



Re-emerging Avian Influenza: Global Situation, Genotype Distribution, and Transmission Patterns

Virology Association of Thailand Academic Workshop

21 July 2025

Dr. Martha Montgomery

Outline

Background

Transmission (birds to people)

Current situation in animals and humans

Clade distribution

One Health strategy for pandemic planning

Background



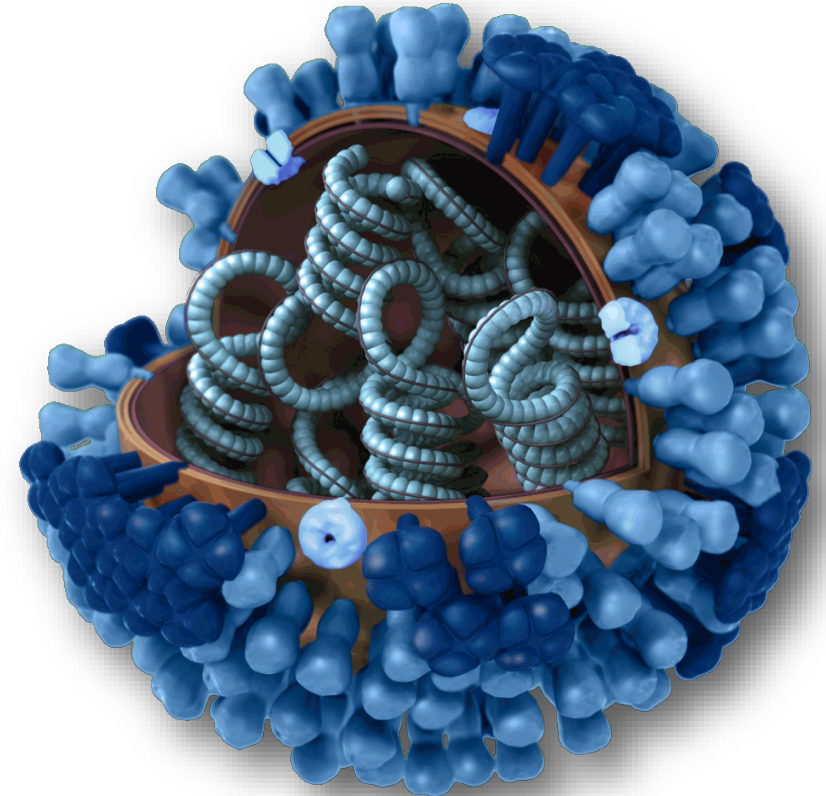
Influenza Virology

- Multiple influenza virus types
 - Two main types in humans
 - One can cause pandemics
-
- Negative-sense, segmented RNA genome
 - 8 gene segments
 - Encode for 11 major proteins
 - Two major surface proteins
 - Hemagglutinin (HA)
 - Neuraminidase (NA)

Influenza A, B, C, D

Influenza A, B

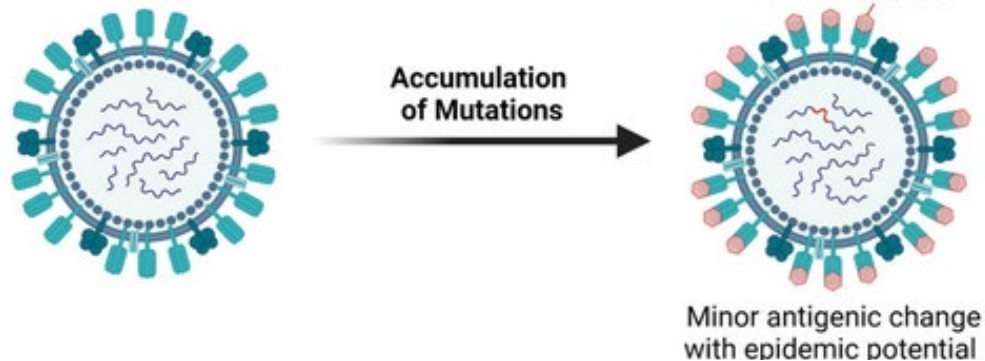
Influenza A



Influenza A pandemic potential is related to genetic reassortment and mutation

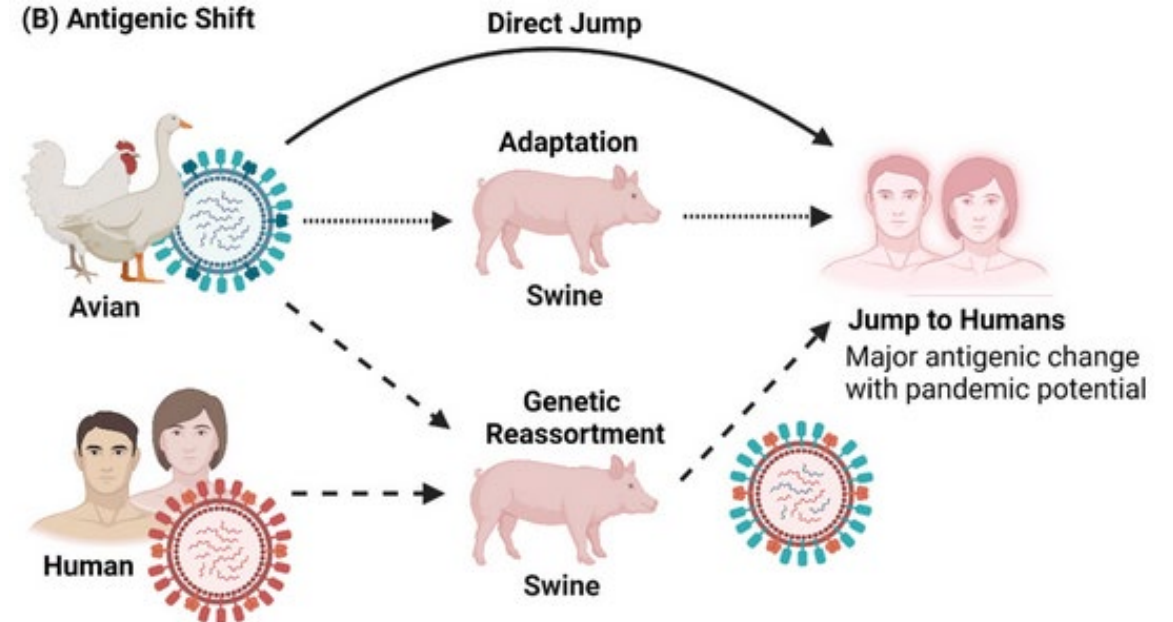
Seasonal influenza

(A) Antigenic Drift



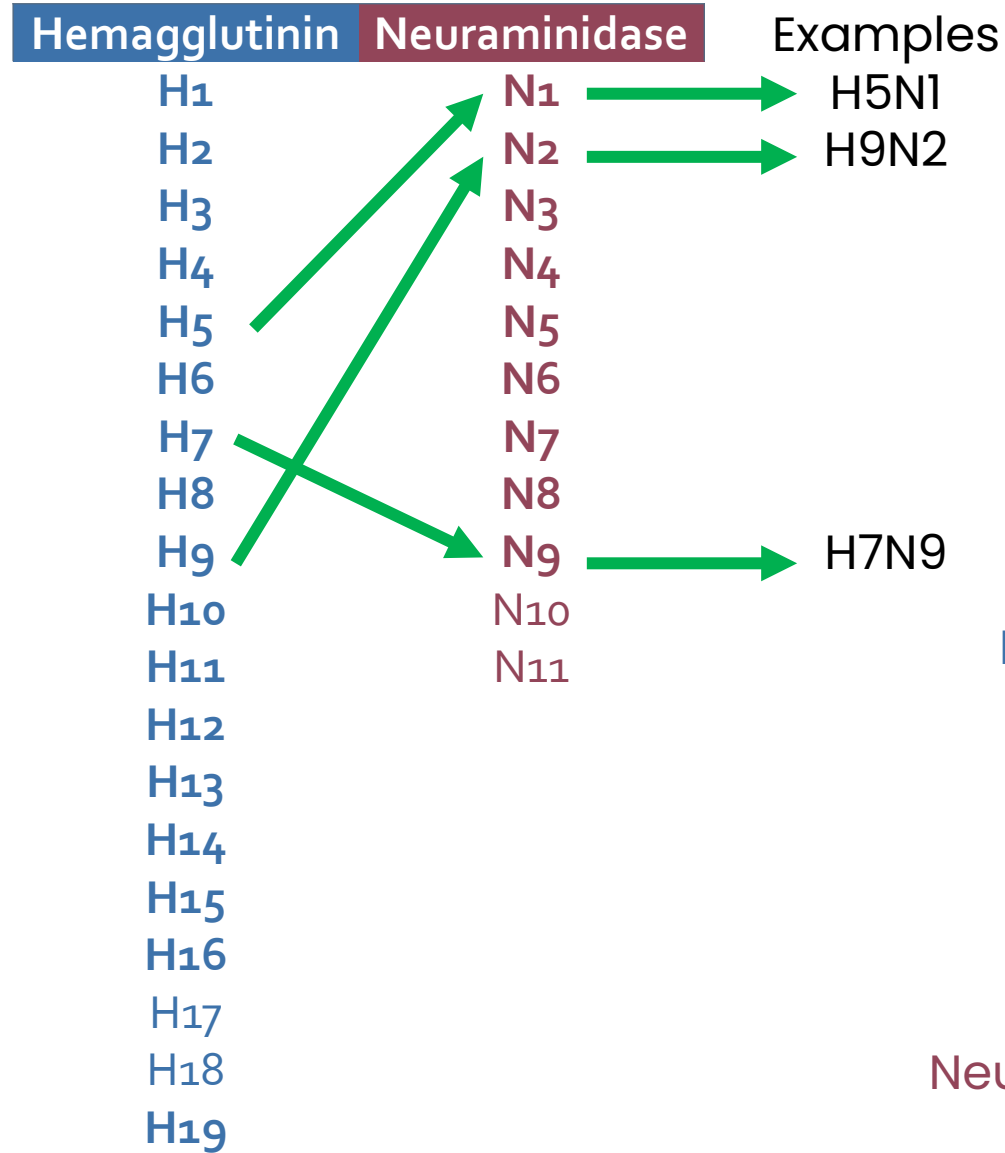
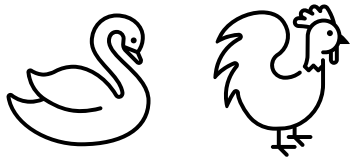
Pandemic influenza

