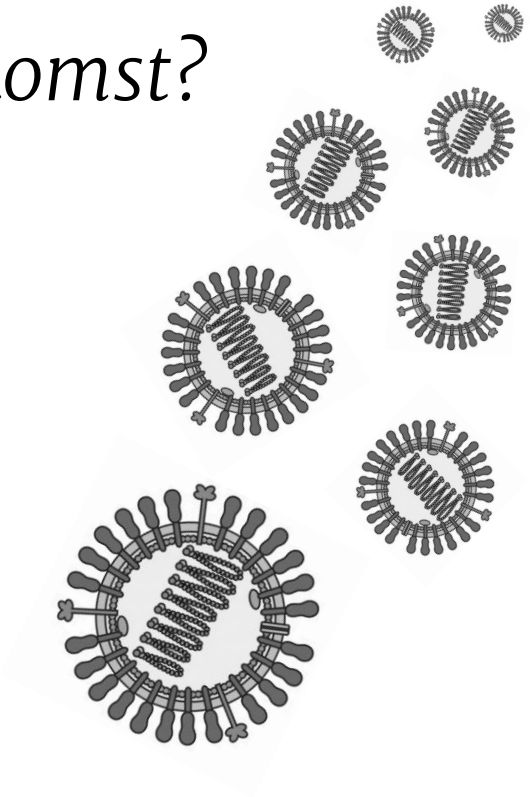
Zijn vaccins de oplossing voor de toekomst?



Flint et al., 2015. Principles of virology 4th edition

Sjaak de Wit

DVM, PhD, EBVS® European Specialist in Poultry Veterinary Science

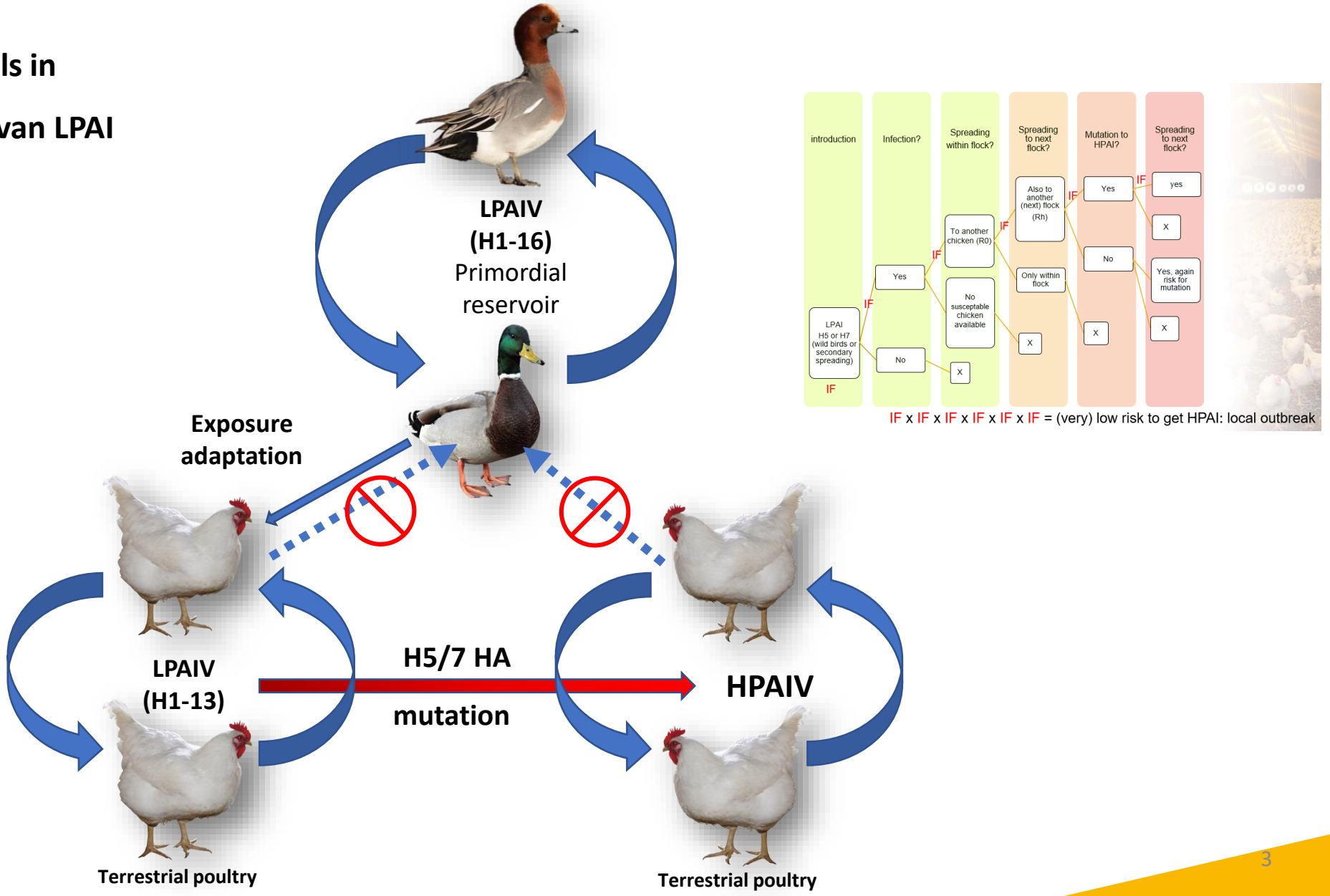
Royal GD and Department Population Health Sciences, Faculty of Veterinary Medicine, Utrecht University

