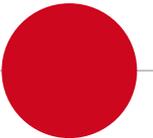


Virus dell'influenza aviaria e spillover nei mammiferi: Cosa sta succedendo?

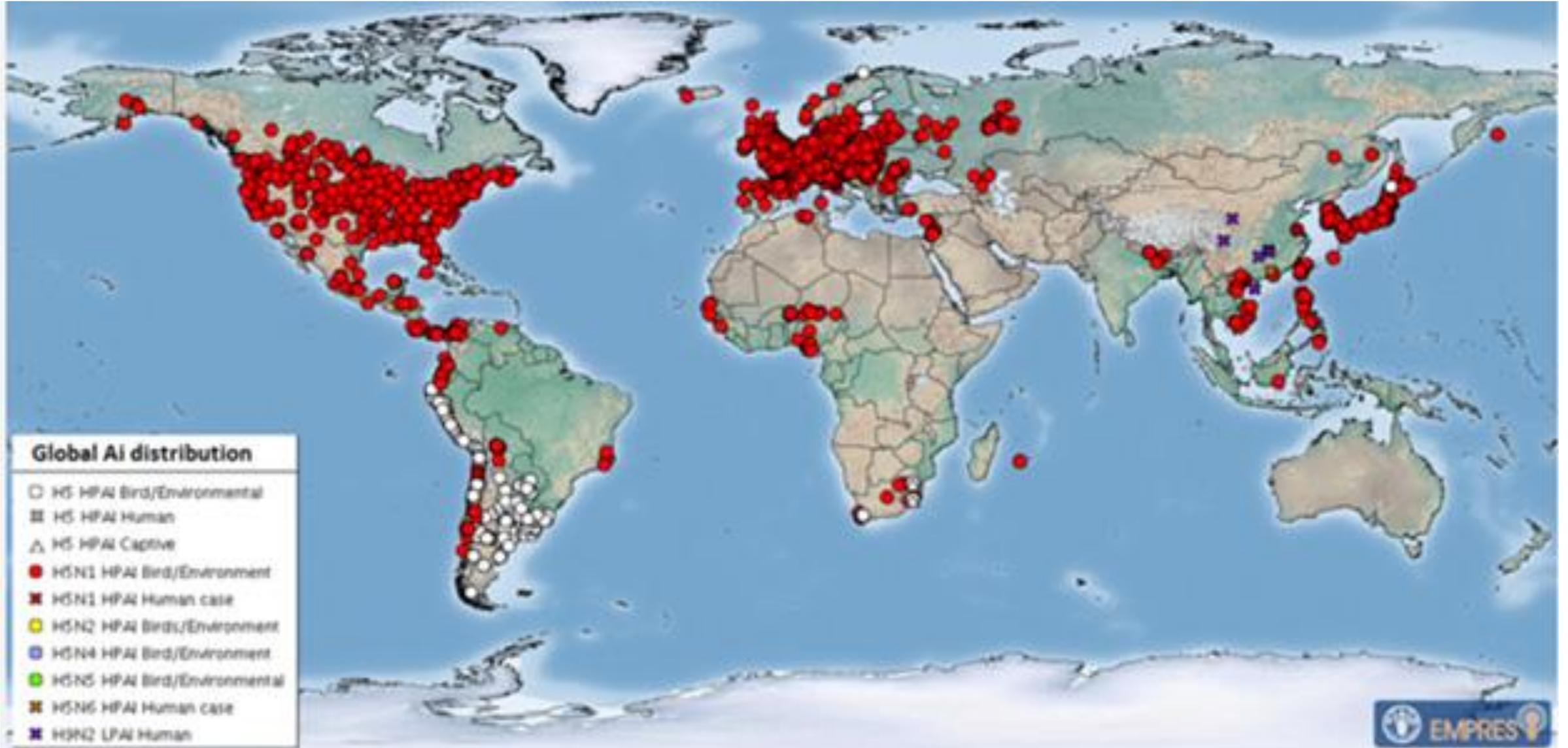
Calogero Terregino

*Laboratorio di Referenza Europeo, WOAH e Nazionale per l'Influenza aviaria e la malattia di Newcastle,
Centro di Referenza FAO per l'influenza animale e la malattia di Newcastle*

Bologna, 30 settembre 2024



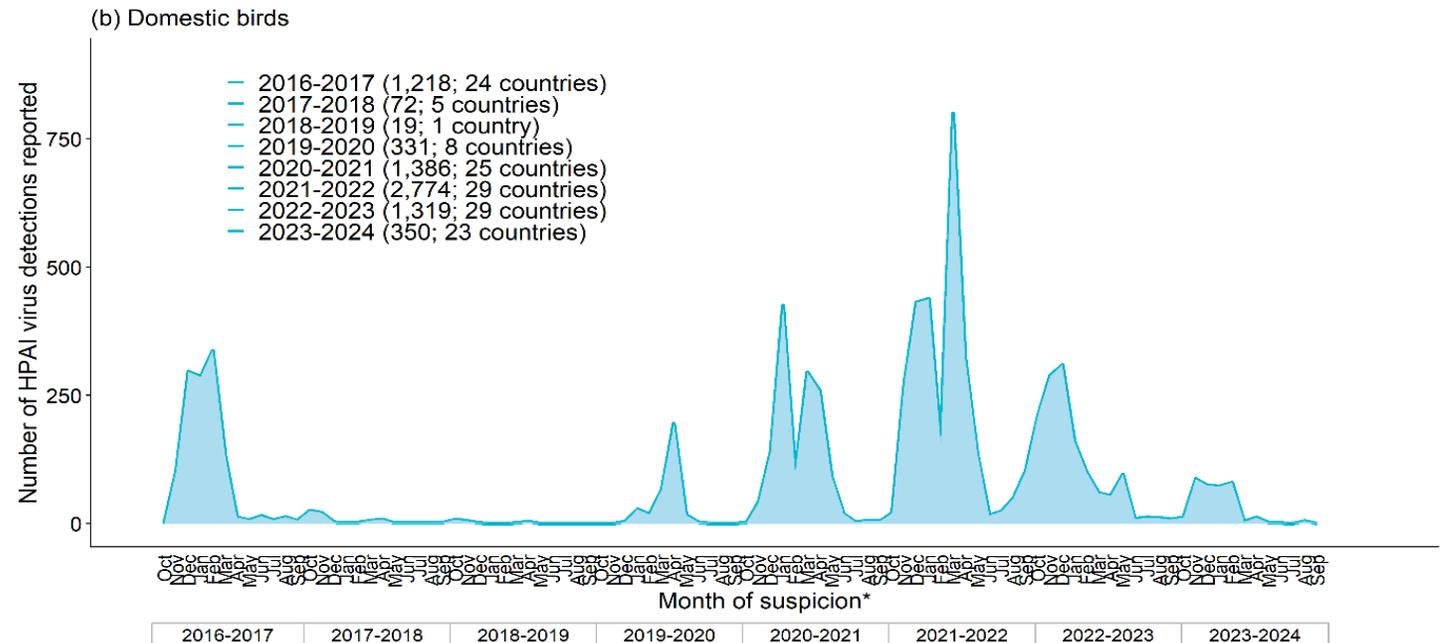
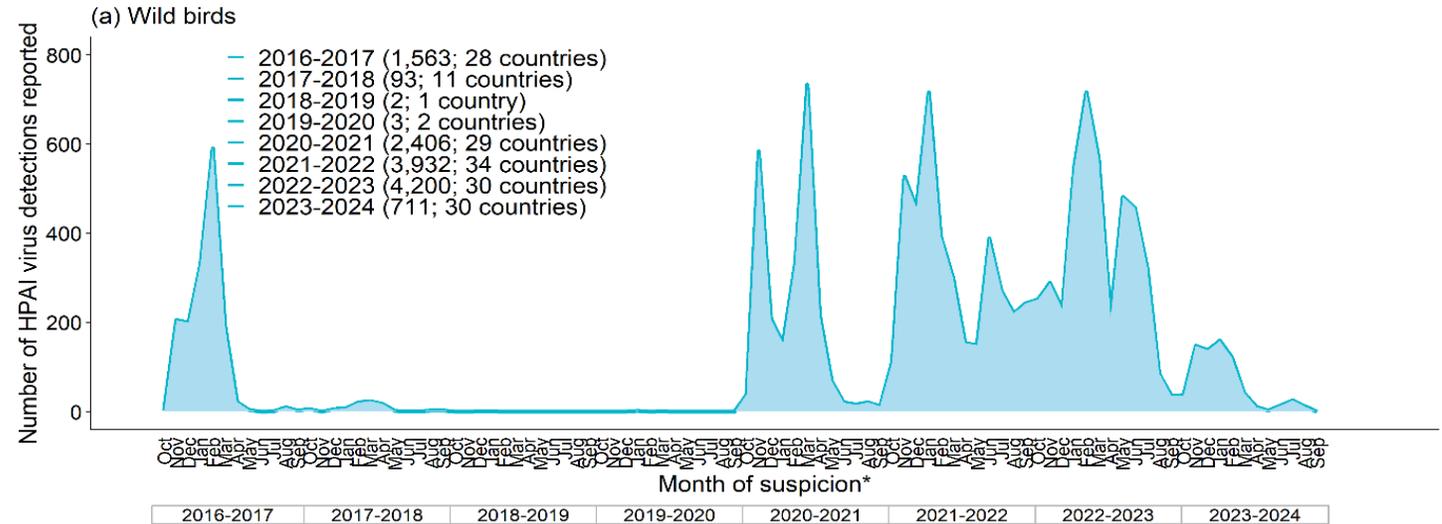
Distribuzione globale del virus H5N1 HPAI e di altri AIV osservati dal 2023



