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# Avian Influenza: Strategies for Prevention & Control

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**Singapore**



# Outlines

- Introduction
- Virus Biology & AIV Current Status
- Epidemiology & Transmission
- Disease, Pathology & Diagnosis
- Control & Prevention Strategies
- Human Infections
- Epilogue



# Asian Top 5 Poultry Health Issues

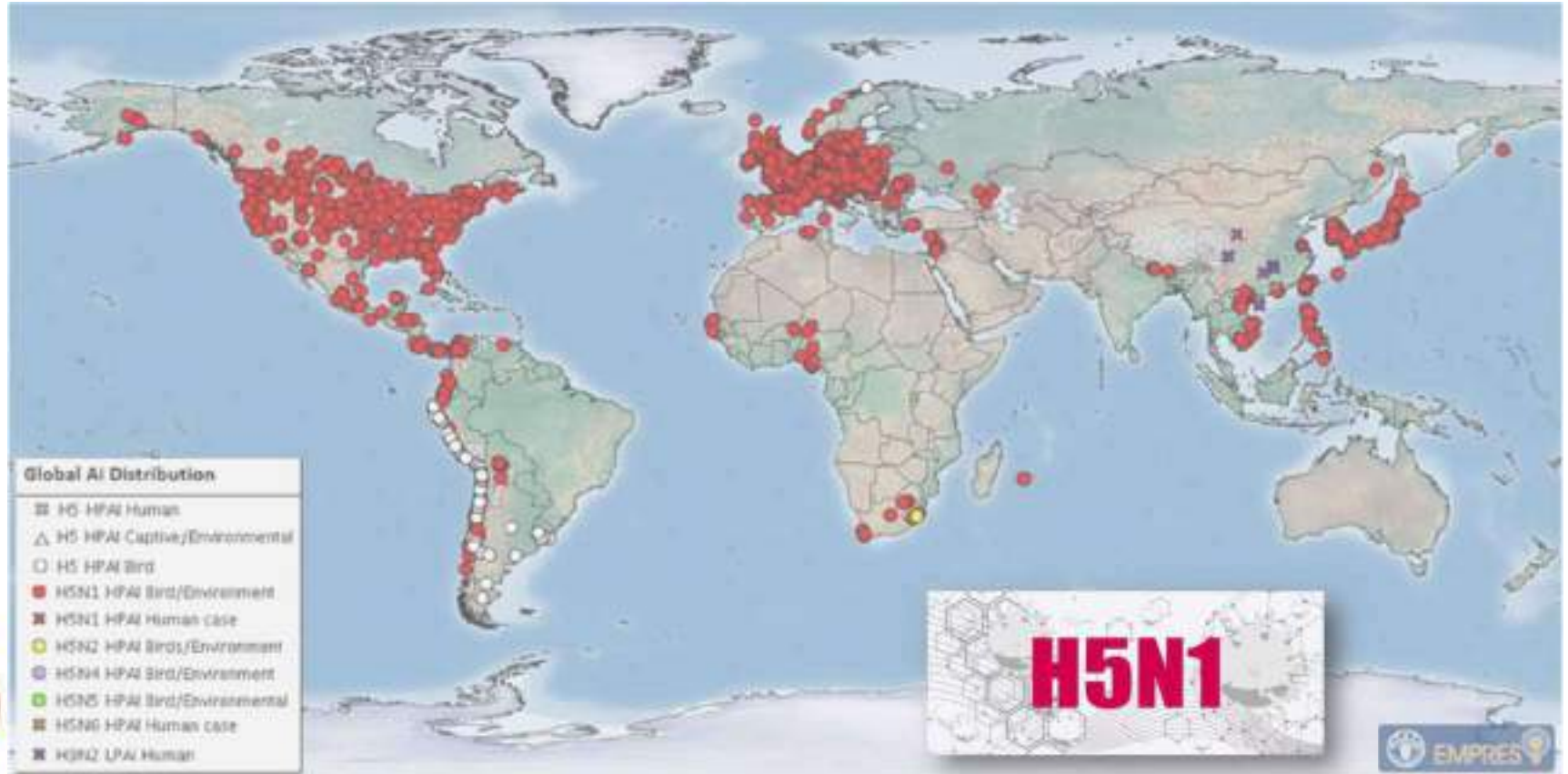
Ranking	Malaysia	Philippines	Thailand	Japan	China	Korea	Vietnam	India	Indonesia
1	ND	AI (H5)	ND	AI (H5)	AI (H7)	AI (H5)	AI (H5)	ABR & Removal	Gut Health
2	IB	ABR & Removal	ABR & Removal	ABR & Removal	Salmon	IB	ND	AI (H9)	AI (H9)
3	Salmon	ND	IB	FAdV	IB	EYP	IB	MG	ND
4	MG	MG	Salmon	Breast muscle myopathy	MG/MS	Salmon	NE/GD	Salmon	NE/GD
5	FAdv	Gut Health	APV	APV	RSS	Cocci	Gut Health	Gut Health	IB



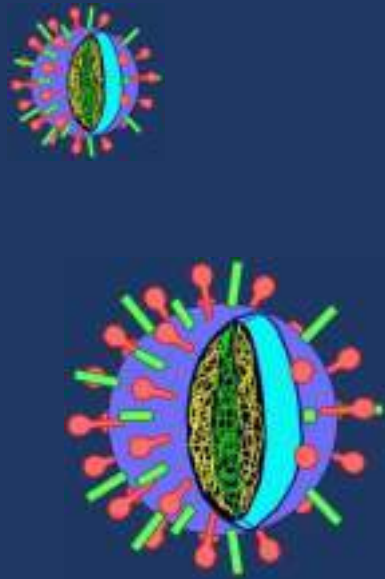
**ABR** = Antibiotic Resistance, **NE** = Necrotic enteritis, **GD** = Gangrenous dermatitis, **EYP** = Egg Yolk Peritonitis, **Salmon** = Salmonellosis, **ND** = Newcastle disease, **AI** = Avian Influenza, **IB** = Infectious bronchitis, **MG/MS** = Mycoplasma, **FAdV** = Fowl adenovirus, **APV** = Avian metapneumovirus

Data Source/references: Breeding Companies, OIE, Industry Veterinarians

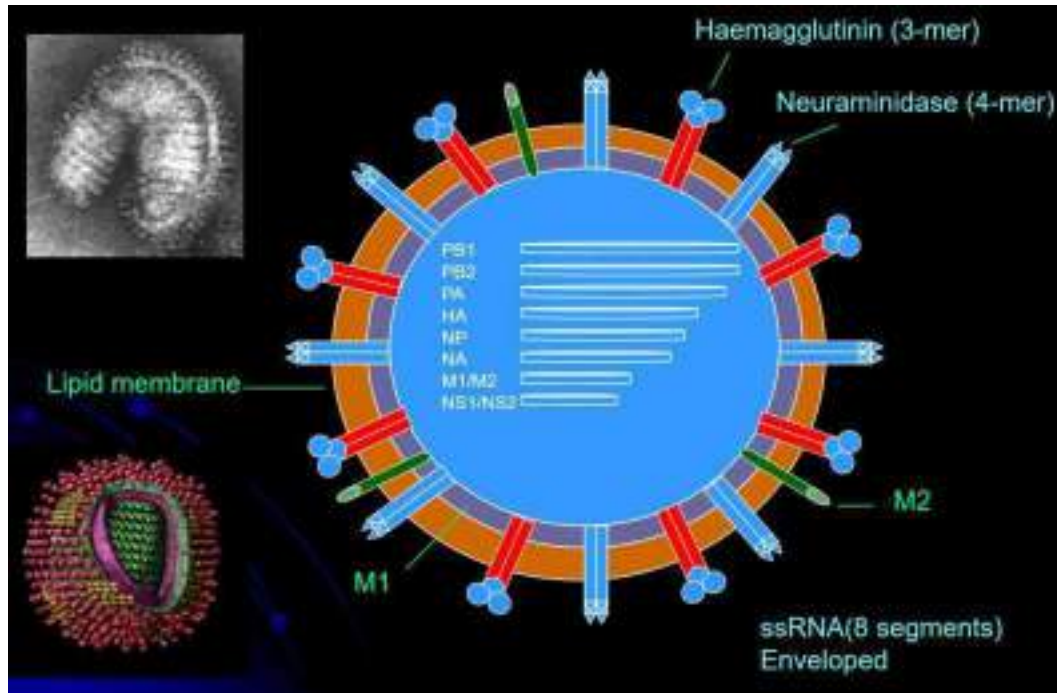
# Global AI Situation: January 2022 – March 2023



# Virus Biology & AIV Status



# Avian Influenza Viruses

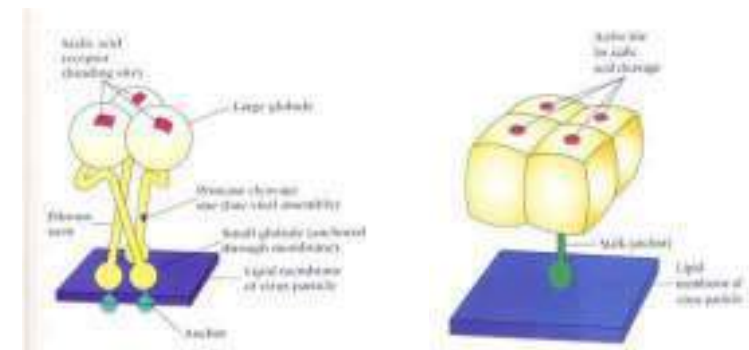


**Surface Antigen Subtype**

Haemagglutinin:		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Human		•	•	•												
Equine				•												
Swine		•		•												
Avian		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
																H16 (17 + 18)

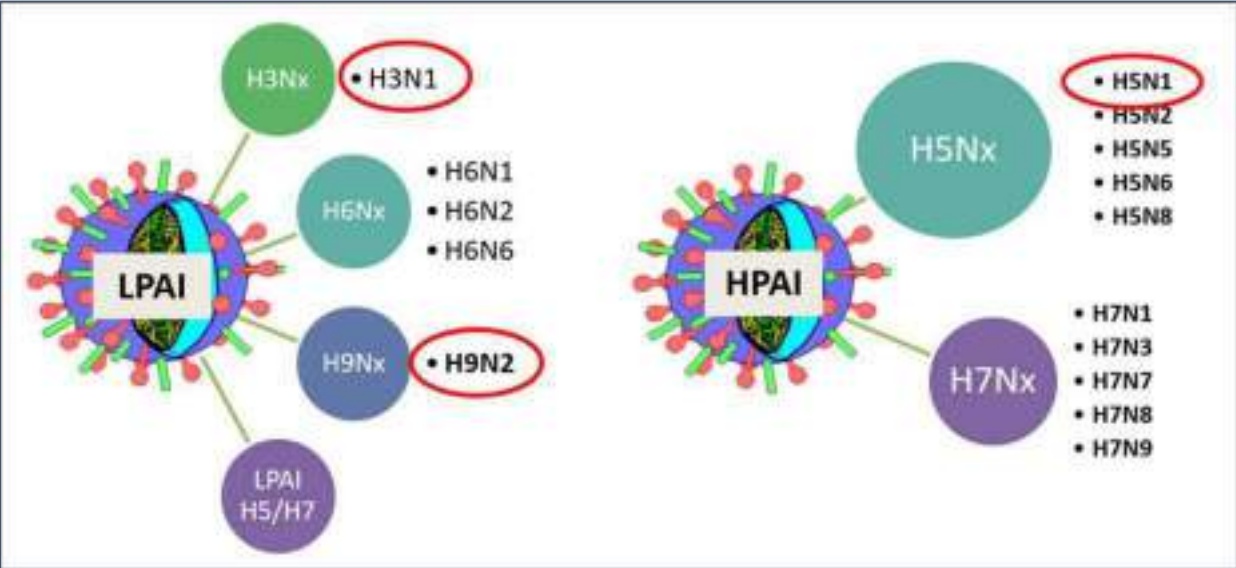
  






Neuraminidase:		1	2	3	4	5	6	7	8	9
Human		•	•							
Equine							•	•		
Swine		•								
Avian		•	•	•	•	•	•	•	•	•



- Potentially there is possible Combination from H and N = 144
- H and N are important in virus entry & exit from the host cell & interaction between virus & host cells

# Important Avian Influenza Viruses



Virus	H5N1	H7N9	H9N2
Host & sialic acid			
	Mild Moderate	Mild	Mild
	Severe	Mild	Mild Moderate
	Moderate	Mild	Mild
	Severe	Moderate Severe	Mild Moderate
	Severe	Severe	Mild Moderate



# AIV Pathotypes & Virus Pathogenicity

## Two Pathotypes of Influenza A in poultry

### Low Pathogenicity

- Mild respiratory disease, depression, egg production problems
- May exacerbate other infections/conditions
- Not in OIE list A disease

### Highly Pathogenicity

- Severe disease
- High mortality up to 100%
- To date only [but not all] viruses of H5 or H7 subtype
- OIE List A disease

### Disease Severity

Localized, -subclinical

Generalized, fatal

### Virus Pathogenicity

Low

High (H5, H7)

## Pathogenicity of AI virus

Replication at point of entry (target receptor)

**LP Strains**  
 HA only cleaved by selected Endoprotease (Trypsin)

**HP Strains**  
 HA cleaved by ubiquitous Endoprotease (Furin, PC6 etc.)

Respiratory / Intestinal Replication

Viremia

Few basic amino acid (B-X-X-R)

Multiple basic amino acid (B-X-B-R)

Systemic Infection



# HPAI Asia Situation

- Currently H5N1 Clade 2.3.4.4b Viruses dominate Globally (> 77 countries)
- Domestic bird outbreaks: not reported from endemic countries



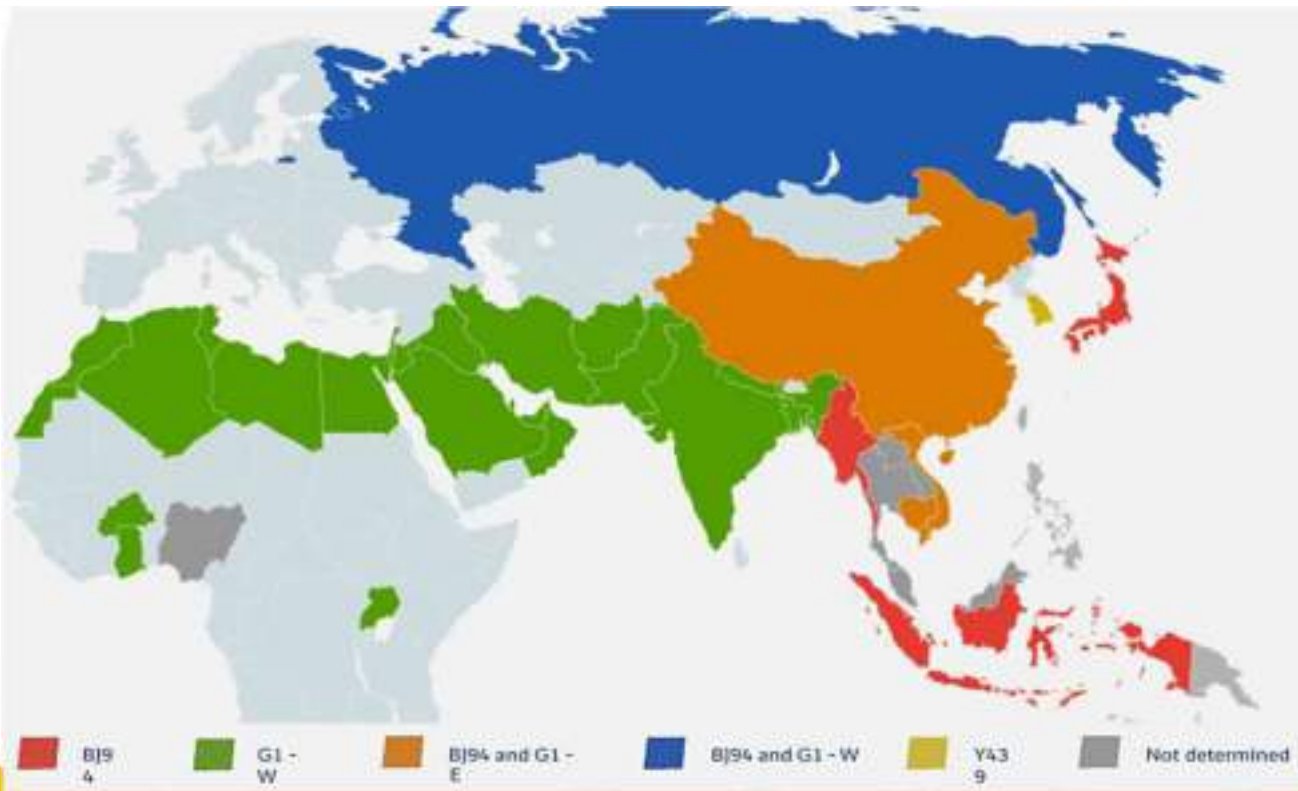
Australia	H7N9, H7N8, H7N3
China	H7N9
South Africa,	H7N6
Mexico	H7N3
Germany	H7N5
Mozambique	H7 (N untyped)

Munir Iqbal (2024)



# Global AI (H9N2) Status

- AI subtype **H9N2** is endemic in many bird species in Asia & the Middle East. Virus has occasionally crossing species barrier to mammals including human beings.
- H9 subtype viruses are **NOT Notifiable** to **OIE**: possible under-reporting on actual field situations.



