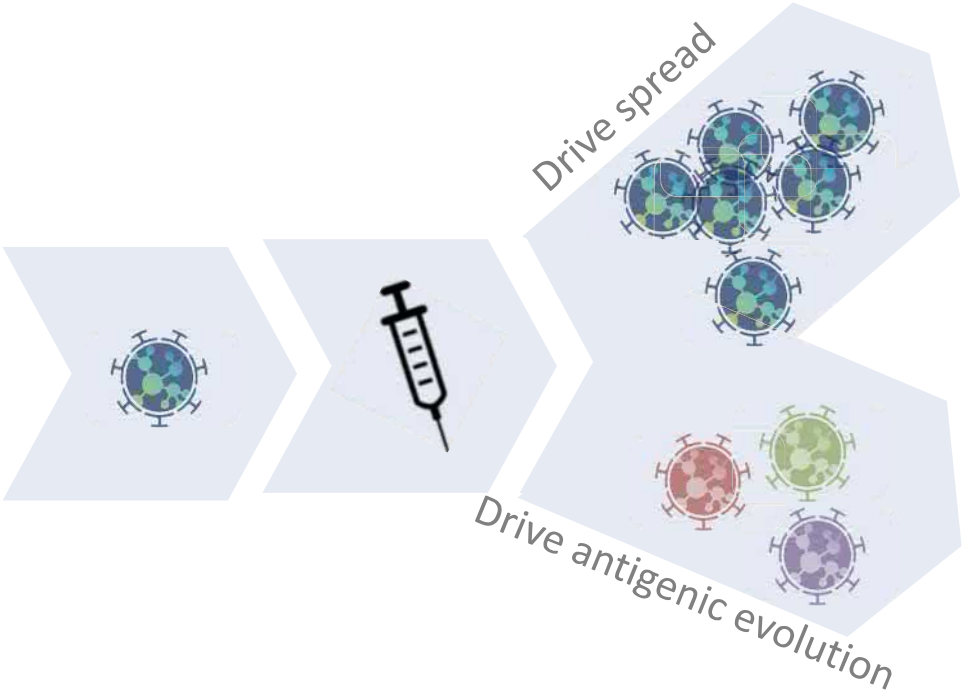
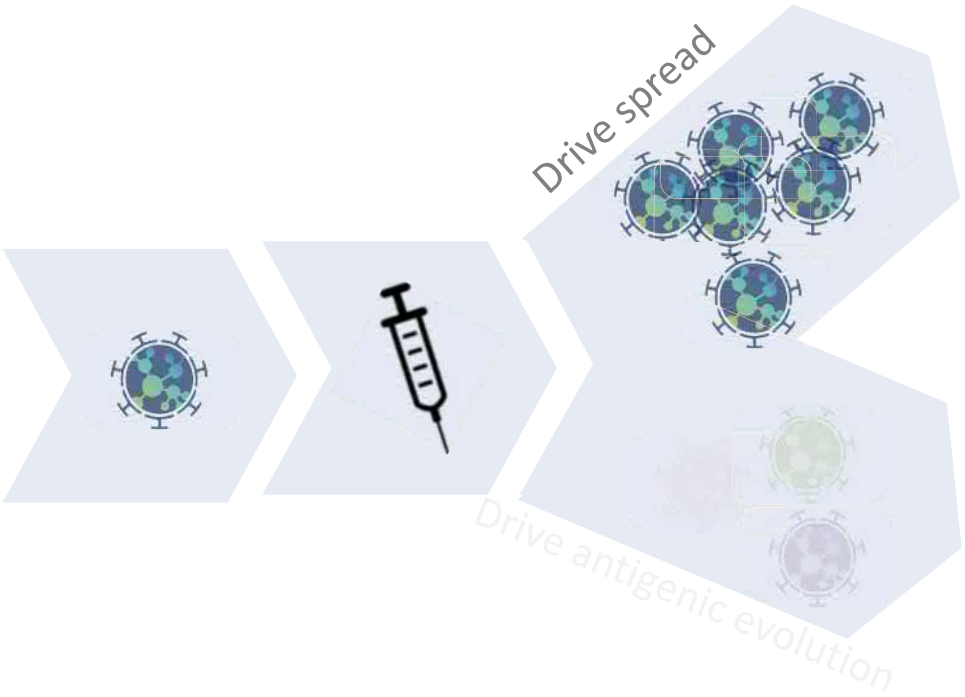
Public health considerations of avian vaccination

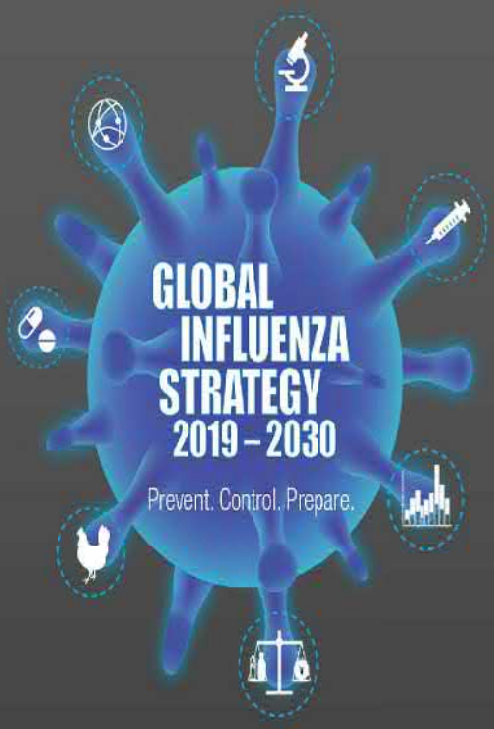
Richard Webby
WHO Collaborating Center for Studies on Ecology of Influenza
St Jude Children's Research Hospital
Memphis, US

Why would public health care?



Would increased or decreased (more likely?) spread impact risk?

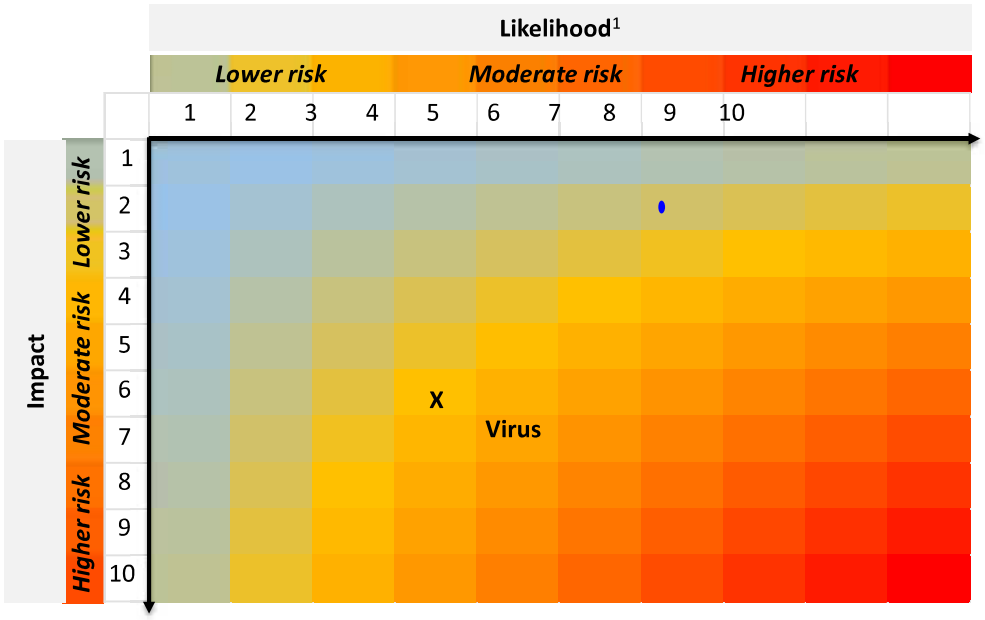




Tool for Influenza Pandemic Risk Assessment (TIPRA)

World Health Organization

WHO's TIPRA: prioritizing preparedness



Built on expert-defined elements

Public Health	1. Human infection 2. Disease severity 3. Population immunity
Animal Health	4. Geographical distribution in animals 5. Infection in animals
Virology	6. Receptor binding properties 7. Transmission in animal models 8. Susceptibility to antiviral treatment 9. Genomic characteristics

Likelihood risk elements

- Receptor binding properties
- Genomic characteristics
- Transmission in animal models
- Human infection
- Infection in animal
- Geographic distribution in animals

Impact risk elements

- Disease severity
- Population immunity
- Susceptibility to antiviral treatment
- Genomic characteristics
- Receptor binding properties
- Human infection

Two elements directly impacted by spread (others indirectly)

Public Health	1. Human infection 2. Disease severity 3. Population immunity
Animal Health	4. Geographical distribution in animals 5. Infection in animals
Virology	6. Receptor binding properties 7. Transmission in animal models 8. Susceptibility to antiviral treatment 9. Genomic characteristics

Likelihood risk elements

- Receptor binding properties
- Genomic characteristics
- Transmission in animal models
- Human infection
- Infection in animal
- Geographic distribution in animals

Impact risk elements

- Disease severity
- Population immunity
- Susceptibility to antiviral treatment
- Genomic characteristics
- Receptor binding properties
- Human infection

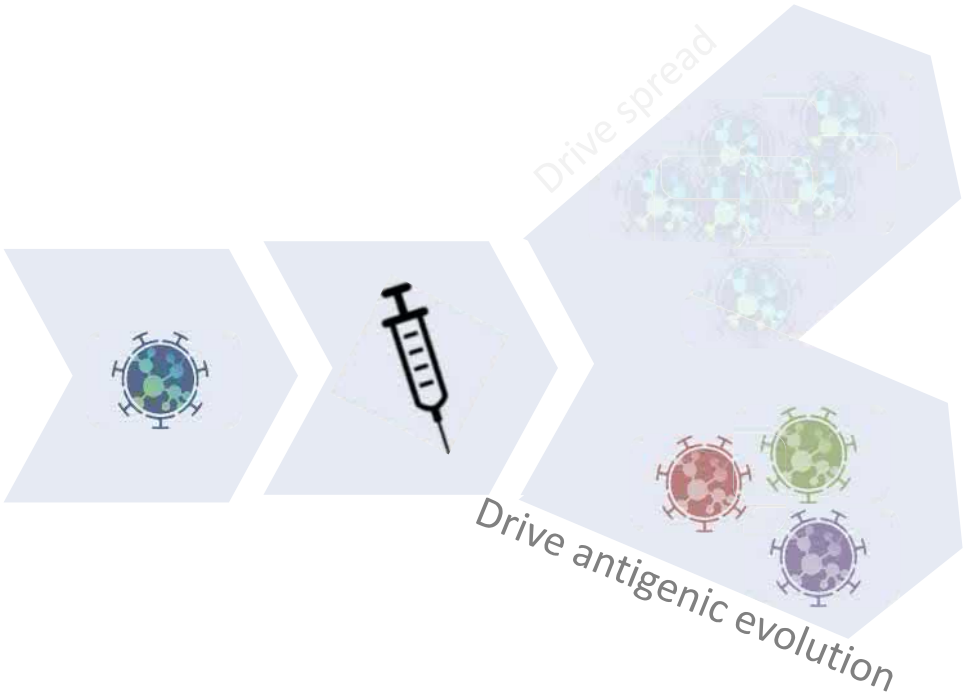
Geographic Distribution in Animals

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

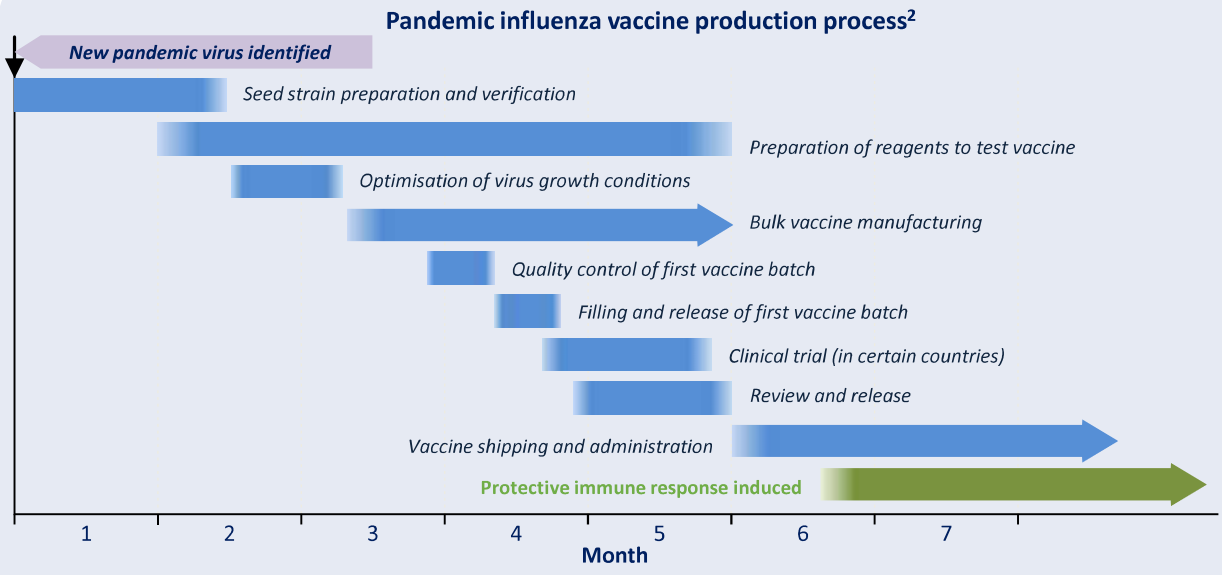
Infections in Animals

This element is defined as the ability of the virus to naturally infect animal[1] species. Factors to consider include the number and diversity of the species, the ability to maintain sustained natural transmission, the environment in which the animals are found (e.g., live poultry market, agricultural fair, back yard, zoo) and the potential for exposure between infected animals and humans.

Would increased antigenic evolution impact human health preparedness?

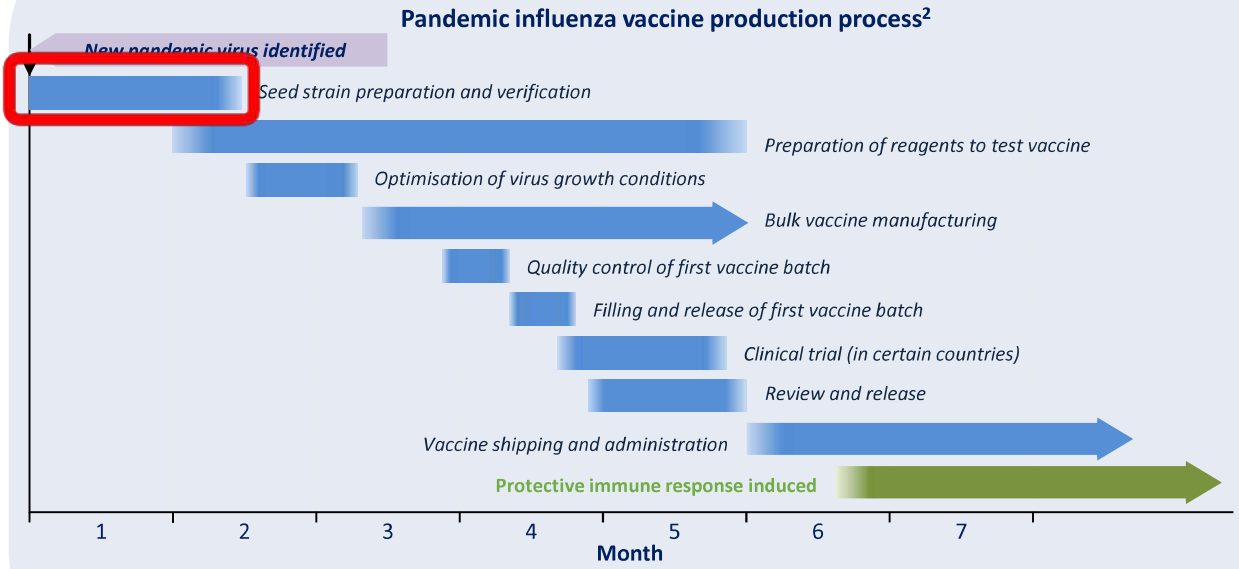


Pandemic influenza vaccine production processes



. *Nat Rev Drug Discov.* Advances in the development of influenza virus vaccines. Krammer F, Palese P. 2015.[2]

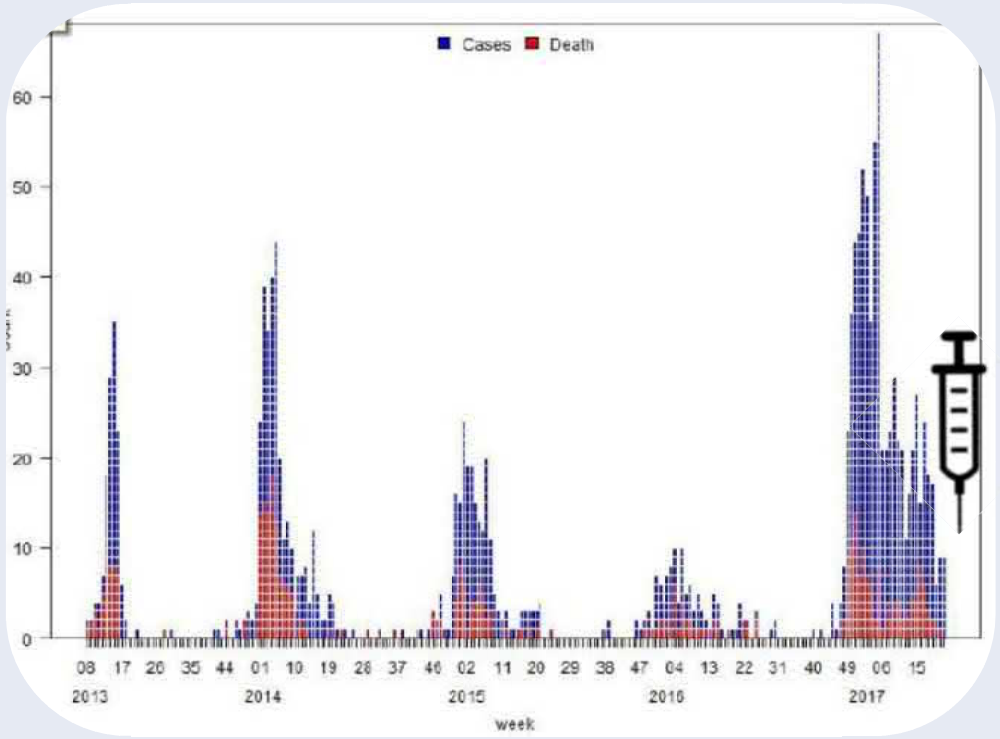
Systems are already in place to monitor antigenic evolution of avian viruses



. *Nat Rev Drug Discov.* Advances in the development of influenza virus vaccines. Krammer F, Palese P. 2015.[2]

This activity a partnership between human and animal health

A(H7N9): a success story?



Conclusions

Spread

- Increased vaccination of birds with robust programs has potential to lower public health risk.

- Primarily though altering exposure of humans to infected birds. Interface species more important.

Immune pressure

- Vaccine-induced pressure unlikely to inherently increase virus capacity to infect humans.

- Vaccine-induced pressure may drive antigenic evolution of the virus, but systems are in place to monitor this. But can always do with improving.

AVIAN INFLUENZA VACCINATION IN FIELD SITUATIONS ESPECIALLY FOR EMERGENCY USE

CAROL CARDONA, BS POMEROY CHAIR IN AVIAN HEALTH
UNIVERSITY OF MINNESOTA, COLLEGE OF VETERINARY MEDICINE

BACKGROUND

- I'm an academic, always have been. My views and opinions are those of third party observer.
- I started my career in California and am now in Minnesota.
- I like working with flu but I don't like what it does to poultry.
- I'm a veterinarian and an advocate for the engagement of qualified poultry veterinarians in the control of poultry diseases, especially avian influenza.

OBJECTIVES

- Tell you a story about a LPAI outbreak that still has relevant lessons
- Where to find the expertise and experience to vaccinate and immunize poultry in their varied settings
- A proposal for private engagement
- And a way to move forward

EXPERIENCE IN THE US IS WITH LPAI VACCINATION

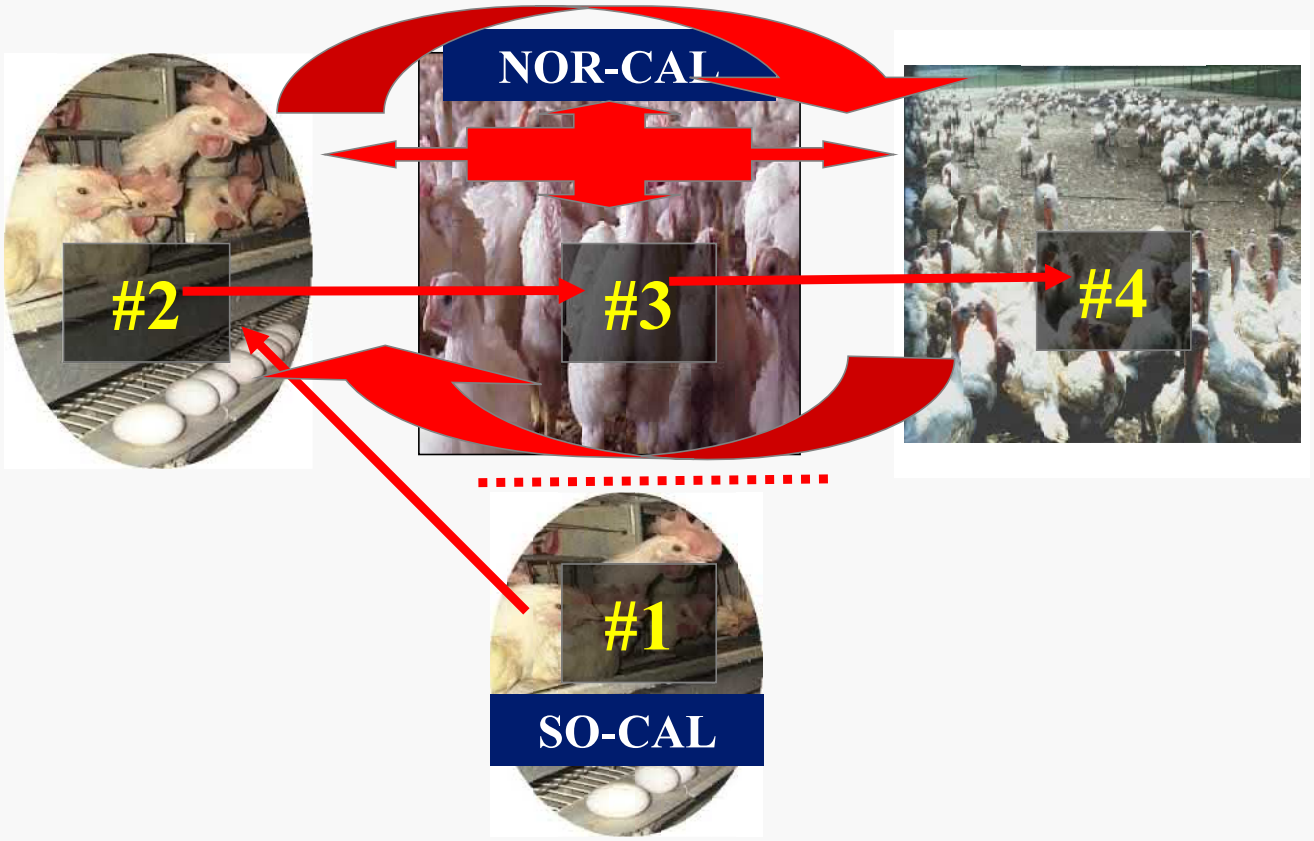
- Not irrelevant but clearly not the same as HPAI vaccination
- The difference, outside of trade implications, comes down to viral transmissibility.
  - Lower infectious doses mean both increased transmissibility but also the need for better immunity to assure protection
- Some LPAIV have been (almost) as transmissible as HPAIV and thus, serve as good models.
  - H7N2 Connecticut
  - H6N2 California

CALIFORNIA AND H6N2, VACCINATION THAT FAILED THEN SUCCEEDED

- California had an H6N2 LPAI outbreak from 2000-2005 that spread and spread and spread
- They vaccinated
  - At first with a mismatched vaccine
    - Allowed the virus to continue to circulate
    - Left flocks susceptible to later infections, which happened
    - Immunity was not tracked
  - At first only layers were impacted
    - No movement controls were in place
    - No end game in place
    - Vaccination was used to prevent egg production losses

SPREAD OF THE OUTBREAK

- The outbreak was localized to egg layers in Southern California
- And then, a company purchased and subsequently closed a spent fowl processing plant in Southern California and spent fowl began to move into Northern California
- Without pre-movement testing, with poorly immunized flocks and new antigenic variants emerging, a fully adapted chicken virus made its way into broiler country



ONCE THE VIRUS WAS IN BROILERS, ALL BETS WERE OFF

- The poultry industry introduced its own movement restrictions and monitoring programs
- Layers:
  - S California layers no longer came to N California
  - N California began vaccinating pullets before movement to lay farms
  - Ended dangerous practices
- Turkeys:
  - Could be held on farm until seroconversion
- Broilers:
  - Only broke after 35 days of age
  - Had to be moved to processing while shedding
  - Cross commodity meetings held weekly to map movements

CASES SLOWED THEN DISAPPEARED

- The outbreak didn't end for another year after the industry control program began
- The California industry learned that monitoring immunity, determining infection status, and movement controls are essential for a vaccination program to succeed
- They also learned that they had to work together to control the outbreak

WHEN THEY DECIDE THEY'RE DONE WITH IT, THEY WILL END IT.

BOB ECKROADE ON HOW TO HELP THE POULTRY INDUSTRY END THE H6N2 OUTBREAK OF IAV

VACCINATION MUST BE A PUBLIC:PRIVATE PARTNERSHIP

- The poultry industry, each individual commodity, must be engaged to make any vaccination program successful
  - The goals of the program have to be agreed upon
    - Immunity may be difficult to achieve, is their commitment to it?
    - Vaccination can be a tool of eradication but only when everyone agrees
- The expertise and manpower to vaccinate is controlled by the poultry industry
  - Only the poultry industry can immunize its birds
  - And only if they want to

ENGAGING PRIVATE INDUSTRY FOR COLLECTIVE GOOD

- The expertise of private resources need to be somehow dedicated to the collective good of the industry and not for the good of an individual company or commodity.
- There may be things that private industry doesn't want to do such as
  - Deliver multiple doses of vaccine
  - Monitor vaccination
  - And monitoring for immunity
  - Perhaps culling of flocks
- In order to successfully eliminate virus, vaccination and immunity have to be equivalent in the field and it will not be easy

THE THREAT OF HPAI DIFFERS FOR EACH COMMODITY THUS TRIGGERS WILL DIFFER

- For the turkey commodity, which have suffered extensive outbreaks, the trigger has likely already been reached
- For broiler companies, which rely heavily on trade and have not experienced the level of outbreaks seen in commercial turkeys, the trigger is likely far away
- The trigger that is used will impact the potential for success of any mass vaccination program
- How can the commodities be engaged to find common ground on vaccination?

REGULATORY AGENCIES MUST ASSURE THAT HPAI DOES NOT CIRCULATE

- The private industry will have a lot to do in the event of HPAI vaccination but regulatory agencies will have the role and responsibility of monitoring for infections
- Providing the scientific basis for determining that virus is not present in an immune population
  - More testing
  - Perhaps use of sentinels
- Controlling the outbreak

IN CONCLUSION

- Consensus on the triggers and goals for the use of vaccination.
  - We need real conversations about triggers
- Implementation of programs with real experts.
  - Field vets, vaccine manufacturers, emergency management experts are needed to collectively undertake the challenges of HPAI vaccination in an emergency situation under a global microscope.
- Surveillance for immunity (and virus) in an ongoing and realistic way.
- The will and thus the funding to do it all.
  - Engage poultry decision makers in real conversations about the tipping points of when vaccination becomes necessary.

MOVING FORWARD

- In the face of a global challenge, we need to stick together
  - We need to remember what we already know
    - Well matched vaccines, delivered appropriately, and monitored can be an effective tool in disease control and eradication
- Its time to rethink the undeclared war called trade and how we can come together to effectively fight this scourge

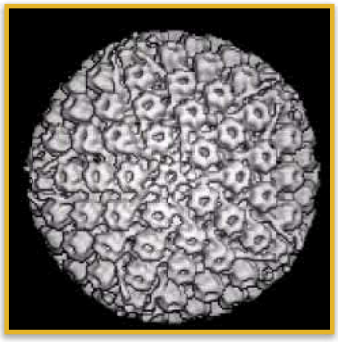
Universiteit Utrecht

DEPARTEMENT POPULATION HEALTH SCIENCES

Vaccination to control transboundary animal pathogens and relevance to Avian Influenza

Arjan Stegeman
Chair Farm Animal Health

Aujeszky's Disease virus: Herpesvirus with pigs as reservoir host



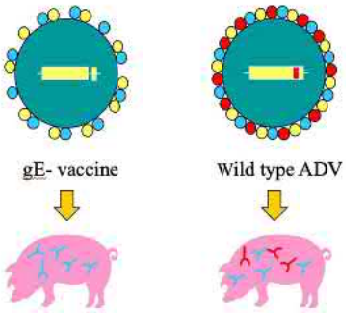
General opinion in 1980's : Vaccination is not a suitable tool to eradicate ADV

Experimental challenge of vaccinated pigs resulted in infection of pigs with subsequent virus excretion.

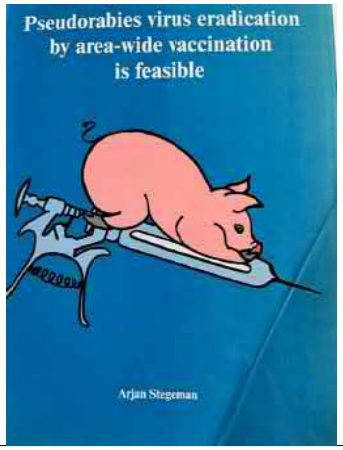
Voluntary vaccination had not resulted in reduced prevalence of infected pigs; >90% of the pig farms in the Netherlands ADV-infected

Stegeman, *Vet Q*, 1995

DIVA vaccine



Vaccination programme with high coverage

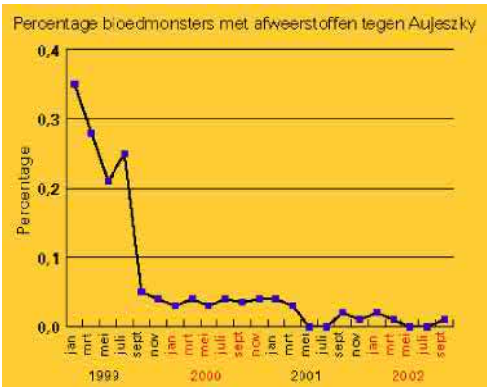


Vaccination does not need to be perfect to be an effective tool in infection control!