HPAI in EU/EEA e UK: distribuzione dei casi dal 2016

Distribuzione del numero di rilevamenti del virus HPAI nei volatili selvatici (12.910) (a) e domestici (7.469) (b) segnalati in Europa durante otto anni epidemiologici per mese, dal 1° ottobre 2016 al 25 ottobre 2024 (**20.379**)

Source: EFSA/ECDC/EURL avian influenza reports
[https://efsa.onlinelibrary.wiley.com/doi/toc/10.1002/\(ISSN\)1831-4732.avianinfluenza](https://efsa.onlinelibrary.wiley.com/doi/toc/10.1002/(ISSN)1831-4732.avianinfluenza)



MINACCIA PER LA SALUTE UMANA

Avian influenza overview December 2023–March 2024

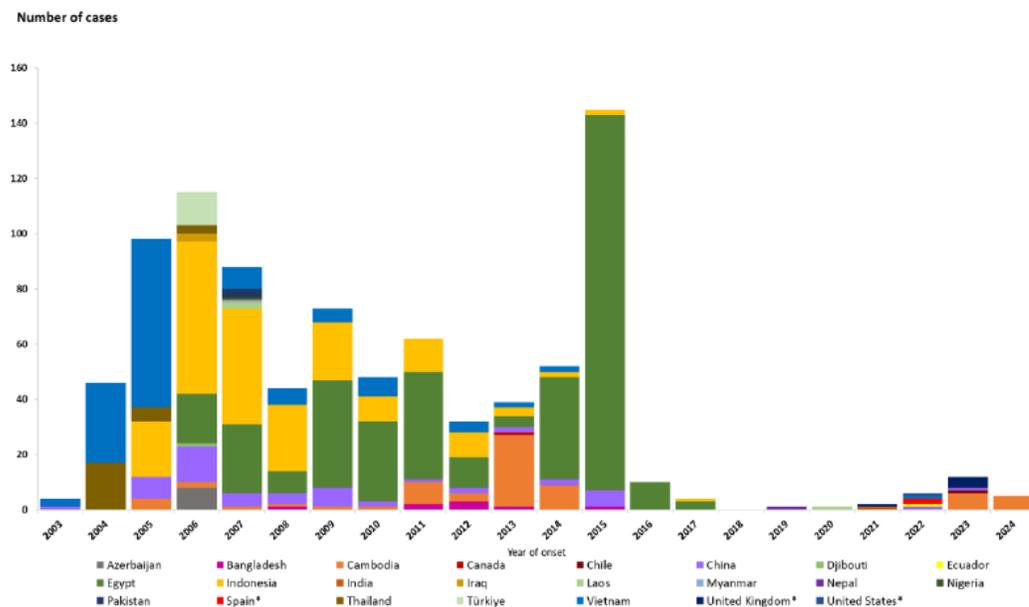


Table 4: Most recent human cases due to avian influenza viruses, by virus subtype

Subtype	New cases reported 1 Dec 2023–12 Mar 2024	Number of reports with disease onset or detection in 2023 and 2024	Total cases (deaths)	Countries reporting human cases
A(H3N8)	-	One case in 2023	3 (1) since 2022	China
A(H5N1)	Five cases in Cambodia, including one death	A total of 12 cases/detections in 2023 Five cases in 2024	887 (462) since 2004	A total of 23 countries reported cases. EU/EEA: Spain, with virus fragment detections in two poultry workers considered contamination and no productive infections.
A(H5N6)	Two cases in China, including one death	Six cases in 2023	90 (35) since 2014	China (89), Laos (1)
A(H9N2)	Four cases in China	Nine cases in 2023 Two cases in 2024	132 (2) since 1998	No EU/EEA country. China (119), Egypt (4), Bangladesh (3), Cambodia (2), Oman (1), Pakistan (1), India (1), Senegal (1)
A(H10N5)	One fatal case in China	One case with onset in 2023	1 (1) first reported in 2024	China (1)

Source: ECDC line list and WHO.

