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HPAI vaccination strategies for prevention and control

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Today's Speakers

Dr. David E. Swayne
Birdflu Veterinarian LLC

Dr. Stephane Lemiere
Boehringer Ingelheim

Dr. David E. Swayne is a veterinarian with specialization as a Veterinary Pathologist and Poultry Veterinarian. For the past 36 years, his personal research has focused on pathobiology and control of avian influenza. He serves in avian influenza leadership roles at the World Organization for Animal Health (WOAH) and OFFLU, the WOAH and Food and Agriculture Organization network of animal influenza experts. Previously, he served for 28 1/2 years as the Laboratory Director of the Southeast Poultry Research Laboratory, U.S. National Poultry Research Center, Agricultural Research Service, U.S. Department of Agriculture in Athens, Georgia, USA and for 7 years as a tenured faculty member at The Ohio State University. He is currently a private veterinarian consulting on avian influenza control.

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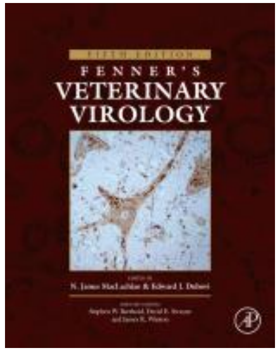
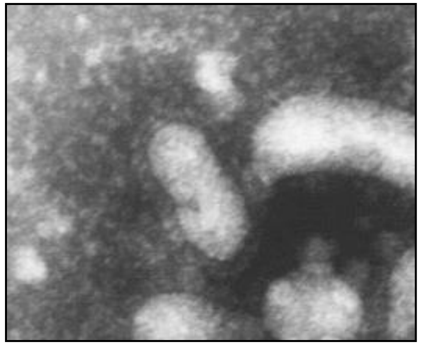
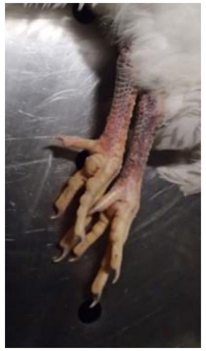
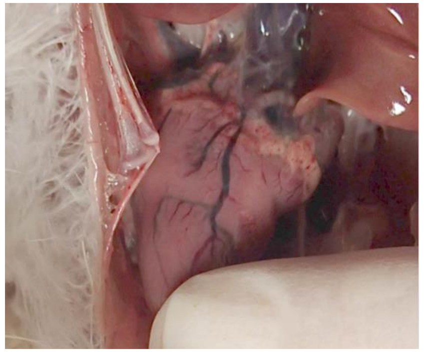
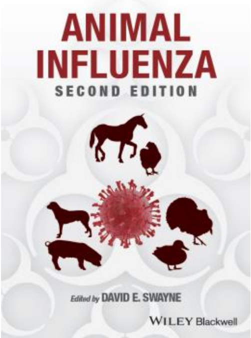
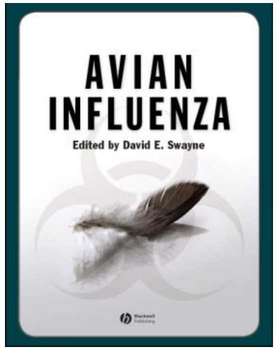




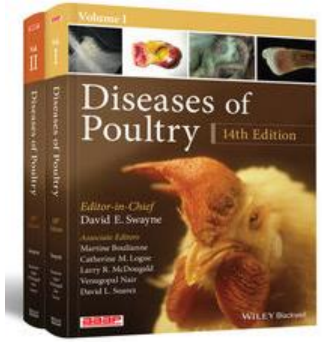








Global Status of Highly Pathogenic Avian Influenza and Its Control



David E Swayne

Private Consultant, Birdflu Veterinarian LLC, Watkinsville, Georgia, USA

Former Laboratory Director, Southeast Poultry Research Laboratory, U.S. National Poultry Research Center, Agricultural Research Service, U.S. Department of Agriculture, Athens, Georgia, USA

Disclaimer: This presentation is based on current scientific data and is not an endorsement of any specific product or company

High Pathogenicity Avian Influenza

1. 1959: Scotland, H5N1
2. 1961: S. Africa, H5N3
3. 1963: England, H7N3
4. 1966: Canada, H5N9
5. 1975: Australia, H7N7
6. 1979: Germany, H7N7
7. 1979: England, H7N7
8. 1983-84: USA, H5N2
9. 1983: Ireland, H5N8
10. 1985: Australia, H7N7
11. 1991: England, H5N1
12. 1992: Australia, H7N3
13. 1994: Australia, H7N3

§ 14. 1994-5: Mexico, H5N2 LPAIV persist

§ 15. 1995 & 2004: Pakistan, H7N3

16. 1997: Australia, H7N4
17. 1997: Italy, H5N2

§ 18. 1996-present: Asia/Europe/Africa/N. & S. America, H5Nx (including N1, 2, 3, 5, 6, 8 reassortants) – Gs/GD Eurasian lineage

19. 1999-2000: Italy, H7N1
20. 2002: Chile, H7N3
21. 2003: Netherlands (BEL, GRM), H7N7
22. 2004: USA, H5N2
23. 2004: Canada, H7N3
24. 2004: S. Africa, H5N2 (ostriches)
25. 2006: S. Africa, H5N2 (ostriches)

§ 26. 2005: N. Korea, H7N7

27. 2007: Canada, H7N3
28. 2008: England, H7N7
29. 2009: Spain, H7N7
30. 2011-3: S. Africa, H5N2 (Ostriches)
31. 2012: Chinese Taipei, H5N2

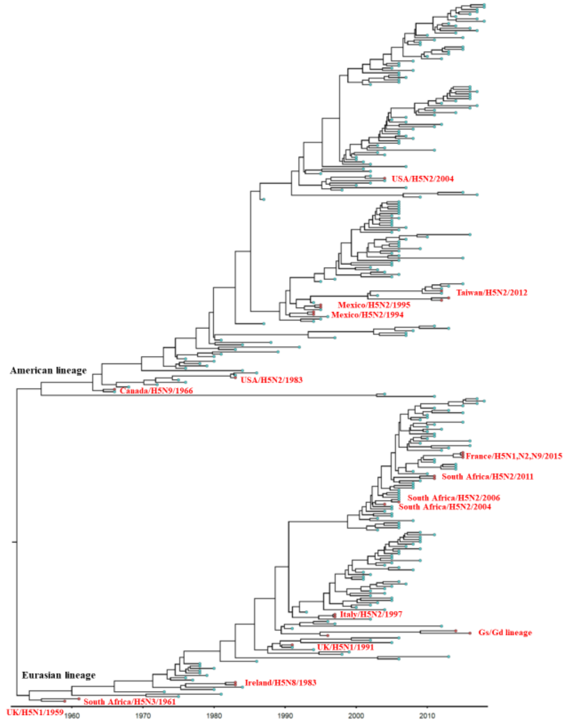
§ 32. 2012-present: Mexico, H7N3

33. 2012: Australia, H7N7
34. 2013: Italy, H7N7
35. 2013: Australia, H7N2
36. 2015: England, H7N7
37. 2015: Germany, H7N7
38. 2015: France, H5Nx
39. 2016: USA (Indiana), H7N8
40. 2016: Italy, H7N7
41. 2017: China, H7N9
42. 2017: USA (Tennessee), H7N9
43. 2020: USA (S. Carolina), H7N3
44. 2020: Australia (Victoria), H7N7

§ Vaccine used in the control strategy

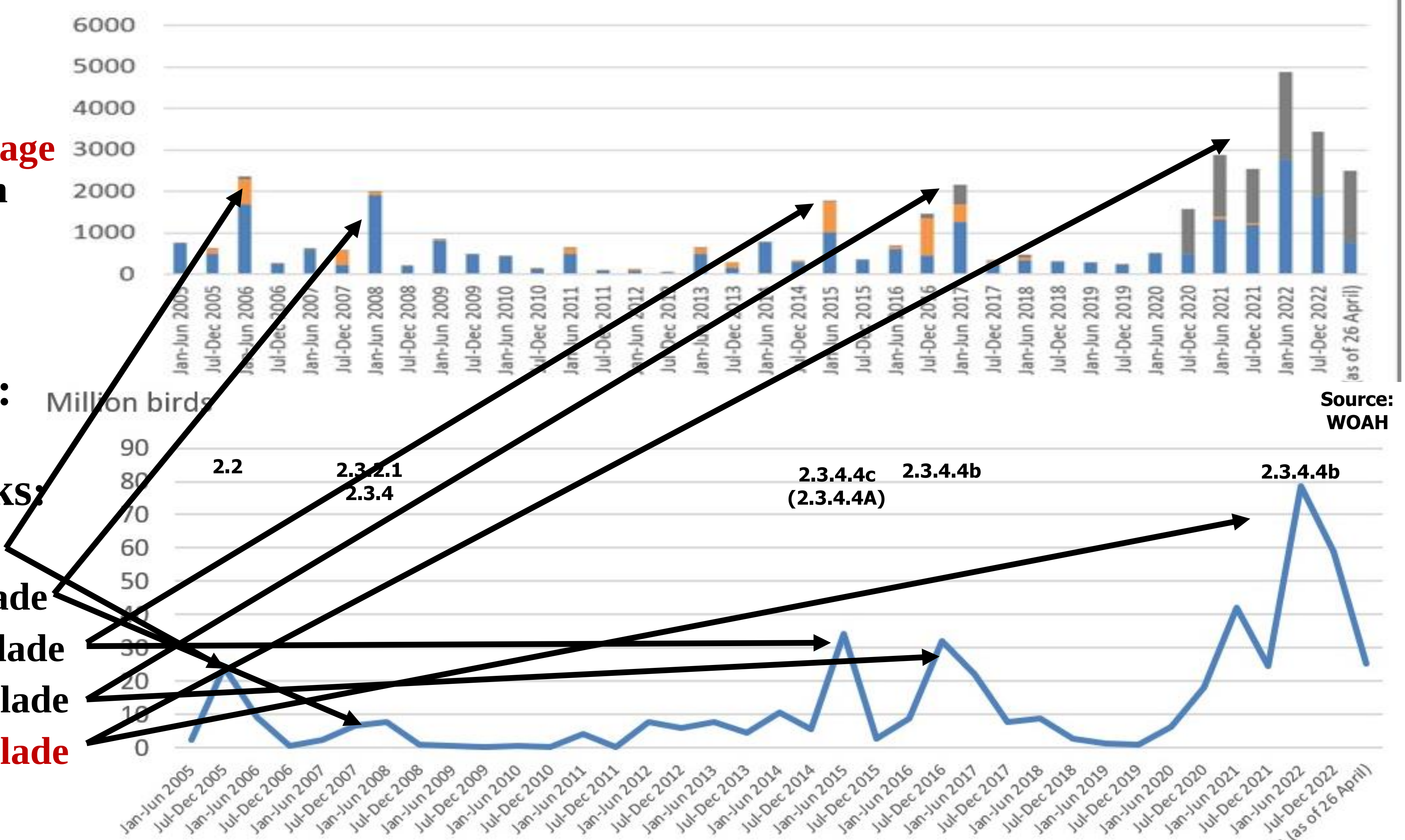
44 HPAI epizootics have distinct virus lineages:

