



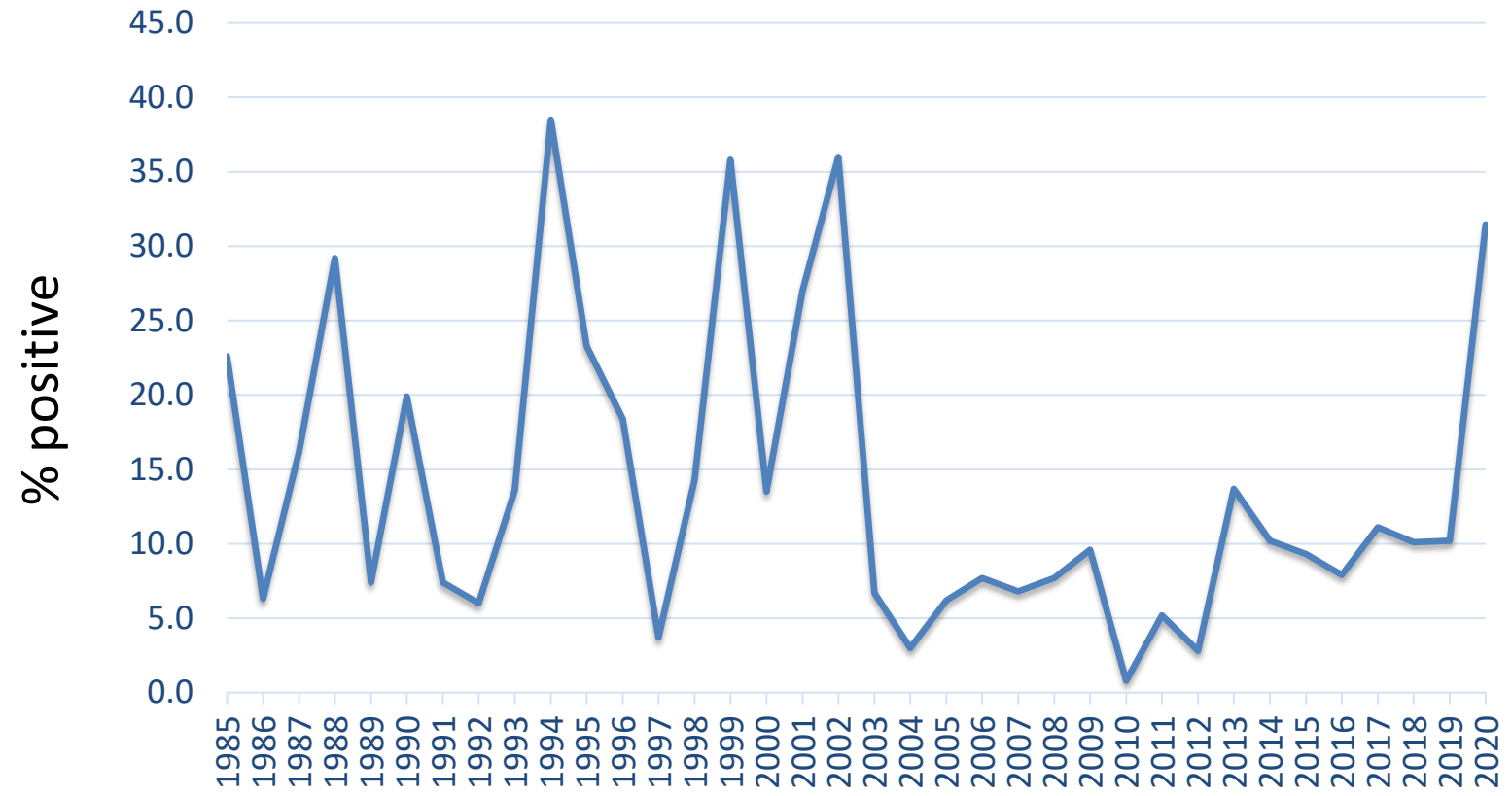
Bird flu the risks and prevention of a future pandemic

