What Providers Need to Know about Zoonotic Influenza

Clinician Outreach and Communication Activity (COCA) Call

Tuesday, June 20, 2023

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Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Discuss the current situation of highly pathogenic avian influenza A(H5N1) virus and variant influenza A viruses in the United States and worldwide, including the epidemiology of human infections with H5N1 viruses and other avian influenza A viruses.
2. Describe diagnostic testing for novel influenza A viruses, limitations of commercially available influenza diagnostic tests, and recommended antiviral treatment for novel influenza A virus infections.
3. Provide updates on current animal outbreaks.
4. Discuss CDC's surveillance and detection of novel influenza A virus infections in people.
5. Review clinical considerations and best practices for managing patients with novel influenza A virus infections.

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov

Today's Presenters

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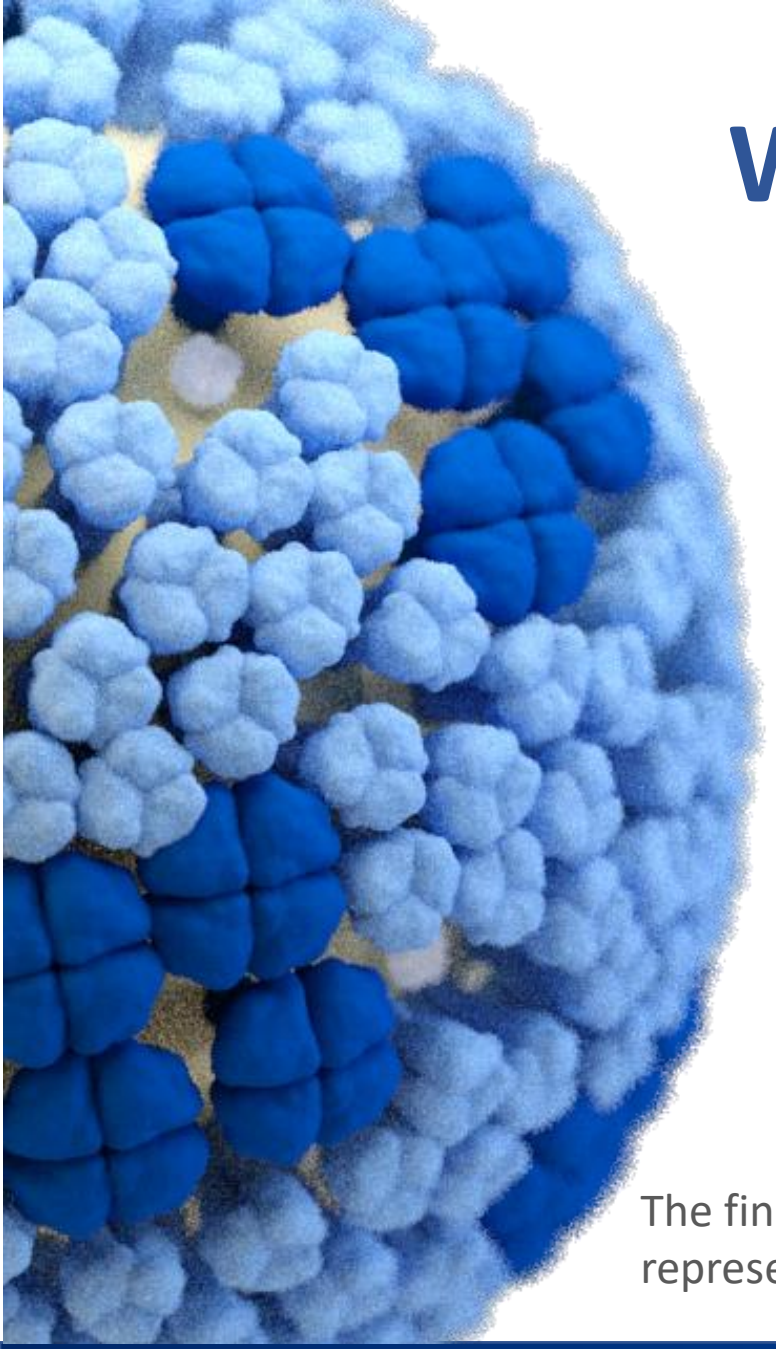

What Providers Need to Know about Zoonotic Influenza

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Overview

- **Avian and swine influenza A virus virology**
  - Types and subtypes
  - Ecology and transmission dynamics
  - Public health impact of zoonotic influenza viruses
- **Surveillance for infections with swine and avian influenza A viruses**
  - Domestic and global strategies – public health
  - Domestic and global strategies – veterinary health
- **Influenza Risk Assessment**
  - Risk assessment tools
  - Genetic and virologic characterization
    - HPAI H5N1
    - Swine influenza viruses
- **Pandemic preparedness**
  - Evaluation of diagnostic tests
  - Characterization of Antiviral drug susceptibility
  - Vaccine development

Influenza Viruses

4 Types of Influenza viruses (A, B, C, D)

Influenza A, B, and C viruses have infected people to cause disease

- **Influenza viruses have 8 gene segments and continue to evolve**
- **Seasonal influenza A and B viruses cause annual epidemics**

Influenza A viruses are important for public health and agriculture

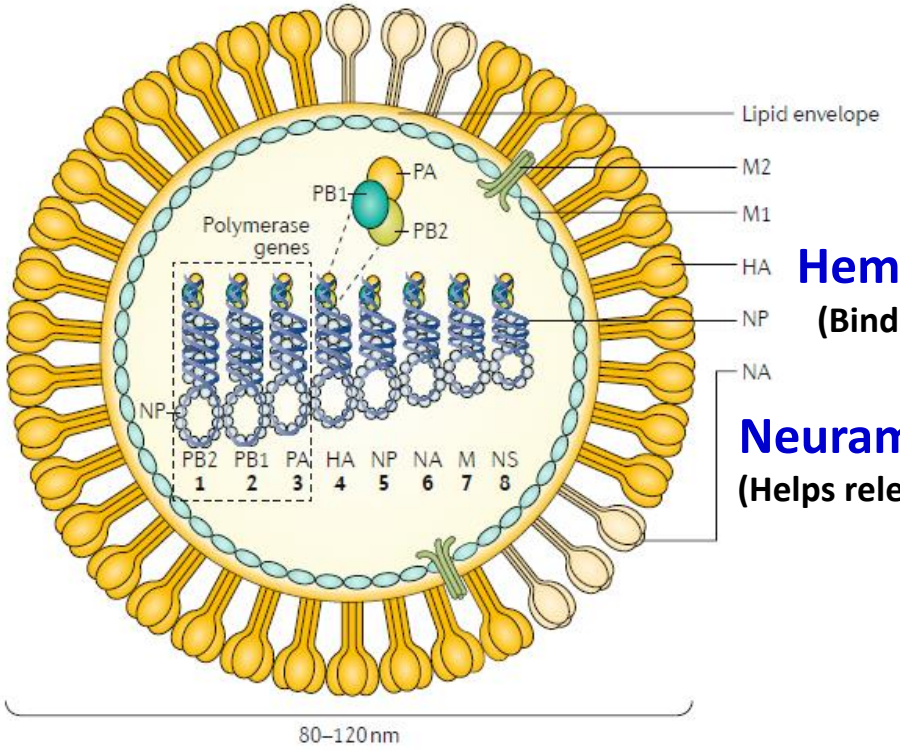
- **Natural reservoir for almost all influenza A viruses is wild waterfowl (wild ducks and geese)**
- **Some influenza A viruses can infect poultry, pigs, and other animals**
- **Some influenza A viruses circulate among animals (established circulation in animal hosts)**

Influenza A viruses are classified into subtypes based on the 2 main surface proteins:

- **Hemagglutinin (HA or H)**

  and

- **Neuraminidase (NA or N)**



Hemagglutinin (HA or H)
(Binds to host cell receptors)

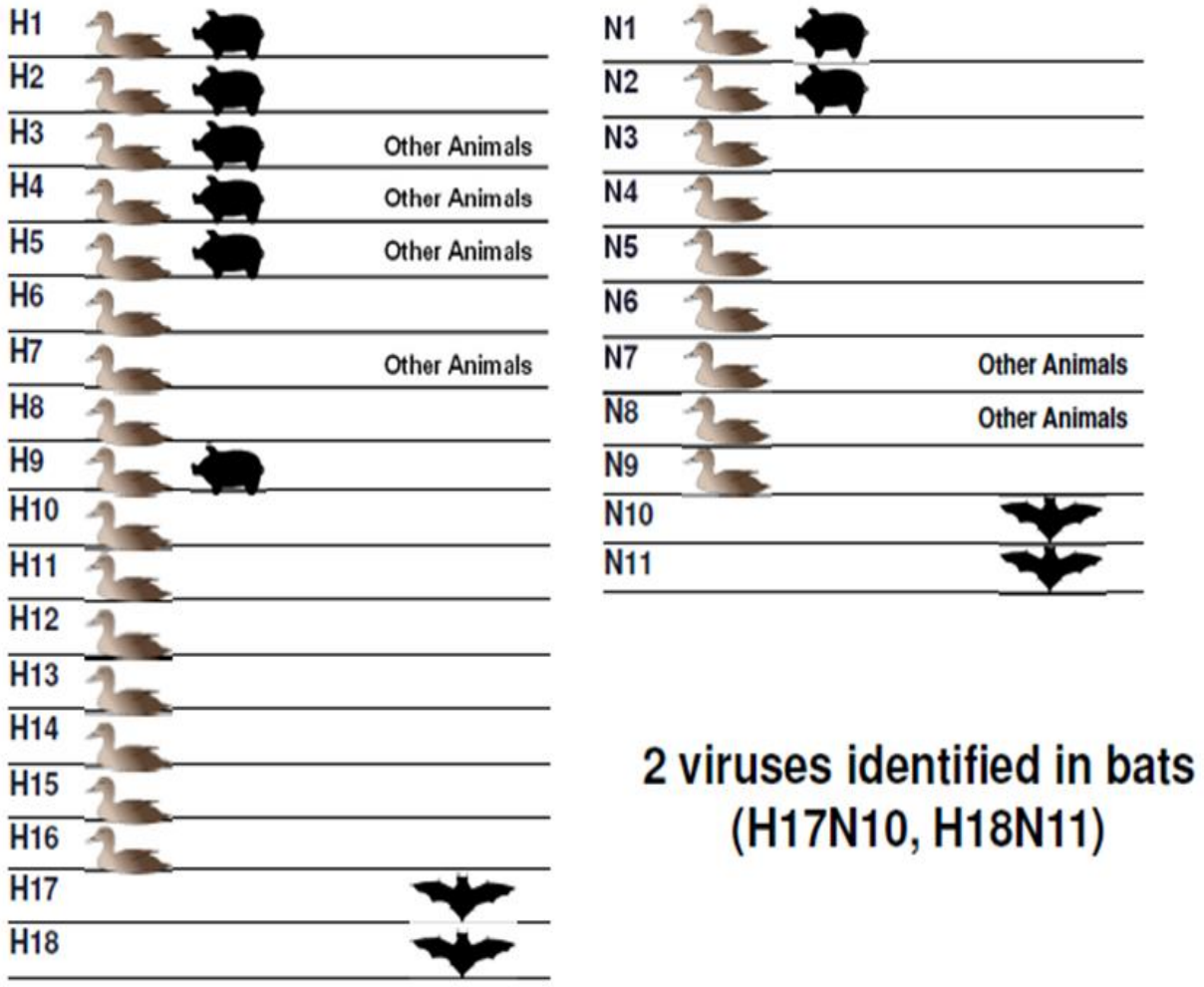
Neuraminidase (NA or N)
(Helps release viral particles from infected cells)

Krammer Nature Reviews Disease Primers 2018

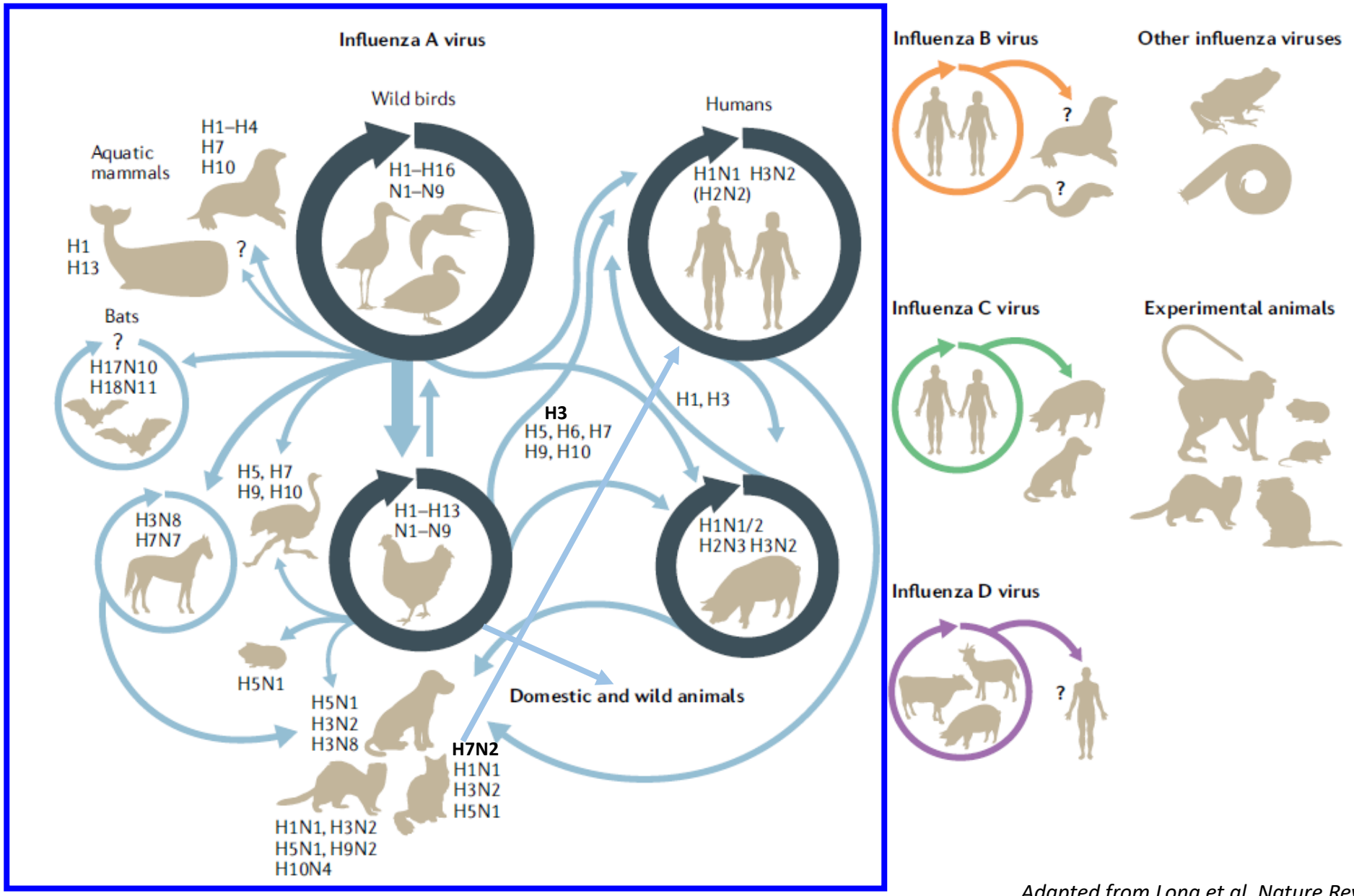
Influenza A Viruses

- **18 HA subtypes; 11 NA subtypes**
  - All but 2 subtypes are found in wild birds
  - Many different animal species can be infected with influenza A viruses
  - Some influenza A viruses circulate among poultry, pigs, and other animals; sporadic avian-to-human or pig-to-human transmission can occur

- **Influenza A viruses can evolve by:**
  - Mutations to genes that result in changes to virus proteins (called “antigenic drift”)
  - Exchanging genes (called “genetic reassortment”)



Ecology of Influenza Viruses



Adapted from Long et al. Nature Reviews Microbiology 2019

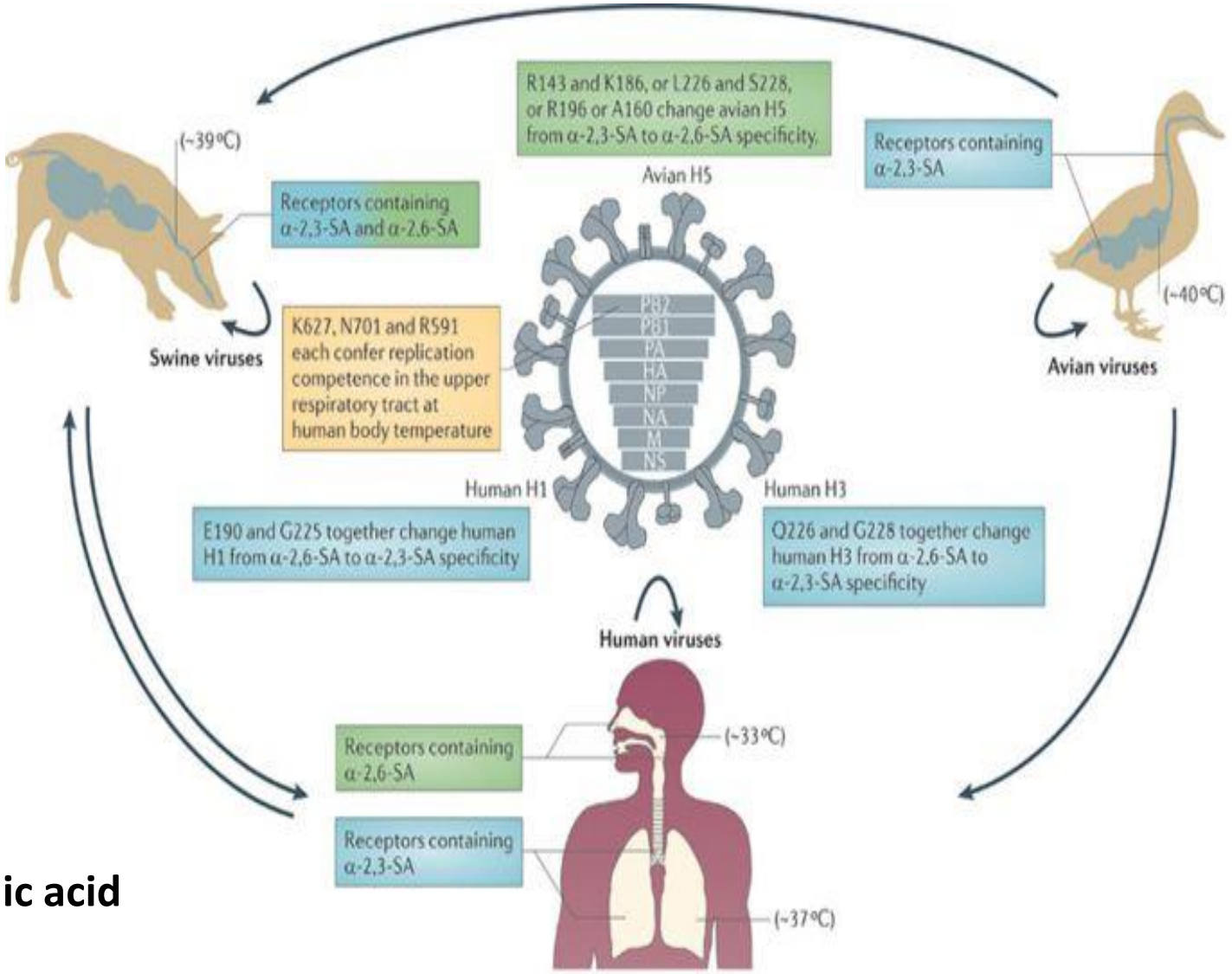
Receptor binding specificity and mammal adaptation of avian influenza viruses