Vroeger, nu, de toekomst?

AI Regelgeving en (non-vaccinatie) beleid zijn gebaseerd op ‘vroeger’

Avian influenza virus: ecologie/epidemiologie (modified from D. Swayne, Feb 2022)

Rol van wilde watervogels in ecologie/epidemiologie van LPAI sinds 1960's



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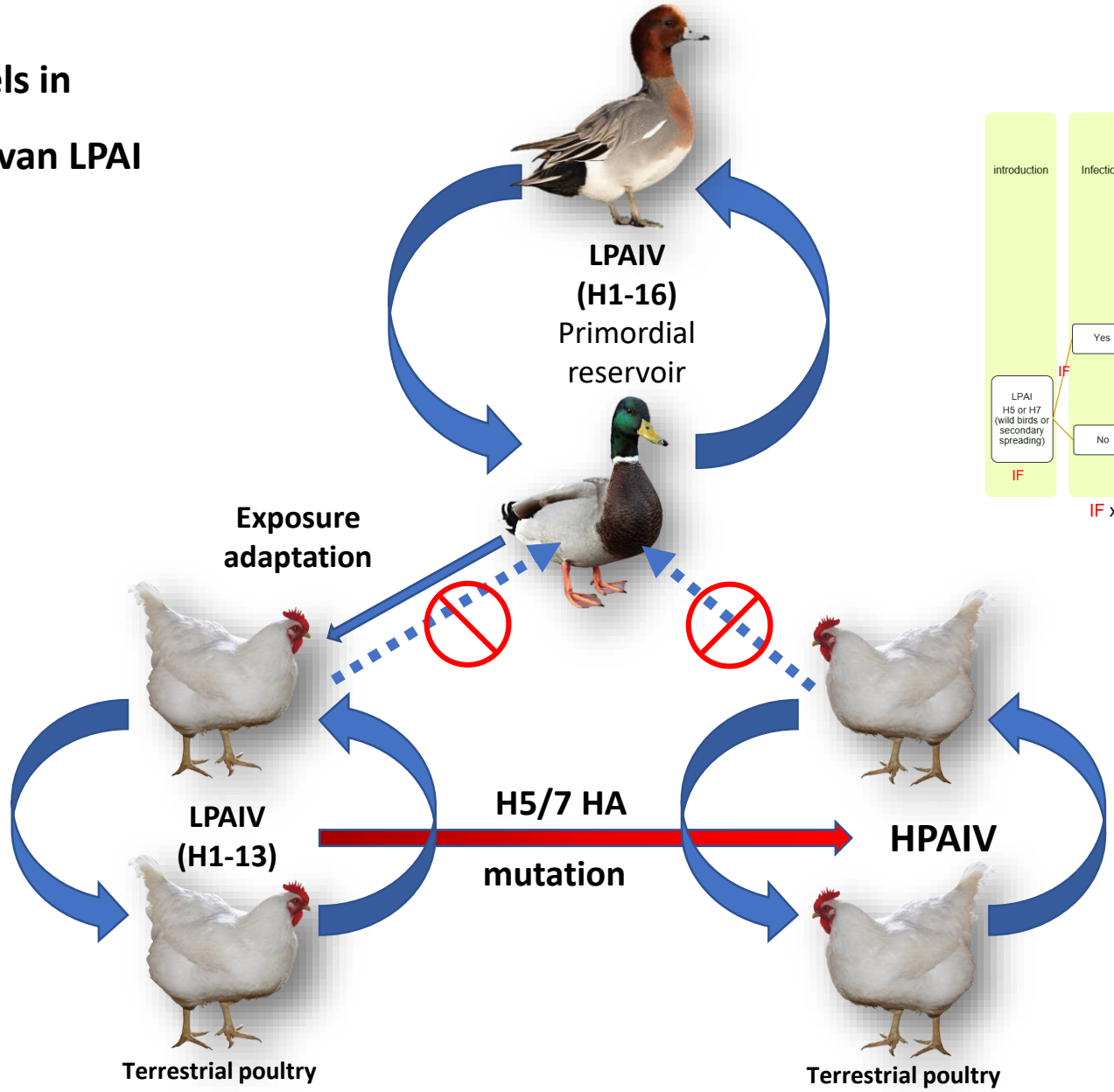
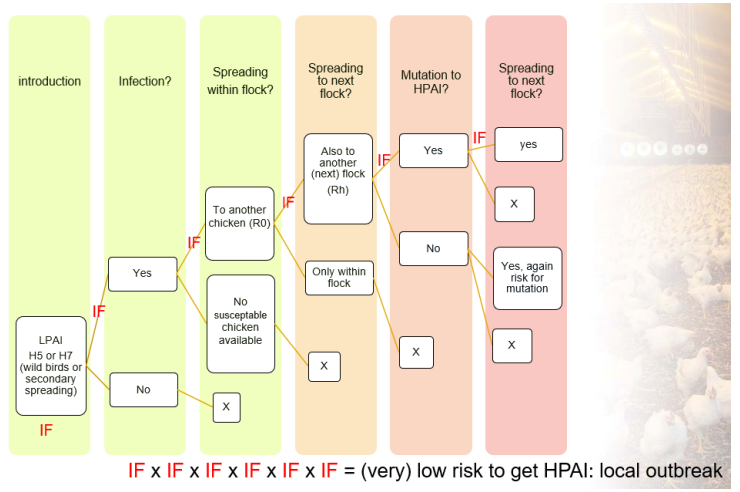