## Three stable HA lineages:

### ❖ G1-W

- Group A
- Group B
- Group C
- Group D

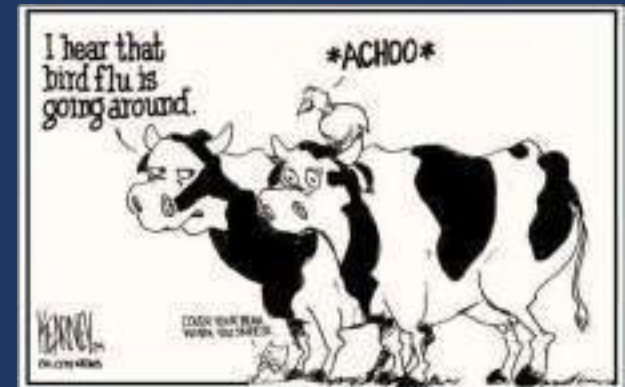
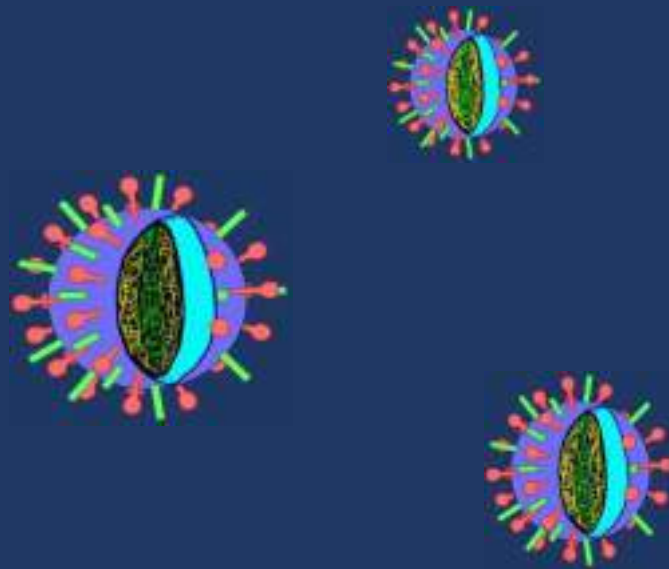
### ❖ Beijing (BJ94/Y280)

### ❖ Korean-like (Y439)

### ❖ Few studies on Antigenicity

Peacock *et al.*, *Viruses* (2019)

# Epidemiology & Transmission



# Avian Influenza Virus : The Hosts

AIV can infect a variety of Domestic & Wild Avian Species (including chickens, turkeys, ducks, domestic geese, quail, pheasants, psittacines, gulls, shorebirds, emu & others). The clinical manifestation of infection ranges from asymptomatic infection to rapidly fatal disease

Aquatic birds, particularly Ducks, Shore Birds & considered the Natural Reservoirs  
These waterfowl generally do not develop disease when infected with AI viruses. Recently, investigators in Asia have shown that asymptomatically infected domestic ducks are shedding more H5N1 to domestic poultry (references: FAO/OIE/WHO 2004)

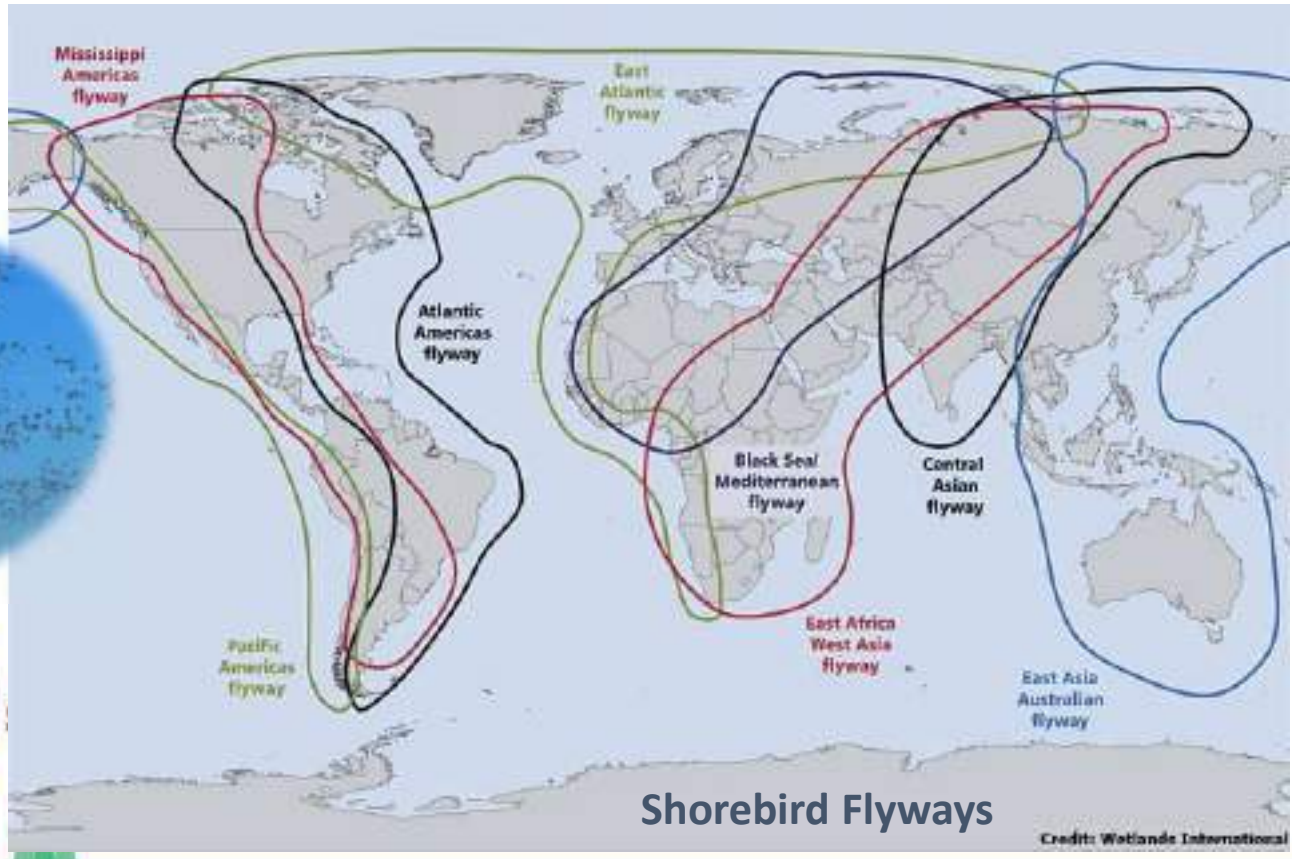


# Influenza A viruses have been isolated from Free-living birds of the following Families

- Very Diverse
- Very Diverse
- High prevalence of infection on a global basis



# Recent Evidences support the Theory that H5N1 being Spread by Migrating Wild Fowls



## The Eastern Asia Flyway



## (East Asia/Australia Flyway)

## The Indo-Asian Flyway



## (Central Asia Flyway)

# AIV Virus Transmission

- Routes of bird-to-bird transmission include :
  - Airborne transmission if birds are in close proximity
  - Direct contact with contaminated respiratory secretions or fecal material
- Vertical transmission is not known to occur (possible cross contamination in hatchery)
- Other factors (spread within & between flocks) :
  - Broken contaminated eggs in incubators infecting healthy chicks
  - Movement of infected birds between flock. Movement of fomites e.g. contaminated equipment, egg flats, feed trucks, clothing & shoes of employee
  - Contact with infected wild birds & waterfowl
  - Fecal contamination of drinking water
  - Garbage flies

How are the virus transmitted & maintained in these species ?



Transmission: Fecal / Oral route

Heavy fecal shedding by infected ducks  
Long term persistence in water  
Isolation of AIVs from surface water

Maintenance: Bird to bird

Persistence in environment

**Peri-domestic Species: The ones most likely in contact with poultry**



• Occasional isolations of AIV from starlings & house sparrows (in contact with infected poultry)

• Replication of some AIVs in these species (experimental)

• Infection - sometimes

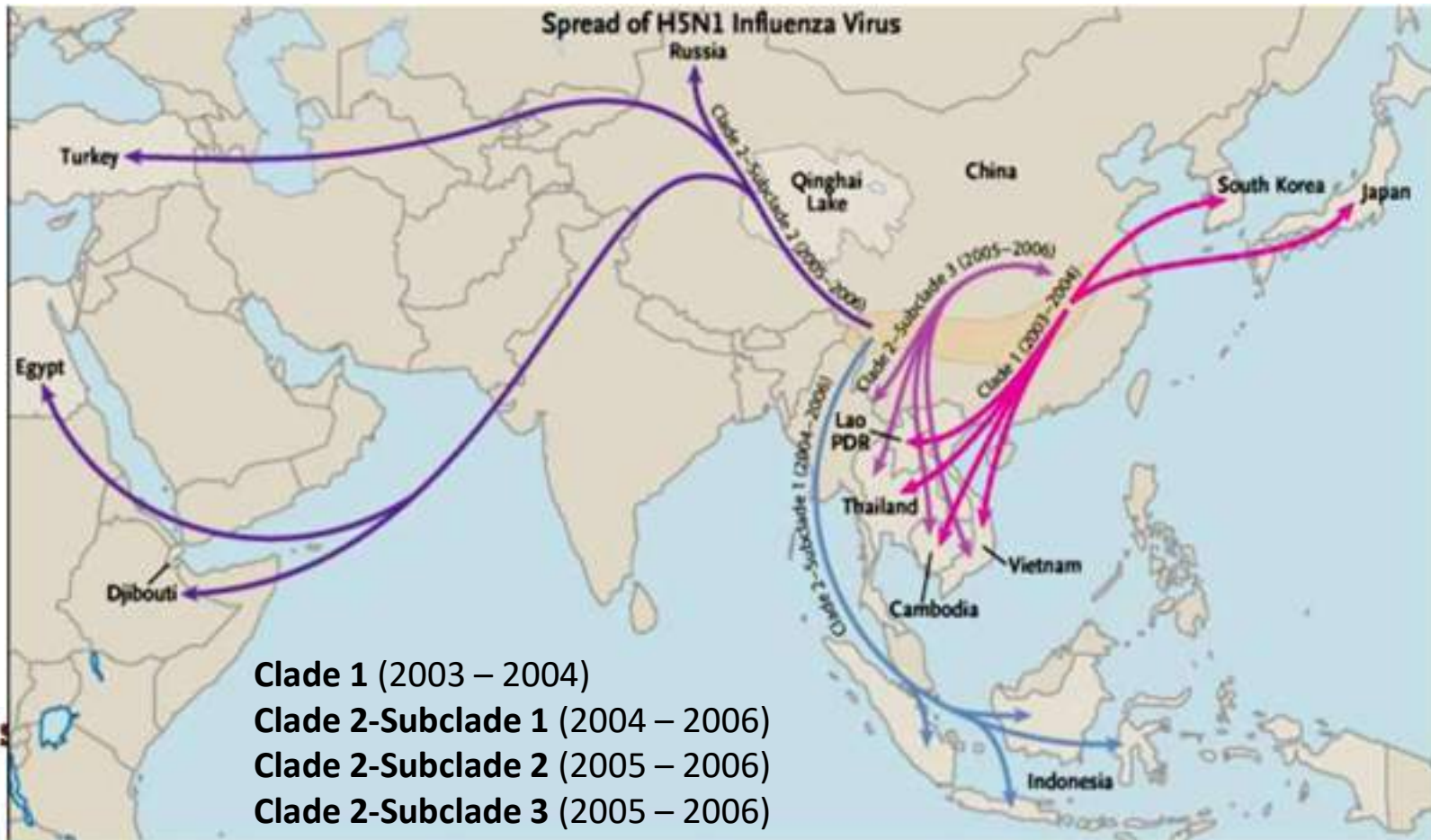
• Reservoir - unlikely

# AIV in Commercial Ducks

- Alexander (1982) reported a 53% isolation rate from pools of cloacal swabs taken from ducks at slaughter
- Shortridge (1982) reported a 6% isolation rate from individual ducks in Hong Kong
- WHO (2005) reported 76% ducks & 21% chicken tested positive for H5N1 in Mekong Delta, South Vietnam



# Early Spread of HPAI (H5N1) in Asia



# Epidemiology of 2024 H5N1 Avian Influenza Outbreaks

- During winter of 2020-2021, a new genotype of highly-pathogenic H5N1 avian influenza A virus emerged in Europe, comprising a (reassortant between the epizootic HP clade 2.3.4.4b H5N8 & local LP wildfowl strains).
- This new genotype caused record levels of infections in farmed poultry throughout Europe and quickly traveled, via waterfowl flyways, into North America, Africa and East Asia
- In following seasons, this panzootic genotype underwent further reassortment with local LP avian strains from waterfowl or seabirds - in Europe, North America & beyond; generating a diverse range of genotypes. One of these North American reassortant genotypes then entered South America and most recently, Antarctica