- Seasonal influenza A and B viruses bind to sialic acid receptors attached to galactose by **α2,6 linkages** on epithelial cells that are primarily found in the ***upper respiratory tract in humans***

- Some influenza viruses can bind to **α2,3 sialic acid receptors** that are primarily found in the ***lower respiratory tract in humans***

- Pigs & humans have similar respiratory tract distribution of α2,6 and α2,3 linkages

- Wild birds & poultry have respiratory and gastrointestinal tract α2,3 linkages
  - Avian viruses adapted for binding α2,3 sialic acid linkages



Nature Reviews | Microbiology

Novel Influenza A Virus Infections of Humans

- **Novel Influenza A virus infection**
  - Human infection with an influenza A virus of animal-origin
    - *Avian influenza A virus (pathogenicity refers to poultry)*
    - *Swine influenza A virus*
    - *Others?*

  - **Different from seasonal influenza A virus infections**
    - Antigenically and Genetically distinct from seasonal influenza A viruses

  - **June 2007, USG made novel influenza A infections nationally reportable to the National Notifiable Diseases Surveillance System**

  - **World Health Organization requires International Health Regulations (IHR) reporting of novel infections**

Public Health Impact of Infection with Zoonotic Influenza Viruses

A pandemic can occur if:

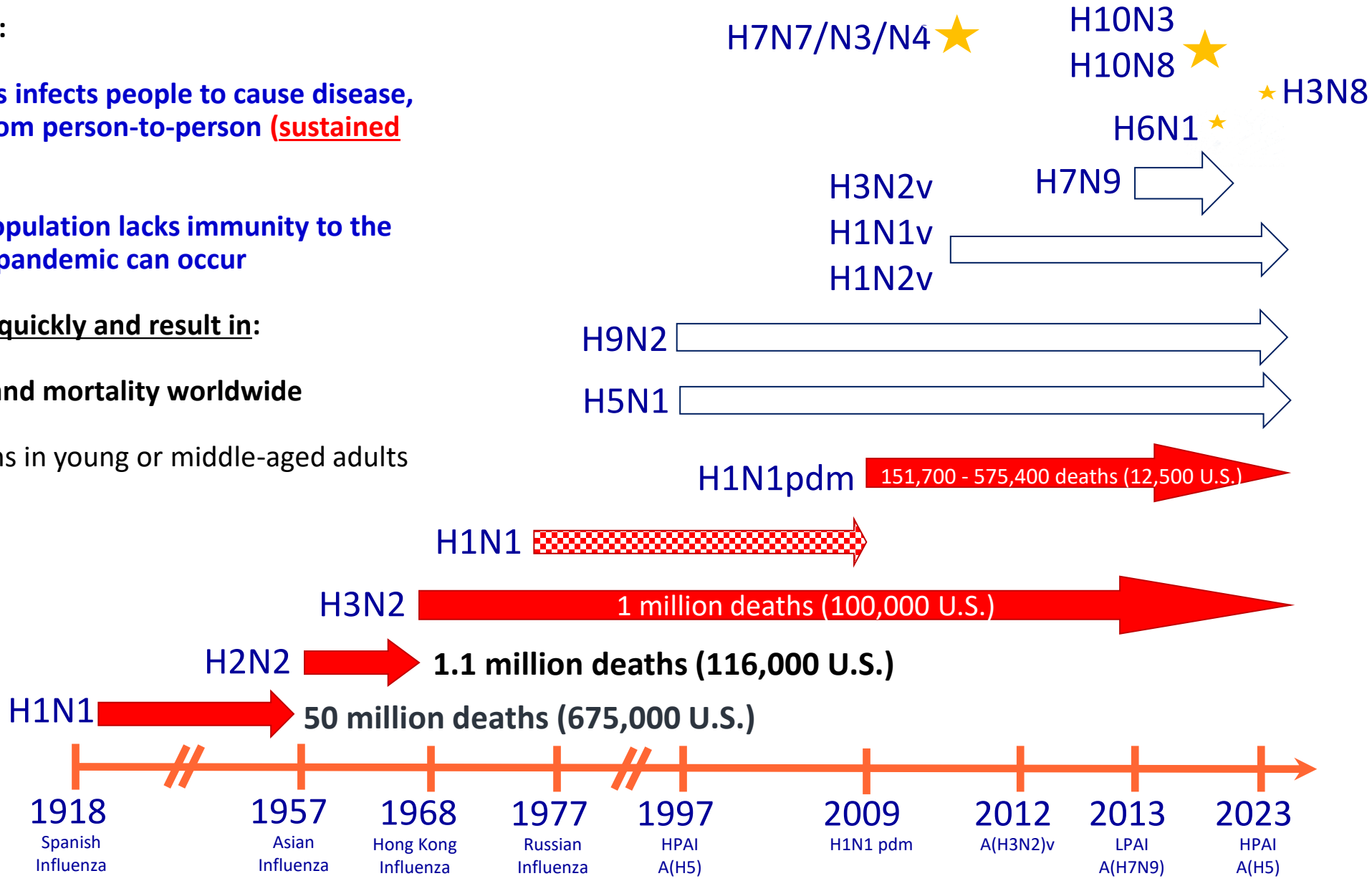
A novel influenza A virus infects people to cause disease, and can spread easily from person-to-person (sustained transmission)

If most of the world's population lacks immunity to the new virus, an influenza pandemic can occur

A pandemic can spread quickly and result in:

Widespread morbidity and mortality worldwide

High proportion of deaths in young or middle-aged adults



Dawood Lancet Infect Dis 2012; Simonsen PLoS Med 2013

Objectives of Influenza Surveillance

Detection	Severity	Populations	Vaccine Match	Changes to Virus	Pandemic Potential	Interventions	Inform
Detect the onset, duration and spread of influenza activity in a geographic area.	Measure and describe the severity of influenza during a season.	Determine the populations affected and identify special risk groups.	Monitor the prevalence of circulating virus types and subtypes and match to annual vaccine strains.	Monitor genetic and phenotypic changes to circulating influenza viruses and evaluate risk and the need for changes to the annual vaccine composition.	Identify and monitor novel subtypes that might signal a pandemic.	Provide data to guide interventions in clinical and public health control measures.	Provide information to key partners including: clinical decision makers, policy makers, emergency response officials, the media, and the public.

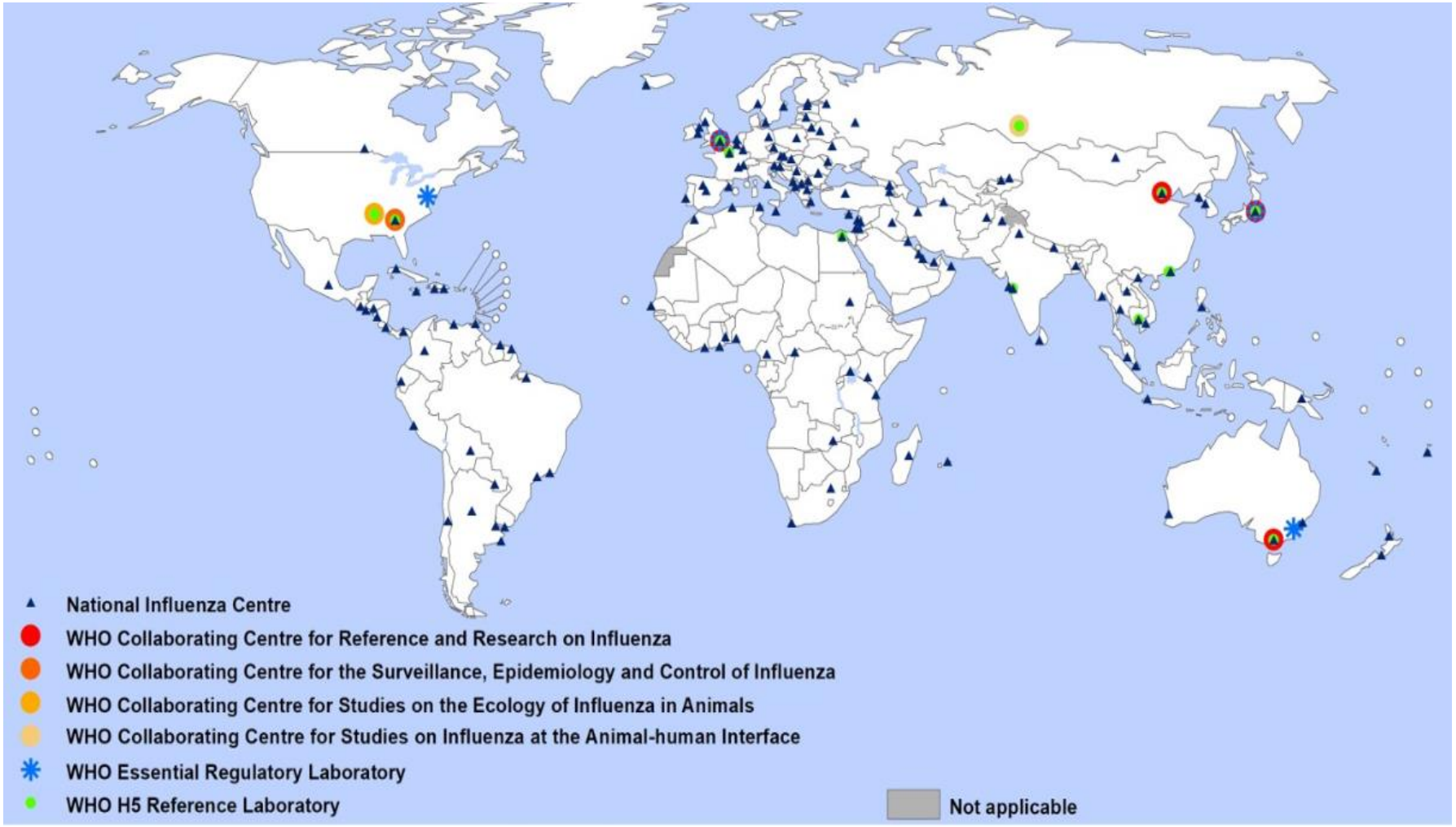
Detecting cases through routine surveillance

- Rare/novel influenza event detection is a component of routine virologic surveillance.
- Specimens should be broadly representative of the population as a whole (age, geography, risk groups, disease severity).
- Routine surveillance to detect 1 novel influenza virus among 700 positive specimens aggregated to the national level during the peak of flu season.
- An unusual laboratory diagnostic result obtained by routine surveillance initiates an investigation including the persons exposure history and follow-up with close contacts.

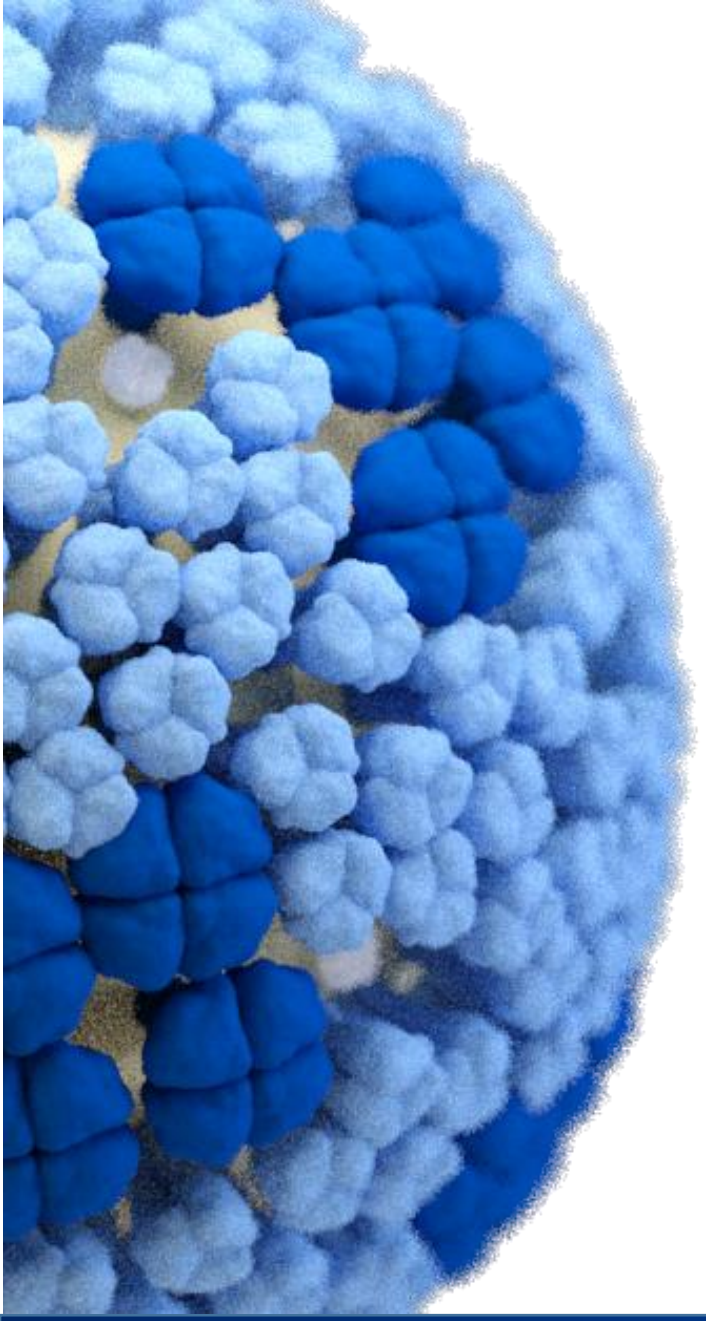
Detecting cases through enhanced surveillance

- Detection of a novel virus may be enhanced with more targeted surveillance in specific populations or risk groups
    - Active symptom monitoring and testing among individuals with exposure to HPAI H5N1 infected birds
- Surrounding an epidemiologic investigation.
    - Linked to another confirmed case (i.e., close contact an index case or exposure where there was a confirmed case)
    - Sick people in close proximity to sick or healthy animals.

CDC supports WHO Global Influenza Surveillance and Response System (GISRS)



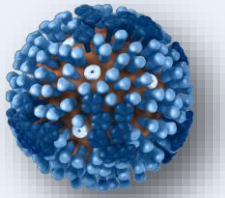
- 147 WHO National Influenza Centers in 123 Member States (CDC Atlanta Influenza Laboratory is one)
- 7 WHO Collaborating Centers for Influenza (CDC is one)
- 12 WHO H5 Reference Laboratories



Influenza Risk Assessment

Influenza Risk Assessment Tool (IRAT)

- Ranks viruses that are circulating in animals but not humans
- Ten risk elements evaluated to develop a risk score:
  - properties of the virus
  - population immunity
  - animal and human ecology
- Evaluative, not predictive

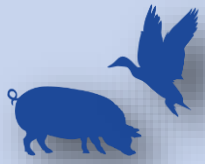


Virus

1. **Genomic Analysis**
2. **Receptor Binding**
3. **Transmission in Animal Models**
4. **Antiviral Treatment Options**

Population

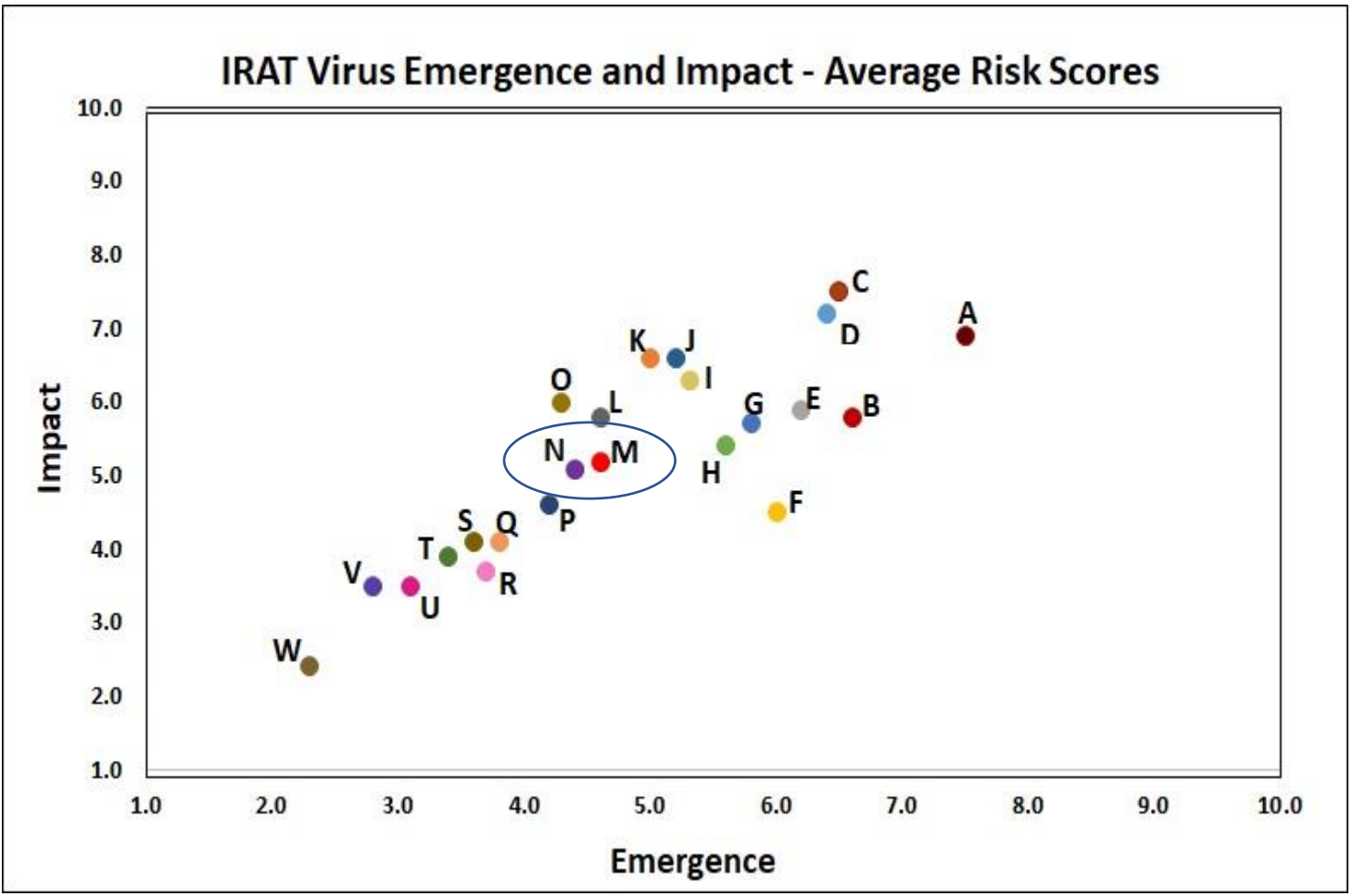
5. **Existing Population Immunity**
6. **Disease Severity and Pathogenesis**
7. **Antigenic Relatedness (to Vaccine Candidates)**