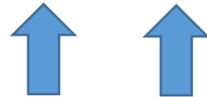
«Il segreto vincente dei virus del clade 2.3.4.4b A(H5)»

Europe: Emergence of H5N1 clade 2.3.4.4b reassortants

Epidemic wave: 2020-2021

W1 - 2020-2021

	PB2	PB1	PA	HA	NP	NA	MP	NS
A	20	20	20	20	20	20	20	20
B	35	23	1	20	1	20	20	20
C	1	1	1	20	1	1	20	1
D	20	20	20	20	20	27	20	20
E	20	20	29	20	20	27	20	20
F	27	20	29	20	37	27	20	20
G	31	31	32	20	12	17	20	1
H	20	31	29	20	27	63	20	20
I	25	14	25	20	26	13	20	28
J	31	23	5	20	26	2	20	28
K	25	1	1	20	1	13	20	1
L	20	20	14	20	20	20	20	20
M	12	33	20	20	36	64	20	20
N	20	29	14	20	20	20	20	20
O	31	23	3	20	26	2	20	28
P	20	20	20	20	26	20	20	20
Q	20	20	29	20	15	27	20	20
R	20	20	29	20	20	20	20	20
S	20	20	29	20	15	20	20	20
T	20	20	29	20	15	20	20	20
U	34	1	1	20	1	1	20	1
V	20	9	14	20	16	61	20	20



Epidemic wave: 2021-2022

W2 - 2021-2022

	PB2	PB1	PA	HA	NP	NA	MP	NS
A	20	20	20	20	20	20	20	20
B	1	1	1	20	1	1	20	1
C	25	14	25	20	26	13	20	28
I	25	14	25	20	26	13	20	28
AA	1	1	1	20	26	1	20	1
AB	31	1	3	20	38	1	20	1
AC	4	1	1	20	1	1	20	1
AD	4	27	1	20	31	1	20	1
AE	4	1	1	20	15	1	20	1
AF	12	6	1	20	50	1	20	29
AG	12	1	1	20	50	1	20	1
AH	12	1	1	20	1	1	20	1
AI	7	1	8	20	37	1	20	29
AJ	10	1	1	20	1	1	20	1
AK	10	1	3	20	38	1	20	1
AL	1	1	1	20	11	1	20	1
AM	1	1	1	20	12	1	20	1
AN	31	1	1	20	1	1	20	1
AO	13	1	1	20	38	1	20	1
AP	45	31	32	20	32	1	20	28
AQ	31	1	8	20	37	1	20	27
AR	1	18	14	20	16	62	16	27
AS	1	1	3	20	38	1	20	1
AT	12	1	1	20	37	1	20	1
AU	19	1	14	20	21	22	20	1
AV	1	1	3	20	1	1	20	1
AW	4	23	1	20	11	1	20	27
AX	31	1	1	20	38	1	20	1
AY	31	1	24	20	38	1	20	1
AZ	1	31	1	20	12	1	20	1
BA	13	1	1	20	1	1	20	1
BB	31	1	43	20	43	1	20	43
BC	45	1	43	20	37	1	20	27
BD	31	31	8	20	26	1	20	1
BE	4	1	14	20	26	1	20	1
BF	13	1	1	20	11	1	20	1



Epidemic wave: 2022-2023

W3 - 2022-2023

	PB2	PB1	PA	HA	NP	NA	MP	NS
C	1	1	1	20	1	1	20	1
I	25	14	25	20	26	13	20	28
AB	31	1	3	20	38	1	20	1
AF	12	6	1	20	50	1	20	29
BB	31	1	43	20	43	1	20	43
CA	31	1	3	20	16	1	16	1
CB	32	1	3	20	38	1	20	1
CC	12	1	8	20	38	1	20	1
CD	31	1	3	20	37	1	20	29
CE	44	1	3	20	38	1	20	1
CF	31	1	3	20	15	1	20	1
CG	4	1	3	20	26	1	20	1
CH	31	1	3	20	26	1	20	1
CI	10	1	12	20	38	1	20	1
CJ	46	6	32	20	26	22	47	1
CK	4	1	3	20	38	1	20	1
CL	31	1	48	20	38	1	20	1
CM	31	49	3	20	38	1	20	1
CN	31	31	3	20	26	1	20	1
CP	31	31	3	20	38	1	20	1
CQ	31	1	3	20	37	1	20	1
CR	31	1	3	20	38	1	20	28
CS	34	1	3	20	38	1	20	51
CU	xxxx	29	xxxx	20	37	1	20	27



Epidemic wave: 2023-2024

W4 - 2023-2024

	PB2	PB1	PA	HA	NP	NA	MP	NS
AB	31	1	3	20	38	1	20	1
AF	12	6	1	20	50	1	20	29
BB	31	1	43	20	43	1	20	43
CH	31	1	3	20	26	1	20	1
CK	4	1	3	20	38	1	20	1
I	25	14	25	20	26	13	20	28
DA	4	52	3	20	38	1	20	27
DB	31	53	3	20	38	1	20	1
DC	41	53	32	20	36	1	20	1
DD	41	1	3	20	26	1	20	56
DE	41	53	3	20	26	1	20	56
DF	4	52	3	20	50	1	20	27
DG	57	1	14	20	38	1	20	1
DH	4	52	3	20	11	1	20	27
DI	14	14	3	20	38	1	20	27
DJ	31	52	3	20	26	1	20	58
DK	4	1	12	20	26	1	20	1
DL	31	1	1	20	38	1	20	1
DM	31	52	3	20	11	1	20	27
DN	4	60	3	20	26	1	20	27
DO	57	1	14	20	26	1	20	1
DP	31	1	65	20	26	1	20	1
DQ	31	1	14	20	38	1	20	1
DR	57	53	3	20	16	1	20	27
DS	57	53	3	20	16	66	20	27

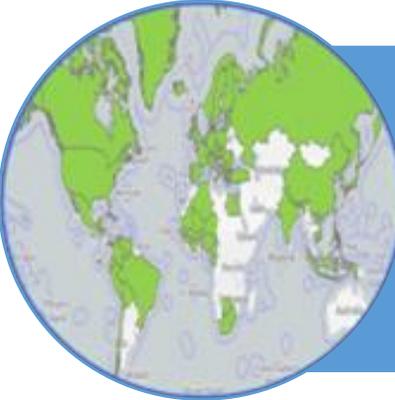


I virus 2.3.4.4b sono più plastici di qualsiasi clade Gs/GD precedente.
Impressionante capacità di riassortimento.

Mantenimento dei geni eurasiatici HA, NA, M.