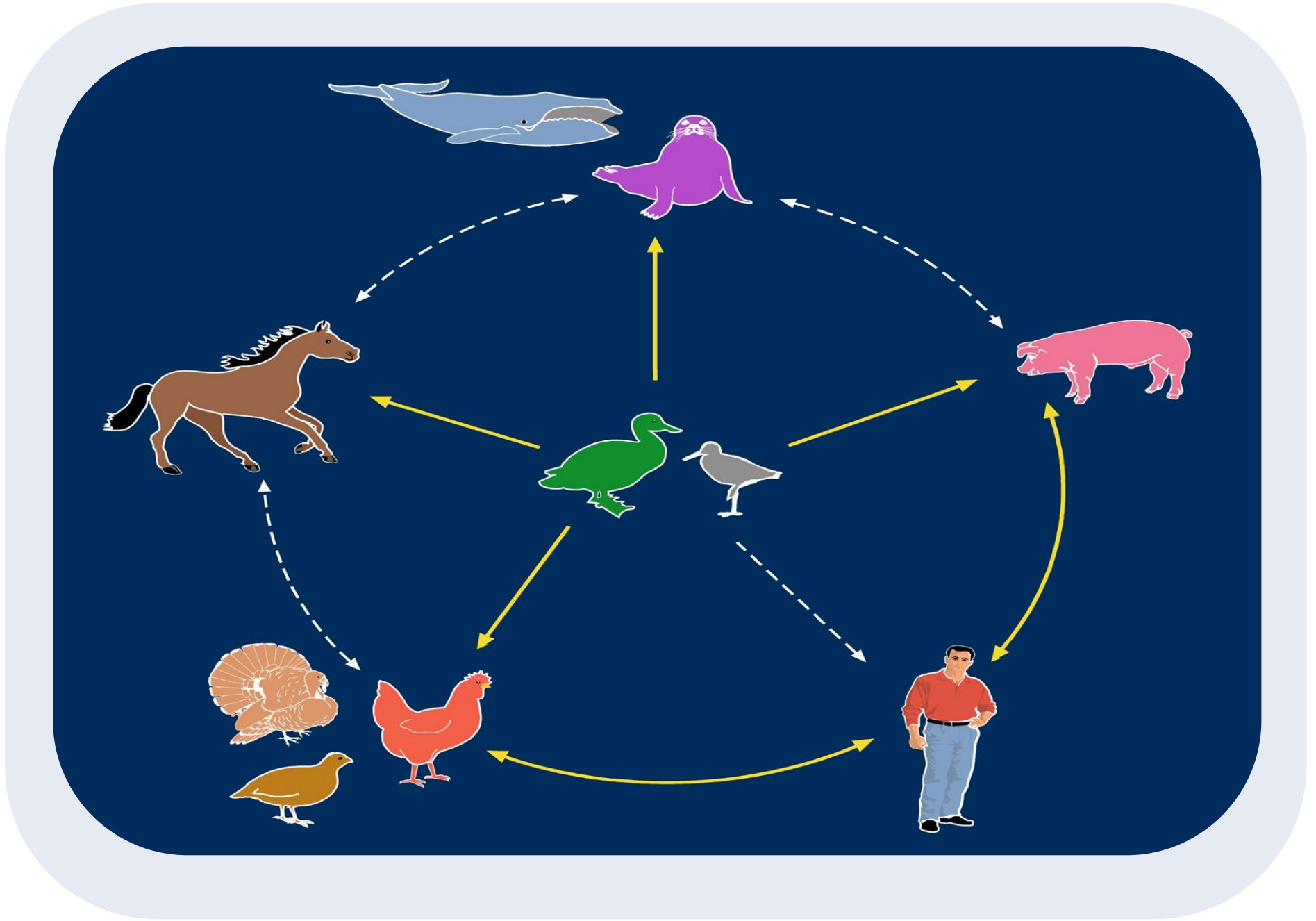
Richard Webby
St Jude Children's Research Hospital



Birds are the major reservoir for influenza A viruses









Non H5 zoonotic infections Sept 2024-Feb 2025

Avian

Country	Subtype (clade)	Cases	Clinical severity	Exposure	Age
China	H9N2	16	Mild to severe	Poultry	13 less than 18, 56, 67, 72
	H10N3	1	Severe	Poultry	23