Ecology

8. **Global Distribution in Animals**
9. **Infection in Animals**
10. **Human Infections and Transmission**

Influenza Risk Assessment Tool



	Influenza Virus	Emergence Score	Impact Score	Risk Assessment Year
A	A(H1N1) [A/swine/Shandong/1207/2016]	7.5	6.9	Jul 2020
B	A(H3N2) variant [A/Ohio/13/2017]	6.6	5.8	Jul 2019
C	A(H7N9) [A/Hong Kong/125/2017]	6.5	7.5	May 2017
D	A(H7N9) [A/Shanghai/02/2013]	6.4	7.2	Apr 2016
E	A(H9N2) Y280 lineage [A/Anhui-Lujiang/13/2018]	6.2	5.9	Jul 2019
F	A(H3N2) variant [A/Indiana/08/2011]	6.0	4.5	Dec 2012
G	A(H1N2) variant [A/California/62/2018]	5.8	5.7	Jul 2019
H	A(H9N2) G1 lineage [A/Bangladesh/0994/2011]	5.6	5.4	Feb 2014
I	A(H5N6) clade 2.3.4.4b [A/Sichuan/06681/2021]	5.3	6.3	Oct 2021
J	A(H5N1) Clade 1 [A/Vietnam/1203/2004]	5.2	6.6	Nov 2011
K	A(H5N6) [A/Yunnan/14564/2015] – like	5.0	6.6	Apr 2016
L	A(H7N7) [A/Netherlands/219/2003]	4.6	5.8	Jun 2012
M	A(H5N8) clade 2.3.4.4b [A/Astrakhan/3212/2020]	4.6	5.2	Mar 2021
N	A(H5N1) clade 2.3.4.4b [A/American wigeon/South Carolina/AH0195145/2021]	4.4	5.1	Mar 2022
O	A(H10N8) [A/Jiangxi-Donghu/346/2013]	4.3	6.0	Feb 2014
P	A(H5N8) [A/gyrfalcon/Washington/41088/2014]	4.2	4.6	Mar 2015
Q	A(H5N2) [A/Northern pintail/Washington/40964/2014]	3.8	4.1	Mar 2015
R	A(H3N2) [A/canine/Illinois/12191/2015]	3.7	3.7	Jun 2016
S	A(H5N1) [A/American green-winged teal/Washington/1957050/2014]	3.6	4.1	Mar 2015
T	A(H7N8) [A/turkey/Indiana/1573-2/2016]	3.4	3.9	Jul 2017
U	A(H7N9) [A/chicken/Tennessee/17-007431-3/2017]	3.1	3.5	Oct 2017
V	A(H7N9) [A/chicken/Tennessee/17-007147-2/2017]	2.8	3.5	Oct 2017
W	A(H1N1) [A/duck/New York/1996]	2.3	2.4	Nov 2011

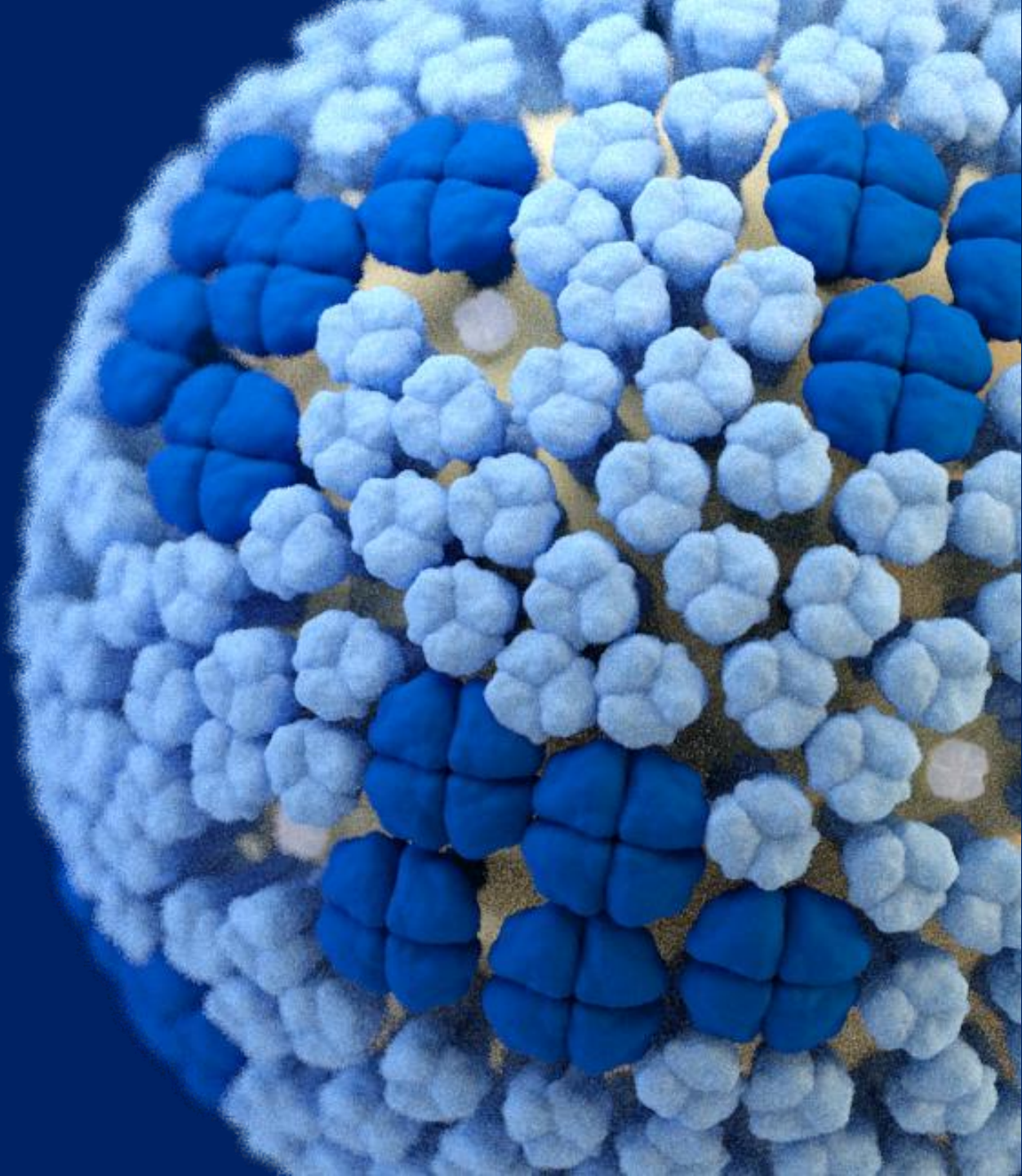
Eurasian Avian/swine H1N1 in China (A) has highest emergence score
Emergence = 7.5, Impact = 6.9
Avian H7N9 in China (C) has highest Impact score
Emergence = 6.5, Impact = 7.5

Avian H5N1 clade 2.3.4.4b [A/American wigeon/South Carolina/AH0195145/2021] (N)
Emergence = 4.4, Impact = 5.1

CDC Influenza

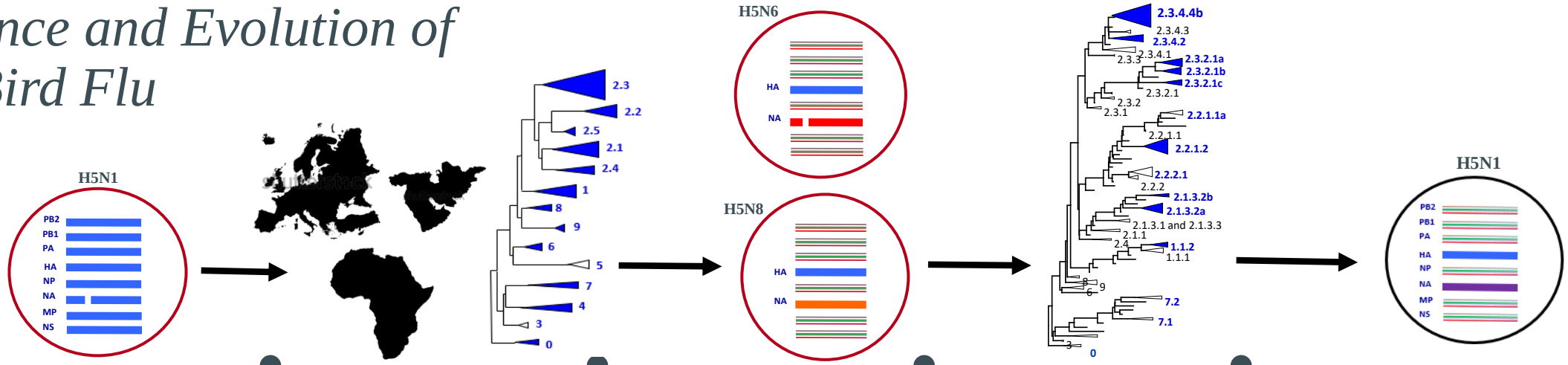
[Influenza Risk Assessment Tool (IRAT) | Pandemic Influenza (Flu) | CDC]

Highly pathogenic avian influenza A(H5N1) viruses detected in birds, mammals and humans since 2022



CDC
Influenza

Emergence and Evolution of H5N1 Bird Flu



1996-1997

H5N1 bird flu virus first detected

In 1996, HPAI H5N1 virus first identified in domestic waterfowl in Southern China. Virus is named A/goose/Guangdong/1/1996.

In 1997, poultry outbreaks detected in China and Hong Kong; 18 human cases (6 fatal) identified.

The original H5N1 virus caused over 860 reported human infections with over 50% mortality.

2003-2005

H5N1 spreads to Africa, the Middle East and Europe

H5N1 re-emerges in 2003 resulting in widespread poultry outbreaks across Asia.

In 2005, wild birds spread H5N1 to poultry in Africa, the Middle East and Europe.

HA gene diversifies into many genetic groups called clades.

Multiple genetic lineages (genotypes) are detected across the Eastern hemisphere.

2014-2016

H5N6 and H5N8 viruses emerge

Reassortment (gene-swapping) of H5 viruses from poultry and wild bird leads to emergence and detection of H5N6 and H5N8 virus subtypes.

HA diversifies further into clade 2.3.4.4 in Asia, Africa, Europe, the Middle East and North America.

H5 viruses with various NA genes continue to be detected, including in U.S. wild birds and poultry.

2018-2020

Clade 2.3.4.4b viruses spread widely

H5N6 and H5N8 viruses become the predominant subtypes detected globally replacing majority of original H5N1 virus.

As of 2022, these subtypes have resulted in 7 confirmed human cases of A(H5N8) and more than 70 A(H5N6) cases.

HA diversifies further into clade 2.3.4.4b and it becomes the predominant clade circulating in Asia, Africa, Europe, and the Middle East.

2021-2023

H5N1 Identified in North and South America

Reassortment leads to emergence of new H5N1 virus belonging to clade 2.3.4.4b with a wild bird adapted N1 NA gene.

Clade 2.3.4.4b H5N1 viruses become the predominant subtype in Asia, Africa, Europe, and the Middle East by the end of 2021.

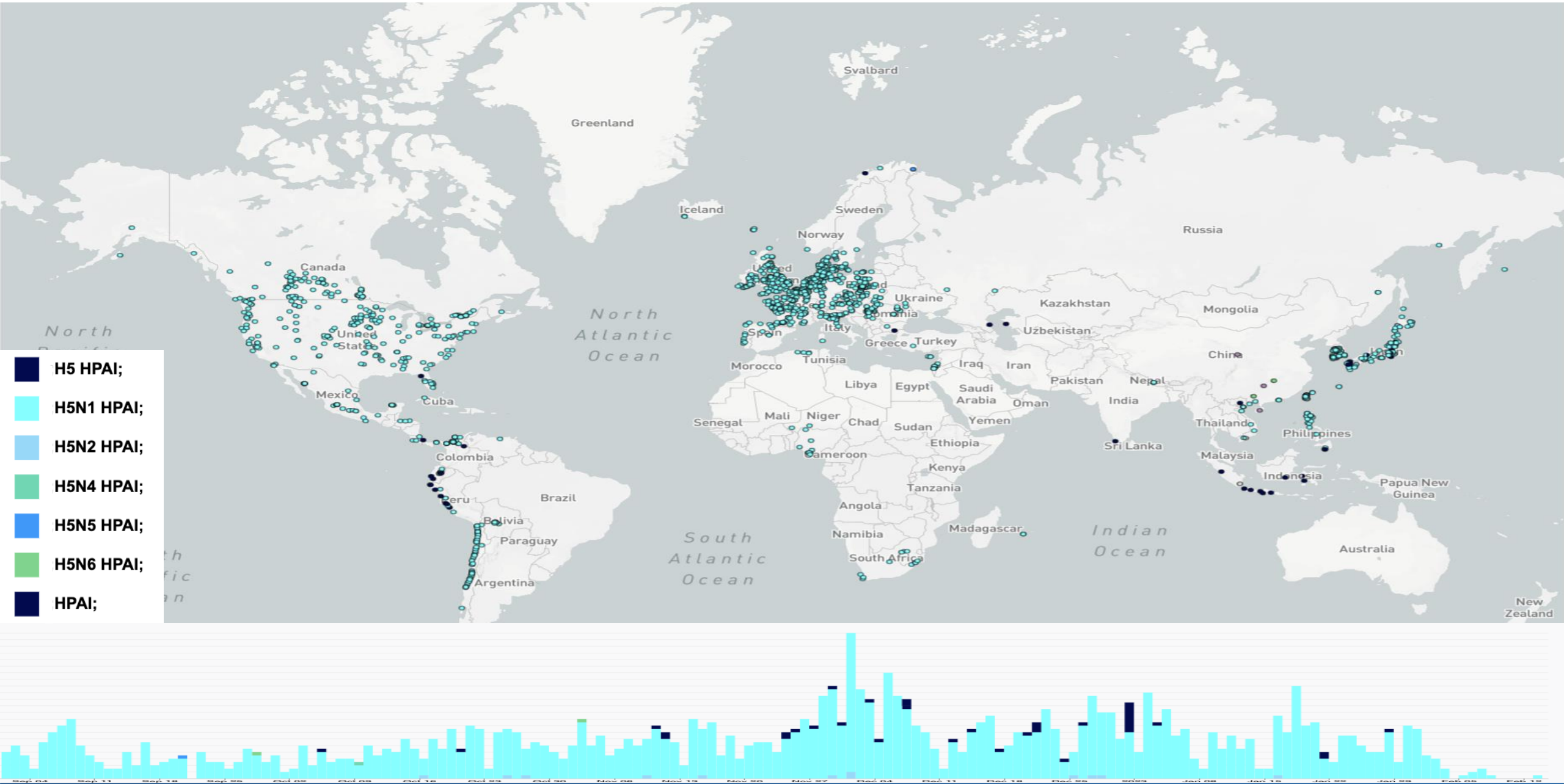
The virus is detected in Canada and U.S. wild birds in late 2021. In February 2022, the virus begins causing outbreaks in U.S. commercial and backyard poultry.

At this time, one human infection with the current H5N1 bird flu virus has been reported in an asymptomatic case in the United Kingdom.

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

CDC Influenza Division / National Center for Immunization and Respiratory Diseases