- **41 EMERGENT**
- **3 ENTRENCHED**



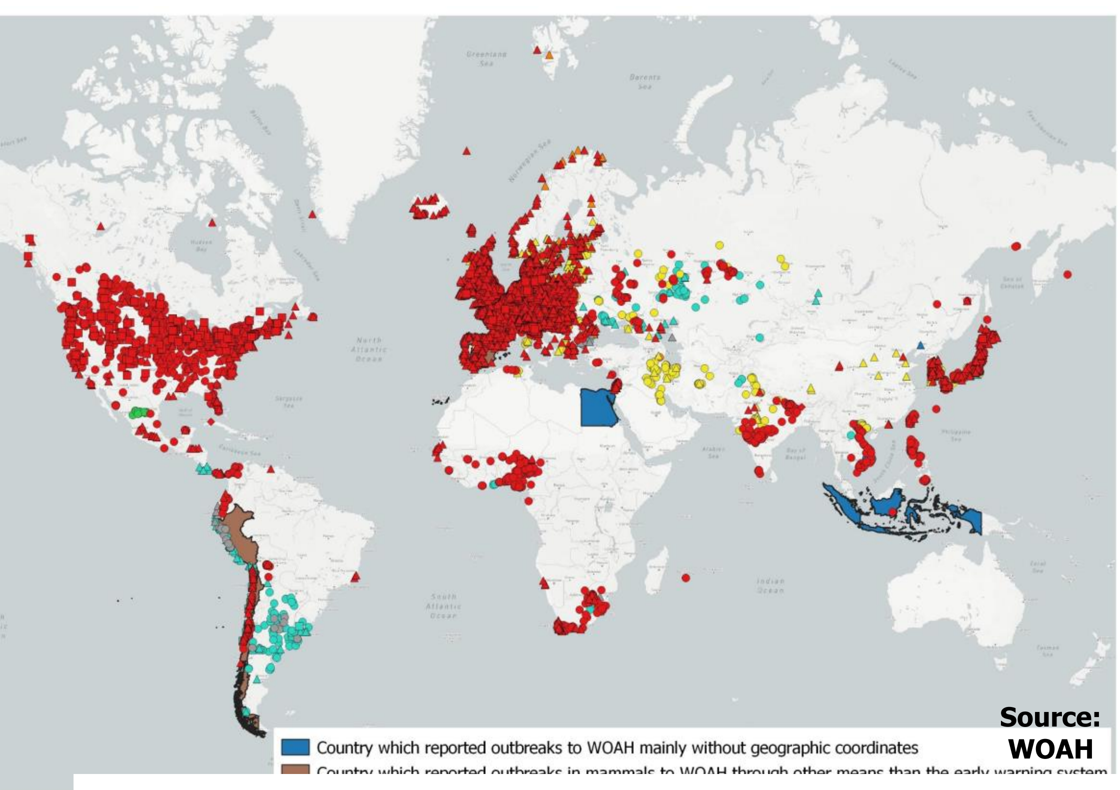
Global HPAI: 2005-2022 Status

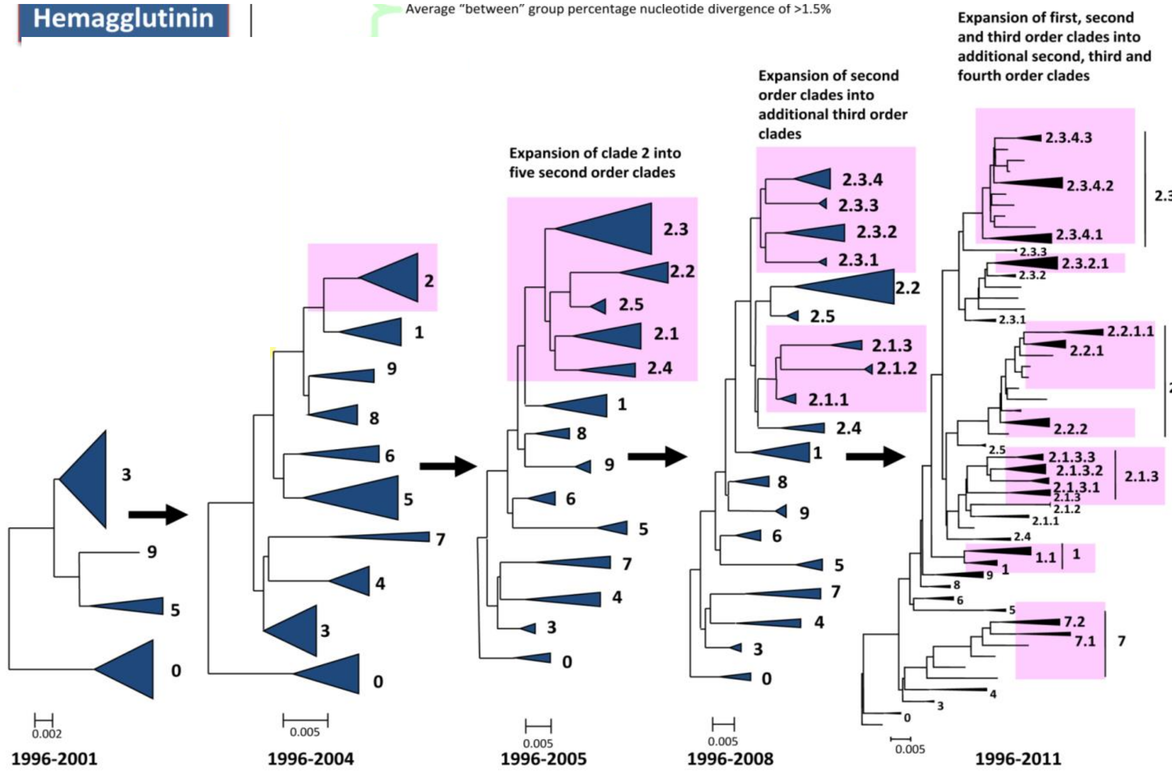
- **Reported cases:**
  - **Entrenched H5Nx Gs/GD Eurasian lineage >>> H7N9 Eurasian lineage >> H7N3 N. American lineage**
  - **Emergent: H7 > H5**
- **Outbreaks 2005-22: Five main H5Nx Gs/GD lineage peaks:**
  - **2005-2006: 2.2 clade**
  - **2007-2008: 2.3.2.1 clade**
  - **2014-2015: 2.3.4.4c clade**
  - **2016-2017: 2.3.4.4b clade**
  - **2020-2023: 2.3.4.4b clade**



Global epizootic: 38,658 outbreaks, >31m bird deaths, >500m birds culled/disposed

Source: WOAH

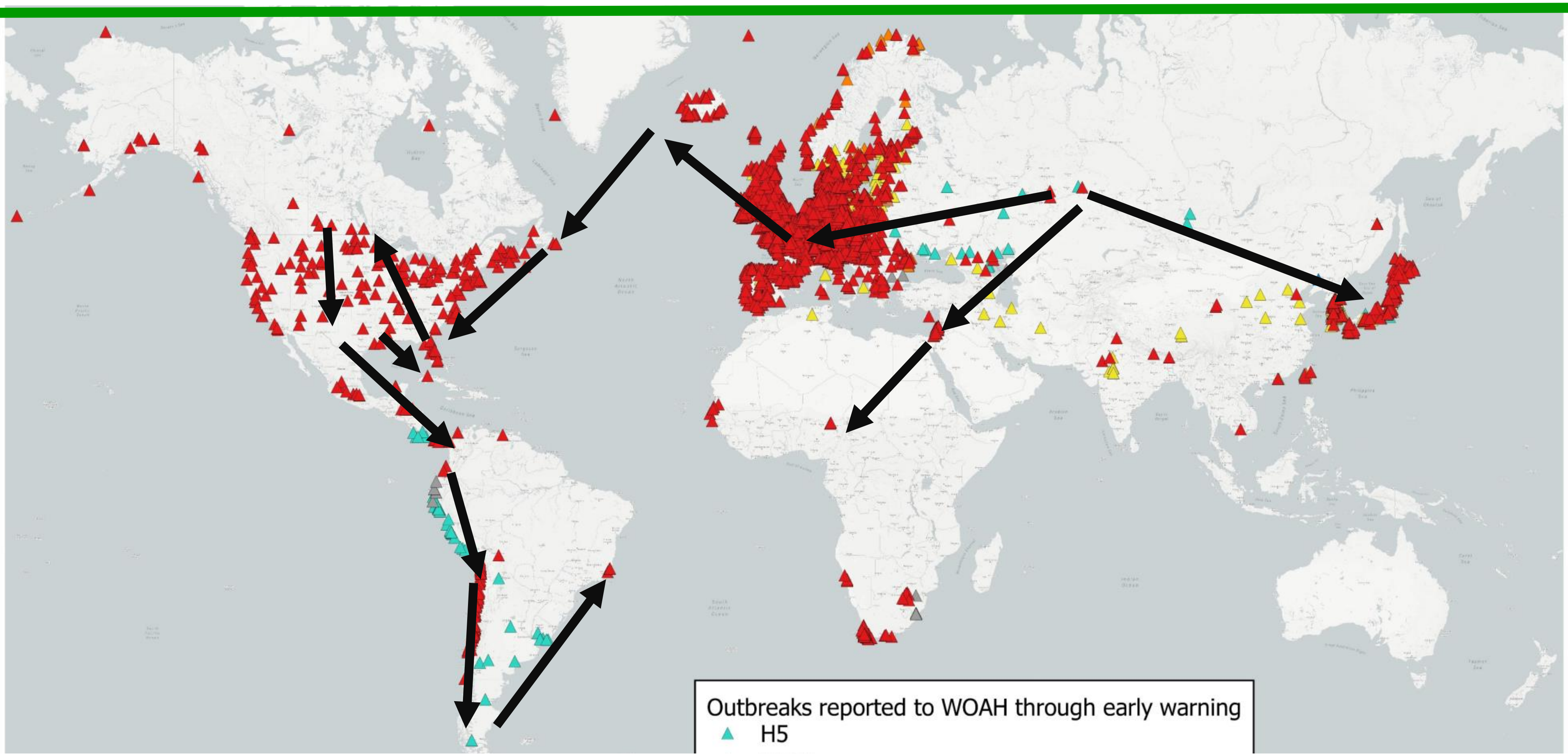




5th order clade: e.g. 2.3.4.4b

- **H5Nx Gs/GD Eurasian lineage affected more poultry than the other 43 HPAI Disease Events combined**
- **>114 countries in poultry, wild birds, wild and captive mammals, and/or humans since 1996**
- **Largest & longest HPAI Outbreak since early 1900's when Fowl Plague ("H7-HPAI") spread across Europe, Asia, Africa, and the Americas**
- **Extensive drift in the hemagglutinin and reassortment of the other 7 gene segments with wild bird LPAIV has impacted the ecology and epidemiology of the epizootic – e.g. HA clades and subclades and genotypes**
- **Evidence of establishment ("endemic") in some wild birds – ecological change (varies from asymptomatic infection to mass die-offs)**

H5Nx Gs/GD Eurasian-lineage HPAIV

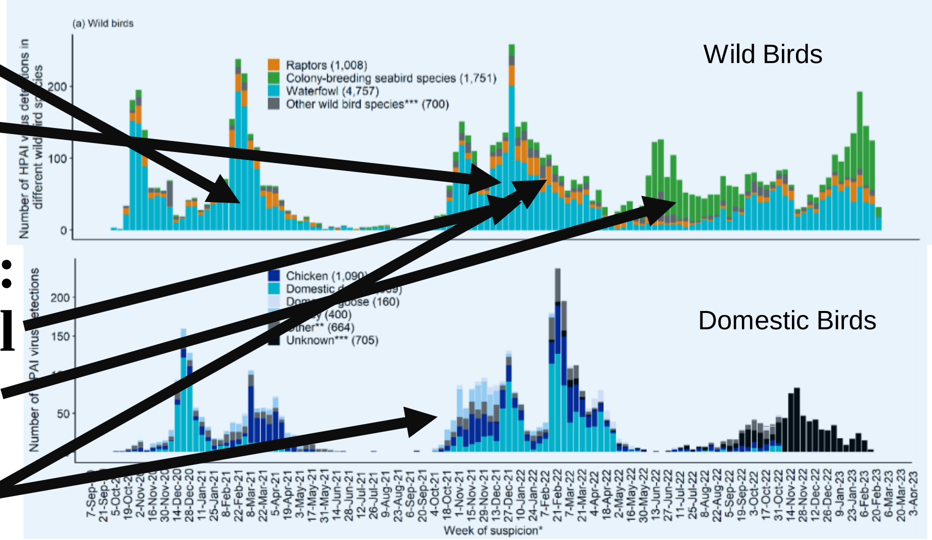


Source: WOAH

- Fall 2020, 2.3.4.4b clade moved by migratory aquatic birds from Central Asia to Europe, Eastern Asia, Middle East, and Africa with evidence of bi-directional movement 2021 spring migrations
- Fall 2021, 2.3.4.4b moved to N. America and winter 2022 down east coast, spring 2022 northward, late summer 2022 southward
- Fall 2022, 2.3.4.4b moved to Central America, Caribbean and northern South America
- Winter 2023. 2344b moved done Pacific Coast and in Spring 2023, detected in southeastern and eastern S. America
- Global (July 2020 to April 2023): 7515 cases, 14 million poultry deaths and 254 million poultry culled