(B) Antigenic Shift

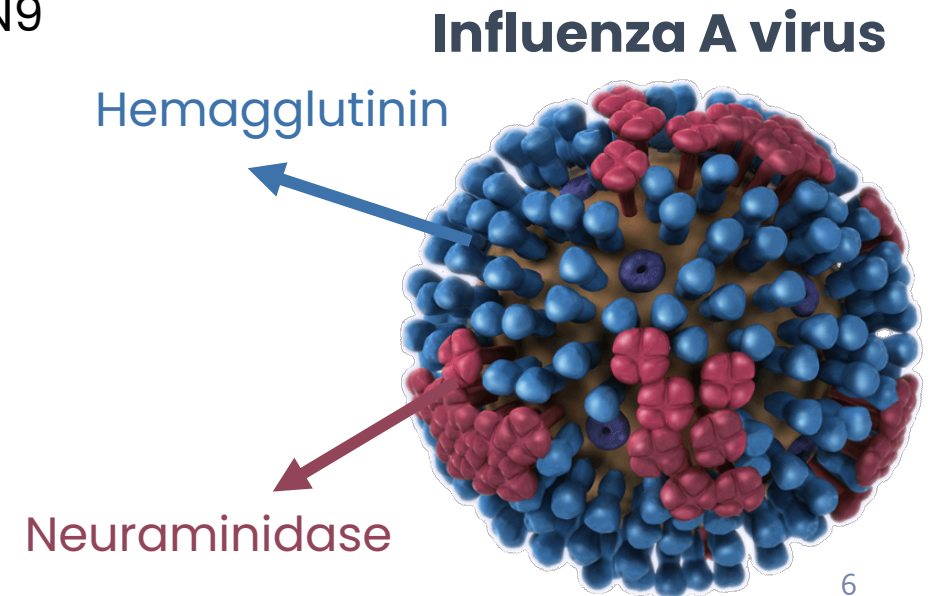


Influenza A virus subtyping

Avian influenza

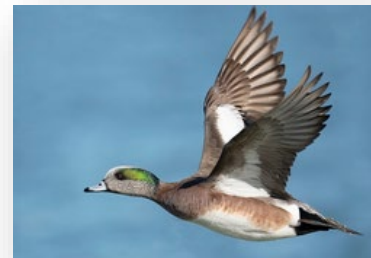
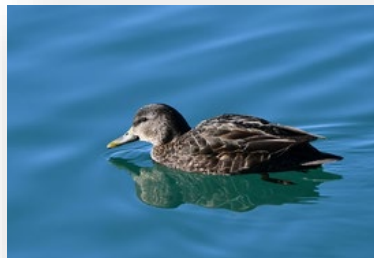


Further classified into clades (eg, A(H5N1) clade 2.3.4.4b or 2.3.2.1e) and subclassified into genotypes (eg, D1.1 or B3.13)



'Avian influenza' is caused by influenza A viruses that normally circulate among birds

- Wild aquatic birds (eg, ducks, geese, swans, gulls, etc.) are the natural hosts of avian influenza A viruses
- Avian influenza A viruses have been isolated from more than 100 different species of wild birds
- Infect predominantly the gastrointestinal tracts of birds



Avian influenza viruses are classified by severity of disease in chickens



- Viruses that cause high mortality in chickens or have specific molecular cleavage sites = *highly pathogenic avian influenza (HPAI)*
- *Low pathogenic avian influenza (LPAI)* causes little or no disease in chickens
- All naturally occurring HPAI are A(H5) or A(H7) although most A(H5) and A(H7) are LPAI
- Severity in chickens **does not predict** severity in humans

Transmission from birds to people

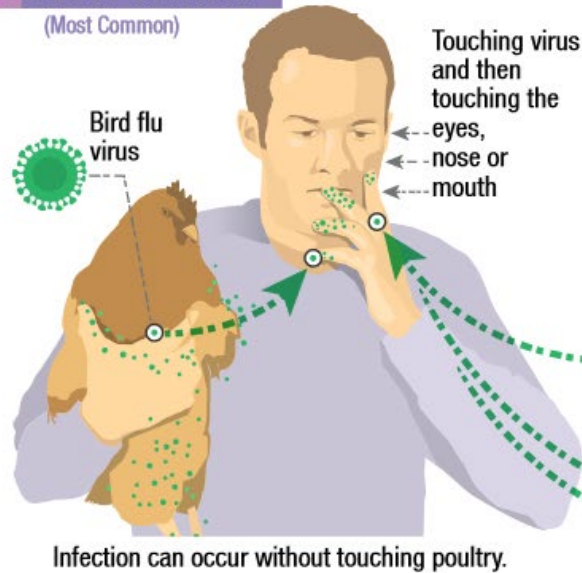
Clinical and epidemiological aspects

How Infected Backyard Poultry Could Spread Bird Flu to People

Human Infections with Bird Flu Viruses Rare But Possible

1 Direct Contact

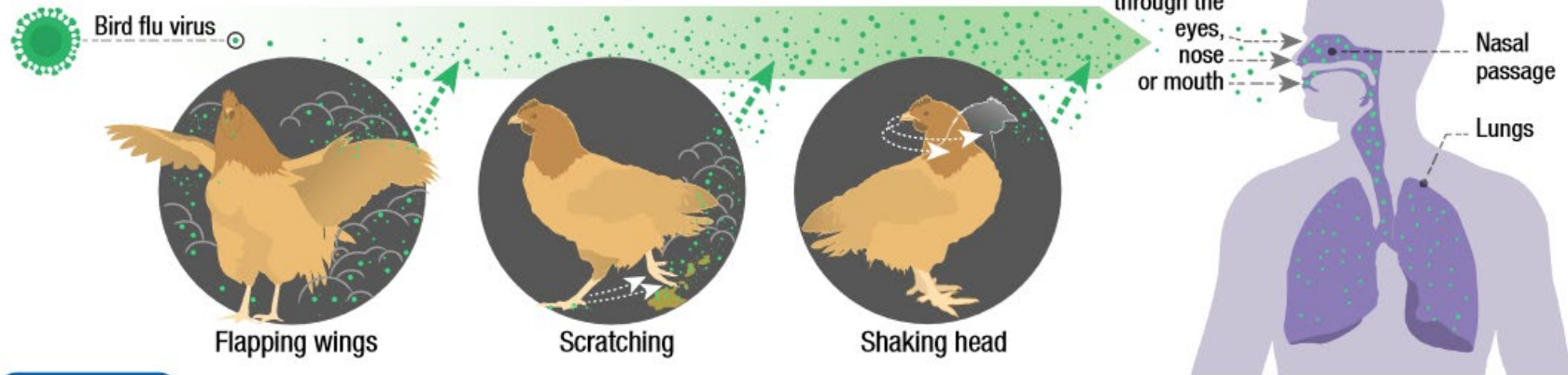
(Most Common)



2 Contaminated Surfaces



3 Bird Flu Virus in the Air (in Droplets or Dust)



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

www.cdc.gov/flu/avianflu/avian-in-humans.htm

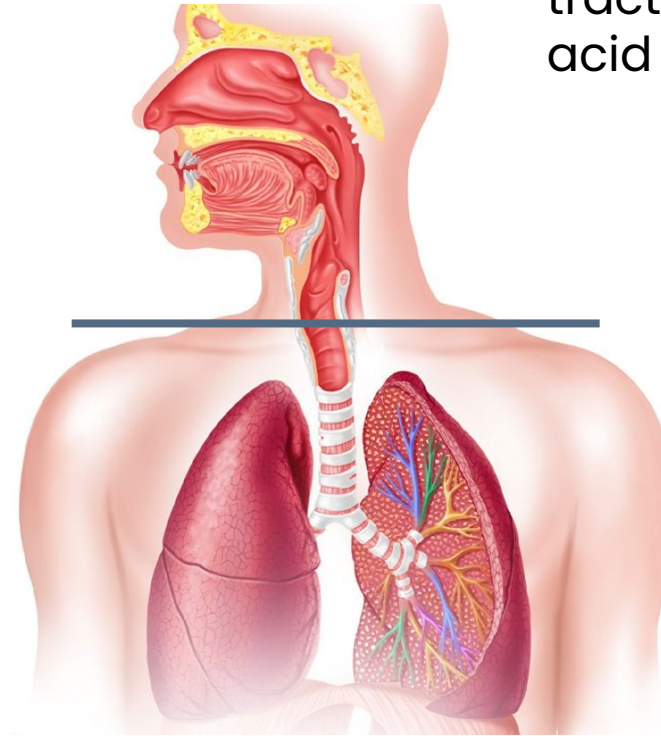
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Influenza A(H5N1) viruses bind preferentially to receptors in human **lower respiratory tract** and **conjunctivae**



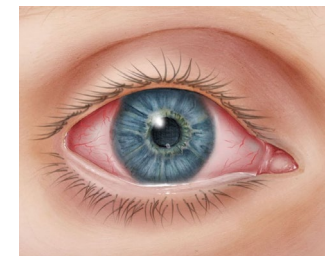
Avian influenza viruses preferentially bind **$\alpha 2,3$ -linked** sialic acid receptors

Found in respiratory and gastrointestinal tract of aquatic birds and poultry



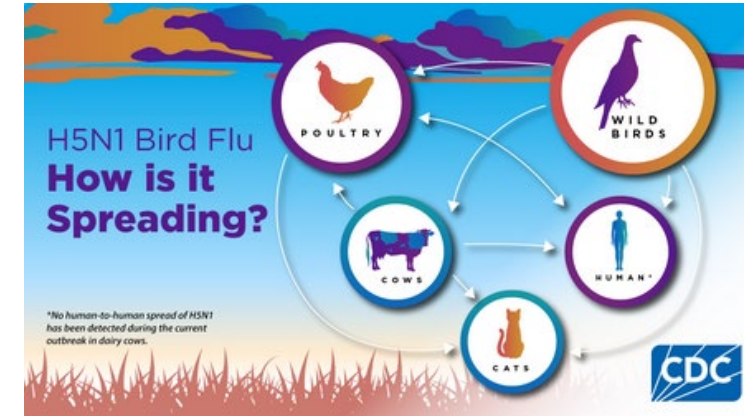
Human upper respiratory tract has **$\alpha 2,6$ -linked** sialic acid receptors

$\alpha 2,3$ -linked sialic acid receptors are found in lower respiratory tract and conjunctivae in humans



Risk factors for human influenza A(H5N1) infections

- Exposure to infected poultry
 - Direct or close contact with sick or dead poultry
 - Visiting a live poultry market
- Exposure to infected wild birds
 - Defeathering wild swans that died of H5N1 virus infection, Azerbaijan 2006
- Exposure to infected dairy cattle in U.S.
- Rare, limited non-sustained human-to-human transmission
 - Household transmission from a sick patient to a family member through **prolonged, unprotected close exposure**
 - Hospital transmission from sick patient to family member, unrelated patient, or health care provider through **prolonged, unprotected close exposure**