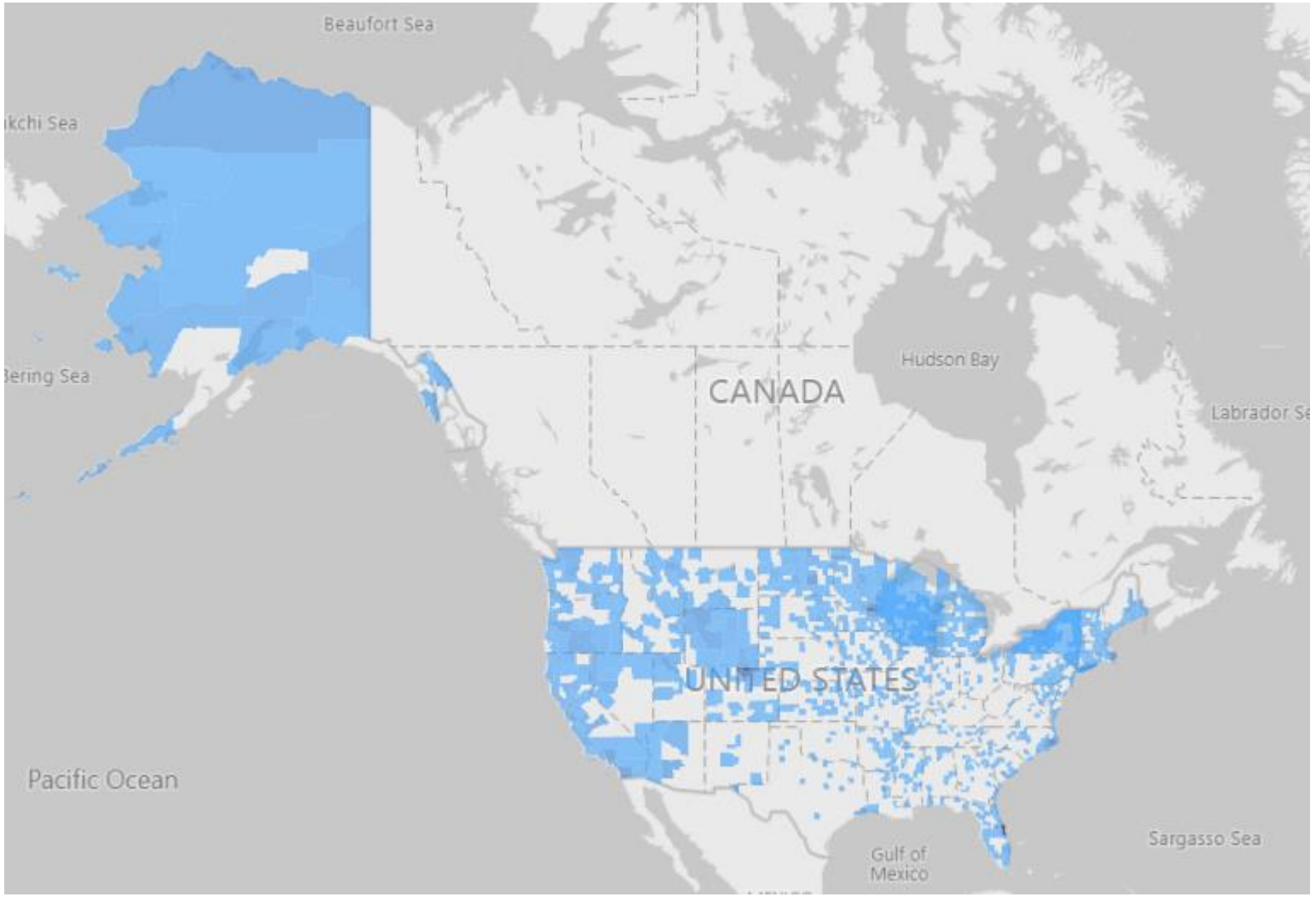
A(H5) activity in birds



U.S. Distribution of Highly Pathogenic Avian Influenza A(H5N1)*

January 2022 – June 2023

A(H5N1) Detections by Number of Wild Birds Impacted



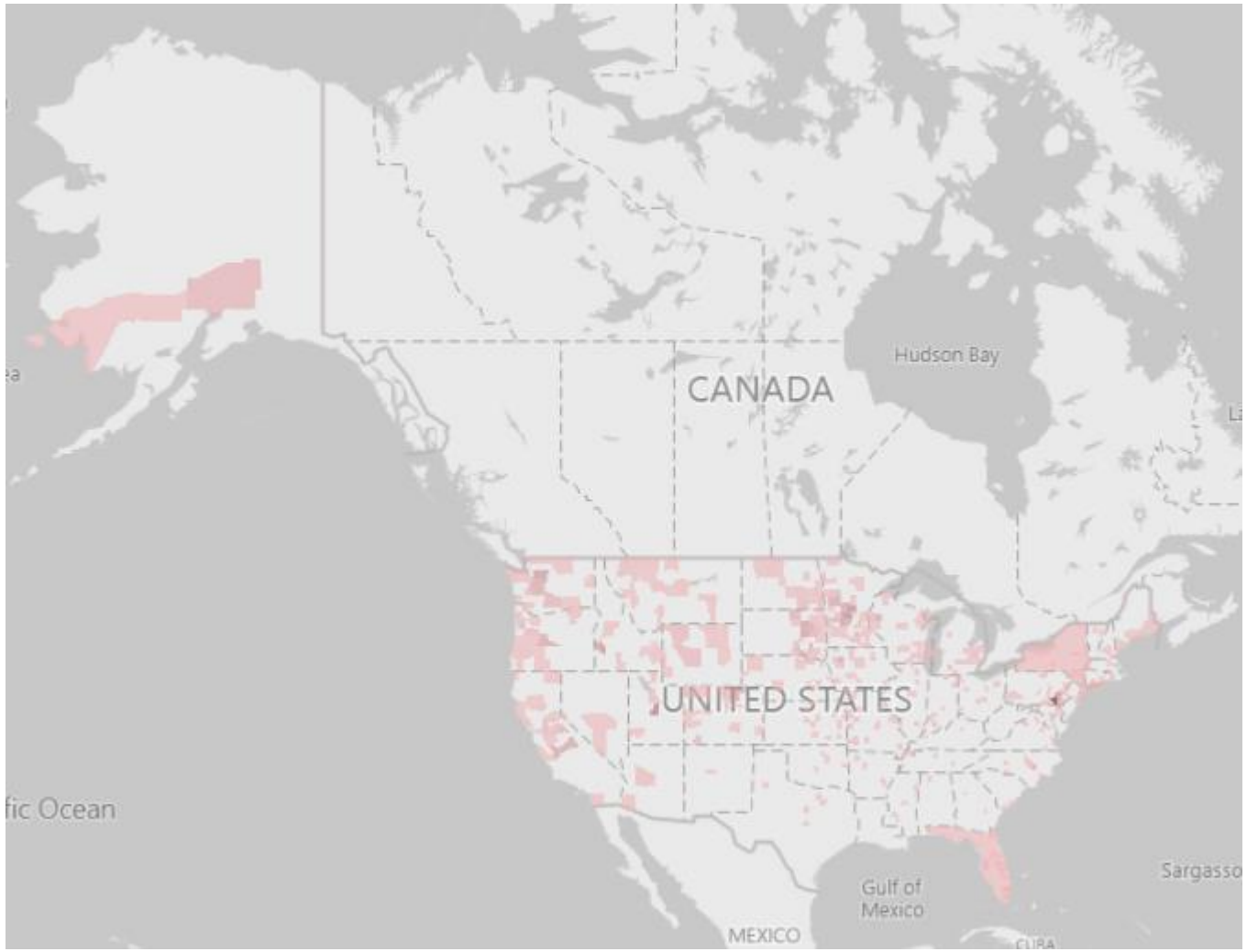
6,737 detections in 49 states

*Data from USDA/APHIS and state updates; data as of May 9, 2023

U.S. Distribution of Highly Pathogenic Avian Influenza A(H5N1)*

January 2022 – June 2023

A(H5N1) Poultry Outbreaks Detected in the US



840 outbreaks detected in 49 states

>58 million birds killed or depopulated

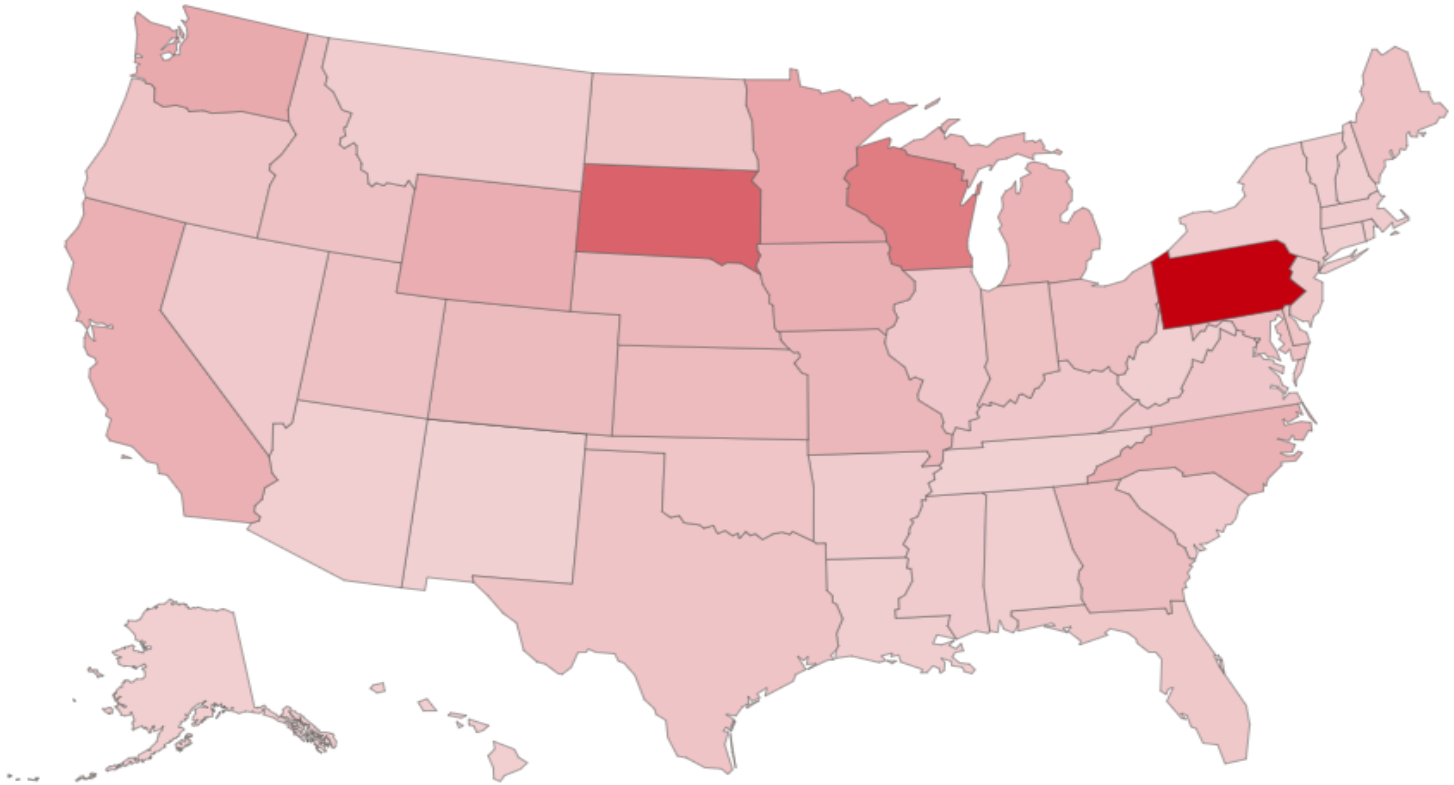
*Data from USDA/APHIS and state updates; data as of May 9, 2023

CDC Influenza

CDC Monitoring for Potential Human Illness*

February 2022 – June 2022

Cumulative Number of Exposed Persons By Resident State



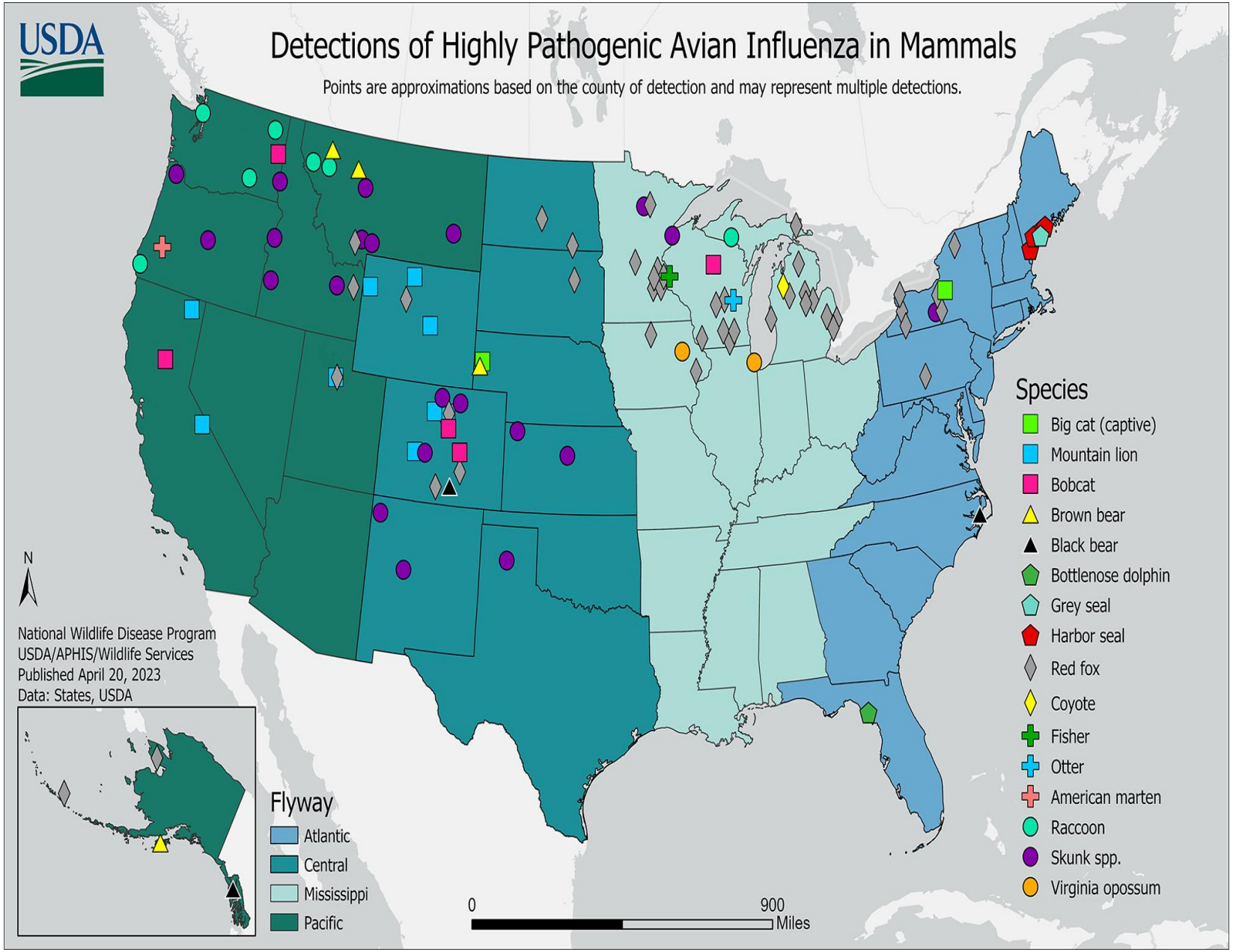
- 6,492 potentially exposed persons in all 50 states
- 35 persons actively being monitored
- 163 persons with Respiratory Symptoms
- 1 positive case

*Data as of May 9, 2023

Kniss K, et al., 2023. Risk for Infection in Humans after Exposure to Birds Infected with Highly Pathogenic Avian Influenza A(H5N1) Virus, United States, 2022. Emerg Infect Dis. Apr 24;29(6).

CDC Influenza

CDC monitoring H5 infected mammals and evidence of adaptation



Globally, sporadic HPAI A(H5N1) virus infections have been reported in farmed mink in Spain, sea lions in Peru and Chile, and foxes in Canada, France, and other countries.

- 24 species of carnivores
- 4 species of cetaceans

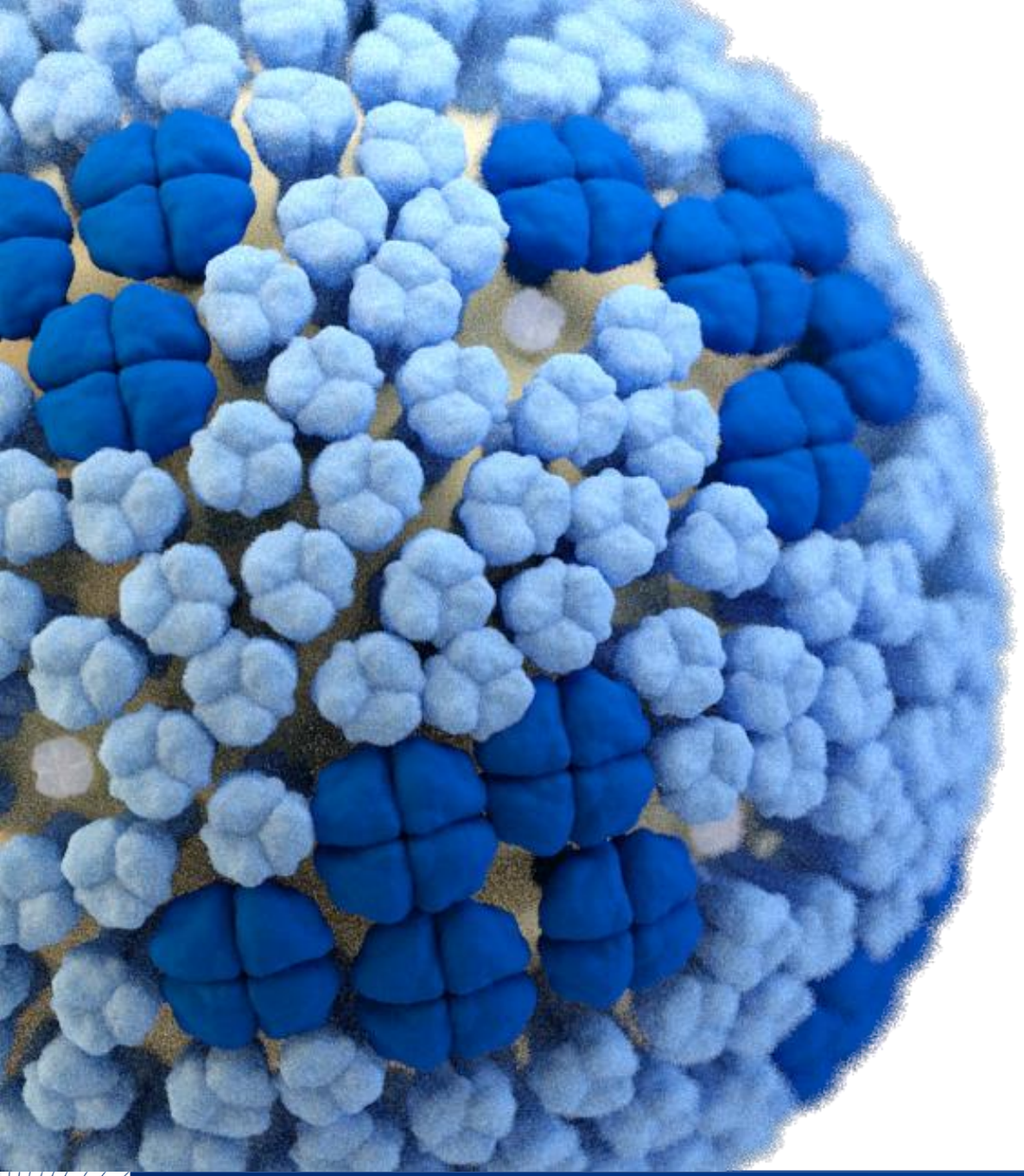
Mutations in the virus that are associated with genetic adaptation to mammals have been detected in many viruses detected in mammals

- About half of the characterized viruses contain at least one of the adaptive markers associated with an increased virulence and replication in mammals in the PB2 protein (E627K, D701N or T271A)

- **No mutations associated with changes in receptor binding specificity have been reported to date**

Wild and captive mammalian infections can be challenging to diagnosis because of **symptomology similar to other pathogens**

- Neurological – tremors, convulsions, paralysis
- Respiratory - dyspnea, tachypnea, nasal and buccal secretions and pulmonary edema



Swine Surveillance for Veterinary and Public Health

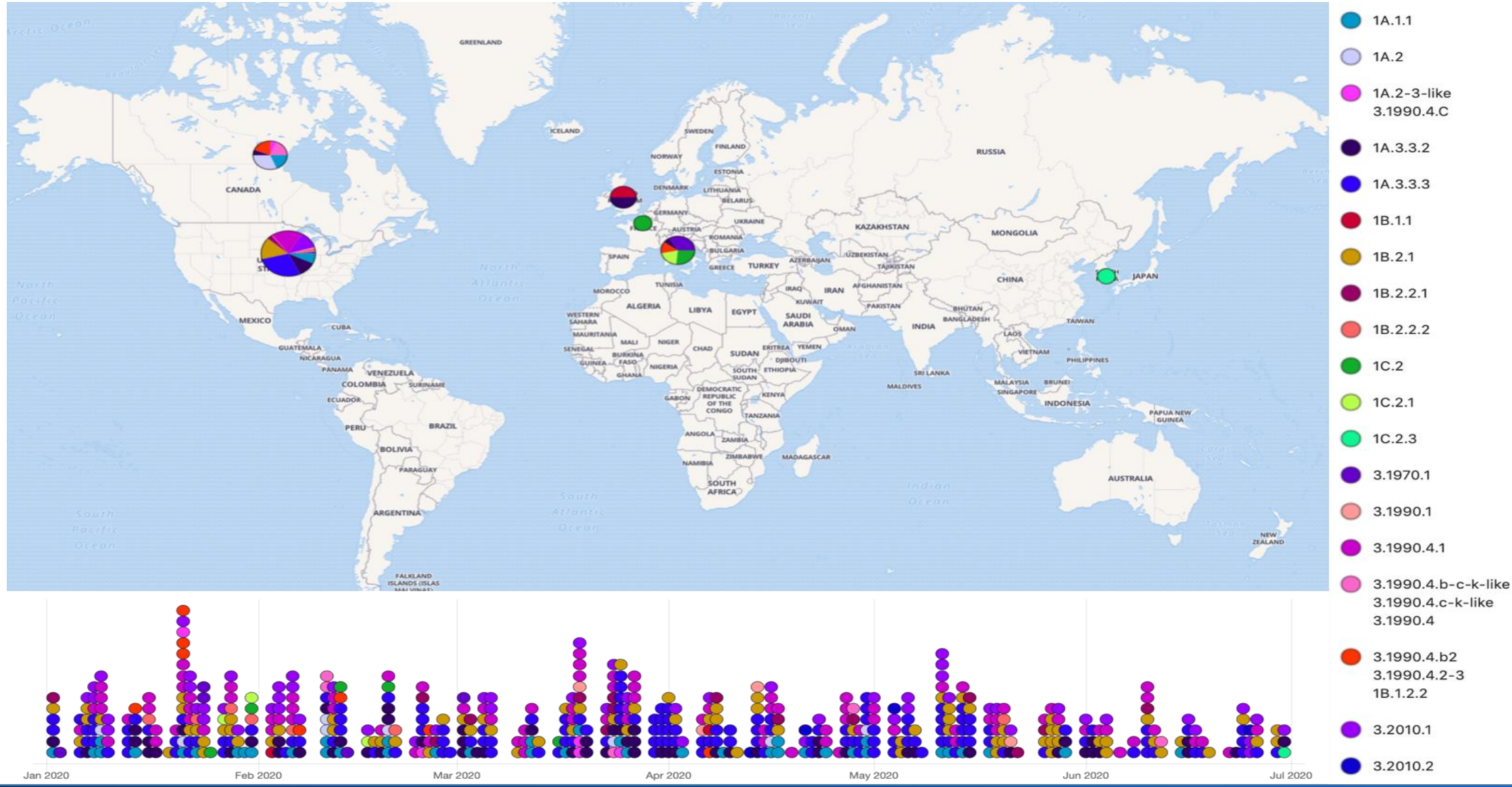
- **USDA IAV-S Surveillance Program**
  - The USDA, in cooperation with State and industry, conducts **voluntary surveillance for IAV-S in the U.S.**
  - Identify viruses that may be circulating in swine, and gain knowledge to contribute to improved animal health diagnostics and vaccines.

