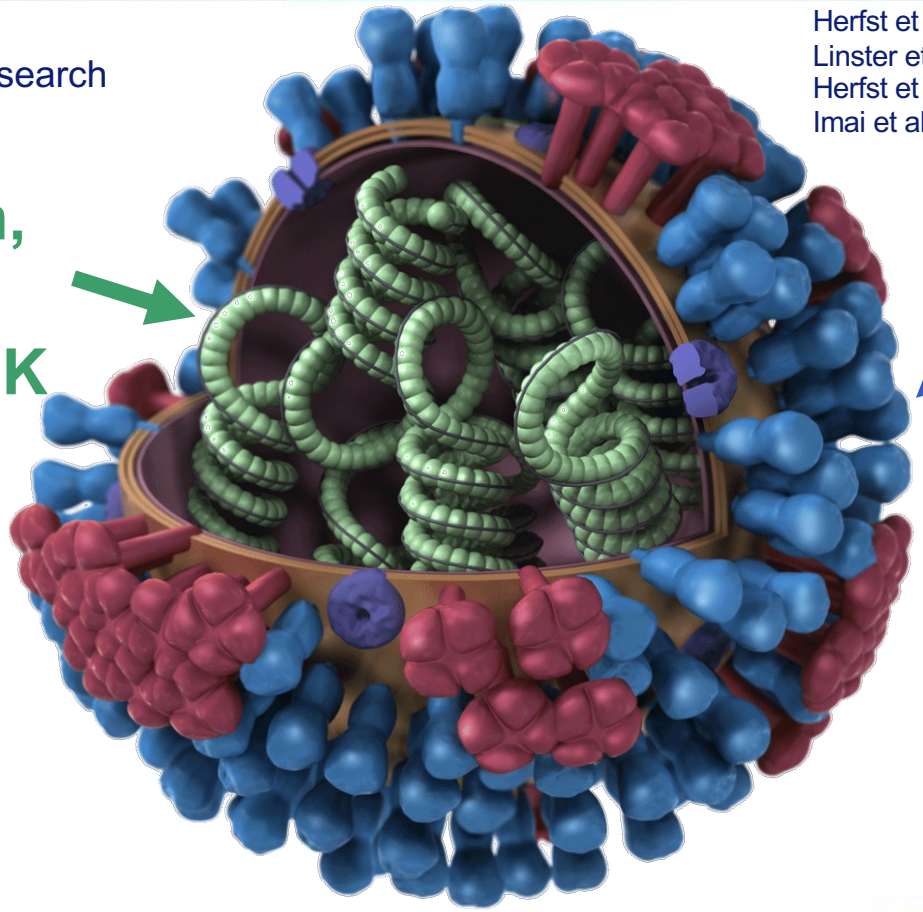
Mammal-mammal transmission ?
Seals (USA), Mink (Spain), Sea Lions (Peru) ?

Avian virus transmission in mammals
- Phenotype/genotype traits; detection -

Based on past pandemics,
natural variants, laboratory research

Herfst et al., Science. 2012 336:1534-41
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

**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/

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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

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

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SCIENTIFIC REPORT

JOURNAL

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Avian influenza overview December 2022 – March 2023

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European Centre for Disease Prevention and Control,
European Union Reference Laboratory for Avian Influenza,
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Other sources:
https://www.who.int/
https://www.woah.org/
https://www.fao.org/
https://www.offlu.org/

GISAID

GISRS GLOBAL INFLUENZA SURVEILLANCE & RESPONSE SYSTEM SINCE 1952

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ΔELTA-FLU

KAPPA-Flu

DURABLE Research Network against Epidemics

VETBIONET

erinha European Research Infrastructure on Highly Pathogenic Agents

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