Utrecht University

Eradication of Aujeszky's Disease virus in the Netherlands by area-wide vaccination

1993: > 90% farms ADV-infected
2000: < 0.1 % infected
2002: officially free
(with vaccination)
2007 vaccination was stopped and no outbreaks have been observed since then



Has been successful in several other countries

Utrecht University

Elbers et al., *Vet Q*, 2000

Vaccination to control transboundary animal pathogens and relevance to Avian Influenza

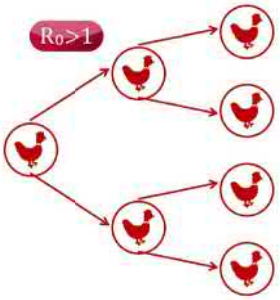
- Foot and Mouth Disease (FMD), picorna virus, cloven hoofed animals
- Classical Swine Fever (CSF), pestivirus, Suidae
- Newcastle Disease (ND), Avian orthoavulavirus 1, birds

Use of vaccination to prevent or control spread of a pathogen

- Stop transmission in an infected region
- Prevent infection in a free region at risk
- Stop spread in a previously free region upon reinfection (emergency vaccination)

To be effective as a stand- alone tool vaccination should reduce transmission: R<1

R_0, Basic Reproduction ratio: average number of secondary infections caused by one infected animal in a fully susceptible population



Heesterbeek et al., 2012

Vaccination as a stand-alone strategy may not always result in R<1

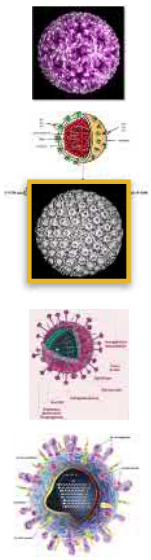
FMD: R<1 in cattle, R>1 in pigs

CSF: R<1

ADV: R<1 in sows, R>1 in finishing pigs

ND: R<1 under experimental condition; protection in field not always sufficient

AI: R<1 under experimental conditions; protection in field may be insufficient



Orsel et al, *Vaccine* 2005, 2007; de Smit et al, *Vaccine* 2001; van Nes et al, Vaccine *1997*, Stegeman et al, *AJVR* 1995, van Boven et al, *Av Path* 2008, Tatar-Kis et al., *Vaccines* 2020, Poetri et al, *Vaccine* 2009, *Res Vet Sci* 2014.

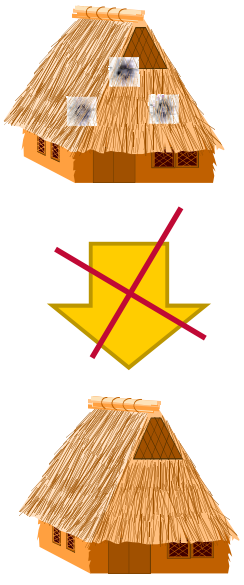
If R>1 in vaccinated populations introductions may result in outbreaks, but between-farm spread may still be stopped

Proportion of introductions resulting in an outbreak decreases (1-1/R).

Proportion of animals affected in an outbreak decreases.

Virus excretion in vaccinated animals decreases.

Vaccination is accompanied by surveillance, movement control and biosecurity



Utrecht University

Heesterbeek et al., 2012

Several other aspects may affect the effectiveness of vaccination programmes

Transboundary Disease	Carriers upon infection	Major exposure source	DIVA test	Quick mass application
Foot and mouth disease 	Yes	Domestic	Yes	Yes
Classical Swine Fever 	Yes	Domestic	No/Yes	Yes
Aujeszky's Disease 	Yes	Domestic	Yes	Yes
Newcastle Disease 	No	Domestic/wild birds	No	Yes
Avian Influenza 	No	Wild birds/ domestic	Yes	Yes/no

Utrecht University

Trade agreements for vaccinated regions differ from those for unvaccinated regions

Serological DIVA surveillance demonstrates infection/freedom in the past

Live animals (vaccinated but infected animals may not show disease) → quarantine

Consumer products (FMD and CSF) may contain virus and end up in feed; less relevant for ND and AI

Utrecht University

Conclusions (1)

- Vaccination does not need to be perfect to help eliminate virus circulation

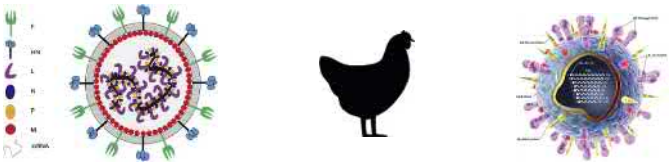
- Vaccination needs to be accompanied with adequate (DIVA) surveillance and biosecurity

- In trade agreements vaccinated animals often have a different status compared to unvaccinated animals

Conclusions (2)

- Vaccination against ND seems most relevant for AI (exposure, no carrier status)

- Important differences between AI and ND include possibilities for mass application, availability of DIVA tests and zoonotic potential



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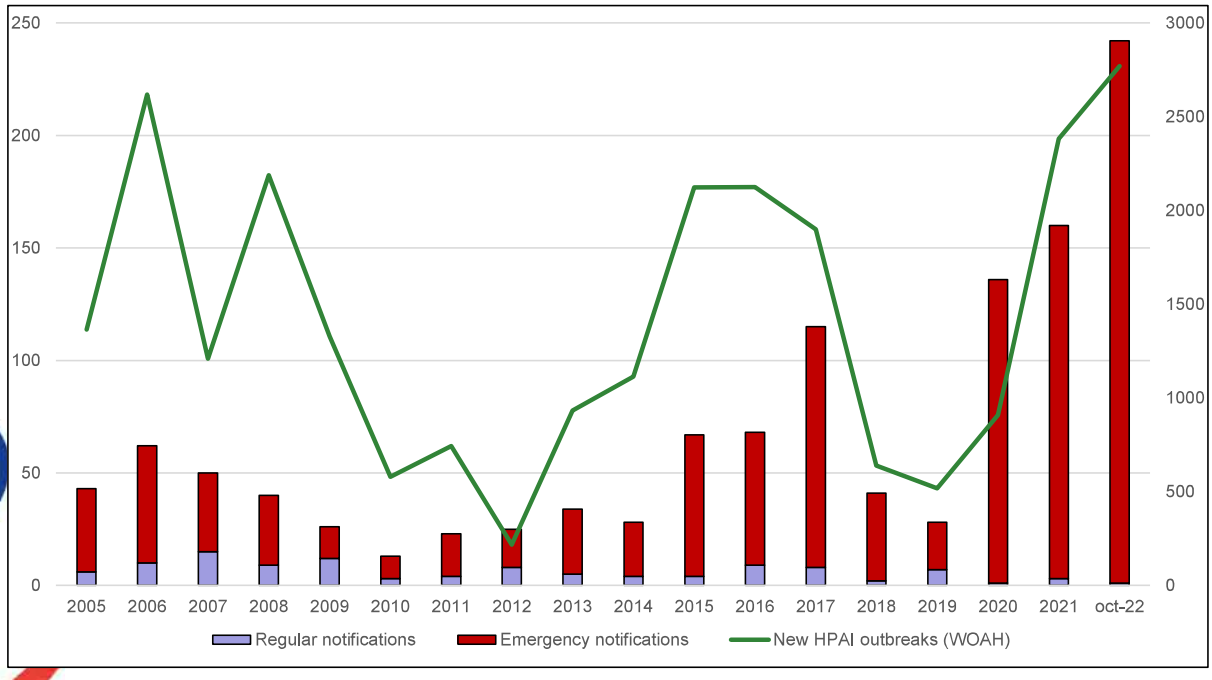
DISCLAIMER

De informatie in deze presentatie is met zorg samengesteld,
maar er kunnen geen rechten ontleend worden aan de inhoud.

WTO perspective of avian influenza and trade in poultry products

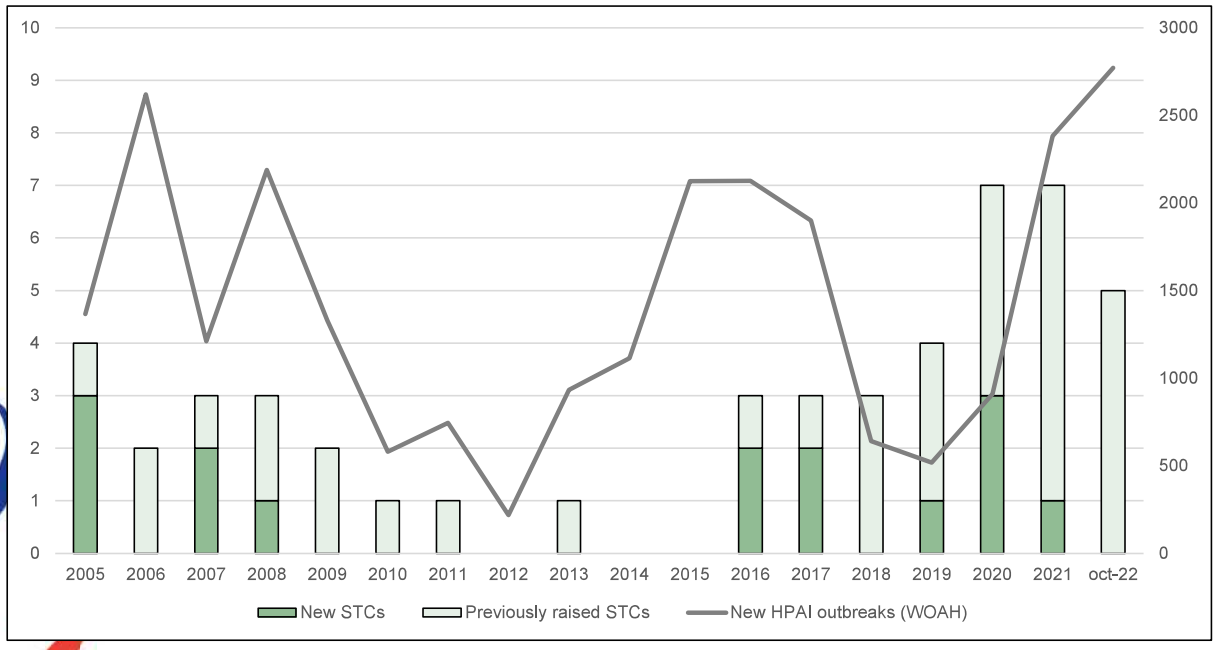
Christiane Wolff
SPS Section
Agriculture and Commodities Division
WTO

WTO Notifications on Avian Influenza* Measures and HPAI Outbreaks Notified to WOAH**



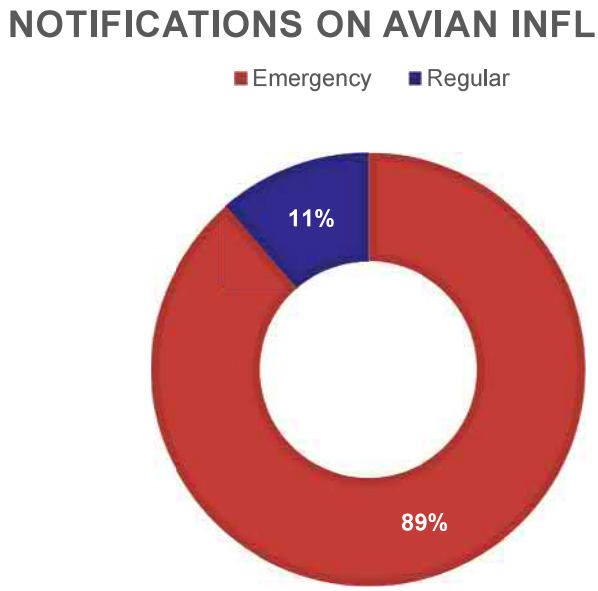
* Data from ePing SPS&TBT Platform.
** Data from the WOAH WAHIS system.

WTO SPS Specific Trade Concerns Related to Avian Influenza* and HPAI outbreaks notified to WOAH

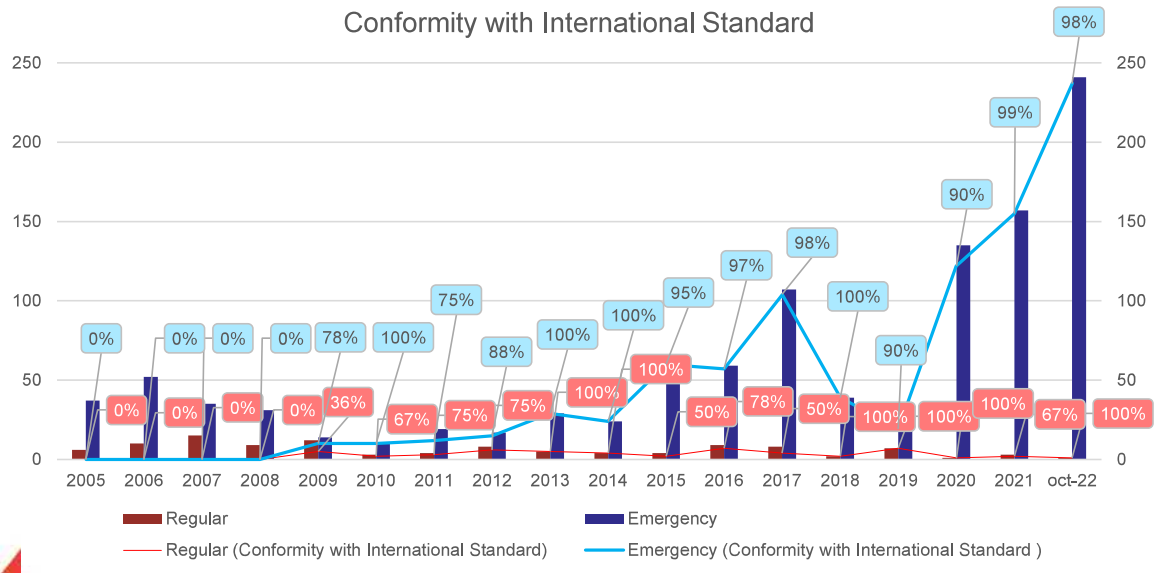


* "Avian Influenza" Keyword on the Trade Concerns Database.

WTO SPS Notifications on Avian Influenza

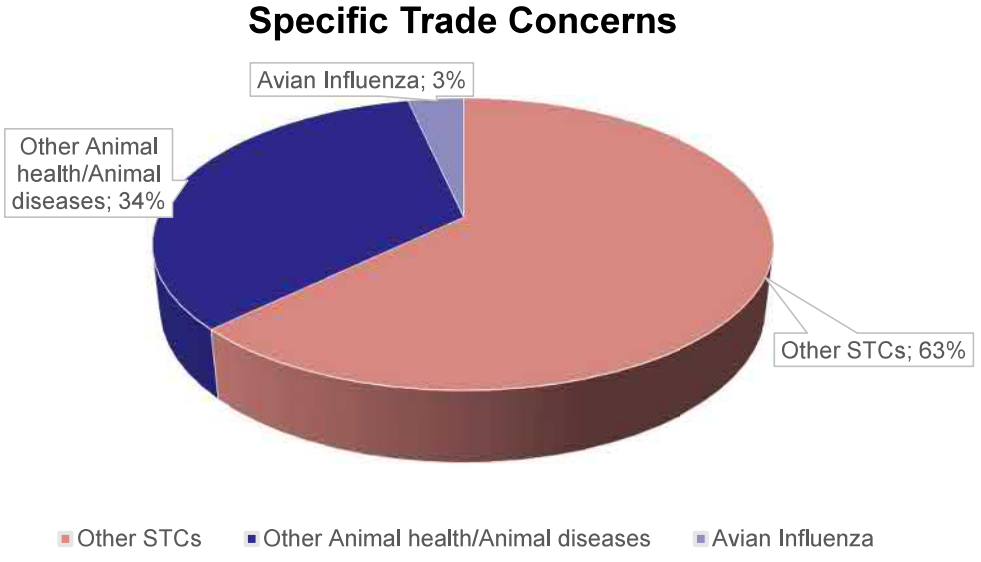


Conformity of Notified AI Measures with WOAH Standards



12 notifications referring to "vaccine" and "vaccination"

Share of Specific Trade Concerns Related to AI



19 STCs raised related to a keyword "Avian Influenza"
(of which **7** were reported as resolved or partially resolved)

Christiane.Wolff@wto.org

www.wto.org/sps

https://eping.wto.org/

Animal & Plant Health Agency

Options for vaccines for emergency use including Mass Applied Vaccines and Pharmaceutical intervention options available and what might be developed

Prof Ian Brown
Head of National and International Reference Laboratory for AI
UK disease expert
APHA
IABS 26TH October 2022
Paris

World Organisation for Animal Health
Founded as OIE

Emergency vaccination

- Option when there is evidence for AI introduction
- Epidemiological evidence supports massive introduction and spread of infection

Purpose

- Protective: vaccination to live
- Suppressive: vaccination to kill

- Protective requires monitoring and surveillance to detect infection in vaccinated flocks

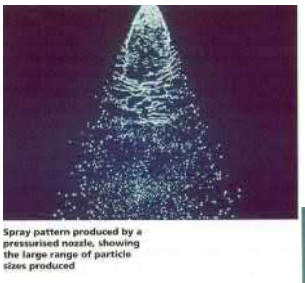
Vaccine requirements for use in an emergency programme

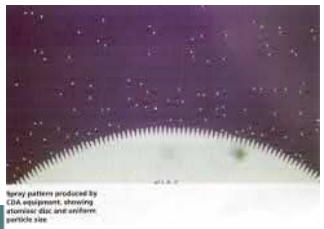
- Vaccine efficacious!
- Ease of delivery on scale to large numbers of birds
- Preferably does not transmit from flock to flock so replication incompetent
- Limited within flock transmission an advantage to enhance flock immunity
  - note not necessarily a problem when using a non-influenza vector.
- Safe
  - will not revert or reassort
- Approach
  - Farm level: as soon as there is an outbreak in one house all other houses are given an emergency spray of live vaccine virus?
  - Population level: targeted based on risk; sector type

Mass vaccination of poultry

Delivered via

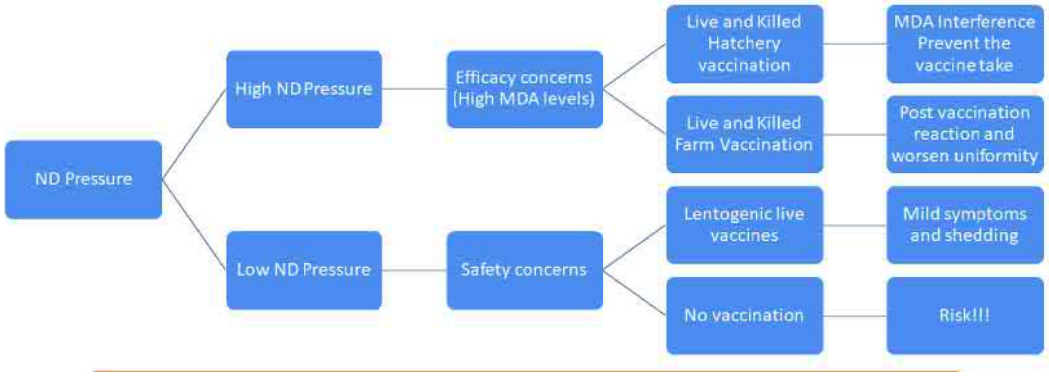
- Spray
- Drinking water
- Feed
- In ovo at hatchery


Spray pattern produced by a pressurised nozzle, showing the large range of particle sizes produced

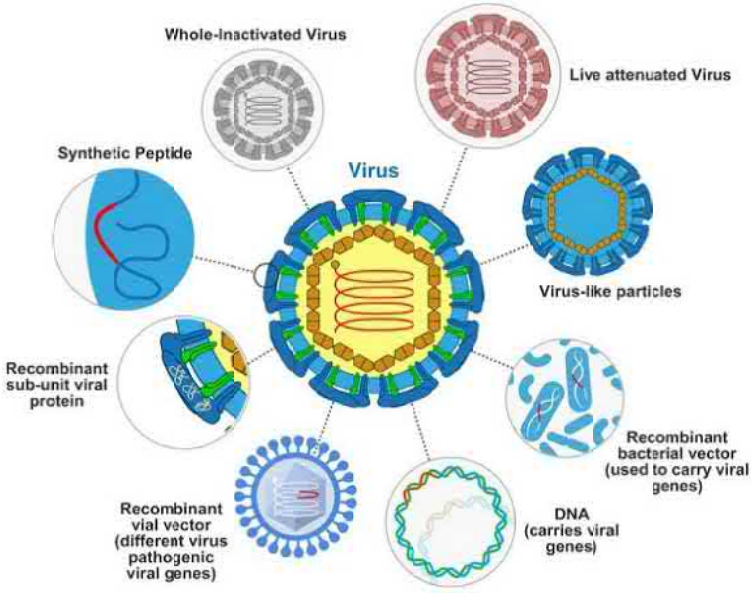

Spray pattern produced by CDA equipment, showing atomiser disc and uniform particle size


Diagrammatic representation of in-ovo administration of vaccine

Learn from experience with other pathogens including in poultry



Types of vaccines and utility for mass application



Inactivated vaccines generally poorly immunogenic when delivered by mass application

There are many other live virus attenuated avian vaccines that are delivered as live viruses (but also concerns about reassortment and recombination) - risk of reassortment for avian influenza must be excluded

Principle options: delivery to mucosal surfaces

- Live virus
- Live attenuated vaccine
- Inactivated vaccines for aerosol delivery
- Viral vectored vaccines
- Recombinant proteins
- Recombinant bacterial vector
- Plant based vectors

- Immune enhancement
- Enhancing regulatory gene expression

Animal & Plant Health Agency

Large body of research underpinning possible options but little taken to field/market

Live attenuated vaccines

- Influenza live wild type X
- Influenza live vaccines can “elicit higher levels of innate responses, mucosal IgA antibodies and heterologous protection compared to inactivated vaccines’
- Modified live influenza vaccines (MLIV) are able to induce a broad humoral (systemic and mucosal) and cellular immune response. Mimicking a natural infection and stimulating the immune system more broadly is advantageous for MLIVs
- MLIVs are based on apathogenic influenza viruses, and attenuation is achieved for example by
  - truncated NS1 proteins
  - restricted replication capacities IE due to cold-adaptation
  - introduction of elastase-specific cleavage sites into the HA precursor protein
- Vector-based vaccines can induce a broader protection than inactivated vaccine,
  - still challenging to express more than the HA protein in the vector backbone, as beneficial to include neuraminidase (NA), the matrix protein (M2), and the nucleoprotein (NP) for a broader and more effective immunity

Live attenuated vaccines: examples

Use of a low pathogenicity H5 virus

- Single administration via drinking water provided complete protection of 30-days-old chickens from lethal challenge with H5 HPAI virus.

Gambaryan A, Gordeychuk I, Boravleva E, Lomakina N, Kropotkina E, Lunitsin A, Klenk HD, Matrosovich M. Immunization of Domestic Ducks with Live Nonpathogenic H5N3 Influenza Virus Prevents Shedding and Transmission of Highly Pathogenic H5N1 Virus to Chickens. Viruses. 2018 Mar 31;10(4):164. doi: 10.3390/v10040164. PMID: 29614716; PMCID: PMC5923458.

- unlikely to get approval (fears of reassortment if used as an emergency vaccine)

Live attenuated vaccines

Attenuate via introduction of influenza gene constellations: 'cold adapted'

- Live attenuated H5N1 vaccine with cold adapted H9N2 internal genes protects (2 doses) chickens from infections by both High Pathogenicity H5N1 and H9N2 Influenza Viruses
  - In vaccinated chickens, IgA and IgG antibody subtypes were induced in lung and intestinal tissue, and CD4+ and CD8+ T lymphocytes expressing interferon-gamma were induced in the splenocytes.

Nang *et al.* (2013) Live attenuated H5N1 vaccine with H9N2 internal genes protects chickens from infections by both Highly Pathogenic H5N1 and H9N2 Influenza Viruses. Influenza and Other Respiratory Viruses 7(2) 120–131.

- Live attenuated influenza H7N3 vaccine is safe, immunogenic and confers protection in animal models

A/mallard/Netherlands/12/00 (H7N3) virus and A/Leningrad/134/17/57 (H2N2) master donor virus. Lack of H7N3 LAIV replication in chicken demonstrated complete safety of this preparation for poultry.

Rekstin A, Desheva Y, Kiseleva I, Ross T, Swayne D, Rudenko L. Live Attenuated Influenza H7N3 Vaccine is Safe, Immunogenic and Confers Protection in Animal Models. Open Microbiol J. 2014 Dec 31;8:154-62. doi: 10.2174/1874285801408010154. PMID: 25685247; PMCID: PMC4323838.

Live attenuated vaccines

Genome manipulation: enable replication and HA cleavage modification to LPAI

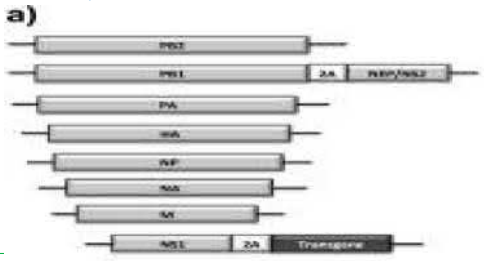
- Cross-clade protective immune responses of NS1-truncated live attenuated H5N1 avian influenza vaccines/HA modified
- A 70-aa amino-terminal fragment of NS1 protein may be long enough for viral replication.
- The recombinant virus was a broad-spectrum live attenuated H5N1 avian influenza vaccine candidate in chicken

Shi et al 2016 Vaccine Volume 34, Issue 3, 12 January 2016, Pages 350-357; DO - 10.1016/j.vaccine.2015.11.045

A modified low pathogenicity virus

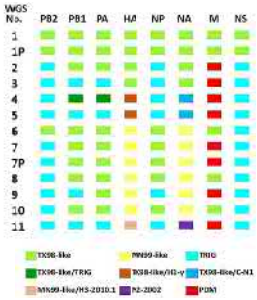
- Rearranged the genome of an avian H9N2 influenza virus
- expressed the entire H5 hemagglutinin open reading frame (ORF) from the segment 8 viral RNA.
- Vectors had reduced polymerase activities as well as viral replication *in vitro* and excellent safety profiles *in vivo*.
- Immunization with the dual H9-H5 influenza virus resulted in protection against lethal H5N1 challenge in mice and ferrets,
- H5 HA is expressed from the H9N2-H5 virus as a chimeric HA segment with the packaging signals of the NS gene, the possibility of reassortment of the H5 HA is considered remote

Pena L, Sutton T, Chockalingam A, Kumar S, Angel M, Shao H, Chen H, Li W, Perez DR. Influenza viruses with rearranged genomes as live-attenuated vaccines. J Virol. 2013 May;87(9):5118-27. doi: 10.1128/JVI.02490-12. Epub 2013 Feb 28. PMID: 23449800; PMCID: PMC3624320.



Experiences of use of live attenuated influenza vaccines in animals

- Live attenuated swine influenza vaccines USA-introduced 2017
- Reassortment with endemic swine viruses in 2018



Sharma A, Zeller MA, Li G, Harmon KM, Zhang J, Hoang H, Anderson TK, Vincent AL, Gauger PC. Detection of live attenuated influenza vaccine virus and evidence of reassortment in the U.S. swine population. J Vet Diagn Invest. 2020 Mar;32(2):301-311. doi: 10.1177/1040638720907918. Epub 2020 Feb 26. PMID: 32100644; PMCID: PMC7081507.

Implications:

If similar viruses used only as an emergency product less chance of reverting to virulence or becoming established in poultry??

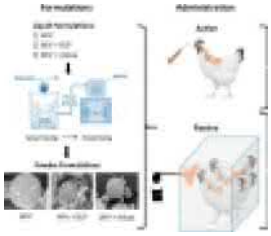
However still concerns about reassortment if applied as an emergency product

Inactivated vaccines for aerosol delivery?

- Pulmonary immunization of chickens using non-adjuvanted spray-freeze dried whole inactivated virus vaccine
- proof-of-concept that pulmonary vaccination protects
  - using non-adjuvanted spray-freeze-dried whole inactivated virus powder vaccine is able to protect chickens from lethal H5N1 HPAI challenge.

Recognised efficacy of pulmonary vaccination by passive inhalation can be improved, this method might be suitable for mass application

Peeters et al 2014 Vaccine Volume 32, Issue 48, 12 November 2014, Pages 6445-6450; DO - 10.1016/j.vaccine.2014.09.048



- Enhanced passive inhalation using Bacterium-like Particles (BLP) with all vaccinated animals surviving a lethal influenza challenge (large reduction in shedding)

Tomar J, Biel C, de Haan CAM, Rottier PJM, Petrovsky N, Frijlink HW, Huckriede A, Hinrichs WLJ, Peeters B. Passive inhalation of dry powder influenza vaccine formulations completely protects chickens against H5N1 lethal viral challenge. Eur J Pharm Biopharm. 2018 Dec;133:85-95. doi: 10.1016/j.ejpb.2018.10.008. Epub 2018 Oct 9. PMID: 30312742; PMCID: PMC7126314.

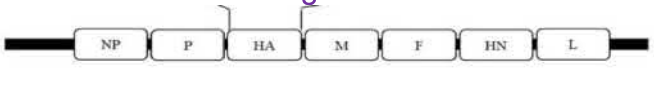
Authors concluded effective and suitable for mass vaccination of chickens if it can be adapted to field settings.

A viral vector that can be delivered by spray

Challenge is to overcome use of a vector to which there is already flock immunity. Any unintended consequences of using a virus of this type ?

Example approaches

- Avian paramyxovirus serotype 2 (APMV-2) as a vector for developing an H9N2 vaccine via intranasal delivery.
- Conferred complete immune protection to prevent viral shedding in the oropharyngeal and cloacal swabs from chickens challenged with H9N2 virus



Yang W, Dai J, Liu J, Guo M, Liu X, Hu S, Gu M, Hu J, Hu Z, Gao R, Liu K, Chen Y, Liu X, Wang X. Intranasal Immunization with a Recombinant Avian Paramyxovirus Serotypes 2 Vector-Based Vaccine Induces Protection against H9N2 Avian Influenza in Chicken. Viruses. 2022 Apr 28;14(5):918. doi: 10.3390/v14050918. PMID: 35632659; PMCID: PMC9144924.

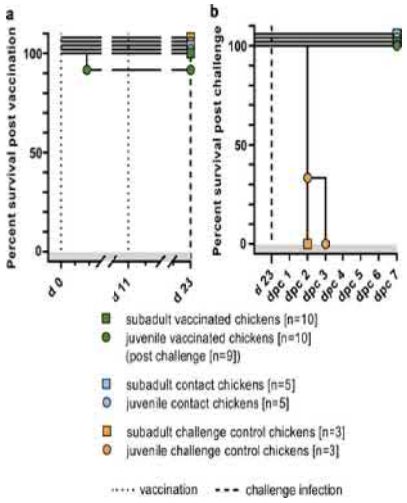
- Immunization of chickens with rAPMV-3 expressing HA protein induced higher level of neutralizing antibodies compared to that of rNDV expressing HA protein

Shirvani, E., Varghese, B.P., Paldurai, A. et al. A recombinant avian paramyxovirus serotype 3 expressing the hemagglutinin protein protects chickens against H5N1 highly pathogenic avian influenza virus challenge. Sci Rep 10, 2221 (2020). https://doi.org/10.1038/s41598-020-59124-x

Vector vaccine utilising an influenza platform?

A bat orthomyxovirus vector: concerns about reassortment?

- generate reassortment incompatible vaccines
- A bat-origin H17N10 shows an incompatibility of the bat influenza packaging signal with conventional IAVs, and therefore reassortment events between bat influenza and AIV are not possible
- MLIV prototype, based on the H17N10 bat influenza virus.
  - H17N10 chimeric virus carrying the NA and HA (modified cleavage site from polybasic to monobasic) genomic segments of H5N1
- Chimeric vaccine strain R65$_{mono}$/H17N10 was able to provide full protection against a lethal challenge infection with HPAIV H5N1 after oronasal immunization.