- **Universities**
  - St. Jude Children's Research Hospital (Dr. Richard Webby)
    - CEIRR network
  - The Ohio State University (Dr. Andy Bowman)
    - Agricultural fairs
    - Swine exhibitions
    - Animal-human interface studies

- **International Veterinary Agencies**
  - Department of Animal Health, MARD, Vietnam
  - National Animal Health Laboratory, MOA, Lao, PDR
  - KEMRI, Nairobi, Kenya

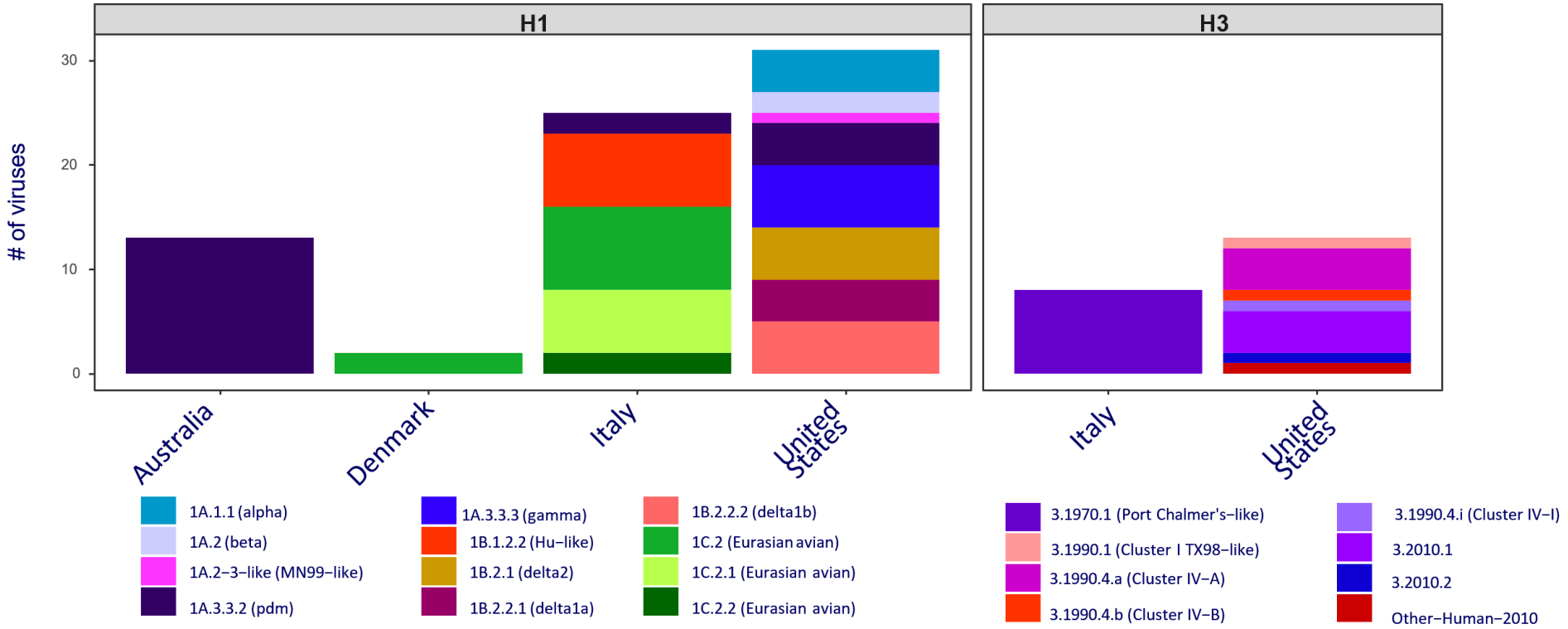
https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/sa_animal_disease_information/sa_swine_health/ct_siv_surveillance/

Many Different Swine Viruses Co-Circulate and Represent Zoonotic/Pandemic Threats



Courtesy OFFLU Technical Advisors

Global Influenza A(H1) and A(H3) Activity in Swine



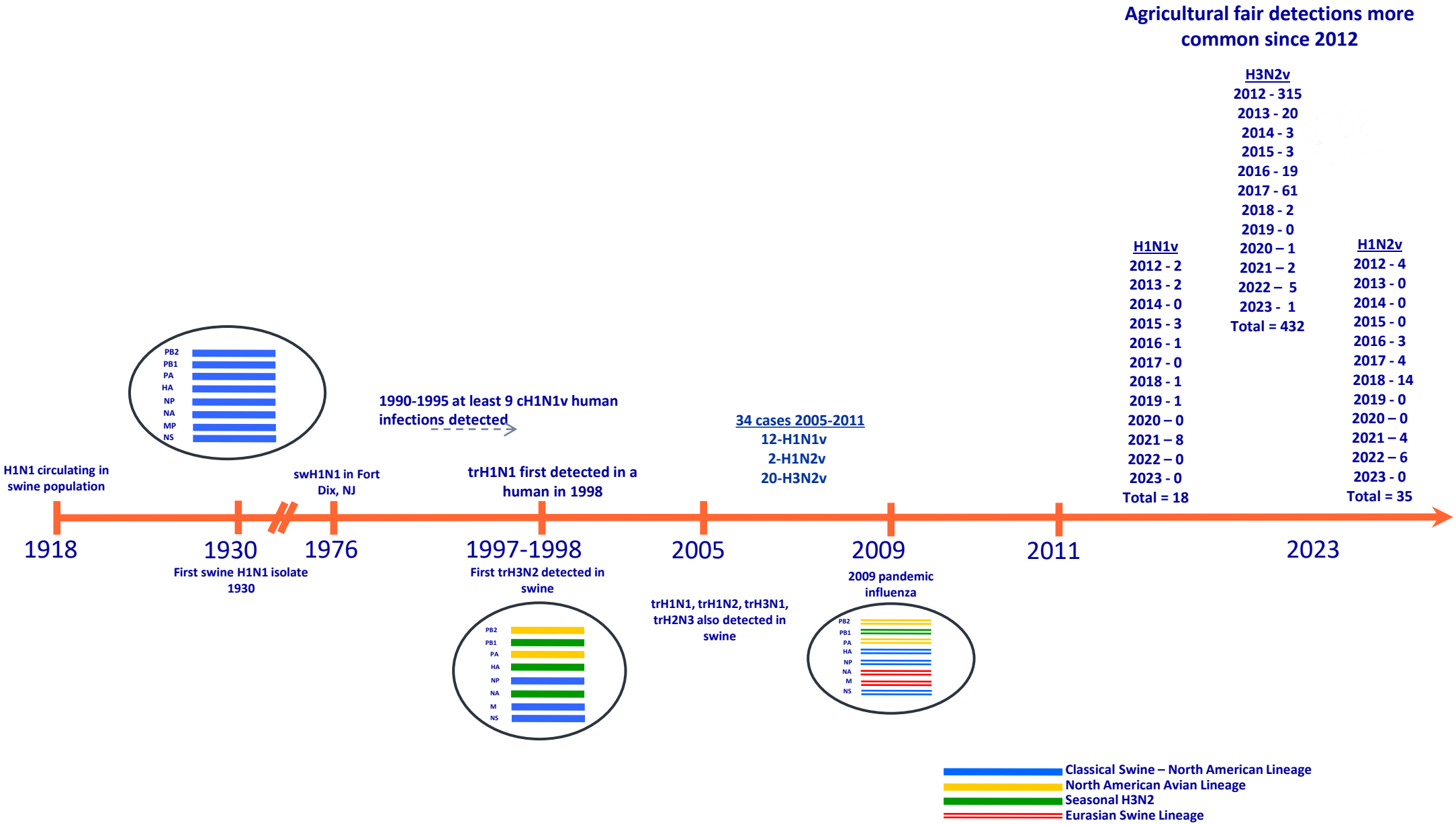
- Global swine influenza virus surveillance is limited, and, unlike HPAI viruses, detection does not mandate reporting to national authorities or global veterinary agencies (i.e., FAO or OIE)

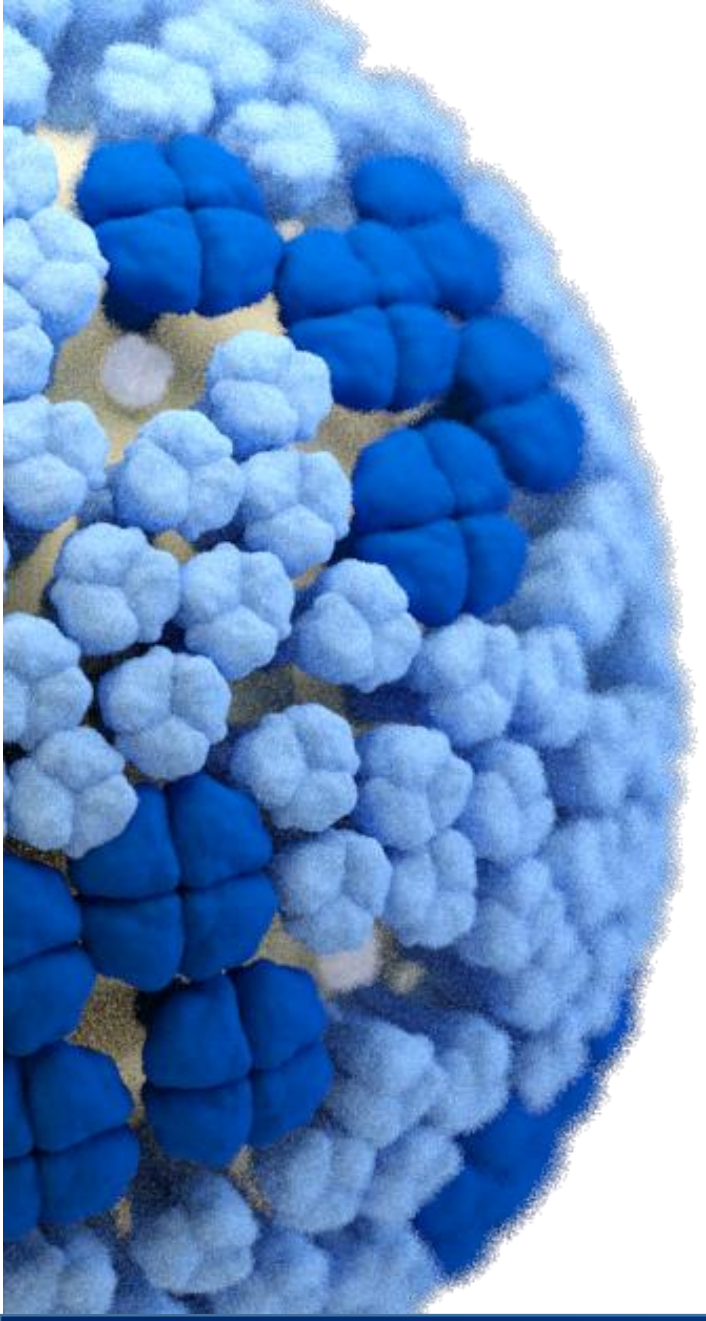
- Where regional surveillance does occur, substantial genetic and antigenic diversity is identified for both H1 and H3 swine influenza viruses

Courtesy OFFLU Technical Advisors

History of swine influenza virus in North America

Influenza



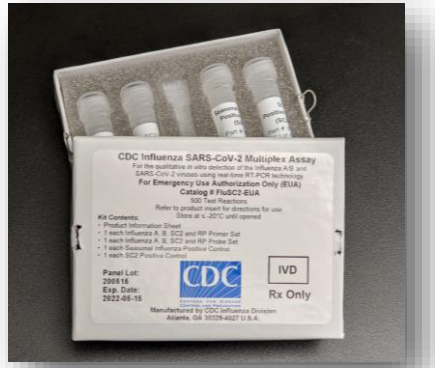


Pandemic Preparedness

- Evaluation of diagnostic test performance
- Sequencing to rapidly characterize viruses
- Antiviral drug susceptibility testing
- Candidate vaccine virus development and stockpiling

Detecting Emerging Influenza A Viruses

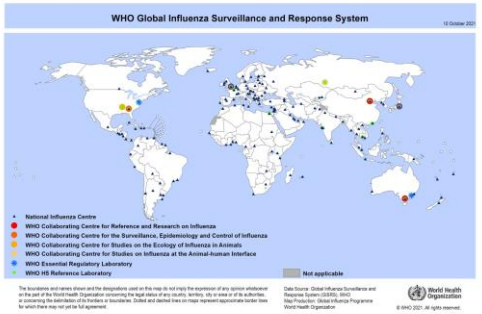
- Detection – Diagnosis
  - CDC's Seasonal Human Influenza Virus Real-Time RT-PCR Diagnostic Panels **will detect novel (non-seasonal) viruses**
    - Flu/SARS-CoV-2 multiplex assay, Influenza A subtyping assay
    - If positive, the test would indicate influenza A virus
    - Available at **>100 public health laboratories** in U.S. and **>120 National Influenza Centers** globally
  - CDC's Human Influenza Virus Real-Time RT-PCR Diagnostic Panel for **influenza A(H5)** detects this new A(H5N1) virus
    - Based on genetic analysis and preliminary laboratory tests
    - Available at **91 public health laboratories** in U.S. and **107 National Influenza Centers** globally
    - Current inventory in the International Reagent Resource **> 350,000 PCR reactions** each for U.S. and global laboratories
    - FDA Cleared (510k) IVD assay



IRR International Reagent Resource

APHL Association of Public Health Laboratories

GISRS Global Influenza Surveillance & Response System



CDC Influenza

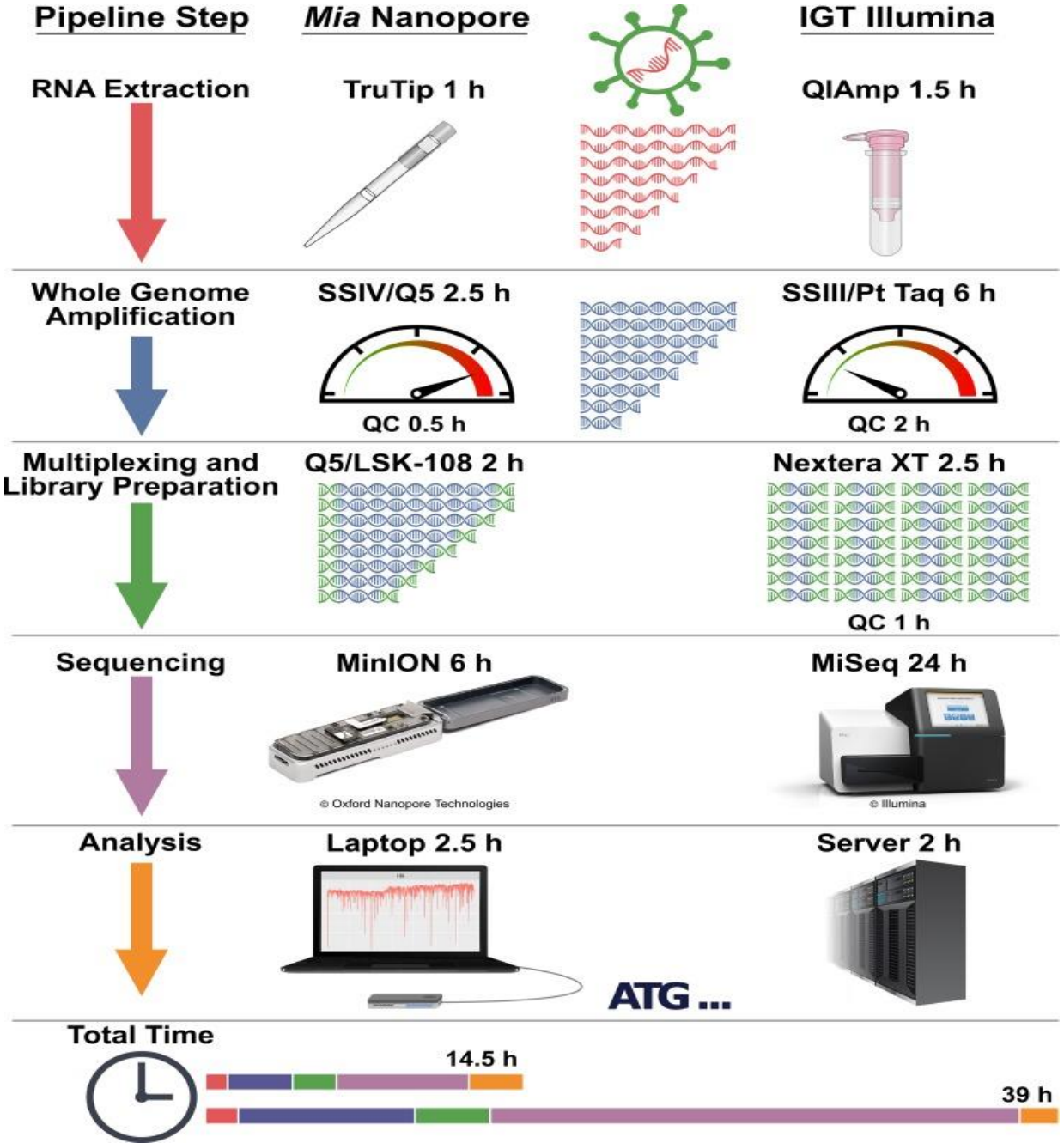
Rapid Response - Oxford Nanopore Technologies