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JOURNAL of MEDICINE

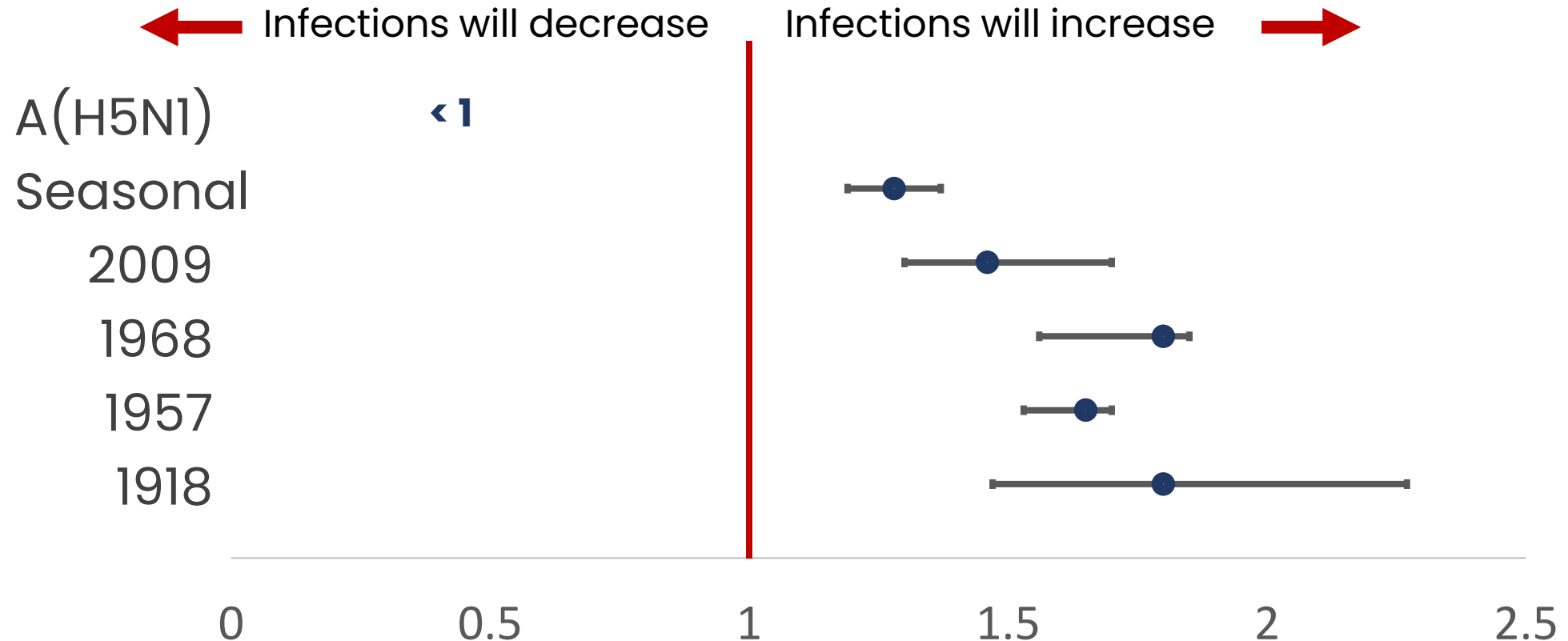
ESTABLISHED IN 1812

JANUARY 27, 2005

VOL. 352 NO. 4

Probable Person-to-Person Transmission
of Avian Influenza A (H5N1)

So far, avian influenza A(H5N1) has not spread easily from person to person



R_0 = expected number of additional infections that result from one initial infection

Symptoms of influenza A(H5N1) in humans

- Wide clinical spectrum – asymptomatic, mild, severe pneumonia, to death
- Symptoms are variable and nonspecific
- Most cases globally are identified in hospitalized patients with severe pneumonia
- Mild cases have been identified in close contacts or through routine surveillance for influenza-like illness
- Detection of virus in asymptomatic persons might not represent infection (transient detection)

Symptoms at illness onset among influenza A(H5N1) human infections			
	Cambodia 2005–2006 (n=6)	China 2003–2013 (n=37)	United States 2024 (n=45)
Fever ≥38 C	100%	65%	49%
Cough	100%	54%	18%
Shortness of breath	100%	8%	16%
Conjunctivitis	Not reported	Not reported	93%
Diarrhea	67%	Not reported	4%
Sore throat	1 of 2	5%	29%
Abdominal pain	2 of 2	Not reported	Not reported
Arthralgia	Not reported	37%	Not reported
Chills	Not reported	35%	Not reported
Sputum	Not reported	32%	Not reported
Fatigue	Not reported	24%	22%
Headache	Not reported	19%	44%
Coryza	Not reported	14%	Not reported

From Buchy et al (2007) J Clin Virology, Cowling et al. (2013) Lancet, Garg et al. (2025) NEJM

Clinical progression of influenza A(H5N1)

- Incubation period (time from infection to symptom onset)
 - Average of 3 days (range 2–7 days) after exposure to sick/dead poultry
- Clinical progression
 - Progression to lower respiratory disease: difficulty/rapid breathing, chest pain
 - Median time from onset to hospitalization for severe pneumonia = 5–6 days
- Hospital admission findings
 - Clinical: hypoxia, signs of pneumonia
 - Laboratory: leukopenia, lymphopenia, mild-to-moderate thrombocytopenia
 - Radiographic findings: patchy, interstitial, lobar, or diffuse infiltrates and opacities, consolidation, pleural effusion

Complications from influenza A(H5N1)

- **Pneumonia** is the most common complication and can progress to respiratory failure and the acute respiratory distress syndrome (ARDS)
- Other complications can include
 - Acute kidney injury
 - Cardiac failure
 - Sepsis, shock, disseminated intravascular coagulation, multi-organ failure, ventilator-acquired pneumonia
- Atypical complications can include
 - Encephalitis
 - Reye syndrome with salicylate exposure
 - Spontaneous miscarriage in pregnant women
 - Vertical transmission to fetus