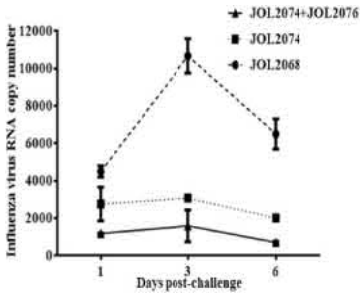
Schön, J., Ran, W., Gorka, M. *et al.* A modified live bat influenza A virus-based vaccine prototype provides full protection against HPAIV H5N1. *npj Vaccines* **5**, 40 (2020). https://doi.org/10.1038/s41541-020-0185-6

Other vectors yet to be used (adeno? other?) again issues of protective immunity and unintended consequences

Delivery of vaccines via drinking water

Oral vaccines could work but need to be constructed in a way that stimulates immunity -eg Salmonella vector or a subunit attached to an immunostimulant

- Salmonella Gallinarum delivering M2eCD40L can act as a bivalent vaccine against Fowl Typhoid and H9N2 infection
- further studies warranted to develop this SG-M2eCD40L vaccine as a broadly protective vaccine against avian influenza virus subtypes. Single shot reduced mortality (75%-12.5%)



Hajam IA, Kim J, Lee JH. Salmonella Gallinarum delivering M2eCD40L in protein and DNA formats acts as a bivalent vaccine against fowl typhoid and H9N2 infection in chickens. Vet Res. 2018 Oct 1;49(1):99. doi: 10.1186/s13567-018-0593-z. PMID: 30285855; PMCID: PMC6389227.

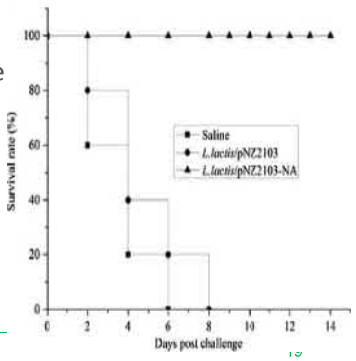
Oral vaccines via bacteria (contd)

Eg Lactobacillus modification and delivery

- oral vaccine based on Lactobacillus plantarum displaying the 3M2e-HA2 protein of the influenza virus
- Mucosal immunity induced with generally protective responses

Li QY, Xu MM, Dong H, Zhao JH, Xing JH, Wang G, Yao JY, Huang HB, Shi CW, Jiang YL, Wang JZ, Kang YH, Ullah N, Yang WT, Yang GL, Wang CF. Lactobacillus plantarum surface-displayed influenza antigens (NP-M2) with FliC flagellin stimulate generally protective immune responses against H9N2 influenza subtypes in chickens. Vet Microbiol. 2020 Oct;249:108834. doi: 10.1016/j.vetmic.2020.108834. Epub 2020 Aug 27. PMID: 32919197.

- Recombinant L.lactis/pNZ2103-NA in the absence of adjuvant was considered an effective mucosal vaccine against H5N1 infection in chickens via oral administration.
- Complete protection in chickens versus lethal challenge
- A platform for mass vaccination in poultry during A/H5N1/x panzootic



Lei H, Peng X, Ouyang J, Zhao D, Jiao H, Shu H, Ge X. Protective immunity against influenza H5N1 virus challenge in chickens by oral administration of recombinant Lactococcus lactis expressing neuraminidase. BMC Vet Res. 2015 Apr 2;11:85. doi: 10.1186/s12917-015-0399-4. PMID: 25880824; PMCID: PMC4389297.

Oral vaccines via bacteria

Indirect benefit by immune up regulation

oral administration of S. enterica serovar Typhimurium expressing chIFN-α can successfully control clinical signs caused by respiratory infection with AIV H9N2,

use of attenuated Salmonella vaccine as an oral delivery system of chIFN-α to prevent the replication of AIV H9N2 in respiratory tract

Rahman MM, Uyangaa E, Han YW, Kim SB, Kim JH, Choi JY, Yoo DJ, Hong JT, Han SB, Kim B, Kim K, Eo SK. Oral administration of live attenuated Salmonella enterica serovar Typhimurium expressing chicken interferon-α alleviates clinical signs caused by respiratory infection with avian influenza virus H9N2. Vet Microbiol. 2011 Dec 29;154(1-2):140-51. doi: 10.1016/j.vetmic.2011.06.034. Epub 2011 Jul 2. PMID: 21764226.

Other platforms for oral vaccine : yeast?

- Yeast display platform technology to prepare oral vaccine against lethal H7N9 virus (challenge in mice)
- Hemagglutinin (HA) of A/Anhui/1/2013 (AH-H7N9) is used as a model antigen
- expression on the surface of Saccharomyces cerevisiae (S.cerevisiae) EBY 100
- significant titers of IgG antibody as well as significant amounts of cytokines IFN-γand IL-4.

Lei H, Xie B, Gao T, Cen Q, Ren Y. Yeast display platform technology to prepare oral vaccine against lethal H7N9 virus challenge in mice. Microb Cell Fact. 2020 Mar 2;19(1):53. doi: 10.1186/s12934-020-01316-1. PMID: 32122351; PMCID: PMC7053147.

Plant based systems for use in feed?

Recently, plant expression systems have gained interest as an alternative for the production of vaccine antigens.

Subunit vaccines from plants can be produced for a low cost, and plant production systems are easily scaled up at low infrastructure cost.

Subunit vaccines generally induce low immunogenicity against influenza

- Nicotiana benthamiana. The construct was cloned into a Cowpea mosaic virus (CPMV)-plus gene regulation enhancers.
- rHA0 maintained its native antigenicity and specificity, providing a good source of vaccine antigen to induced immune response in poultry

Kanagarajan S, Tolf C, Lundgren A, Waldenström J, Brodelius PE (2012) Transient Expression of Hemagglutinin Antigen from Low Pathogenic Avian Influenza A (H7N7) in *Nicotiana benthamiana*. PLoS ONE 7(3): e33010. https://doi.org/10.1371/journal.pone.0033010

- M2e conserved virus protein. Relatively high yield holds promise for the development of a duckweed-based expression system to produce an edible vaccine against avian influenza?

Firsov, A., Tarasenko, I., Mitiouchkina, T. *et al.* High-Yield Expression of M2e Peptide of Avian Influenza Virus H5N1 in Transgenic Duckweed Plants. *Mol Biotechnol* **57**, 653–661 (2015). https://doi.org/10.1007/s12033-015-9855-4

Agents that stimulate innate immunity or perhaps some cross immunity

Options include

- H9N2 but will this generate sufficient response to stop a subsequent H5 virus from replicating.
  - Issues regarding reassortment.
- Toll-like receptor agonists

Ie novel chicken adjuvant with potent immune-potentiating capability by incorporating avian toll-like receptor 21 agonist nanoparticle platform

This enhanced immune stimulation benefits from high stability and controlled release of internal component of nanoparticles that improve cellular delivery, lymphoid organ targeting and sustainable

Lin SY, Yao BY, Hu CJ, Chen HW. Induction of Robust Immune Responses by CpG-ODN-Loaded Hollow Polymeric Nanoparticles for Antiviral and Vaccine Applications in Chickens. Int J Nanomedicine. 2020 May 11;15:3303-3318. doi: 10.2147/IJN.S241492. PMID: 32494131; PMCID: PMC7227821.

Learn from other hosts: dogs

- Wheat W, Chow L, Kuzmik A, Soontararak S, Kurihara J, Lappin M, Dow S. Local immune and microbiological responses to mucosal administration of a Liposome-TLR agonist immunotherapeutic in dogs. BMC Vet Res. 2019 Sep 13;15(1):330. doi: 10.1186/s12917-019-2073-8. PMID: 31519215; PMCID: PMC6743184.

Vectors that stimulate production of relevant interferons (experience from other sectors)

- Kim A, Lee G, Hwang JH, Park JH, Lee MJ, Kim B, Kim SM. BacMam Expressing Highly Glycosylated Porcine Interferon Alpha Induces Robust Antiviral and Adjuvant Effects against Foot-and-Mouth Disease Virus in Pigs. J Virol. 2022 Jun 22;96(12):e0052822. doi: 10.1128/jvi.00528-22. Epub 2022 May 23. PMID: 35604219; PMCID: PMC9215255.
- Kim A, Lee G, Hwang JH, Park JH, Lee MJ, Kim B, Kim SM. BacMam Expressing Highly Glycosylated Porcine Interferon Alpha Induces Robust Antiviral and Adjuvant Effects against Foot-and-Mouth Disease Virus in Pigs. J Virol. 2022 Jun 22;96(12):e0052822. doi: 10.1128/jvi.00528-22. Epub 2022 May 23. PMID: 35604219; PMCID: PMC9215255.

Immunomodulation and intracellular delivery of antigen/adjuvant by nanocarriers eliciting enhanced T cell responses

Barman S, Borriello F, Brook B, Pietrasanta C, De Leon M, Sweitzer C, Menon M, van Haren SD, Soni D, Saito Y, Nanishi E, Yi S, Bobbala S, Levy O, Scott EA, Dowling DJ. Shaping Neonatal Immunization by Tuning the Delivery of Synergistic Adjuvants via Nanocarriers. ACS Chem Biol. 2022 Sep 16;17(9):2559-2571. doi: 10.1021/acschembio.2c00497. Epub 2022 Aug 26. PMID: 36028220; PMCID: PMC9486804.

Enhancing immune modulators

- The rational design of novel mucosal-inactivated vaccines against AIV
  - requires a comprehensive knowledge of the structure and function of the lung-associated immune system in birds in order to target vaccines appropriately and to design efficient mucosal adjuvants.

ie Toll like receptors (TLR) ligand as AIVs adjuvants can activate dendritic cells to improve immune responses

- Zhang A, Li D, Song C, Jing H, Li H, Mi J, Zhang G, Jin S, Ren X, Huangfu H, Shi D, Chen R. Evaluation of different combination of pam2CSK4, poly (I:C) and imiquimod enhance immune responses to H9N2 avian influenza antigen in dendritic cells and duck. PLoS One. 2022 Jul 19;17(7):e0271746. doi: 10.1371/journal.pone.0271746. PMID: 35853030; PMCID: PMC9295992.
- Singh SM, Alkie TN, Nagy É, Kulkarni RR, Hodgins DC, Sharif S. Delivery of an inactivated avian influenza virus vaccine adjuvanted with poly(D,L-lactic-co-glycolic acid) encapsulated CpG ODN induces protective immune responses in chickens. Vaccine. 2016 Sep 14;34(40):4807-13. doi: 10.1016/j.vaccine.2016.08.009. Epub 2016 Aug 16. PMID: 27543454.

Enhancing immune modulators

- Bacterially synthesized modular capsomere comprising influenza M2e, previously shown to confer complete protection in challenged mice, for application in poultry.

Wibowo et al (2015). Non-chromatographic preparation of a bacterially produced single-shot modular virus-like particle capsomere vaccine for avian influenza Vaccine; Volume 33, Issue 44, https://doi.org/10.1016/j.vaccine.2015.08.100.

- Salmonella typhimurium flagellin-based hemagglutinin globular head (HA1) fusion proteins and characterized their immunogenicity and efficacy. HA1-ΔfliC can protect chickens against H9N2 AIV by eliciting the efficient mucosal immune responses.

Wang T, Wei F, Liu L, Sun Y, Song J, Wang M, Yang J, Li C, Liu J. Recombinant HA1-ΔfliC enhances adherence to respiratory epithelial cells and promotes the superiorly protective immune responses against H9N2 influenza virus in chickens. Vet Microbiol. 2021 Nov;262:109238. doi: 10.1016/j.vetmic.2021.109238. Epub 2021 Sep 15. PMID: 34560407.

RNA vaccines for the future; application to AI

- Delivery of RNA vaccines using an ND vector

mRNA vaccines consists in the intramuscular injection of an mRNA encoding a vaccine antigen

SARS-CoV-2, the S protein model for HPAI?

translation into protein that is presented to the immune system

stimulation of antigen-specific T and B cells, generating protective antibody and T cell responses.

García-Sastre A. Mucosal delivery of RNA vaccines by Newcastle disease virus vectors. Curr Res Immunol. 2022;3:234-238. doi: 10.1016/j.crimmu.2022.10.001. Epub 2022 Oct 11. PMID: 36245642; PMCID: PMC9552541.

- new generation of intranasally administered HPAI vaccines to stimulate protective mucosal immunity
- vaccine vectors consist on the use of a harmless avian negative strand RNA virus to deliver intranasally a self-replicating RNA expressing the vaccine antigen in the cells of the respiratory mucosa.
- Initially applied to SARs-CoV2

Recombinant protein technology

- Rapid expression of HA immunogens in mammalian cells from emerging influenza strains.

Lu H, Khurana S, Verma N, Manischewitz J, King L, Beigel JH, Golding H. A rapid Flp-In system for expression of secreted H5N1 influenza hemagglutinin vaccine immunogen in mammalian cells. PLoS One. 2011 Feb 28;6(2):e17297. doi: 10.1371/journal.pone.0017297. PMID: 21386997; PMCID: PMC3046144.

- M2e and HA2-specific immunity in chicken to develop broad protective influenza vaccine against HPAI H5N1 expressed in e coli

Kalaiyarasu S, Bhatia S, Mishra N, Senthil Kumar D, Kumar M, Sood R, Rajukumar K, Ponnusamy B, Desai D, Singh VP. Elicitation of Highly Pathogenic Avian Influenza H5N1 M2e and HA2-Specific Humoral and Cell-Mediated Immune Response in Chicken Following Immunization With Recombinant M2e-HA2 Fusion Protein. Front Vet Sci. 2021 Feb 5;7:571999. doi: 10.3389/fvets.2020.571999. PMID: 33614753; PMCID: PMC7892607

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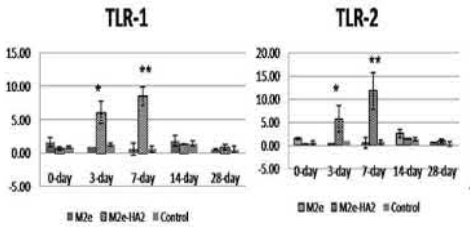


Key conclusions

- Substantial research effort at global scale
- Some of these options provide innovation for possible improved prevention and control of HPAI
- How do we consider these options and feed into next generation approaches?
- 21st century science for 21st century solutions

Animal & Plant Health Agency

Thank you for your attention

IABS Meeting on High Pathogenicity Avian Influenza
OCTOBER 25 - 26, 2022
Paris, France

"Cull plus vaccination"—a strategy adopted in China for highly pathogenic avian influenza control

Hualan Chen

Harbin Veterinary Research Institute, CAAS, China

Topics

- H5 influenza control in China.
- H7N9 influenza control in China.

China is the largest poultry-producing country in the world

- Over 17 billion poultry, including 4 billion ducks, are reared annually in China.



China is the largest poultry-producing country in the world

- Over 17 billion poultry, including 4 billion ducks, are reared annually in China.
- Many birds, especially ducks and geese, are often reared in open fields with no biosecurity measures, which could be easily attacked by wild bird viruses.

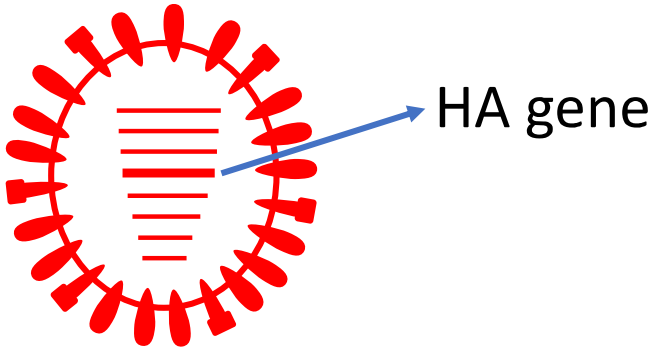


Avian influenza control strategies

- Many countries in Europe and North America control highly pathogenic influenza by culling infected and suspected poultry.
- Some countries, including China, have adopted a "cull plus vaccination" strategy.

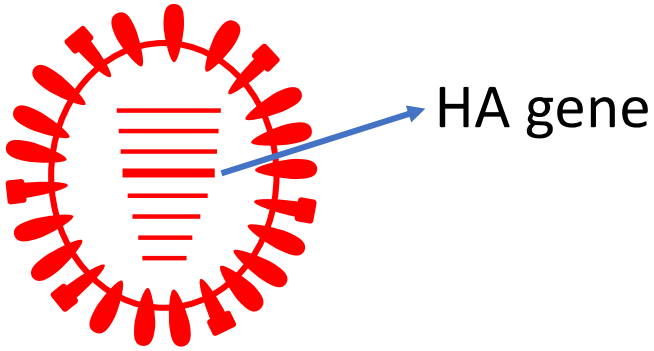
Challenge for the vaccination strategy

- Influenza virus mutates easily, and mutation of the HA gene often causes antigenic variation, which compromises the protective efficacy of vaccine.



Challenge for the vaccination strategy

- Influenza virus mutates easily, and mutation of the HA gene often causes antigenic variation, which compromises the protective efficacy of vaccine.
- The biggest challenge for the vaccination strategy is ensuring that the vaccine matches the circulating virus.



Surveillance and analysis the strains

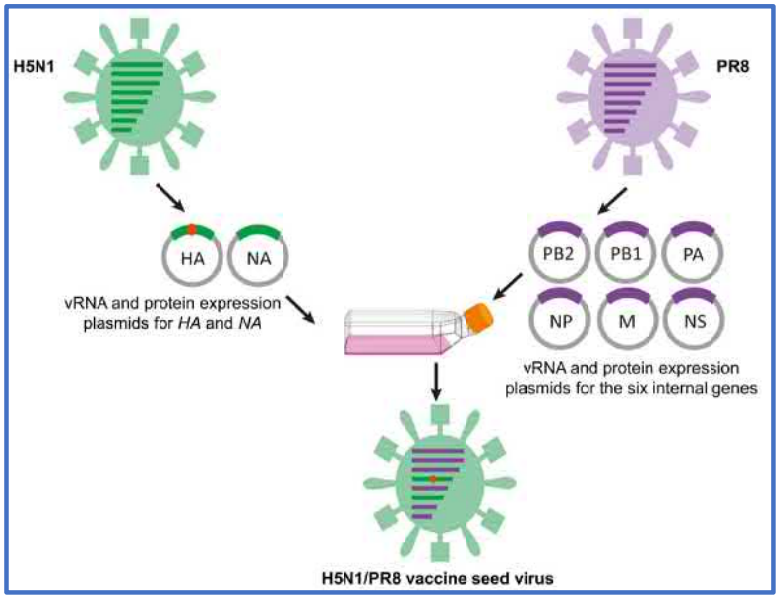
- We continuously perform active surveillance in wild birds and domestic poultry to monitor the newly introduced viruses (about 40,000 samples per year collected by our lab).

Surveillance and analysis the strains

- We continuously perform active surveillance in wild birds and domestic poultry to monitor the newly introduced viruses (about 40,000 samples per year collected by our lab).
- We compare the antigenic properties of the newly detected H5 virus with the vaccine seed virus, if a clear difference is observed, the vaccine will be updated

Inactivated vaccine development platform

Vaccine seed virus generation by reverse genetics

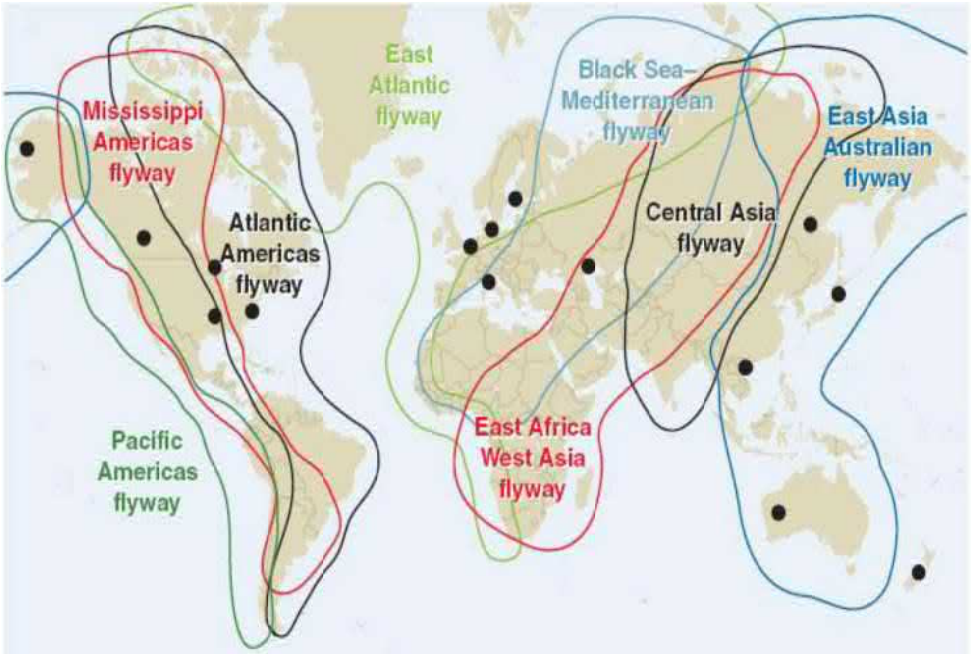


Tian et al., Virology, 2005

An ideal vaccine seed virus can be generated within a week

A large number of migratory birds fly over China, and they introduced different H5 influenza viruses into China in the past years.

Chen H., JVI, 2006;
Li Y., EID, 2010;
Cui Y., EMI, 2020;
Li Y., EID, 2020;
Cui P., SCLS, 2022;
Cui P., EMI, 2022



Viruses carrying different clades or subclades of HA that have been introduced into China before 2020

Year	Subtype/clade	Representative strain
2005	H5N1/clade 2.2	A/bar-headed goose/Qinghai/3/2005
2006	H5N1/clade 7.2	A/chicken/Shanxi/2/2006
2006	H5N1/clade 2.3.4	A/duck/Anhui/1/2006
2010	H5N1/clade 2.3.2	A/duck/goose/S1322/2010
2013	H5N1/clade 2.3.4.4g	A/chicken/Guizhou/4/2013
2017	H5N6/clade 2.3.4.4h	A/duck/Guizhou/S4184/2017
2017	H5N1/clade 2.3.2.1f	A/chicken/Liaoning/SD007/2017

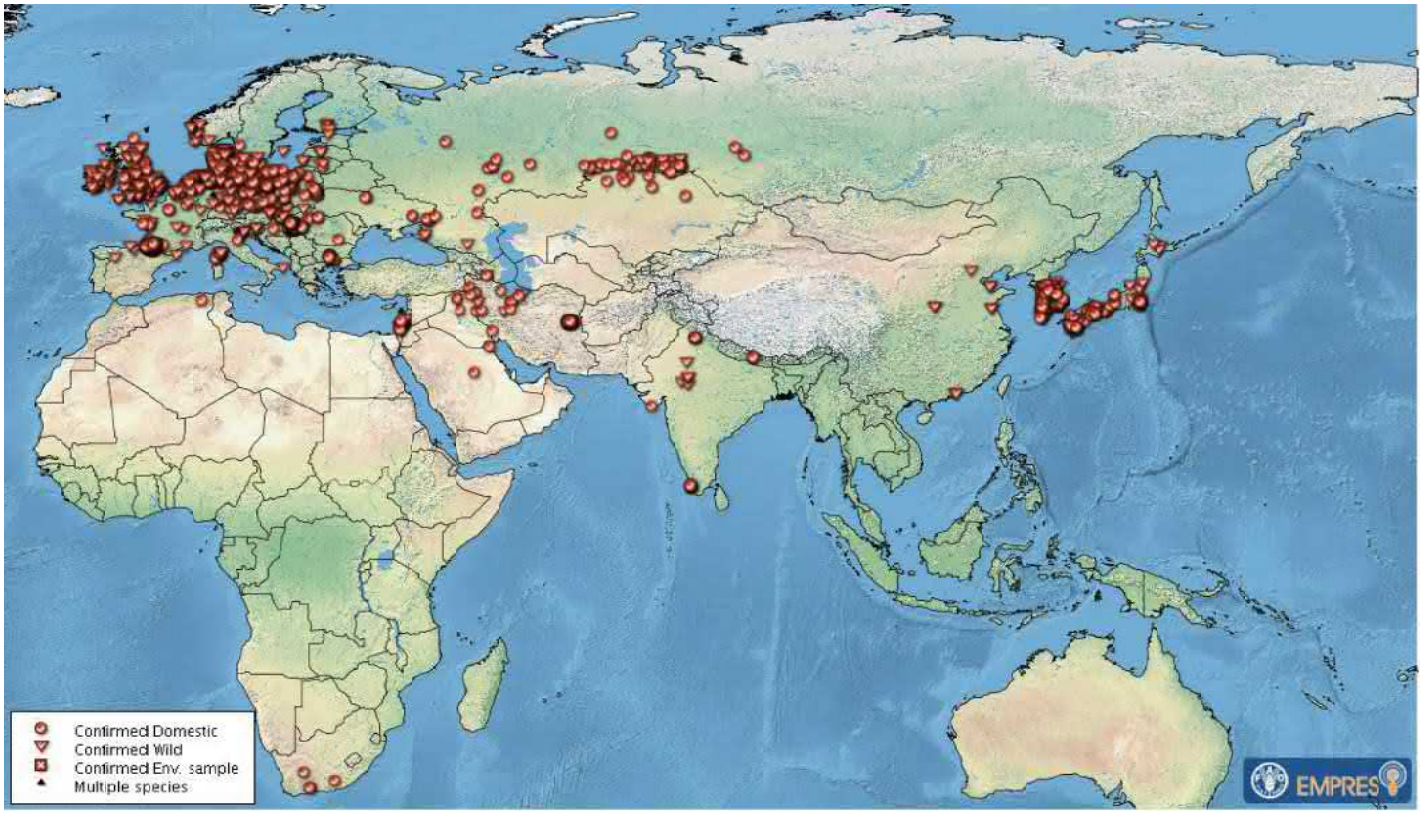
Eight H5 vaccine seed viruses had been used in China from 2004 to 2021

Seed virus	HA donor virus (clade)	Application period	Complete protection against the clade of
H5-Re1	GD/GD/1/1996(H5N1) (0)	03/2004–03/2008	0, 1, 2.2, 2.3.4
H5-Re4	CK/SX/2/2006(H5N1) (7.2)	07/2006–04/2014	7.2
H5-Re7	CK/LN/S4092/2011(H5N1) (7.2)	04/2014–09/2017	7.2
H5-Re6	DK/GD/S1322/2010(H5N1) (2.3.2)	06/2012–09/2017	2.3.2
H5-Re12	CK/LN/SD007/2017(H5N1) (2.3.2.1f)	12/2018–12/2021	2.3.2.1f
H5-Re5	DK/AH/1/2006(H5N1) (2.3.4)	03/2008–06/2012	2.3.4
H5-Re8	CK/GZ/4/2013(H5N1) (2.3.4.4g)	12/2015–12/2018	2.3.4.4g
H5-Re11	DK/GZ/S4184/2017(H5N6) (2.3.4.4h)	12/2018–12/2021	2.3.4.4h

Viruses bearing the clades 7.2, 2.3.4, 2.3.2, 2.3.2.1f, and 2.3.4.4g HA gene have been eliminated in China

Seed virus	HA donor virus (clade)	Application period	Complete protection against the clade of	Virus eliminated in China
H5-Re1	GD/GD/1/1996(H5N1) (0)	03/2004–03/2008	0, 1, 2.2, 2.3.4	**Yes**
H5-Re4	CK/SX/2/2006(H5N1) (7.2)	07/2006–04/2014	7.2	**Yes**
H5-Re7	CK/LN/S4092/2011(H5N1) (7.2)	04/2014–09/2017	7.2	
H5-Re6	DK/GD/S1322/2010(H5N1) (2.3.2)	06/2012–09/2017	2.3.2	**Yes**
H5-Re12	CK/LN/SD007/2017(H5N1) (2.3.2.1f)	12/2018–12/2021	2.3.2.1f	**Yes**
H5-Re5	DK/AH/1/2006(H5N1) (2.3.4)	03/2008–06/2012	2.3.4	**Yes**
H5-Re8	CK/GZ/4/2013(H5N1) (2.3.4.4g)	12/2015–12/2018	2.3.4.4g	**Yes**
H5-Re11	DK/GZ/S4184/2017(H5N6) (2.3.4.4h)	12/2018–12/2021	2.3.4.4h	Not yet, but very soon

H5N8 viruses bearing the clade 2.3.4.4b HA gene caused disease outbreaks in European countries since 2020



Introduction of H5N8 virus into China by wild birds

Surveillance performed from September 2020 to June 2021

Samples collected		H5N8 viruses isolated
Wild bird	317	22
Duck	13,908	8
Goose	1,552	6
Pigeon	189	0
Chicken	25,532	0
Total	41,172	36

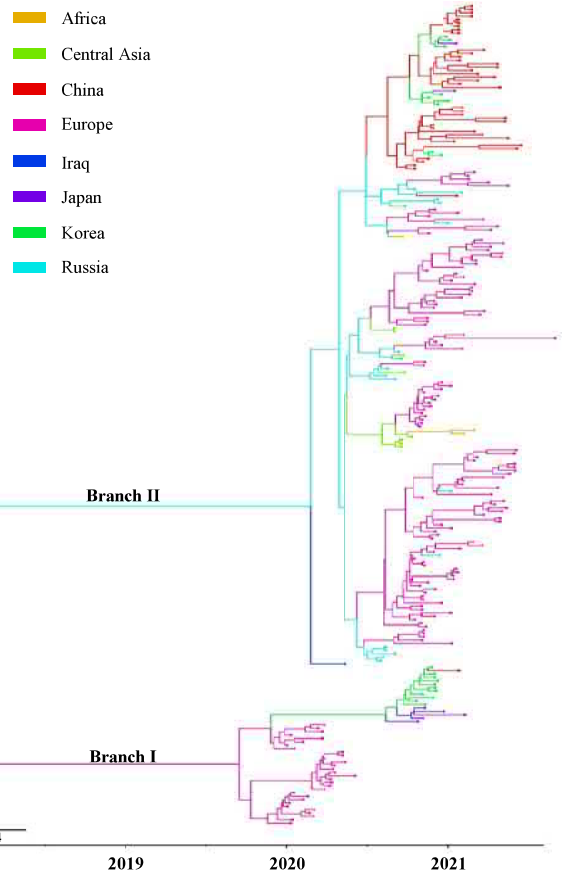
Time	Location	Host
November 2020	Shanxi	
January 2021	Shandong	
	Guangdong	
	Beijing	
	Jiangsu	
February 2021	Guangxi	
	Shandong	
March 2021	Guangdong	
	Jiangxi	
	Zhejiang	
	Hunan	
	Jiangsu	
April 2021	Liaoning	
	Henan	
	Hebei	
May 2021	Guangxi	
	Tibet	
June 2021	Shaanxi	
	Ningxia	

Jan. 2020 in Europe

Jan. 2021 in China

Branch I

Time	Location	Host
January 2020	Poland, Hungary, Germany, Czech Republic	
February 2020	Germany, Poland, Czech Republic	
March 2020	Poland, Germany, Hungary	
April 2020	Hungary	
May 2020	Hungary	
June 2020	Hungary	
October 2020	Korea, Japan	
November 2020	Korea, Japan	
December 2020	Korea, Japan	
January 2021	China	
February 2021	Japan	