Nanopore sequencing and on-site analytics

- Unsubtypable clinical specimens
- Novel influenza A virus detections (H5/H7/H9/H1v/H3v)
- Field-based surveillance/outbreak response
  - Agricultural fair
  - Live poultry market
  - Farms

- National Strategy for Pandemic Preparedness exercise
  - the sequences from a swine exhibition were emailed to ID colleagues
  - developed a synthetically derived vaccine designed to match the viruses at the exhibition

- Training and deploying



B. L Rambo-Martin, et. al., 2020/2/26, Msphere Vol 5.

NGS-based identification of drug-resistant A(H5N1) viruses

- Source: **GISAID**; clade 2.3.4.4b HPAI A(H5N1) viruses collected in US during 2022
- Genomes: **1,015** (apparent duplicates excluded)

Molecular markers of drug resistance with known clinical relevance:

- **M2 blockers**: **3** viruses with **M2-V27A**
  - Cluster

M2-V27A

A/domestic_duck/SD/22-033350-004-original/2022	10/18/2022
A/turkey/SD/22-033350-005-original/2022	10/18/2022
A/chicken/SD/22-033350-001-original/2022	10/18/2022

- **NAI oseltamivir** (and peramivir): **4** viruses with **NA-H275Y**
  - Not a cluster

NA-H275Y

A/turkey/NH/22-007886-001-original/2022	3/15/2022
A/chicken/ME/22-008540-001-original/2022	3/22/2022
A/great_horned_owl/MA/22MM00199/2022	3/3/2022
A/Canada goose/MA/22-025071-002-original/2022	7/21/2022

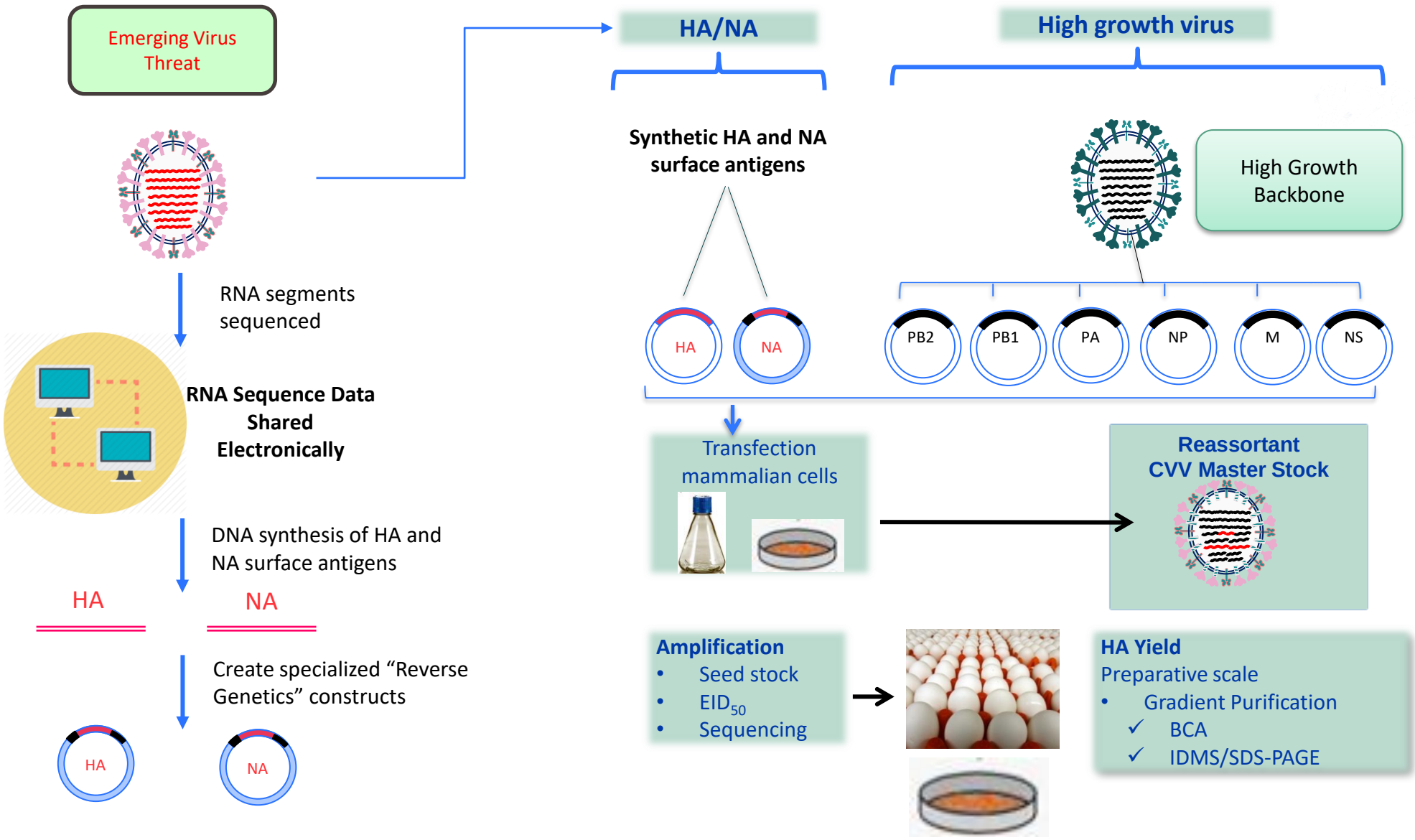
- PA CENI **baloxavir**: **1** virus with **PA-I38T**

PA-I38T

A/chicken/MI/22-013961-001-original/2022	5/4/2022

- Viruses resistant to any of FDA-approved antivirals were detected at low frequency (0.8%)

Synthetic Virology Used to Generate Viruses for Testing and Potential CVVs



Courtesy Dr. Bin Zhou, Vaccine Preparedness Team/VSDB, Influenza Division

Clade 2.3.4.4b A(H5) Candidate Vaccine Virus Development

Candidate vaccine viruses	Subtype	Clade	Institution	Availability
IDCDC-RG42A (A/Sichuan/26211/2014-like)	H5N6	2.3.4.4a	CDC	Yes
Seqirus (A/Fujian-Sanyuan/21099/2017-like)	H5N6	2.3.4.4b	Seqirus	Yes
CNIC-21099 (A/Fujian-Sanyuan/21099/2017-like)	H5N6	2.3.4.4b	CCDC	Pending
IDCDC-RG71A (A/Astrakhan/3212/2020-like)	H5N8	2.3.4.4b	CDC	Yes
CBER-RG8 (A/Astrakhan/3212/2020-like)	H5N8	2.3.4.4b	FDA	Pending
A/chicken/Ghana/AVL-763/21VIR7050-39/2021-like	H5N1	2.3.4.4b	CDC	Pending
A/American Wigeon/South Carolina/22-000345-001/2021-like	H5N1	2.3.4.4b	CDC	Pending
IDCDC-RG43A (A/gyrfalcon/Washington/41088-6/2014-like)	H5N8	2.3.4.4c	CDC	Yes
Seqirus (A/Hubei/29578/2016-like)	H5N6	2.3.4.4d	Seqirus	Yes
CNIC-29578 (A/Hubei/29578/2016-like)	H5N6	2.3.4.4d	CCDC	Pending
NIID-001 (A/duck/Hyogo/1/2016-like)	H5N6	2.3.4.4e	NIID	Yes
A/chicken/Vietnam/NCVD-15A59/2015-like	H5N6	2.3.4.4f	SJCRH	Pending
IDCDC-RG69A (A/chicken/Vietnam/RAHO4-CD-20-421/2020-like)	H5N6	2.3.4.4g	CDC	Pending
IDCDC-RG56A (A/Guangdong/18SF020/2018-like)	H5N6	2.3.4.4h	CDC/CCDC	Pending

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Novel Influenza A Virus Infections Epidemiology and Clinical Issues

Tim Uyeki, MD, MPH, MPP

Influenza Division, CDC

June 20, 2023

Overview

- **Human infections with avian influenza A viruses**
  - Epidemiology, risk factors, clinical characteristics
    - Focus on highly pathogenic avian influenza A(H5N1) virus infections
- **Human infections with swine influenza A viruses (variant influenza A viruses)**
  - Epidemiology, risk factors, clinical characteristics
- **Diagnostic testing for novel influenza A viruses**
- **Clinical management**
  - Infection prevention and control measures
  - Antiviral treatment
  - Supportive care

Human Infections with Avian Influenza A Viruses

- **Many different subtypes of avian influenza A viruses have caused sporadic human infections, with a wide clinical spectrum of illnesses**
  - **Low pathogenic avian influenza (LPAI) A viruses**
    - A(H3): H3N8
    - A(H6): H6N1
    - A(H7): H7N2, H7N3, H7N4, H7N7, H7N9
    - A(H9): H9N2
    - A(H10): H10N3, H10N7, H10N8
  - **Highly pathogenic avian influenza (HPAI) A viruses**
    - A(H5): H5N1, H5N6, H5N8
    - A(H7): H7N3, H7N7, H7N9

Risk Factors for Avian Influenza A Virus Infection

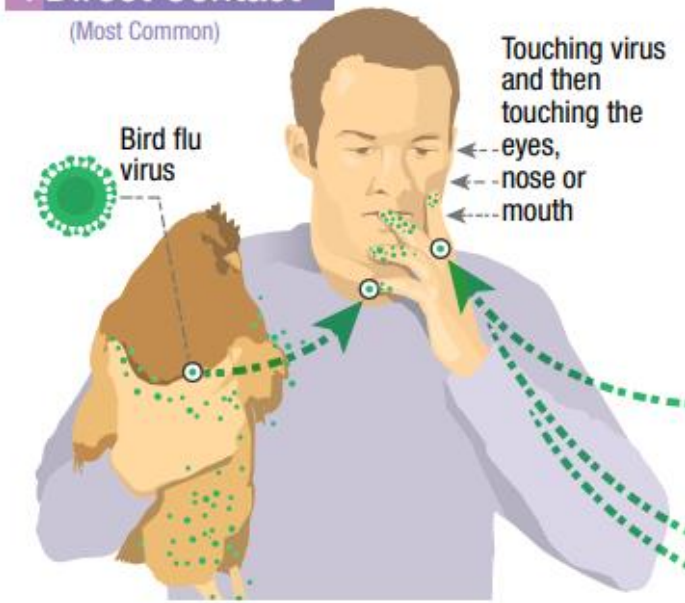
- **Exposure to infected poultry**
  - **Direct or close unprotected exposure to sick/dead poultry**
    - **Poultry infected with HPAI A viruses (e.g., H5N1, H5N6, H7N7, H7N9)**
  - **Direct or close unprotected exposure to well-appearing poultry**
    - **Poultry infected with LPAI A viruses (e.g., H7N9, H9N2)**
    - **Ducks infected with HPAI A viruses**
  - **Raising backyard poultry that were sick/died**
    - **Poultry infected with HPAI A viruses (e.g., H5N1, H5N6)**
  - **Visiting a live poultry market**
    - **Chickens and other poultry species infected with LPAI A viruses (e.g., H7N9)**
    - **Poultry infected with HPAI A viruses (e.g., H5N1, H5N6)**

Mounts J Infect Dis 1999; Dinh Emerg Infect Dis 2004; Zhou J Infect Dis 2009; Zhou Open Forum Infect Dis 2016

Human Infections with Bird Flu Viruses Rare But Possible

1 Direct Contact

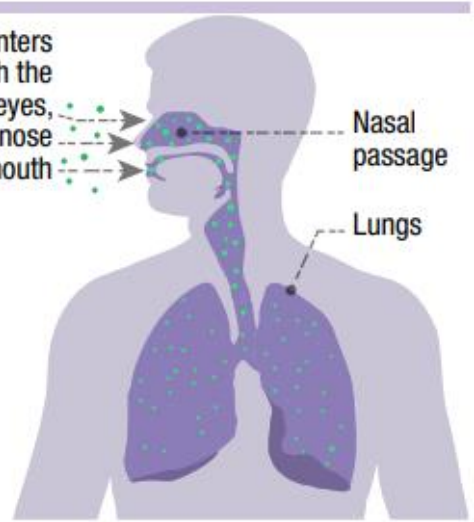
(Most Common)



Infection can occur without touching poultry.

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

CS330154

Risk Factors for Avian Influenza A Virus Infection

- **Exposure to infected wild birds**
  - **Defeathering wild swans that died of HPAI A(H5N1) virus infection (Azerbaijan, 2006)**
    - **7 cases: 6 family members, 1 neighbor became ill during February 15 - March 4, 2006, 4 died**
    - **All cases had direct contact with dead wild birds (swans) and removed the birds' feathers**

Gilsdorf Eurosurveillance 2006

Risk Factors for Avian Influenza A Virus Infection

- **Rare, Limited, non-sustained human-to-human transmission**
  - **Household transmission: Spread from a *sick case-patient to a family member* through prolonged, unprotected close exposure**
    - **HPAI A(H5N1) virus**
    - **LPAI A(H7N9) virus**
  - **Hospital transmission: Spread from a *sick case-patient to a family member* through prolonged, unprotected close exposure**
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  - **Hospital transmission: Spread from a *sick case-patient to an unrelated patient or healthcare provider* through prolonged, unprotected close exposure**
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    - **LPAI A(H7N9) virus**

Ungchusak N Engl J Med 2005; Kandun N Engl J Med 2006; Wang Lancet 2007; WHO N Engl J Med 2008; Bridges J Infect Dis 2000; Katz J Infect Dis 1999; Zhou Emerg Infect Dis 2018; Qi BMJ 2013; Xiao Eurosurveillance 2014; Chen Emerg Infect Dis 2016

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Clusters of Cases of Avian Influenza A Virus Infection

- **Cases epidemiologically-linked by location and time**
  - **Clusters mostly with small numbers of cases in family members**
  - **Nearly all cases had common exposures to poultry**
    - **HPAI A(H5N1) virus**
    - **LPAI A(H7N9) virus**
  - **A small number of case clusters have been identified in which limited, non-sustained human-to-human transmission likely occurred (secondary cases without poultry exposures)**
    - ***Blood-related family members**
      - **2nd generation transmission (e.g. H5N1 Thailand 2004, H5N1 China 2007; China H7N9 2013-2017)**
      - **3rd generation transmission (e.g., H5N1 Indonesia 2006, H5N1 Pakistan 2007)**
    - ****Some cases have also been identified in non-blood-related individuals**
      - **Patient-to-healthcare worker or Patient-to-patient (e.g. H5N1 Vietnam; H7N9 China)**

Zhou Emerg Infect Dis 2018; Ungchusak N Engl J Med 2005; Wang Lancet 2007; WHO Wkly Epi Rec 2008

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    - **3rd generation transmission (e.g., H5N1 Indonesia 2006, Pakistan 2007)**

    ****Some cases have also been identified in unrelated individuals**
    - **Patient-to-Healthcare worker (e.g., H5N1 Vietnam); Patient-to-Patient (e.g., H7N9 China)**

Zhou Emerg Infect Dis 2018; Ungchusak N Engl J Med 2005; Wang Lancet 2007; WHO Wkly Epi Rec 2008; WHO N Engl J Med 2008

Human Infections with Avian Influenza A Viruses – Additional Considerations

- **The source of infection is not always identified - unknown for some cases**
- **No cases of mammal-to-human transmission of avian influenza A viruses reported**
  - **Wide range of terrestrial and marine mammals have been infected with avian influenza A viruses, especially HPAI A(H5N1) viruses**
  - ➢ **Potential for human infection from direct or close exposure to any animal infected with avian influenza A viruses (wild birds, poultry, pet birds, domesticated animals, wild mammals)**
- A few cases have been reported in travelers
  - Pneumonia and meningoencephalitis (fatal H5N1 case) in Canada after returning from China in 2013
  - Mild respiratory illness (H7N9) in 2 cases in Canada after returning from China in 2015
  - Severe pneumonia (H7N9) diagnosed in Taiwan after returning from China in 2013
  - Severe pneumonia (H7N9) diagnosed in Malaysia in a Chinese tourist in 2014
- ➢ Comprehensive epidemiological and laboratory investigations (public health, animal health) are needed to assess potential sources of infection with avian influenza A viruses

Rajabali Can J Infect Dis Med Micro 2015; Skowronski Emerg Infect Dis 2016; Lin Clin Infect Dis 2014; William Emerg Infect Dis 2014

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Rajabali Can J Infect Dis Med Micro 2015; Skowronski Emerg Infect Dis 2016; Lin Clin Infect Dis 2014; William Emerg Infect Dis 2014

Many Avian Influenza A Viruses Have Caused Human Infections

- **Different Highly Pathogenic and Low Pathogenic Avian Influenza A virus subtypes have infected people and caused a wide spectrum of disease worldwide**
  - **Pathogenicity in infected poultry does not necessarily translate to pathogenicity in infected people**

Clinical Characteristics	LPAI virus subtypes	HPAI virus subtypes
Uncomplicated Disease		
Conjunctivitis	**H7N2, H7N3, H7N7, H10N7**	**H7N3, H7N7**
Upper respiratory tract illness	**H3N8, H7N2, H7N3, H7N9, H9N2, H10N7**	**H5N1, H5N6, H7N7**
Severe Disease		
Lower respiratory tract disease, pneumonia	**H3N8, H6N1, H7N2, H7N4, H7N9, H9N2, H10N3, H10N8**	**H5N1, H5N6, H7N7, H7N9**
Respiratory failure, acute respiratory distress syndrome	**H3N8, H7N9, H9N2, H10N3, H10N8**	**H5N1, H5N6, H7N7, H7N9**
Multi-organ failure	**H7N9, H10N8**	**H5N1, H5N6, H7N7, H7N9**
Encephalopathy or encephalitis	**H7N9**	**H5N1, H5N6**
Fatal outcomes	**H3N8, H7N9, H9N2, H10N8**	**H5N1, H5N6, H7N7, H7N9**