- AB (H5N1-A/duck/Saratov/29-02V/2021-like) EPI_ISL_5463797
- AF (H5N1-A/chicken/Italy/IZSLT-122448_21VIR9218-1/2021-like) EPI_ISL_7733644
- BB (H5N1-A/Herring_gull/France/22P015977/2022-like) EPI_ISL_13519451
- CH (H5N1-A/Eurasian_Wigeon/Netherlands/3/2022-like) EPI_ISL_15925882
- CK (H5N1 A/Cormorants/Sweden/SVA240102520114/FB000004/M-2023-like) EPI_ISL_18815224
- I (H5N5-A/whooper_swan/Romania/10123_21VIR849-1/2021-like) EPI_ISL_1665268
- DA (H5N1-A/mute_swan/Slovenia/PER1486-23TA_23VIR10323-22/2023-like) EPI_ISL_18612233
- DB (H5N1-A/herring_gull/Germany-NI/2023AI08764/2023-like) EPI_ISL_18526630
- DC (H5N1-A/Common_Buzzard/Netherlands/23023642-002/2023-like) EPI_ISL_18506031
- DD (H5N1-A/Pheasant/England/113705/2023-like) EPI_ISL_18538399
- DE (H5N1-A/Chicken/Scotland/114176/2023-like) EPI_ISL_18538402
- DF (H5N1_A/hens/Bulgaria/309_24VIR2991-20/2024-like) \
- DG (H5N1-A/Gallus_gallus/Belgium/11307_0002/2023-like) EPI_ISL_18607170
- DH (H5N1-A/teal/Italy/23VIR11492-4/2023-like) EPI_ISL_18812084
- DI (H5N1-A/mute_swan/Poland/MB008-1/2024-like) EPI_ISL_18787976
- DJ (H5N1 A/Barnacle_Goose/Netherlands/24000825-002/2024-like) EPI_ISL_18918831
- DK (H5N1-A/barnacle_goose/Denmark/09539-1.02/2023-like) \
- DL (H5N1-A/Chicken/England/005435/2024-like) EPI_ISL_18927384
- DM (H5N1-A/cygnus-olor/Romania/16868_24VIR1002-1/2023-like) EPI_ISL_18956171
- DN (H5N1-A/peregrine-falcon/Cyprus/24VIR1053/2024-like) EPI_ISL_18956184
- DO (H5N1 A/fox/Germany-BW/2024AI00417/2024-like) EPI_ISL_18937337
- DP (H5N1 A/turkey/Poland/H40-T2/2024-like) EPI_ISL_19033547
- DQ (H5N1_A/chicken/Germany-MV/2024AI00860/2024-like) EPI_ISL_19014079
- DR (H5N1_A/Red_Knot/Germany-SH/2024AI01285/2024-like) EPI_ISL_19014084
- DS (H5N8_A/Red_Knot/Germany-SH/2024AI01485/2024-like) EPI_ISL_19030161

HPAI: Challenging dogmas



Paradigma

“I virus presenti negli uccelli delle Americhe e dell'Eurasia rientrano in due clade distinti, indipendentemente dal sottotipo”.

“New challenge: la globalizzazione di un clade plastico (2.3.4.4b) e il rischio per l'emergere di virus con nuove capacità”

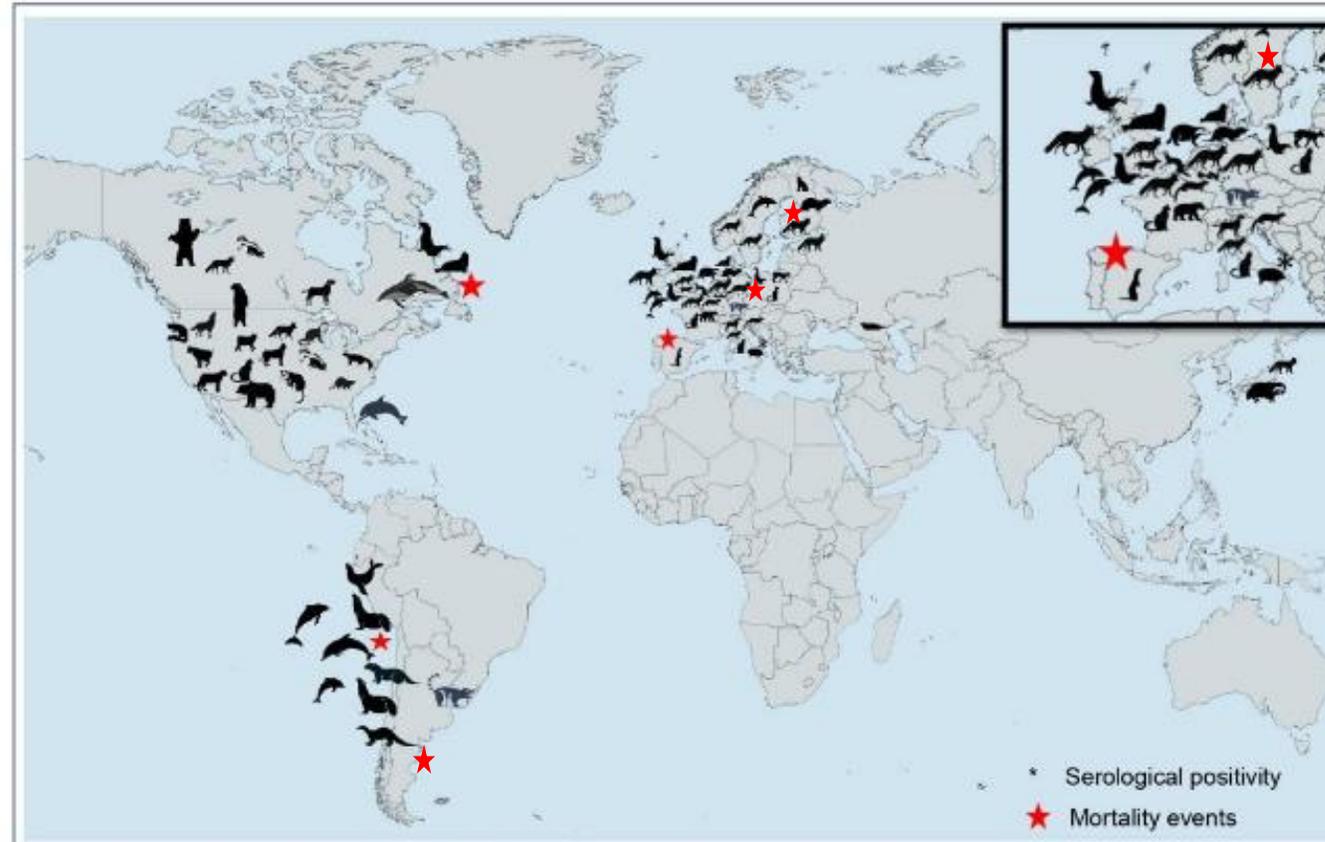
HPAI: Challenging dogma

Paradigma
“Sporadica
diffusione
dell'HPAIV nei
mammiferi”



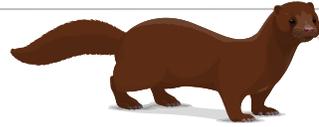
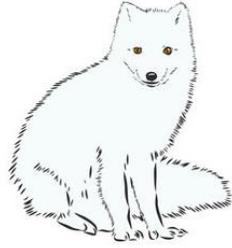
«New challenge:
Infezione di una vasta gamma
di mammiferi”