Current Situation of Avian Influenza

Animals

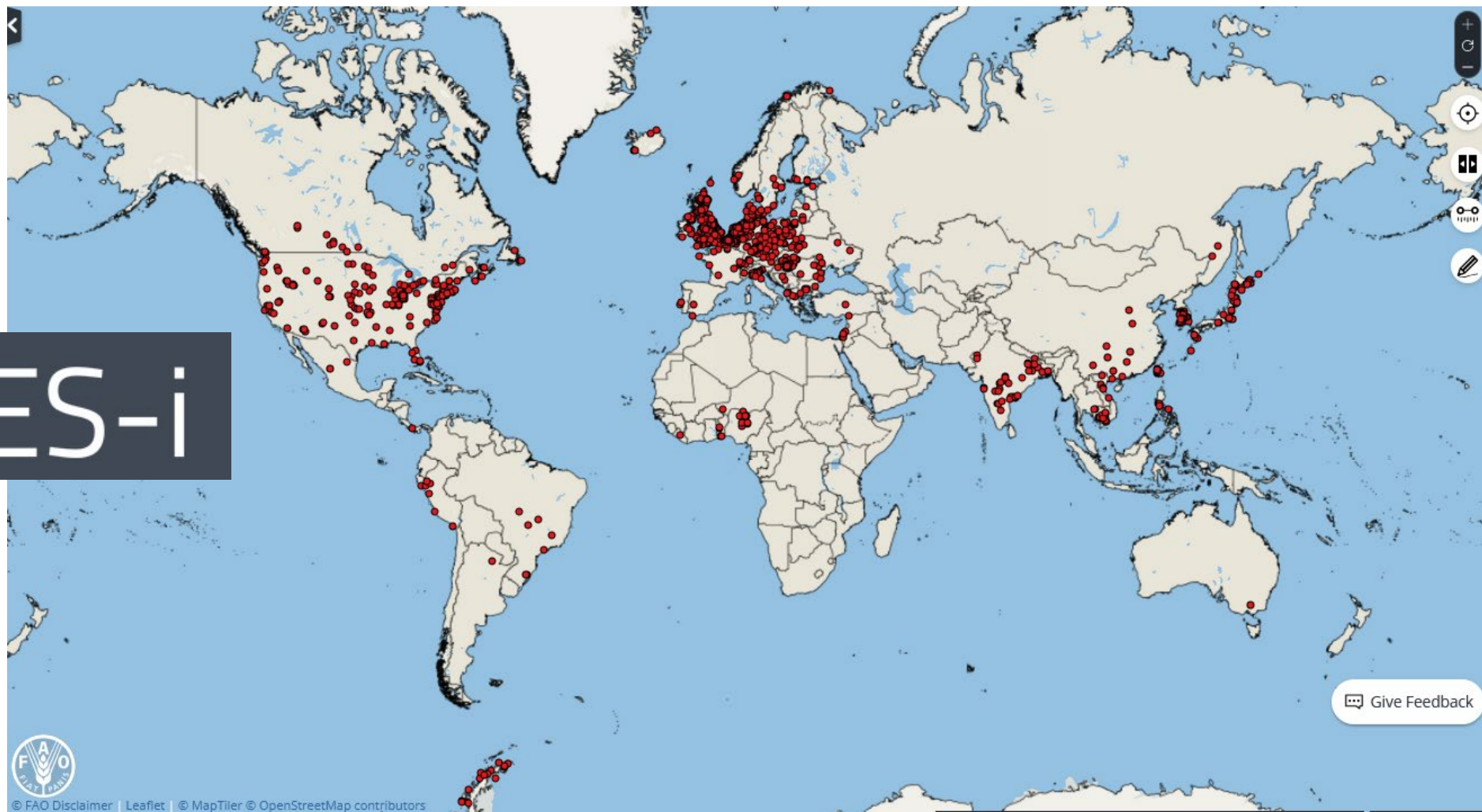
Humans

Avian influenza events in animals reported to FAO

1 January 2025
– 20 June 2025



EMPRES-i



Avian influenza events in animals reported to FAO

1 January 2025
– 20 June 2025

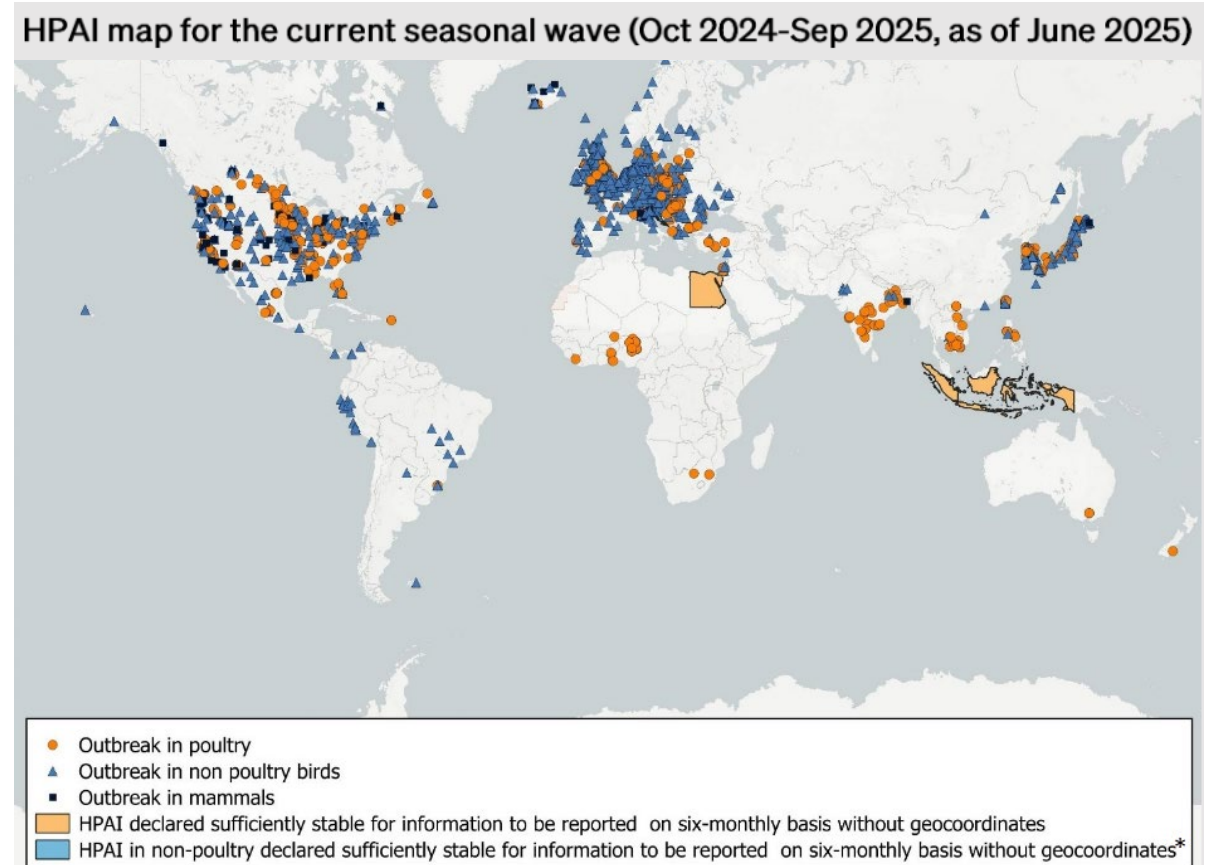
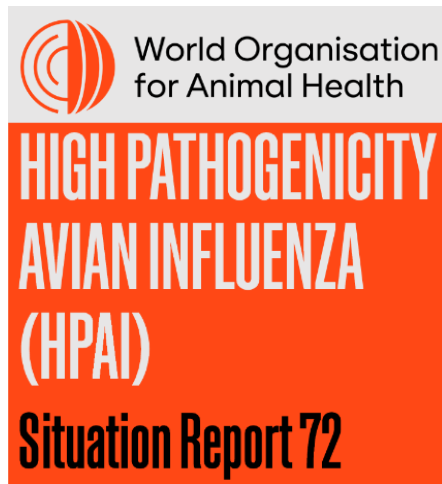


EMPRES-i

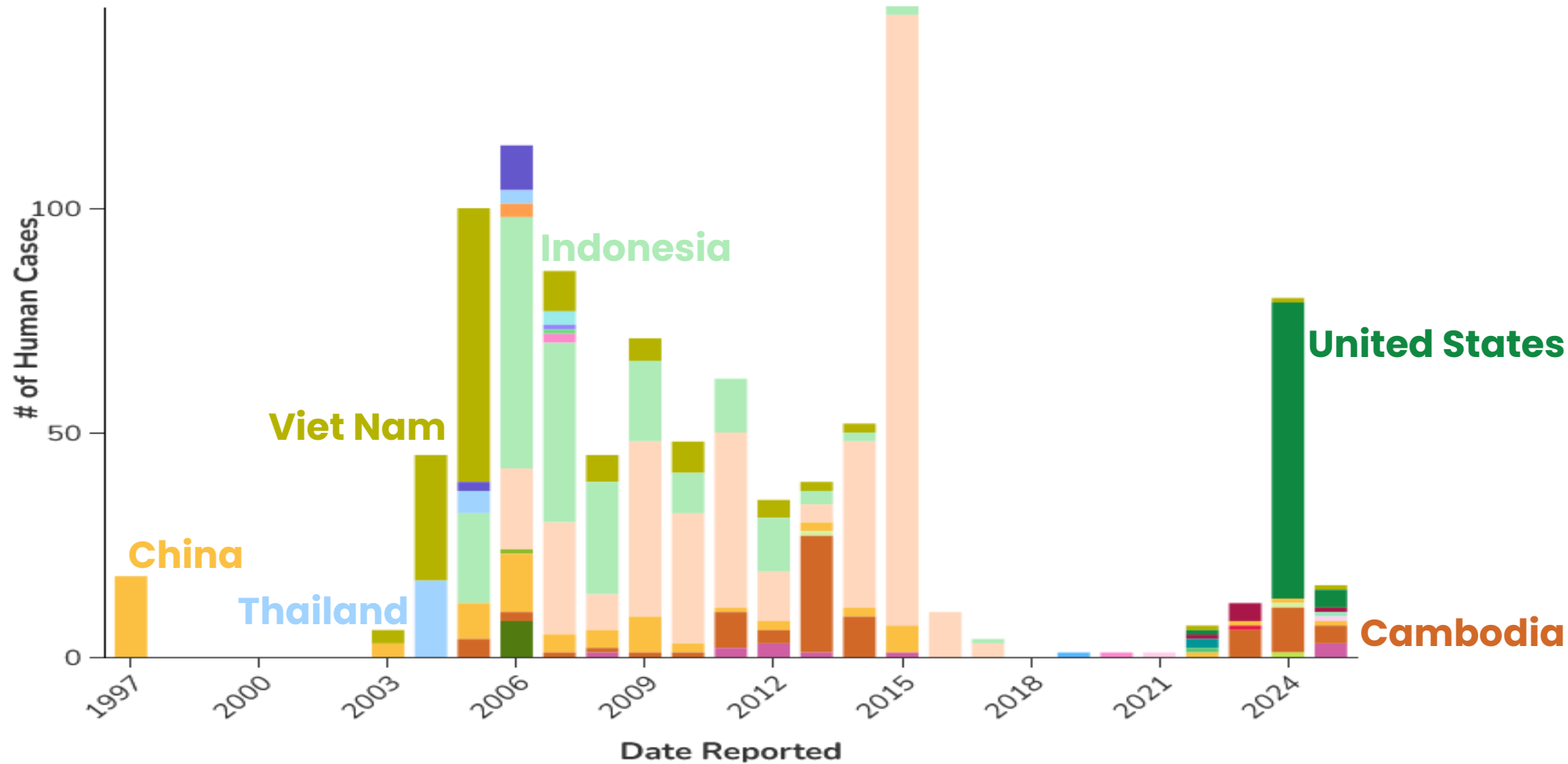


Avian influenza events in animals reported to World Organization for Animal Health (WOAH)

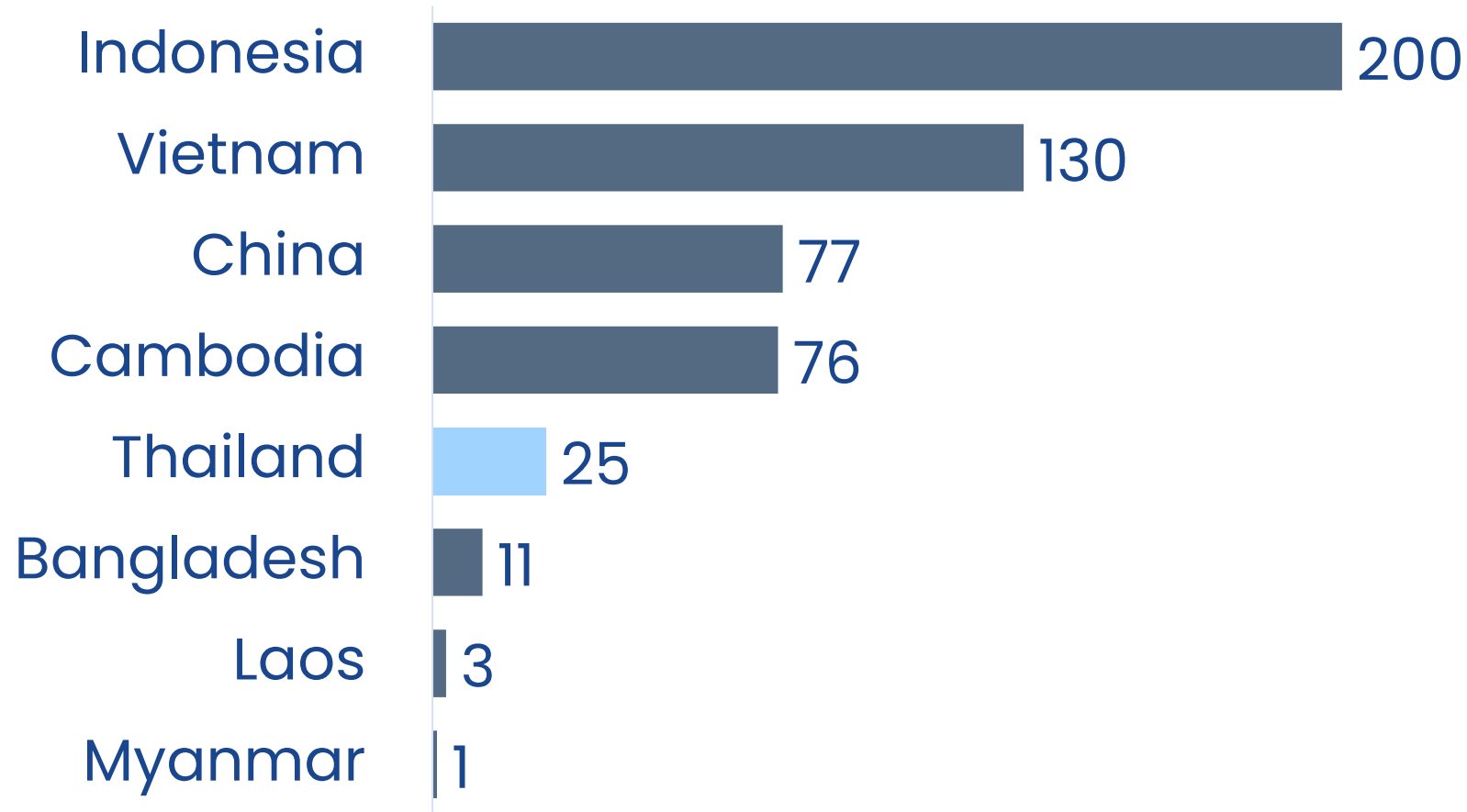
- Countries are required to report highly pathogenic avian influenza through the World Animal Health Information System (WAHIS)