Swine

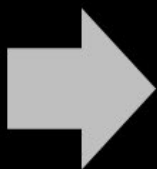
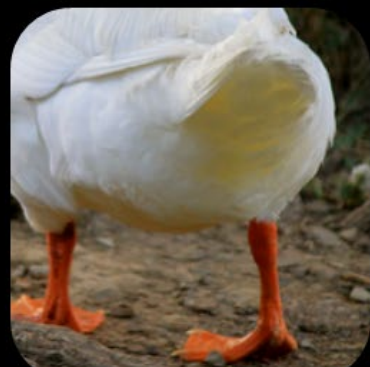
Country	Subtype (clade)	Cases	Clinical severity	Exposure	Age
China	H1N1 (1B.2.1)	1	Mild	Swine	1
United States	H1N2 (1C.2.3)	1	Severe	Unknown	<18



A(H5) Sept 2024-Feb 2025

Country	Subtype (clade)	Cases	Clinical severity	Exposure	Age
Cambodia	H5N1 (2.3.2.1e/previously 2.3.2.1c)	1	Fatal	Poultry	28
Canada	H5N1 (2.3.4.4b)	1	Severe	Unknown	<18
United Kingdom	H5N1 (2.3.4.4b/unknown)	2	Asymptomatic /mild	Poultry	adults
United States of America	H5N1 (2.3.4.4b)	56	Mild to fatal	Bovine/poultry/unknown	range
Viet Nam	H5	1	Severe	Poultry	18

A(H5) Feb 2025 - present 9 Cambodia, 2 Bangladesh, 2 India, China, Mexico, VietNam