# Recent Spread of H5N<sub>x</sub> (Gs/GD Euroasian lineage) HPAI Virus (2.3.4.4b Clade)

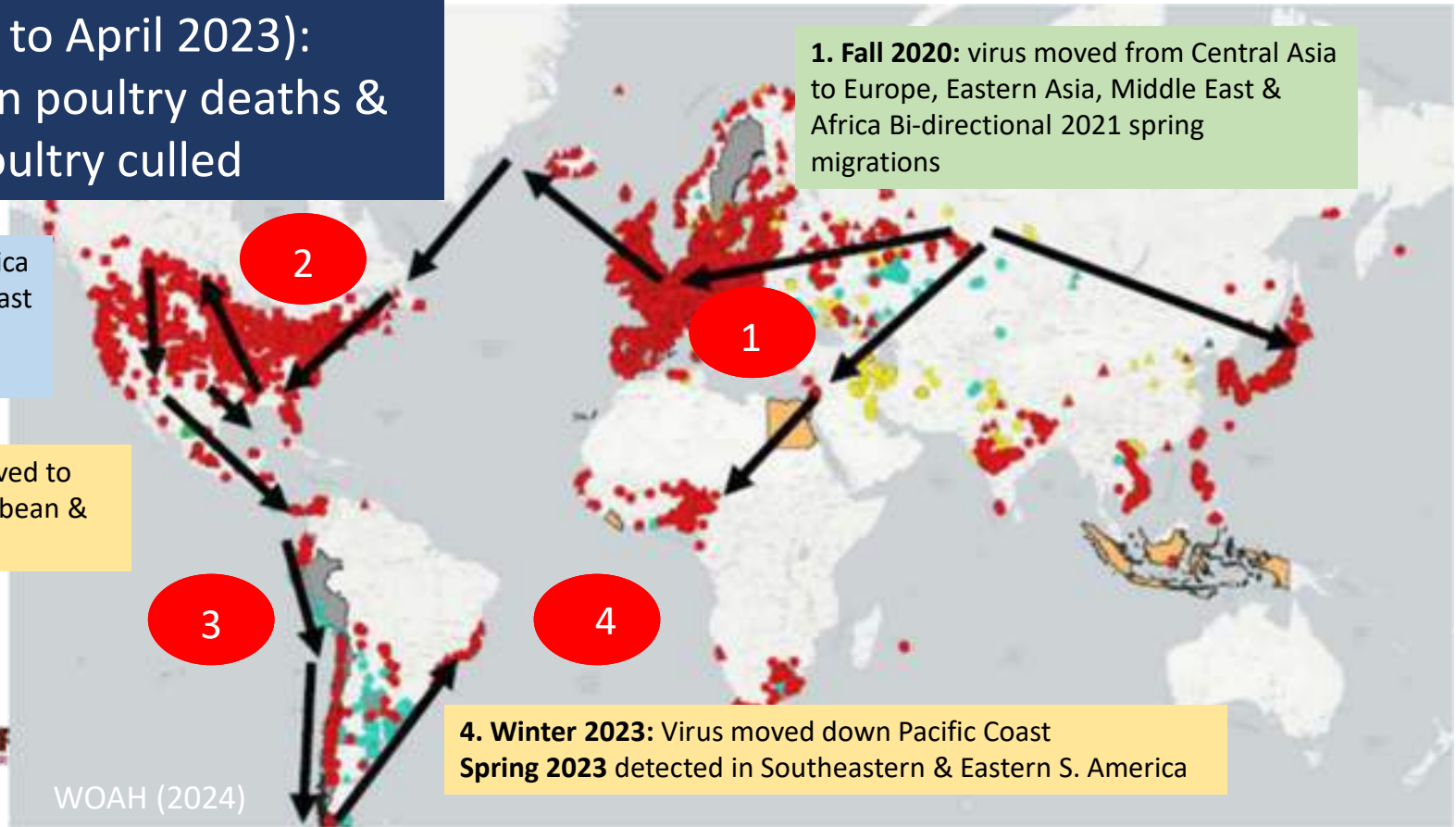
Global (July 2020 to April 2023):  
 7515 cases, 14 million poultry deaths &  
 254 million poultry culled

- 2. Fall 2021:** Virus moved to N. America
- Winter 2022 move down East Coast
  - Spring 2022 Northward
  - Late Summer 2022 Southward

**3. Fall 2022:** Virus moved to Central America, Carribean & Northern S. America

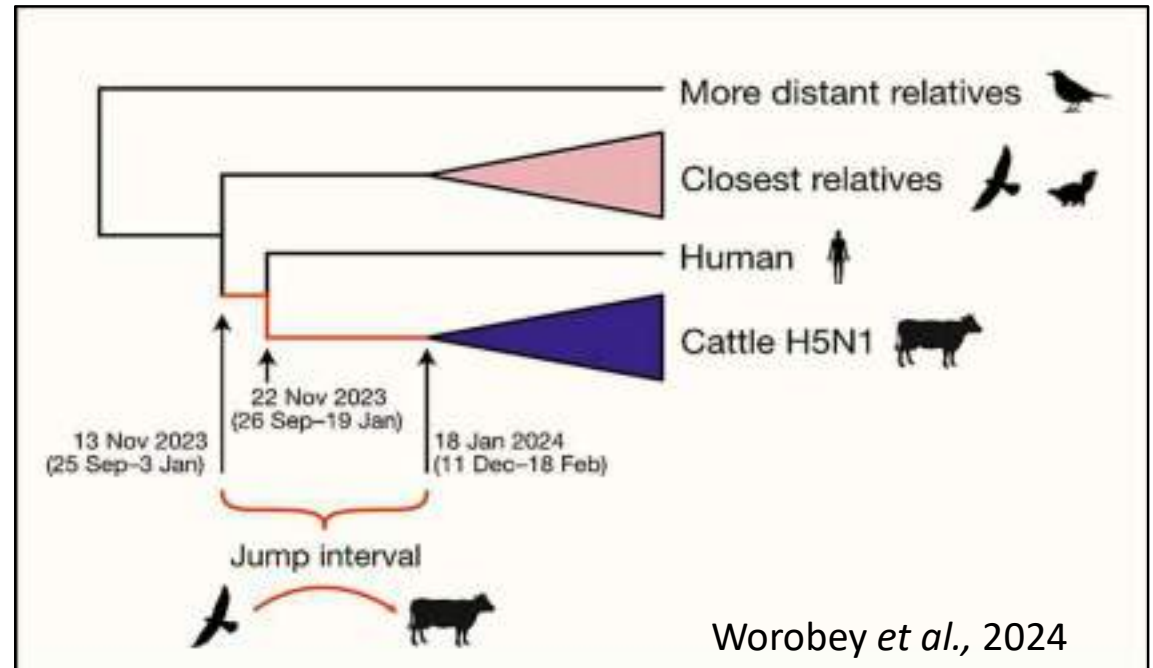
**4. Winter 2023:** Virus moved down Pacific Coast  
 Spring 2023 detected in Southeastern & Eastern S. America

**1. Fall 2020:** virus moved from Central Asia to Europe, Eastern Asia, Middle East & Africa Bi-directional 2021 spring migrations



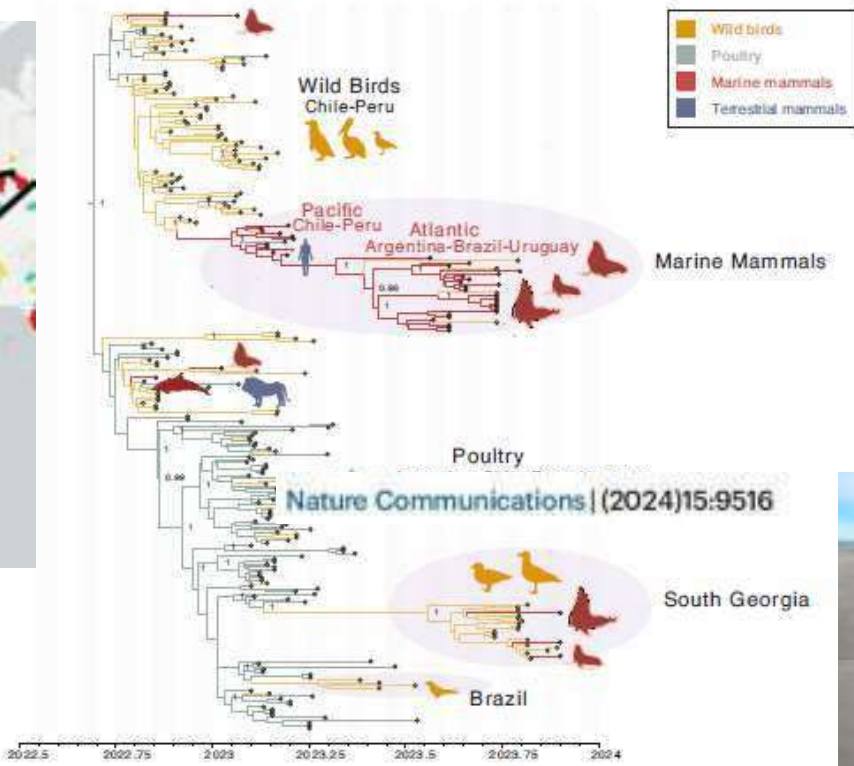
# Spillover of HPAI H5N1 virus to Dairy Cattle

## Cow Flu: H5N1 Clade 2.3.4.4b (2024)



Schematic depicting the phylogenetic relationships between the HA segment of the viral genomes in different host species & when H5N1 likely spilled over into cattle

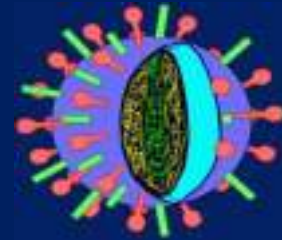
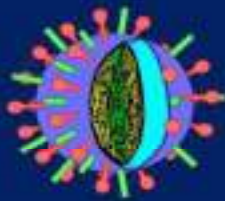
# Virus Expansion to Marine Animals



Uhart *et al.*, Nature Communications (2024)



# Pathology & Diagnosis



# Highly Pathogenic Avian Influenza (HPAI)

## Clinical Signs:

Sudden, high mortality (up to 100%)

## Other Signs:

cessation of egg-laying, respiratory, excessive lacrimation, oedema of head, subcutaneous haemorrhage. Diarrhoea, neurological signs.



# HPAI: Clinical Signs & Pathology



HPAI: Clinical & pathological signs

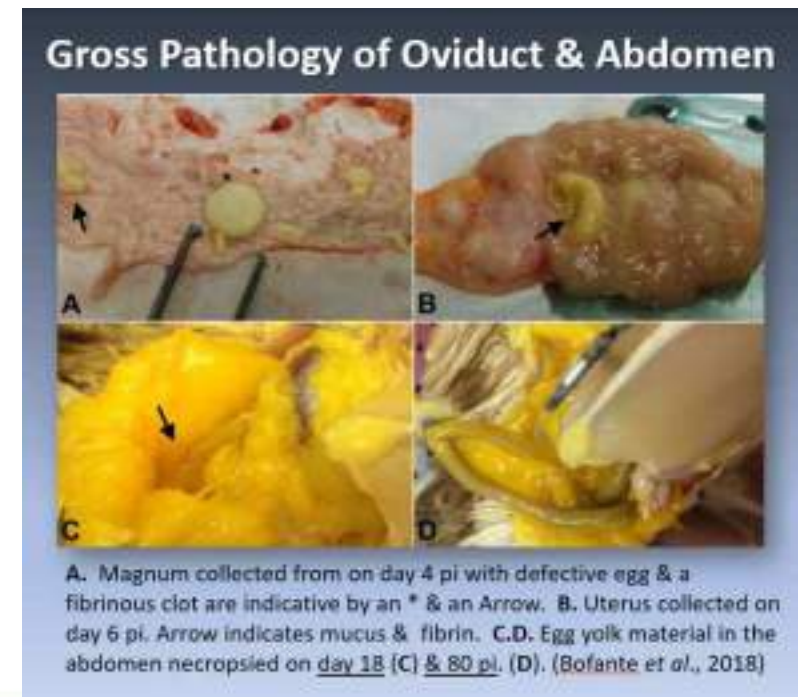
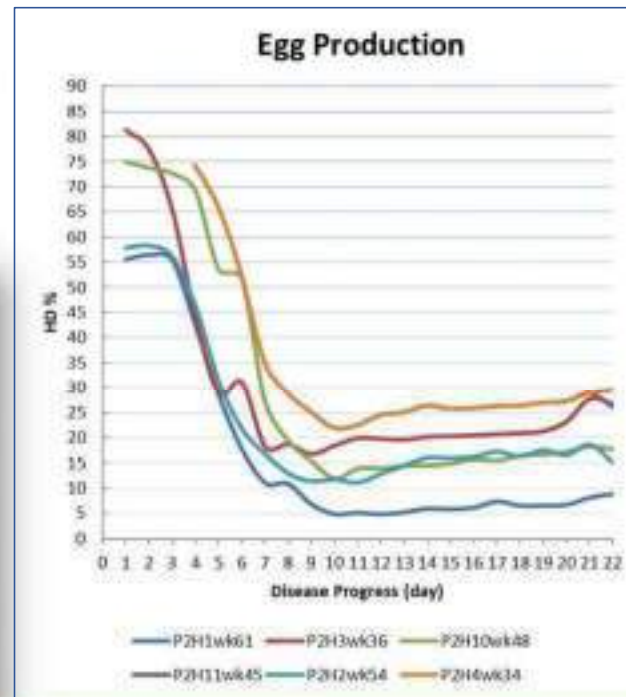


# HPAI: Clinical Signs & Pathology

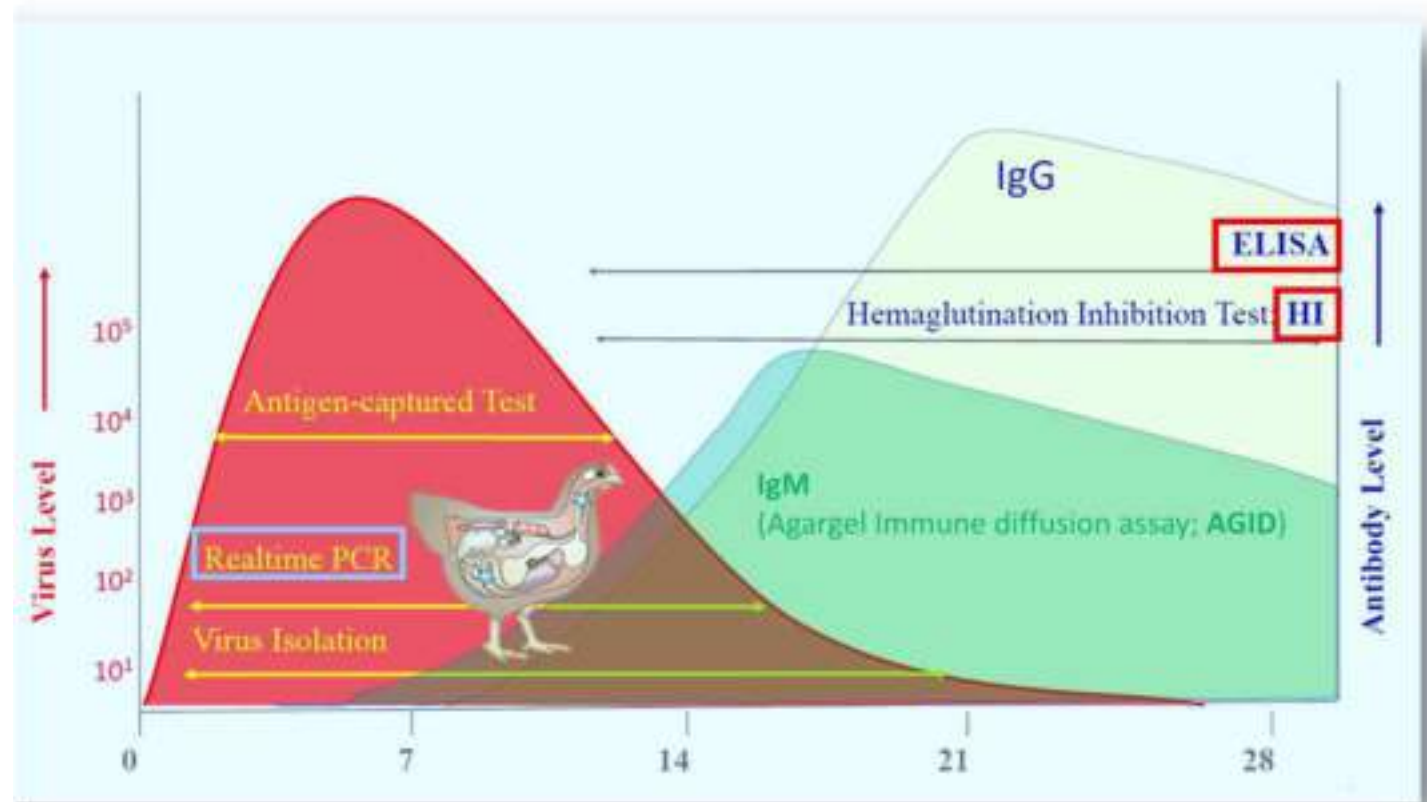
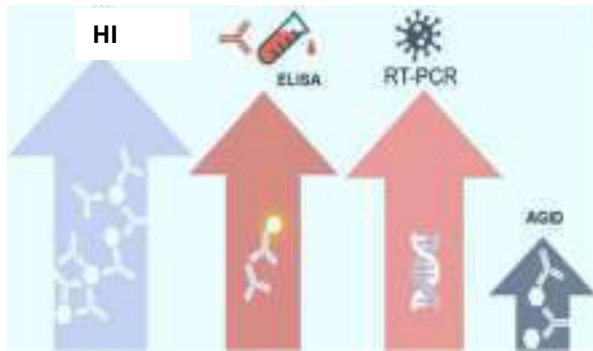


# LPAI H9N2 in Poultry

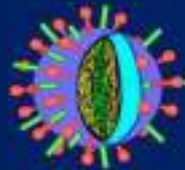
- Virus is spread & disseminated via air sacs & serosal route to oviduct.
- Course of infection: loss of appetite, reduced feed intake & egg production drop (transient yolk follicle atresia, acute necrotic inflammation of oviduct: permanent low egg production with quality issues).
- **H9N2** is Self-limiting disease, affected birds recover after 2 weeks. Mortality observed more in older birds (> 55 wks) or birds with complicated secondary pathogens.