Lokale uitbraak van HPAI: ruimen van besmet pluimvee was tevens het uitroeien van de HPAI stam

2003 H7N7 uitbraken

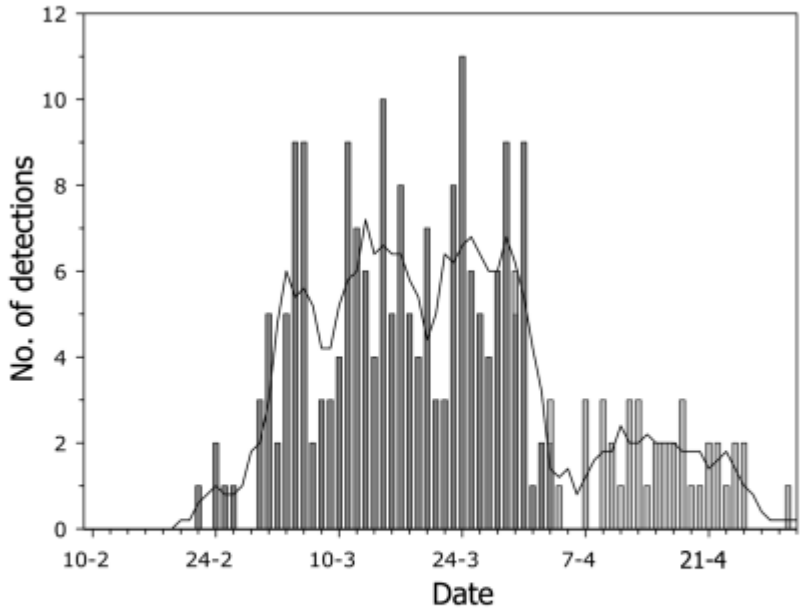


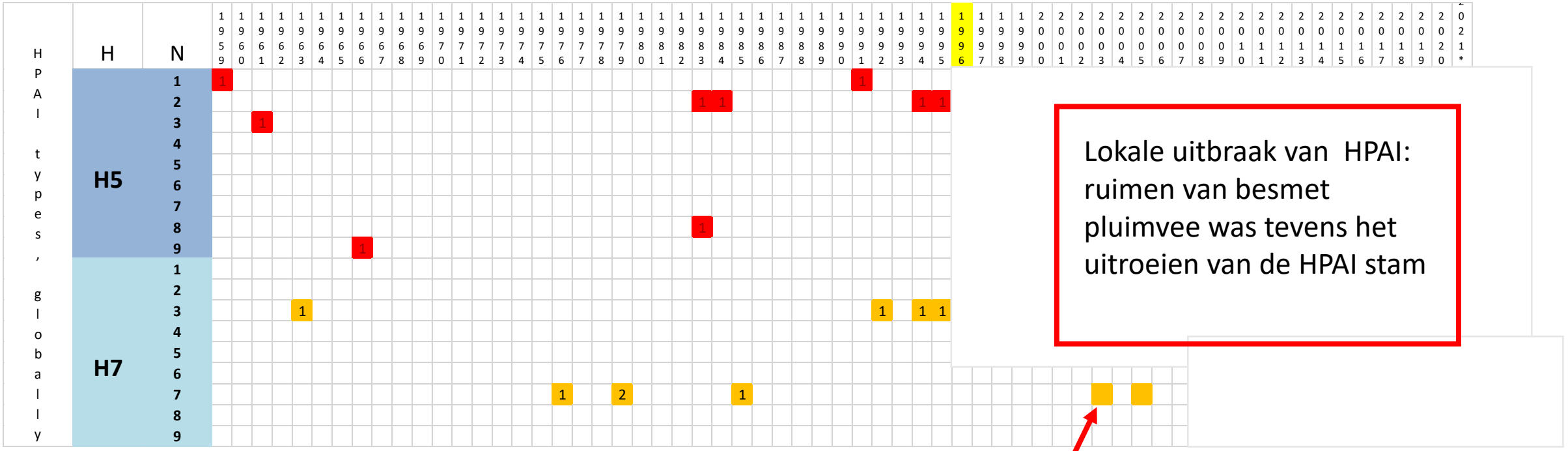
Figure 2. Course of the no. of detected outbreaks during the 2003 epidemic of avian influenza (AI) in The Netherlands. *Dark bars*, Gelderse Vallei; *light bars*, Limburg; *lines*, 5-day moving average.