Clade 2.3.4.4b: Unprecedented impacts on mammals



- | | | | |
|---|---|---|--|
| American black bear (<i>Ursus americanus</i>) | Caracal (<i>Caracal caracal</i>) | Ferret (<i>Mustela fura</i>) | Raccoon (<i>Procyon lotor</i>) |
| American mink (<i>Neogale vison</i>) | Caspien seal (<i>Pusa caspica</i>) | Fisher cat (<i>Pekania pennanti</i>) | Red fox (<i>Vulpes vulpes</i>) |
| American pine marten (<i>Martes americana</i>) | Cat (<i>Felis catus</i>) | Grey seal (<i>Halichoerus grypus</i>) | Skunk (<i>Mephitis mephitis</i>) |
| Amur leopard (<i>Panthera pardus orientalis</i>) | Chilean dolphin (<i>Cephalorhynchus eutropia</i>) | Harbour porpoise (<i>Phocoena phocoena</i>) | South American coati (<i>Nasua nasua</i>) |
| Amur tiger (<i>Panthera tigris</i>) | Common dolphin (<i>Delphinus delphis</i>) | Harbour seal (<i>Phoca vitulina</i>) | South American fur seal (<i>Arctocephalus australis</i>) |
| Asiatic black bear (<i>Ursus thibetanus</i>) | Coyote (<i>Canis latrans</i>) | Japanese raccoon dog (<i>Nyctereutes viverrinus</i>) | South American bush dog (<i>Speothos venaticus</i>) |
| Beech marten (<i>Martes foina</i>) | Dog (<i>Canis lupus familiaris</i>) | Kodiak grizzly bear (<i>Ursus arctos harribilis</i>) | South American sea lion (<i>Otaria flavescens</i>) |
| Bobcat (<i>Lynx rufus</i>) | Eurasian badger (<i>Meles meles</i>) | Marine otter (<i>Lontra felina</i>) | Southern river otter (<i>Lontra provocax</i>) |
| Bottlenose dolphin (<i>Tursiops truncatus</i>) | Eurasian lynx (<i>Lynx lynx</i>) | Mountain lion (<i>Puma concolor</i>) | Virginia opossum (<i>Didelphis virginiana</i>) |
| Brown bear (<i>Ursus arctos</i>) | Eurasian otter (<i>Lutra lutra</i>) | North American river otter (<i>Lontra canadensis</i>) | White-sided dolphin (<i>Lagenorhynchus acutus</i>) |
| Burmeister's porpoise (<i>Phocoena spinipinnis</i>) | European polecat (<i>Mustela putorius</i>) | Pig (<i>Sus scrofa</i>) | |

Outbreaks in mammals caused by 2.3.4.4b H5 HPAI



Animali da pelliccia in
Spagna (n. 1) e in
Finlandia (n.76)

Bovini da latte (> 200
allevamenti) in USA



Fonte?



35 gatti (+1 caracal e 1
dog) in Polonia;
2 ricoveri per gatti in
South Korea;
Casi multipli in USA



Migliaia di leoni marini in Perù, Cile
e Argentina. Migliaia di elefanti
marini in Argentina

Clusters of infection caused by 2.3.4.4b H5 HPAI



Wild birds?

Rapid communication

Open Access

Highly pathogenic avian influenza A(H5N1) virus infection in farmed minks, Spain, October 2022

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Montserrat Agüero^{1,*}, Isabella Monne^{2,*} , Azucena Sánchez¹, Bianca Zecchin² , Alice Fusaro² ,
María José Ruano¹, Manuel del Valle Arrojo³, Ricardo Fernández-Antonio⁴ , Antonio Manuel Souto⁵, Pedro Tordable⁵, Julio Cañas⁵,
Francesco Bonfante², Edoardo Giussani², Calogero Terregino², Jesús Javier Orejas⁶

Individuato l'H5N1 nei visoni che presentavano segni respiratori e neurologici.

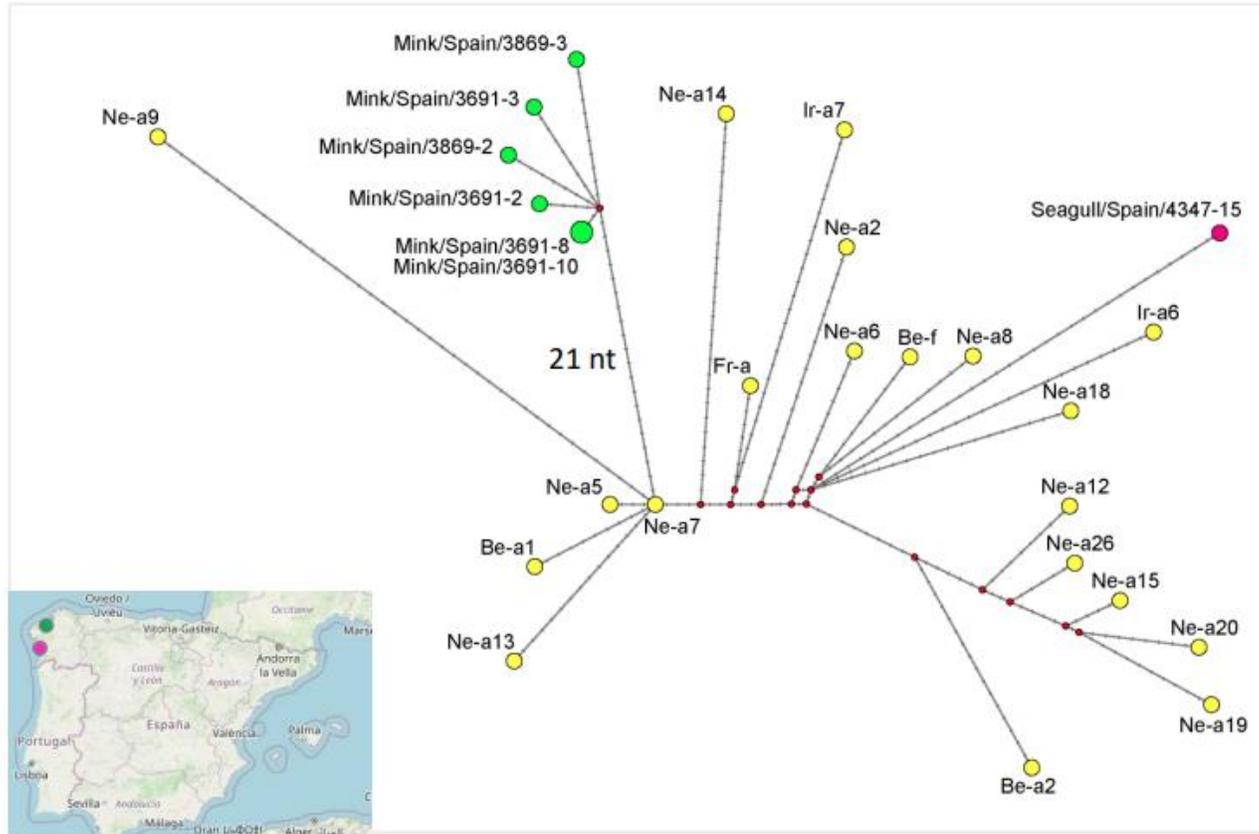
Insights from the epidemiological investigation

Ottobre 2022, Spagna

- La malattia si è diffusa in poche settimane in tutto l'allevamento.
- Nelle settimane precedenti l'epidemia nell'allevamento di visoni, il virus era stato rilevato negli uccelli selvatici della regione.
- I visoni erano ospitati in ricoveri non completamente chiusi sui lati.
- Nessuna prova che gli allevamenti di pollame che fornivano mangime agli allevamenti di visoni avessero registrato focolai di AIV.
- L'allevamento era frequentemente visitato da uccelli selvatici (ad esempio, gabbiani).