Since 1997, over 1,000 human infections with influenza A(H5N1) have been reported to WHO from 25 countries

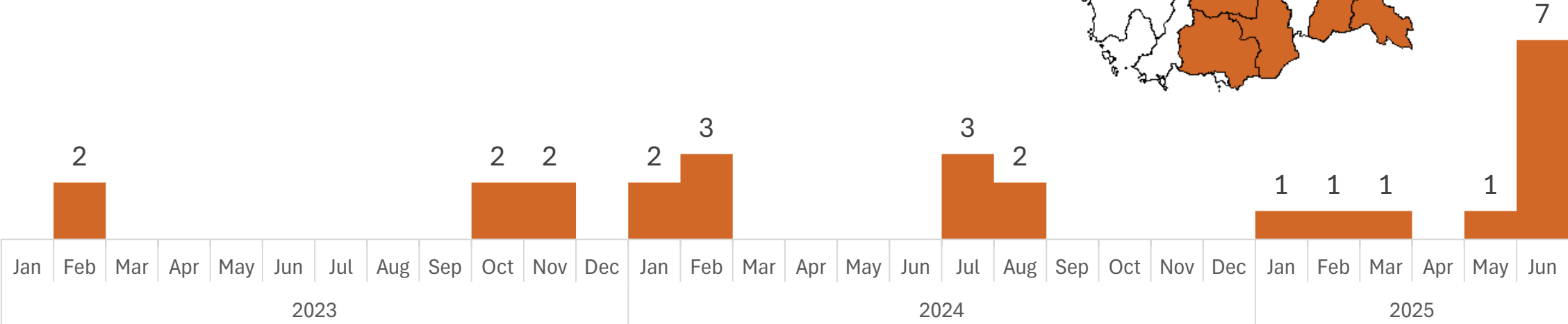
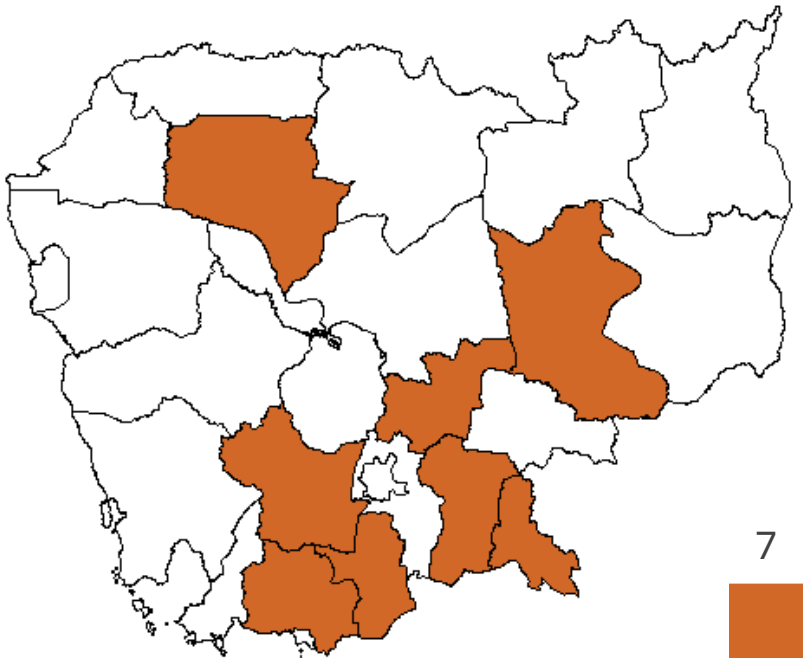


523 influenza A(H5N1) cases were reported from East Asia and Southeast Asia



In Cambodia (Feb 2023–June 2025), 27 human cases of influenza A(H5N1) have been reported

- Most infections were caused by influenza A(H5N1) clade 2.3.2.1e virus (2.3.2.1e formerly 2.3.2.1c)
- At least 13 fatal cases



Symptom onset

Three human A(H5N1) cases reported from Bangladesh in 2025

- All three cases had mild or moderate severity
- Two cases A(H5N1) were clade 2.3.2.1a
- This same clade was reported in one fatal case from India and one non-fatal case in Australia with recent travel to India



EMERGING INFECTIOUS DISEASES®

DISPATCHES

Influenza A(H5N1) Virus Clade 2.3.2.1a in Traveler Returning to Australia from India, 2024

Yi-Mo Deng,¹ Michelle Wille,¹ Clyde Dapat, Ruopeng Xie, Olivia Lay, Heidi Peck, Andrew J. Daley, Vijaykrishna Dhanasakeran, Ian G. Barr

 **FINANCIAL EXPRESS**
Read to Lead

Infant girl succumbs to bird flu in Andhra Pradesh

As a precaution, officials conducted a survey but found no new cases, including among the girl's family members.

Influenza A(H5N1) human cases in United States 2024–2025

As of July 19, 2025

- 70 confirmed A(H5N1) cases in 13 states
 - 41 cases associated with dairy cow exposure
 - 24 cases associated with commercial poultry exposure
 - 2 cases associated with backyard poultry exposure
 - 3 cases with unknown exposures
- Severity
 - 4 of 70 cases required hospitalization
 - 3 cases with pneumonia
 - 1 death
- No human-to-human A(H5N1) transmission identified in U.S. to date



Other avian influenza A viruses (non-H5) with zoonotic potential



Food and Agriculture Organization
of the United Nations

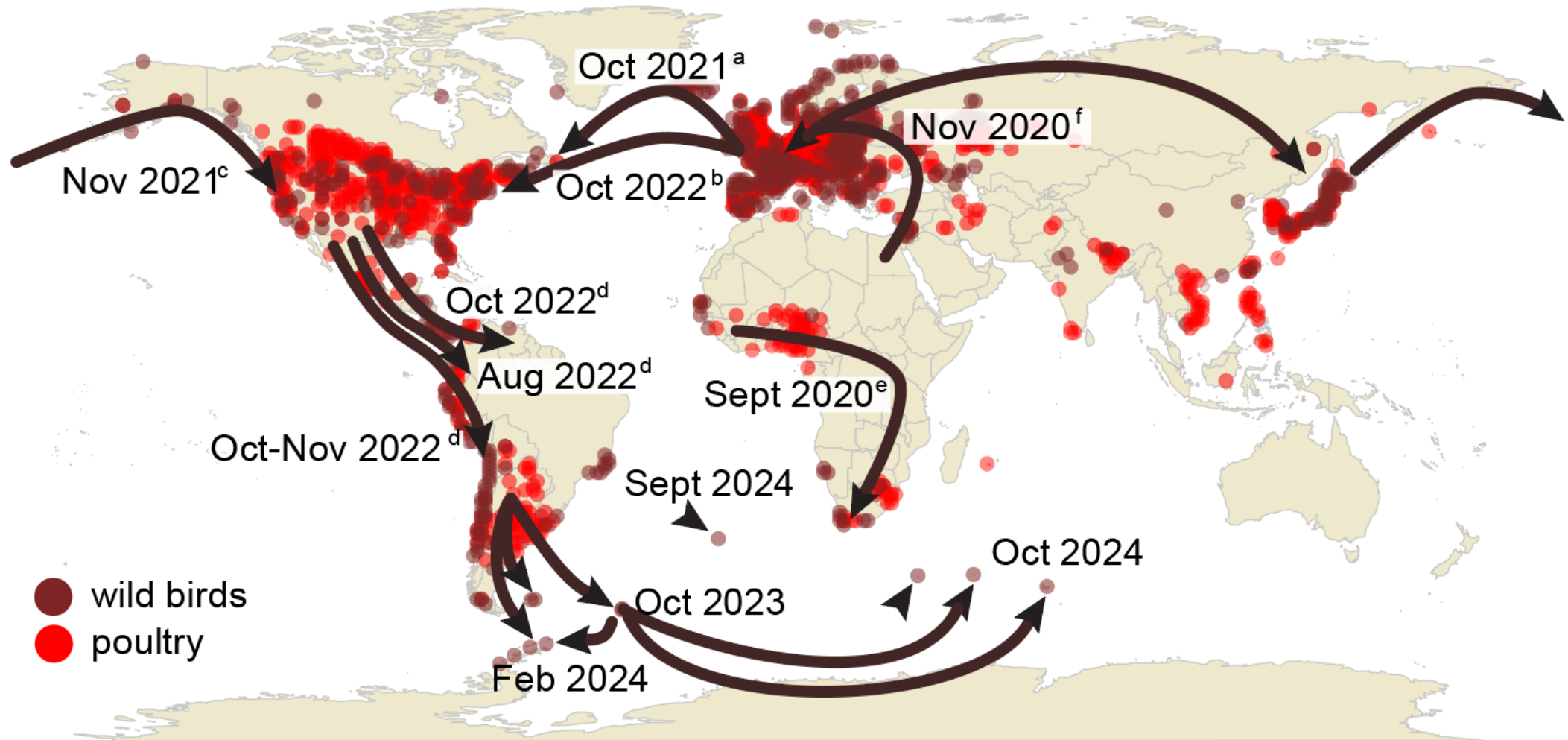
As of 22 May 2025

- H3N8
 - Emerged in live bird markets in China in 2021
 - 3 human cases reported in 2022–2023 in China
- H7N4
 - One human case in China in 2017, exposed to poultry
- H7N9
 - Over 1,000 human cases in China, mostly 2013–2017
 - Poultry vaccination campaign started in 2017
 - Last reported human case 2019
- H9N2
 - First case reported 1998
 - Around 100 human cases, 2 reported fatalities, mostly in China
- H10Nx
 - Around 10 cases reported from China, Egypt, and Australia