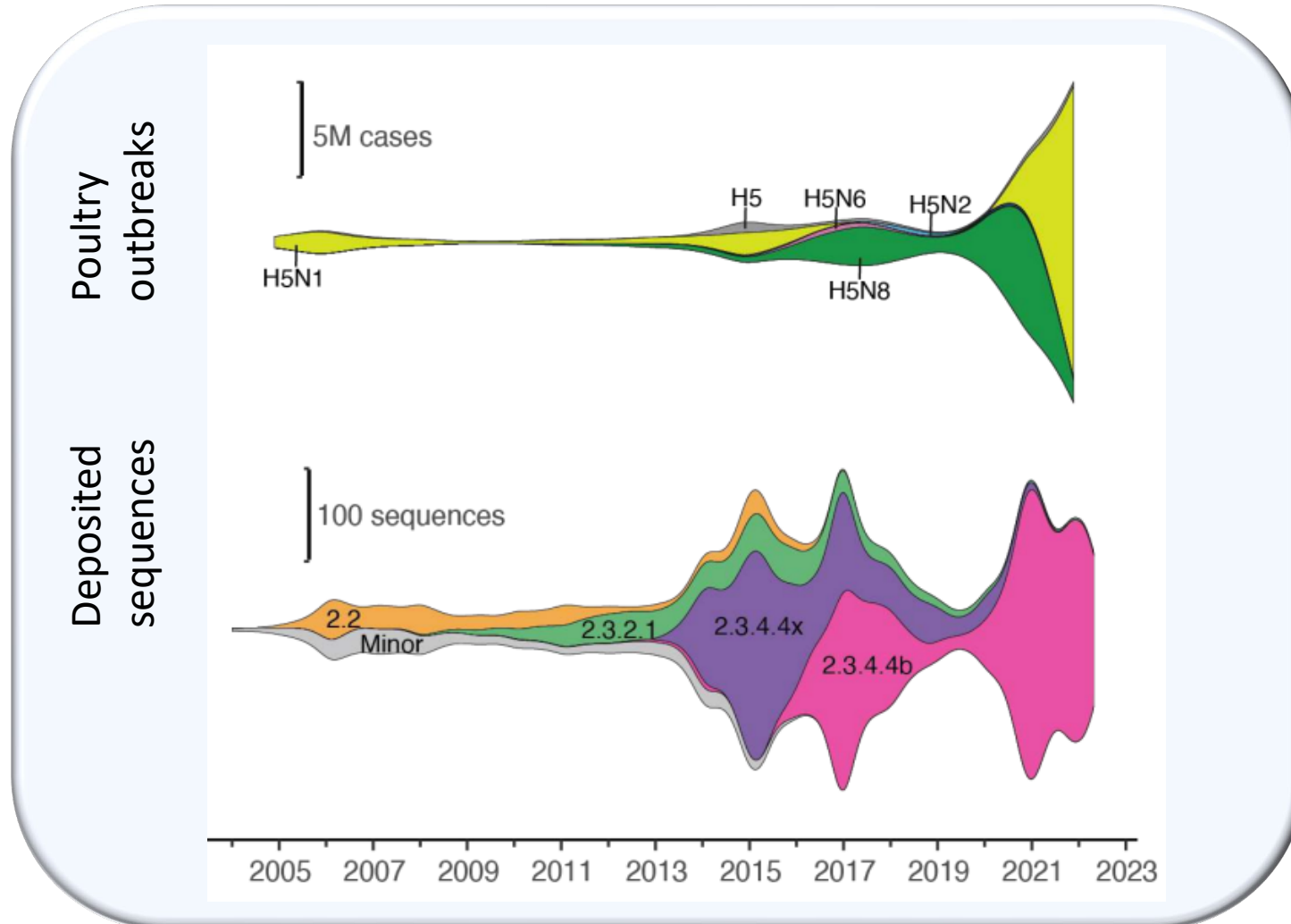


We have long been warning of the H5 threat





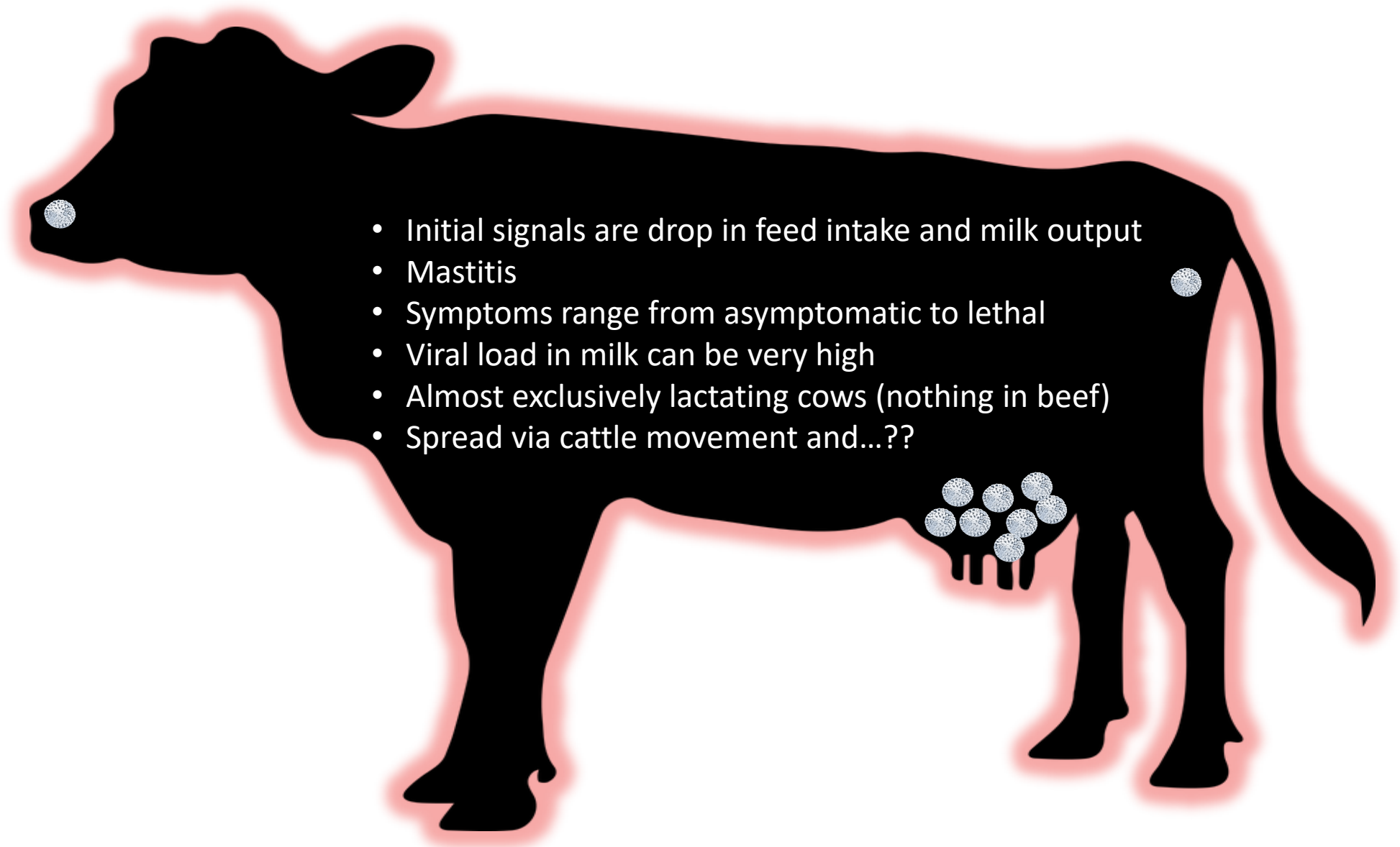
The 2.3.4.4b H5 viruses are different







H5N1 in cows





Cattle to human infections



The NEW ENGLAND
JOURNAL of MEDICINE

CORRESPONDENCE

f X i

Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker

Published May 3, 2024 | DOI: 10.1056/NEJMc2405371



- Most all worked on dairy farms
- All had signs of conjunctivitis, some mild respiratory as well
- Sporadic detection of adaptive mutations

What is the
impact of
sustained
transmission in
cows?



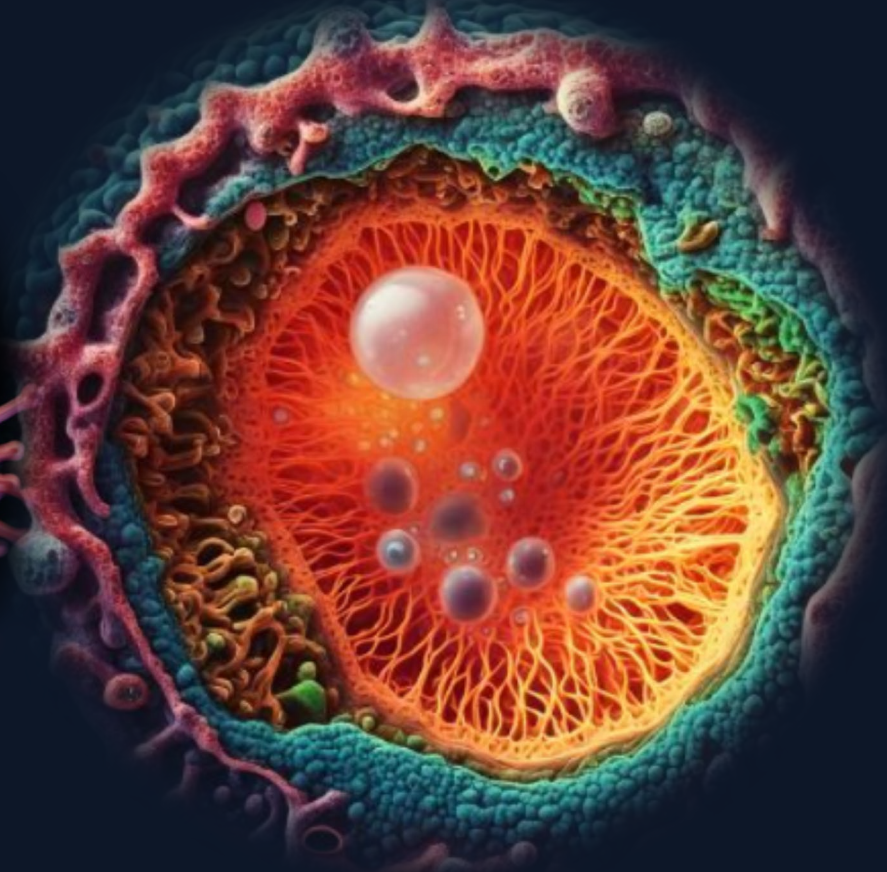
What drives pandemic risk?



Exposure to infected host



Receptor preference



Replication

Bovine outbreak current status





Modulating public health risk

Geographic Distribution in Animals

This element is defined as the spatial geographic distribution of the virus in animals at the time of scoring. Factors to consider include the potential exposure of infected animals to humans, the density of the human population in the geographic area (e.g., the risk might be higher in a densely human populated area than a similarly sized area less densely populated), the density of the animal species, the animal production/management system(s) involved and the availability of proven and effective control measures (e.g., culling) to limit further spread.