Approfondimenti dall'indagine genetica: Come si è diffuso il virus all'interno dell'azienda?

Spain H5N1 clade 2.3.4.4b, 2022



Network analysis of the concatenated complete genomes of viruses belonging to the A/Herring_gull/France/22P015977/2022-like genotype (Bel: Belgium, Fra: France, Ne: The Netherlands, Ir: Ireland).

I virus rilevati negli allevamenti di animali da pelliccia si distinguono dai virus aviari del clade 2.3.4.4b H5N1: Presentano marcatori di adattamento ai mammiferi nel gene PB2 (T271A); Possibile trasmissione da mammifero a mammifero

Outbreaks

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Highly pathogenic avian influenza A(H5N1) virus infections on fur farms connected to mass mortalities of black-headed gulls, Finland, July to October 2023

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Lauri Kareinen¹, Niina Tammiranta¹, Ari Kauppinen¹, Bianca Zecchin², Ambra Pastori², Isabella Monne², Calogero Terregino², Edoardo Giussani², Riikka Kaarto³, Veera Karkamo³, Tanja Lähteinen¹, Hanna Lounela¹, Tuija Kantala¹, Ilona Laamanen¹, Tiina Nokireki¹, Laura London¹, Otto Helve⁴, Sohvi Kääriäinen⁴, Niina Ikonen⁴, Jari Jalava⁴, Laura Kalin-Mänttari⁴, Anna Katz⁴, Carita Savolainen-Kopra⁴, Erika Lindh⁴, Tarja Sironen⁵, Essi M Korhonen⁵, Kirsi Aaltonen⁵, Monica Galiano⁶, Alice Fusaro², Tuija Gadd¹

Luglio-ottobre, 2023, Finlandia

-76 allevamenti colpiti

-Il virus è stato sequenziato in 27 diversi allevamenti di animali da pelliccia.

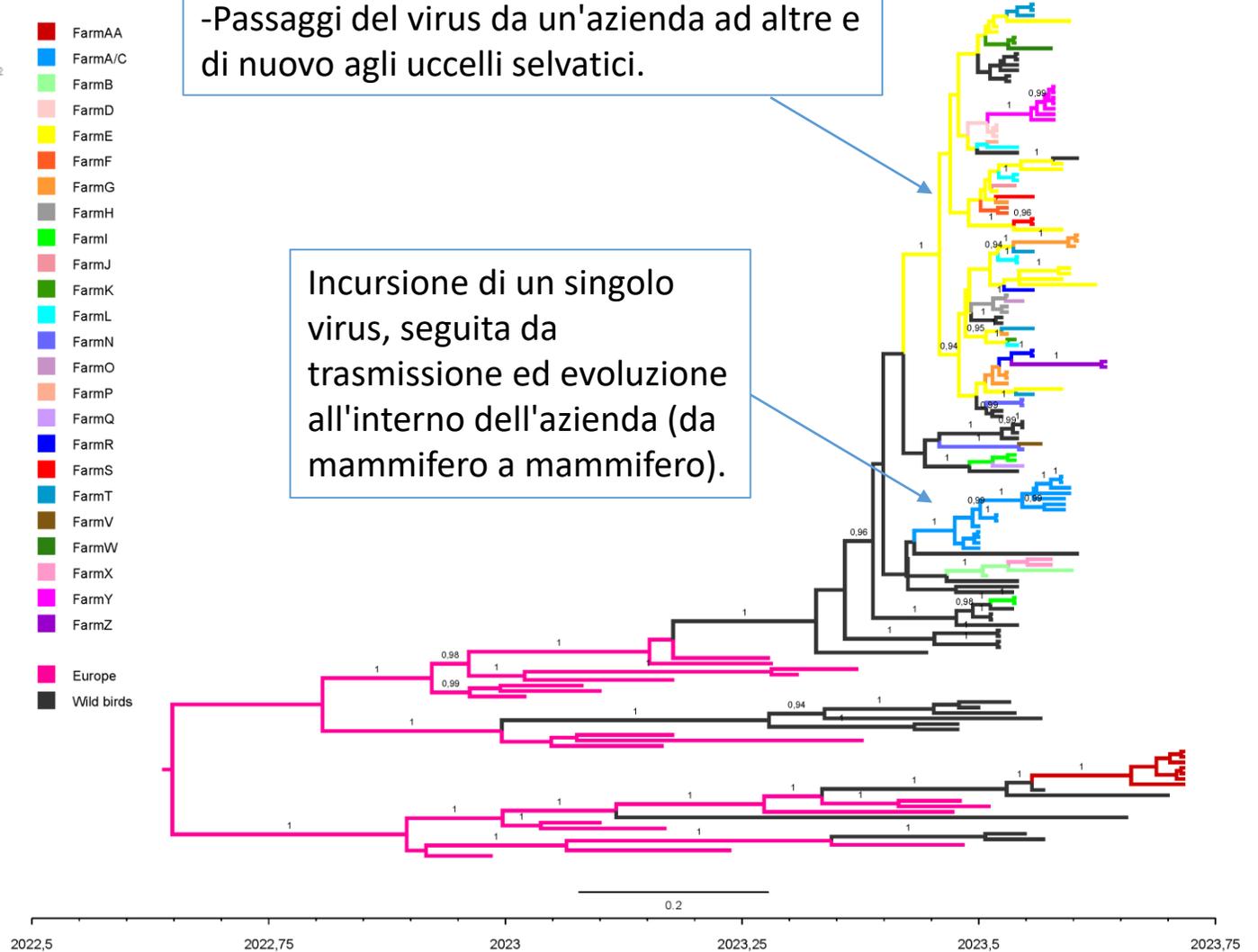
-Genotipo BB

-Introduzione da parte di uccelli selvatici

- FarmAA
- FarmA/C
- FarmB
- FarmD
- FarmE
- FarmF
- FarmG
- FarmH
- FarmI
- FarmJ
- FarmK
- FarmL
- FarmN
- FarmO
- FarmP
- FarmQ
- FarmR
- FarmS
- FarmT
- FarmV
- FarmW
- FarmX
- FarmY
- FarmZ
- Europe
- Wild birds

-Passaggi del virus da un'azienda ad altre e di nuovo agli uccelli selvatici.

IncurSIONE di un singolo virus, seguita da trasmissione ed evoluzione all'interno dell'azienda (da mammifero a mammifero).