H5N8 2.3.4.4b HPAI wave began Fall 2020 in Central Asia

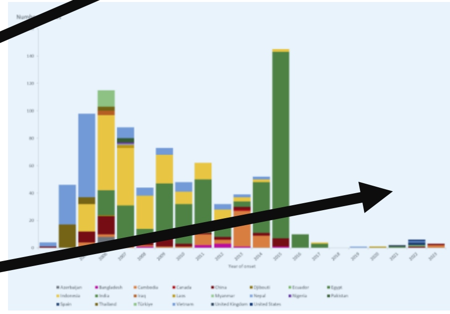
- **Fall 2021, H5N1 reassortant emerged causing infection in diverse wild bird species (>350 species, 51 Families, 20 Orders) with illness and death, and continuous cases**
- **Spread by migratory birds across large geographic regions: asymptomatic infections in many waterfowl with individual bird deaths to massive die-offs of colony breeding seabirds (e.g. Peruvian pelicans, boobies, gannets, terns)**
- **Spill-over to predatory-scavenger species of wild birds**
- **Spill-over into poultry from:**
  - **Direct spread by wild aquatic bird into outdoor reared poultry**
  - **Indirect spread by wild aquatic bird feces contaminating environment around poultry premises and moved into the barn by human activity (clothes, shoes, equipment, water or feed)**
  - **Some countries: farm-to-farm spread through human activity**
- **Spill-over to 35 species of wild carnivorous terrestrial mammals and 11 species of sea mammals with large die-offs harbor seals (2022) and sea lions (2023) & 1 mink farm**
- **Sporadic human cases mostly from direct poultry exposure**



https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2023.7917

https://en.wikipedia.org/wiki/Red_fox

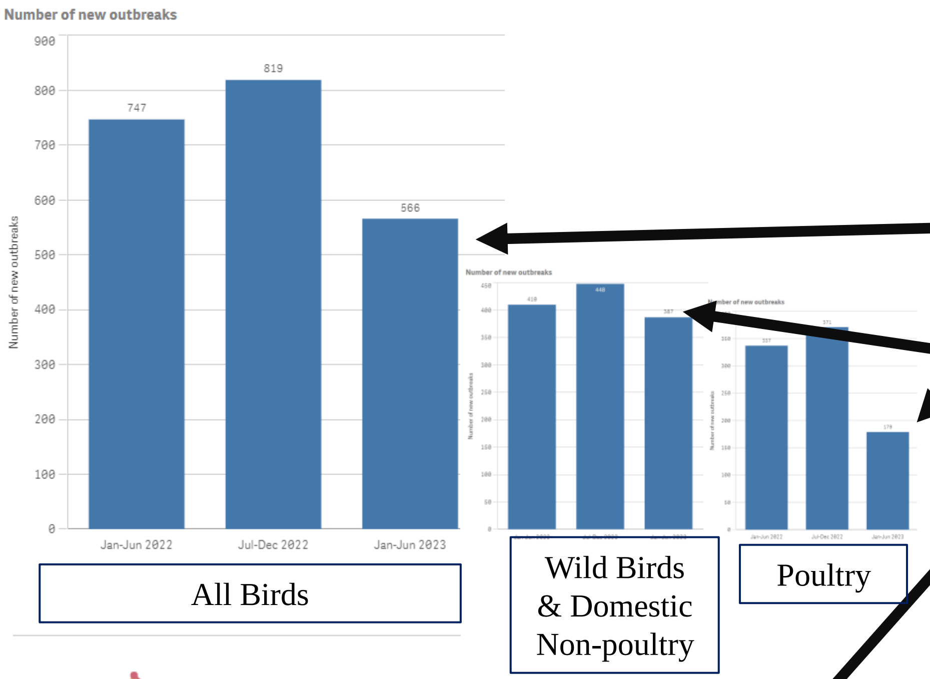
https://en.wikipedia.org/wiki/Harbor_seal



EFSA Scientific Reports - doi:10.2903/j.efsa.2023.7786

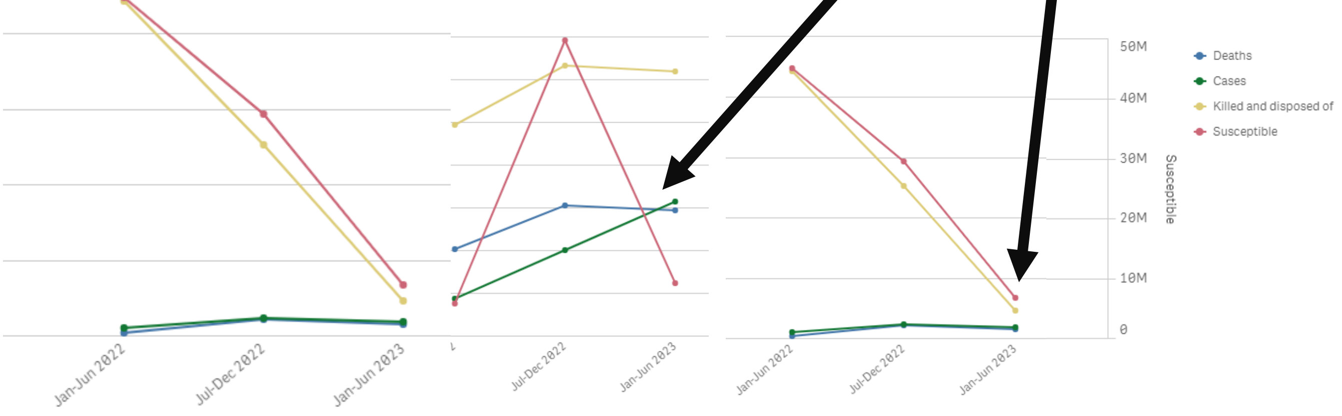
https://en.wikipedia.org/wiki/South_American_sea_lion

Americas HPAI (1-2022 to 6-20-2023)



Source: WOAH

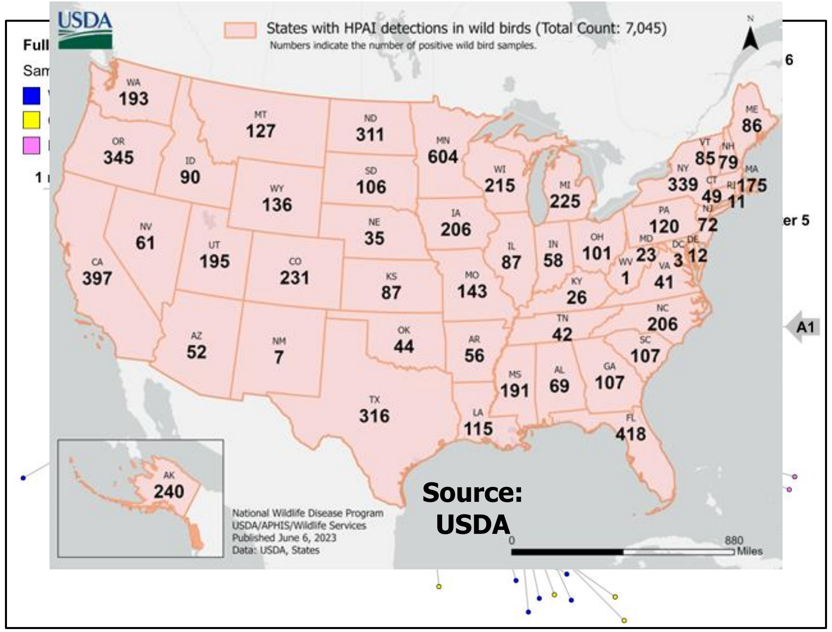
- **First case in N. America – Canada, Great black backed gull sample collected 11-2021**
- **Jan-Jun 2023 decline in total bird cases from a decline in poultry cases & deaths**
- **Wild bird deaths continue at a similar detection rate**



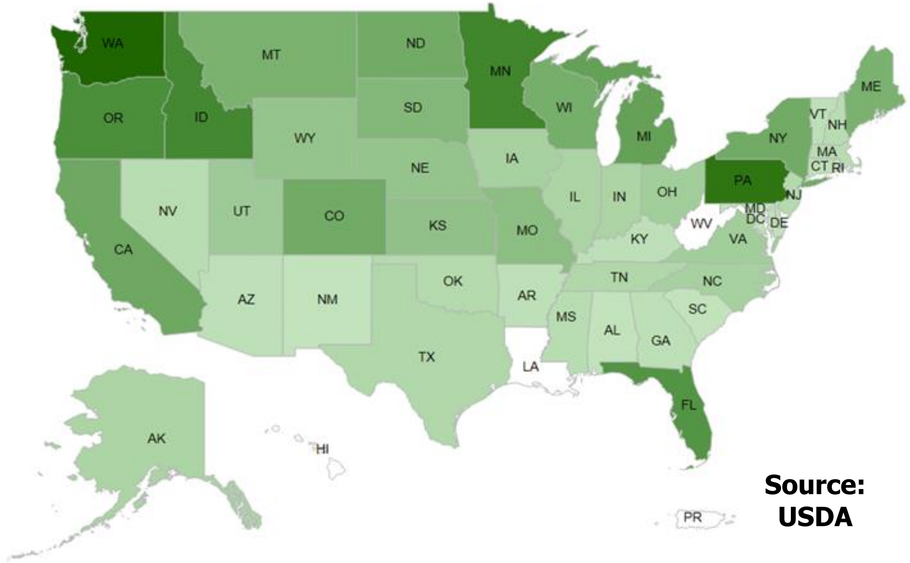
Source: WOAH

H5 Gs/GD Eurasian-lineage HPAIV: Epidemiology in poultry varies with countries and region

- **Asia: Continuing farm-to-farm and along value chains of live poultry markets (LPM) spread with 2.3.4.4b and other Gs/GD clades of virus**
- **USA: first year, 83% point source introductions and 17% possible onward spread (farm-to-farm)**
- **Backyard/village poultry are sentinels for environmental contamination from wild aquatic birds**



Courtesy: Sungsu Youk and Mary Pantin-Jackwood

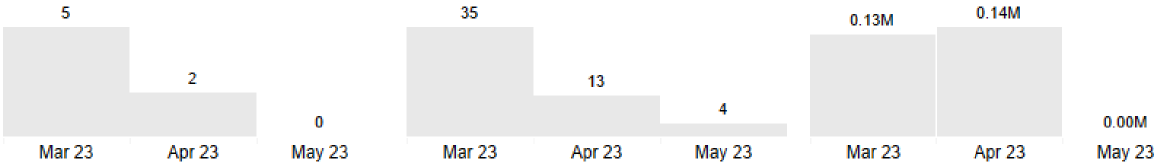


Source: USDA

836 Confirmed Flocks
0 confirmed last 30 days
Birds tested and confirmed having HPAI

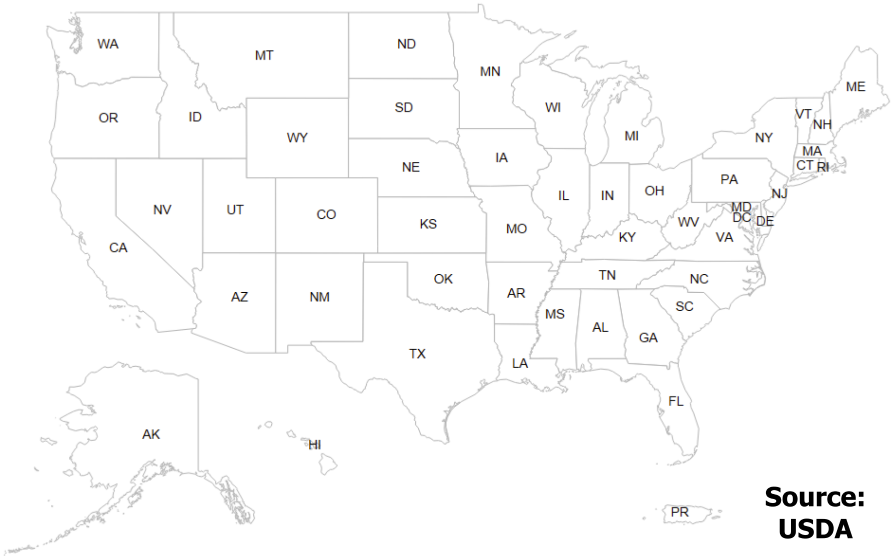
47 Affected States
0 states last 30 days
States with at least one confirmed infected flock