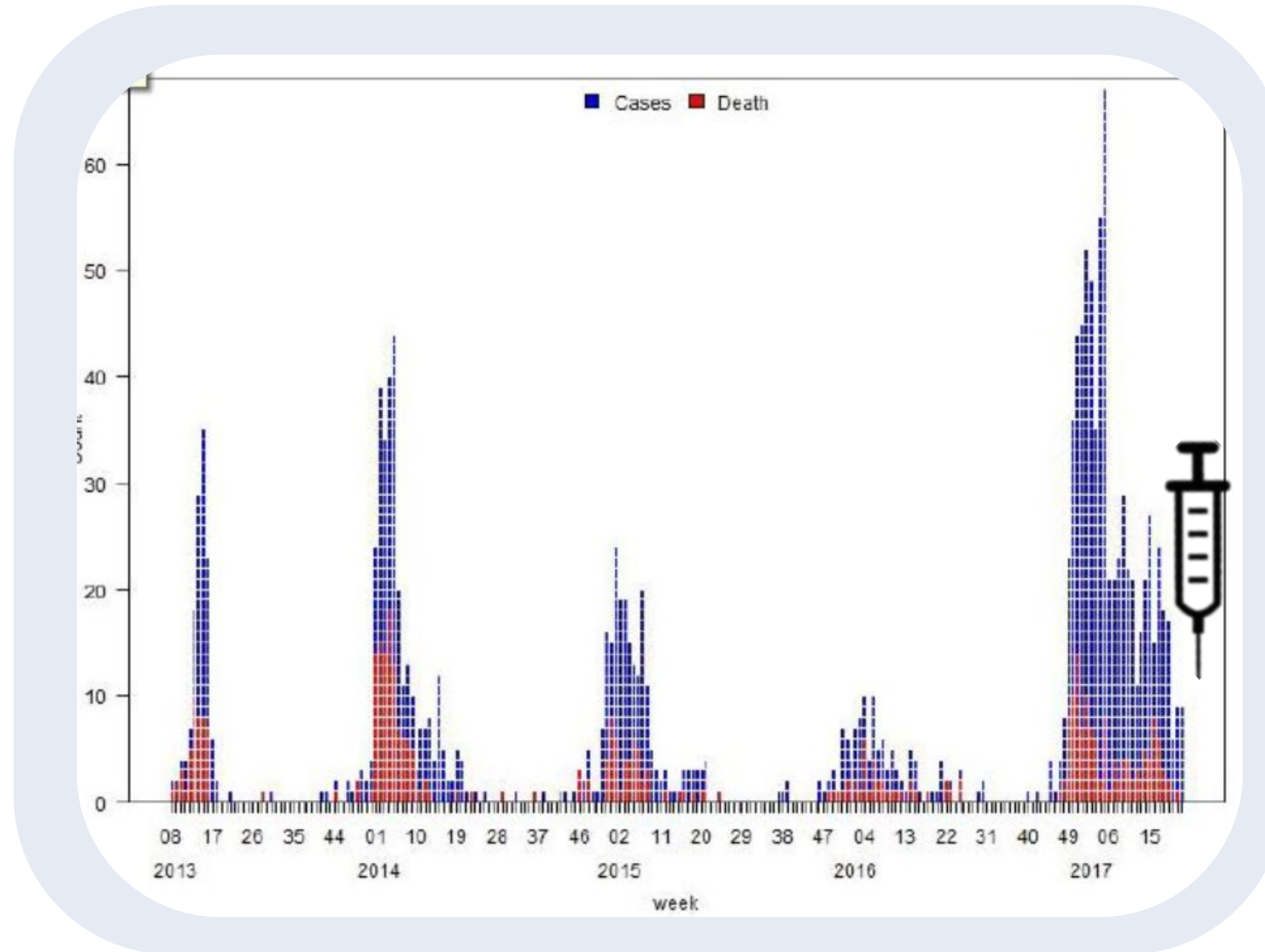
Infections in Animals

This element is defined as the ability of the virus to naturally infect animal¹ species. Factors to consider include the number and diversity of the species, the ability to maintain sustained natural transmission, the environment in which the animals are found (e.g., live poultry market, agricultural fair, back yard, zoo) and the potential for exposure between infected animals and humans.

Comes down to control in source populations



A(H7N9) in China: a vaccine success story?