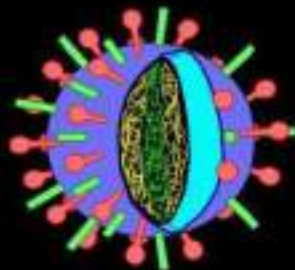
# AIV Diagnostics: Serology & Molecular Methods



# Disease Control & Prevention Strategy



# Disease Control & Prevention Strategy

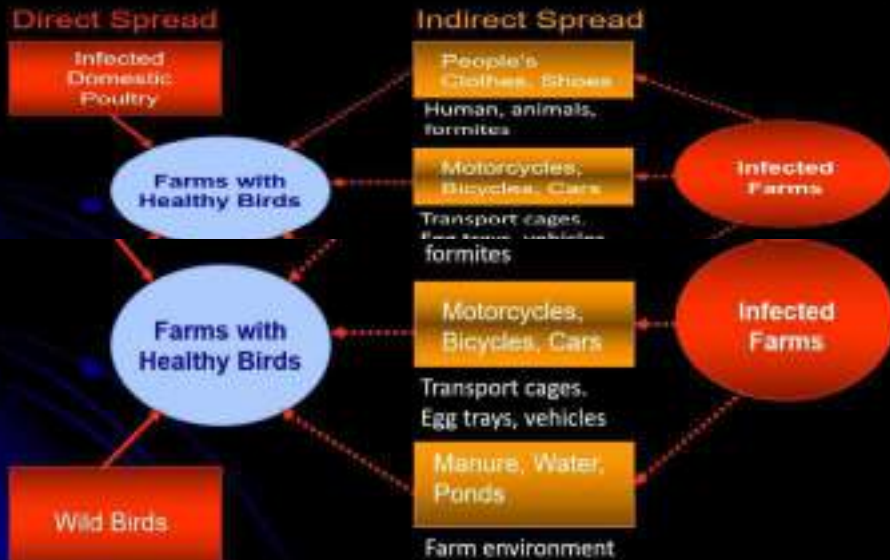


## Containment of HPAI Spread

- Quarantine of area and infected premises
- Restrict movement of birds, product & manure
- Move by Permit only
- Strict Monitoring of Dead bird disposal
- Increased Biosecurity
- Surveillance of all poultry in a 3-5 mile area

# Avian Influenza Control Measures

## Spread of H5N1 Virus



## AIV in Live Bird Markets (LBM)

1. Very important source of contamination
2. Virus is maintained in these large markets
3. Trucks carrying these birds go back to the farm



# Avian Influenza Control Measures

## Control Measures during Outbreaks (Emergency Situation)

- Rapid destruction ("Culling" or "Stamping Out") of all infected or exposed birds
- Proper disposal of carcass
- Quarantine & rigorous disinfection of farm with disinfectant e.g. formalin, iodine compounds

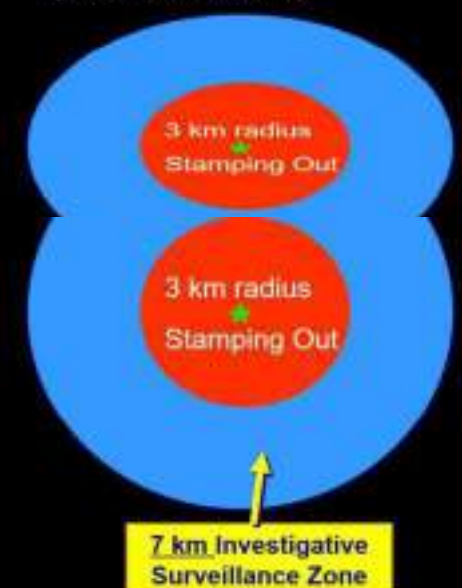


## HPAI Control Strategies in Asian Countries

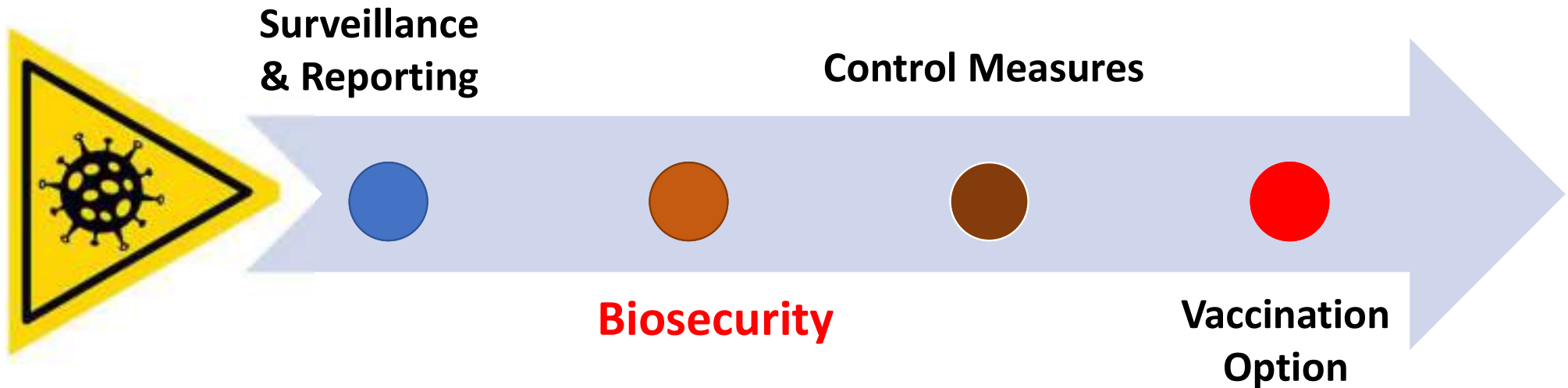
**China** : Combinations of culling & vaccination measures



**Vietnam, Thailand, Cambodia** : Combinations of Culling & Surveillance (Vietnam: Vaccination)



# Control Measures of Avian Influenza



- Bio-security
- Stamping-out infected and at-risk flocks (sporadic infections)
- Vaccination

# Control of Avian Influenza Surveillance & Reporting

## Early Detection is the Key to Control AIV Spread

1. Routine Submission of Eggs or Blood to Lab for testing
  - Broilers/turkeys – 10 blood samples per flock at slaughter
  - Layers/breeders – 30 eggs per month
2. Routine Submission to Lab for diagnosis of any Disease Problems
3. Training of local poultry industry of Danger of Avian Influenza
  - Prevent introduction through good biosecurity
  - Recognition of the disease
  - Testing for avian influenza



# Control of Avian Influenza

## Biosecurity: Cleaning & Disinfection



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# Control of Avian Influenza

## Biosecurity - Biosecurity – Biosecurity

We know where the virus comes from

- Wild water fowl
- Live bird markets/Sunday markets
- Backyard flocks/Mixed farming
- Pet birds
- Other infected commercial poultry flocks



# Biosecurity: AI Virus Inactivation

1. AIV are not very hardy, killed or inactivated by heat, drying, UV light & common chemical disinfectants e.g. sodium hypochlorite, phenolic compounds, quaternary ammonium compounds, iodine compounds, formalin & other aldehydes.
2. AIV inactivated within 6 days with field manure at an ambient temp (approx. 15°C) condition (Lu *et al.*, 2003).
3. AIV (H7N2) loss infectivity in 24 hrs under 30 – 37°C & less than a week under 15 – 20°C temperatures (Lu *at al.*,2003).



# Effect of One hour Exposure of Different Disinfectants on the ability to inactivate AIV

- All 5 disinfectants are effective at inactivating AIV @ recommended concentrations.
- Only the Chlorine & Peroxygen compounds damaged the RNA (could not be detected by RT-PCR).



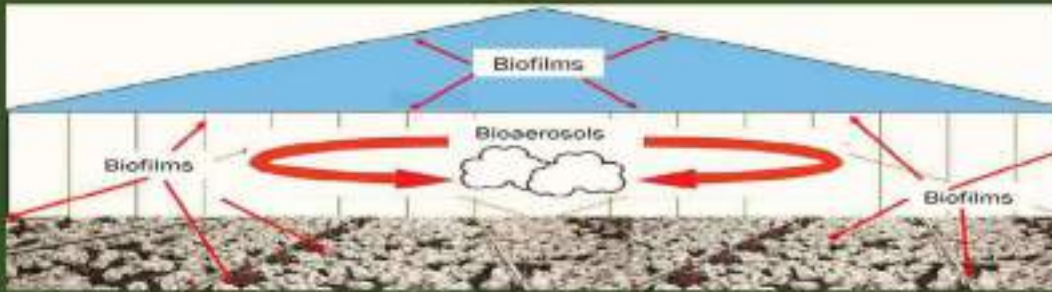
Disinfectant/dilution	1/10	1/100	1/256	1/1000
Sodium hypochlorite*	NT <sup>A</sup> /(-) <sup>B</sup>	(-) <sup>C</sup> /(+)	(-)/(+)	(-)/(+)
Phenolic		NT/(+)	(-)/(+)	(-)/(+)
Lysol		NT/(+)	(-)/(+)	(-)/(+)
Quaternary ammonia		NT/(+)	(-)/(+)	(+)/(+)
Peroxygen compound*		NT/(-)	(-)/(-)	(-)/(+)
Peroxygen Compound (10 day old)		NT/(+)	(+)/(+)	(+)/(+)



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<sup>A</sup>NT = not tested. <sup>B</sup>(-) = negative for RT-PCR. <sup>C</sup>(-) = negative by virus (Suarez *et al.*, 2003)

# Environmental Challenges : Biofilms



Temperature, Relative Humidity, Air Flow

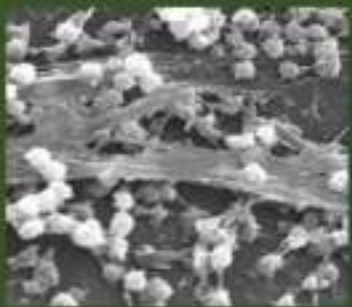
Source: C.M. Wether (2004)	Typical Concentration	Inhaled burden/day
Inhalable dust	7 mg/m <sup>3</sup>	7.7 mg
Respirable dust	0.8 mg/m <sup>3</sup>	0.88 mg
Inhalable endotoxin	1600 ng/m <sup>3</sup>	1.6 mg
Respirable endotoxin	80 ng/m <sup>3</sup>	0.09 mg
Bacteria	$5 \times 10^6$ c.f.u./m <sup>3</sup>	$5.5 \times 10^6$ c.f.u.
Fungi	$1.6 \times 10^5$ c.f.u./m <sup>3</sup>	$1.8 \times 10^5$ c.f.u.
Ammonia	17 ppm	13 mg

Calculated assuming a minute volume of 700 ml for a 1.6 kg broiler chicken



- Biofilms are the most common form of microbial populations in poultry facilities
- Almost all pathogens are able to form Biofilm (facilitated by Quorum Sensing)
- Biofilms in poultry units are common in flocks with Chronic Respiratory Tract

Calculated assuming a minute volume of 760 ml for a 1.6 kg broiler chicken



- Biofilms are the most common form of microbial populations in poultry facilities
- Almost all pathogens are able to form Biofilm (facilitated by Quorum Sensing)
- Biofilms in poultry units are common in flocks with Chronic Respiratory Tract infections (Pasteurella, Mycoplasma...)
- Biofilms development in poultry facilities can be due to:
  - Oral medication or nutrient supplement via drinking water
  - Sub MIC concentrations of antibiotics/disinfectant stimulate Biofilm formation

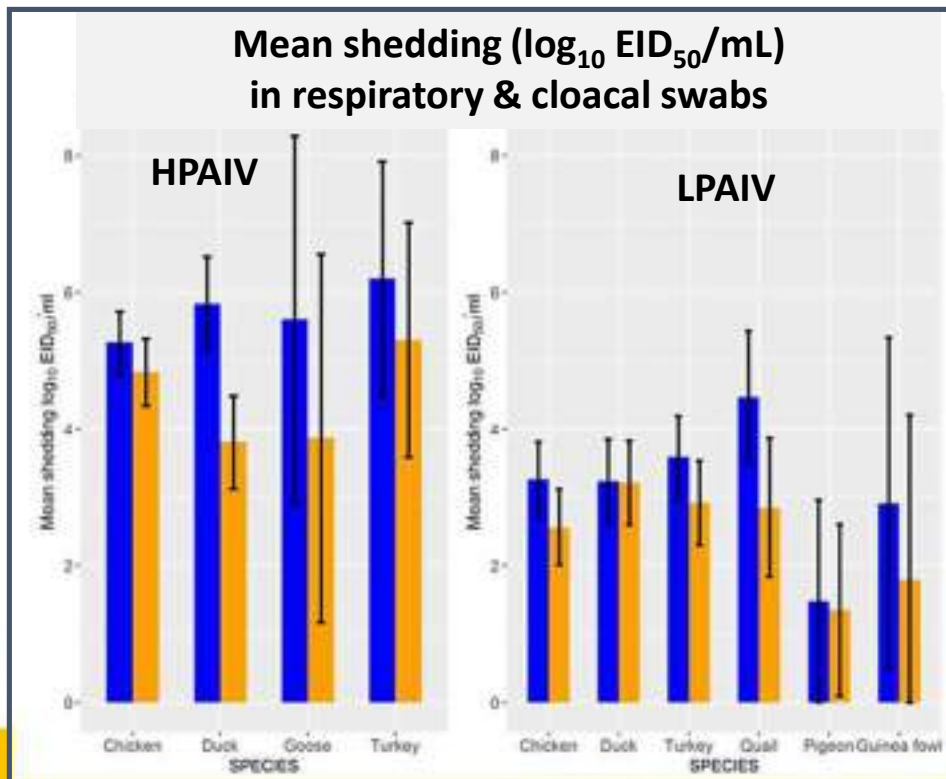
# New Idea in Air Sanitation: In-housing Fogging & Disinfection

Contaminated air is one way that diseases and viruses like HPAI can be transmitted into a facility



# Avian Influenza Virus Shedding

- Avian influenza viruses are shed in the saliva, mucous, feces, & respiratory secretions of infected birds
- The virus can also be found in the body fluids of other infected animals, such as cow milk
- LPAI viruses can be shed in asymptotically infected or minimally affected flocks



**An Indication of AIV shedding length in days in multiple poultry species**

Pathotype	Poultry Species	Length of Respiratory Virus Shedding (Days)		Length of Cloacal Virus Shedding (Days)	
HPAI	Chicken	2.6	(1.1-6.5)	2.5	(1.0-6.2)
	Duck	6.9	(2.8-17.1)	6.6	(2.7-16.3)
LPAI	Chicken	6.2	(0.8-17.8)	5.5	(0.7-15.7)
	Duck	5.3	(0.7-15.3)	8.2	(1.0-23.3)
	Turkey	10.0	(1.3-28.7)	14.1	(1.8-40.2)
	Guinea fowl	3.3	(0.4-9.4)	3.3	(0.4-9.4)
	Pigeon	3.6	(0.4-10.2)	2.8	(0.3-8.0)
	Quail	NA		6.9	(0.9-19.8)

NA = not applicable.