Commercial Flocks	Backyard Flocks	Birds Affected*
325	**511**	**58.79M**

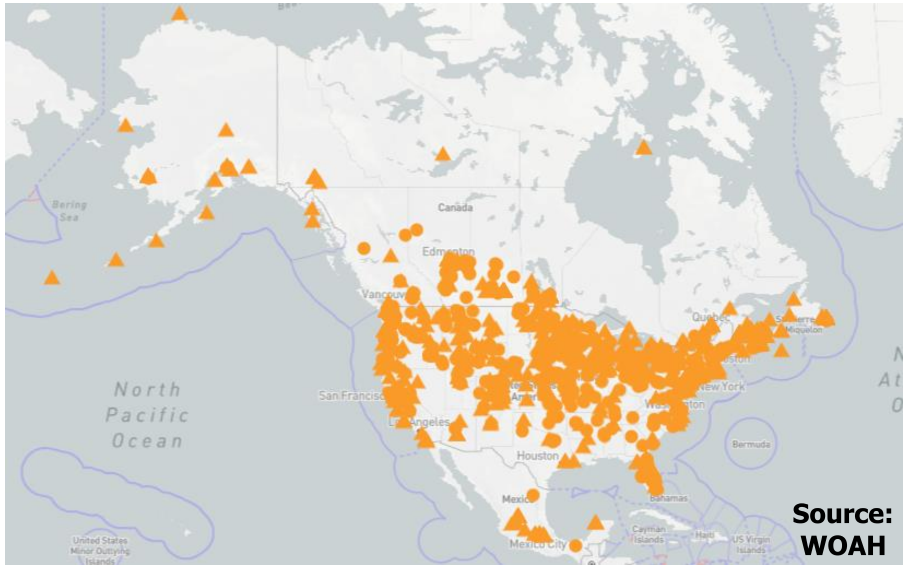


*Number of birds on confirmed infected premises.
Bars reflect most recent 4 months (numbers may not add up to total).

USA Cases HPAI (1-1-2023 to 6-20-2023)



Commercial poultry and backyard since 5-20-2023



Last Backyard (non-poultry): 18 May 2023

Last Commercial flocks (cases since 1-2023):

- **Meat Turkeys, 19 April 2023, ND & SD (8)**
- **Broiler Flocks: 21 February 2023, PA (3)**
- **Commercial Table Egg, 20 December 2023, CO**

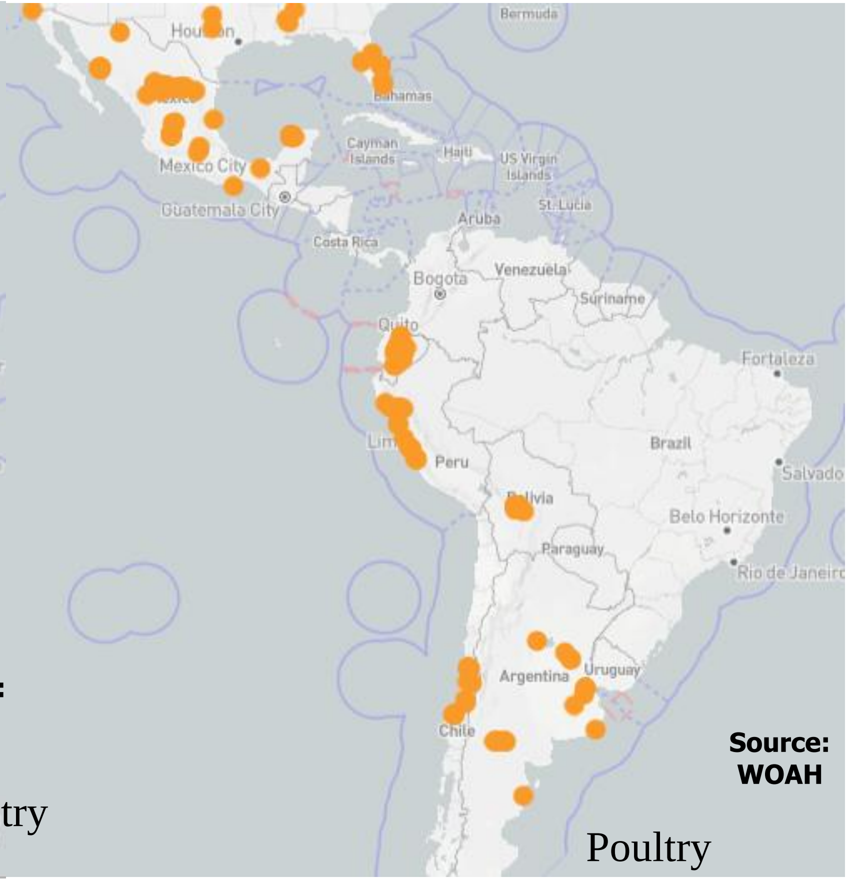
Wild Birds: Continuing detection (North America = 9229 cases; USA = 7093, Canada = 2136)

- **Raptors**
- **Dabbling ducks**
- **Geese**
- **Gulls**

https://en.wikipedia.org/wiki/Gadwall#/media/File:Gadwall-Anas-strepera.jpg

C. & S. America HPAI (1-1-2022 to 6-20-2023)

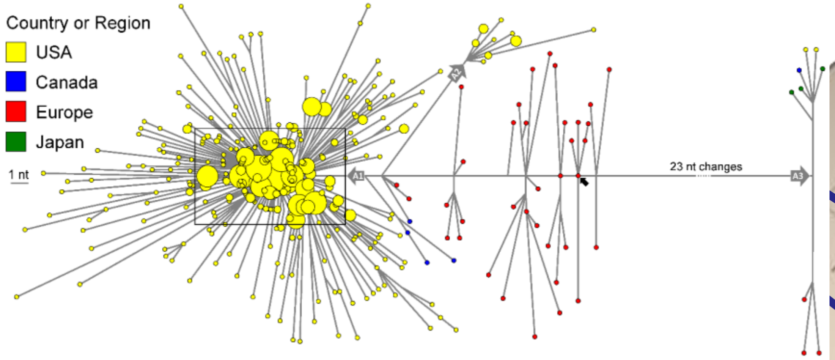
Wild and non-poultry domestic Birds



Poultry

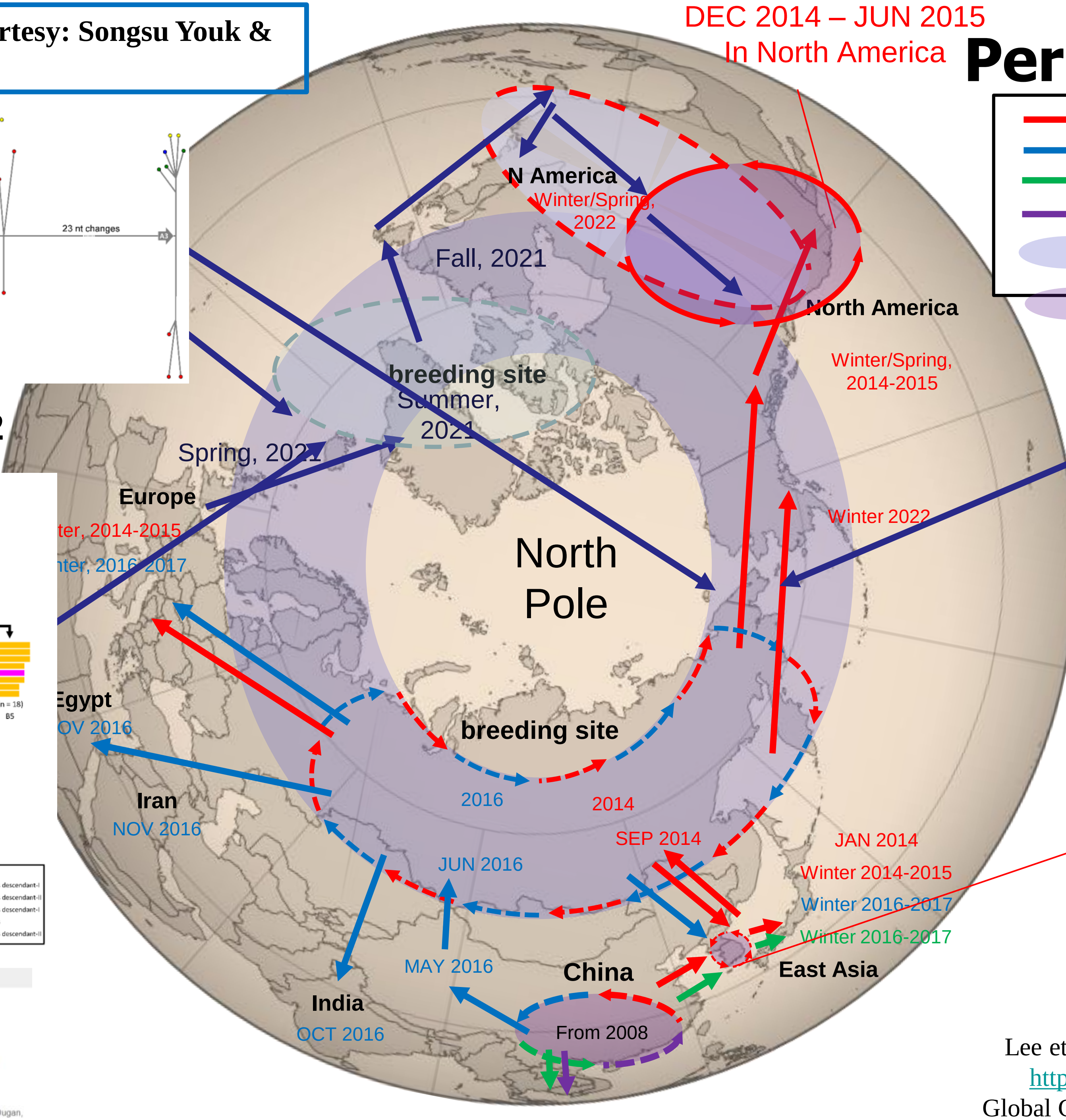
- **Wild bird cases wide geographic spread – most countries lack robust wild bird surveillance programs – major die-offs Peruvian pelicans, boobies and sea lions**
- **Backyard flocks are sentinels for environmental contamination**
- **Geographically restricted reports of HPAI in commercial poultry**

Phylogenetic Network Analysis Courtesy: Songsu Youk & Mary Pantin-Jackwood

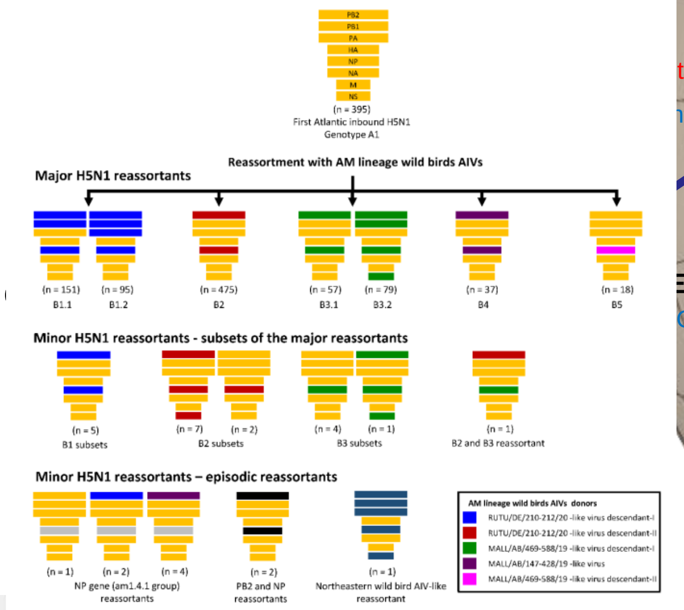


Peripolar Ecology

- Viral migration of 2.3.4.4c HPAI
- Viral migration of 2.3.4.4b HPAI
- Viral migration of 2.3.4.4d-f HPAI
- Viral migration of 2.3.4.4a HPAI
- Breeding site of migratory wild birds
- Virus circulation in poultry



3 introductions by April 2022



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RESEARCH ARTICLE

North Atlantic Migratory Bird Flyways Provide Routes for Intercontinental Movement of Avian Influenza Viruses

Robert J. Dusek, Gunnar T. Hallgrimsson, Hon S. Ip, Jón E. Jónsson, Srinand Sreevatsan, Sean W. Nashold, Joshua L. TeSlaa, Shinichiro Enomoto, Rebecca A. Halpin, Xudong Lin, Nadia Fedorova, Timothy B. Stockwell, Vivien G. Dugan, David E. Wentworth, Jeffrey S. Hall

JVI

Intercontinental Spread of Asian-Origin H5N8 to North America through Beringia by Migratory Birds

Dong-Hun Lee et al., 2015. J Virol 89:6521–6524.