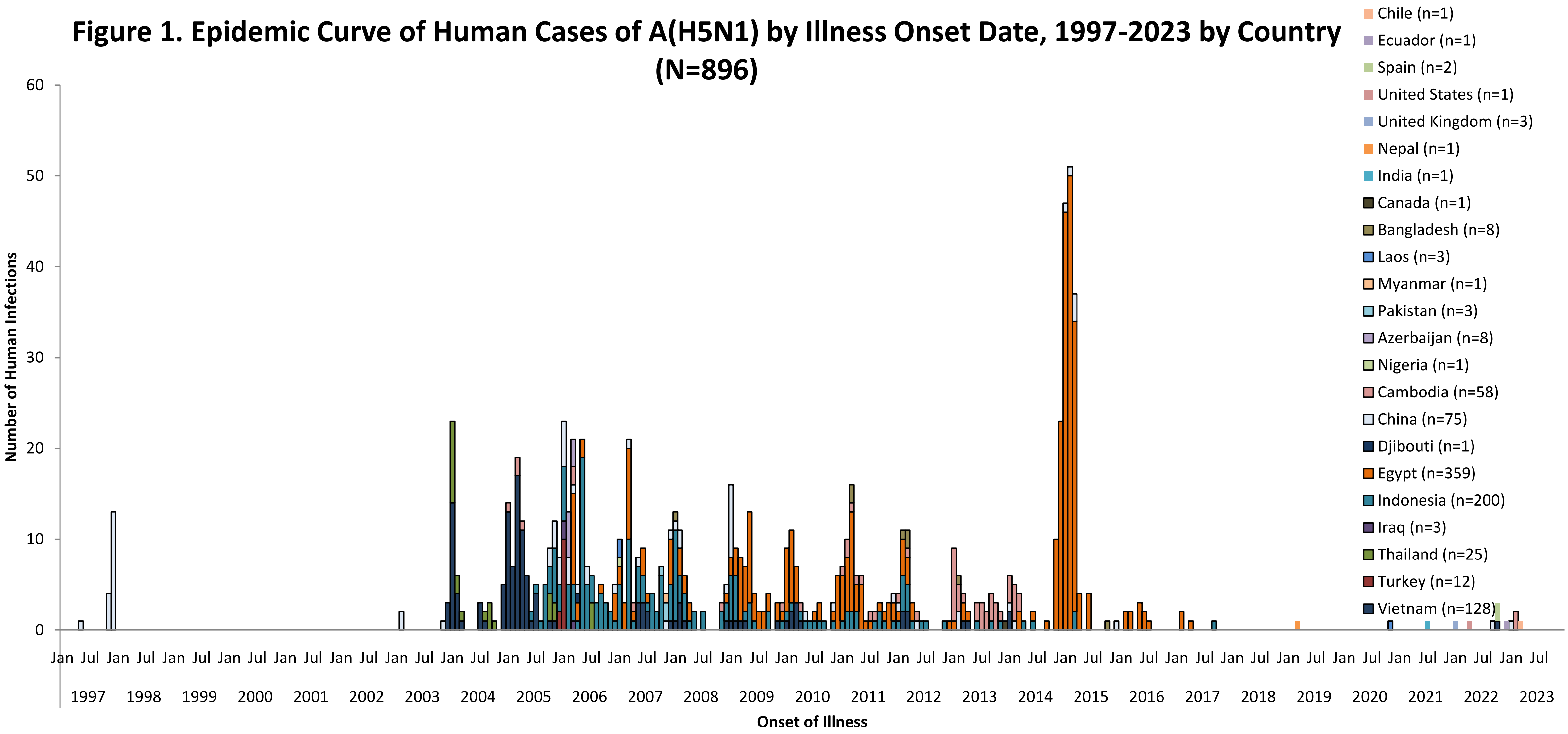
Adapted from Uyeki Lancet 2022 and Uyeki Infect Dis Clinics N America 2019

Epidemiology of Human Cases of HPAI A(H5N1)

- **First human infections identified in Hong Kong, 1997 (18 cases, 6 deaths)**
  - **Serologic evidence of additional cases**
- **2 H5N1 cases, one probable case, identified in a Hong Kong family that traveled to Fujian Province, China February 2003**
- **Re-emergence in humans: November 2003-2005 (China, Southeast Asia)**
- **Cases identified in other regions since 2006 (Middle East, Europe, Africa)**
- **2022-2023: Cases identified in the Americas**
- **Since 1997: 896 H5N1 cases with >50% mortality reported from 22 countries (most cases with severe pneumonia)**
  - ***Few cases reported worldwide since 2015-2016***

Chan Clin Infect Dis 2002; Bridges J Infect Dis 2000; Katz J Infect Dis 1999; Peiris Lancet 2004; WHO N Engl J Med 2005; WHO N Engl J Med 2008

Figure 1. Epidemic Curve of Human Cases of A(H5N1) by Illness Onset Date, 1997-2023 by Country (N=896)



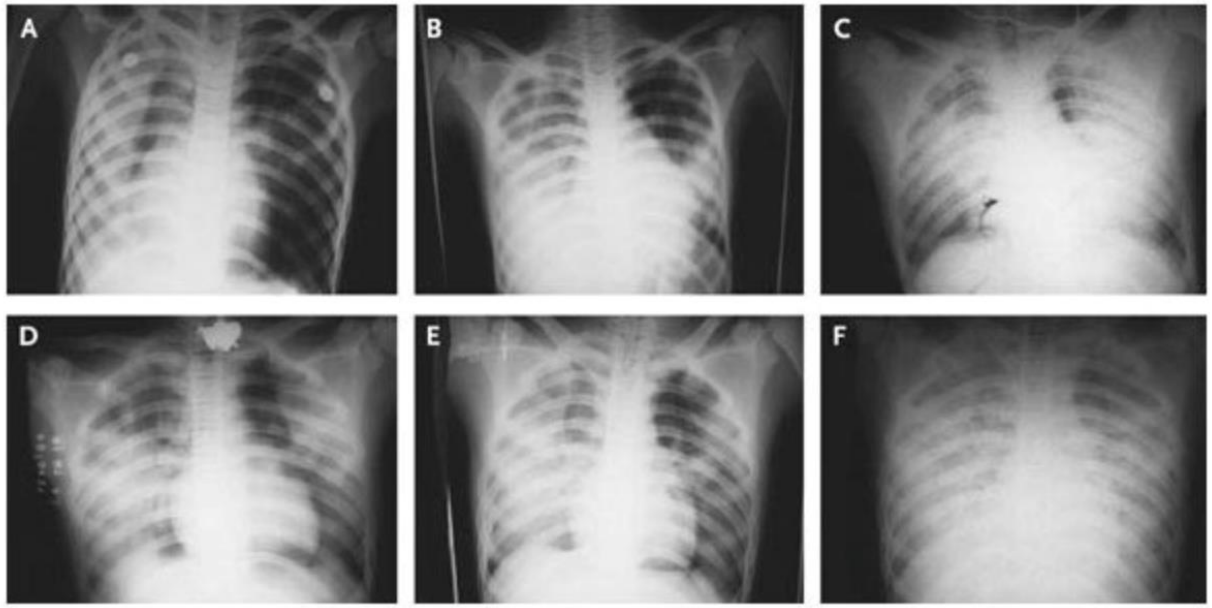
Clinical Presentation

- **Incubation period after poultry exposure: mean: 3 days (2-5 days, up to 7 days)**
  - **Clinical progression:**
    - **Fever or feverishness, nonproductive cough, muscle aches, malaise, headache, sore throat, myalgia, abdominal pain, vomiting and diarrhea can occur**
    - ➢ **Progression to lower respiratory tract disease: difficulty breathing, shortness of breath, chest pain, tachypnea**

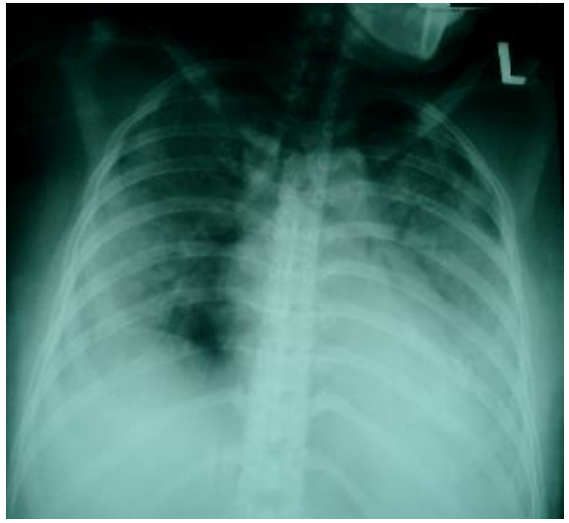
- **Patients with severe disease: median time onset to hospitalization: @6 days**
  - **Hospital admission findings:**
    - **Clinical: hypoxia, signs of pneumonia**
    - **Laboratory: leukopenia, lymphopenia, mild-to-moderate thrombocytopenia**
    - **Radiographic findings: patchy, interstitial, lobar, and/or diffuse infiltrates and opacities, consolidation, pleural effusion**

Uyeki Clin Infect Dis 2009; Virlogeaux Am J Epidemiology 2015; Cowling Lancet 2013

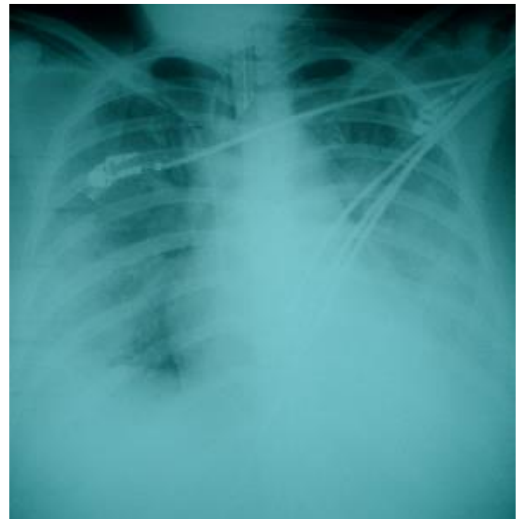
Examples of H5N1-associated severe pneumonia cases



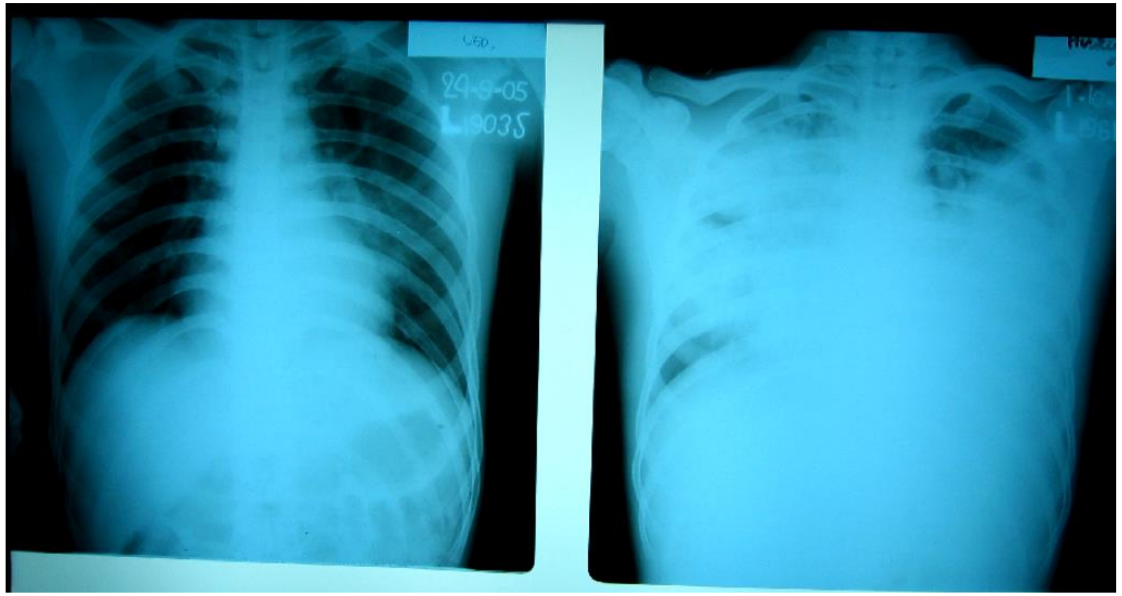
Hien N Engl J Med 2004



37-yo woman, illness day #7
Admission CXR



Illness day #10; died day #11



21-yo male, illness day #5
Admission CXR

Illness day #12; survived
(not ventilated)

T Uyeki, CDC September 2005

Complications of H5N1 Virus Infection

- **Pneumonia is the most common complication**
  - **Progression to respiratory failure, ARDS**
    - **Community-acquired bacterial co-infection is rare; VAP can develop in ventilated patients**

- **<u>Other complications</u>**
  - **Acute kidney injury**
  - **Cardiac failure**
  - **Sepsis, shock, DIC, multi-organ failure (respiratory and renal failure)**
  - **Atypical complications**
    - **Encephalitis with diarrhea and pneumonia; encephalitis with obstructive hydrocephalus; meningoencephalitis with pneumonia**
    - **Reye syndrome with salicylate exposure**
    - **Spontaneous miscarriage in a pregnant woman**
    - **Vertical transmission (mother-to-fetus)**

Current Situation and Recent H5N1 Cases

- **Human H5N1 cases reported 2022 to date (N = 13, 8 countries)** ***(most had recent poultry exposures)***
  - **Severe illness: 6 cases (2 deaths); Mild illness: 2 cases; Asymptomatic: 5 cases**
    - **UK (Dec. 2021):** Elderly asymptomatic man who raised ducks in England, clade 2.3.4.4b
    - ***US (April 2022): Adult involved in poultry culling, reported fatigue,** clade 2.3.4.4b
    - **Vietnam (October 2022): child developed critical illness, survived**
    - **China (September/October 2022): adult developed critical illness, died,** clade 2.3.4.4b
    - ***Spain (September): 2 asymptomatic adult poultry workers,** clade 2.3.4.4b
    - **Ecuador (Dec 2022/January 2023): child developed critical illness, survived,** clade 2.3.4.4b
    - **China (January 2023): adult developed severe illness,** clade 2.3.4.4b
    - **Cambodia (February 2023): 2 cases, girl (critical illness, died)** and father (mild illness), clade 2.3.2.1c
    - **Chile (March 2023): adult developed critical illness**, clade 2.3.4.4b
    - ***U.K. (May 2023): 2 asymptomatic adult poultry workers,** clade 2.3.4.4b

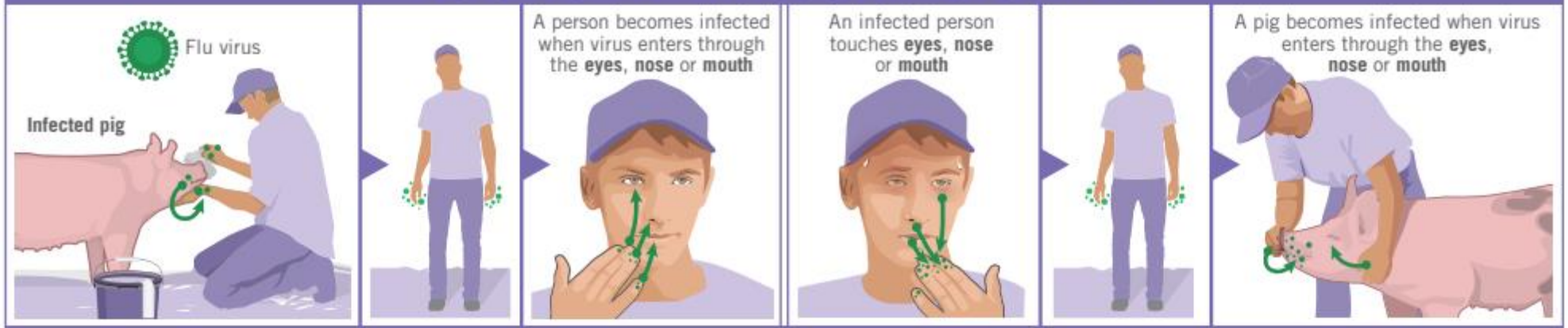
***May not represent infection**

UK Health Security Agency Technical Briefing 4, June 2, 2023; CDC H5N1 Technical Report March 17, 2023; Aznar et al. Euro Surveill. Feb. 23, 2023

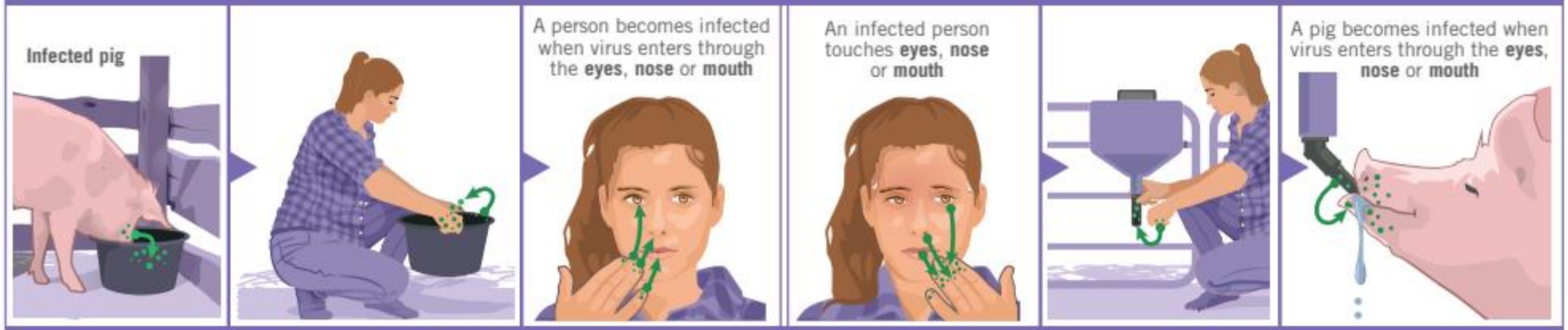
Human Infections with Swine Influenza A Viruses

- **Swine influenza A viruses that have infected humans are referred to as variant influenza A viruses (denoted with “v” after the subtype)**
- **Variant influenza A viruses that have caused sporadic human infections:**
  - A(H1): H1N1v, H1N2v
  - A(H3): H3N2v
- **Most variant influenza A virus infections have been reported in children, and most illnesses have generally been mild**

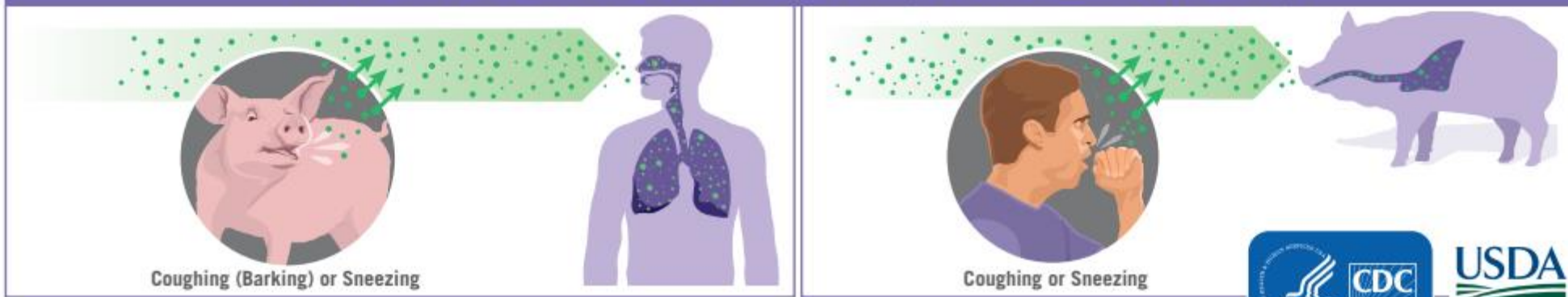
FLU CAN SPREAD THROUGH DIRECT CONTACT



FLU CAN SPREAD THROUGH SURFACE CONTACT



FLU CAN SPREAD THROUGH THE AIR (IN DROPLETS OR DUST)