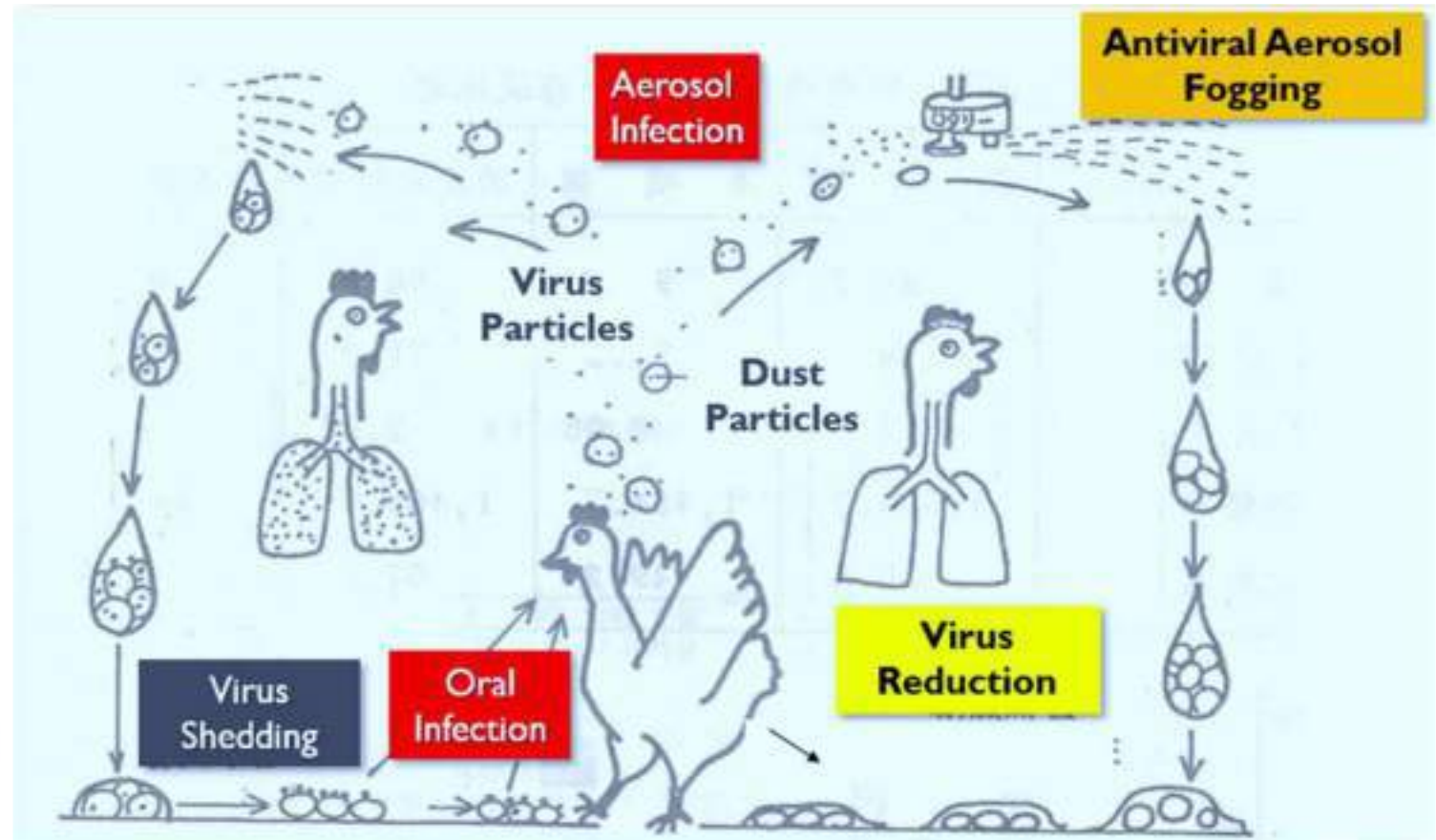
Germeraad *et al.*, (2019)

Shedding route  
■ Respiratory  
■ Cloacal

# Reduce Virus Shedding & Contamination by Aerosol Fogging

## House & Environment Decontamination

- Washing with surfactant, disinfectant spraying, thermal fogging...
- Consider Foaming disinfection in severe outbreak case
- Continuous use of water sanitizer



# Application of Foggers

## Fogger Cooling System

## Description

### Low Pressure Fogging

100 – 200 psi (7 – 14 bar), droplet sizes > 30 microns may cause wet litter at high humidity

### High Pressure Fogging

400 – 600 psi (28 – 41 bar), droplet sizes of 10 – 15 microns minimal residual moisture giving extended humidity range

### High Pressure Fogging

Air is drawn through water-soaked filter (pad) by tunnel ventilation + Foggers inside house

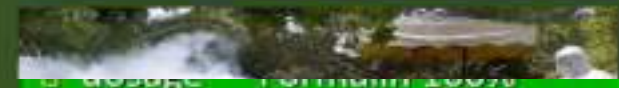
### Fogger + Cooling Pads

Air is drawn through water-soaked filter (pad) by tunnel ventilation + Foggers inside house

## Environmental Fogging

### "Fog" Machines

- ❑ especially for disinfecting
- ❑ works on the basis of combustion & pressure (heat)
- ❑ use: 1.5 – 1.7 ltr/ 100m<sup>3</sup>
- ❑ dosage: Formalin 100%  
Peroxides 20 -25 %



- ❑ dosage: Formalin 100%  
Peroxides 20 -25 %



# Microaerolized H<sub>2</sub>O<sub>2</sub> on Bacterial & Viral Poultry Pathogens

## Efficacy of Vaporized H<sub>2</sub>O<sub>2</sub> against Exotic Animal Viruses (Heckert *et al.*, 1997)

TABLE 2. Titres of several different exotic animal viruses, suspended in liquid or dried onto a glass or steel surface, before and after exposure to VPHP gas.

Virus	Titre (mean ± SD, log <sub>10</sub> /ml) of virus <sup>a</sup> in:									
	Liquid suspension					Dried state				
	No VPHP		VPHP, in			No VPHP		VPHP, in		
	Out of box		In box			Out of box		In box		
	Glass	Steel	In box	VPHP, in	VPHP, in	Glass	Steel	Glass	Steel	VPHP, in
AIV	ND	ND	4.5 <sup>b</sup>	0	5.68 ± 0.14	5.68 ± 0.14	2.60 ± 0.14	2.91 ± 0.63	0 ± 0.0	0 ± 0.0
ASFV	6.73 ± 0.8	6.35 ± 0.58	5.96 ± 1.06	<1 <sup>c</sup>	5.89 ± 0.29	6.05 ± 0.25	0.06 ± 0.04	0.06 ± 0.01	<1	<1
BTV	4.43 ± 0.14	4.35 ± 0.14	4.39 ± 0.35	<1	4.43 ± 0.14	4.55 ± 0.25	1.32 ± 0.72	1.31 ± 0.8	<1	<1
HCV-CC	6.55 ± 0.25	6.85 ± 0.14	6.0 <sup>b</sup>	<1	58.5 ± 0.14	5.74 ± 0.29	0 ± 0.0	0 ± 0.0	<1	<1
HCV-WB	6.99 ± 0.29	6.71 ± 0.29	5.64 ± 0.18	5.5 ± 0.0	6.8 ± 0.25	6.86 ± 0.43	4.3 ± 0.25	3.81 ± 0.8	4.18 ± 0.14	4.35 ± 0.14
NDV	ND	ND	8.25 <sup>b</sup>	0 ± 0.0	9.34 ± 0.29	8.5 ± 0.0	6.5 ± 0.0	6.1 ± 0.14	0 ± 0.0	0 ± 0.0
PRV	6.95 ± 0.38	7.24 ± 0.29	6.75 ± 0.8	<1	6.1 ± 0.14	6.1 ± 0.14	4.35 ± 0.14	4.43 ± 0.14	<1	<1
SVDV	7.8 ± 0.25	8.18 ± 0.14	7.79 <sup>b</sup>	<1	7.7 ± 0.38	8.01 ± 0.38	0 ± 0.0	0 ± 0.0	<1	<1
VEV	7.7 ± 0.38	8.0 ± 0.8	2.0 ± 0.8	<1	2.26 ± 0.38	2.55 ± 0.25	0.1 ± 0.0	0.1 ± 0.0	<1	<1
VSV-CC	5.04 ± 1.15	5.99 ± 0.29	4.75 <sup>b</sup>	<1	3.04 ± 1.5	4.55 ± 0.25	0 ± 0.0	0 ± 0.0	<1	<1
VSV-AF	6.06 ± 0.43	7.01 ± 0.38	7.75 <sup>b</sup>	<1	5.34 ± 0.52	4.34 ± 0.66	3.68 ± 0.14	3.89 ± 0.29	<1	<1

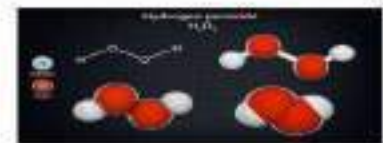
<sup>a</sup> AIV, avian influenza virus; ASFV, African swine fever virus; BTV, bluetongue virus; HCV-CC, hog cholera virus in cell culture medium; HCV-WB, hog cholera virus in whole blood; NDV, Newcastle disease virus; PRV, pseudorabies virus; SVDV, swine vesicular disease virus; VEV, vesicular exanthema virus; VSV-CC, vesicular stomatitis virus in cell culture medium; VSV-AF, vesicular stomatitis virus in allantoic fluid. Out of box, samples not placed in decontamination chamber; in box, samples placed in decontamination chamber; ND, not done.

<sup>b</sup> Not replicated.  
<sup>c</sup> Sample could not be assayed at a dilution of less than 1/10 because of toxicity in the assay system at lower dilutions.

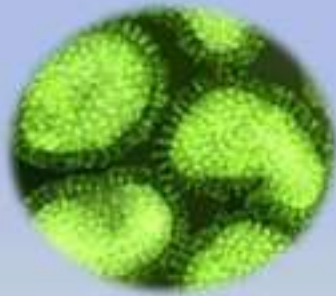
VPHP = vapor-phase of hydrogen peroxide

## Silver Stabilized Hydrogen Peroxide

- Silver stabilized H<sub>2</sub>O<sub>2</sub> and is a very effective, multipurpose disinfectant & work effectively across wide pH range.
- Silver combines with H<sub>2</sub>O<sub>2</sub> to enhance stability & to boost performance to clean effectively with short contact time (almost 20X more powerful). A potent Biofilm remover!
- It works as bactericidal, fungicidal & also against viruses and it works effectively in cold water (does not require any heat to inactivate). short contact time (almost 20X more powerful). A potent Biofilm remover!
- It works as bactericidal, fungicidal & also against viruses and it works effectively in cold water (does not require any heat to inactivate).
- It is safe, colorless liquid with no smell or taints and is Non-carcinogenic.



# HPAI/LPAI Prevention Approach



**3. Vaccination**

**2. Management Practice GMP**

**Triangle of  
HPAI & LPAI  
Control**

**1. Biosecurity**



# Use of AI Vaccines

## What We Want? Objectives

- Increase immunity against AIV.
- Prevent mortality, reduce symptoms and economic losses.
- Reduce shedding and spreading of AIV, if infected.
- It does not prevent infection = No Sterile Immunity
- Vaccination against Avian Influenza is: to control the diseases, not to eradicate the virus

Antigen

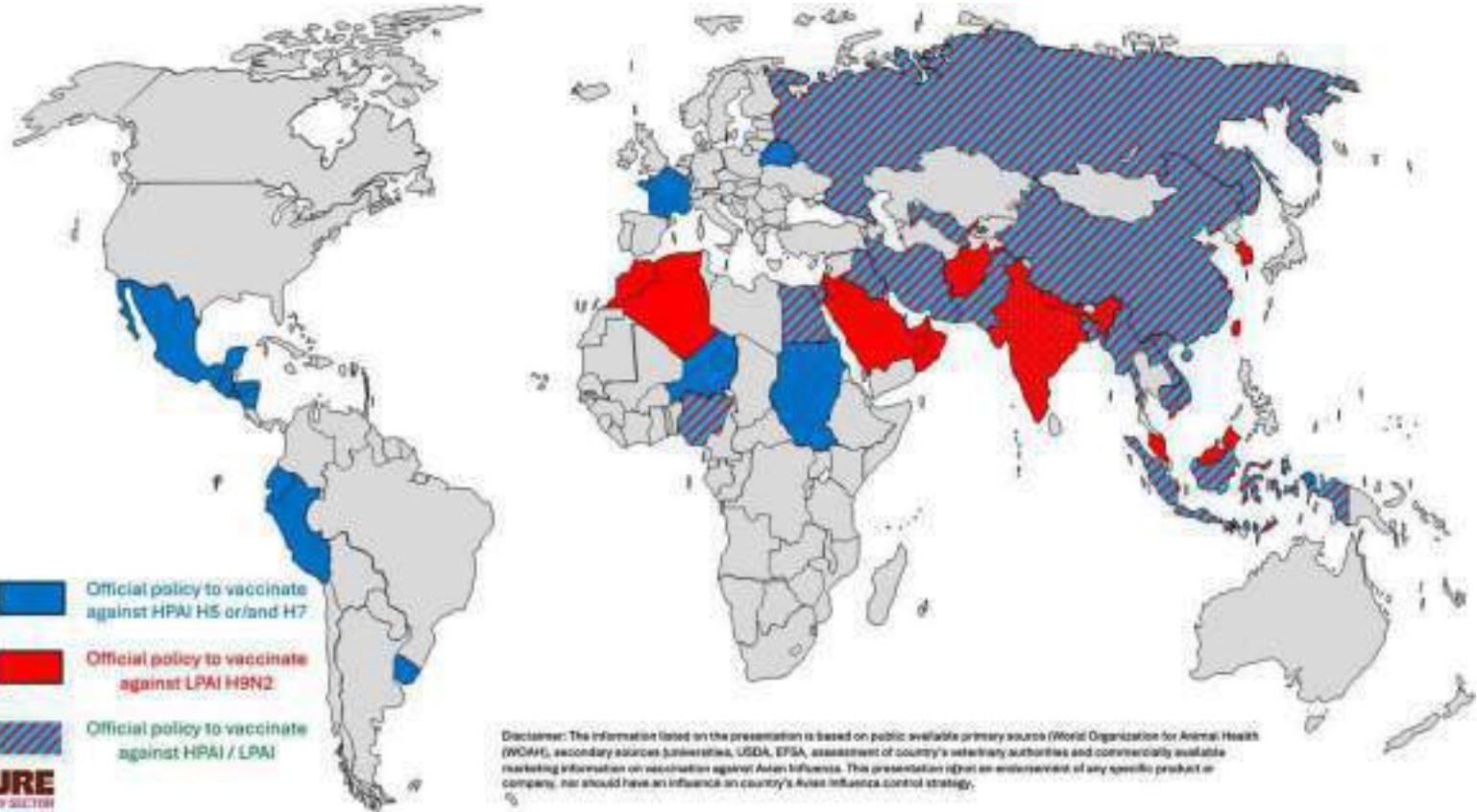
Vehicle

Vaccine &  
Vaccination

Adjuvant

Delivery

# Countries officially vaccinating against LPAI & HPAI



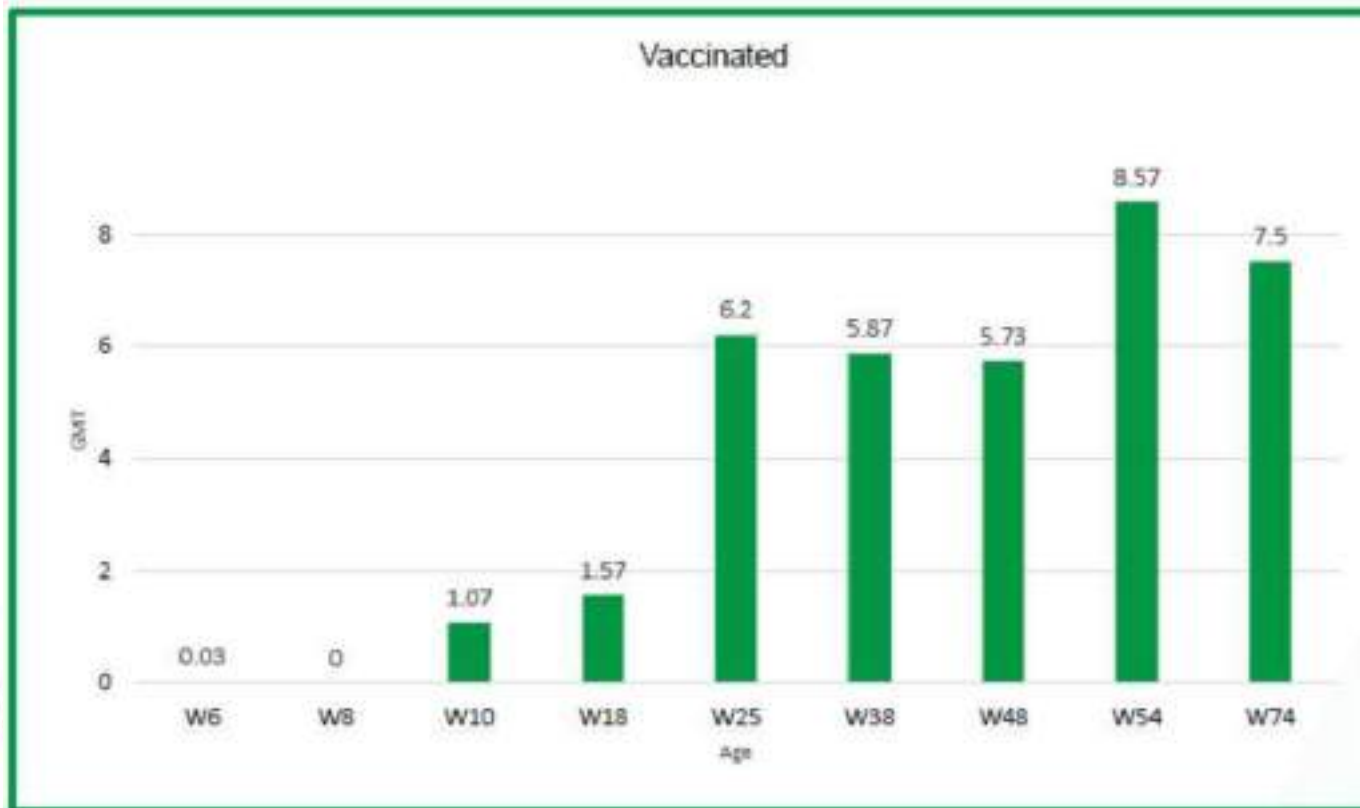
**SHAPING THE FUTURE**  
 OF INDIAN POULTRY SECTOR