Clade Distribution

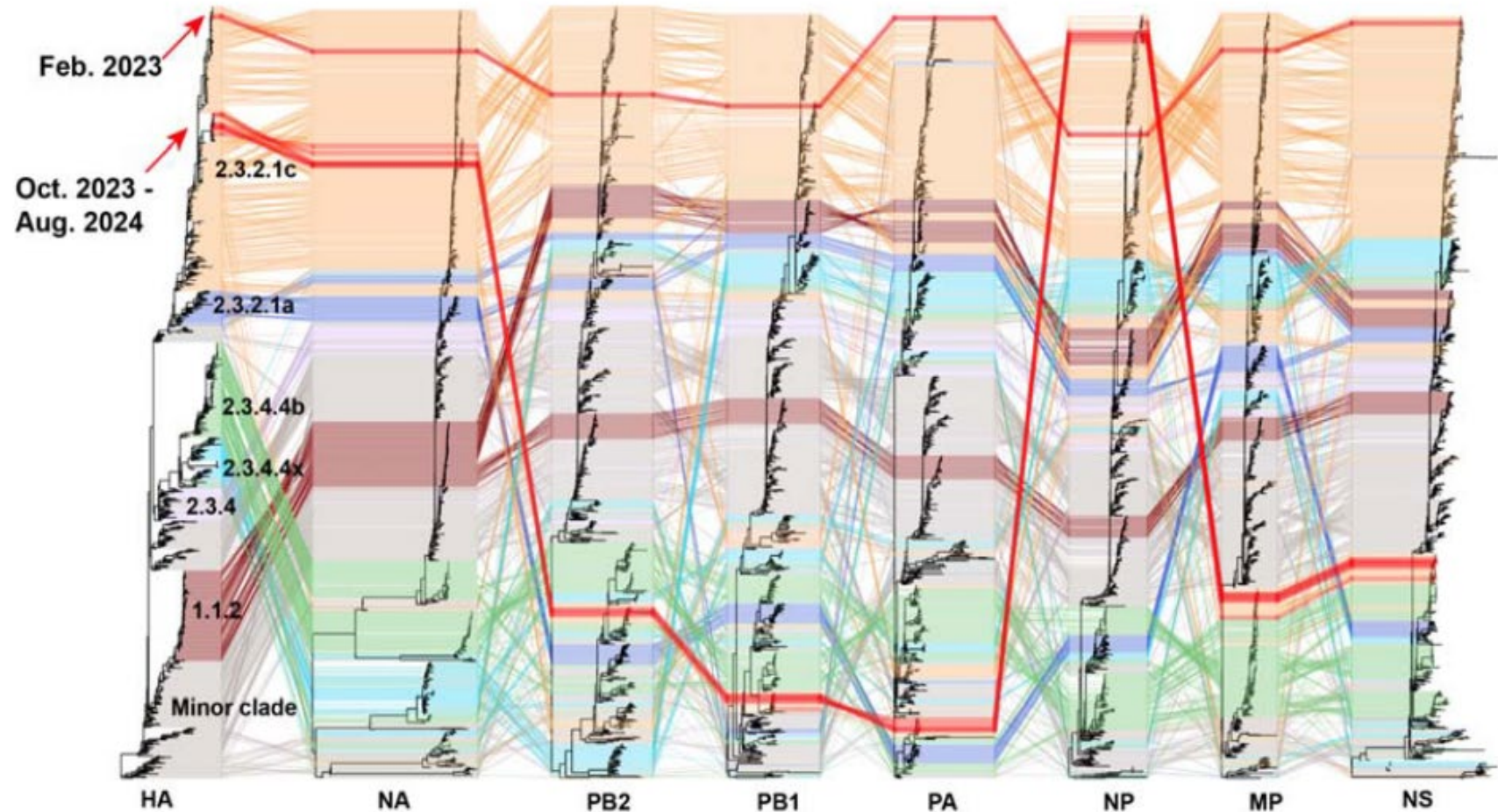


Influenza A(H5N1) clade 2.3.4.4b emerged in 2020 and caused a panzootic among birds

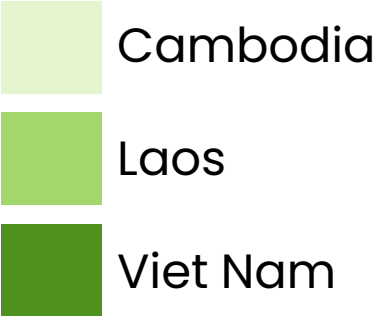


Genetic reassortment of A(H5N1) virus clade 2.3.2.1e (formerly 2.3.2.1c) in Southeast Asia

- 2.3.2.1e/c in **orange**
- 2.3.4.4b in **green**
- Human A(H5N1) cases from Cambodia in **red**
- Evidence of reassortment of internal genes (PB2, PB1, PA, MP, NS) after February 2023

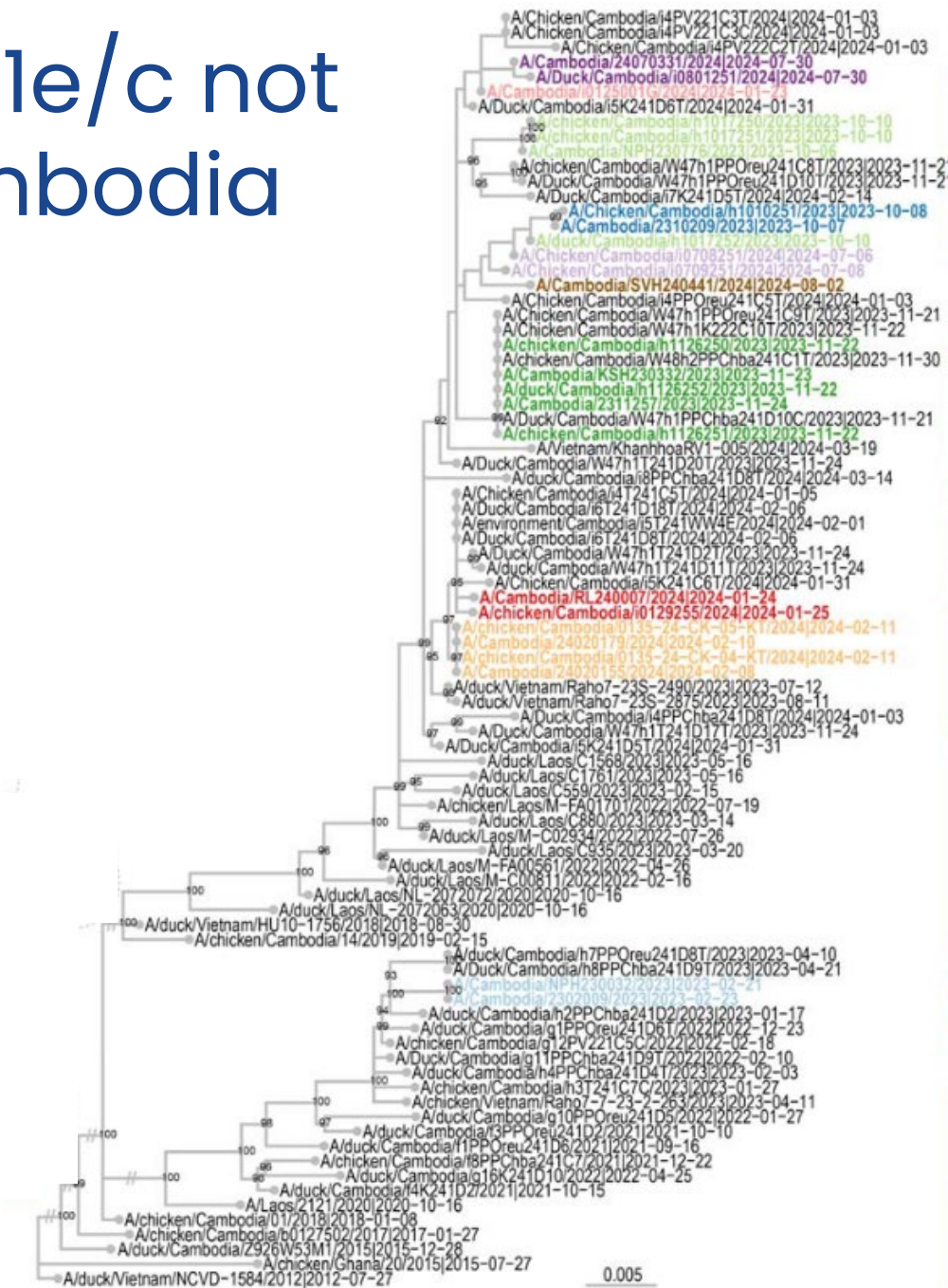


Clade 2.3.2.1e/c not only in Cambodia



Siegers JY et al. (2025) medRxiv preprint.
<https://www.medrxiv.org/content/10.1101/2024.11.04.24313747v2.full>

Clade 2.3.2.1e/c not only in Cambodia

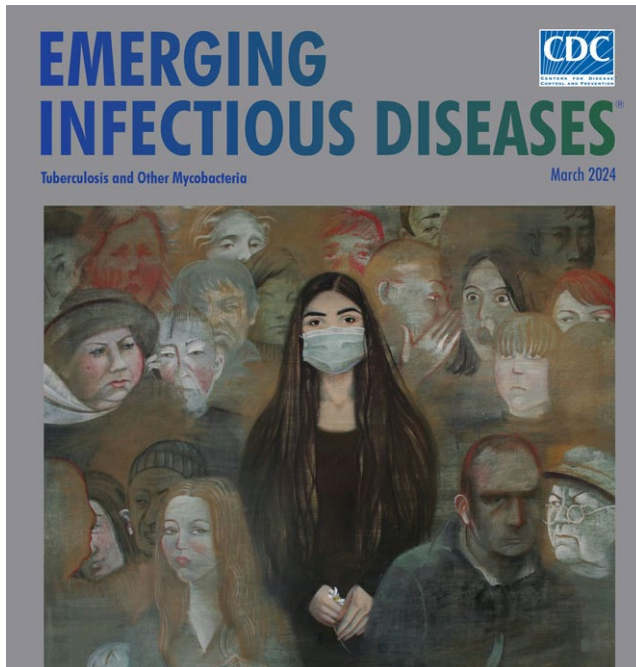


Human infection
Viet Nam 2024

Human infection
Lao 2020

A(H5N1) clades 2.3.2.1e/c and 2.3.4.4b have spread to mammals

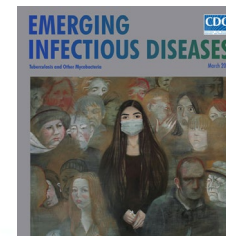
- Spread to unprecedented number of animals and to mammals