Stegeman et al, JID 2004

- Eind februari tot begin mei

- 255 besmette koppels (incl hobby)
  - Ongeveer 5 miljoen dieren
- Preventieve ruiming 1255 bedrijven en 17421 hobbykoppels
  - Ongeveer 30 miljoen dieren

Bekende HPAI uitbraken in de wereld 1959-2021



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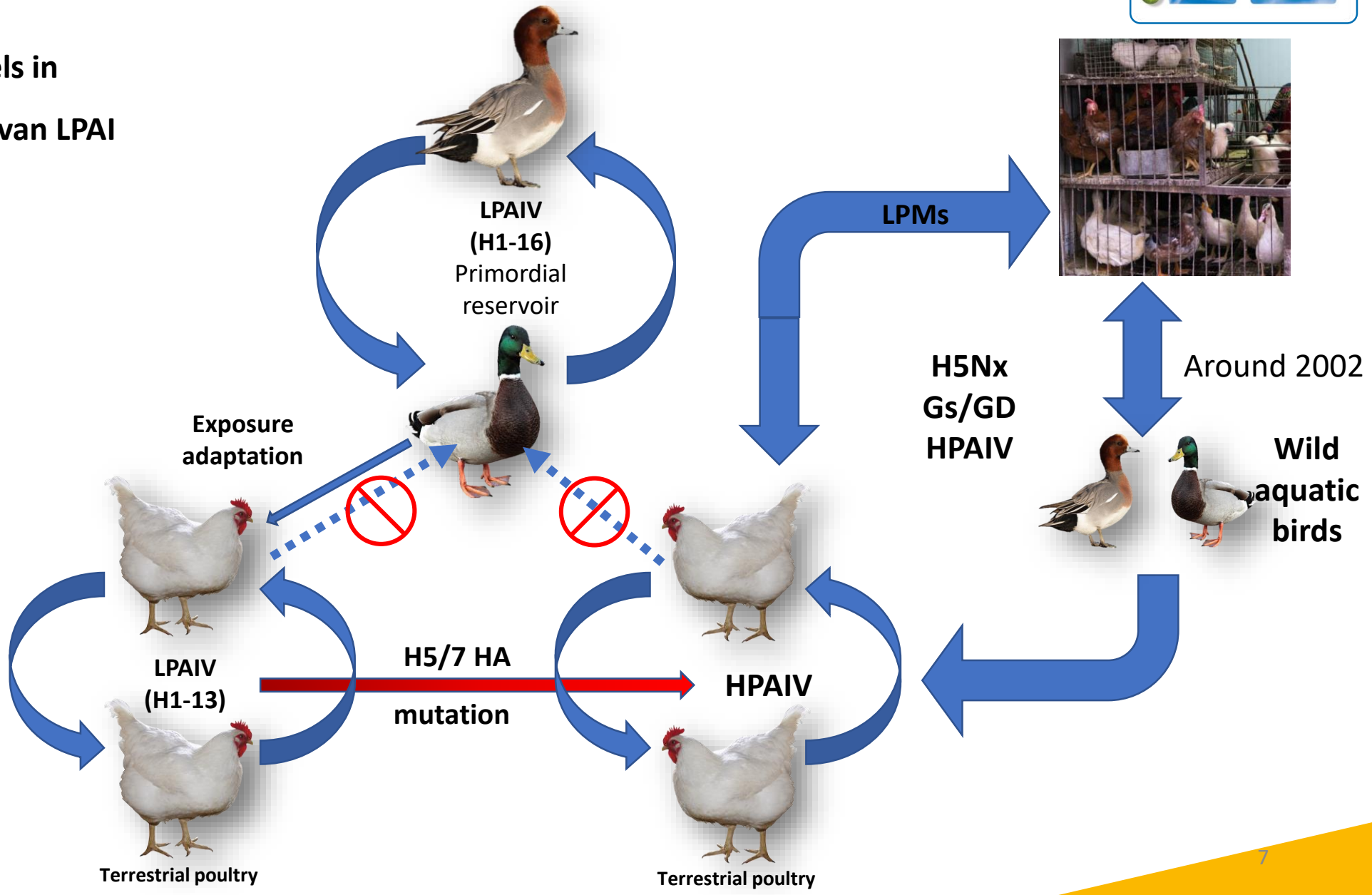