Lee et al. J Vet Sci 2017, 18(S1), 269-280, 2017
https://doi.org/10.4142/jvs.2017.18.S1.269,
Global Consortium et al. Science 354:213-217, 2016

World Organization for Animal Health (WOAH)

- **WOAH Guidelines:**
  - Terrestrial Animal Health Code – chapter 10.4. Infection with High Pathogenicity Avian Influenza Viruses
  - Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2022 - Chapter 3.3.4. Avian influenza (including infection with high pathogenicity avian influenza viruses) (version adopted in May 2021)
- **Outcome- and risk-based provisions to control & prevent the spread of HPAI through international trade while avoiding unjustified restrictions**
- **Code contains specific considerations:**
  - For defining a country or zone free from HPAI
  - For considerations for the possible use of vaccination
  - For considerations for free compartments
  - For localization HPAI outbreak to a containment zone, and
  - Providing specific recommendations for the recovery of the free status of a country or zone after an outbreak

World Organisation for Animal Health
Founded as OIE

World Organization for Animal Health (WOAH)

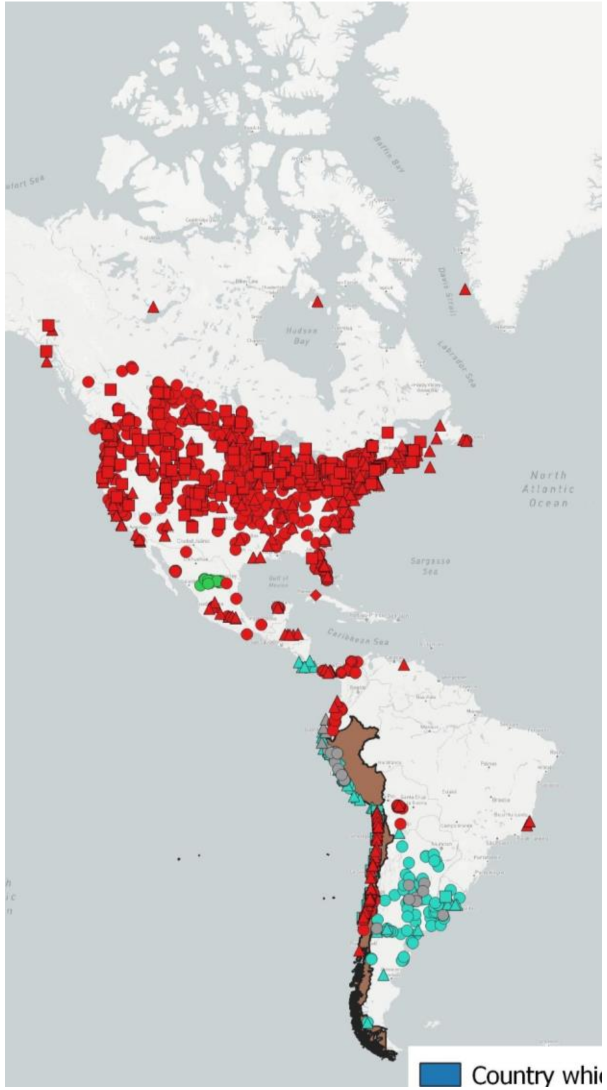
- **WOAH Code**
  - Specific provisions for the importation of various poultry commodities safely
  - Alternatives being provided according to the animal health status of the population at the origin
  - List of commodities considered safe irrespective of HPAI status of the exporting country or zone
  - Imply certain standard processing which would inactivate HPAI virus
  - Supports trade in vaccinated or non-vaccinated poultry in the presence of appropriate surveillance to demonstrate freedom from HPAI virus infection

General Control of HPAI

- Today: World Organization for Animal Health (WOAH) consensus for severe transboundary animal diseases (e.g. HPAI) is elimination and stamping-out has been the preferred strategy
- H5Nx Gs/GD Eurasian HPAI has challenged a single view-point and strategy
  - Many countries eliminated Gs/GD HPAI through stamping-out program, but some have had multiple re-introduction and elimination cycles (e.g. South Korea and Japan)
  - Other countries had delays in elimination associated with various reasons - limited veterinary services, restricted finances, delayed logistics, inadequate diagnostic systems, lack indemnities, etc., and the HPAI virus became entrenched in poultry
  - Some countries with entrenched HPAI have undertaken systematic vaccination for national food security needs without likelihood of elimination in immediate future (e.g. China, Egypt, Indonesia, Vietnam, Bangladesh)
  - Other countries have done targeted/ring emergency vaccination programs to limit the virus, in order to allow stamping-out programs to catch-up and have led to elimination in the mid-2000's (e.g. Coite d'Ivoire, Sudan)
  - Global re-examination of vaccination as a supplemental control tool

H5N1 Gs/GD Eurasian-lineage HPAIV: Vaccine in Americas

- **Control in the Americas – vaccination for H5N1 Eurasian lineage HPAI**
  - **Mexico and Guatemala: added emergency H5 Eurasian vaccines - ongoing vaccination with H5N2 LPAI and H7N3 HPAI N. American strains**
  - **Ecuador (14 million doses) and Bolivia (10 million doses): vaccination of long-lived poultry**
  - **Columbia: examining vaccination of egg-layers in high-risk areas**
  - **Peru: vaccinated egg layers and pullets (28M), light breeders (1.5M), heavy breeders (7.2M) and approved turkey breeders and meat turkeys**
  - **USA: approved vaccination of California Condors (testing in vultures in Rehab Center)**

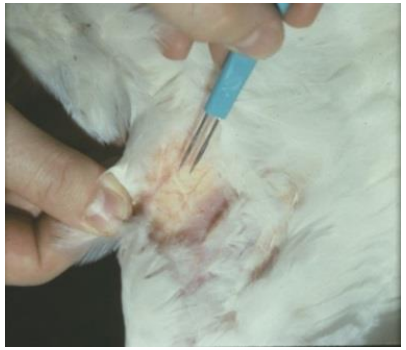


https://en.wikipedia.org/wiki/California_condor

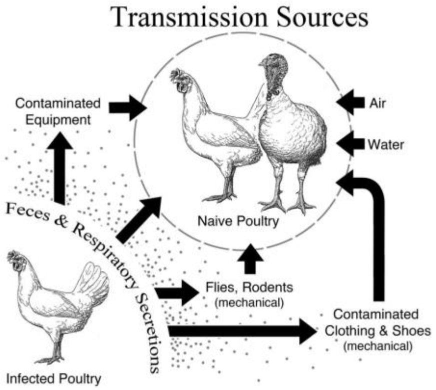
General Session Outcomes

Strategic Challenges in the Global Control of HPAI

- **Members maintain transparency through timely and comprehensive reporting of avian influenza events to WOAH**
- **Members respect and implement the adopted WOAH standards and recognise compliant zones and compartments of their trade partners**



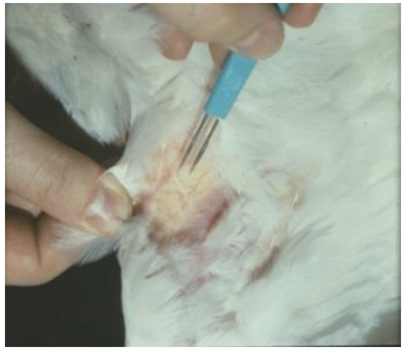
- **Members, conduct appropriate, risk-based, comprehensive and systematic monitoring and surveillance in domestic birds, wild birds (e.g., along flyways) and in other susceptible animal species to support early warning and risk management at the human–animal–environment interface.**
- **Members, in consultation with the poultry sector may consider the implementation of vaccination as a complementary disease control tool**
- **Members adopt vaccine best practices (stewardship) and reassess on an ongoing basis the use of appropriately field matched vaccine strains and the continuing need for update of vaccines**

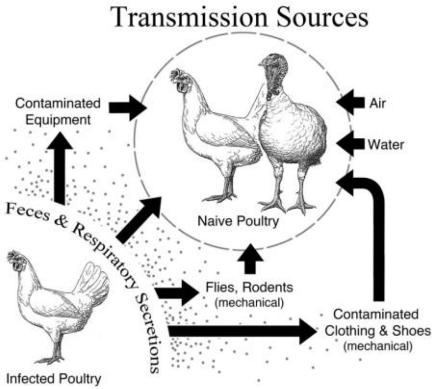


General Session Outcomes

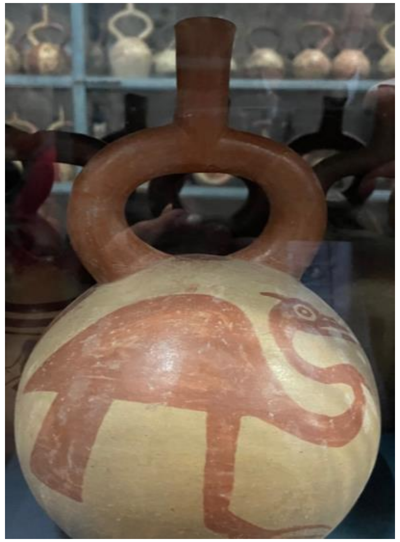
Strategic Challenges in the Global Control of HPAI

- **Members respect and implement the adopted WOAH standards and recognise compliant use of vaccination without negative consequences on trade: vaccination monitoring and disease surveillance**
- **WOAH provide up-to-date information on the genetic and antigenic characterisation of circulating virus strains, including comparison with existing vaccines, to infer levels of protection.**
- **Members ensure the use of authorised vaccines manufactured according to WOAH standards that are effective against circulating strains and regularly share information related to the effectiveness of the vaccination programme and their surveillance system to inform changes in vaccination strategies and policy**





Thank You for Your Attention!



Dr. Stephane Lemiere is a doctor in Veterinary Medicine recognized specialist in poultry pathology. Member of the American Association of Avian Pathologists, the French Branch of the World Veterinary Poultry Association, the World Poultry Science Association Course Master Broiler Chicken Production WVEPAH. Boehringer Ingelheim Global Head, Technical Services, Lyon, France Leading the Global Poultry Veterinary Technical Services group.