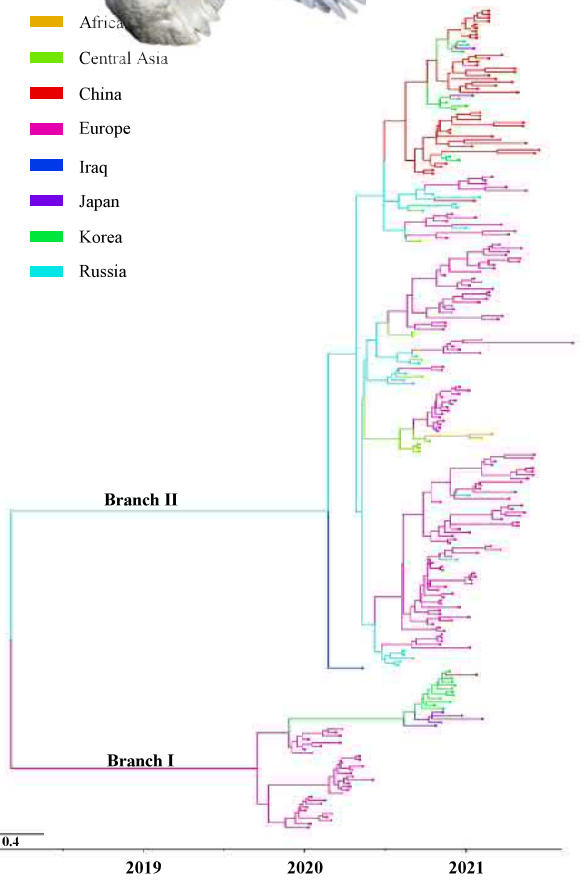


May 2020 in Iraq

October 2020 in China

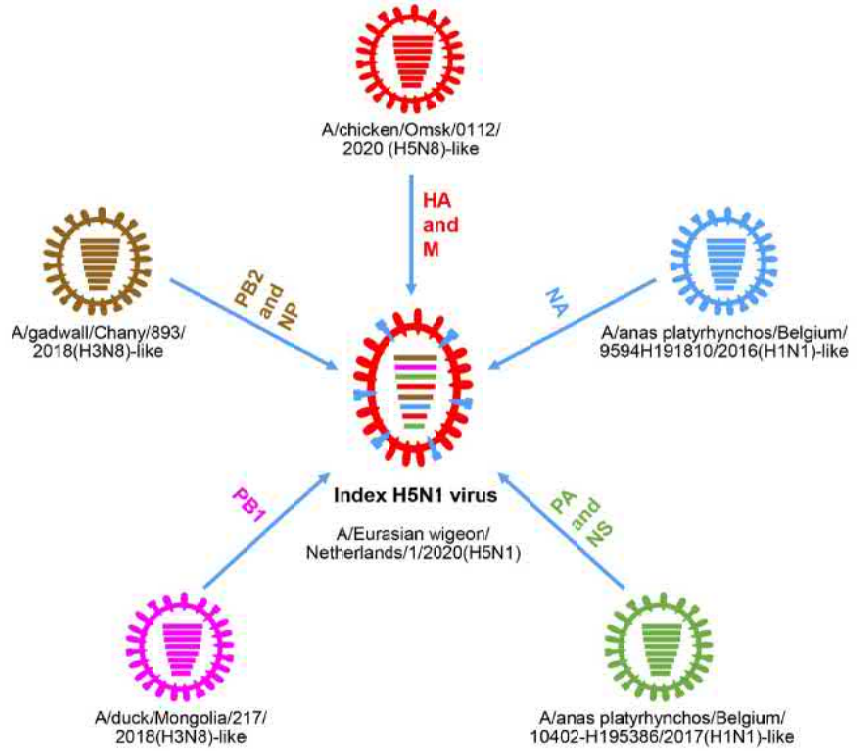
Branch II

Time	Location	Host
May 2020	Iraq	
July 2020	Russia	
August 2020	Russia	
September 2020	Russia, Kazakhstan	
October 2020	Russia, Kazakhstan, Netherlands, Germany, UK	
	China	
November 2020	Netherlands, UK, Denmark, Italy, Belgium, France, Sweden, Slovenia, Korea, Spain, Poland, Norway	
	China	
December 2020	Russia, UK, Slovenia, Italy, Korea, Poland	
January 2021	Russia, UK, Italy, Korea, Spain, Norway, Slovakia, Romania, Japan, Czech Republic	
	China	
February 2021	Italy, Poland, Czech Republic, Bulgaria, Austria, Latvia, Nigeria, Lithuania	
	China	
March 2021	Poland, Hungary, Czech Republic, Nigeria, Croatia, Lithuania, Greece	
	China	
April 2021	Poland, Czech Republic, Romania, Bulgaria, Austria	
	China	
May 2021	Poland, Bulgaria, Romania, Czech Republic, Kosovo, Albania	
	China	
June 2021	Kosovo, Albania	
	China	
August 2021	Belgium	



Cui et al., SCLS, 2022

Emerging of the H5N1 virus in Northern Europe



Gu et al., EMI, 2022

Evolution and spread of H5N1 virus bearing the clade 2.3.4.4b HA since October 2020

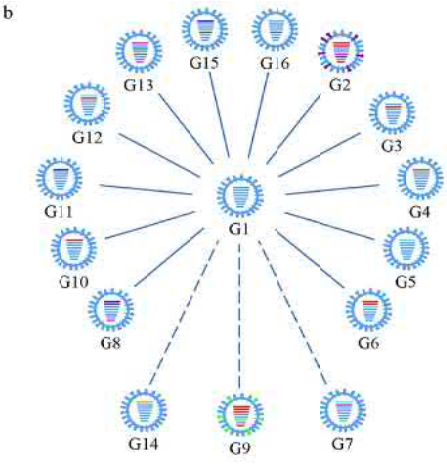
October 2020 in The Netherlands

November 2021 in China

a

Time	Location: Europe	Africa	Asia -Others	Asia -China	North America
Oct. 2020	G1				
Nov. 2020	G1, C2				
Dec. 2020	G1	G1			
Jan. 2021	G1	G1			
Feb. 2021	G1	G1			
March 2021	G1	G1			
April 2021	G1				
May 2021	G1				
June 2021	G1				
July 2021	G1				
Aug. 2021	G1				
Sept. 2021	G1, C3, G4				
Oct. 2021	G1, G4, G5, G6, G8, G10		G7		
Nov. 2021	G1, G4, G8, G11, G12, G13,		G7	G1, G9	
Dec. 2021	G1, G4, G5, G8, G12, G15		G14	G7, G9	G1
Jan. 2022	G1, G4, G8, G16	G1		G7, G9, G10	G1
Feb. 2022	G1, G4			G7	G1
March 2022				G9	

b



Gene conor:

- A/anas platyrhynchos/Belgium/10402-H195386/2017 (H1N1)-like
- A/wild duck/South Korea/KNU2020-58/2020(H1N1) -like
- A/mallard/Novosibirsk region/1894k/2019(H4N6)-like
- A/anas platyrhynchos/Belgium/827/2020(H3N8)-like
- A/duck/Moscow/5586/2018(H3N2)-like
- A/common Teal/Amur region/31b/2019(H3N6)-like
- A/anas platyrhynchos/Belgium/204-0003/2020(H4N6) -like
- A/green sandpiper/Kurgan/1050/2018(H3N8)-like
- A/mallard/Denmark/12947-12/2020(H7N5)-like
- Wild bird H5N8

Evolution and spread of H5N1 virus bearing the clade 2.3.4.4b HA since October 2020

October 2020 in The Netherlands

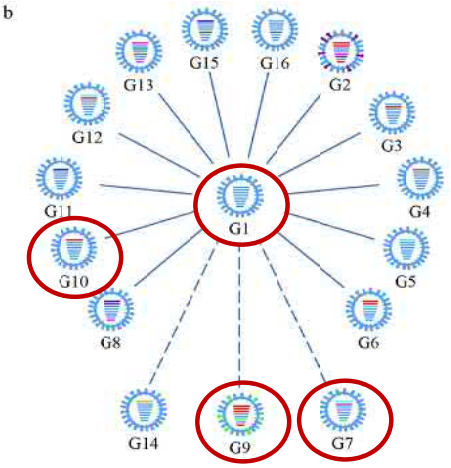
November 2021 in China

a

Time	Location: Europe	Africa	Asia -Others	Asia -China	North America
Oct. 2020	G1				
Nov. 2020	G1, G2				
Dec. 2020	G1	G1			
Jan. 2021	G1	G1			
Feb. 2021	G1	G1			
March 2021	G1	G1			
April 2021	G1				
May 2021	G1				
June 2021	G1				
July 2021	G1				
Aug. 2021	G1				
Sept. 2021	G1, G3, G4				
Oct. 2021	G1, G4, G5, G6, G8, G10		G7		
Nov. 2021	G1, G4, G8, G11, G12, G13,		G7	G1, G9	
Dec. 2021	G1, G4, G5, G8, G12, G15		G14	G7, G9	G1
Jan. 2022	G1, G4, G8, G16	G1		G7, G9, G10	G1
Feb. 2022	G1, G4			G7	G1
March 2022				G9	

16 genotypes formed

b



Gene conor:

- A/anas platyrhynchos/Belgium/10402-H195386/2017 (H1N1)-like
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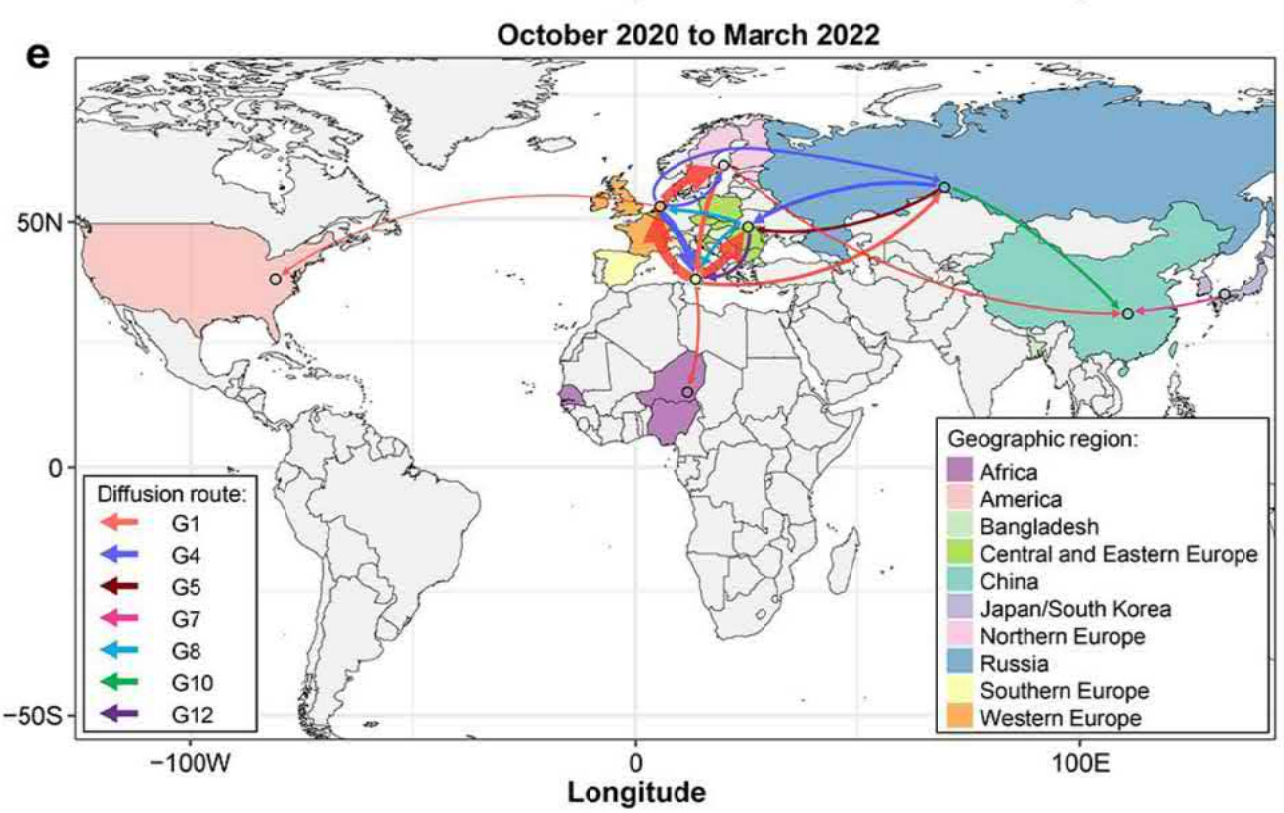
- A/anas platyrhynchos/Belgium/827/2020(H3N8)-like
- A/duck/Moscow/5586/2018(H:N2)-like
- A/common Teal/Amur region/31b/20:9(H3N6)-like
- A/anas platyrhynchos/Belgium/204-0003/2020(H4N6) -like
- A/green sandpiper/Kurgan/1050/2018(H3N8)-like
- A/mallard/Denmark/12947-12/2020(H7N5)-like
- Wild bird H5N8

Three different H5N1 viruses were respectively spread to China from Northern Europe, Russia, and Japan/Korea



The newly introduced H5N8 viruses shows clear antigenic difference with the previously used vaccines H5-Re11 and H5-Re12

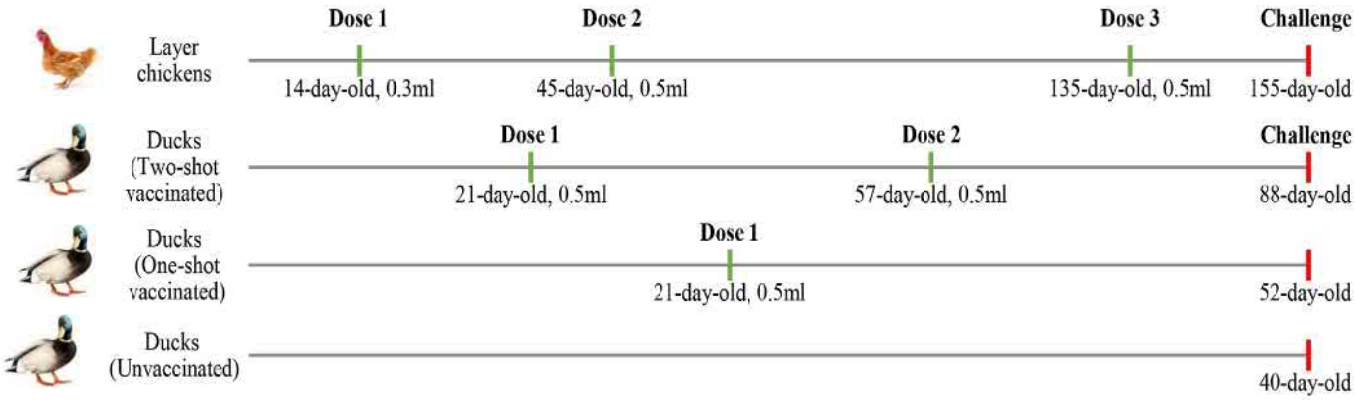
	HA clade	HI antibody titer of antiserum	
		Re-11	Re-12
Re-11	2.3.4.4h	**512**	32
Re-12	2.3.2.1d	16	**512**
WS/SX/4-1/2020(G1)	2.3.4.4b	16	8
BS/BJ/1/2021(G1)	2.3.4.4b	16	8
GS/HuN/S11288/2021(G1)	2.3.4.4b	16	8
WS/SD/SC195/2021(G2)	2.3.4.4b	16	8

Cui et al., SCLS, 2022

The first H5N8 strain:
A/swan/Shanxi/4-1/2020 (H5N8)

Could our vaccinated poultry be well protected against this newly invasive virus?

Chickens and ducks from different poultry farms that were routinely vaccinated or unvaccinated were challenged with H5N8 virus in the laboratory setting



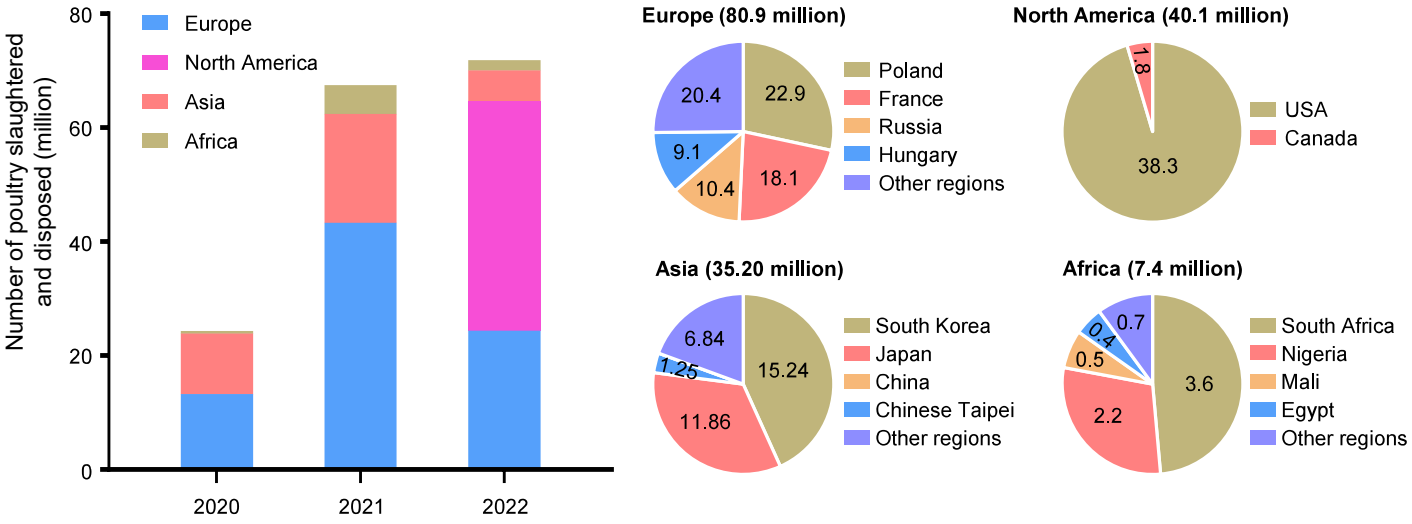
Cui et al., SCLS, 2022

Vaccinated poultry were completely protected against the newly introduced H5N8 virus challenge

Group	Virus shedding (shedding/total)				Shedding/ Total	Survival /Total
	Day 3 post challenge		Day 5 post challenge			
	Oropharynx	Cloacae	Oropharynx	Cloacae		
Vaccinated layer chickens (three doses)	0/10	0/10	0/10	0/10	0/10	10/10
SPF chickens	10/10	10/10	/	/	10/10	0/10
Vaccinated ducks (one dose)	0/10	0/10	0/10	0/10	0/10	10/10
Vaccinated ducks (two doses)	0/10	0/10	0/10	0/10	0/10	10/10
Unvaccinated ducks	10/10	10/10	10/10	10/10	10/10	8/10

Cui et al., SCLS, 2022

Over 163 million poultry died or were destroyed due to H5 virus infection from January 2020 to March 2022; of note, Mainland China lost only 10, 000 birds during this period

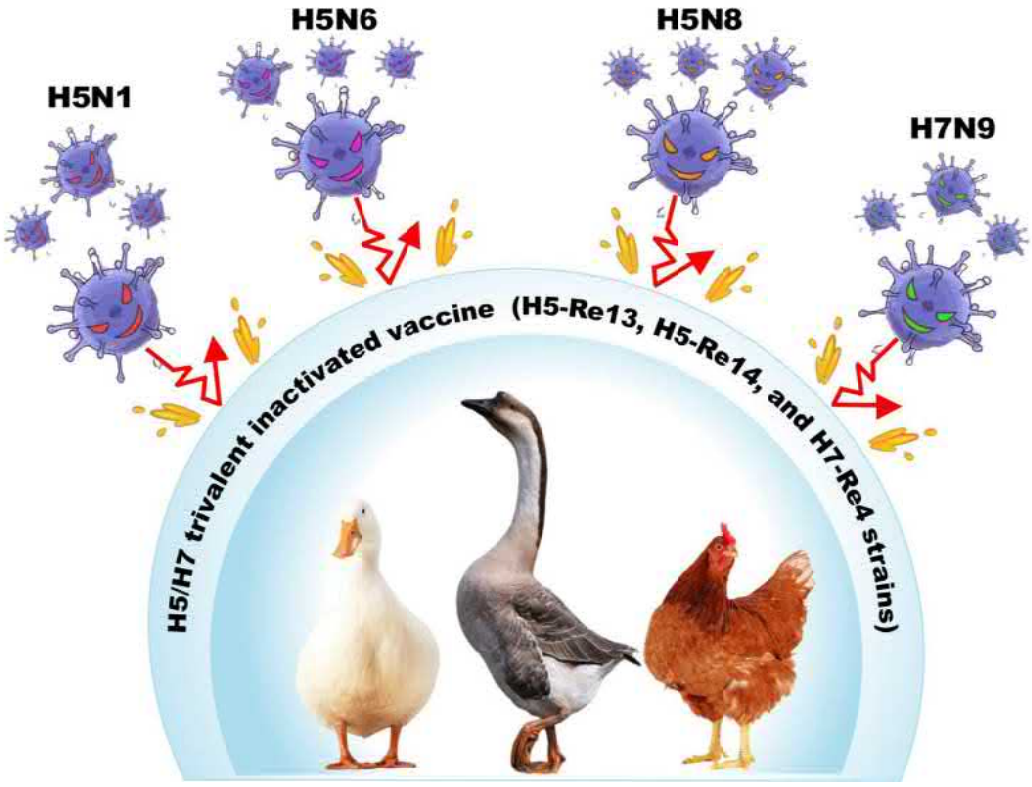


The H5 vaccine seed viruses have been updated in 2022, even though the previous vaccine could still provide complete protection against the emerging H5N8 virus.

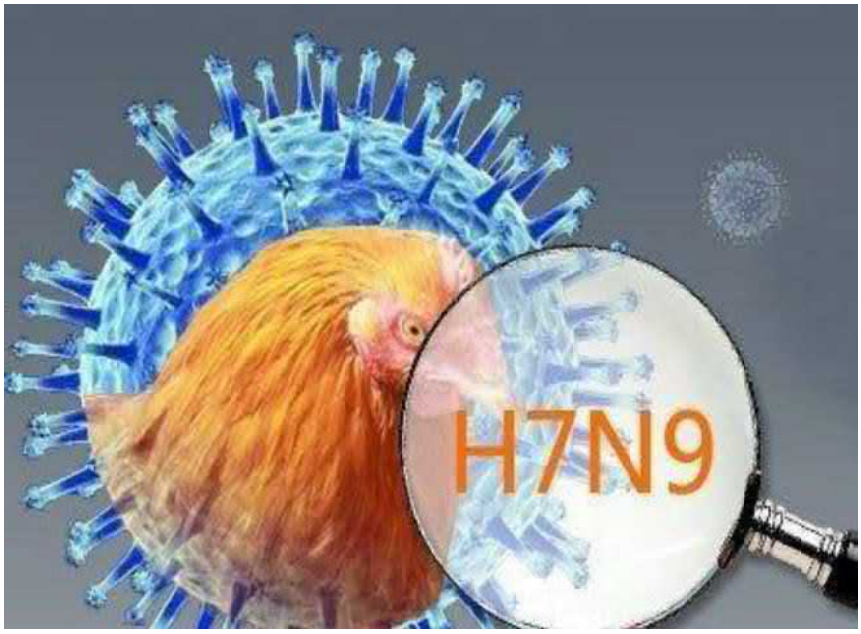
Seed virus	HA donor virus (clade)	Application period	Complete protection against the clade of
H5-Re13	DK/FJ/S1424/2020(H5N6) (2.3.4.4h)	01/2022–	2.3.4.4h
H5-Re14	WH/SX/4-1/2020(H5N8) (2.3.4.4b)	01/2022–	2.3.4.4b

Zeng et al., Protective efficacy of an H5/H7 trivalent inactivated vaccine (H5-Re13, H5-Re14, and H7-Re4 strains) in chickens, ducks, and geese against newly detected H5N1, H5N6, H5N8, and H7N9 viruses.

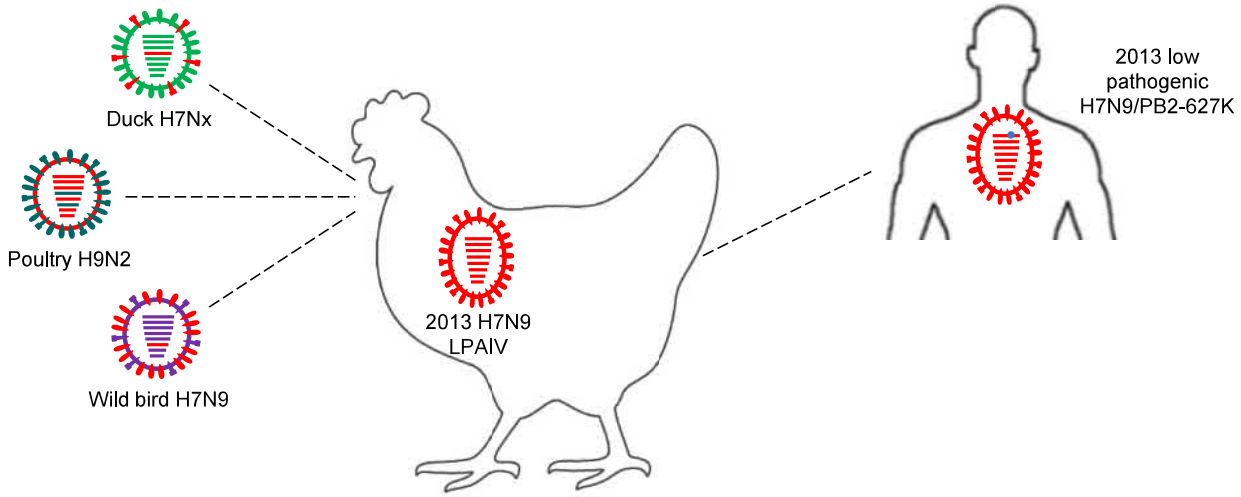
Journal of Integrative Agriculture, 2022, 21(7): 2086–2094



Control of H7N9 virus in China

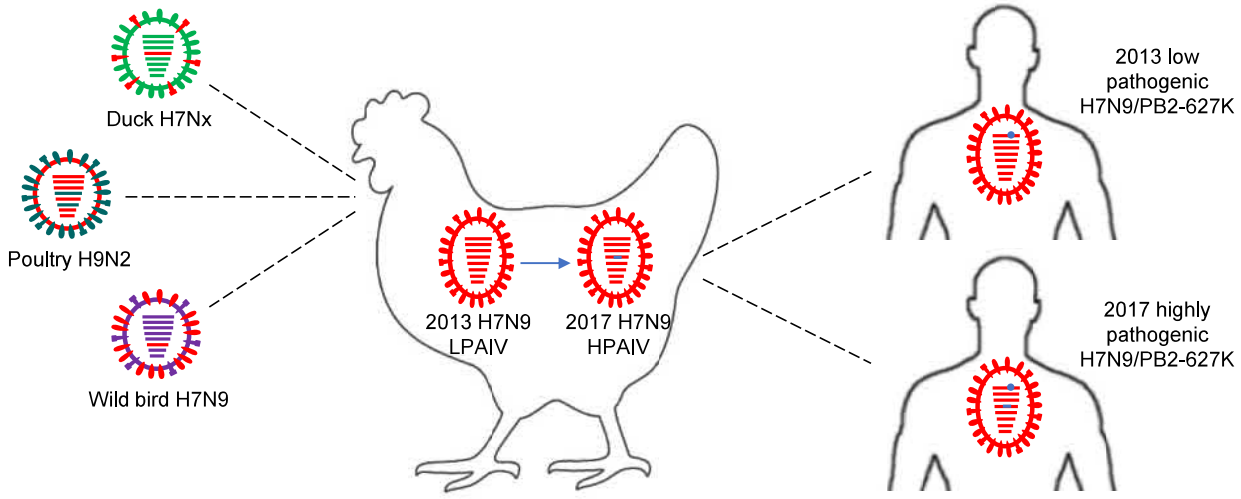


Emergence and evolution of H7N9 viruses in China



Zhang Q., et al, Science, 2013

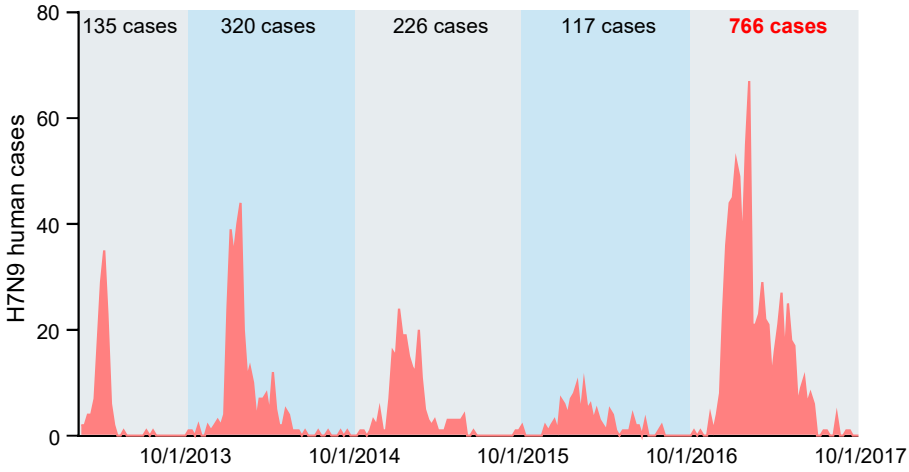
Emergence and evolution of H7N9 viruses in China



Shi et al, Cell Research, 2017
Yang et al., JVI, 2018

Damage to humans and poultry industry caused by H7N9 viruses in China

The virus caused over 1,560 human infections in five waves from February 2013 to September 2017, with a mortality rate of nearly 40%.



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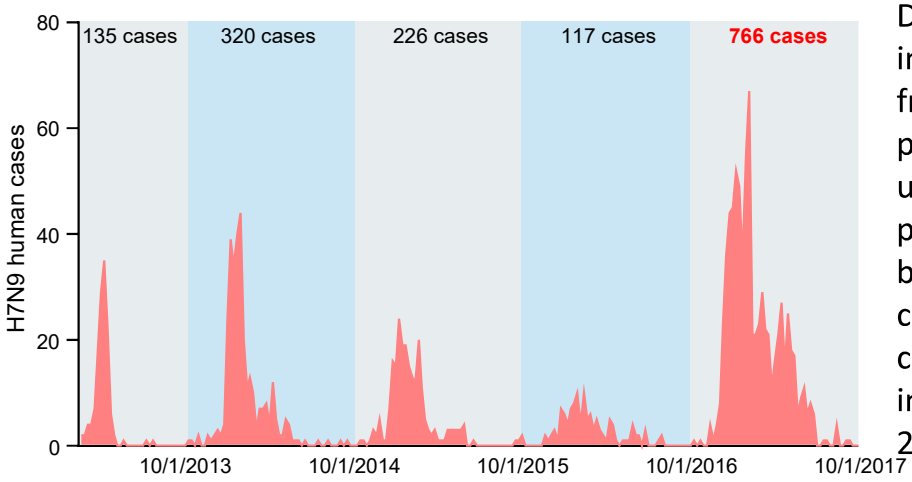


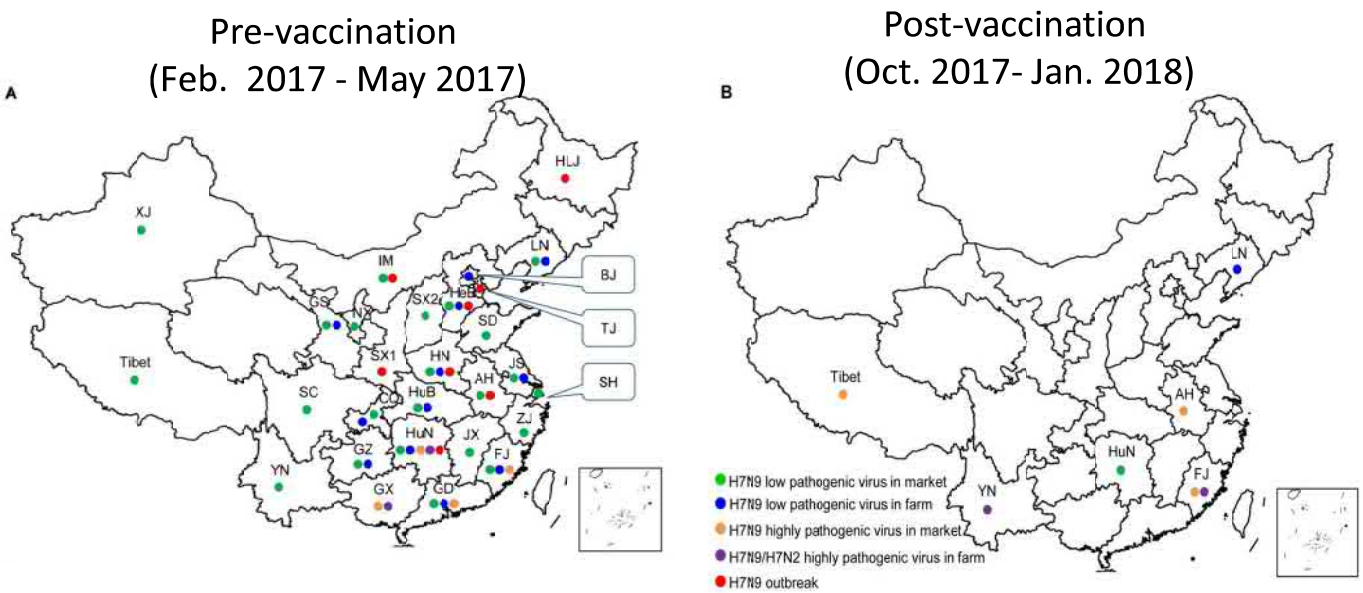
During the human H7N9 waves, in addition to culling poultry from poultry markets that were positive for the virus, tons of uninfected poultry and poultry products were destroyed because people were afraid to consume them, which caused considerable damage to poultry industries in China from 2013-2017.