Game changer

Changing Role of Wild Birds in the Epidemiology of Avian Influenza A Viruses

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[1]Corresponding author: e-mail address: r.bodewes@uu.nl

Contents

Abstract

Waterbirds are the main reservoir for low pathogenic avian influenza A viruses (LPAIV), from which occasional spillover to poultry occurs. When circulating among poultry, LPAIV may become highly pathogenic avian influenza A viruses (HPAIV). In recent years, the epidemiology of HPAIV viruses has changed drastically. HPAIV H5N1 are currently endemic among poultry in a number of countries. In addition, global spread of HPAIV H5N*x* viruses has resulted in major outbreaks among wild birds and poultry worldwide. Using data collected during these outbreaks, the role of migratory birds as a vector became increasingly clear. Here we provide an overview of current data about various aspects of the changing role of wild birds in the epidemiology of avian influenza A viruses.

Advances in Virus Research, 2018

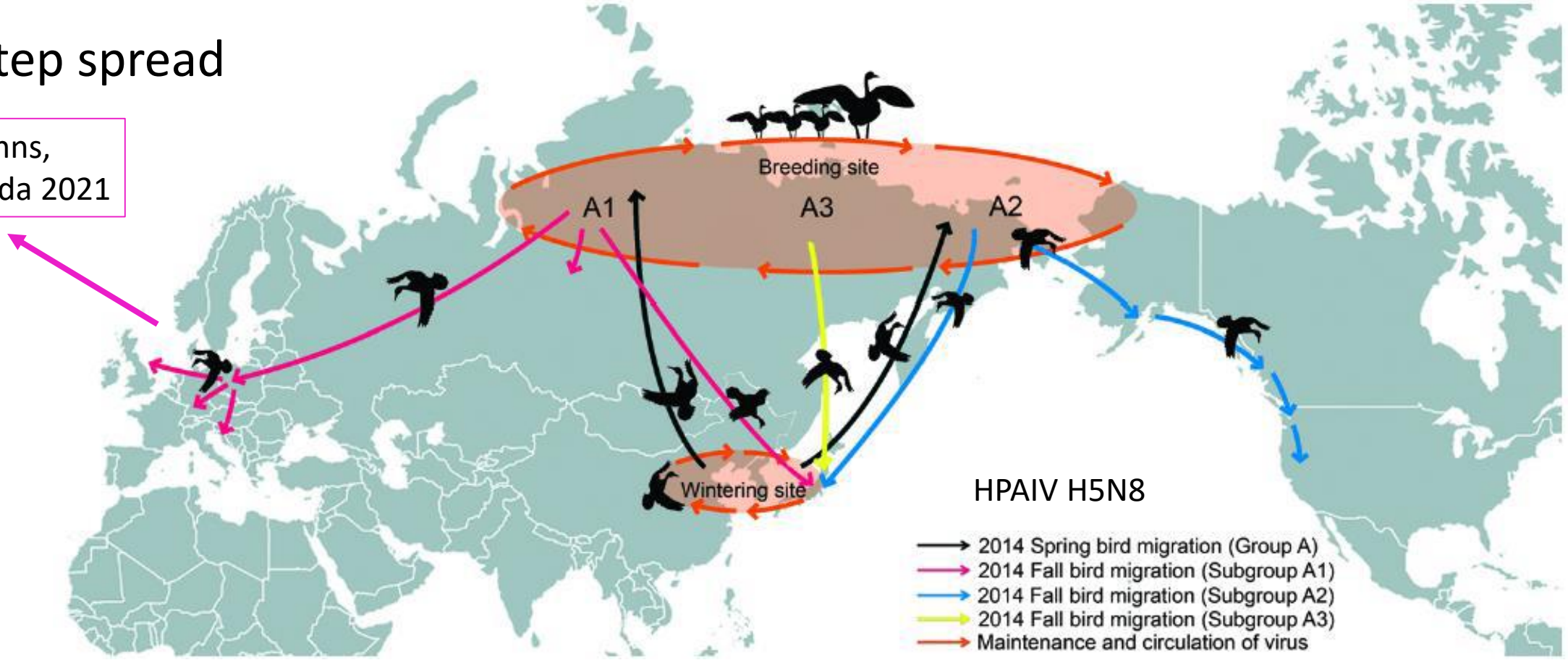
Waterbirds are the main reservoir for low pathogenic avian influenza A viruses (LPAIV), from which occasional spillover to poultry occurs. When circulating among poultry, LPAIV may become highly pathogenic avian influenza A viruses (HPAIV). In recent years, the epidemiology of HPAIV viruses has changed drastically. HPAIV H5N1 are currently endemic among poultry in a number of countries. In addition, global spread of HPAIV H5N*x* viruses has resulted in major outbreaks among wild birds and poultry worldwide.

the epidemiology of HPAIV viruses has changed drastically.