Boehringer Ingelheim

GLOBAL APPROACH FOR AVIAN INFLUENZA H5N1 VACCINATION

July 11th, 2023

Dr Stephane Lemiere

AVIAN INFLUENZA VACCINES

Experience of BOEHRINGER INGELHEIM since the years 1980:

1980s: AI vaccines full virus subtypes H6 & H9 for turkeys & broiler breeders in Italy

1996: AI vaccine full virus sub-type H7N3 Pakistan

1998: AI fowl pox vector vaccine platform vAIV-H5 (original insert, updated insert AIV-H5N2 Mex, AIV-H7N3 Mex)

1999: AI vaccines full virus sub-type H9N2 for Middle-east countries (maybe combined with ND)

2000s: AI vaccine full virus sub-type H5N9 for Europe & Asia

[2010s: AI 'reverse genetics' sub-type H5N1 for China, Africa & Asia / Re-1, Re-5, Re-6, Re-7, Re-8]

2015: B.E.S.T Baculovirus Expression System Technology AIV-H5 2.3.2-based optimized design cross-protective

2021 (on-going development): vHVT-IBD-IBD AIV-H5 hemagglutinin 'COBRA' (computationally optimized broadly reactive antigen)

AVIAN INFLUENZA H5 VACCINES – AVAILABLE VACCINES

In vivo presentation of the AIV-H5 antigen (s):

- **Full inactivated virus (original strain or reverse genetics) Vaccines**
- **Sub-Unit Vaccines**

In vivo expression of the AIV-H5 antigen – the hemagglutinin:

- **Viral Vectors**
- **RNA Vaccines**

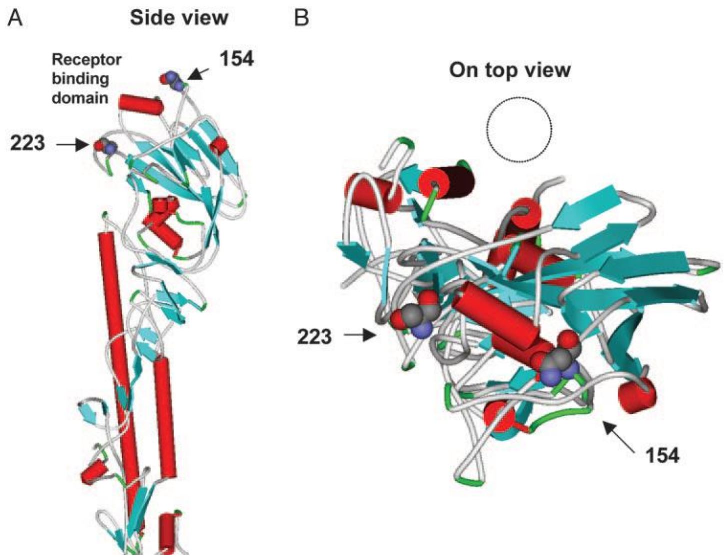
B.E.S.T. AI H5+ND – INACTIVATED SUB-UNIT VACCINE

Avian Influenza H5 Expression systems: for example Baculovirus (Baculovirus Expression System Technology B.E.S.T.)

Optimized HA genetic sequence to enhance immunogenicity & enlarge cross-clade clinical protection

DIVA: HA only expressed

→ anti-NP *ELISA antibodies detected post-infection*



S223N, S120N, S155N, +328K

HA from clade 2.3.2
A/duck/China/E319-2/03

B.E.S.T. AI H5+ND – INACTIVATED SUB-UNIT VACCINE

Group	Country of Origin of challenge virus	Species of Origin of challenge virus	Year of isolation	Virus Clade	Protection against mortality and clinical signs	Maximum shedding in days (Positives by PCR)
1	Mexico (H5N2)	Chicken	2004	0	100%	Not done
2	Vietnam	Duck	2005	2.3.2	100%	3
3	Spain	Chicken	2006	2.2	100%	4
4	Egypt	Chicken	2008	2.2.1.1**	90%	3
5	Egypt	Chicken	2010	2.2.1*	100%	Absent
6	Egypt	Chicken	2010	2.2.1.1**	80%	7
7	Egypt	Chicken	2012	2.2.1*	100%	7

* Also known as Clade A
** Also known as Clade B

AVIAN INFLUENZA H5N1 2.3.4.4b - PROJECTS

A/chicken/egypt/Elmenofia/AH14/2020

Phylogroup	Virus/aa Position (H5 Numbering) *	72	94	140	169	188	236	268	522	532
Vaccine strain	A/green-winged teal/Egypt/877/2016	R	S	T	R	T	N	E	V	V
	A/Duck/Egypt/Elbehera_AH2/2019	N	.	.	.	.	.	G	.	.
	A/chicken/Egypt/kafrelsheik_AH/2019	N	.	.	.	I	.	G	.	.
	A/chicken/Egypt/Alex_AH1/2020	N	.	.	.	I	.	G	A	.
Egypt-II	A/chicken/Egypt/Alex_AH/2020	N	.	.	.	I	.	G	A	M
	A/chicken/Egypt/Alex_AH2/2020	N	.	.	.	I	.	G	.	.
	A/chicken/Egypt/Elmonufia_AH/2020	S	R	.	Q	.	.	G	.	M
	A/turkey/Egypt/Cairo/AH/2019	S	R	.	Q	.	.	G	.	.
	A/turkey/Egypt/Alex_AH/2019	S	R	.	Q	.	.	G	.	.
	A/duck/Egypt/Behera_AH1/2019	S	R	.	Q	.	.	G	.	.
	A/chicken/Egypt/behera-AH/2021	.	.	A	Q	.	.	G	A	.
	A/chiken/Egypt/Alex-Breeder-AH/2021	.	.	A	Q	.	.	G	A	M
	A/chicken/Egypt/Giza-AH/2020	.	.	A	.	.	D	G	A	M
	A/chicken/Egypt/Elmonufia-backyard-AH/2019	.	.	A	.	.	D	G	A	M
	A/chicken/Egypt/qalyubia-layer-AH/2020	.	.	A	.	N	D	G	A	M
Egypt-III	A/chicken/Egypt/sohag-AH/2020	.	.	A	.	.	D	G	A	M
	A/chicken/Egypt/Assuit-AH/2019	.	.	A	.	.	D	G	A	M
	A/Duck/Egypt/Behera-HB2-AH/2020	.	.	A	.	.	D	G	A	M
	A/Chicken/Egypt/Giza-HG4L-AH/2020	.	.	.	.	.	D	G	A	M
	A/Chicken/Egypt/Cairo-HC11B-AH/20	.	.	A	.	.	D	G	A	M
	A/turkey/Egypt/Alex-AH1/2019	.	.	A	.	.	.	G	A	M

viruses MDPI

Communication

Isolation of Genetically Diverse H5N8 Avian Influenza Viruses in Poultry in Egypt, 2019–2021

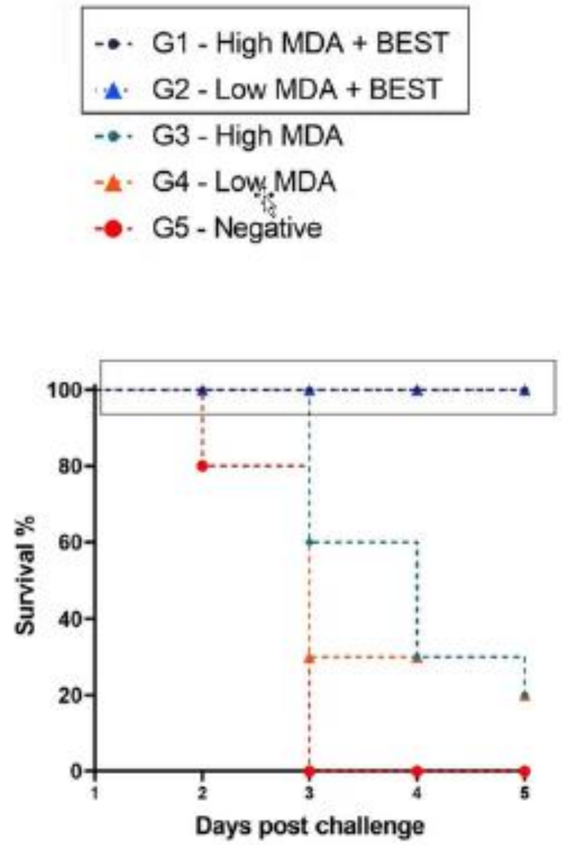
Ahmed H. Salaheldin [1,*], Ahmed R. Elbestawy [2], Abdelkader M. Abdelkader [3], Hesham A. Sultan [4], Awad A. Ibrahim [5], Hatem S. Abd El-Hamid [2,*] and Elsayed M. Abdelwhab [6,*]

AVIAN INFLUENZA H5N1 2.3.4.4b - PROJECTS

Type	Group	No	Administration of homologous chicken antiserum (MDA) (7 days)	Serology & Vaccination (10 days)	Serology & Challenge (31 days)	Tracheal and cloacal swabs	Serology (45 days)
Commercial broiler (Ross 308)	G1	15	High (12-14 HIU*)	+	Serology for all birds Challenge of 10 birds per group (IZSVe) (2 isol. A and B)	Daily (first 5 days) + days 7 and 10 p.i./p.c.	All survived birds (isol. A)
	G2	15	Low (6-7 HIU)	+			
	G3	15	High (12-14 HIU*)	-			
	G4	15	Low (6-7 HIU)	-			
	G5	15	Negative serum	-			