In September 2017, the control strategy of H7N9 influenza was changed from “stamping-out” to “massive vaccination”, and an H5+H7 bivalent vaccine was started to be used to control both H5 and H7 avian influenza in China.

Shi J., et al, Cell Host & Microbe, 2018

Vaccination dramatically prevented the prevalence of H7N9 virus in poultry

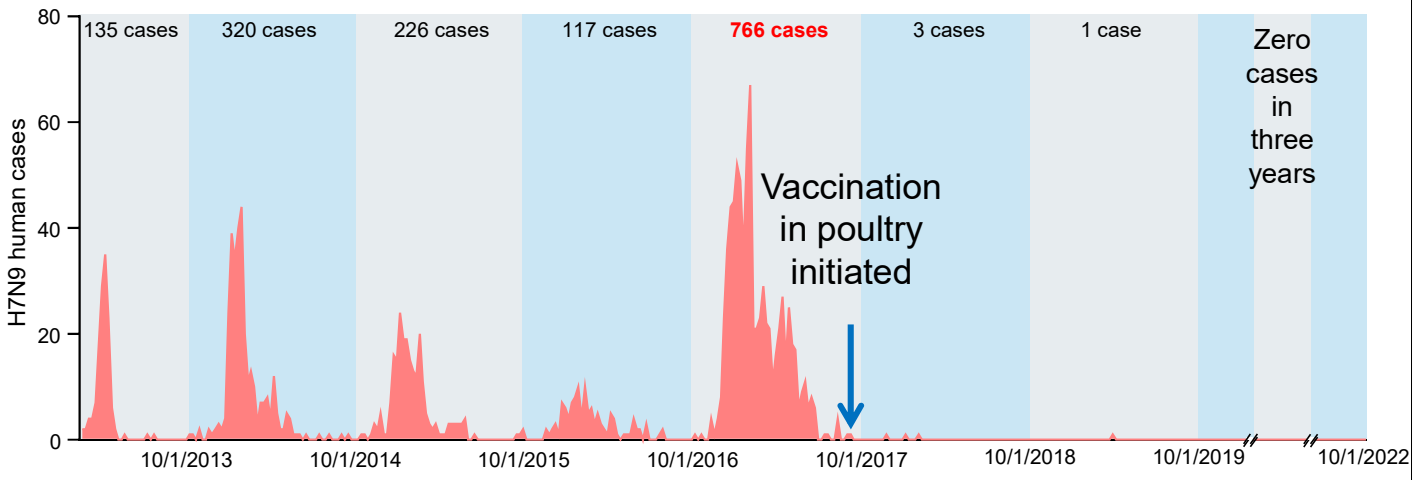
The isolation rate of H7N9 virus in poultry was immediately reduced by 93.3% after birds were inoculated with the H5/H7 vaccine



Shi J., et al, Cell Host & Microbe, 2018

Vaccination of poultry successfully eliminated human infection with H7N9 virus

Only three human cases and one human case were reported during the sixth and seventh waves, respectively, and no human case has been detected since April 2019



Conclusion and suggestions

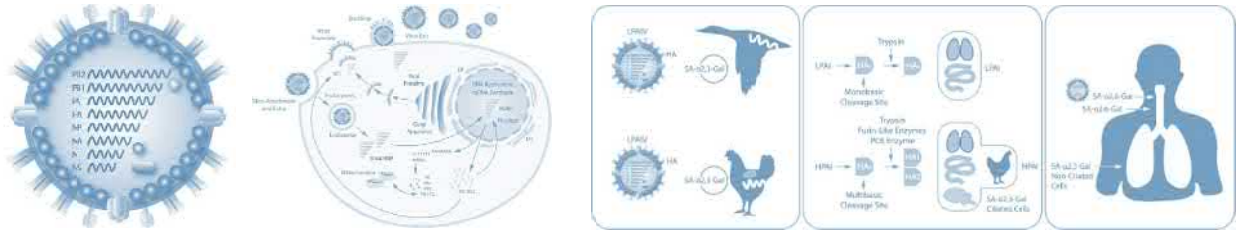
- Vaccination strategy is very successful in China, as evidenced by the facts that several clades of H5 viruses have been eradicated and the pervasive H7N9 viruses have been nearly eliminated in China.

Conclusion and suggestions

- Vaccination strategy is very successful in China, as evidenced by the facts that several clades of H5 viruses have been eradicated and the pervasive H7N9 viruses have been nearly eliminated in China.

- To improve animal welfare, reduce economic damage, and reduce human infection potential, vaccination should be immediately and seriously considered as a control strategy. Any unnecessary obstacles to vaccination strategies should be removed immediately and forever.

Thank you very much for your attention!

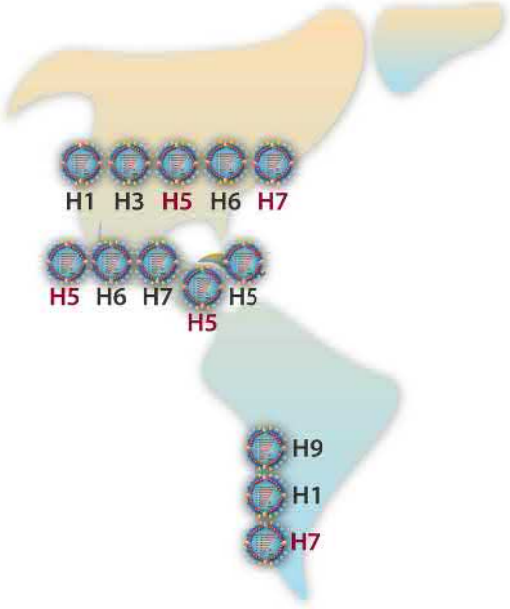


Avian Influenza in Latin America
A Field Perspective

Guillermo Zavala
Avian Health International, LLC

Relevant AI Outbreaks in Latin America

- Mexico
  - HPAI H5N2 (1994)
  - LPAI H5N2 (1996) - Enzootic
  - H6Nx (Uncharacterized)
  - H7N3 (c. 2013) - Enzootic
- Guatemala LPAI H5N2 (Periodical)
- Belize LPAI H5N2 (Periodical)
- Dominican Republic H5N2 (Periodical)
- Chile LPAI (H1, H9) (Occasional Incursions)
- Chile HPAI H7N3 (2002) Single Outbreak



Published Reports of AIV in Latin America
(2000 – 2015)

AIV Subtype	Country	Year	Species
H5N2 H5N2	Guatemala	2000 2002-2003	Chicken Chicken
H7N3 H7N3 H1N1	Chile	2002 2002 2009	Chicken Chicken Turkey
H9N2 H5N2 H5N2	Colombia	2005	Chicken Chicken Japanese quail
H5N2 H5N2 H7N3	Mexico	2001 (1994) 2001 (c. 1996) 2012	Chicken Chicken Chicken
H5N2	Honduras	2001	Chicken

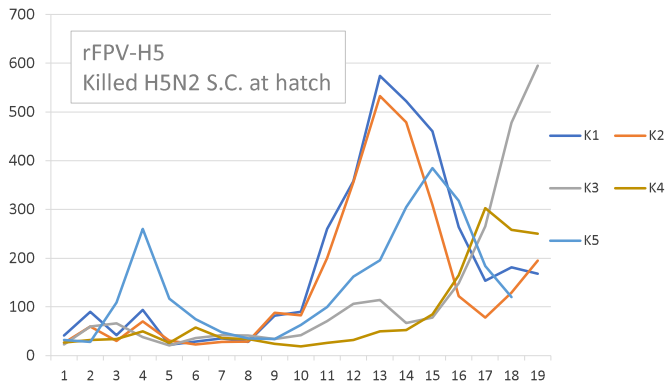
Partial data extracted from: Afanador-Villamizar, A. et al. Avian influenza in Latin America: A systematic review of serological and molecular studies from 2000-2015. PLoS ONE 12 (6): e0179573 https://doi.org/10.1371/journal. pone.0179573

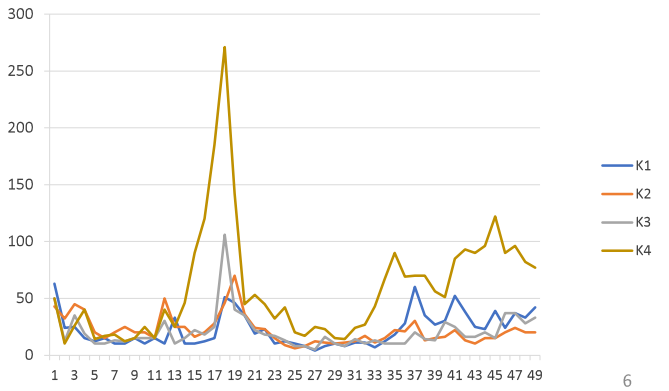
Stories of Success and Failure

Characteristic	Success	Failure
Geography	E.U., North America, Japan, N. Korea, Australia	Mexico, L.A. Egypt, Middle East, Africa, Southeast Asia
Surveillance	Intensive	Insufficient or absent
Diagnostics	High capability	Limited capability
Reporting	Always	Seldom, selectively or never
Emergency Preparedness	High preparedness	Low or no preparedness
Quarantine	Rapid, Enforced	Slow, not enforced (biosecurity is generally very good)
Depopulation	Mostly effective and rapid	Slow, poor knowledge and technique or no depopulation
Disposal	Mostly effective and rapid	Slow, inadequate, poor knowledge and technique
Compensation	Very effective	Insufficient or absent
Virus elimination	Effective and monitored	Unknown
Testing	Intensive	Limited or absent
Restocking	Only after demonstrable virus elimination	Usually, no requirements
Biosecurity	Acceptable to excellent	Poor to excellent

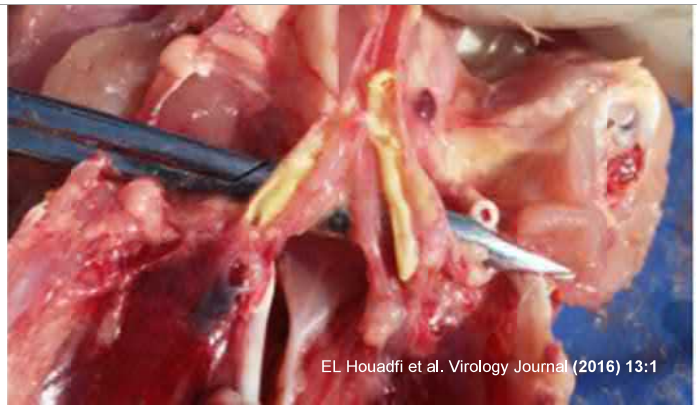
Countries Adopting Vaccination

Country	Subtype	Vaccine Type	Remarks
Guatemala	H5N2 H5N2 H5 H7N3	Killed conventional H5N2 Killed reverse genetics NDV GV + H5N2 Live rFPV-H5 Killed rgH7N3	Broiler breeders, Commercial layers, and Broiler chickens
Chile	H1N1 H9Nx	Killed H1 None	Turkeys
Colombia	H9N2 H5N2	None	N/A
Dominican Republic	H5N2	Killed conventional H5N2 Live rFPV-H5	Broiler Breeders, Commercial Layers, and Broilers
El Salvador	?	Killed conventional H5N2	Broiler Breeders, Commercial Layers
Mexico	H5N2 H5N2 H5 H5 H7N3 H7N3 H7 H7	Killed conventional H5N2 Killed reverse genetics NDV GV + H5N2 Live rFPV-H5 Live rNDV-H5 Conventional H7N3 Killed rgH7N3 Live rFPV-H7 Live rNDV-H7	Broiler breeders, Commercial layers, Broiler chickens





H9N2 North Africa, Middle East, Central and Southeast Asia

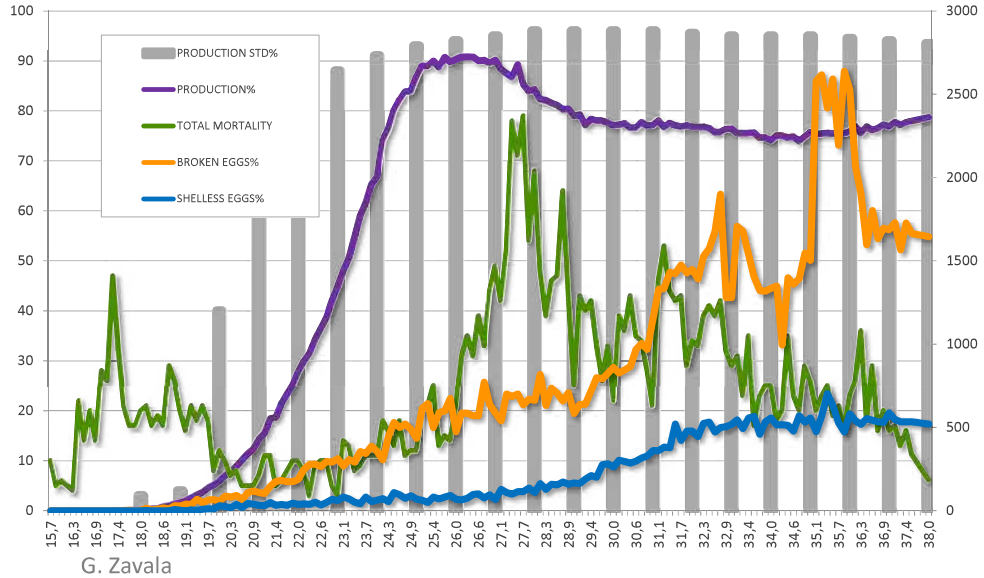


- Coinfection with multiple pathogens including H9N2
- MG, MS, IBV (nephropathogenic), aMPV subtype B
- H9N2 belongs to G1 lineage from Middle East
- Moroccan isolates: virulent; potential for human adaptation

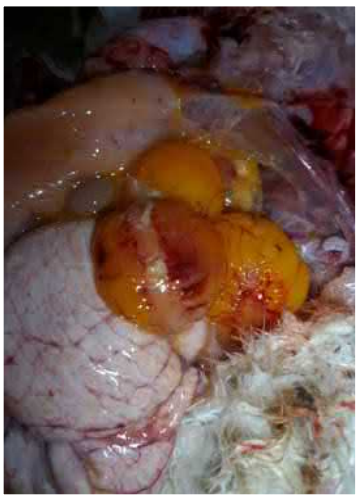
[1] Avian Diseases 59(3):440-446. 2015

[2] EL Houadfi et al. Virology Journal (2016) 13:140

Impact of H7N3 in [3X] Vaccinated Egg Layers
Mexico – High Challenge Area



G. Zavala



Vaccine and Vaccination Cost - Mexico

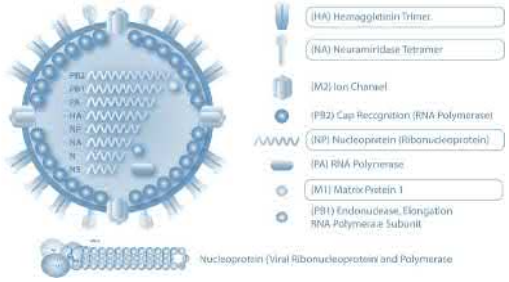
Type of Bird	Vaccination and Prevalence	Total Cost/Bird ($ USD)	Cost/1000 Doses ($ USD)
Broilers	Hatchery	0.018	$18.00
Broilers	Hatchery and farm	0.033	$33.00
Layers	Low prevalence	0.041	$41.00
Layers	High prevalence	0.251	$251.00
Breeders	Low prevalence	0.041	$41.00
Breeders	High prevalence	0.058	$58.00

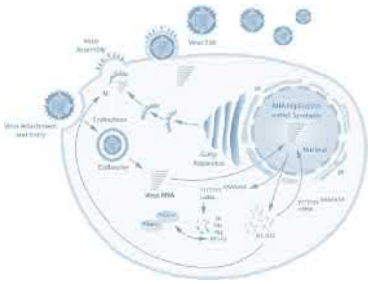
Cost by Vaccine Type - Mexico

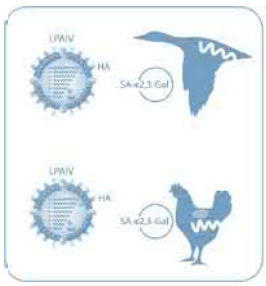
Vaccine	Type	Strain	Route	Cost/1000 Doses ($ USD)
rFPV+AIH5	Recombinant	FPV+H5	SC	$6.66
Inactivated AIH5+ND	Inactivated	AIH5+NDV LaSota	SC	$11.66
rNDV+AIH5	Recombinant	rNDV LaSota+H5	Eye	$5.55
Inactivated AIH5+ND	Inactivated	H5+NDV LaSota	SC/IM	$10.55
Inactivated rgAIH7	Reverse Genetics (Inactivated)	rgAIH7	SC/IM	$17.77

Primary Challenges for Successful Vaccination

- Absence of reliable **surveillance** programs
- Insufficient capacity of **accredited laboratories**
- Lack of emergency response **preparedness**
- **Governance** and coordinated response
- **Under-reporting** of HPAI and LPAI
- Variation of **vaccine quality**
  - Quality; updated master seeds
- **Cost** of vaccines and vaccination
- Poultry **concentration**
- **Biosecurity** and added challenges
  - Live bird commercialization
  - Thinning practices (broilers and commercial egg layers)
  - On-site sales of spent fowl and undergrade eggs
  - Manure handling and transportation







Thank You

Guillermo Zavala
Avian Health International, LLC

World Organisation for Animal Health
Founded as OIE

Food and Agriculture Organization of the United Nations

Ministry of Agriculture
Republic Indonesia

Highly Pathogenic Avian Influenza Vaccination Strategy: Lesson Learned from The Implementation of Influenza Virus Monitoring in Indonesia

KEMENTERIAN PERTANIAN
REPUBLIK INDONESIA

Hendra Wibawa

Disease Investigation Center Wates
(National Reference Laboratory for Avian Influenza in Indonesia),
Directorate General Livestock and Animal Health Services,
Ministry of Agriculture, Republic of Indonesia.
Jl. Wates KM 27, Kulon Progo, Yogyakarta, Indonesia

Poultry Production Type, Avian Influenza Outbreaks, and Virus Evolution

Poultry Production Type

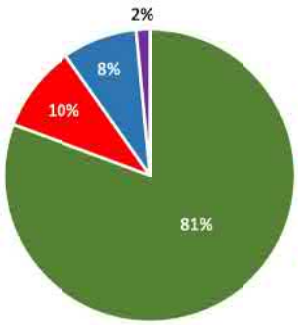
Sector 1 — Industrial integrated system; high level biosecurity

Sector 2 — Semi-vertical integrated system; Moderate level biosecurity

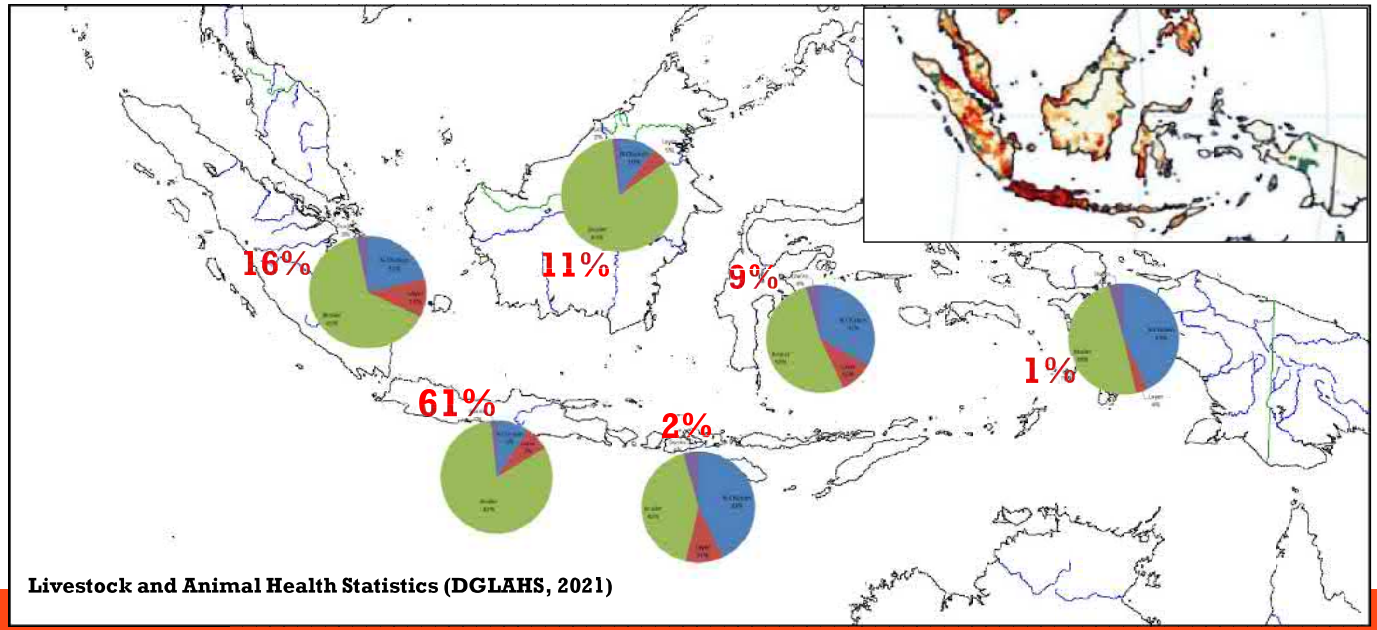
Sector 3 — Small commercial poultry production; low level biosecurity

Sector 4 — Village or backyard poultry; no biosecurity, mix farming

ISLAND-BASED POULTRY POPULATION



Total Population:
3.851.045.000 birds (in 2021)

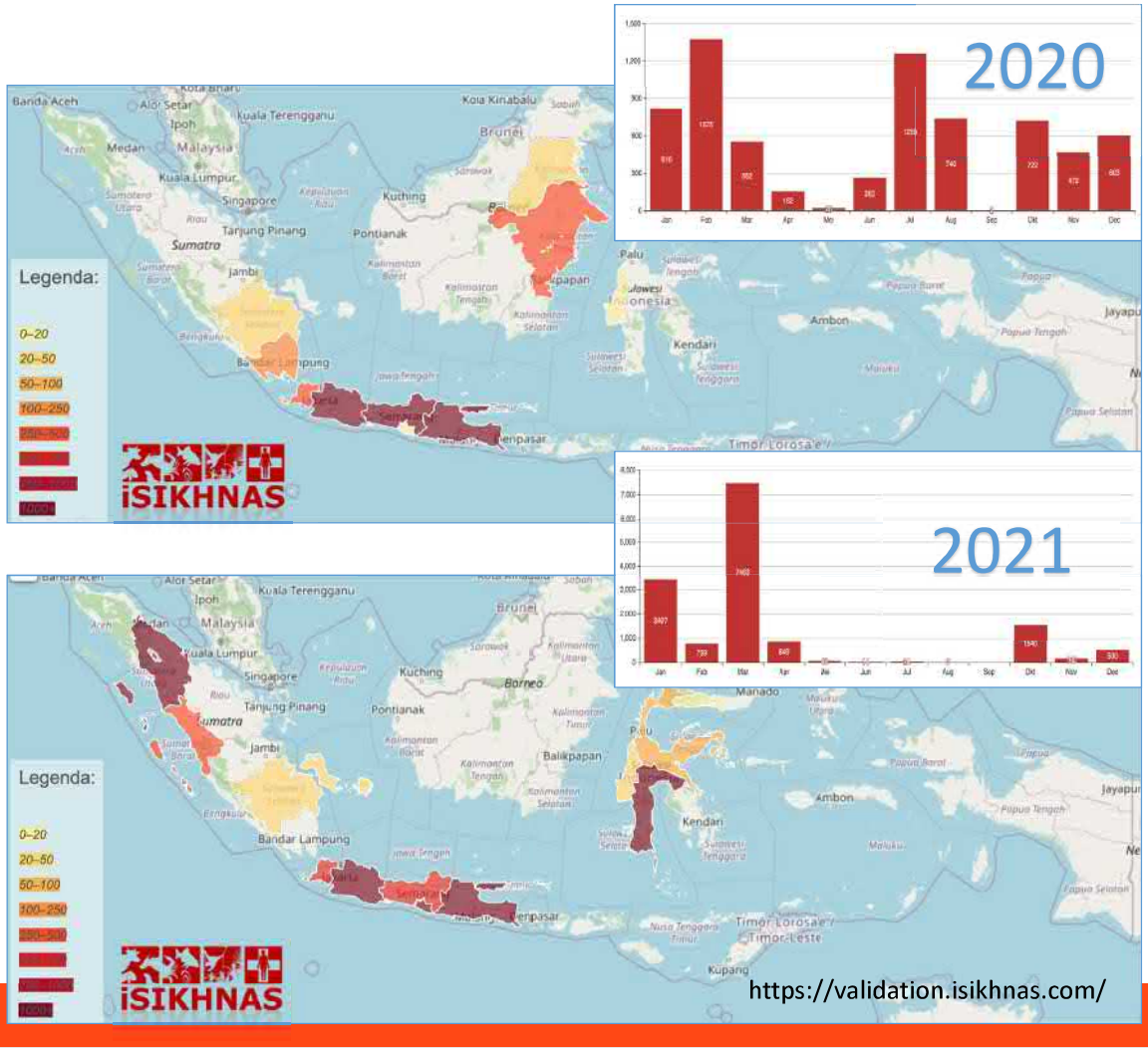


Livestock and Animal Health Statistics (DGLAHS, 2021)

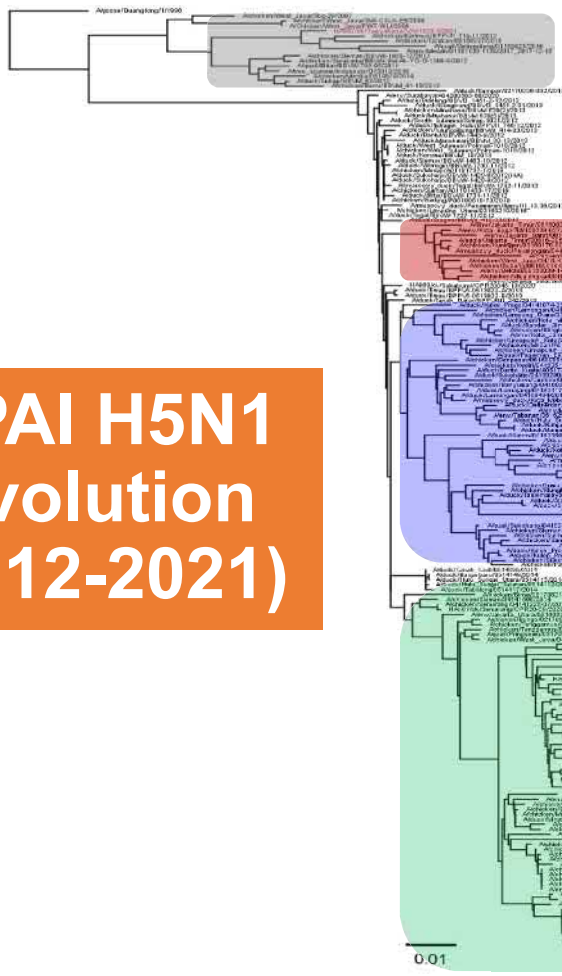
TIMELINE OF AIV OUTBREAKS IN INDONESIA

- Mid-2013 : Outbreak HPAI H5N1 Clade 2.1 di Jawa
- 2004-2005 : H5N1 telah menyebar di 30 dari 33 provinsi di Indonesia
- Mid-2005 : Kasus human-H5N1 pertama di Indonesia
- 2005-2007 : H5N1 clade 2.1 → clade 2.1.1, 2.1.2, 2.1.3
- 2007-2010 : H5N1 clade 2.1.3 → clade 2.1.3.1, 2.1.3.2, 2.1.3.3
- 2010-2012 : H5N1 Clade 2.1.3.2 → clade 2.1.3.2a dan 2.1.3.2b
- Mid-2012 : Outbreak HPAI H5N1 clade 2.3.2.1c
- Late-2016 : Outbreak LPAI H9N2
- 2017-now : Co-circulation HPAI H5N1 clade 2.3.2.1c dan LPAI H9N2

HPAI Situation in Poultry



HPAI H5N1 Evolution (2012-2021)



2.1.3.2)
(2006-2017, 2021)

Initial
(2012-2013)

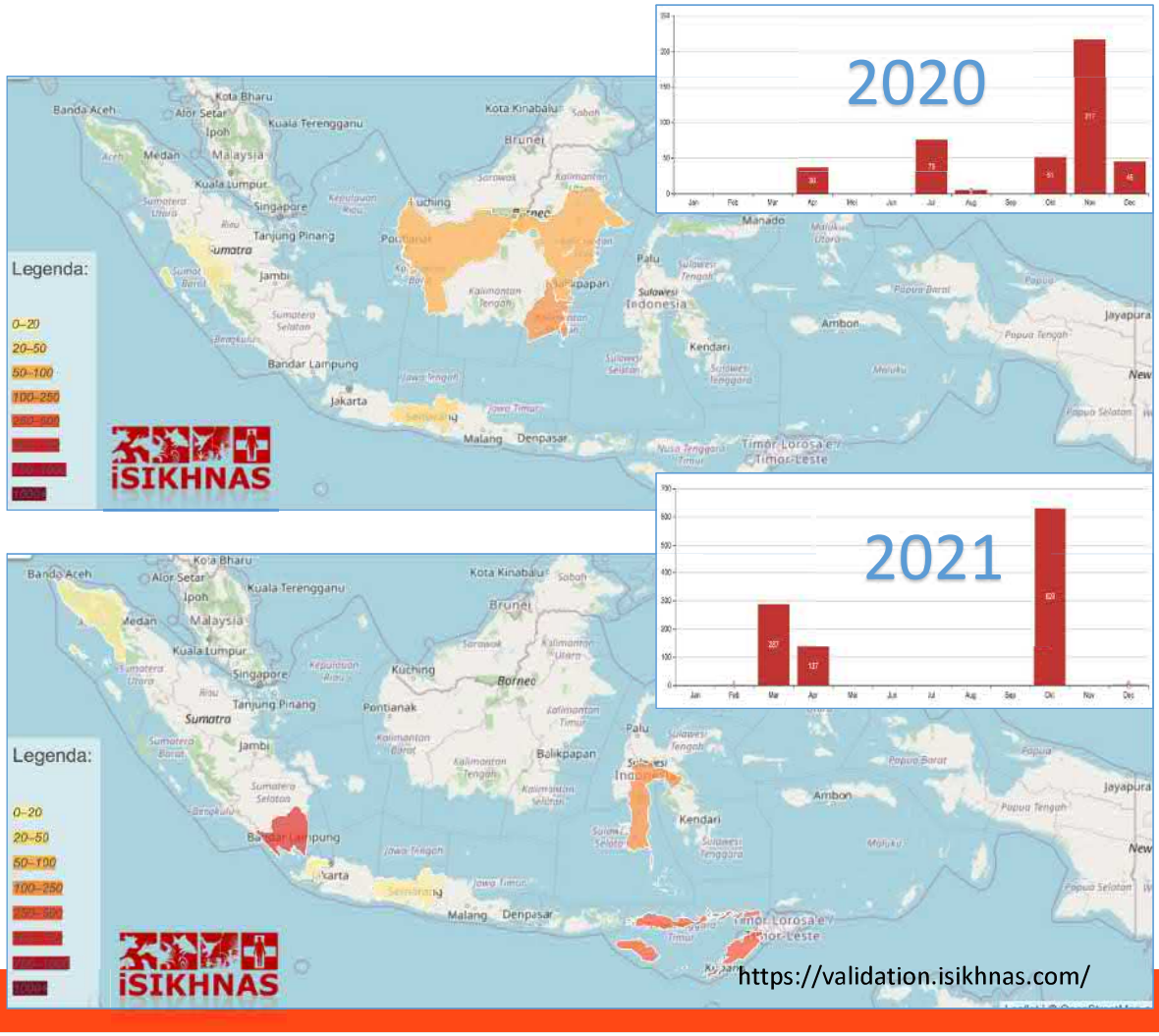
Group III
(2016-2017)