III - What is the role of wild birds? Long-distant spread of HPAIVs

2-step spread

St Johns, Canada 2021



Lee et al 2015 Journal of Virology
Caliendo et al 2021 BioRix

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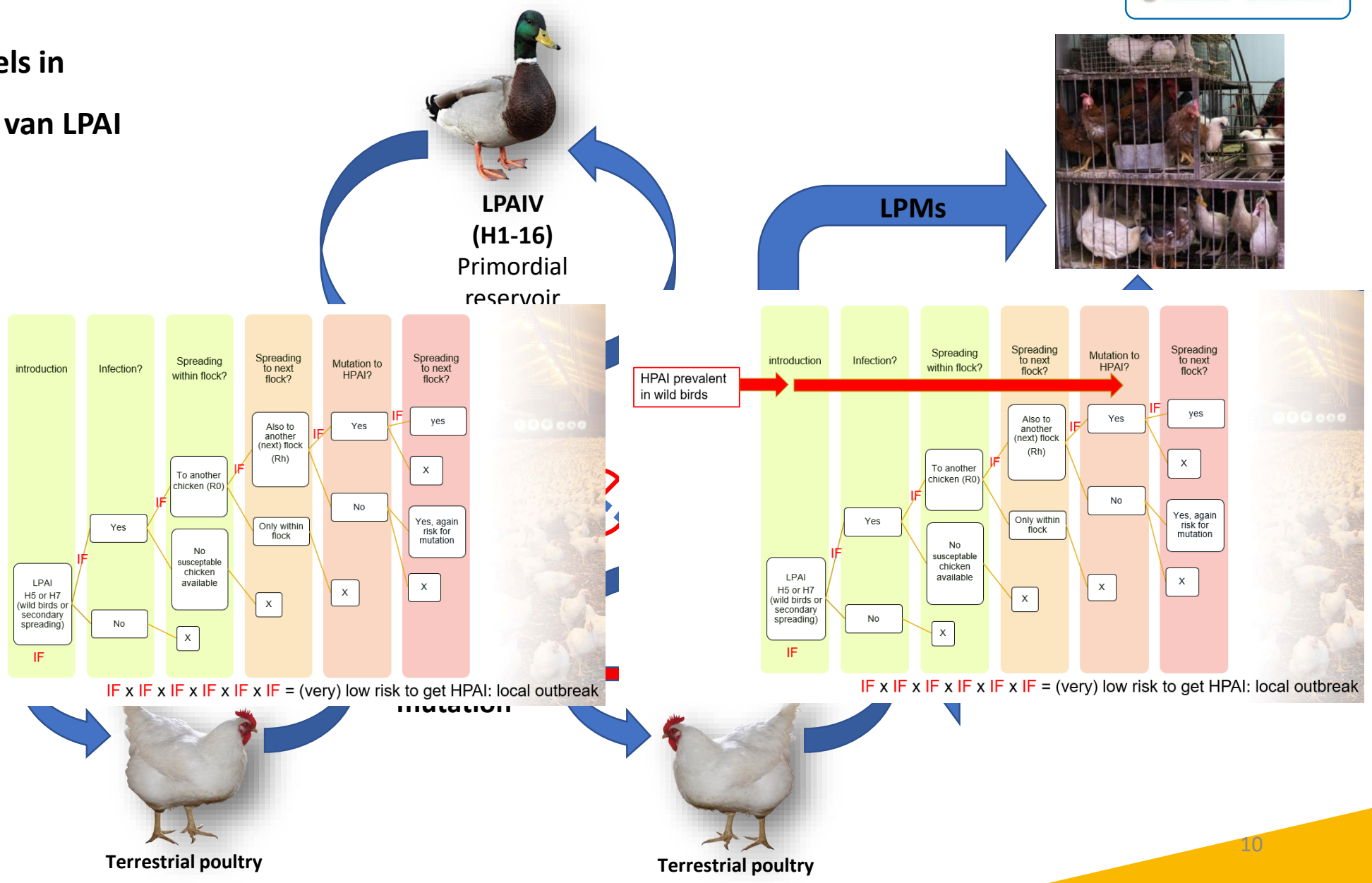