Marine mammals, South America clade 2.3.4.4b H5 HPAI



Gamarra-Toledo *et al.*, 2023 EID

- Dalla fine del 2022, sono state segnalate molteplici infezioni da clade 2.3.4.4b A(H5N1) nei mammiferi marini lungo le coste sudamericane di Perù, Cile, Argentina, Uruguay e Brasile, compreso un evento di mortalità di massa senza precedenti (~17.000 individui) nell'ottobre 2023 negli elefanti marini meridionali (*Mirounga leonina*) a Península Valdés, Argentina.
- Sintomi nervosi (tremori e convulsioni) oltre a dispnea e altri sintomi respiratori.



Research

Open Access

Outbreak of highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in cats, Poland, June to July 2023

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Katarzyna Domańska-Blicharz¹, Edyta Świętoń², Agnieszka Świątalska³, Isabella Monne⁴, Alice Fusaro⁴, Karolina Tarasiuk¹, Krzysztof Wyrostek¹, Natalia Styś-Fijoł¹, Aleksandra Giza², Marta Pietruk², Bianca Zecchin⁴, Ambra Pastori⁴, Łukasz Adaszek⁵, Małgorzata Pomorska-Mól⁶, Grzegorz Tomczyk¹, Calogero Terregino⁴, Stanisław Winiarczyk^{5,7}

Raw poultry meat:
most probable source of
infection

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Emerging seasonal and pandemic influenza infections

Characterization of highly pathogenic avian influenza A (H5N1) viruses isolated from cats in South Korea, 2023

Kyungmoon Lee, Minjoo Yeom, Thi Thu Hang Vu, Hai-Quynh Do, Woonsung Na, Mikyung Lee, ...show all

Article: 2290835 | Published online: 22 Jan 2024

Cite this article https://doi.org/10.1080/22221751.2023.2290835

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H5N1(HPAI) Detections in Livestock in USA

Singola introduzione del virus da uccelli selvatici a bovini da latte con una data stimata di dicembre 2023 (4 mesi prima del rilevamento);

Genotipo B3.13 (descritto finora solo negli USA);

Dopo l'introduzione, persistenza del virus nelle popolazioni bovine e trasmissione da bovino a bovino;

Le movimentazioni di bovini hanno permesso la diffusione del virus;

La trasmissione tra vacche in lattazione avviene probabilmente durante le operazioni di mungitura.

HPAI data among people in the USA

Current HPAI in Cattle Outbreak (2024)

CDC and state and local health departments monitor people exposed to infected cattle for 10 days after exposure. Between March 2024 and now, there have been

- At least 1,570 people monitored
- At least 62 persons tested for novel influenza A

Case Reporting

Total Reported Human Cases of H5 in the United States since 2022: 11

Human Cases of H5 Following Exposure to Dairy Cattle since April 1, 2024: 4

Human Cases of H5 Following Exposure to Poultry since April 28, 2022: 7 (6 in 2024)

States with Reported Case(s): Colorado, Michigan, Texas



10 human infections in the USA in 2024

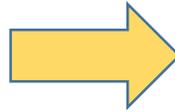
Pandemic risk posed by currently circulating H5 Gs/GD/96 viruses

Evades restriction factors

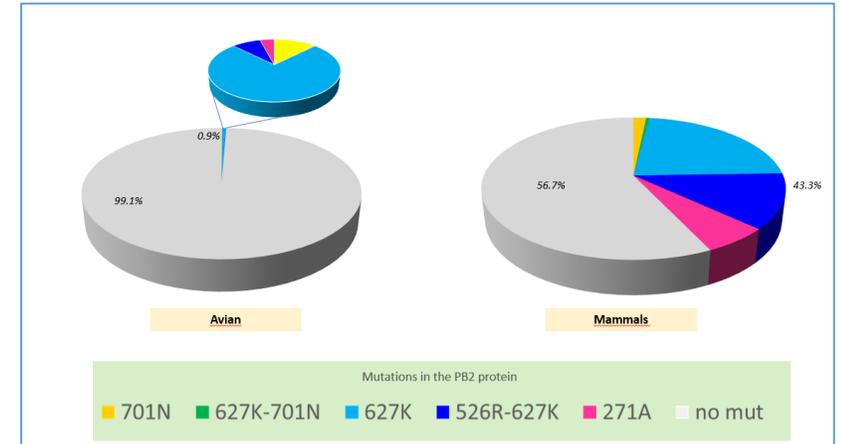
Polymerase changes
(PB2 627K, 590/91SR
701N, 271°)

HA mutated to α 2-6 SA
preference

Lower pH of fusion and
more heat stable



- **Polimerasi**
- **Fattori di restrizione**
- **Legame con il recettore umano**
- **Efficiente trasmissione aerogena**



Ad oggi, nessun riassortimento con virus umani

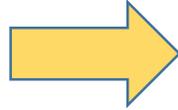
Pandemic risk posed by currently circulating H5 Gs/GD/96 viruses

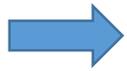
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- **Polimerasi**
- **Fattori di restrizione** 
- **Legame con il recettore umano**
- **Efficiente trasmissione aerogena**

Protein	Mutation	Effect
NP	Y52N	Evasion of human BTN3A3 (a potent inhibitor of avian but not human influenza A viruses replication)