Group I
(2016-now)

Group II
(2014-now)

2.3.2.1c
(2012-now)

LPAI Situation in Poultry



https://validation.isikhnas.com/

LPAI H9N2 Evolution (2016-2021)

HPAI Control Strategy in Indonesia

HPAI Control Strategy

- AI control in Indonesia is focused on enhancing **surveillance** (in poultry and live bird markets), improving **biosecurity** in livestock, **vaccination** in poultry supported by **monitoring of AI virus dynamics**, and **certifying AI free compartments**,
- It is very difficult for countries with endemic status, including Indonesia, to obtain and maintain AI free status for all regions of the country.
- A more feasible concept is to obtain and maintain different animal health status for a poultry compartments within the country. **HPAI-free compartments** provide private sectors with an opportunity to protect their investments by establishing segregation between livestock and wild species.
- MoA Indonesia has implemented of HPAI-free compartments through the Minister of Agriculture Decree Number 28/Permentan/OT.140/ 5/2008 since 2008 in accordance with the Terrestrial Animal Health Code (2021): Chapter 1.4. Animal Health Surveillance; Chapter 4.4. Zoning and Compartmentalisation; Chapter 4.5. Application of Compartmentalisation; and Chapter 10.4. on Infection with High Pathogenicity Avian Influenza Viruses

Outcome HPAI-Free Compartment

- Facilitating safe inter-provinces trade: Live birds, Hatching Eggs, DOC must originate from HPAI free compartment certified by MoA
- International Market Access: Recognition of HPAI free compartments by trading partners as a basis of exportation of poultry and poultry products from Indonesia:
  - **Bangladesh**: Processed Poultry Products
  - **Japan**: Processed Poultry Products
  - **Myanmar**: Chicken Hatching Eggs
  - **PNG**: Processed Poultry Products
  - **Qatar**: Processed Poultry Products
  - **Singapore**: Chicken Carcasses, DOC (establishment approval)
  - **Timor Leste**: DOC, Chicken Carcasses, Processed Poultry Products

Status	Number of Compartments
Self declared HPAI Free Compartment status (sent to WOAH 4 March 2021) https://www.woah.org/app/uploads/2021/07/2021-01-indonesia-hpai-compartement-eng.pdf	100
Additional HPAI Free Compartment certified by MoA (by 18 October 2022) Self declaration to be sent to WOAH	80

AI Vaccination Strategy in Indonesia

Vaccination Strategies

Phase 2004-2006:

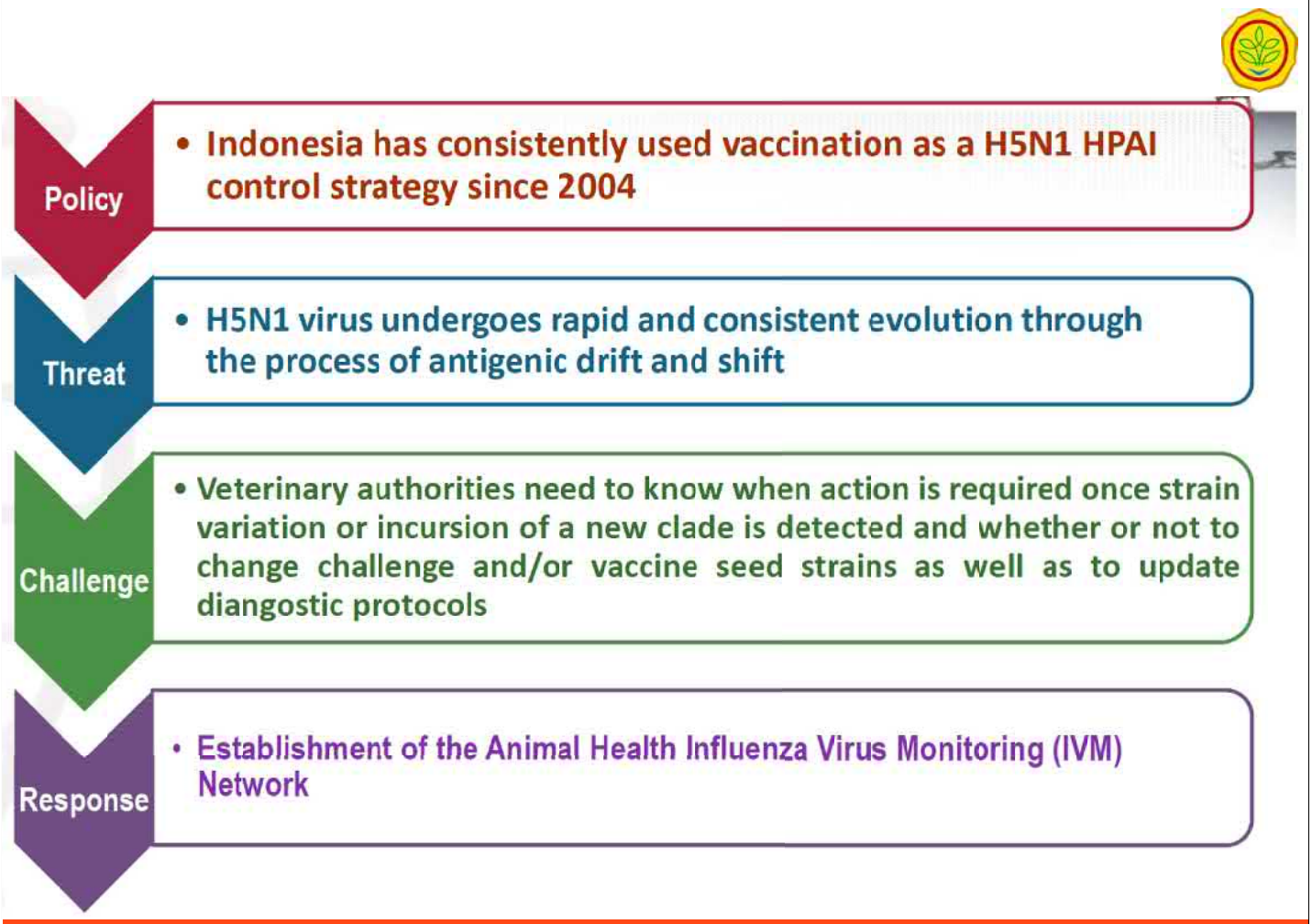
- **Mass vaccination** in mid 2004:
  - 300 M doses available.
  - Inactivated H5N1 local isolate (Legok/03-based vaccine seed).
  - **Free of charge**: backyard and small farmers (sector 4) of **any species.**
- Mass vaccination continued **in 2005** and **early 2006**
- **Mid 2006** due to limited vaccines - **targeted vaccination in sector 3**:
  - Inactivated H5N1 local isolate
  - Inactivated LPAI vaccine (H5N2)
- **Vaccination in sectors 1, 2 and 3** (breeders and layers)
  - **At their own cost.**
  - With coverage estimated to be 90% in commercial layer and 100% in breeding flocks.

Phase 2007-2011:

- **Vaccination in sector 4 discontinued** due to logistic problems and task of administrating vaccines to free-ranging birds.
- **Continued targeted vaccination** of some populations in high. risk/endemic areas for small-holder commercial farms (Sector 3) done by the district livestock services (Dinas Peternakan).
- **Vaccination in sectors 1, 2 and 3** (breeders and layers) **at their own cost.**
- **OFFLU Projects started for the selection of master seed vaccines and challenge antigens** based on genetic (phylogenetics), antigenic cartography and challenge studies.

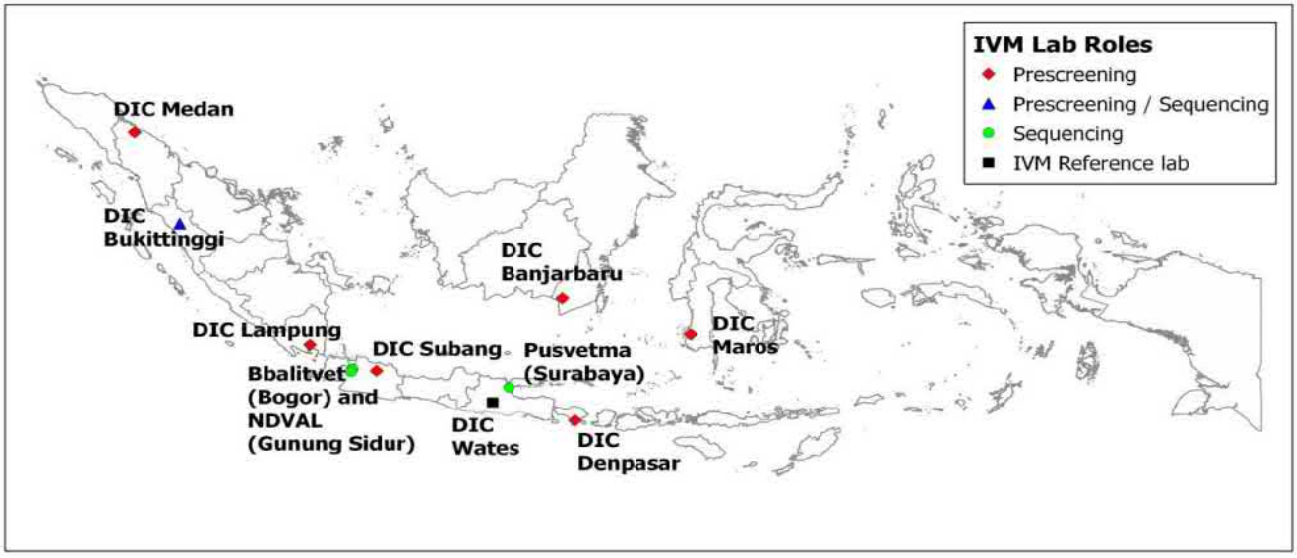
Vaccination Strategies (Phase III: 2011-Now)

- Recommendation Meeting OFFLU Oct-2010 (at this stage clade 2.1.3.2 was dominant H5N1 virus circulating in poultry). At this time master seed vaccines were based on 4 local isolates and 2 isolates as antigen challenge strains.
- The vaccine that used virus seed other which had been set by the government, particularly those of imported vaccines, then immediately withdrawn from circulation and ended in December 2011.
- Another seed vaccine (A/duck/Sukoharjo/BBVW-1428-9/12) has been introduced following the introduction and spread of Clade 2.3.2.1c viruses since 2012.
- Vaccine companies are allowed to make monovalent or bivalent vaccines from combination of clade 2.1.3.2 and clade 2.3.2.1, or use their own seed **strain as long as originated from local isolates and they must be characterized and passed** from registration procedures (in National Veterinary Drug Assay Laboratory)
- An H9N2 local strain (master seed) has been characterized and prepared during 2017 for a new H9N2 vaccine.



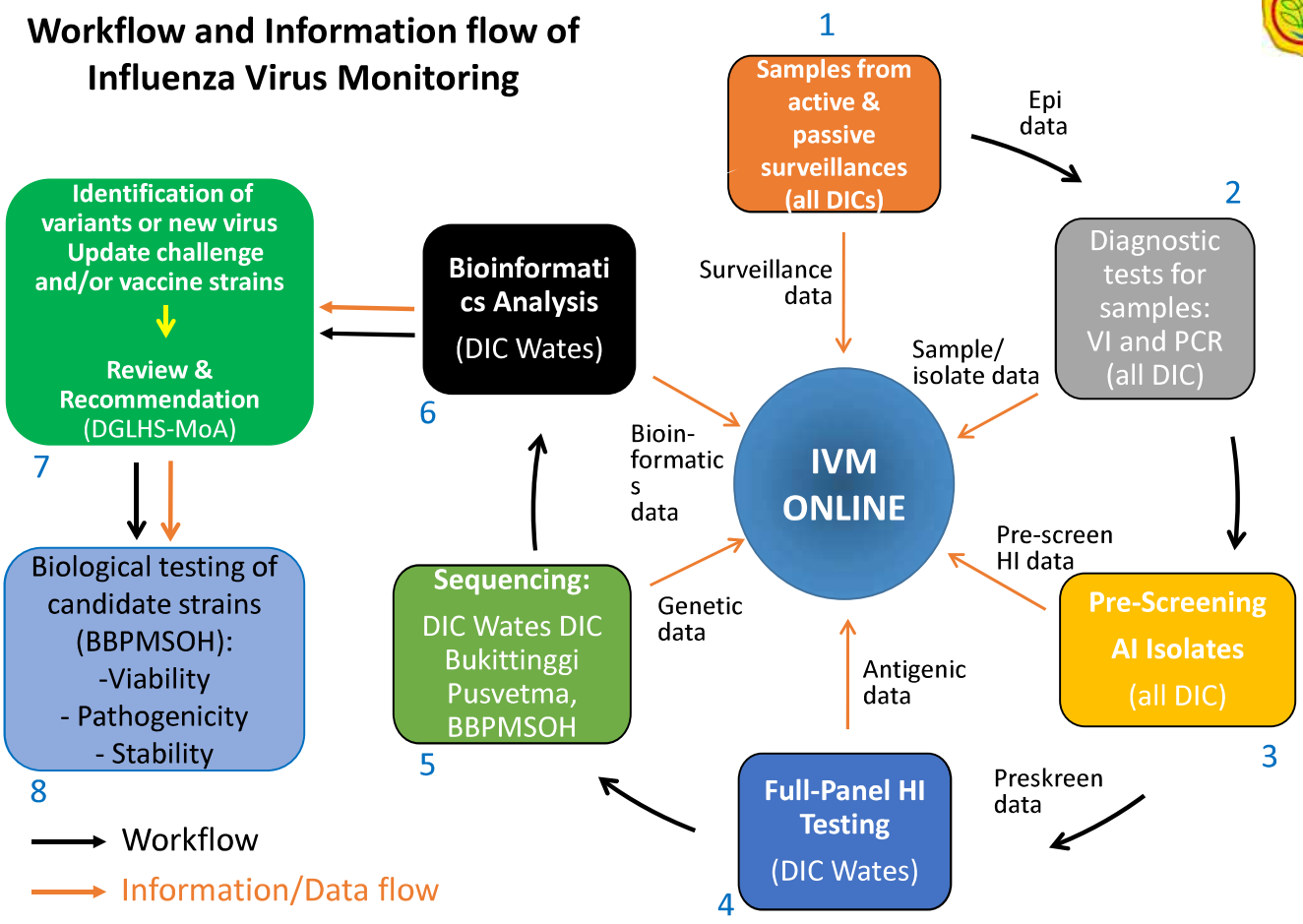
Influenza Virus Monitoring (IVM) Network

IVM: an integrated and coordinated HPAI surveillance at the molecular level conducted by veterinary laboratory network in Indonesia

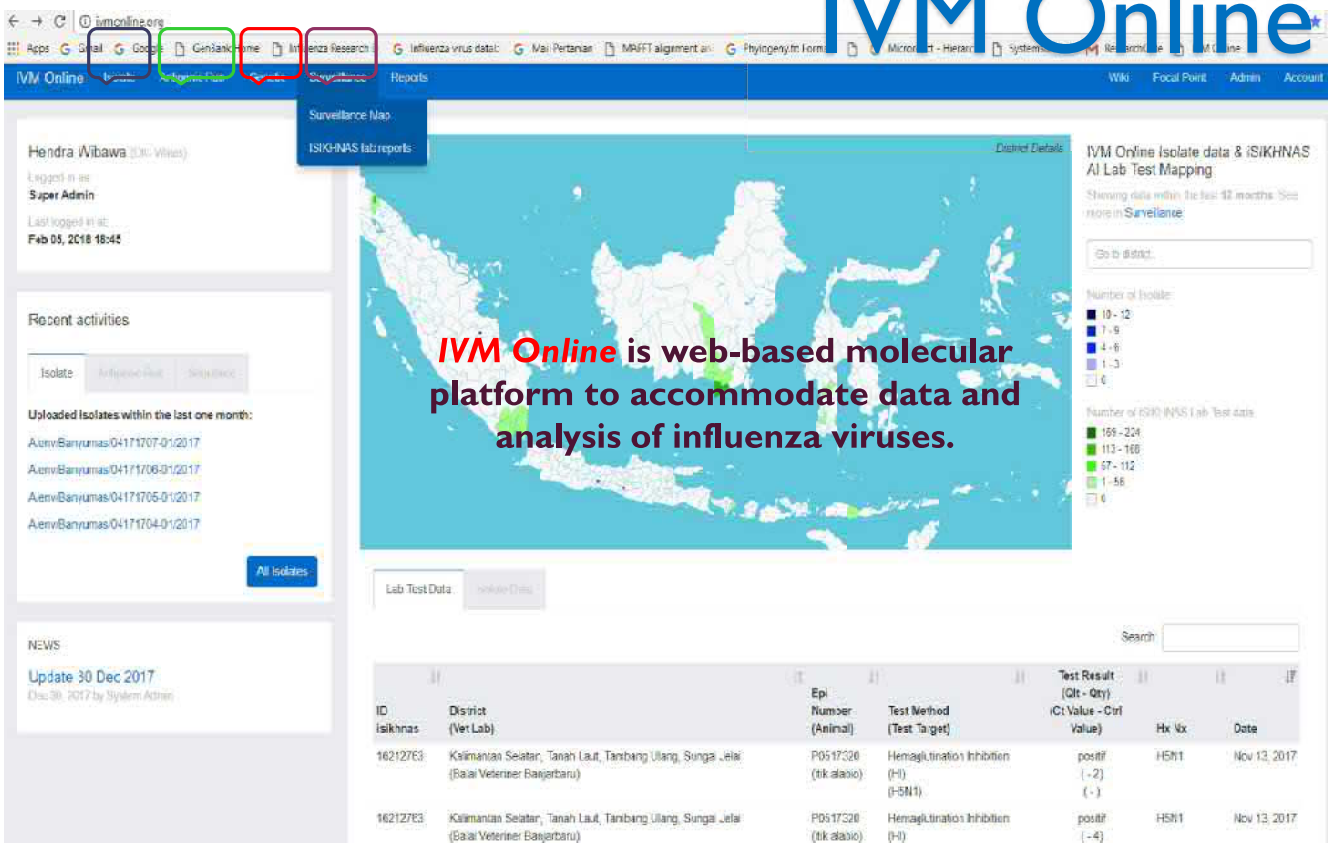


- **Aim and Objectives:**
  - ✓ To monitor the dynamic of influenza virus circulating in animal in Indonesia and to accelerate the reporting of virus monitoring to decision makers at the national level.
- **IVM Network Activities**
  - ✓ Included the use of virology and molecular detection and identification using virus isolation and PCR, followed by DNA sequencing, antigenic cartography, and bioinformatic analysis for vaccine seed and challenge strain selection to ensure a close antigenic match.

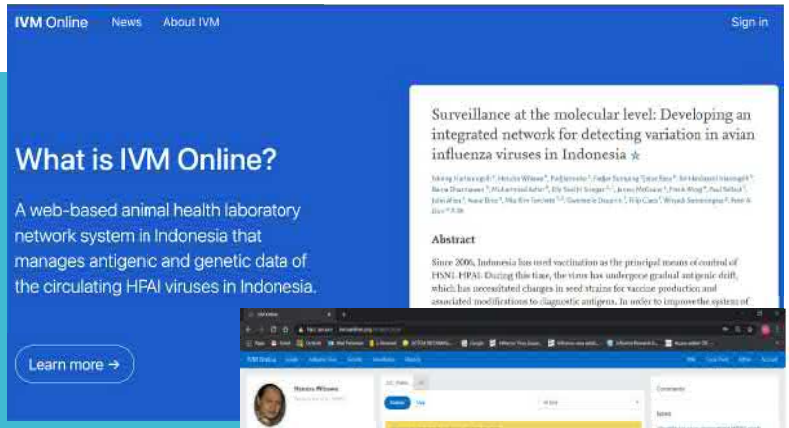
Workflow and Information flow of Influenza Virus Monitoring



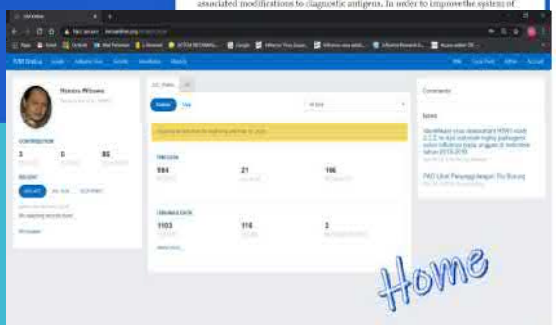
IVM Online

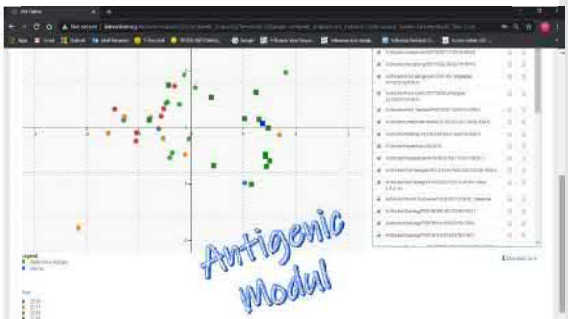


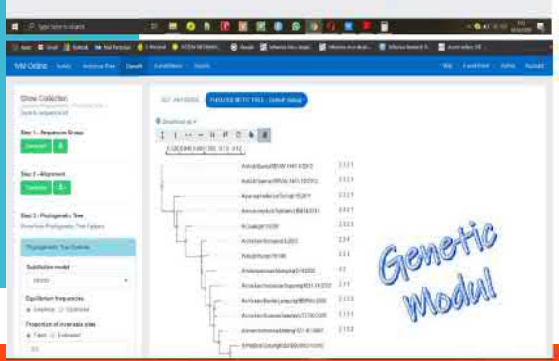
- Developed in collaboration with the Directorate General of PKH-Ministry of Agriculture, FAO-Indonesia, and assisted by experts from ACDP Australia
- Since December 2017, real-time infolab data (particularly related to AI test results) from iSIKHNAS (*National Animal Health Information System*) are shown automatically into IVM Online

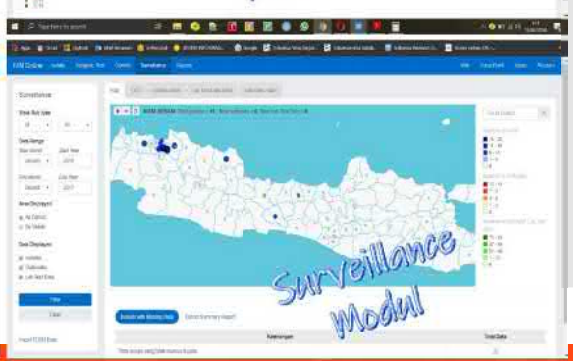


IVM Online

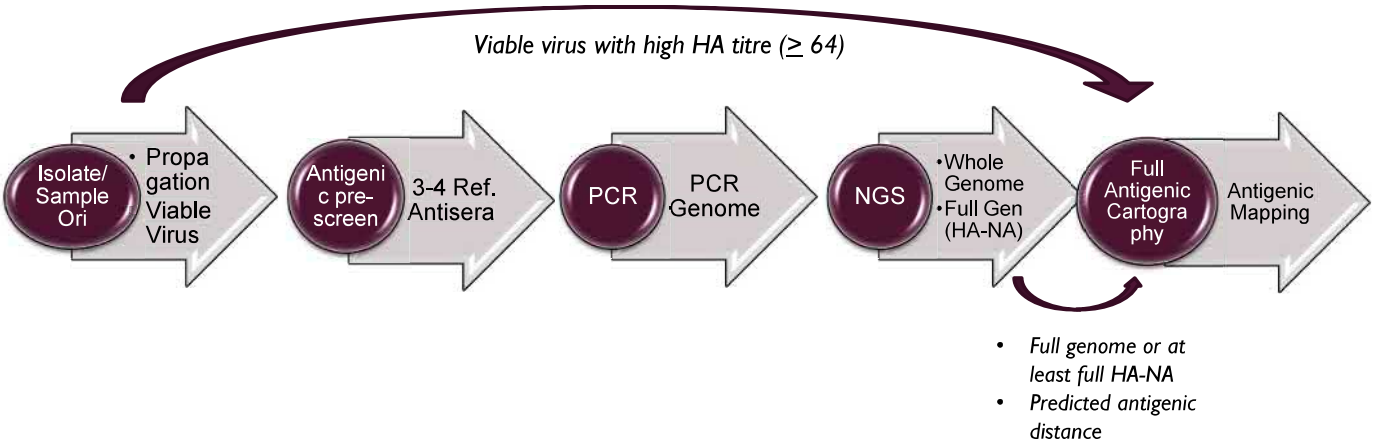






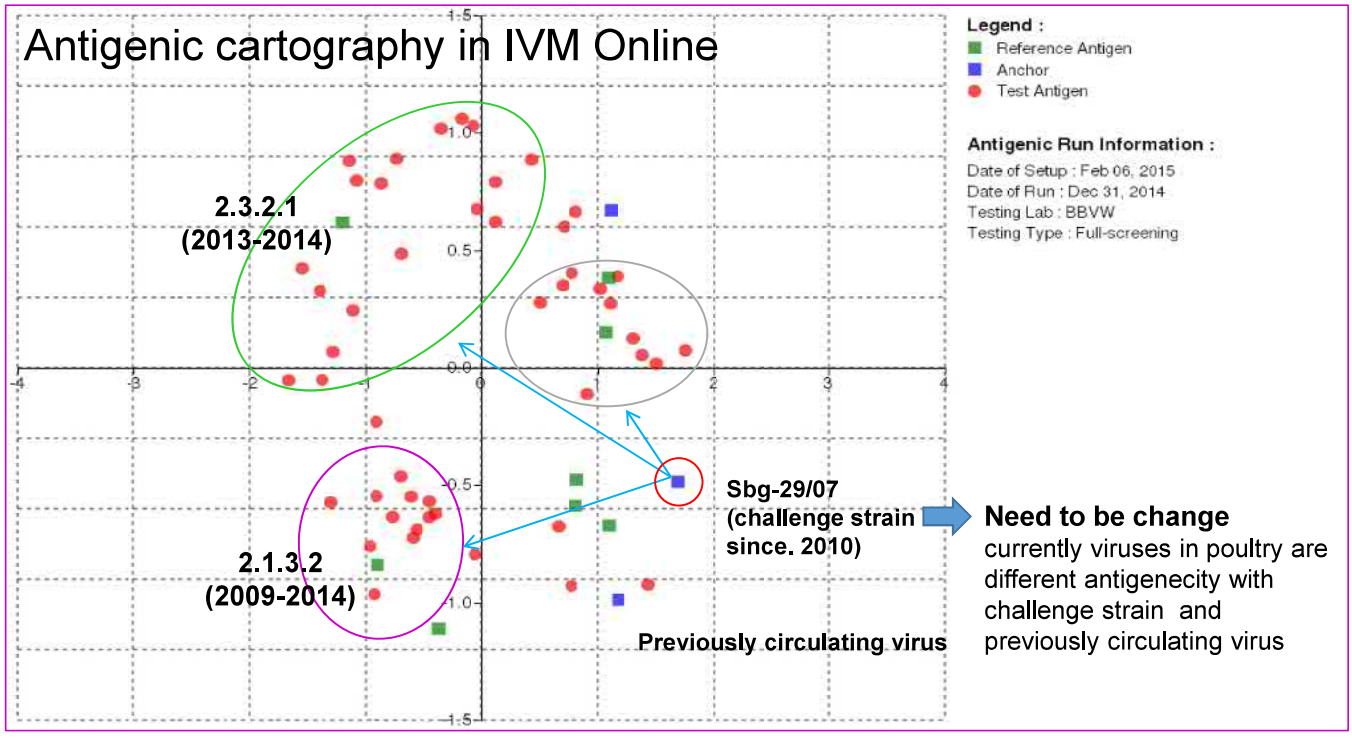


DEVELOPMENT OF NEXT GENERATION SEQUENCING: CHANGE OF THE PROCESS OF CHARACTERIZATION (GENETIC → ANTIGENIC)



Example: Detection of antigenic variation of HPAI H5N1

The results of post vaccination monitoring show that the 2.1.3 reference antigen showed low cross protection → significant antigenic distances of newly viruses to previously circulating virus → need to change the challenge strain antigen

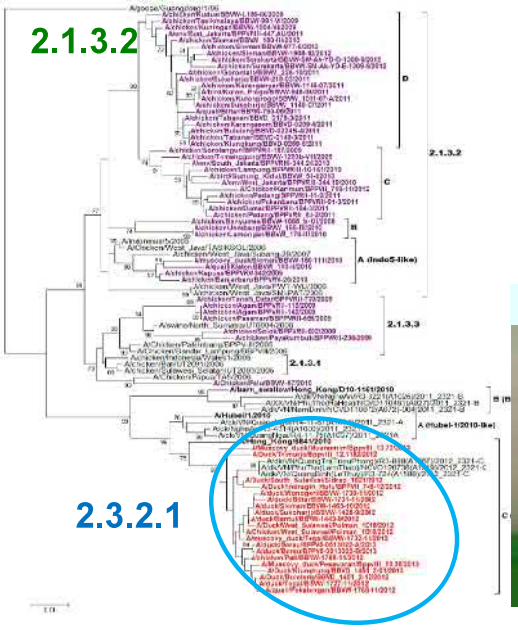


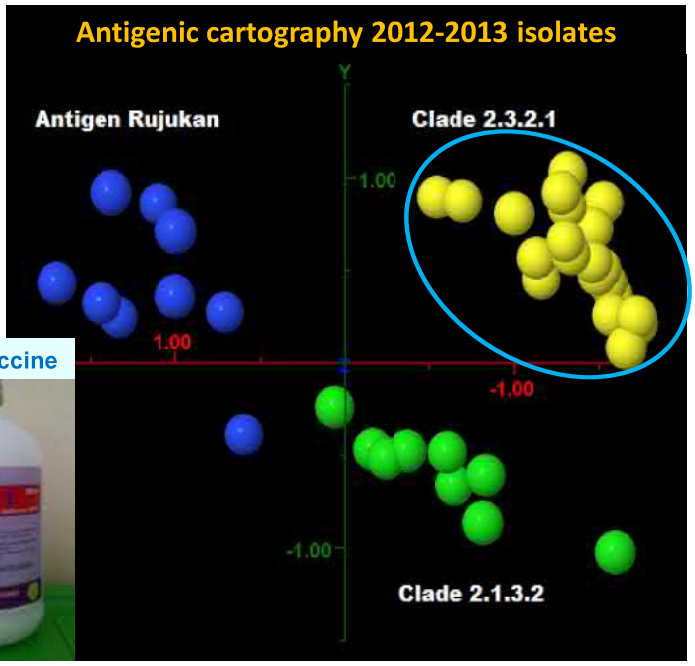
The Benefits of IVM Network for AI Surveillance & Vaccination