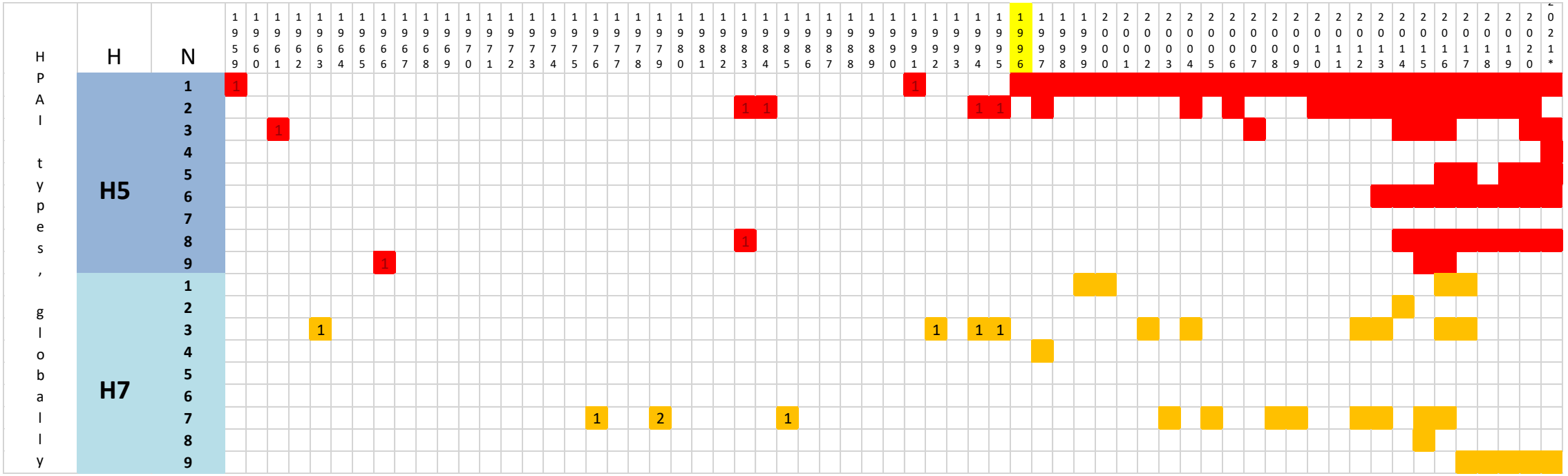


Bekende HPAI uitbraken in de wereld 1959-2021

Appearance of the Goose/Guadong H5Nx



Lokaal dieren ruimen roeit het virus niet meer uit!
= Dweilen met de kraan open!

Vroeger, nu, toekomst?