# Avian Influenza Poultry Vaccines

- ✓ Inactivated “Whole virus” vaccines
- ✓ Inactivated “Reverse Genetic” vaccines
- ✓ Recombinant vaccines
  - Baculovirus as the vector
  - Poxvirus as the vector
  - Newcastle Disease virus as the vector
  - Herpesvirus of Turkey (HVT) as vector



# Example: Inactivated “Whole Virus” Vaccine Response (H9 HI titers)



Vaccination	Age
1 <sup>st</sup> dose	W5
2 <sup>nd</sup> dose	W14
3 <sup>rd</sup> dose	W45

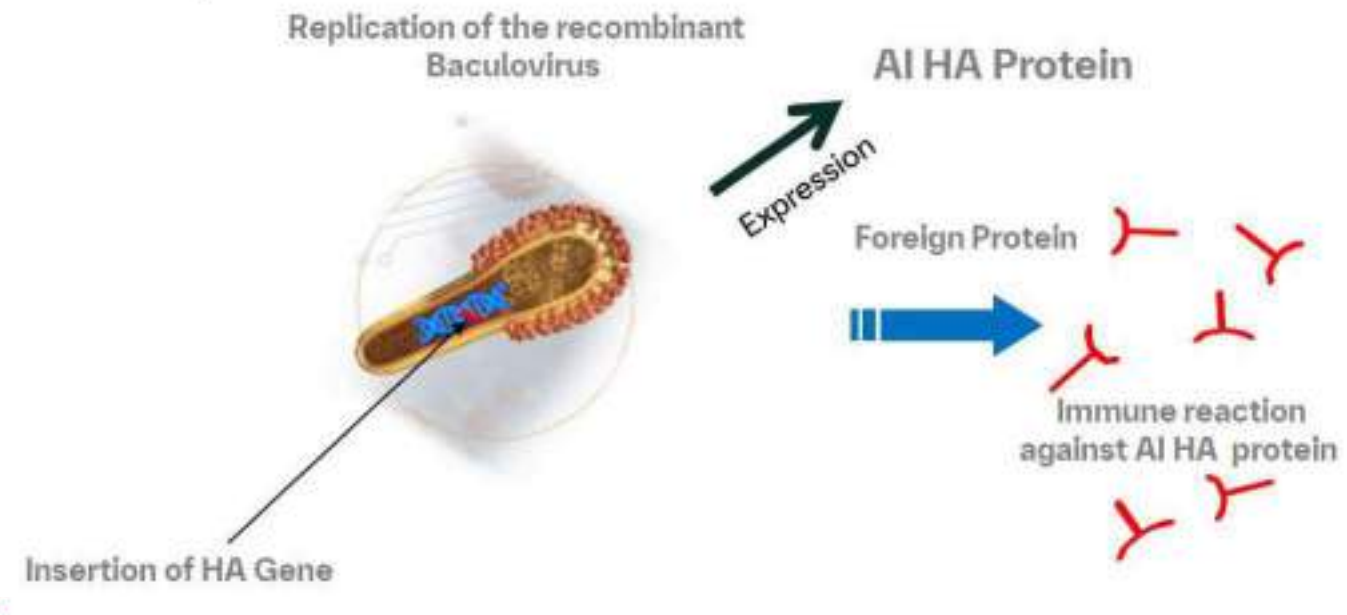
Good seroconversion  
seen after 2 doses of  
vaccine administered



# Example: Inactivated Recombinant Vaccine against AIV H5 (B.E.S.T. Technology)

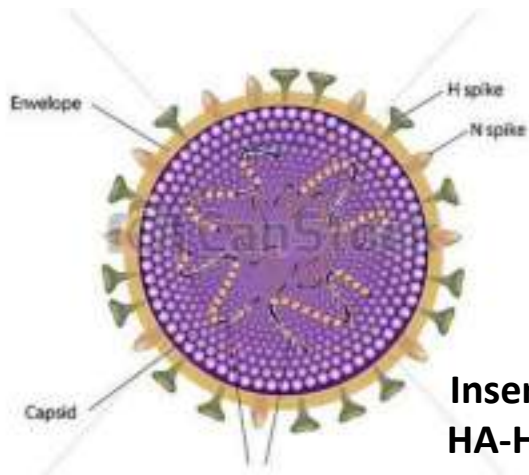
## Baculovirus Expression System Technology B.E.S.T.

Antigen was expressed in insect cells after infection with a recombinant baculovirus encoding for inserted sequence

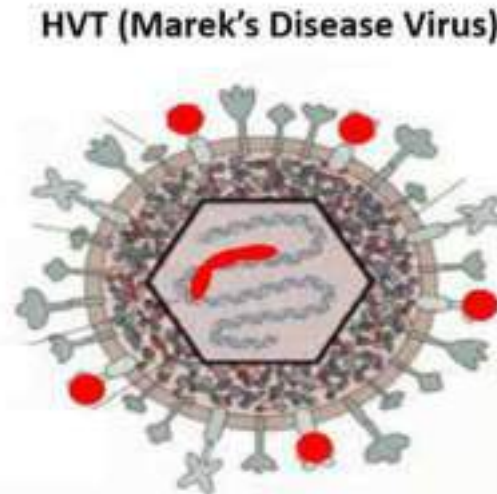


Stephane Lemiere (2024)

# Example: HVT-vectored H5 Vaccine



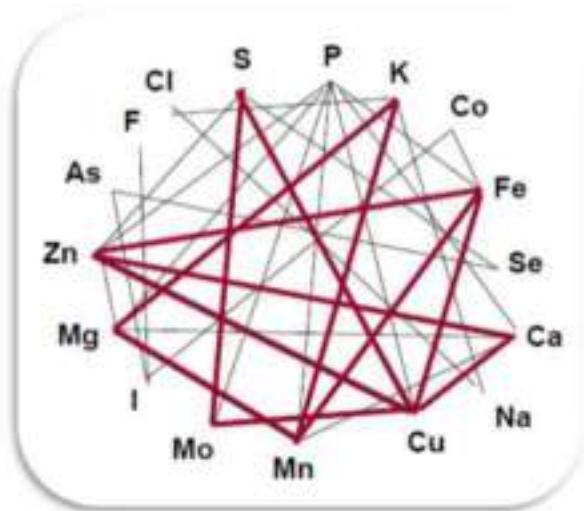
Insertion of  
HA-H5 gene



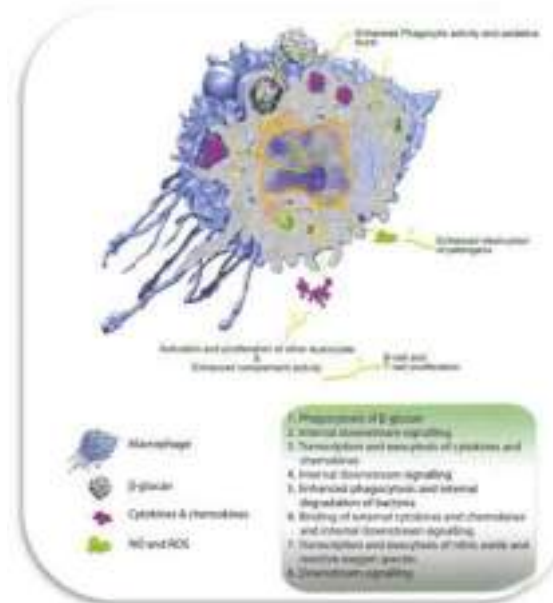
- HVT-H5 vaccine was constructed by inserting a recombinant HA-H5 gene into the genome of HVT FC126.
- The recombinant HA-H5 was derived from a compilation of HPAI H5N1, clade 2.2, 2005 strains (GenBank: MW310457).



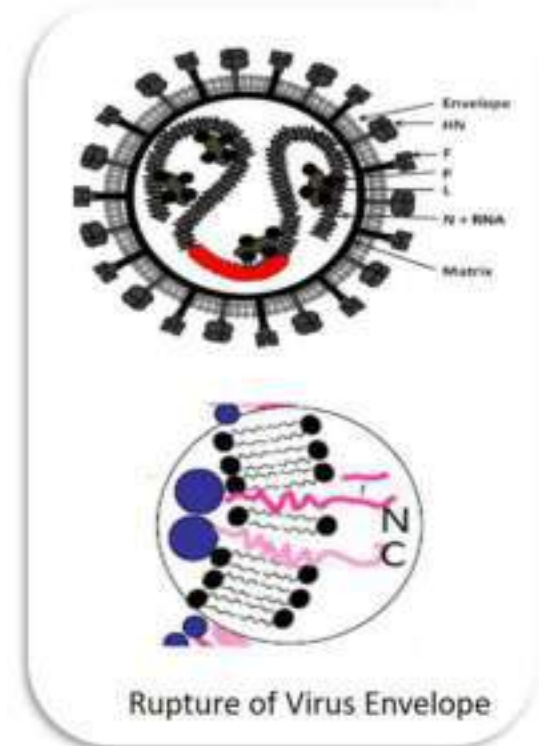
# Recent Focus on Avian Immune System under Virus Challenge Situation



Nutrient Uplift & Consider  
 Micro-nutrient Support



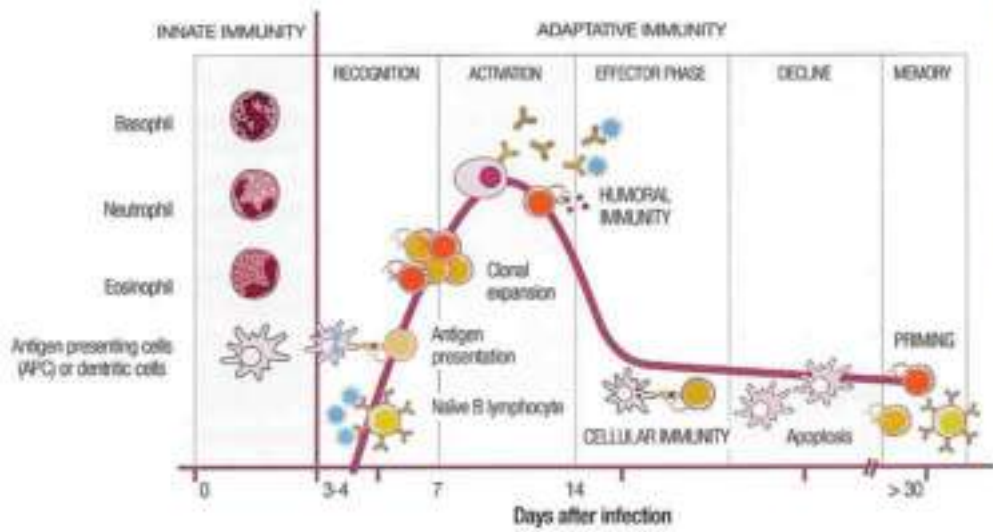
Apply Immune  
 Modulating Agents



Rupture of Virus Envelope  
 Feed Sanitation  
 & Water Hygiene



# Role of Cell-mediated Immunity in Support of Inactivated Vaccination

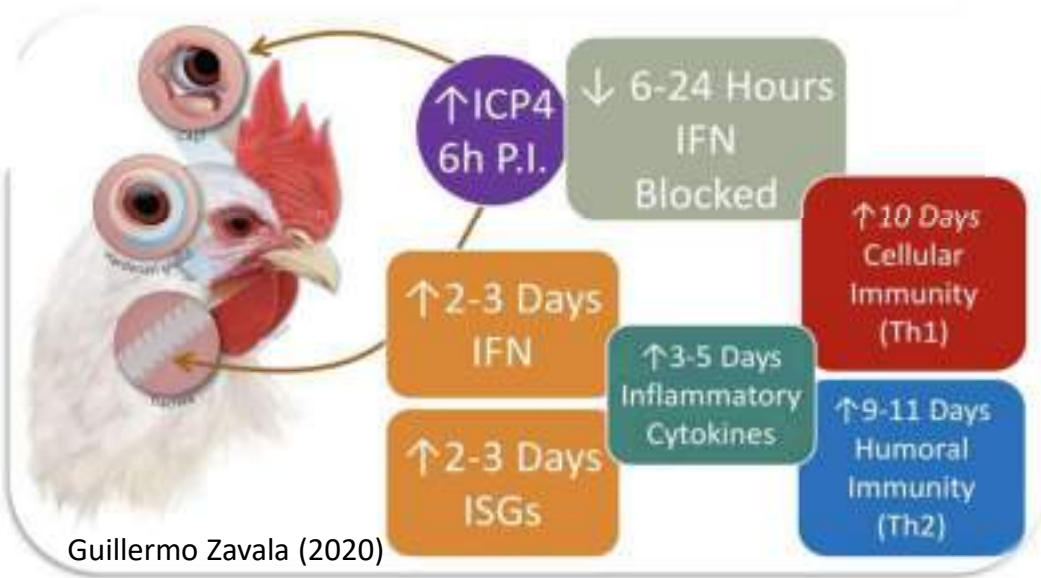


Type of Immunity		Killed Vaccines
Local Immunity	Humoral (Ab IgA)	No
	Cell-mediated (CTLs)	No
Systemic Immunity	Humoral (Ab IgY, IgM)	Yes
	Cell-mediated (CTLs)	No

Thiery van den Berg (2014)

**Head-associated Lymphoid Tissues** are important secondary tissues in the fight against Respiratory Pathogens

- CALT (Conjunctiva)
- HALT (Hardenian gland)
- NALT (Nasal)
- TALT (Trachea)

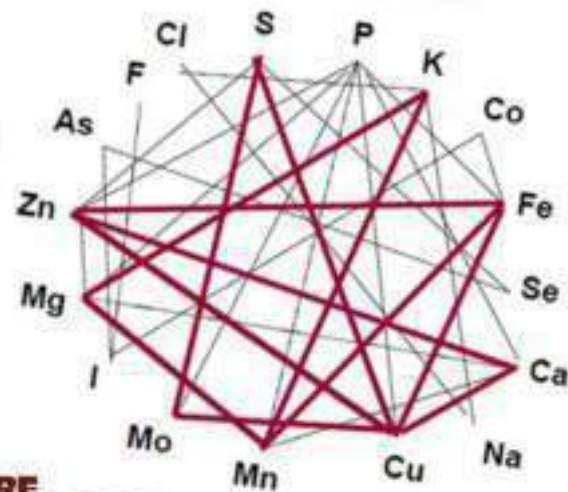


Guillermo Zavala (2020)