AVIAN INFLUENZA H5N1 2.3.4.4b - PROJECTS

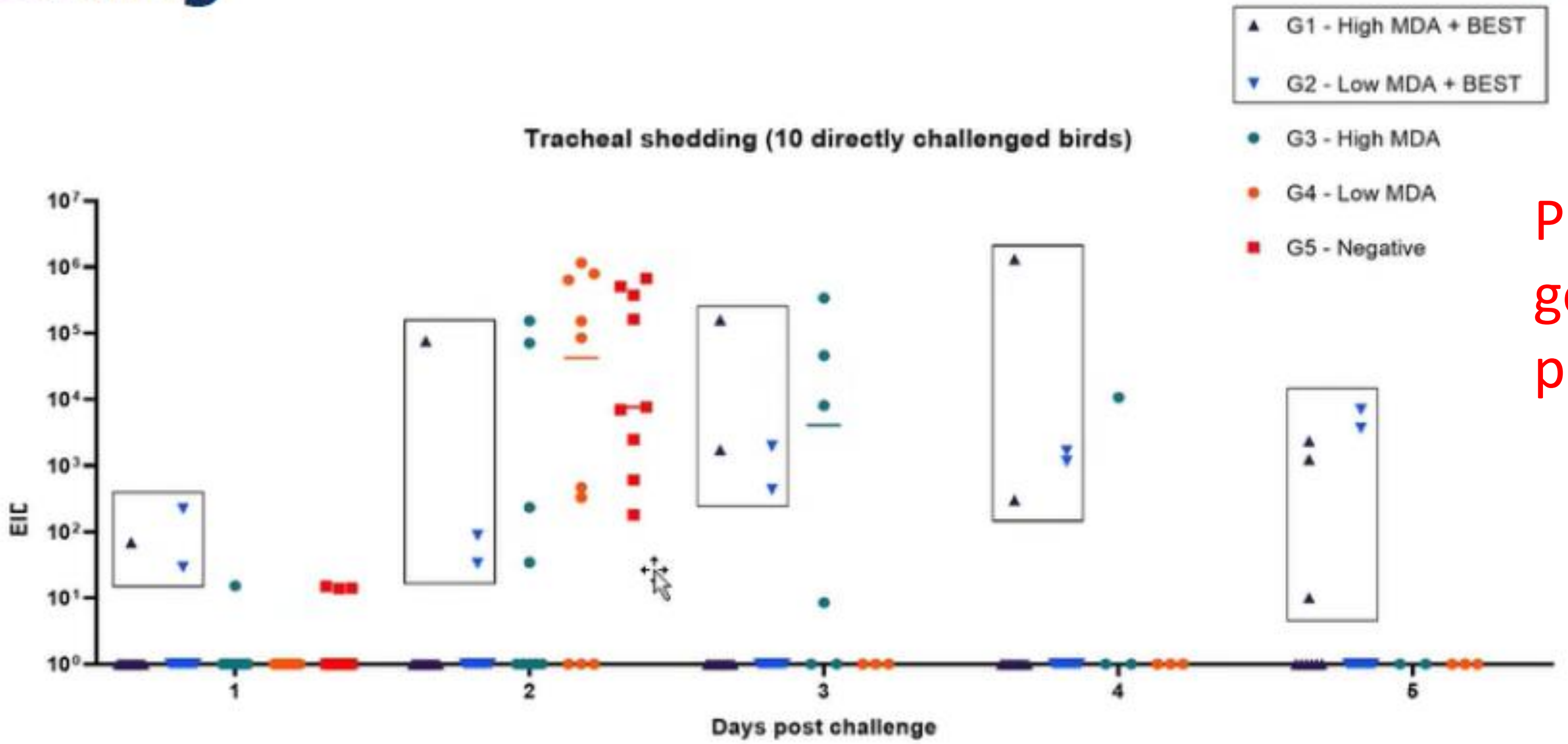
iProtection



Preliminary results – on-going analysis & data processing

AVIAN INFLUENZA H5N1 2.3.4.4b - PROJECTS

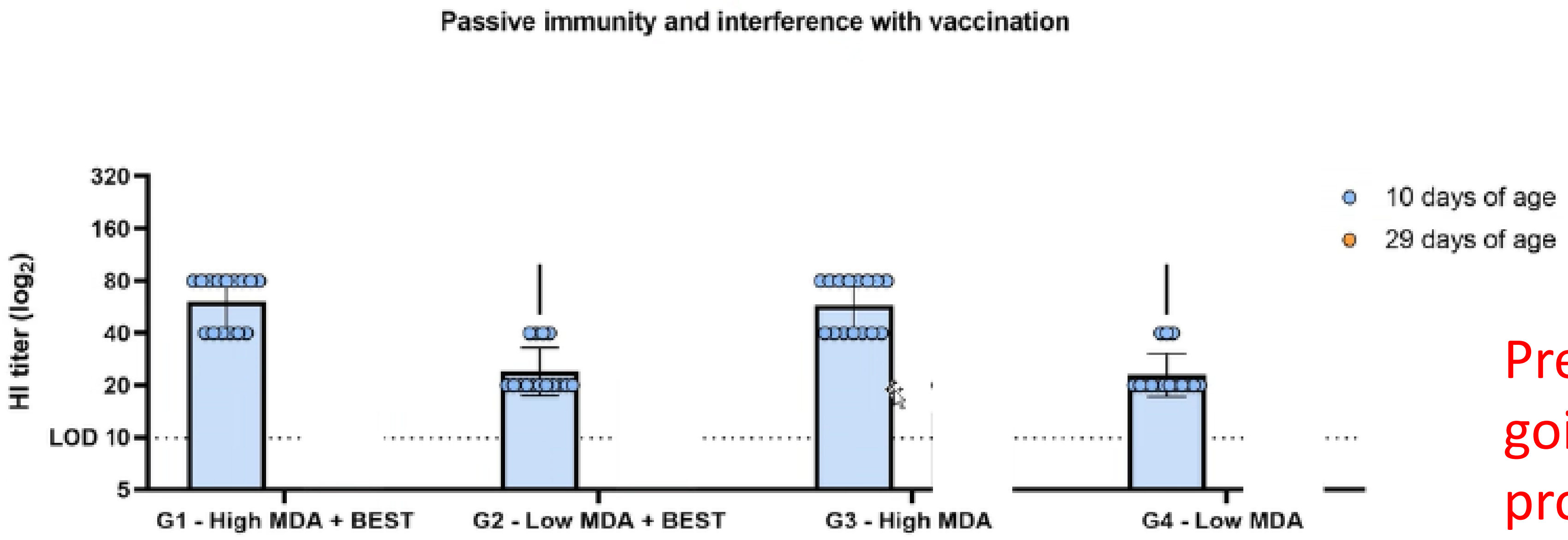
Shedding



Preliminary results – on-going analysis & data processing

AVIAN INFLUENZA H5N1 2.3.4.4b - PROJECTS

Serology (HI Volvac BEST Ag)



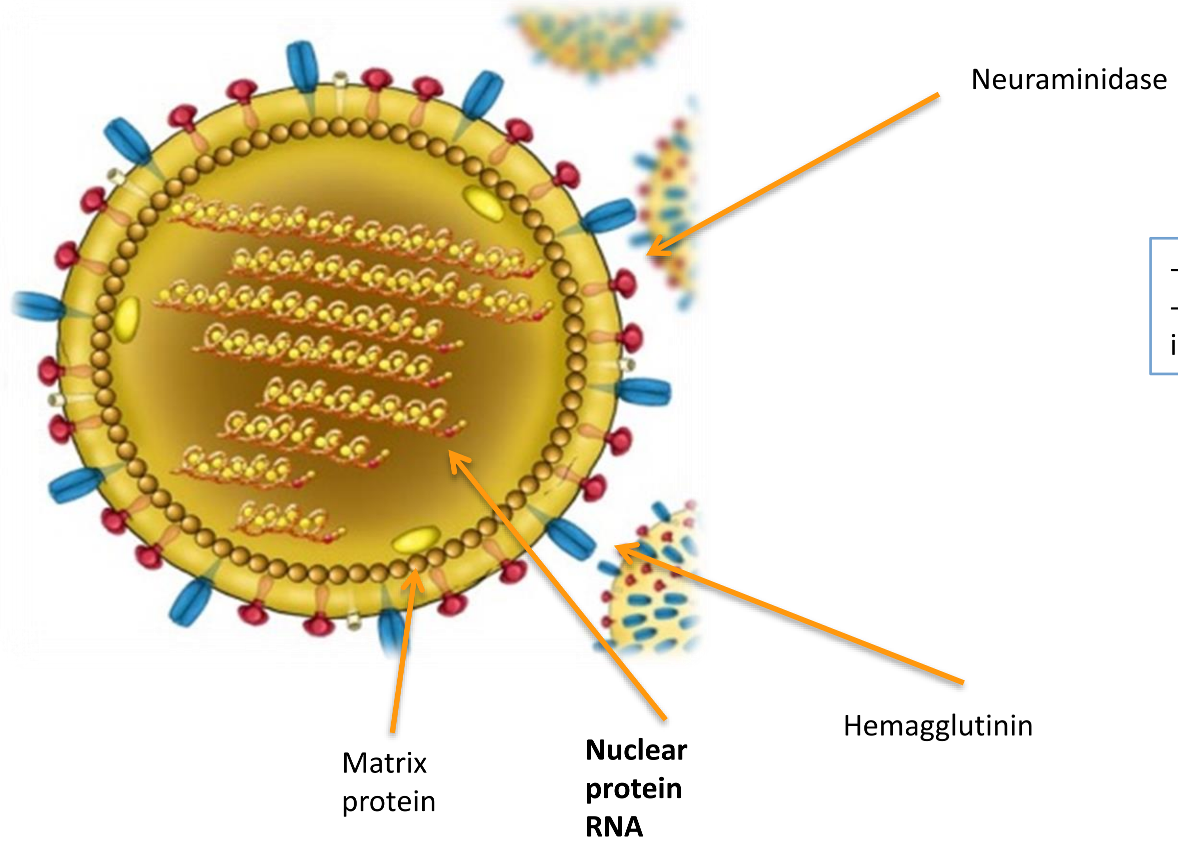
Preliminary results – on-going analysis & data processing

HI titers against the vaccine homologous antigen, at 10 days of age.

Boehringer Ingelheim

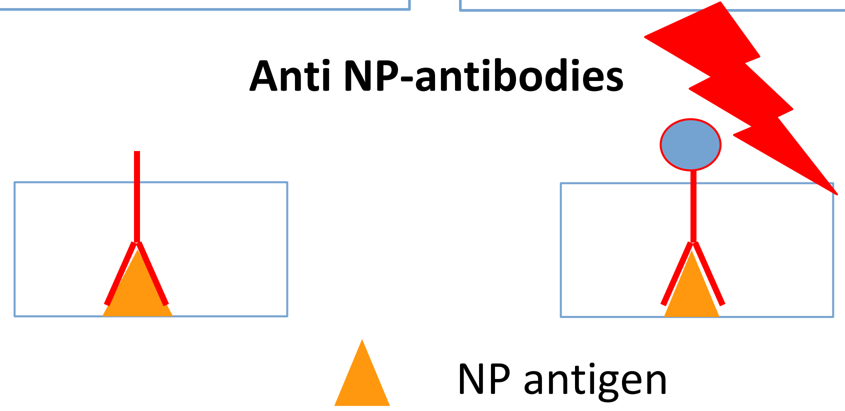
B.E.S.T. AI H5+ND – INACTIVATED SUB-UNIT VACCINE

DETECTION OF VACCINATED AND SUBSEQUENTLY INFECTED ANIMALS (DIVA-APPROACH)



- Only infected
- Vaccinated with only HA and infected

- Not infected
- Vaccinated with HA and not infected



[Mundt, 2012, Encyclopedia of Molecular Mechanism of Disease]

B.E.S.T. AI H5+ND – INACTIVATED SUB-UNIT VACCINE

Age	Gp1	Gp2	Gp3	Gp4
Zero day	9.00±0.00	9.00±0.00	9.00±0.00	9.00±0.00
First week	7.37±0.52	7.37±0.52	7.37±0.52	7.37±0.52
Second week	3.75±0.46[c]	3.87±0.64b[c]	3.87±0.83[bc]	3.75±0.46[c]
Third week	1.50±0.53[c]	5.50±0.53[a]	5.50±0.53[a]	5.50±0.53[a]
Fourth week	0.62±0.52[d]	7.00±0.53[b]	7.00±0.00[ab]	7.50±0.53[a]
Fifth week	0.40±0.35[e]	8.50±0.53[b]	8.50±0.53[b]	10.00±0.53[a]
Sixth week	0.25±0.46[d]	9.50±0.53[b]	9.50±0.53[b]	10.50±0.53[a]
Seven week	0.00±0.00[d]	8.37±0.52[b]	8.25±0.46[b]	10.50±0.53[a]
Eight week	0.00±0.00[e]	7.37±0.52[c]	7.25±0.71[c]	10.00±0.76[a]
Nine week	0.00±0.00[e]	6.37±0.52[d]	7.75±0.46[c]	9.62±0.52[a]
Ten week	0.00±0.00[d]	6.12±0.83[c]	8.75±0.89[a]	9.00±0.53[a]
Eleven week	0.00±0.00[d]	5.25±0.89[c]	9.00±0.93[ab]	8.00±0.76[b]
Twelve week	0.00±0.00[d]	5.25±0.71[c]	9.25±0.89[a]	7.50±0.76[b]
Thirteen week	0.00±0.00[d]	4.75±0.46[c]	9.50±0.53[a]	7.50±0.76[b]
Fourteen week	0.00±0.00[d]	3.62±1.07[c]	10.12±0.83[a]	7.00±0.53[b]
Fifteen week	0.00±0.00[d]	3.00±1.06[c]	10.00±0.76[a]	6.50±0.76[b]
Sixteen week	0.00±0.00[d]	2.37±0.52[c]	9.75±0.89[a]	6.37±0.52[b]

*HI mean titers ($\log_2 \pm$ SD) using 4 HA units of the AI H5N2 Ag (A/Chicken/Mexico/232/94 /CPA)

Different superscript letters (a, b, c, d or e) in the same raw indicate a significant difference between the value of the geometric mean titers at the same time point with a ($P \leq 0.05$)

Group 1 (did not receive any AIV vaccine), group 2 (received only one injection of Baculo-H5 prototype vaccine at 8 days of age), group 3 (received two injections of Baculo-H5 prototype vaccine at 8 and 53 days of age), group 4 (received two injections of Baculo-H5 prototype vaccine at 8 and 18 days of age),

Veterinary Research Communications
https://doi.org/10.1007/s11259-018-9717-1

ORIGINAL ARTICLE

CrossMark

Effectiveness of different avian influenza (H5) vaccination regimens in layer chickens on the humoral immune response and interferon-alpha signalling immune marker

Mustafa Hamad[1] · Omar Amen[1] · Mohamed Mahmoud[1] · Ola Hassanin[2] · Mostafa Saif-Edin[1]

Received: 2 December 2017 / Accepted: 9 March 2018

Highest level of seroconversion with the 2-vaccination regimen 8-53D > than 8-18D > than 8D alone