Output and Outcome IVM (2012-2013):

Identification of a new clade (2.3.2.1) H5N1 virus incursion into Indonesia through bioinformatics analyses (phylogenetics and antigenic cartography) lead to the successful and timely development H5N1 clade 2.3.2.1 vaccine that produced locally

Phylogenetic analysis 2012-2013





2.3.2.1. vaccine

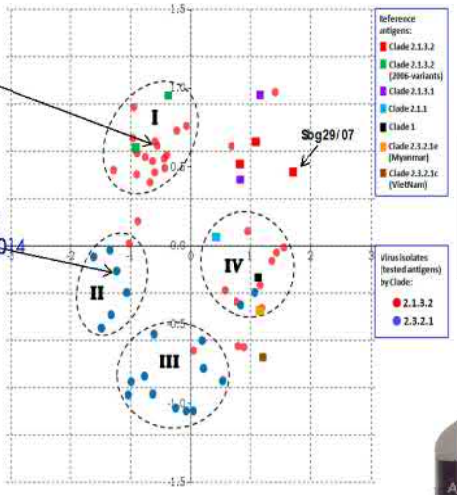
The Benefits of IVM Network for AI Surveillance & Vaccination

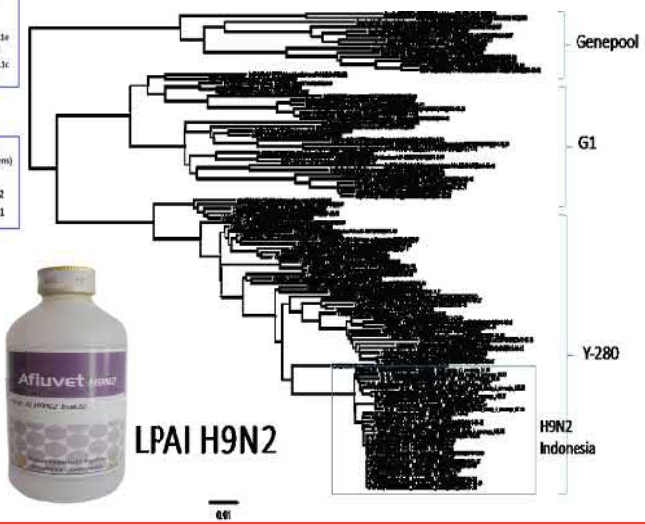
Output and Outcome IVM (2014-2017):

Updated challenge strains for vaccine efficacy due to mutation of HPAI H5N1 clade 2.3.2.1c and clade 2.1.3.2 and provided recommendation for master seed vaccine following the identification of LPAI H9N2

2.1.3.2 challenge strain candidate:
A/chicken/Barru/BBVM 41-13/2013

2.3.2.1 challenge strain candidates:
A/chicken/Semarang/0401225-07/2014



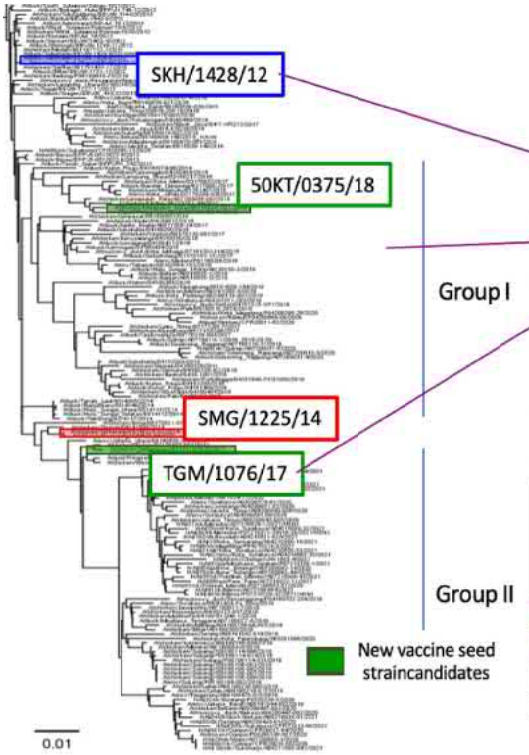


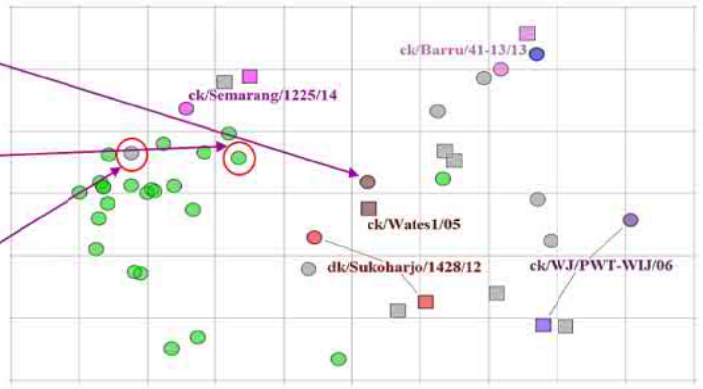
LPAI H9N2

The Benefits of IVM Network for AI Surveillance & Vaccination

Output and Outcome IVM (2018-2021):

- **Provided recommendation to update master seed vaccine due to significant mutations (genetically and antigenically) of HPAI H5N1 clade 2.3.2.1c**





Tested Antigen	HA Titer	HI Titer			Antigenic Distance (AD) to SKH/1428/12		AD pattern to SKH/1428/12
		SMG/1225/14 (2.32.1)	TGM/1076/17 (2.3.2.1)	SKH/1428/12 (2.3.2.1)	Antigen	Antisera	
ck/Limapuluh Kota/A02180375-001/201	2048	512	512	32	1.7	3.6	Moderate AD
ck/Tanggamus/031711076-65/2017	256*	256	256	16	3	4.9	Strong AD
dk/Sukoharjo/BBVW1428-9/2012	256*	512	128	512			

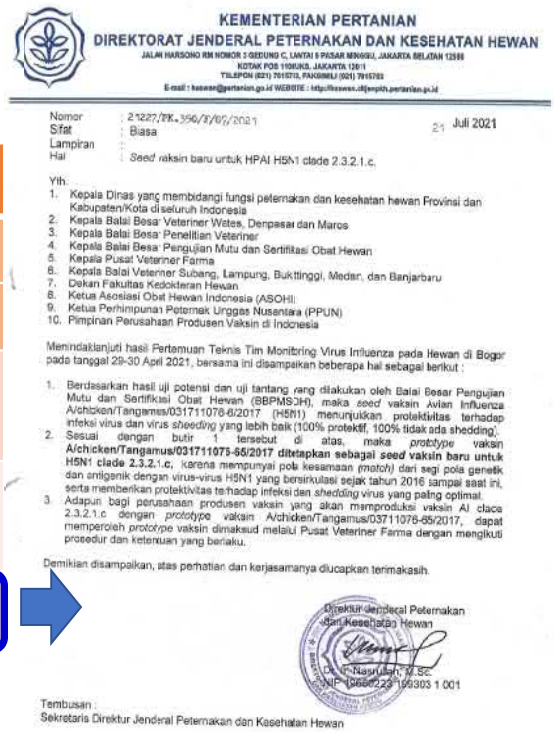
* HA dari inactivated antigen. Titer HI dengan warna merah adalah dari homologous antigen-antisera

The Benefits of IVM Network for AI Surveillance & Vaccination

Results of Challenge Study of HPAI H5N1 Clade 2.3.2.1c (Source: NVDAL - IVM Network)

Vaccine Seed Strain (Clade 2.3.2.1c)	Challenge Strain(Clade 2.3.2.1c)					
	TGM/1076/2017		50-KT/0376/2018		SMG/1225/2014	
	Dead/ Survive	Shedding	Dead/ Survive	Shedding	Dead/ Survive	Shedding
SKH/1428/2012	0/10	Yes (Day 3-6)	0/10	Yes (Day 3-6)	**1/9**	Yes (Day 3-6)
50-KT/0376/2018	0/10	No	0/10	No	**1/9**	Yes (Day 3-6)
TGM/1076/2017	**0/10**	**No**	**0/10**	**No**	**0/10**	**No**

From the process of virus characterization through IVM Network, IVM Team recommended to MoA to update vaccine seed strain for H5N1 clade 2.3.2.1c : A/chicken/Tanggamus/031711076-65/2017 (TGM/1076/2017)



KEMENTERIAN PERTANIAN
DIREKTORAT JENDERAL PETERNAKAN DAN KESEHATAN HEWAN

Nomor : 21227/PK.350/F/07/2021
Sifat : Biasa
Lampiran :
Hal : *Seed* vaksin baru untuk HPAI H5N1 clade 2.3.2.1.c.

21 Juli 2021

Yth.
1. Kepala Dinas yang membidangi fungsi peternakan dan kesehatan hewan Provinsi dan Kabupaten/Kota di seluruh Indonesia
2. Kepala Balai Besar Veteriner Wates, Denpasar dan Maros
3. Kepala Balai Besar Penelitian Veteriner
4. Kepala Balai Besar Pengujian Mutu dan Sertifikasi Obat Hewan
5. Kepala Pusat Veteriner Farma
6. Kepala Balai Veterner Subang, Lampung, Bukttinggi, Medan, dan Banjarbaru
7. Dekan Fakultas Kedokteran Hewan
8. Ketua Asosiasi Obat Hewan Indonesia (ASOHI)
9. Ketua Perhimpunan Peternak Unggas Nusantara (PPUN)
10. Pimpinan Perusahaan Produsen Vaksin di Indonesia

Menindaklanjuti hasil Pertemuan Teknis Tim Monitoring Virus Influenza pada Hewan di Bogor pada tanggal 29-30 April 2021, bersama ini disampaikan beberapa hal sebagai berikut :

1. Berdasarkan hasil uji potensi dan uji tantang yang dilakukan oleh Balai Besar Pengujian Mutu dan Sertifikasi Obat Hewan (BBPMSOH), maka *seed* vaksin Avian Influenza A/chicken/Tanggamus/031711076-6/2017 (H5N1) menunjukkan protektivitas terhadap infeksi virus dan virus *shedding* yang lebih baik (100% protektif, 100% tidak ada shedding).
2. Sesuai dengan butir 1 tersebut di atas, maka *prototype* vaksin **A/chicken/Tanggamus/031711075-65/2017 ditetapkan sebagai seed vaksin baru untuk H5N1 clade 2.3.2.1.c**, karena mempunyai pola kesamaan (*match*) dari segi pola genetik dan antigenik dengan virus-virus H5N1 yang bersirkulasi sejak tahun 2016 sampai saat ini, serta memberikan protektivitas terhadap infeksi dan *shedding* virus yang paling optimal.
3. Adapun bagi perusahaan produsen vaksin yang akan memproduksi vaksin AI clade 2.3.2.1.c dengan *prototype* vaksin A/chicken/Tangamus/031711076-65/2017, dapat memperoleh *prototype* vaksin dimaksud melalui Pusat Veteriner Farma dengan mengikuti prosedur dan ketentuan yang berlaku.

Demikian disampaikan, atas perhatian dan kerjasamanya diucapkan terimakasih.

Direktur Jenderal Peternakan dan Kesehatan Hewan

Dr. I Nasrullah, M.Sc.
NIP. 19660223 199303 1 001

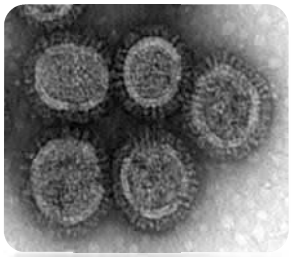
Tembusan :
Sekretaris Direktur Jenderal Peternakan dan Kesehatan Hewan

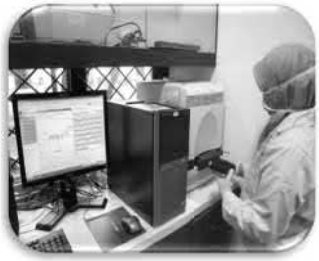
SUMMARY

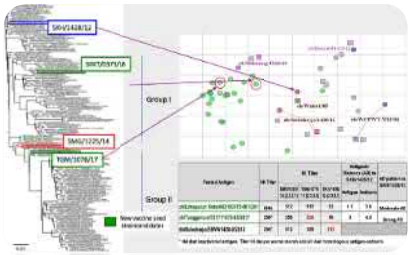
- HPAI H5N1 in poultry remains endemic in some areas, particularly in Java, with Clade 2.3.2.1c now is predominant clade since 2015 replacing clade 2.1.3.2.
- LPAI H9N2 virus was detected in late 2016 caused LPAI outbreaks in several poultry farms (particularly in layer farms).
- The government of Indonesia has taken several strategies to control AI virus in poultry, including improve surveillance and diagnostic capacity for early detection and respond, improve biosecurity practices for poultry farms, improve the quality of vaccines (antigenically matched to circulating viruses to provide good protectivity), and increase HPAI-free poultry compartments.
- Vaccination is an important approach for HPAI control strategy in endemic countries, but it should be supported by post-vaccination monitoring and evaluation and should be strengthened by continued molecular surveillance to provide better understanding on the HPAI virus dynamic and evolution.
- IVM network is quite relevant to other countries seeking to establish a laboratory network for the surveillance of avian influenza and other pathogens.

Acknowledgements

- Director General Livestock and Animal Health Services, Ministry of Agriculture, Indonesia
- Director of Animal Health, Directorate General Livestock and Animal Health Services (DGLAHS), Ministry of Agriculture, Indonesia
- Directors of Veterinary Laboratories under DGLAHS, Ministry of Agriculture, Indonesia
- Food and Agriculture Organization of the United Nations, Emergency Centre for Transboundary Animal Diseases (FAO-ECTAD), Jakarta, Indonesia
- Influenza Virus Monitoring Network Laboratories in Indonesia







Vaccination Strategies to prevent and control HPAI: Removing unnecessary barriers for usage

VACCINATION IN PLACES WHERE VIRUS IS ENDEMIC:
Egypt Practice to control HPAI

Abdelsatar Arafa

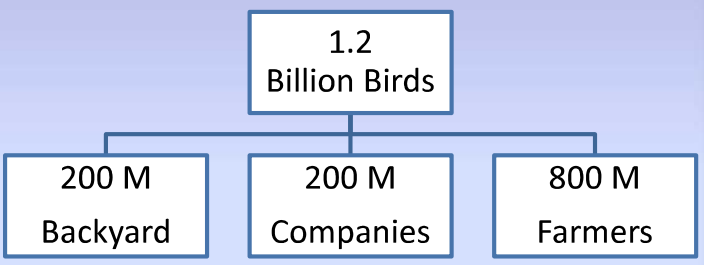
PhD, Head of Reference Laboratory for Veterinary Quality Control on Poultry Production,
Animal Health Research Institute, Agriculture Research Center, Egypt

WOAH Reference Laboratory for Avian Influenza

WOAH Headquarter, Paris
October 25-26, 2022

Background:

Egyptian Broilers Production



Egypt, administrative divisions map

Egyptian Broilers Production Distributions

- Upper Egypt — 8%
- Middle Egypt — 15%
- Lower Egypt — 65%
- Out of Valley — 12%

H5 HAPI in Egypt

HPAI (H5N1) first reported in Egypt in 2006, the disease was widely spread in both commercial and household sectors.

Endemic status of HPAI in Egypt since 2008

H5N1 HPAI clade 2.2.1 was the ancestral strain in 2006, and subjected for several mutations that lead to emergence of variant clades 2.2.1.1 and 2.2.1.1a in 2008.

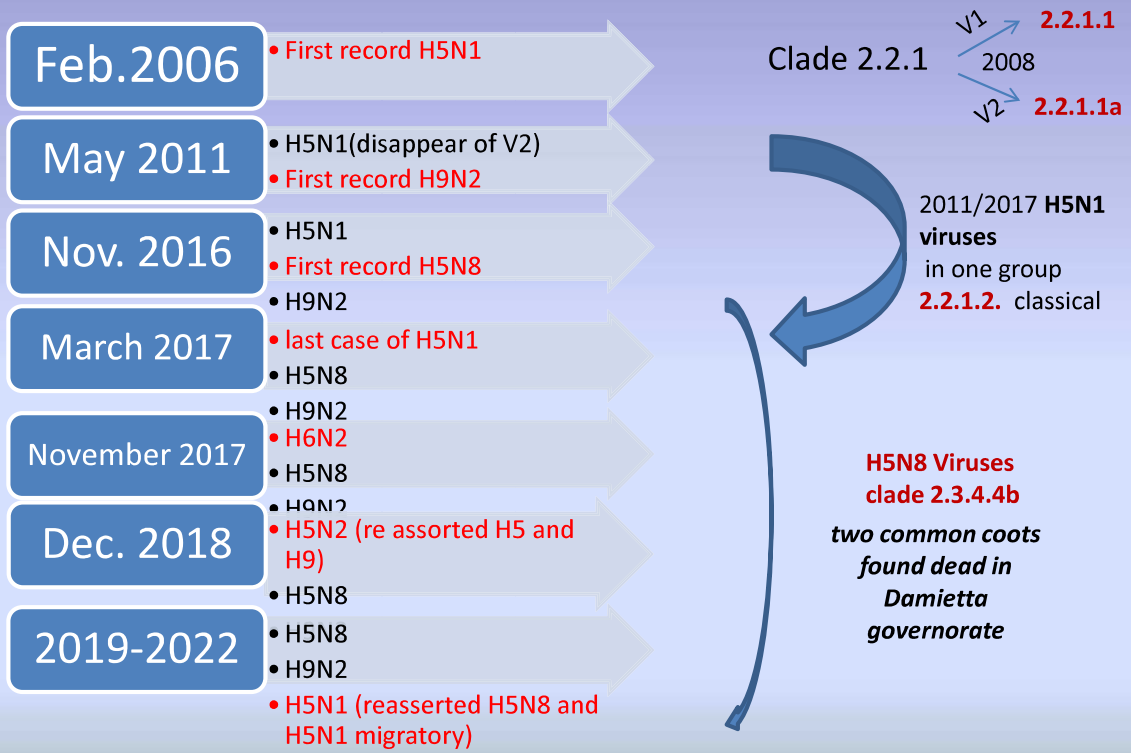
In 2014, new clade was emerged (2.2.1.2) that lead to exacerbated increase in the number of human cases.

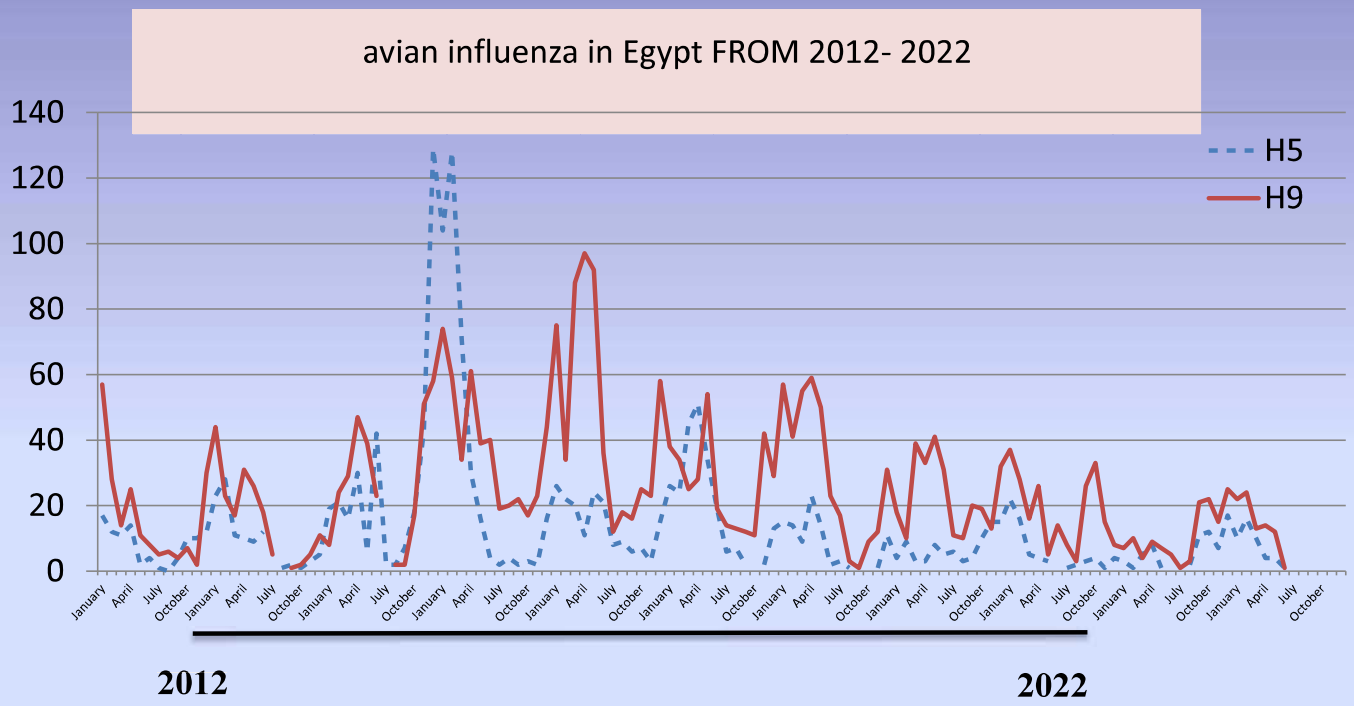
On the other hand, H9N2 LPAI is endemic in Egypt since its first record in 2011as well as H5N8 HPAI since 2016.

The continuous circulation of these subtypes for several years led to the emergence of the first natural reassortment event in domestic poultry in Egypt, the HPAI (H5N2) virus that was isolated from a commercial duck farm in 2018.

Since late 2020, a new variant H5N1 2.3.4.4b has been spreading widely in Europe, Asia and western and south Africa causing infection of both humans and birds.

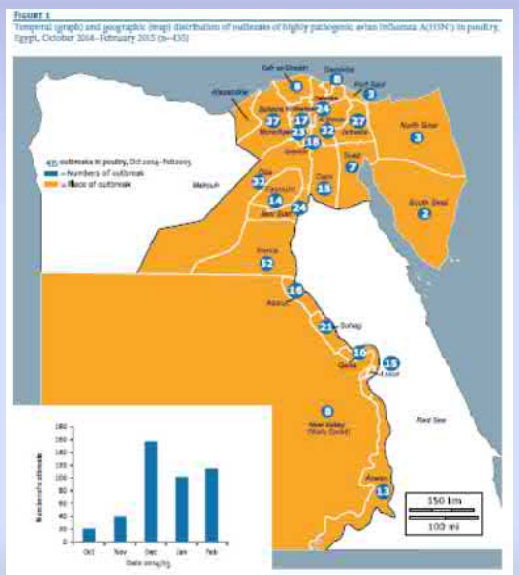
Time flow of avian influenza in Egypt 2006 -2022

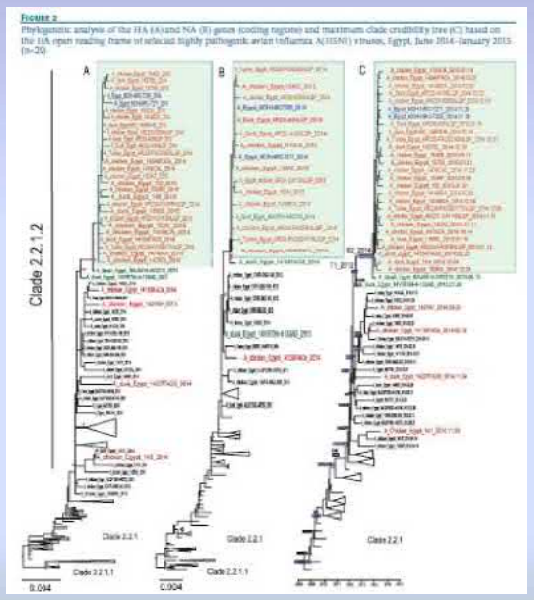




Avian Influenza H5N1

- **2014-2015; cl 2.2.1.2 (Arafa et al, 2015)**





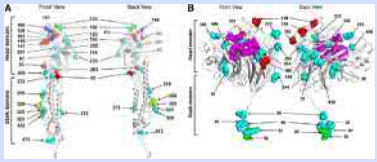
Avian Influenza H5N1

Virol J. 2017 Mar 9;14(1):48. doi: 10.1186/s12985-017-0697-5.

Isolation and genetic characterization of a novel 2.2.1.2a H5N1 virus from a vaccinated meat-turkeys flock in Egypt.

Salaheldin AH[1,2], Veits J[3], Abd El-Hamid HS[4], Harder TC[3], Devrishov D[5], Mettenleiter TC[3], Hafez HM[6], Abdelwhab EM[3]

- Case report in turkeys
- Inactivated vaccines (8 & 34 days)
- 72 days of age – AI infection



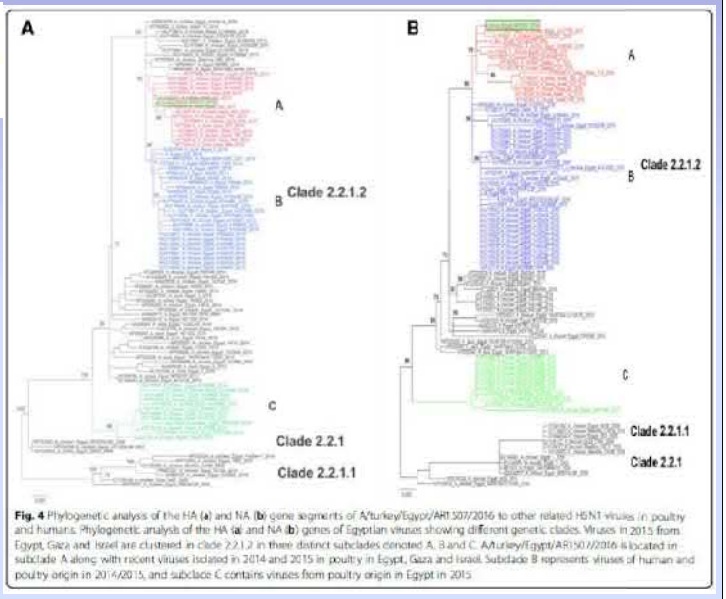


Fig. 4 Phylogenetic analysis of the HA (**a**) and NA (**b**) gene segments of A/turkey/Egypt/AR1507/2016 to other related H5N1 viruses in poultry and humans. Phylogenetic analysis of the HA (**a**) and NA (**b**) genes of Egyptian viruses showing different genetic clades. Viruses in 2015 from Egypt, Gaza and Israel are clustered in clade 2.2.1.2 in three distinct subclades denoted A, B and C. A/turkey/Egypt/AR1507/2016 is located in subclade A along with recent viruses isolated in 2014 and 2015 in poultry in Egypt, Gaza and Israel. Subclade B represents viruses of human and poultry origin in 2014/2015, and subclace C contains viruses from poultry origin in Egypt in 2015

Transbound Emerg Dis. 2018 Jan 24. doi: 10.1111/tbed.12816. [Epub ahead of print]

An Egyptian HPAI H5N1 isolate from clade 2.2.1.2 is highly pathogenic in an experimentally infected domestic duck breed (Sudani duck).

Samir M[1,2], Hamed M[3], Abdalla F[4], Kinh Nguyen V[5], Hernandez-Vargas EA[5], Seehusen F[6], Baumgärtner W[6], Hussein A[7], Ali AAH[4], Pessler F[1,8]

Avian Influenza H5N8

- H5N8 in Dec 2016 (cl 2.3.4.4b)

JOURNAL OF GENERAL VIROLOGY

RESEARCH ARTICLE

Kandeil et al., Journal of General Virology 2017;98:1573–1586
DOI 10.1099/jgv.0.000847

MICROBIOLOGY SOCIETY

Genetic characterization of highly pathogenic avian influenza A H5N8 viruses isolated from wild birds in Egypt

Ahmed Kandeil,[1] Ahmed Kayed,[1] Yassmin Moatasim,[1] Richard J. Webby,[2] Pamela P. McKenzie,[2] Ghazi Kayali[3,4,*] and Mohamed A. Ali[1,*]

Abstract

A newly emerged H5N8 influenza virus was isolated from green-winged teal in Egypt during December 2016. In this study, we provide a detailed characterization of full genomes of Egyptian H5N8 viruses and some virological features. Genetic analysis demonstrated that the Egyptian H5N8 viruses are highly pathogenic avian influenza viruses. Phylogenetic analysis revealed that the genome of the Egyptian H5N8 viruses was related to recently characterized reassortant H5N8 viruses of clade 2.3.4.4 isolated from different Eurasian countries. Multiple peculiar mutations were characterized in the Egyptian H5N8

Co-circulation of H5N1, H5N8 and H9N2 can lead to possible reassotments

Avian Influenza H5N2

- **H5N2 was reported in Egypt in March 2019**

viruses

MDPI

Communication

Isolation of a Novel Reassortant Highly Pathogenic Avian Influenza (H5N2) Virus in Egypt

Naglaa M. Hagag [1], Ahmed M. Erfan [1], Mohamed El-Husseiny [1], Azhar G. Shalaby [1], Mohamed A. Saif [1], Maram M. Tawakol [1], Ahmed A. Nour [1], Abdullah A. Selim [1], Abdel-Satar Arafa [1], Mohamed K. Hassan [1], Wafaa M. M. Hassan [1], Hanan A. Fahmy [1], Essam Ibraheem [1], Mohamed Attia [2], Ali M. M. Abdelhakim [2], Momtaz A. Shahein [1] and Mahmoud M. Naguib [1,3,*]

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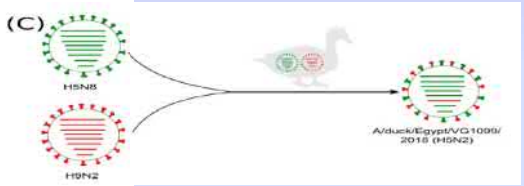
2 General Organization for Veterinary Services, Nadi El-Said Street P.O. Box, 12619 Dokki, Cairo, Dokki-Giza, Egypt; ashrafatea@yahoo.com (M.A.); Hakam2060@gmail.com (A.M.M.A.)

3 Zoonosis Science Centre, Department of Medical Biochemistry and Microbiology, Uppsala University, Husargatan 3, P.O. Box 582, 75123 Uppsala, Sweden

* Correspondence: Mahmoud.naguib@imbim.uu.se



Avian influenza current situation

Outbreaks in poultry

- There were 6 commercial farms recorded H5N8 (in 5 Governorates)
- 1 household birds (in Menia)
- 46 live bird markets (in 12 Governorates)
- 1 slaughter house (in Menia)
- 1 case H5N1
- A total of 54 cases

Human cases

- There is no human cases since 2017

Laboratory findings

- The genetic analysis of recent H5N8 isolates revealed that they were clustered to clade 2.3.4.4b
- Multiple basic amino acid pattern of cleavage sites of the HA that characterizes the high pathogenicity of AIVs
- The genetic analysis of NA gene of the H5N8 isolates revealed that these viruses are related to the Russian like reassortant H5N8 viruses clade 2.3.4.4.b that introduced to Egypt in 2016
- NA protein did not show any marker of resistance to Tamiflu.