Ad oggi, nessun riassortimento con virus umani

Marker	Effects	Notes	Counting	Samples if n<=2	SamplesAll	Cit
HA(H5):D94N	Increased pseudovirus binding to α 2-6	H3 numbering: 101		3	A/turkey/Poland/H1A/turkey/Poland/H1	Suttie A. et al., (2019); Su Y. et al., (2008)
HA(H5):E251K	Increased virus binding to α 2-6	H3 numbering: 255		8	A/chicken/Northern/Spain/89	Suttie A. et al., (2019); Chen L.M. et al., (2012)
HA(H5):E75K;HA(H5):S123P	Increased virus binding to α 2-6	H3 numbering: 83;128		1	A/chicken/Scotland/A/chicken/Scotland	Suttie A. et al., (2019); Yamada S. et al., (2006)
HA(H5):N154D	Decreased virulence in mice	H3 numbering: 158		4	A/peregrine_falcon/A/peregrine_falcon	Suttie A. et al., (2019); Jin F. et al., (2019)
HA(H5):P235S	Increased virus binding to α 2-6	H3 numbering: 239		6	A/great_crested_gull/A/great_crested_gull	Suttie A. et al., (2019); Watanabe Y. et al., (2011)
HA(H5):Q192R	Increased virus binding to α 2-6	H3 numbering: 196		2	A/chicken/Spain/89	Suttie A. et al., (2019); Watanabe Y. et al., (2011); Ch
HA(H5):S123P;HA(H5)2-5:R167K	Increased virus binding to α 2-6	H3 numbering: 128,496		6	A/domestic_goose/A/domestic_goose/	Suttie A. et al., (2019); Yamada S. et al., (2006)
HA(H5):S133A	Increased pseudovirus binding to α 2-6	H3 numbering: 137	3362		A/fox/England/0158	Suttie A. et al., (2019); Yang Z.Y. et al., (2007)
HA(H5):S133A;HA(H5):T188I	Increased pseudovirus binding to α 2-6	H3 numbering: 137;192		6	A/Caspian_tern/Ast/A/Caspian_tern/Ast	Suttie A. et al., (2019); Yang Z.Y. et al., (2007)
HA(H5):S154N	Increased virus binding to α 2-6	H3 numbering: 158	3356		A/fox/England/0158	Suttie A. et al., (2019); Wang W. et al., (2010)
HA(H5):S155N	Increased virus binding to α 2-6	H3 numbering: 159		16	A/northern_gannet/A/northern_gannet	Suttie A. et al., (2019); Wang W. et al., (2010)
HA(H5):S155N;HA(H5):T156A	Increased virus binding to α 2-6	H3 numbering: 159;160		16	A/northern_gannet/A/northern_gannet	Suttie A. et al., (2019); Wang F. et al., (2015); Wang V
HA(H5):T156A	Increased virus binding to α 2-6;Increased transmission in guinea pigs	H3 numbering: 160	3350		A/fox/England/0158	Suttie A. et al., (2019); Wang W. et al., (2010); Gao Y.
HA(H5):T188I	Increased pseudovirus binding to α 2-6	H3 numbering: 192		6	A/Caspian_tern/Ast/A/Caspian_tern/Ast	Suttie A. et al., (2019); Yang Z.Y. et al., (2007)
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186	3363		A/fox/England/0158	Suttie A. et al., (2019); Lu X. et al., (2013)
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				Watanabe Y. et al., (2011)
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				X. et al., (2019)
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				N. et al., (2015)
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				A. et al., (2019)
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				A. et al., (2019)
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				n W.J. et al., (1989); Ilyush
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				Y. et al., (2010); Bean W.J.
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				Y. et al., (2010); Bean W.J.
HA(H5):V182N	Increased virus binding to α 2-6;Decreased virus binding to α 2-3	H3 numbering: 186				Y. et al., (2010); He G. et al.
NA(N1):A369I	Disruption of the second sialic acid binding site (258)		351		A/TOX/England/0158	
NA(N1):D199Y	Reduced inhibition to Oseltamivir;Reduced inhibition to Zanamivir;Normal Inhibition to Peramivir;Normal Inhibition to Laninamivir			1	A/goose/Spain/472;A/goose/Spain/472;	Takashita E. et al., (2020)
NA(N1):E119G	Reduced susceptibility to zanamivir;Reduced susceptibility to peramivir			4	A/canada_goose_/S/A/canada_goose_/S	Suttie A. et al., (2019); Baek Y.H. et al., (2015)
NA(N1):E119G	Normal Inhibition to Oseltamivir;Highly reduced inhibition to Zanamivir;From reduced to highly reduced inhibition to Peramivir			4	A/canada_goose_/S/A/canada_goose_/S	Hurt A.C. et al., (2009); Baek Y.H. et al., (2015)
NA(N1):E119G	Normal Inhibition to Oseltamivir;Highly reduced inhibition to Zanamivir;From reduced to highly reduced inhibition to Peramivir;Highly reduced inhibition to Peramivir			4	A/canada_goose_/S/A/canada_goose_/S	Baek Y.H. et al., (2015); Lloren K.K.S. et al., (2019); Pi
NA(N1):H275Y	Reduced susceptibility to oseltamivir;Reduced susceptibility to peramivir			1	A/swan/Italy/22VIR	A/swan/Italy/22VIR Suttie A. et al., (2019); Nguyen H.T. et al., (2013); Gul
NA(N1):H275Y	From reduced to highly reduced inhibition to Oseltamivir;Normal inhibition to Zanamivir;From reduced to highly reduced inhibition to Peramivir			1	A/swan/Italy/22VIR	A/swan/Italy/22VIR Nguyen H.T. et al., (2013); Ilyushina N.A. et al., (2010)
NA(N1):H275Y	Highly reduced inhibition to Oseltamivir;Normal inhibition to Zanamivir;From reduced to highly reduced inhibition to Peramivir;Normal inhibition to Peramivir			1	A/swan/Italy/22VIR	A/swan/Italy/22VIR Baz M. et al., (2009); Okomo-Adhiambo M. et al., (20
NA(N1):H275Y	Highly reduced inhibition to Oseltamivir;Normal inhibition to Zanamivir;Highly reduced inhibition to Peramivir			1	A/swan/Italy/22VIR	A/swan/Italy/22VIR Okomo-Adhiambo M. et al., (2010); Choi W.Y. et al., (
NA(N1):I117T	Reduced susceptibility to oseltamivir;Reduced susceptibility to zanamivir			19	A/Great_black-back	A/Great_black-back Suttie A. et al., (2019); Kode S.S. et al., (2019)
NA(N1):I117T	Reduced inhibition to Oseltamivir;Reduced inhibition to Zanamivir			19	A/Great_black-back	A/Great_black-back Kode S.S. et al., (2019)
NA(N1):I117V	Normal Inhibition to Oseltamivir;Normal Inhibition to Zanamivir			8	A/pheasant/England	A/pheasant/England Kode S.S. et al., (2019); Ilyushina N.A. et al., (2010); L
NA(N1):I223K	Reduced inhibition to Oseltamivir;Normal Inhibition to Zanamivir;Normal Inhibition to Peramivir;Normal Inhibition to Laninamivir			1	A/Chicken/Sweden	A/Chicken/Sweden/Takashita E. et al., (2015); Nguyen H.T. et al., (2010);

Sviluppo di un nuovo strumento per identificare automaticamente nei genomi di AIV i determinanti molecolari coinvolti nell'attraversamento della barriera delle specie ospiti (aviari-mammiferi) (disponibile on line)

Rischio zoonotico: lo scenario attuale

- La trasmissione tra mammiferi è stata ipotizzata sulla base delle indagini genetiche ed epidemiologiche condotte, soprattutto negli allevamenti di animali da pelliccia e di bovini da carne.
- La trasmissione da uccelli infetti all'uomo rimane un evento raro. La trasmissione da un mammifero infetto all'uomo è stata osservata nei bovini da carne.
- I virus continuano a diversificarsi a livello globale e, con la migrazione degli uccelli selvatici, altri ceppi di AIV portatori di potenziali mutazioni di adattamento ai mammiferi potrebbero spostarsi attraverso i continenti.

To do list

- L'accesso a processi diagnostici rapidi, sostenibili ed economici deve essere mantenuto anche in contesti con risorse limitate.
- È necessario potenziare la sorveglianza nell'uomo e negli animali (compresi i mammiferi, con particolare attenzione alle specie altamente suscettibili all'infezione da influenza A), nonché l'analisi genomica e la condivisione dei dati di sequenza.
- Forte collaborazione tra i settori animale e umano.
- È fondamentale migliorare le misure di biosicurezza negli allevamenti di specie sensibili ad AIV.
- È necessario pensare ad un'attenta riorganizzazione degli allevamenti zootecnici

Grazie dell'attenzione!

Calogero Terregino

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