Trade, not scientific, reasons blocking implementation of animal vaccination





February 2025

		subtype	clade	Astrakhan	Am wild/SC	Ghana	Ezo fox	Gyrfalcon		Collection date	Passage history
Reference antigen											
1	CEBR-RG8A (A/Astrakhan/3212/2020-like)	H5N8	2.3.4.4b	160	40	40	40	160			V1E2/E1
2	IDCDC-RG78A (A/Am wigeon/South Carolina/22-000345-001/2021-like)	H5N1	2.3.4.4b	80	320	80	80	80			V1E2/E1
3	IDCDC-RG80A (A/chicken/Ghana/AVL-763_21VIR7050-39/2021-like)	H5N1	2.3.4.4b	40	20	80	80	<			V1E2/E1
4	NIID-002 (A/Ezo red fox/Hokkaido/1/2022)	H5N1	2.3.4.4b	160	160	80	80	160			EX/E1
5	IDCDC-RG43A (A/gyrfalcon/Washington/41088-6/2014-like)	H5N8	2.3.4.4c	160	40	<	20	320			V1E2/E1
Test antigen											
6	A/British Columbia/PHL-2032/2024	H5N1	D1.1	80	160	80	40	20		Nov. 2024	C2/HCH
7	A/American black duck/Tennessee/141/2024	H5N1	D1.1	<	40	40	10	<		11/21/2024	E1
8	A/ring-necked duck/Tennessee/148/2024	H5N1	D1.1	<	40	40	10	<		11/23/2024	E1
9	A/ring-necked duck/Tennessee/155/2024	H5N1	D1.1	10	80	40	10	<		11/23/2024	E1
10	A/Northern pintail/Tennessee/158/2024	H5N1	D1.1	<	40	40	10	<		11/23/2024	E1
11	A/bovine/California/CL001/2024	H5N1	B3.13	10	160	80	40	<		11/27/2024	E1
12	A/blue-winged teal/Louisiana/LA24-1082/2024	H5N1	D1.1	10	80	40	20	<		11/25/2024	E1
13	A/Canada goose/Kansas/W24-962/2024	H5N1	D1.1	20	80	80	40	<		11/15/2024	E1
14	A/green-winged teal/Florida/W24-974A/2024	H5N1	A3	80	40	40	40	80		11/20/2024	E1
15	A/snow goose/Arkansas/AR24-105/2024	H5N1	D1.1	<	40	40	10	<		12/6/2024	E1
16	A/cackling goose/Kansas/W24-1006/2024	H5N1	D1.1	10	80	40	20	<		12/2/2024	E1
17	A/snow goose/Kentucky/W24-1021B/2024	H5N1	D1.1	80	80	40	40	40		12/4/2024	E1
18	A/snow goose/Louisiana/W24-1010A/2024	H5N1	D1.1	10	80	40	40	<		12/3/2024	E1
19	A/snow goose/Louisiana/W24-1087OR/2024	H5N1	D1.1	10	80	40	20	<		12/5/2024	E1
20	A/wood duck/Florida/W24-974B/2024	H5N1	A3	80	80	40	40	80		11/20/2024	E1
21	A/Ross's goose/Kansas/W24-1015/2024	H5N1	D1.1	10	40	40	20	<		12/3/2024	E1
22	A/snow goose/Kentucky/W24-1021D/2024	H5N1	D1.1	<	40	40	10	<		12/4/2024	E1
23	A/snow goose/Arkansas/AR24-102/2024	H5N1	NA	40	40	40	20	20		12/6/2024	E1
24	A/snow goose/Arkansas/AR24-104/2024	H5N1	NA	10	80	40	20	<		12/6/2024	E1
Serum production: P=prime, B=boost, B*= boost + adjuvant, C= concentrated; NA=Not Available; ***= low reactors					P/B*/B*	CDC	P/B*	NIID	P/B/B*C		

Serum production: P=prime, B= boost, B*= boost + adjuvant, C= concentrated; NA=Not Available; ***= low reactors