GENETIC CHARACTERIZATION OF H5N8

•The receptor binding pocket of the HA protein of all sequenced Egyptian isolates revealed amino acids H103, N182, G221, Q222, and G224 suggesting an avian-like α2,3-sialic acid receptor binding preference.

GENETIC CHARACTERIZATION OF A/H5N8

•However, mutations N94S detected in the HA protein were linked to enhanced binding affinity to human-type alpha 2,6 sialic acid receptors.

•Mutations in the antigenic sites both (A) T140A & P144Q and (B) A196V were detected in 2021/22 isolates.

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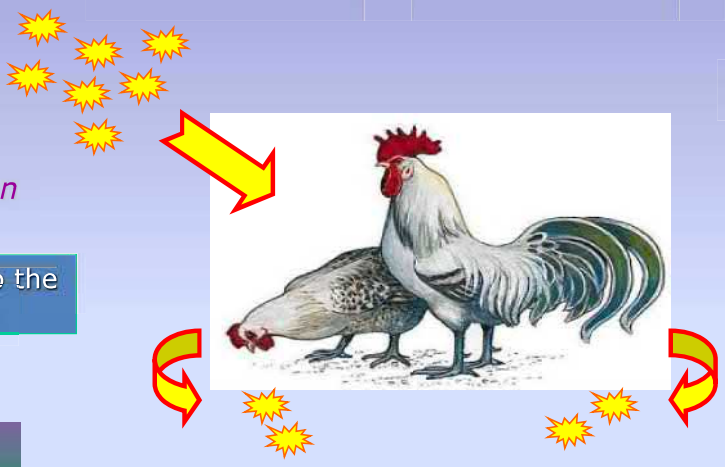
Immunity to control H5 HPAI



Infection

Resistance to the infection

Local and cell mediated immunity

Clinical signs, egg drop, growth retardation, …

Clinical protection

Humoral and cell mediated immunity

Excretion (oral and cloacal)

Reduction of shedding

Humoral, cell mediated & mucosal immunity

Measures for containment of outbreaks in poultry

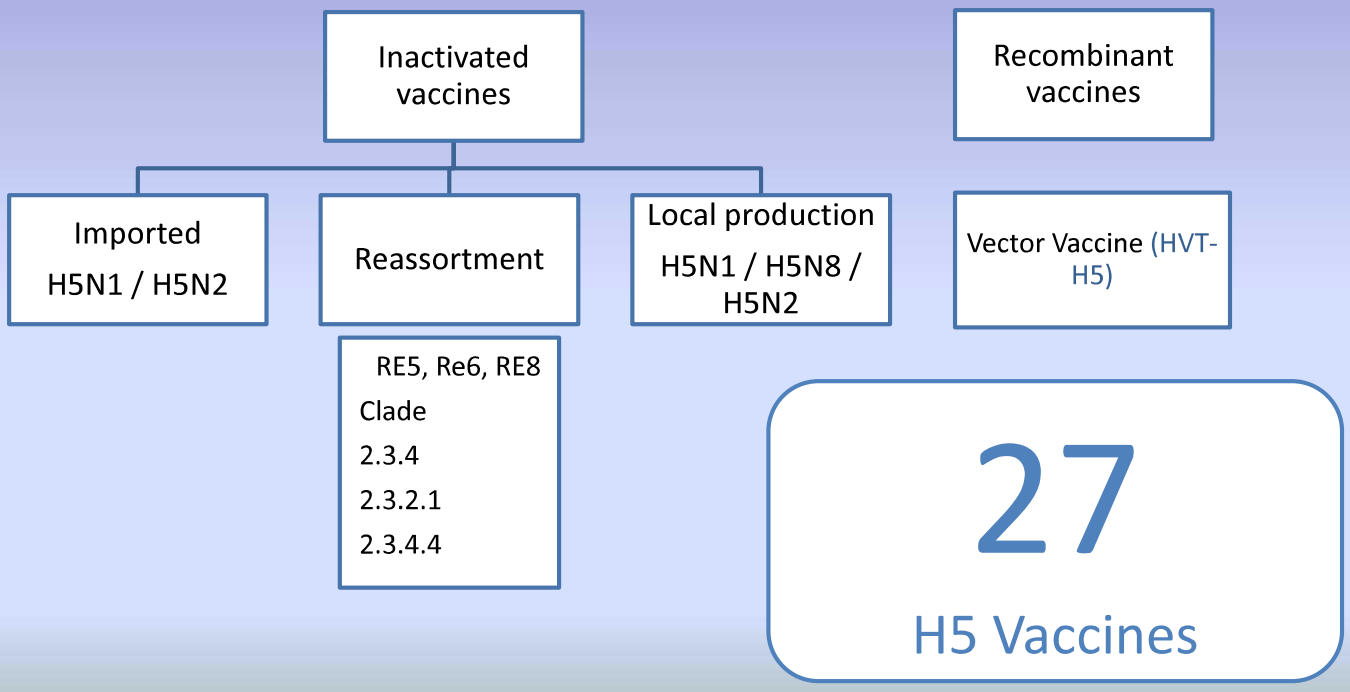
- Rapid Response measures are implemented by RRT teams at each districts and include:
- Culling of the infected birds depending on the culling policy in household, farms (if symptoms are clear).
- Sanitary and safe disposal of dead, culled birds, litter and infected premises.
- Cleaning and disinfection of the infected area.
- Targeted Surveillance in farms within 3-5 km around the center of the outbreak.

Epidemiological investigations




- **Conducting awareness/educational seminars to educate people about the disease.**
- **A 21 day surveillance was carried out to find out the disease situation in the infected village (symptomatic surveillance)**
- **Ring vaccination from outside to inside of household birds (within 9 km).**

- **Types of H5 Vaccines that used in the Egyptian country**



- **H5 Vaccine Distribution & Usage**

- For broilers Most of flocks vaccinated during the winter cycle (around 80%)
- During the summer months they refrain the usage to overcome the production cost (around 40%)
- Layer and breeders used the H5 vaccines all over the year regardless the seasons

- **Percentage of Usage**

25%	40%	35%
Reassortment HIV vaccines	Local inactivated	Imported inactivated

•28 million H5N2 doses were distributed in Egypt, making it the country that received the most significant level of distribution

Currently used seed vaccines

No.	Vaccine Seed Virus	Subtype	Abbreviation	Clade/Lineage	Accession Numbers (aa)	Company	AA Identity to Egyptian H5N8 (Min–Max)
1	A/chicken/Mexico/232/1994	H5N2	Mexico/H5N2	North American	AAR88841	Ceva, Mexico	75.3–90.1
2	A/duck/Potsdam/1402-6/1986	H5N2	Potsdam/H5N2	Eurasian	ABI84497	Intervet, The Netherlands	87.2–92.0
3	A/chicken/Egypt/18-H/2009	H5N1	EGY09/H5N1	2.2.1.1	ADG28676	Harbin Veterinary Research Institute, China	88.7–94.2
4	A/duck/Egypt/M2583D /2010	H5N1	EGY10/H5N1	2.2.1.1	AEP37317	ME-VAC, Egypt	90.8–96.4
5	A/chicken/Vietnam/C58/2004	H5N1	Vietnam/H5N1	1	AAW80718.1	Zoetis, USA	90.9–96.7
6	A/duck/China/E319-2/2003	H5N1	CN03/H5N1	2.3.2	AAR99628	Boehringer Ingelheim, Germany	92.5–98.4
7	A/duck/Anhui/1/2006	H5N1	Re5	2.3.4	ADG59091	QYH, China	92.9–98.4
8	A/chicken/Guizhou/4/2013	H5N1	Re8	2.3.4.4	EPI675769	Merial, USA & QYH, China	94.9–97.1
9	A/green-winged teal/Egypt/877/2016	H5N8	EGY16/H5N8	2.3.4.4b	ART29489	ME-VAC, Egypt	97.8–100

Common vaccines

Vaccine subtype	Seed virus	clade	Origin	Technology
H5N2	A/chicken/Mexico/232/1994 (H5N2)	classic	Mexican	Inactivated
H5N1	RG A/duck/Anhui/1/2006(H5N1) (Re-5)	2.3.4	China	Inactivated
H5N6/H5N8	Re6+Re8	2.3.2.1	China	Inactivated
H5N1	RG A/chicken/Egypt/18-H/2009 (H5N1)	2.2.1.1	Egypt	Inactivated
H5N3	A/chicken/Vietnam/C58/2004 (H5N3)	1	Vietnam	Inactivated
H5	A/Swan/Hungary/499/2006	2.2.1	Hungary	Recomb-HVT
H5+ND	A/duck/China/E319-2/03	2.3.2	China	Bacluovirus
H5N2+ND	A/duck/Potsdam/1402-6/1986(H5N2)	classic	Germany	Inactivated
H5N1+ND	RG A/duck/ Egypt /M2583D /2010 (H5N1)	2.2.1.2	Egypt	Inactivated
H5N1	local	2.2.1.2	Egypt	Inactivated
H5N1+H5N8	local	2.3.4.4	Egypt	Inactivated

Vaccine efficacy Evaluation

Emerg Infect Dis. 2016 Mar; 22(3): 379–388.
doi: 10.3201/eid2203.150593
PMCID: PMC4766899
PMID: 26886164

Avian Influenza A(H5N1) Virus in Egypt

Ghazi Kayali, Ahmed Kandeil, Rabeh El-Shesheny, Ahmed S. Kayed, Asmaa M. Maatouq, Zhipeng Cai, Pamela P. McKenzie, Richard J. Webby, Samir El Refaey, Amr Kandeel, and Mohamed A. Ali

- The poultry vaccination program is failing. (based on data available through their surveillance program)

DOI:10.1111/irv.12290
www.influenzajournal.com
Original Article

Variation in protection of four divergent avian influenza virus vaccine seed strains against eight clade 2.2.1 and 2.2.1.1. Egyptian H5N1 high pathogenicity variants in poultry

Erica Spackman,[a] David E. Swayne,[a] Mary J. Pantin-Jackwood,[a] Xiu-Feng Wan,[b] Mia K. Torchetti,[c,d,e] Mohammad Hassan,[f] David L. Suarez,[a] Mariana Sá e Silva[a]

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Accepted 9 September 2014. Published Online 4 October 2014.

There were differences in protection among the vaccines relative to one another based on challenge virus.

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Available at www.veterinaryworld.org/Vol.14/August-2021/20.pdf

RESEARCH ARTICLE
Open Access

Discrepancies in the efficacy of H5 inactivated avian influenza vaccines in specific-pathogen-free chickens against challenge with the Egyptian H5N8 clade 2.3.4.4 Group B virus isolated in 2018

Amena Abd El-Moeid[1], Ayman Hany EL-Deeb[1], Marwa Fathy Elsaied[2], Reem Ahamed Soliman[2], Mounir Mohamed EL-Safty[1] and Hussein Aly Hussein[1]

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doi: www.doi.org/10.14202/vetworld.2021.2131-2141 **How to cite this article:** El-Moeid AA, EL-Deeb AH, Elsaied MF, Soliman RA, EL-Safty MM, Hussein HA (2021) Discrepancies in the efficacy of H5 inactivated avian influenza vaccines in specific-pathogen-free chickens against challenge with the Egyptian H5N8 clade 2.3.4.4 Group B virus isolated in 2018, *Veterinary World*, 14(8): 2131-2141.

Abstract

Background and Aim: Highly pathogenic avian influenza H5N8 virus of clade 2.3.4.4 was newly emerged to Egypt and firstly detected in carcasses of wild birds in November 2016. This study assessed the protection efficacy and virus shedding reduction of three different inactivated avian influenza (AI) H5 (H5N1, H5N2, and H5N3) commercial vaccines against challenge with two newly emerging highly pathogenic AI virus H5N8 Egyptian isolates in specific-pathogen-free (SPF) chicks.

Virus shedding reduction and protection efficacy of studied vaccines were variable and the field vaccine should be reconsidered.

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Virology®

GENETIC DIVERSITY AND EVOLUTION
1 September 2011 Volume 85 Issue 17
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Antigenic Drift in H5N1 Avian Influenza Virus in Poultry Is Driven by Mutations in Major Antigenic Sites of the Hemagglutinin Molecule Analogous to Those for Human Influenza Virus

Giovanni Cattoli[1,*], Adelaide Milani[1], Nigel Temperton[2], Bianca Zecchin[1], Alessandra Buratin[1], Eleonora Molesti[2], Mona Meherez Aly[3], Abdel Arafa[3], and Ilaria Capua[1]

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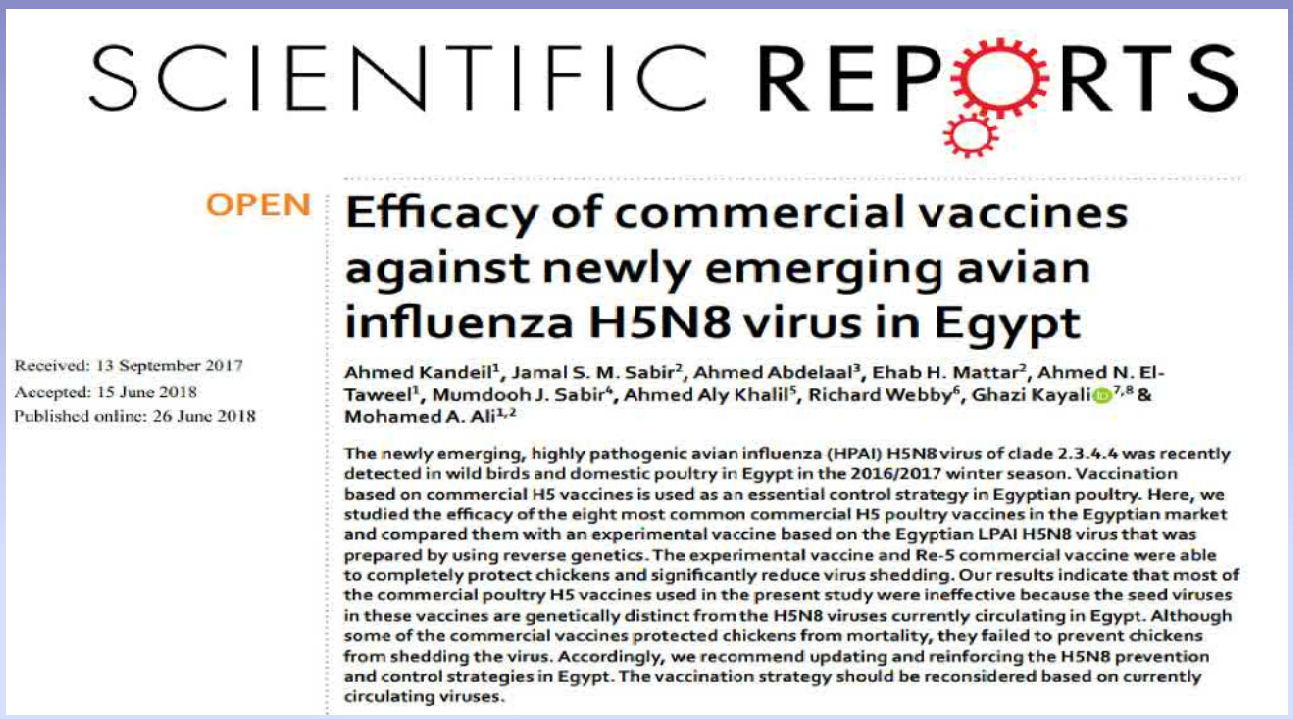
[2]School of Pharmacy, University of Kent at Medway, Chatham Maritime, Kent ME4 4AG, United Kingdom
[3]National Laboratory for Veterinary Quality Control on Poultry Production, Animal Health Research Institute, P.O. Box 264, Dokki, Giza 12618, Egypt

ABSTRACT H5N1 highly pathogenic avian influenza virus has been endemic in poultry in Egypt since 2008, notwithstanding the implementation of mass vaccination and culling of infected birds.

Antigenic drift of H5N1 viruses in Egypt was initiated and driven by mutations primarily occurring in the RBD and decreasing HI antibody activities

- Previous publications suggested that extensive vaccination of poultry for avian influenza can favor the emergence of viruses antigenically drifted from the vaccines applied in the field. This could potentially reduce vaccine efficacy and be responsible for vaccination failures



SCIENTIFIC REPORTS

OPEN

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Efficacy of commercial vaccines against newly emerging avian influenza H5N8 virus in Egypt

Ahmed Kandeil[1], Jamal S. M. Sabir[2], Ahmed Abdelaal[3], Ehab H. Mattar[2], Ahmed N. El-Taweel[1], Mumdooh J. Sabir[4], Ahmed Aly Khalil[5], Richard Webby[6], Ghazi Kayali[7,8] & Mohamed A. Ali[1,2]

The newly emerging, highly pathogenic avian influenza (HPAI) H5N8 virus of clade 2.3.4.4 was recently detected in wild birds and domestic poultry in Egypt in the 2016/2017 winter season. Vaccination based on commercial H5 vaccines is used as an essential control strategy in Egyptian poultry. Here, we studied the efficacy of the eight most common commercial H5 poultry vaccines in the Egyptian market and compared them with an experimental vaccine based on the Egyptian LPAI H5N8 virus that was prepared by using reverse genetics. The experimental vaccine and Re-5 commercial vaccine were able to completely protect chickens and significantly reduce virus shedding. Our results indicate that most of the commercial poultry H5 vaccines used in the present study were ineffective because the seed viruses in these vaccines are genetically distinct from the H5N8 viruses currently circulating in Egypt. Although some of the commercial vaccines protected chickens from mortality, they failed to prevent chickens from shedding the virus. Accordingly, we recommend updating and reinforcing the H5N8 prevention and control strategies in Egypt. The vaccination strategy should be reconsidered based on currently circulating viruses.

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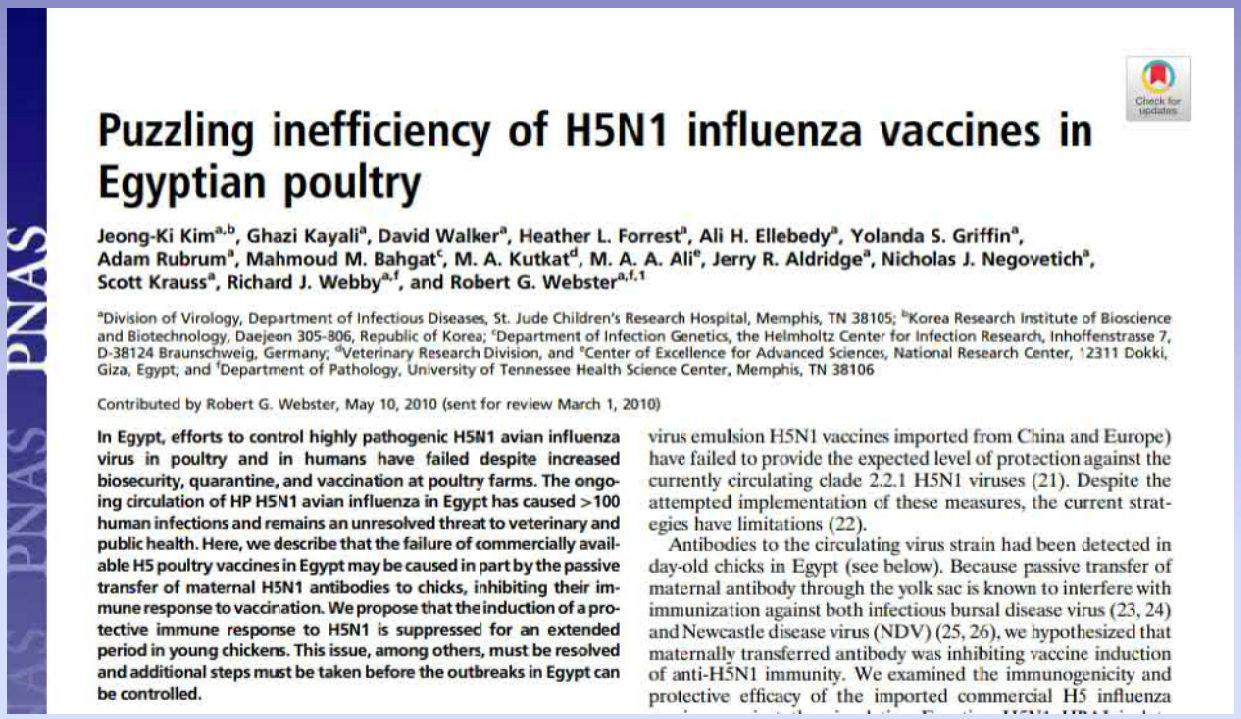

Puzzling inefficiency of H5N1 influenza vaccines in Egyptian poultry

Jeong-Ki Kim[a,b], Ghazi Kayali[a], David Walker[a], Heather L. Forrest[a], Ali H. Ellebedy[a], Yolanda S. Griffin[a], Adam Rubrum[a], Mahmoud M. Bahgat[c], M. A. Kutkat[d], M. A. A. Ali[e], Jerry R. Aldridge[a], Nicholas J. Negovetich[a], Scott Krauss[a], Richard J. Webby[a,f], and Robert G. Webster[a,f,1]

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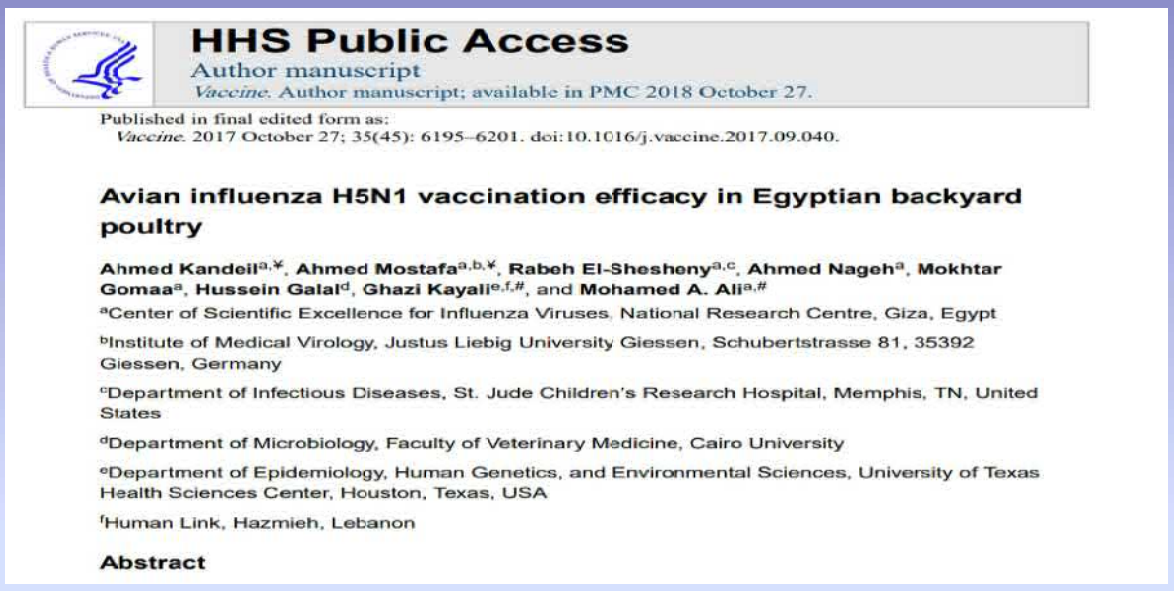
Contributed by Robert G. Webster, May 10, 2010 (sent for review March 1, 2010)

In Egypt, efforts to control highly pathogenic H5N1 avian influenza virus in poultry and in humans have failed despite increased biosecurity, quarantine, and vaccination at poultry farms. The ongoing circulation of HP H5N1 avian influenza in Egypt has caused >100 human infections and remains an unresolved threat to veterinary and public health. Here, we describe that the failure of commercially available H5 poultry vaccines in Egypt may be caused in part by the passive transfer of maternal H5N1 antibodies to chicks, inhibiting their immune response to vaccination. We propose that the induction of a protective immune response to H5N1 is suppressed for an extended period in young chickens. This issue, among others, must be resolved and additional steps must be taken before the outbreaks in Egypt can be controlled.

virus emulsion H5N1 vaccines imported from China and Europe) have failed to provide the expected level of protection against the currently circulating clade 2.2.1 H5N1 viruses (21). Despite the attempted implementation of these measures, the current strategies have limitations (22).

Antibodies to the circulating virus strain had been detected in day-old chicks in Egypt (see below). Because passive transfer of maternal antibody through the yolk sac is known to interfere with immunization against both infectious bursal disease virus (23, 24) and Newcastle disease virus (NDV) (25, 26), we hypothesized that maternally transferred antibody was inhibiting vaccine induction of anti-H5N1 immunity. We examined the immunogenicity and protective efficacy of the imported commercial H5 influenza

the failure of commercially available H5 poultry vaccines in Egypt may be caused in part by the passive transfer of maternal H5N1 antibodies to chicks, inhibiting their immune response to vaccination.



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Avian influenza H5N1 vaccination efficacy in Egyptian backyard poultry

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Abstract

Our data indicates that vaccination can be effective in the backyard setting in Egypt, although planning should consider the species covered.

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,*]

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- The efficiency of current vaccines should be regularly evaluated and updated to fully protect poultry flocks in Egypt against H5N8 viruses.

Controlled Clinical Trial > Poult Sci. 2013 Jan;92(1):114-8. doi: 10.3382/ps.2012-02637.

Do commercial avian influenza H5 vaccines induce cross-reactive antibodies against contemporary H5N1 viruses in Egypt?

G Kayali [1], A Kandeil, R El-Shesheny, A S Kayed, M R Gomaa, M A Kutkat, J Debeauchamp, P P McKenzie, R G Webster, R J Webby, M A Ali

Affiliations + expand

PMID: 23243237 DOI: 10.3382/ps.2012-02637

Free article

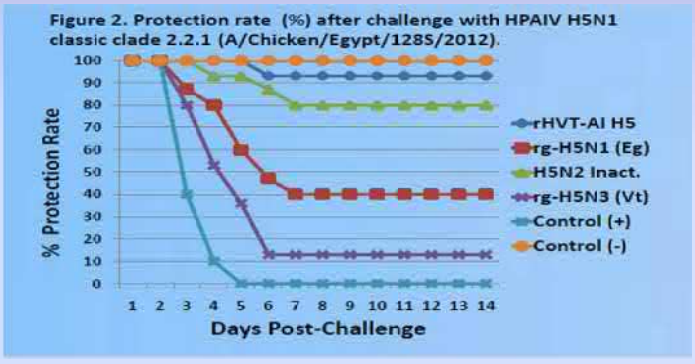
Abstract

After emerging in Egypt in 2006, highly pathogenic avian influenza H5N1 viruses continued to cause outbreaks in Egyptian poultry and sporadic human infections. The strategy used by Egyptian

The group studied the cross-reactivity of six commercially available H5 poultry vaccines against recent H5N1 Egyptian isolates in a field setting in Egypt. Only one vaccine based on an Egyptian H5N1 virus induced high cross-reactive antibody titres.

H5N1 cl 2.2.1 and H5N1 cl 2.2.1.1

- Commercial DOCs with MDA
- Vaccinated with different types of AI vaccines
- Challenged with two different clades of HPAI at 29 days of age
- rHVT-H5-vaccinated chickens showed the highest protection rates



AAAP 2014 Annual Meeting
Colorado Convention Center
Denver, Colorado, USA, 2014

Research Article

Efficacy of a Recombinant Turkey Herpesvirus AI (H5) Vaccine in Preventing Transmission of Heterologous Highly Pathogenic H5N8 Clade 2.3.4.4b Challenge Virus in Commercial Broilers and Layer Pullets

Vilmos Palya,[1] Tímea Tatár-Kis,[1] Edit Walkóné Kovács,[1] István Kiss,[1] Zalán Homonnay,[1] Yannick Gardin,[2] Krisztián Kertész,[3] and Ádám Dán[4]

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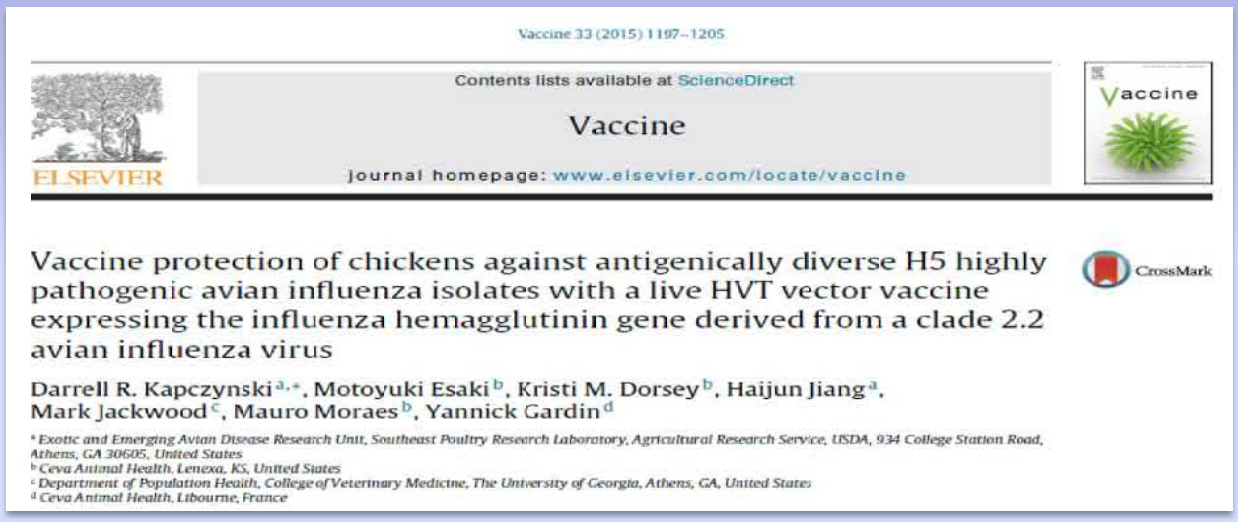
Correspondence should be addressed to Vilmos Palya; vilmos.palya@ceva.com

HVT-H5 and cross-clade protection in chickens



Vaccine 33 (2015) 1197–1205

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journal homepage: www.elsevier.com/locate/vaccine

Vaccine protection of chickens against antigenically diverse H5 highly pathogenic avian influenza isolates with a live HVT vector vaccine expressing the influenza hemagglutinin gene derived from a clade 2.2 avian influenza virus

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[b] Ceva Animal Health, Lenexa, KS, United States
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[d] Ceva Animal Health, Libourne, France

Conclusion

- Egypt is endemic for H5N8 since 2016
- H5N8 virus reported in 54 positive cases from the beginning of January 2022 throughout the country in Live bird markets, back yard poultry and commercial farms.
- vaccination is employed as part of control strategy to limit disease.
- widely used vaccines include (H5N1) (Re-5) clade 2.3.4 virus, (H5N2) classical virus and H5N3 clade 1 virus. And local Egyptian viruses clade 2.2.1.2 & 2.3.4.4
- The vaccines are evaluated against recent circulating virus H5N8/2021

Conclusion

- Vaccination can be a useful tool for controlling the disease and prevent sudden loss of birds due to a new virus introduction.
- However, long term vaccinating can develop variant strains causing vaccination failure.
- Selection a good vaccine candidate still the main target for vaccine producers (with GMP and vaccine know how) to pass the challenge against field viruses.

Conclusion

- Vaccine evaluation against recent circulating viruses is important to update knowledge about vaccine efficacy over time.

Recommendations

- **Strengthening plans of avian influenza surveillance , prevention and control.**
- **Enhance public awareness and awareness at various sectors.**
- **Enhance sequencing activity of whole genome sequence using NGS to surveillance.**
- **Sustainable professional Training between different sectors in poultry producers**
- **Sustainable fund resources for different activities of lab diagnosis**
- **Mutual collaboration between Veterinary authorities and WOAH Reference labs to support data sharing and rapid response.**

Thank You