B.E.S.T. AI H5+ND – INACTIVATED SUB-UNIT VACCINE

Current challenge = AIV-H5 clade 2.3.4.4b

Proven clinical protection

Proven reduction of AIV-H5 virus shedding

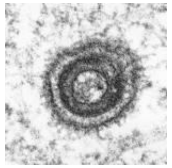
Continuous support with on-going updates on cross-protections (currently Egyptian strain checked for protection)

Continuous effort on serological monitoring systems – AIV-H5 B.E.S.T antigen, NP & AIV-H5 ELISAs (id-vet)

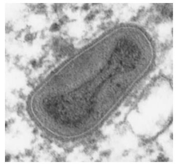
AVIAN INFLUENZA H5 VACCINES – VECTOR VACCINES

4 used vectors:

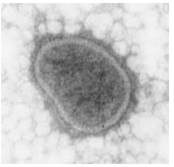
Fowlpox (not for ducks)



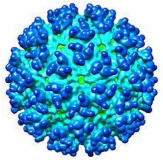
HVT (not for ducks)



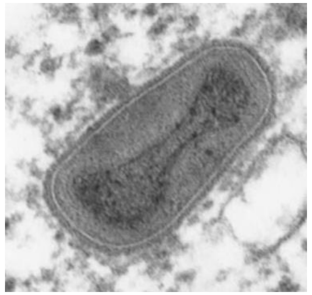
~~**NDV**~~



RNA Replicon



AVIAN INFLUENZA H5 VACCINES – FOWLPOX VECTORS



Vaccine application:

- Hatchery: sub-cutaneous route

In vivo replication pattern:

- 1-2 weeks → **quick onset**
- skin → **systemic immunity**

Interferences:

- **Maternal antibodies**: mostly the **anti-insert** antibodies

  …but no inhibition of the **priming effect**

AVIAN INFLUENZA H5 VACCINES – HVT VECTORS

Administration: **hatchery** (SC or *in ovo*)

Established safety for HVT

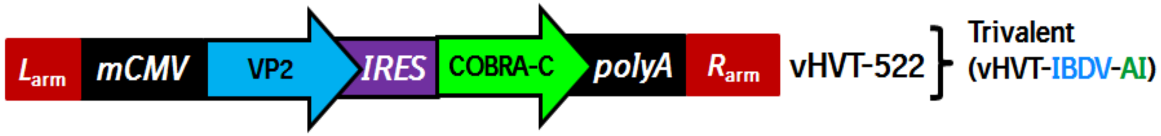
Replication pattern:

- Persistent → **long lasting** immunity
- Lymphocytes & skin tropism → **systemic** immunity

Interferences:

- **other HVTs**

HVT-IBD-AIV-H5 (INNOVATION ONGOING PROJECT)



Based on Mortality, Shedding and hemagglutination assays, *COBRA-C* (between A,B & C candiadtes) was selected as best H5 antigen

VAXXITEK HVT+IBD+AIV-H5

Recombinant HVT with COBRA-C was designed in trivalent context, either as **HVT-AI-IBD** (or HVT-AI-ND not developed) and bivalent HVT-AI

Protection against mortality (100%) demonstrated by challenge:

- Tk/MN/15 Clade 2.3.4.4a
- Tk/Hungary/16 clade 2.3.4.4b
- Egypt/14 clade 2.2.1

Protection against shedding:

- All candidates were able to decrease at least 2 logs compared to shams (for 2dpc)

Based on comparison of **overall distance** (% identity) of isolates tested in the challenge study and sequences from the current outbreaks (clade 2.3.4.4b) the candidate is expected to protect birds

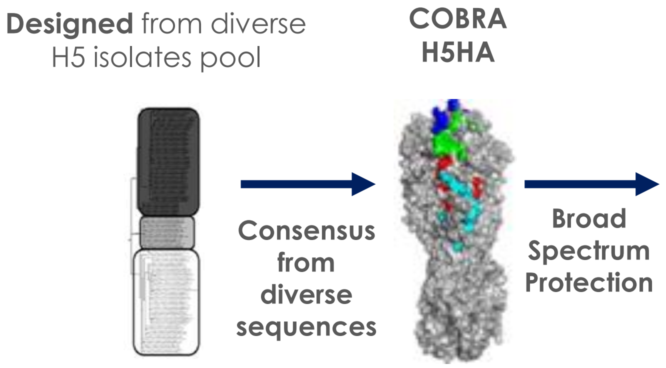
HVT-IBD-AIV-H5 (INNOVATION ONGOING PROJECT)

Computationally Optimized Broadly Reactive Antigen

A computationally optimized H5 HA sequence, termed COBRA, where the polybasic cleavage sites of H5 sequence was modified to low pathogenic (LP) type

(*Bertran K, Kassa A, Criado MF, Nuñez IA, Lee D-H, Killmaster L, et al. Efficacy of recombinant Marek's disease virus vectored vaccines with computationally optimized broadly reactive antigen (COBRA) hemagglutinin insert against genetically diverse H5 high pathogenicity avian influenza viruses. Vaccine 2021;39] https://doi.org/10.1016/j.vaccine.2021.02.075*)

COBRA H5 HA was inserted into the backbone of a commercially licensed vaccine HVT-IBD, VAXXITEX – DOUBLE INSERT PLATFORM



Broad Spectrum Protection
Against a variety of clades of isolates

Virus		Clade	
A/Vietnam/1203/2004		1	★
A/chicken/Vietnam/NCVD-016/2008		7.1	
A/IN/05/05		2.1.3	★
A/Whooper Swan/244/2005		2.2	★
A/Egypt/N03072/2010		2.2.1	★
A/Egypt/321/2007		2.2.2	★
A/Anhui/01/2005		2.3.4	
A/Hubei/1/2010		2.3.2.1a	★
A/Guizhou/1/2013		2.3.4.2	★
A/Sichuan/26221/2014 (H5N6)	★	2.3.4.4	
A/gyrfalcon/Washington/41088-6/2014 (H5N8)	★	2.3.4.4	
A/chicken/Egypt/CAL3-RLQP/2017	★	2.2.1.2	★
A/duck/Egypt/S78-RLQP/2017 (H5N8)		2.3.4.4	★

★ 509 (Cobra-C)
★ 510 (H5N2wt)

AVIAN INFLUENZA H5 VACCINES – PRIME-BOOST

« Prime »

Hatchery

« Boost »

Field

→Homogeneous & wide immunity

Swayne *et al.* (1997) Avian Dis. 41, 910-22 ; Swayne *et al.* (2000) Vaccine 18, 1088-95 ; Swayne *et al.* (2000) Vet. Microbiol. 74, 165-72 ; Bublot *et al.* (2007) Avian Dis. 51, 498-500 ; Bublot *et al.* (2010) Avian Dis. 54, 257-61 ; Eggert *et al.* (2010) Vaccine 28, 4609-15 ; Richard-Mazet *et al.* (2014) Vet Res, 45: 107

AVIAN INFLUENZA H5N1 2.3.4.4b - PROJECTS

Netherlands - GD Deventer & Lelystad Institute: Vectored HVT+IBD+AIV-H5 lab study in SPF chicks. Clinical protection shown against H5N1 2.3.4.4b. Check on vaccination plans in of chickens – long live birds, such as layer pullets

Italy - Istituto Zooprofilattico Sperimentale delle Venezie (IZSVe), Padua: IZSVe is going to check with the Italian Ministry of Health on the possibility to import some doses of the vaccine from the US. On-going test with a recent Egyptian isolate, 2.3.4.4b. Recent protection data of clinical protection, protection against shedding & DIVA seroconversion on-going. Test in turkeys on-going with B.E.S.T AIV-H5 & Vectored HVT+IBD+AIV-H5

France - ANSES: on-going test in the field in ducks with B.E.S.T AIV-H5. Ducks challenged with the 2022 challenge strain. Clinical protection proven against challenge - DIVA seroconversion proven with HI test & id-vet ELISA

Mexico – SENASA: selection of B.E.S.T AIV-H5 for control of AIV-H5 2.3.4.4b outbreaks

Algeria – launch of B.E.S.T. AIV-H5 in November 2022

Use of B.E.S.T. AIV-H5 as the reference vaccine in **Egypt, Kazakhstan, Jordan,** etc.

AVIAN INFLUENZA H5N1 2.3.4.4b – BI OPTIONS

VAXXITEK PLATFORM - HVT-IBD-AIV-H5 (C.O.B.R.A technology): Option for hatchery priming & broilers vaccination program in enzootic countries

AVIAN INFLUENZA H5N1 2.3.4.4b – BI OPTIONS

B.E.S.T SUB-UNIT H5 INACTIVATED PLATFORM - AIV-H5 (+ND): Option for long-live bird vaccination programs & broiler vaccination programs in enzootic countries

THANK YOU!

Boehringer Ingelheim GmbH

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Question and Answer

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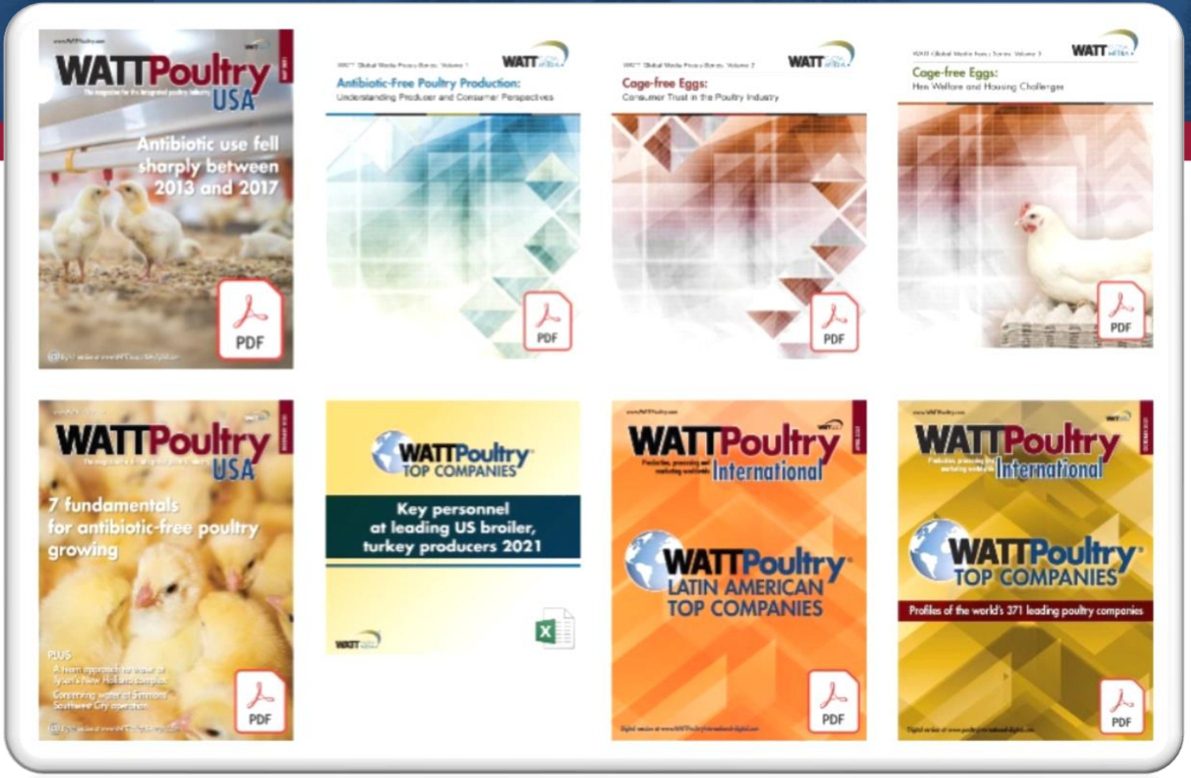
birdfluvet@gmail.com

Dr. Stephane Lemiere

Stephane.LEMIERE@boehringer-ingelheim.com

Thank you for attending!

How can you grow **<u>your success</u>** in the agrifood industry with exclusive industry knowledge?



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