≤ 2 fold	4 fold	8 fold	≥ 16 fold	Closest CVV
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	Clade	Institution ²	Available
NBRG-88 (A/Viet Nam/1194/2004)	1	CDC	Yes
IDCDC-RG34B (A/Cambodia/R0405050/2007)	1	SJCRH	Yes
SJRG-166614 (A/duck/Human/X0810301/2013)	1.1	MHRA	Yes
CDC-RG2 (A/Indonesia/5/2005)	1.1.2	MHRA	Yes
NIDRG-9 (A/Indonesia/NHRD11771/2011)	2.1.1	CDC	Yes
SJRG-163222 (A/bar-headed goose/Qinghai/1A/2005)	2.1.3.2	SJCRH/HKU	Yes
IBCDC-RG7 (A/chicken/India/NIV33487/2006)	2.1.3.2a	CDC	Yes
SJRG-163243 (A/whooper swan/Mongolia/244/2005)	2.2	NIID	Yes
IDCDC-RG11 (A/Egypt/2321-NAMRU3/2007)	2.2	SJCRH/HKU	Yes
NBRG-23 (A/turkey/Turkey/1/2005)	2.2	CDC/NIV	Yes
IDCDC-RG29 (A/Egypt/N03072/2010)	2.2	SJCRH	Yes
IDCDC-RG13 (A/Egypt/3300-NAMRU3/2008)	2.2.1	CDC	Yes
NBRG-306 (A/Egypt/N04915/2014)	2.2.1	MHRA	Yes
SJRG-166615 (A/common magpie/Hong Kong/5052/2007)	2.2.1	CDC	Yes
IDCDC-RG30 (A/Hubei/1/2010)	2.2.1.1	CDC	Yes
SJ007 (A/duck/Bangladesh/19097/2013)	2.2.1.2	CDC	Yes
IDCDC-RG63A (A/duck/Bangladesh/17D1012/2018)	2.3.2.1	MHRA	Yes
SJ003 (A/barn swallow/Hong Kong/D10-1161/2010)	2.3.2.1a	SJCRH/HKU	Yes
NBRG-301 (A/duck/Viet Nam/NCVD-1584/2012)	2.3.2.1a	CDC	Yes
SJ009 (A/chicken/Guiyang/1153/2016)	2.3.2.1a	SJCRH	Yes
SJ002 (A/chicken/Hong Kong/AP156/2008)	2.3.2.1b	CDC	Yes
IBCDC-RG6 (A/Anhui/1/2005)	2.3.2.1e	SJCRH/HKU	Yes
CBER-RG1 (A/duck/Laos/3295/2006)	2.3.2.1d	MHRA	Yes
SJRG-164281 (A/Japanese white eye/Hong Kong/1038/2006)	2.3.4	SJCRH/HKU	Yes
IDCDC-RG36 (A/chicken/Bangladesh/11rs1984-30/2011)	2.3.4	SJCRH/HKU	Yes
IDCDC-RG35 (A/Guizhou/1/2013)	2.3.4	CDC	Yes
IDCDC-RG42A (A/Sichuan/26221/2014) (HSN6)	2.3.4	FDA	Yes
IDCDC-RG71A (A/Astrakhan/3212/2020) (HSN8)	2.3.4.2	SJCRH/HKU	Yes
CBER-RG8A (A/Astrakhan/3212/2020) (HSN8)	2.3.4.2	CDC	Yes
IDCDC-RG78A (A/Am. Wigeon/South Carolina/22-000345-001/2021)	2.3.4.4a	CDC/CCDC	Yes
NIID-002 (A/Ezo red fox/Hokkaido/1/2022)	2.3.4.4b	CDC/CCDC	Yes
CNIC-JSN210 (A/Jiangsu/NJ210/2023)	2.3.4.4b	CDC	Yes
IDCDC-RG43A (A/gyrfalcon/Washington/41088-6/2014) (HSN8)	2.3.4.4b	FDA	Yes
NIID-001 (A/duck/Hyogo/1/2016) (HSN6)	2.3.4.4b	CDC	Yes
IDCDC-RG65A (A/Guangdong/18SF020/2018) (HSN6)	2.3.4.4b	NIID	Yes
IDCDC-RG69A (A/ck/Vietnam/RAHO4-CD-20-421/2020-like) (HSN6)	2.3.4.4c	CCDC	Yes
SJRG-165396 (A/goose/Guiyang/337/2006)	2.3.4.4e	CDC	Yes
	2.3.4.4h	NIID	Yes
	2.3.4.4g	CDC	Yes
		CDC	Yes



Human H5 vaccines

- have been clinically evaluated in at least 32 000 individuals, including healthy adults, children, older adults, and individuals with underlying health conditions.
- at least 20 H5 influenza vaccines licensed by regulatory bodies in the Americas, Asia, Australia, and Europe
- only one country (Finland) has implemented an A(H5) vaccination program



Summary

- H5 bird flu has settled into a seasonal disease in US coinciding with migratory bird movement
- We are currently in a lull, but birds are on the move
- The current form of the virus is of low risk for human infection
- The pathogenic potential of the virus is scary



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