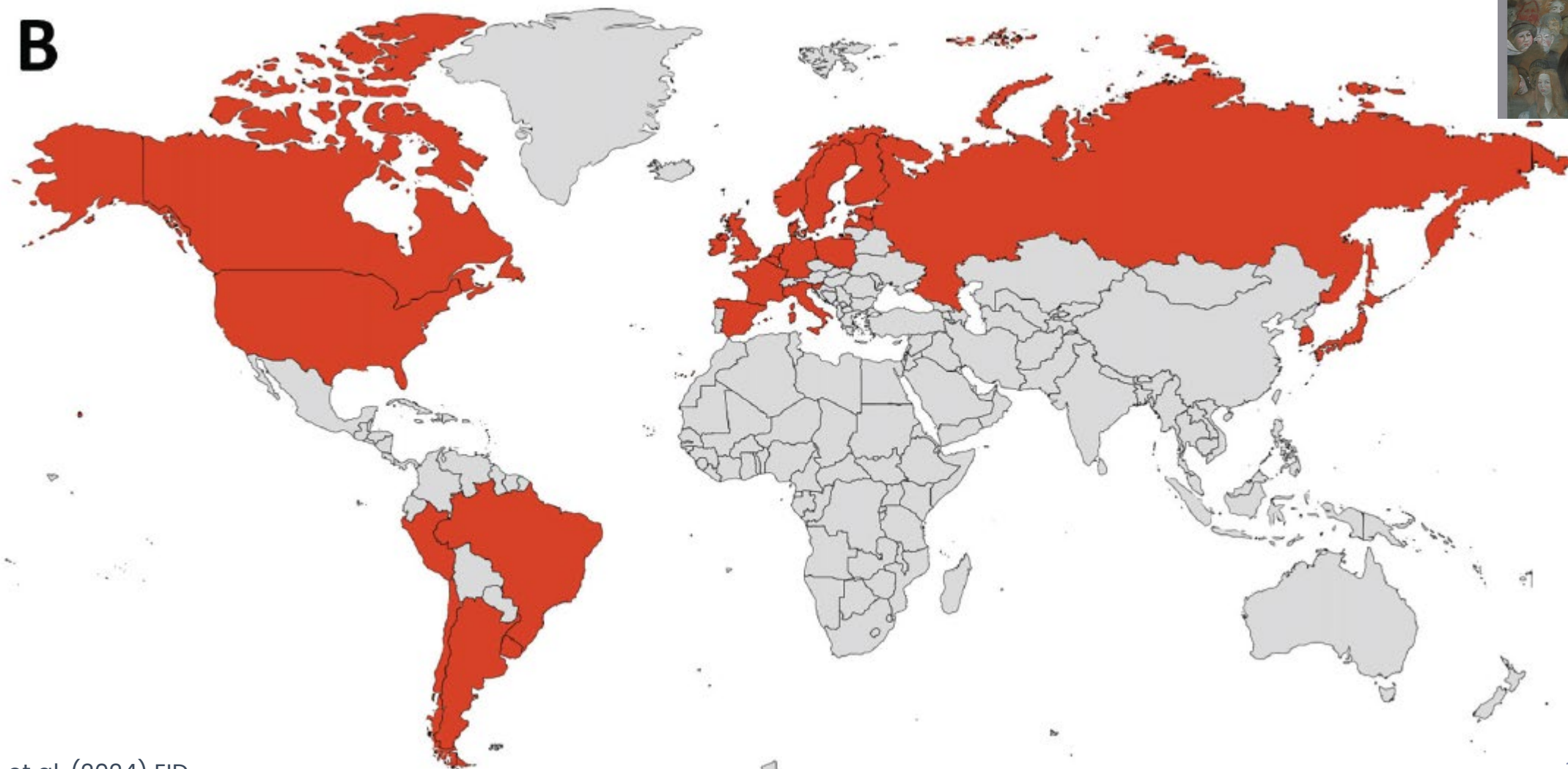
Recent Changes in Patterns of Mammal Infection with Highly Pathogenic Avian Influenza A(H5N1) Virus Worldwide

Pablo I. Plaza, Víctor Gamarra-Toledo, Juan Rodríguez Euguí, Sergio A. Lambertucci

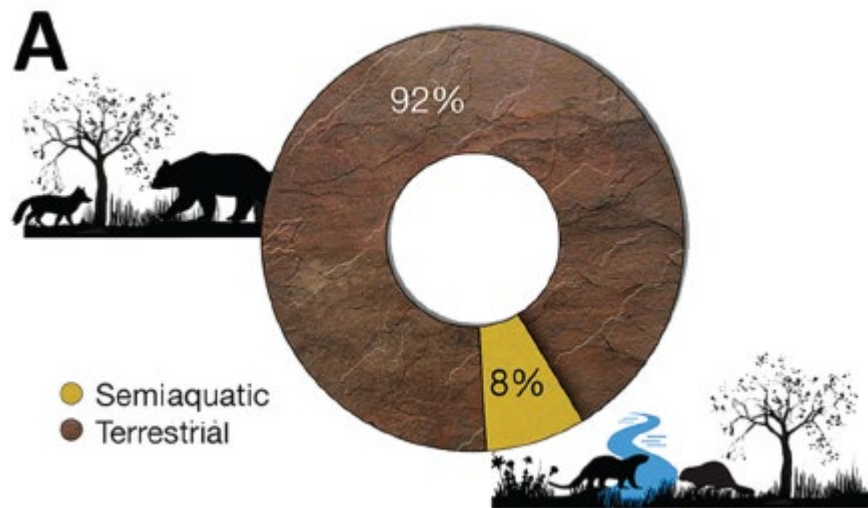
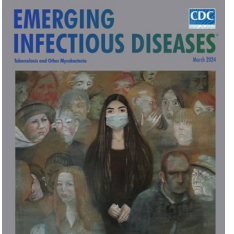
Location of mammal species infected with A(H5N1) virus in current panzootic (2020–2023)



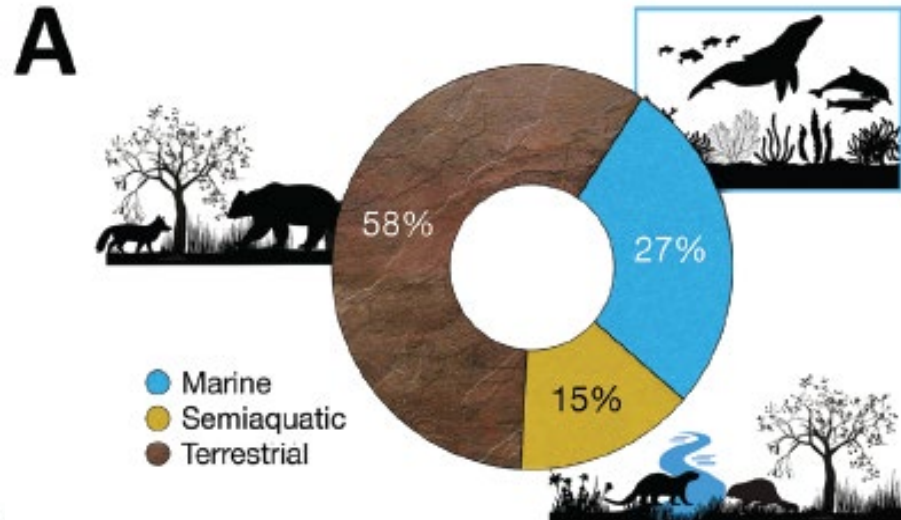
B



Habitats of mammal species affected by A(H5N1)



2003–2019

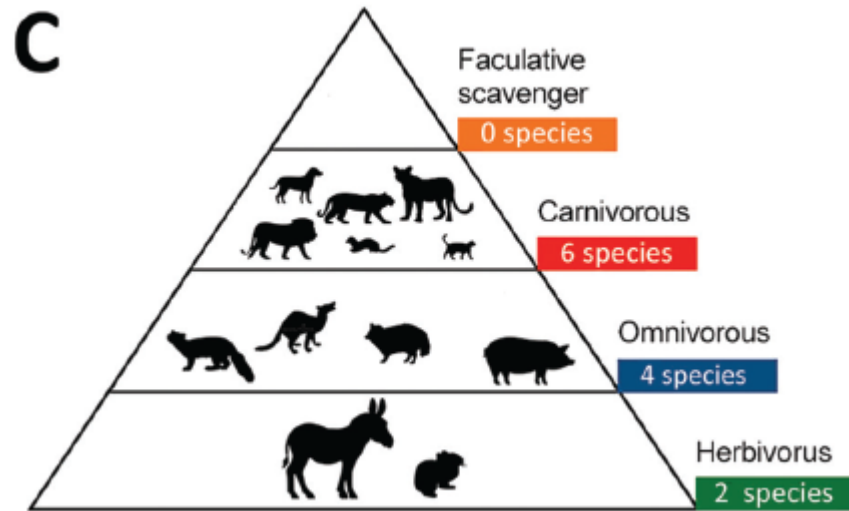
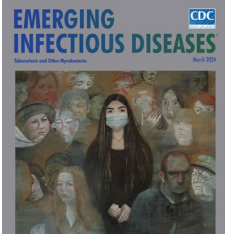


2020–2023

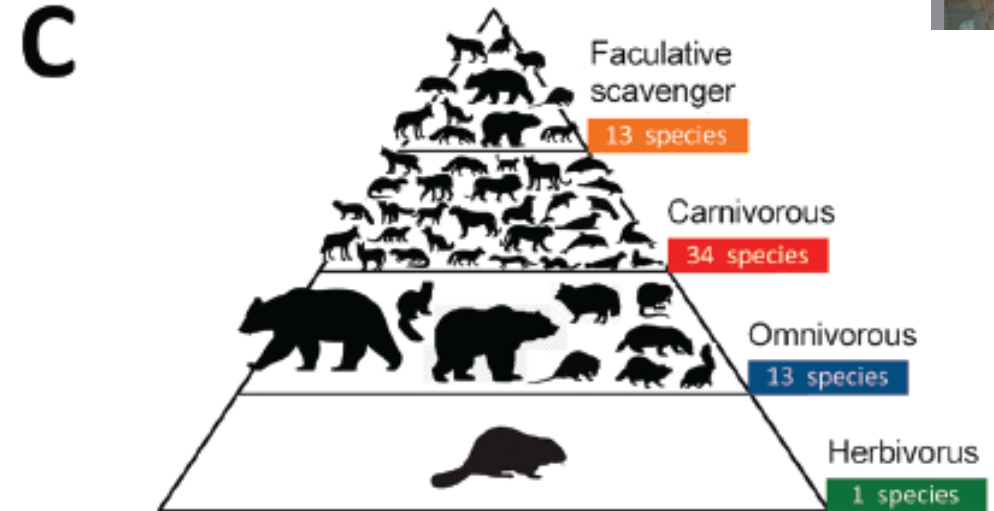
Hypotheses:

- higher environmental circulation of A(H5N1)
- changes in viral dynamics

Trophic level of mammal species affected by A(H5N1)