# Use of Antioxidants, Probitoics, Immuno-modulators, Organic Minerals & Vitamins ...

**Example: Organic Zinc & Selenium** reduce symptoms of vaccination stress by supporting the Immune system



## Zinc

- Skin/gut integrity, Keratin formation, Lymphocyte & SOD production. Glutathione production

## Manganese

- Macrophage killing ability, Steriodogenesis
- Chondroitin sulfata production

## Copper

- Neutrophil activation, Cross-linking collagen, Lysyl oxidase

## Selenium

- Cellular protection

## Chromium

- Insulin sensitivity

## Iodine

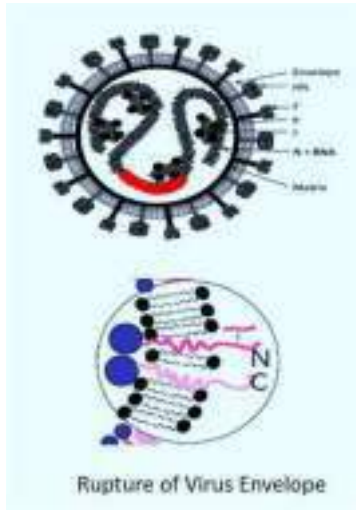
- Metabolic rate



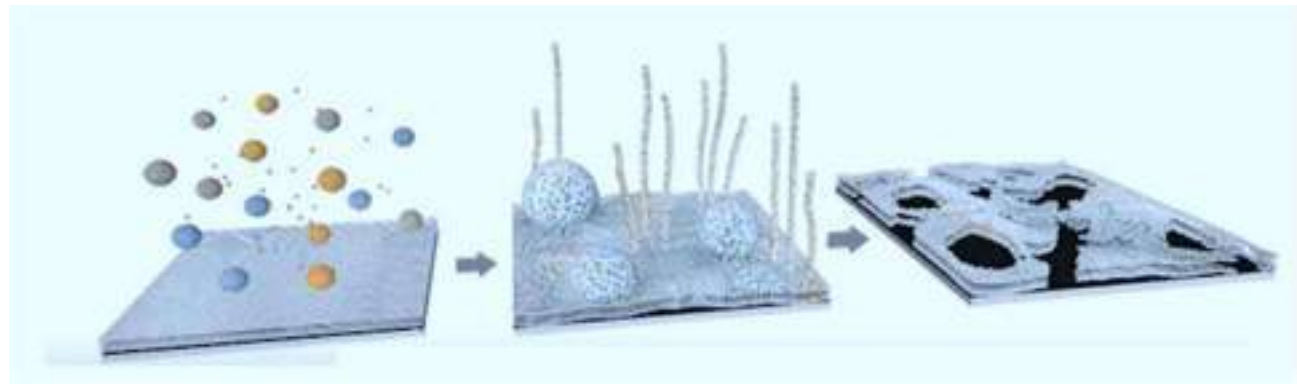
**SHAPING  
THE FUTURE**  
OF ORGAN POULTRY SECTOR



# Antiviral Effect of Medium Chain Fatty Acid (MCFA) Application through Feed/drinking water



- Micelles from **MCFA (Caprylic acid, Monocaprylin)** interact with virus membranes, causing buds or tubules formation which will rupture, leaving holes in the membrane, killing microbial pathogens & inactivating virus particles.
- Supplementation of MCFA Caprylic acid through feed or water could kill the virus in live birds.
- MCFA & MCMG are potent antimicrobials & antiviral with anti-inflammatory & growth promoting effects on recovery Pullets/Layers.



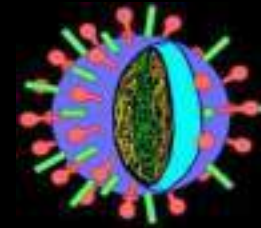
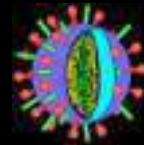
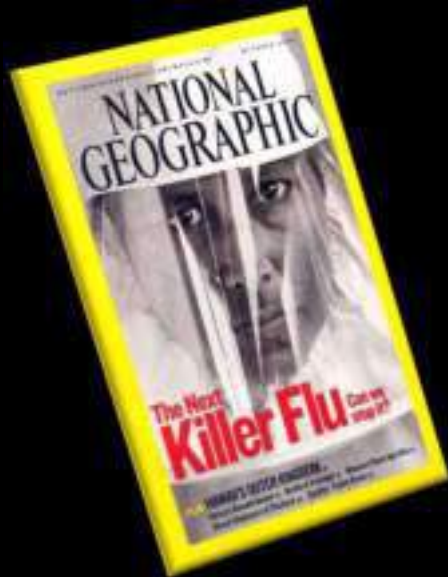
# Guidelines & Application of Control Policies for Avian Influenza

<u>H5/H7 virus Pathogenicity</u>	<u>Index Case Flock</u>	<u>Evidence of Spread to Industrial Sector</u>	<u>Population Density in area</u>	<u>Policy</u>
<u>HPAI/LPAI</u>	Backyard	No	High/Low	Stamping out
<u>HPAI/LPAI</u>	Backyard	Yes	Low	Stamping out
			High	Vaccination
<u>HPAI/LPAI</u>	Industrial	No	High/Low	Stamping out
<u>HPAI/LPAI</u>	Industrial	Yes	Low	Stamping out
			High	Vaccination

After Capua & Marangon (2003)



# Human Infection



# Zoonotic Disease



South China Morning Post 20<sup>th</sup> June 2005



# Bird Flu Virus Infection in Humans



## Influenza A H5

- Potentially of 9 different subtypes
- Can be highly pathogenic or low pathogenic
- H5 infection have been documented among humans, sometimes causing severe illness & death

## Influenza A H9

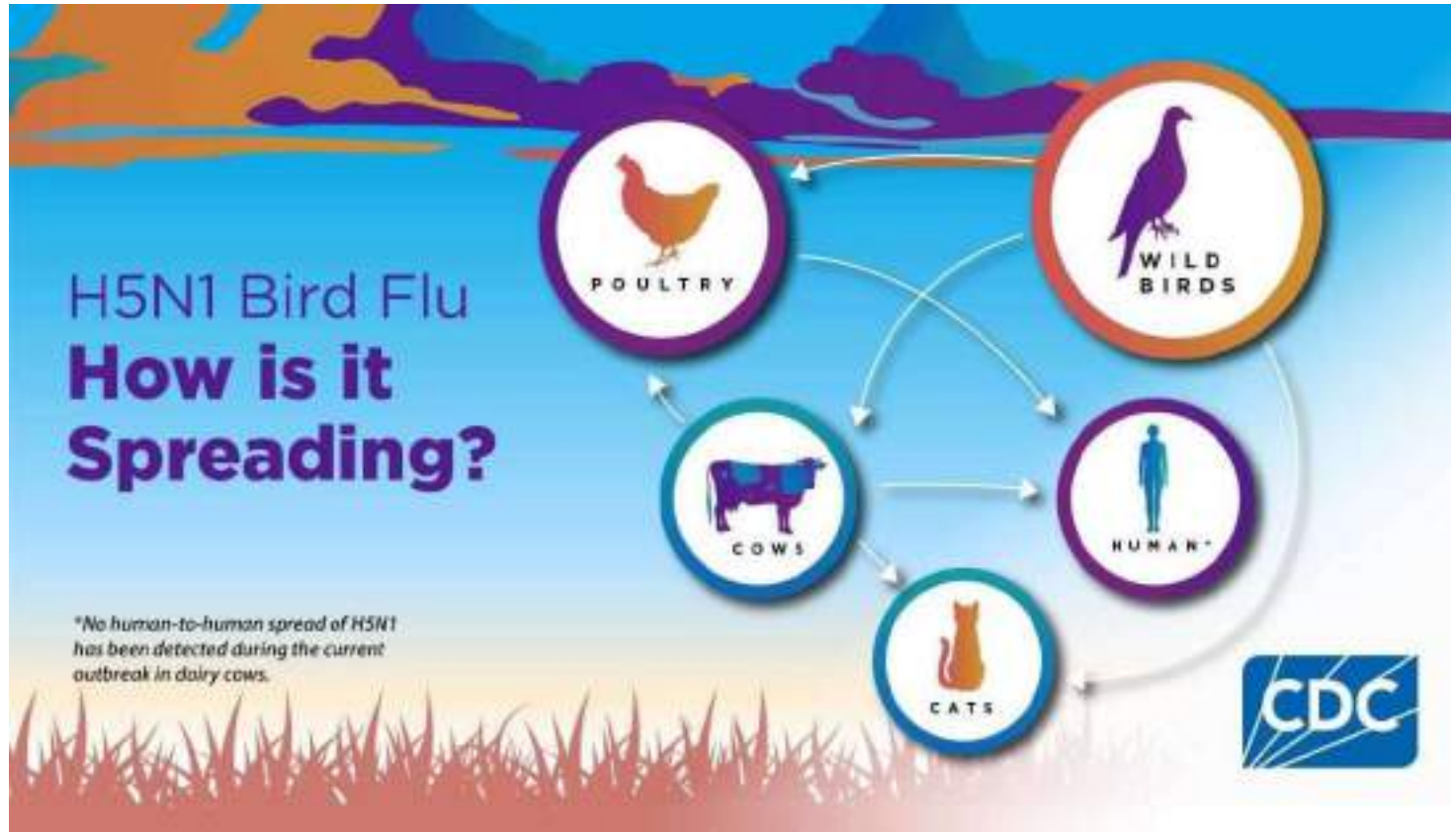
- Potentially 9 different subtypes
- Documented only in low pathogenic form
- H9 infections in humans have been confirmed

## Influenza A H7

- Potentially 9 different subtypes
- Can be highly pathogenic or low pathogenic
- H7 infection in human is rare, but can occur any persons who have close contact with infected birds, symptoms may include conjunctivitis/ or upper respiratory symptom



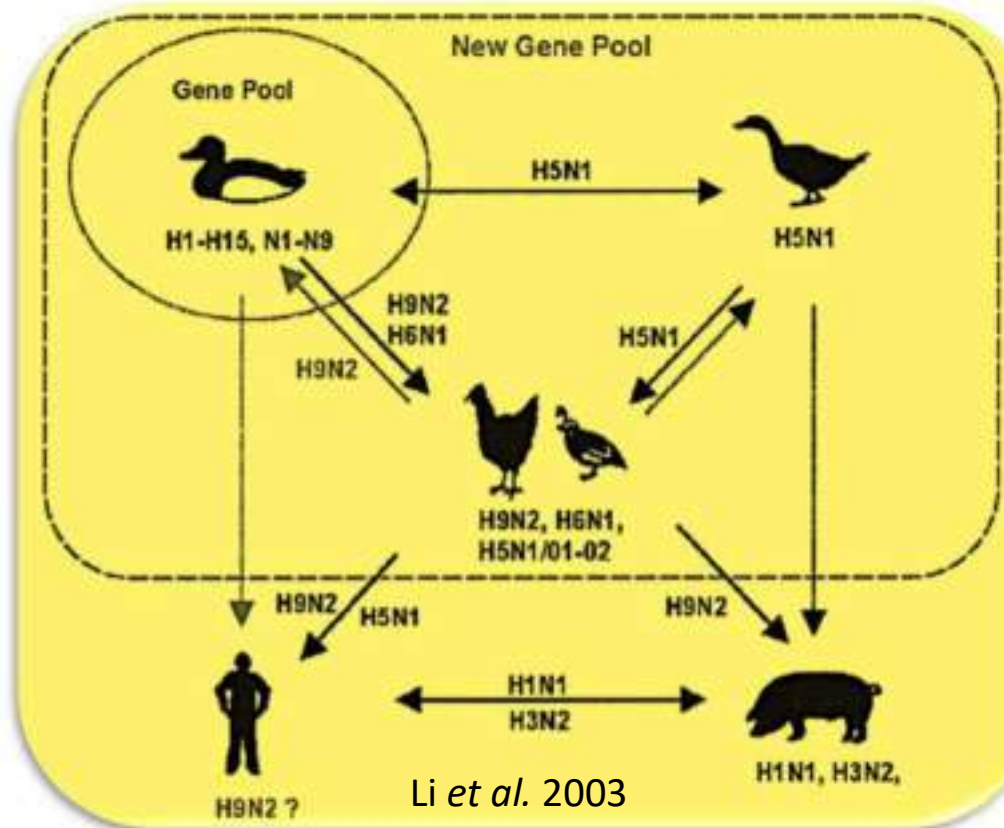
# Bird Flu Virus Infection in Humans



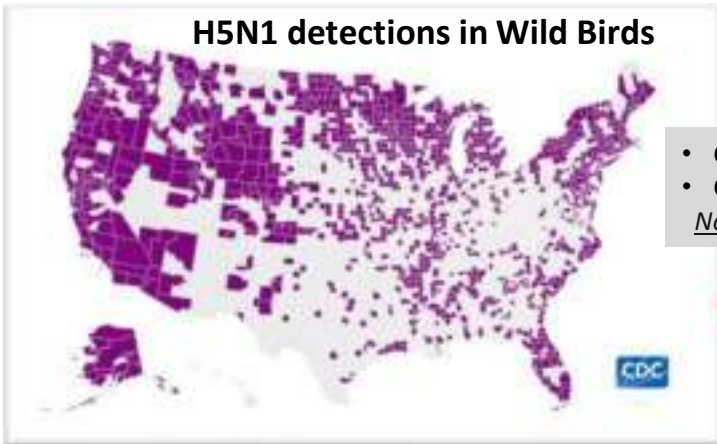
# Zoonotic Potential of H9 Subtypes

## Properties which may influence zoonotic transmission

	H5	H9
Worldwide interface	✓	✓✓
α2-6 receptor binding	x	✓
Signature residues for human transmission	✓	✓
Natural transmission to pigs	x	✓
Respiratory transmission	x	✓



# US Bird Flu Virus Infection in Humans



- Case detected **10,563**
- Counties affected 1,185

*November 12, 2024*



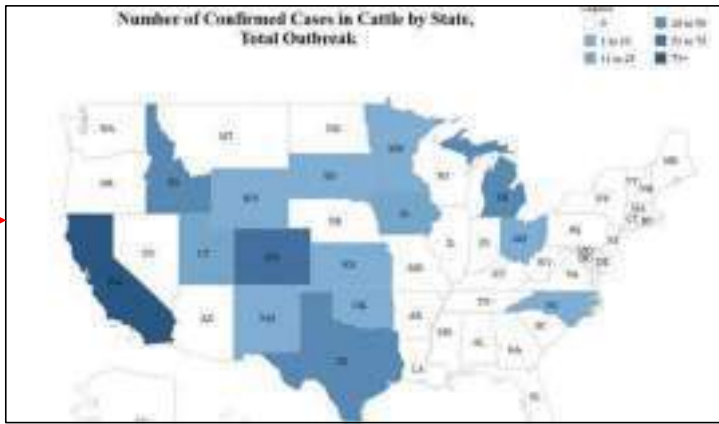
Since February 2022 Outbreak

- **108.41 million** birds have been affected
- Total 1,218 flocks in 48 States
- 533 flocks Commercial & 685 flock Backyard

*November 15, 2024*

- Total Outbreak in Cattle **549** confirmed in 15 States

*July 03, 2024*



**Confirmed Total Reported Human Cases**

State	Cattle	Poultry	Unknown	State Total
California	27	0	0	27
Colorado	1	9	0	10
Michigan	2	0	0	2
Missouri	0	0	1	1
Oregon	0	1	0	1
Texas	1	0	0	1
Washington	0	11	0	11
<b>Source Total</b>	<b>31</b>	<b>21</b>	<b>1</b>	<b>53</b>

*NOVEMBER 18, 2024*



Failure to control H5N1 among American livestock could have global consequences. The US vaccine supply is inadequate and slow with too few genome sequences of H5N1 virus to fit an antibody made publicly available for scientific review. See the writer's PHOTO REPORT.