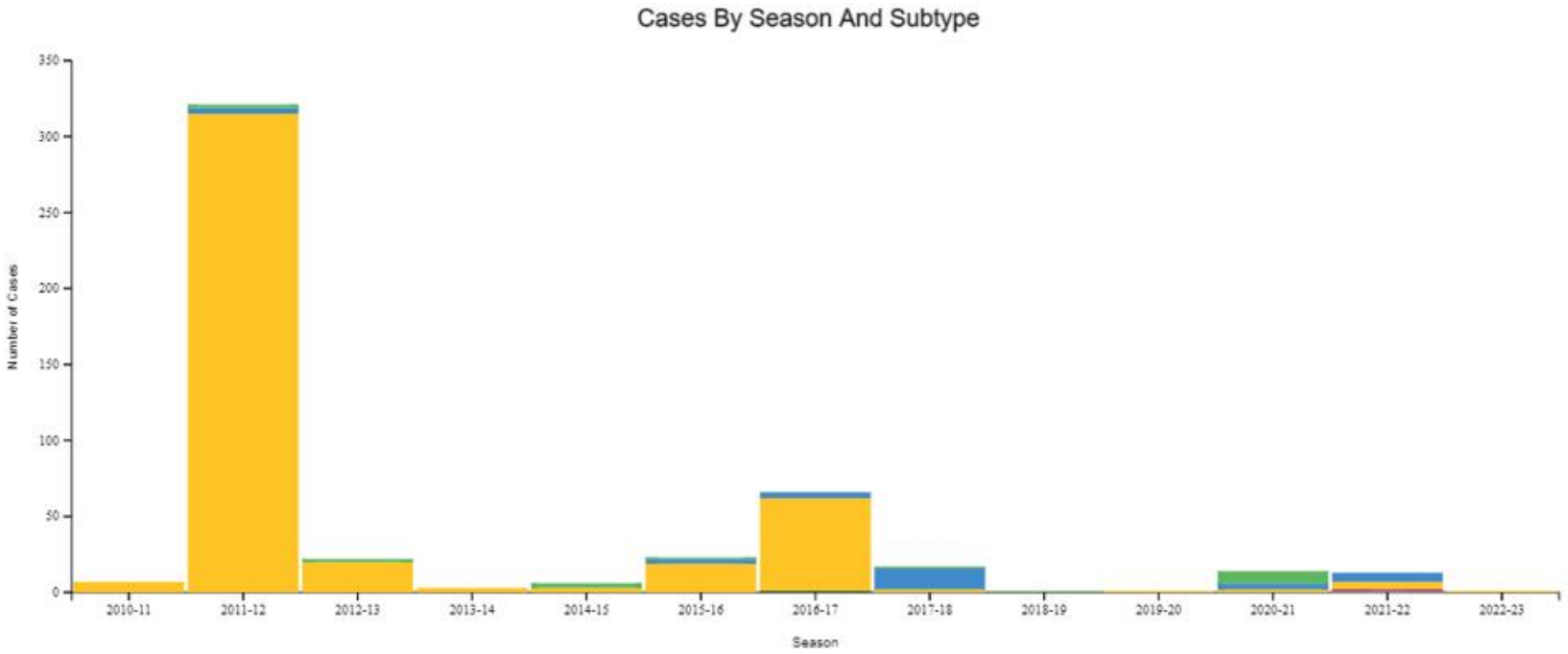


www.cdc.gov/flu/swineflu/index.htm

CDC USDA

Variant Influenza A Virus Infections, U.S. 2010 to date

FLUVIEW interactive



	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	2022-23	Total
Influenza A H1N1v	0	2	2	0	3	1	0	1	1	0	8	0	0	18
Influenza A H1N2v	0	4	0	0	0	3	4	14	0	0	4	6	0	35
Influenza A H3N2v	7	315	20	3	3	19	61	2	0	1	2	5	1	439

https://gis.cdc.gov/grasp/fluview/Novel_Influenza.html

Variant (Swine-origin) Influenza A Virus Infections and Disease Severity

- **306 human H3N2v infections reported** (2012)
  - **Median age: 7 years**
  - **Associated with swine exposure at agricultural fairs**
  - ➢ **Most cases were clinically mild (uncomplicated influenza)**
  - ➢ **16 (5.2%) hospitalizations, 1 death**
  - ➢ ***Some limited human-to-human transmission may have occurred (n=15)***

MAJOR ARTICLE

Outbreak of Variant Influenza A(H3N2) Virus in the United States

Michael A. Jhung,[1] Scott Epperson,[1] Matthew Biggerstaff,[1] Donna Allen,[8] Amanda Balish,[1] Nathelia Barnes,[1] Amanda Beaudoin,[9] LaShondra Berman,[1] Sally Bidol,[6] Lenee Blanton,[1] David Blythe,[15] Lynnette Brammer,[1] Tiffany D'Mello,[1] Richard Danila,[7] William Davis,[1] Sietske de Fijter,[12] Mary DiOrio,[12] Lizette O. Durand,[2] Shannon Emery,[1] Brian Fowler,[12] Rebecca Garten,[1] Yoran Grant,[5] Adena Greenbaum,[2] Larisa Gubareva,[1] Fiona Havers,[2] Thomas Haupt,[13] Jennifer House,[8] Sherif Ibrahim,[14] Victoria Jiang,[1] Seema Jain,[1] Daniel Jernigan,[1] James Kazmierczak,[13] Alexander Klimov,[1] Stephen Lindstrom,[1] Allison Longenberger,[10] Paul Lucas,[4] Ruth Lynfield,[7] Meredith McMorrow,[1] Maria Moll,[10] Craig Morin,[7] Stephen Ostroff,[10] Shannon L. Page,[12] Sarah Y. Park,[11] Susan Peters,[6] Celia Quinn,[3] Carrie Reed,[1] Shawn Richards,[8] Joni Scheftel,[7] Owen Simwale,[10] Bo Shu,[1] Kenneth Soyemi,[4] Jill Stauffer,[8] Craig Steffens,[1] Su Su,[1] Lauren Torso,[10] Timothy M. Uyeki,[1] Sara Vetter,[7] Julie Villanueva,[1] Karen K. Wong,[2] Michael Shaw,[1] Joseph S. Bresee,[1] Nancy Cox,[1] and Lyn Finelli[1]

RAPID COMMUNICATIONS

Swine influenza A (H1N1) virus (SIV) infection requiring extracorporeal life support in an immunocompetent adult patient with indirect exposure to pigs, Italy, October 2016

F Rovida [1 2], A Piralla [1 2], FC Marzani [3], A Moreno [4], G Campanini [1], F Mojoli [3 5], M Pozzi [3], A Girello [1], C Chiapponi [6], F Vezzoli [7], P Prati [8], E Percivalle [1], A Pavan [9], M Gramegna [10], GA Iotti [3 5], F Baldanti [1 11]
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11. Dipartimento di Scienze Clinico-Chirurgiche, Diagnostiche e Pediatriche, Università degli Studi di Pavia, Pavia, Italy

RAPID COMMUNICATIONS

Severe acute respiratory infection caused by swine influenza virus in a child necessitating extracorporeal membrane oxygenation (ECMO), the Netherlands, October 2016

PLA Fraaij [1 2], ED Wildschut [3], RJ Houmes [3], CM Swaan [4], CJ Hoebe [5 6], HCC de Jonge [7], P Tolsma [8], I de Kleer [9], SD Pas [1], BB Oude Munnink [1], MVT Phan [1], TM Bestebroer [1], RS Roosenhoff [1], JJA van Kampen [1], M Cotten [2], N Beerens [10], RAM Fouchier [1], JH van den Kerkhof [4], A Timen [4], MP Koopmans [1]
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3. Intensive Care and Department of Pediatric Surgery, Erasmus MC-Sophia, Rotterdam, The Netherlands
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6. Faculty of Health, Medicine and Life Sciences Department of Medical Microbiology, Maastricht Infection Center (MINC),School of Public Health and Primary Care (CAPHRI),Maastricht University Medical Center (MUMC+), Maastricht, The Netherlands
7. Gemeentelijke Gezondheidsdienst Rotterdam-Rijnmond, Rotterdam, The Netherlands
8. Gemeentelijke Gezondheidsdienst Brabant zuidoost, Eindhoven, The Netherlands
9. Department of Paediatrics, Subdivision of pulmonary medicine, Erasmus MC – Sophia, Rotterdam, The Netherlands
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11. Wageningen University and Research, Wageningen the Netherlands

Jhung Clin Infect Dis 2013; Fraaij Eurosurveillance 2016; Rovida Eurosurveillance 2017

Variant (Swine-origin) Influenza A Virus Infections and Disease Severity

Table 2. Demographic and Exposure Characteristics, Symptoms, and Clinical Course of Cases of Influenza A(H3N2) Variant Virus Infection—United States, July–September 2012 (N = 306)

Characteristic	No. (%)
Male sex	145 (47)
Age, y, median (range)	7 (3 mo–74 y)
<1 y	7 (2.2)
1–4 y	93 (30)
5–11 y	152 (50)
12–17 y	31 (10)
18–49 y	18 (6)
≥50 y	5 (1.6)
Race (n = 288)	
White	279 (97)
Black	3 (1.0)
Asian	3 (1.0)
Multiracial	3 (1.0)
Ethnicity (n = 235)	
Hispanic	8 (3.4)
Non-Hispanic	227 (97)
Signs and symptoms	
Fever/feverishness	294/300 (98)
Cough	241/285 (85)
Fatigue	214/258 (83)
Sore throat	171/253 (68)
Headache	161/240 (67)
Myalgia	139/227 (61)
Vomiting	80/265 (30)
Diarrhea	66/264 (25)
Eye irritation/redness	57/243 (23)
Estimated incubation period, d, mean (95% confidence interval)[e]	2.9 (2.7–3.1)
Illness duration, d, median (range)	4 (1–16)
Household size, median (range)[f]	4 (1–12)
Underlying medical condition[g]	61/271 (23)
Received antiviral treatment	170/281 (60)
Received influenza vaccination in past year	135/244 (55)
Sought healthcare for illness	282/293 (96)
Hospitalized	16 (5.2)
Fatal	1 (<1)
Exposure characteristic[a]	
Any (direct or indirect) swine contact within ≤4 d of illness onset[b]	281/296 (95)
Direct contact with swine within ≤4 d of illness onset[b]	205/296 (69)
Indirect contact with swine within ≤4 d of illness onset[b]	76/296 (26)
Attended fair within ≤4 d of illness onset but swine exposure denied or unknown[c]	19/296 (6.4)
Agricultural fair attendance ≤4 d of illness onset	274/296 (93)
Swine contact in a nonfair setting only within ≤4 d of illness onset	7/296 (2.4)
Swine contact or fair attendance > 4 d prior to illness onset[d]	10/296 (3.4)
No swine contact or fair attendance reported prior to illness onset[d]	5/296 (1.7)
No. of days with swine contact in week prior to illness (n = 238)	
1 d	83 (35)
2–3 d	42 (18)
4–6 d	48 (20)
7 d	65 (27)

Jhung Clin Infect Dis 2013

Infection Prevention and Control Recommendations

Novel influenza A viruses associated with severe disease*

- **Potential for close range large droplet and small particle (aerosol) spread, and high mortality (e.g., H5N1 virus infection)**

➢ **Place patient in airborne infection isolation room (AIIR)**

- **If not available, isolate in single-patient room, place facemask on patient, keep door closed; arrange transfer to facility with an AIIR (negative-pressure, HEPA filtration)**

➢ **Standard, contact, airborne precautions recommended**

➢ **PPE: single-use gown, gloves, eye protection (goggles), fit-tested N95 respirator**

Novel influenza A viruses not associated with severe disease

- Standard, contact, and droplet precautions

**CDC. Interim Guidance for Infection Control Within Healthcare Settings When Caring for Confirmed Cases, Probable Cases, and Cases Under Investigation for Infection with Novel Influenza A Viruses Associated with Severe Disease: https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm*

Infection Prevention and Control Recommendations

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Diagnostic Testing and Specimen Collection

- **Commercially available influenza assays**
  - **Cannot specifically identify any avian or variant influenza A virus**
    - **Tests that identify influenza A virus do not distinguish seasonal influenza A viruses from novel influenza A viruses in respiratory specimens**
    - **If influenza A positive, and novel influenza A virus infection is suspected because of animal exposures: need subtyping performed**
- **Patients with mild disease:**
  - **Collect NP swab, and combined nasal & throat swabs for rRT-PCR testing for influenza A and B viruses at public health laboratories (e.g., using the CDC Flu rRT-PCR Dx Panel)**
    - **Influenza A positives are subtyped for H1, H3**
      - **If influenza A positive and not subtypeable (H1 negative, H3 negative), send to CDC**
      - **If H5 is suspected, test by CDC H5 primer/probe set; confirm presumptive positive at CDC**
        - **Throat swabs have higher sensitivity to detect H5N1 virus >nasal >NP specimens**
    - **If recent swine exposure and H1 or H3 is positive, and subtyping is presumptive positive for a variant influenza A virus, confirm at CDC**

Diagnostic Testing and Specimen Collection

- **Patients with lower respiratory tract disease:**
  - If influenza A positive on a commercial influenza molecular assay, collect respiratory specimens for influenza A virus subtyping at a public health laboratory
  - Collect NP swab, and combined nasal & throat swabs, and sputum for rRT-PCR testing for influenza A virus subtypes H1, H3, at public health laboratories
  - ➢ Intubated patients: Also collect endotracheal aspirate specimens (or BAL fluid)
    - If A positive, H1 negative, H3 negative: perform H5 subtyping (or other subtypes: H7)
    - Confirm presumptive positives or A nonsubtypeable results at CDC
  - ➢ Collect multiple respiratory tract specimen from multiple sites on multiple days for patients with suspected avian influenza A virus infection to maximum potential for diagnosis

Clinical Management - Antiviral Treatment

- **Antiviral Treatment: Start oseltamivir or other neuraminidase inhibitor (zanamivir, peramivir) empirically as soon as possible for novel influenza A viruses associated with severe disease in humans* (based on history of exposures):**
  - **Oseltamivir is recommended for progressive/severe disease & hospitalized patients**
    - **Oseltamivir standard dosing: twice daily x 5 days (mild disease); longer duration for severe disease (optimal duration unknown)**
      - **Case reports of emergence of oseltamivir resistant H5N1 viruses during treatment**
      - **No data for baloxavir treatment of H5N1 patients**
    - **No clinical trials - Observational studies: starting oseltamivir treatment soon after illness onset is associated with greater survival versus later treatment**
    - ***No markers of resistance to recommended antivirals in H5N1 viruses circulating in birds or detected in humans***
  - **Oseltamivir or other neuraminidase inhibitors or baloxavir are recommended for outpatients at increased risk for influenza complications and suspected or confirmed variant influenza A virus infection**

**CDC. Interim Guidance on the Use of Antiviral Medications for Treatment of Human Infections with Novel Influenza A Viruses Associated with Severe Human Disease: https://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm*

Clinical Management - Antiviral Chemoprophylaxis

- **Consider post-exposure antiviral chemoprophylaxis based on clinical judgment:**
  - **If less than 2 days from unprotected exposure or breech in PPE (without respiratory and eye protection), based on: duration of exposure, known infection status of the birds or sick person**
  - **If post-exposure antiviral chemoprophylaxis is initiated, use *treatment dosing with* oseltamivir (twice daily x 5 days) for avian influenza A viruses associated with severe disease (e.g., H5N1, H5N6)**

CDC. Interim Guidance on Influenza Antiviral Chemoprophylaxis of Persons Exposed to Birds with Avian Influenza A Viruses Associated with Severe Human Disease or with the Potential to Cause Severe Human Disease: https://www.cdc.gov/flu/avianflu/guidance-exposed-persons.htm

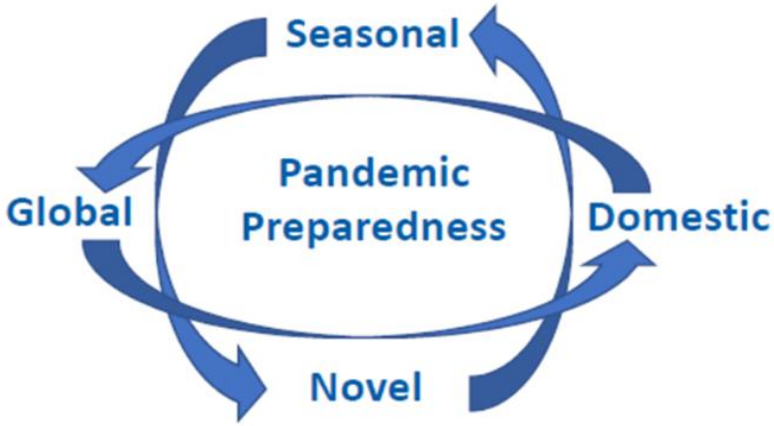
Clinical Management - Supportive Care

- **Clinical management of severe disease → supportive care of complications**
  - **Respiratory support: may require invasive mechanical ventilation**
  - **Other advanced organ support:**
    - **Extracorporeal membrane oxygenation (ECMO) has been used for H5N1 and H7N9 patients**
    - **Renal replacement therapy (dialysis) for kidney failure**
  - **Adjunctive therapy**
    - **Avoid moderate to high-dose corticosteroids**
      - **Associated with prolonged viral shedding**
      - **May increase the risk for ventilator-associated pneumonia and death**

Key Points

- **Sporadic novel influenza A virus infections of humans are expected to continue to occur (avian-origin, swine-origin)**
  - **Highly pathogenic avian influenza A(H5N1) virus is not the only novel influenza A virus with pandemic potential – all novel influenza A viruses are of public health concern**
- **Wide range of clinical severity in patients with novel influenza A virus infections**

➢**Improving our response to seasonal influenza and novel influenza A virus infections (zoonotic influenza) will also improve preparedness and response to the next influenza pandemic**



Resources

Human infections with avian influenza A viruses

- Case definitions: https://www.cdc.gov/flu/avianflu/case-definitions.html
- Monitoring & post-exposure antiviral prophylaxis: https://www.cdc.gov/flu/avianflu/guidance-exposed-persons.htm
- Follow-up of close contacts: https://www.cdc.gov/flu/avianflu/novel-av-chemoprophylaxis-guidance.htm
- Summary for clinicians: https://www.cdc.gov/flu/avianflu/clinicians-evaluating-patients.htm
- Specimen collection & testing: https://www.cdc.gov/flu/avianflu/severe-potential.htm
- Infection prevention and control: https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm
- Antiviral guidance: https://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm
- Current situation: https://www.cdc.gov/flu/avianflu/avian-flu-summary.htm
- CDC H5N1 Technical Report: https://www.cdc.gov/flu/avianflu/spotlights/2022-2023/h5n1-technical-report.htm

Human infections with variant influenza A viruses

- Background and reporting: https://www.cdc.gov/flu/swineflu/variant.htm
- Clinical guidance: https://www.cdc.gov/flu/swineflu/interim-guidance-variant-flu.htm
- Figure on transmission: https://www.cdc.gov/flu/pdf/swineflu/transmission-between-pigs-people.pdf
- General information: https://www.cdc.gov/flu/swineflu/index.htm

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov

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- Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **July 25, 2023,** and **July 25, 2025,** and use course code **WD4520-062023.** The access code is **COCA062023.**

- Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CEs obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

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- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage https://emergency.cdc.gov/coca/calls/2023/callinfo_062023.asp

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