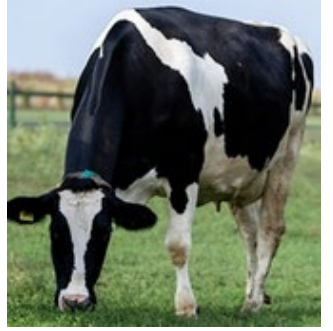
2003–2019



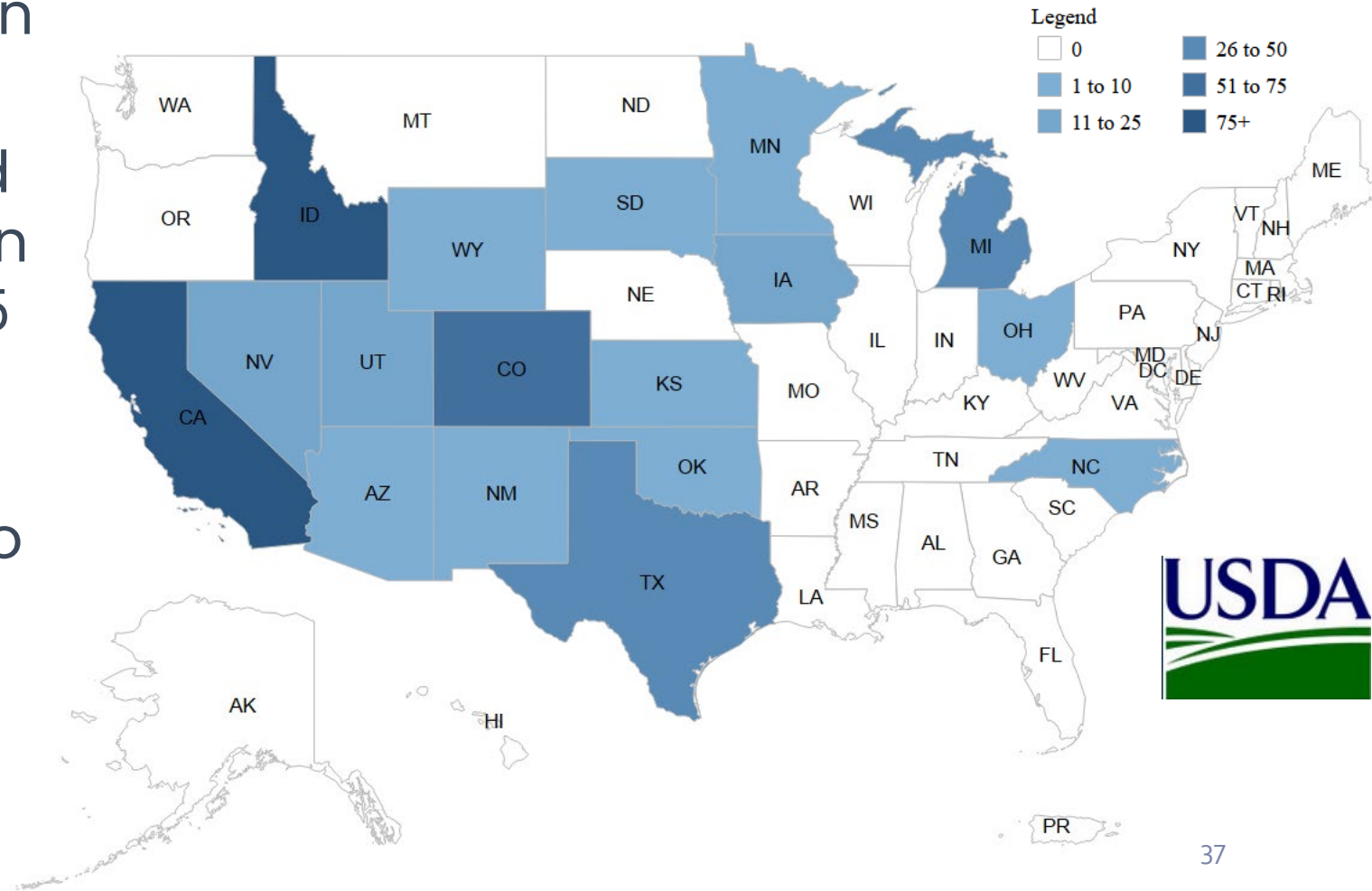
2020–2023

“40 (42) new mammal species have been reported as infected by [A(H5N1)] during the current panzootic”

Influenza A(H5N1) cases in dairy cattle in United States 2024–2025



- First A(H5N1) case in dairy cattle confirmed in Texas in March 2024
- Overall, A(H5N1) confirmed in 1,073 dairy cattle herds in 17 states as of June 3, 2025
- At least 3 independent introductions of clade 2.3.4.4b from wild birds into dairy cattle
- Genotype B3.13 (most prevalent), D1.1



One Health Approach to Pandemic Planning



A One Health approach is needed to plan, detect, and respond to avian influenza

Why **ONE HEALTH** is Important

As Earth's population grows, our connection with animals and the environment changes:



People live closer together



Changes in climate and land use



More global travel and trade



Animals are more than just food

These factors make it easier for diseases to spread between animals and people.

A One Health approach tackles shared health threats by looking at all angles—human, animal, plant, and environmental

www.cdc.gov/onehealth



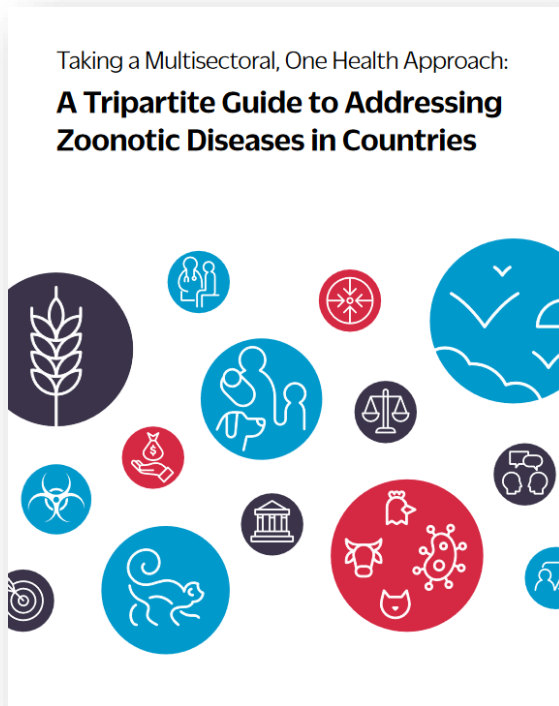
A One Health approach is needed to **plan**, detect, and respond to avian influenza



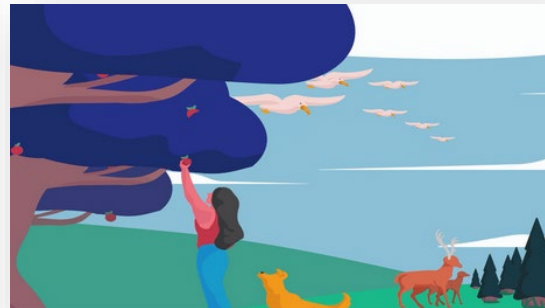
Food and Agriculture
Organization of the
United Nations



World Health
Organization



Joint Risk Assessment



Surveillance and
Information Sharing



Multisectoral, One Health,
Coordination Mechanism



A One Health approach is needed to plan, **detect**, and respond to avian influenza

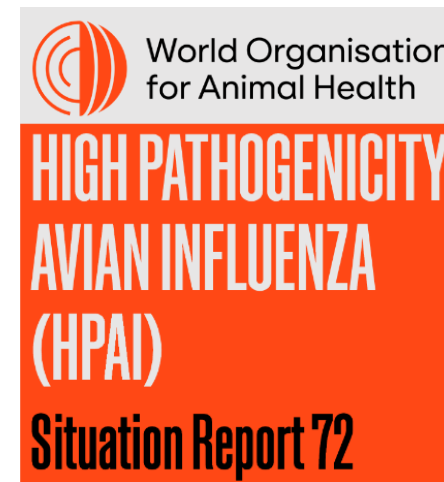
Human



- A single surveillance system won't address respiratory disease broadly
- Need multiple surveillance systems and complementary studies



Animal



A One Health approach is needed to plan, **detect**, and respond to avian influenza



Food and Agriculture
Organization of the
United Nations



World Health
Organization



World Organisation
for Animal Health

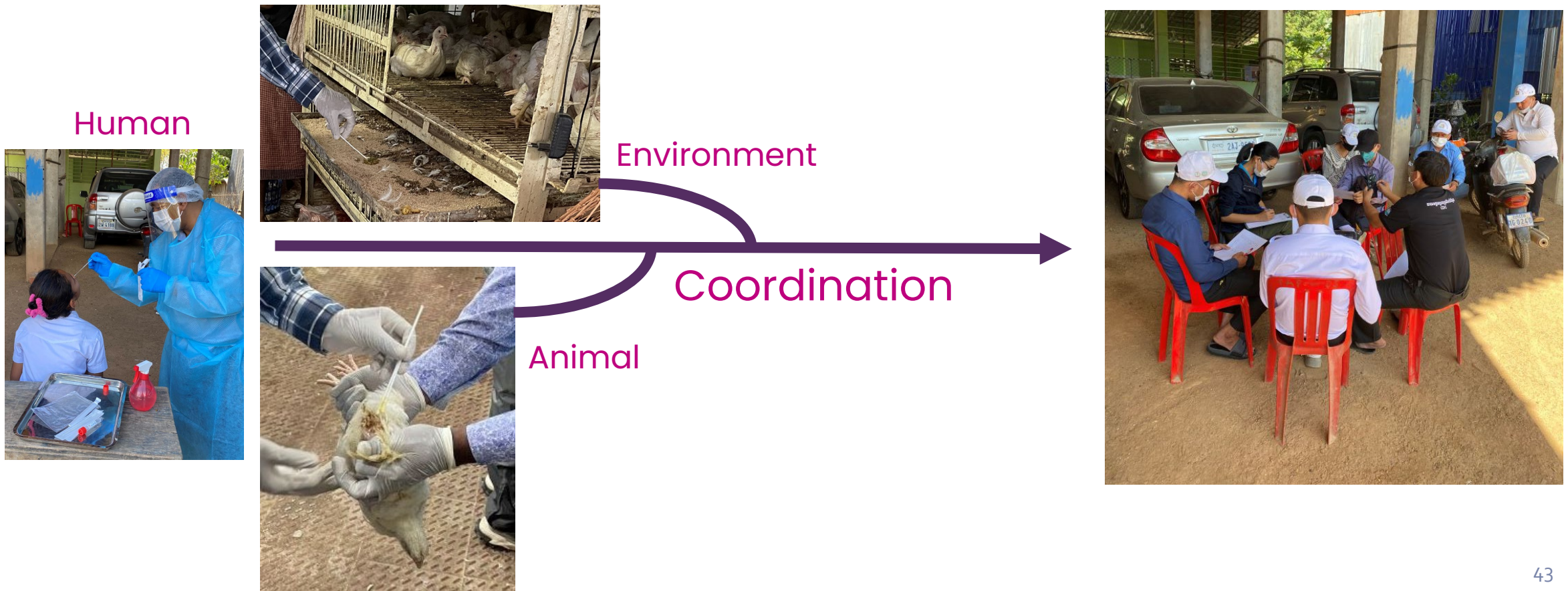
Updated joint FAO/WHO/WOAH public health assessment of recent influenza A(H5) virus events in animals and people

Assessment based on data as of 1 March 2025

17 April 2025

A One Health approach is needed to plan, detect, and **respond** to avian influenza

Investigations of avian influenza cases, clusters, and outbreaks involve **multiple sectors** at **multiple levels**



Thank you

Many thanks to Drs. Tim Uyeki, Sonja Olsen, Bill Davis, and Joshua Mott for developing slides

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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