That's why I'm so frustrated that genomic sequences of H5N1 animal cases in the US are not quickly made available. Sharing genomic data is essential for understanding the threat and giving the world time to prepare, including developing antiviral and vaccine. Amanda, for example, can't even hold

**Beyond the risks to its own citizens (there are more than 45 cases of people in the US getting the virus in 2024), America should remember that the country where a pandemic emerges can be accused of not doing enough to control it. We still hear how China did not do enough to stop the Covid-19 pandemic. None of us would want a new pandemic labelled the "American virus", as this could be very damaging for the US' reputation and economy.**

## The world is watching the US deal with bird flu, and it is scary

The US needs to reassure the world it has the outbreak under control.

### Tulio de Oliveira

As a virus spreader in South Africa, I've been watching with dread as H5N1 bird flu spreads among animals in the United States. The pathogen poses a serious pandemic threat and has been detected in more than 500 dairy herds in 25 states - which is probably an underestimate. And yet, the US vaccine supply is inadequate and slow, with too few genomic sequences of H5N1 virus to fit an antibody made publicly available for scientific review.

Failure to control H5N1 among American livestock could have global consequences, and this demands urgent attention. The US has done little to reassure the world that it has the outbreak contained.

The recent infection of a pig at a farm in Oregon is especially concerning, as pigs are known to be "mixing bowls" for influenza viruses. Pigs can be infected by both avian and human influenza viruses, creating a risk for the viruses to exchange genetic material and potentially spawning adaptations for human transmission. The H5N1 pandemic in 2009 was created and spread initially by pigs.

Beyond the risk to its own citizens (there are more than 45 cases of people in the US getting the virus in 2024), America should remember that the country where a pandemic emerges can be accused of not

doing enough to control it. We still hear how China did not do enough to stop the Covid-19 pandemic. None of us would want a new pandemic labelled the "American virus", so this could be very damaging for the US' reputation and economy.

The US should learn from how the Global South responds to infectious diseases. Those of us working in the region have a good track record of responding to epidemics and emerging pandemics, and can help the US identify new virus variants and other insights into how to control H5N1. This knowledge has not come easily or without suffering, it has developed from decades of dealing with deadly diseases. We're just one step in time. We need to learn about your country as quickly as possible in order to fight it.

We did this during the Covid-19 pandemic. In November 2020, my

**Beyond the risks to its own citizens (there are more than 45 cases of people in the US getting the virus in 2024), America should remember that the country where a pandemic emerges can be accused of not doing enough to control it. We still hear how China did not do enough to stop the Covid-19 pandemic. None of us would want a new pandemic labelled the "American virus", as this could be very damaging for the US' reputation and economy.**

colleagues and I, and others in Botswana, discovered the "Sherrin virus". We quickly and publicly warned the world that it could rapidly spread. This kind of transparency is not always easy because it can occur at large economic cost. For example, after we shared our findings, discovery countries around the world

imposed travel bans on South Africa ahead of December holidays, opening businesses. Our team received death threats, and we avoided society for our lab. Our estimate suggests South Africa lost US\$60 million (US\$4 million) in cancelled bookings from December to March. But it was the right thing to do

in many cases. Countries need to continue to support one another: we need an increase of scientific and public data that can work together to respond to new epidemics and potential pandemics, including diagnosing and genotyping every single sample of H5N1.

I understand that it's not easy to persuade business, such as the meat and dairy industries, to allow the testing of all of their animals and staff, and to make that data public quickly. But I also know that in the end, doing so protects lives, limits economic damage and crosses a wider world.

The world cannot afford to gamble with this virus, letting it spread in a track and hoping it never reaches a certain threshold - or crossing our fingers that its spread won't be serious to people. Time will tell. I hope we are not watching the start of a new pandemic unfold, with both the Americas and the future global community keeping our heads in the sand rather than confronting potential danger. <https://www.who.int>

Dr Tulio de Oliveira is the director of the Centre for Epidemic Response and Innovation at Stellenbosch University in South Africa and an associate professor of global health at the University of Washington. He has received numerous awards for his work in infectious diseases.

The US needs to reassure the world it has the outbreak under control.

# Human Exposure to H5 Avian Influenza near Migratory Shorebird Habitats

Article

<https://doi.org/10.1038/s41467-024-53036-y>

## Serological analysis in humans in Malaysian Borneo suggests prior exposure to H5 avian influenza near migratory shorebird habitats

Received: 6 March 2024

Accepted: 25 September 2024

Published online: 17 October 2024

[Check for updates](#)

Hannah Klim<sup>1</sup>, Timothy William<sup>2,3,4</sup>, Jack Mellors<sup>1</sup>, Caolann Brady<sup>1</sup>,  
Giri S. Rajahram<sup>5</sup>, Tock H. Chua<sup>5,6</sup>, Helena Brazal Monzó<sup>7</sup>,  
Jecelyn Leslie John<sup>8</sup>, Kelly da Costa<sup>9</sup>, Mohammad Saifree Jeffree<sup>10</sup>,  
Nigel J. Temperton<sup>9</sup>, Tom Tipton<sup>9</sup>, Craig P. Thompson<sup>11</sup>,  
Kamruddin Ahmed<sup>8,12,13</sup>, Chris J. Drakeley<sup>7</sup>, Miles W. Carroll<sup>1</sup> &  
Kimberly M. Fornace<sup>7,14</sup>

Cases of H5 highly pathogenic avian influenza (HPAI) are on the rise. Although mammalian spillover events are rare, H5N1 viruses have an estimated mortality rate in humans of 60%. No human cases of H5 infection have been reported in Malaysian Borneo, but HPAI has circulated in poultry and migratory avian species transiting through the region. Recent deforestation in coastal habitats in Malaysian Borneo may increase the proximity between humans and migratory birds. We hypothesise that higher rates of human-animal contact, caused by this habitat destruction, will increase the likelihood of potential zoonotic spillover events. In 2015, an environmentally stratified cross-sectional survey was conducted collecting geolocated questionnaire data in 10,100 individuals. A serological survey of these individuals reveals evidence of H5 neutralisation that persisted following depletion of seasonal H1/H3 HA binding antibodies from the plasma. The presence of these antibodies suggests that some individuals living near migratory sites may have been exposed to H5 HA. There is a spatial and environmental overlap between individuals displaying high H5 HA binding and the distribution of migratory birds. We have developed a novel surveillance approach including both spatial and serological data to detect potential spillover events, highlighting the urgent need to study cross-species pathogen transmission in migratory zones.

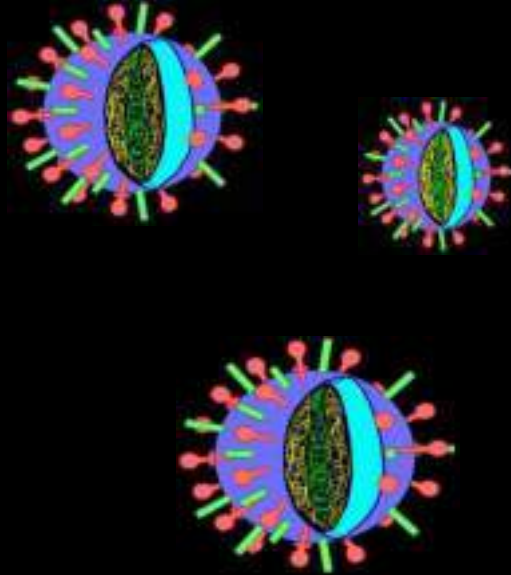


# Bird Flu H5N1 Treatment in Human

1. There is No Effective Treatment for HPAI in Poultry
2. Drug Treatment possible in Human Cases
  - Amantadine, Rimantadine used, resistance development quickly (Webster 1985)
  - Newer analogues of Sialic acid (GG167, 4-guanidineNeu5AC2en) effective in animal models (Hayden *et al.*,1992)
  - Current available antiviral drugs : Oseltamivir, Zanamivir ....



# Epilogue



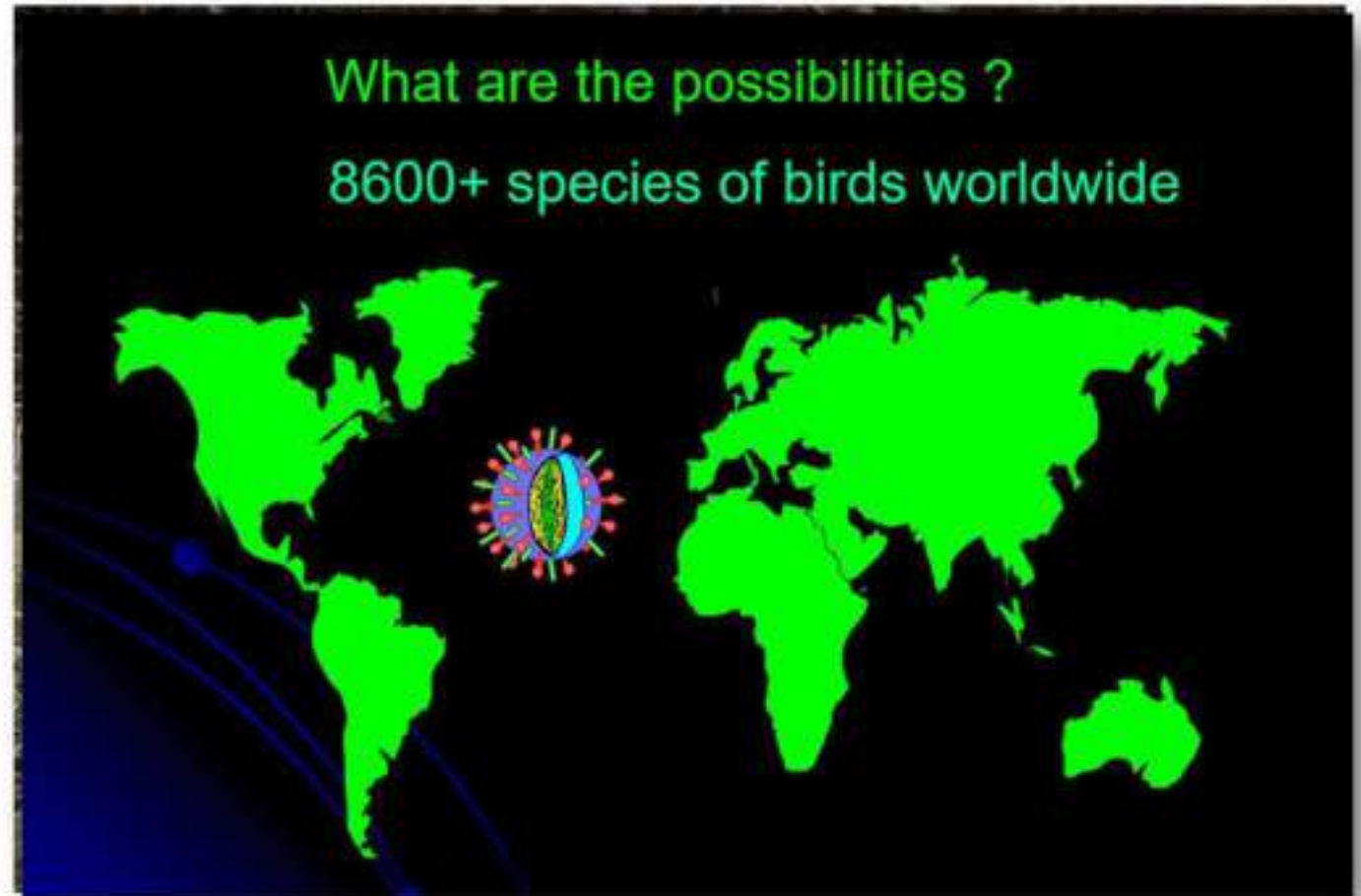
# Multiage Flocks ?

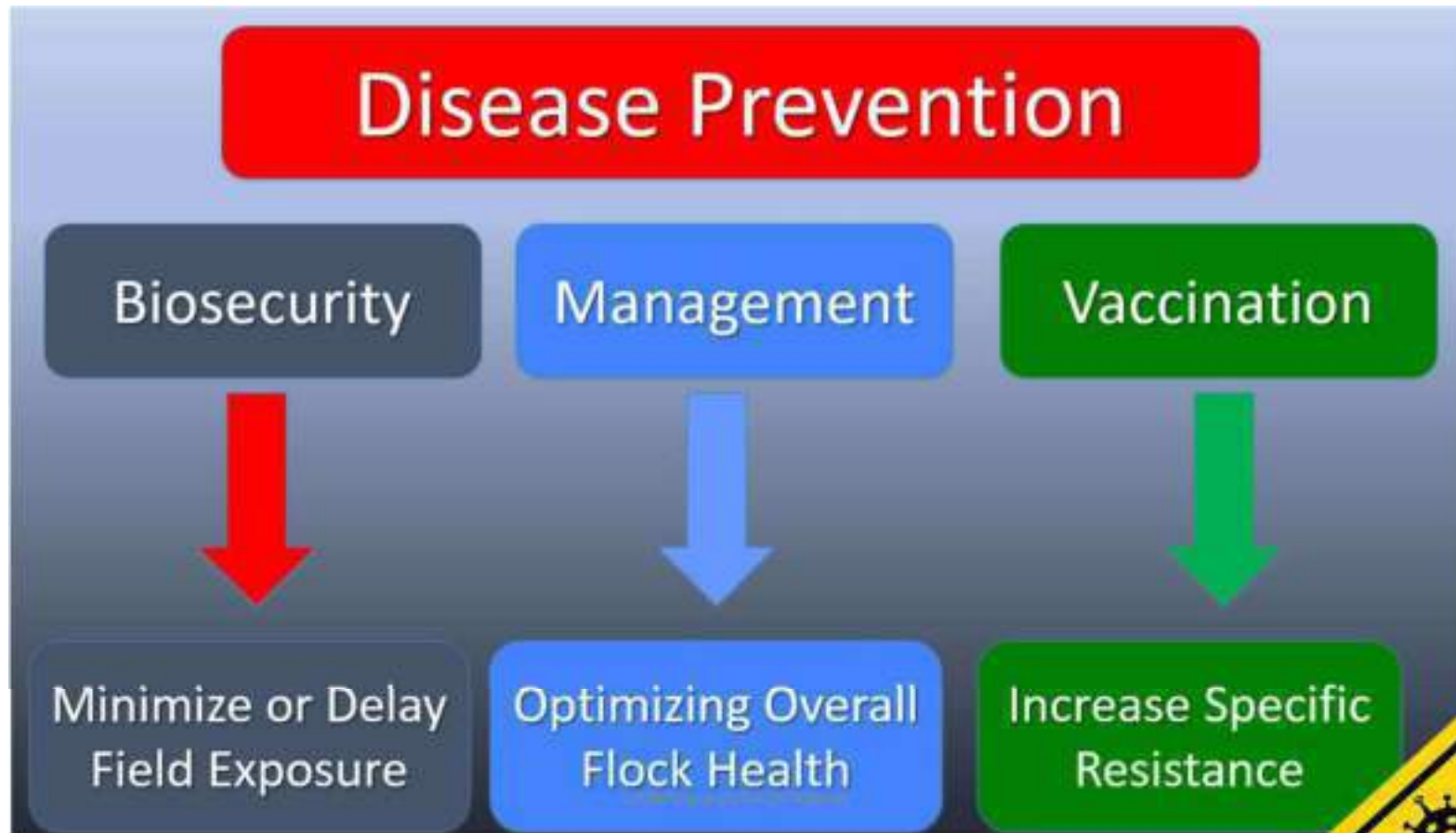


# Avian Host & Avian Reservoir



What are the possibilities ?  
8600+ species of birds worldwide





**SHAPING  
THE FUTURE**  
OF Poultry Sector

**Biosecurity - Biosecurity – Biosecurity**



# Take Home Message

- **Natural reservoirs of AIV infection are abundant & will not go away**
- **Disease surveillance & Early Detection** is the key to Control AIV Spread
- **Enhanced Biosecurity & Change of Farming Practice** are the best long term Strategy to Prevent AIV infection
- **Vaccination Strategy** (in addition to Mass Culling method) will be more effective to stop the rapid spread
- **Industry & Public Sector Corporation** is vital for Successful Control & Eradication
- A need of **Transparency & Openness** in Disease Information Exchange & Reporting
- **Need for a Global Approach in AI Control Strategy**





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**SHAPING  
THE FUTURE**  
OF INDIAN POULTRY SECTOR