Parameter	Before 1996	From 1996, last years
Frequency HPAI outbreaks	Rare	Frequent
Size outbreak	Small area, short period	Countries/continents, endemic in big areas
Eradication HPAI strain post culling	Yes	No, only locally
HP in wild (migratory) birds (mammals)	No	Yes
Illness/mortality in humans	No	Yes (mainly in developing countries)
Housing chickens	Inside	Increasing free range/organic
Image/understanding of public, politicians, media	Understanding	Decreasing
Trade problems	Relatively limited (frequency, size)	More often, longer
Vaccines	Only inactivated vaccines, complete virus, drift, homology	Also new technology, genetically modified live vector vaccines, RNA vaccines (replication)
Mass application	No (2x injection in field)	Mostly no (hatchery injection)
DIVA monitoring possible	Hardly, very complicated, limited	Yes (new technology vaccines)

Doel van vaccinatie, eis aan vaccins

- Bescherming tegen
  - **ziekte/sterfte**
  - **Besmetting/transmissie (R<1)**
- DIVA (opsporen veenbrand/aantonen vrij zijn): zoonotische kant en handel
- Liefst ook met test die niveau van aanslaan/bescherming aangeeft
- Geschikt voor gewenste diersoorten (kip, kalkoen, eend?)
- Gewenste snelheid en lengte van bescherming
- Werken in aanwezigheid van MDA?

Susceptibility of non-vaccinated vs vaccinated layers

Table 2
Lethal dose 50% endpoint titrations of HPAIV H5N1 R65 in layer hens with different vaccination status and age.

Challenge trial	Immunization status	LD_{50} (log_{10})	Average MDT (days)
C1	NV	4.5	3.7
C2	NV	2.5	2
C3	NV	<2	2.7
C4	NV	2.2	1.7
C5	NV	3.5	3.3
C1	BI	5.7	4
C2	BI	>6.5	–
C3	BI-6	6.0	5.5
C4	BI-12	5.7	4.8
C4	RV1-6	>6.5	7
C5	BI-18	5.2	6.8
C5	RV1-12	>6.5	5
C5	RV2	>6.5	7

MDT—mean death time; NV—non-vaccinated; BI—basically immunized (6, 12 or 18 months ago); RV1—revaccinated once (6 or 12 months ago); RV2—revaccinated twice.

C1, 2, 3, 4, 5: H5N1, clade 2.2 challenge at week 23, 27, 48, 74 and 101

- Non-vaccinated birds: highest susceptibility to H5N1 at W48
- Vaccinated birds needed 1000-10,000x more virus to get infected

Utrecht University

Rudolf *et al.* Longitudinal 2 years field study of conventional vaccination against highly pathogenic avian influenza H5N1 in layer hens Vaccine 2010, 6832-6840

Universiteit Utrecht

Several examples of vaccination induced reduced HPAIv transmission $R < 1$ in experiments

Subtype	$Host$	R_0	Reference
H7N7	chicken	0.03-0.2	Van der Goot et al. PNAS 2005
H5N1	ducks	0.2-0.6	Van der Goot et al. Virology 2008
H5N1	chicken	0.12	Sitaras et al., J. R Soc Int, 2016
H5N1	chicken	0.0	Poetri et al., Res Vet Sci 2017
H5N1	turkey	0.0	Bos et al., Vaccine, 2008

Universiteit Utrecht

Using inactivated vaccines, the homologous HI titer (HI≥3) seems crucial for protection against infection and such titers are difficult to obtain in the field

Subtype	*Titer*	R_v	Reference
H5N1	<3 (field)	3.1	Poetri et al., Res. Vet Sci 2014
H7N7	<3 (field)	>1	Koch et al., unpublished
H5N1	<3	6.6	Sitaras et al., J. R Soc Int, 2016
H5N1	<3	1.7	Poetri et al., Res Vet Sci 2017

Humoral and/or cellular protection, inactivated vs replicating vaccines

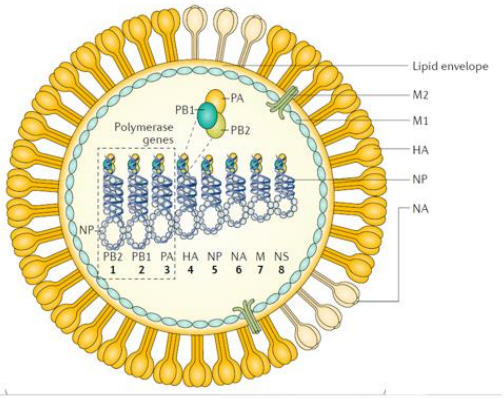
Inactivated antigens induce ‘only’ antibodies (MHC-2), mainly humoral

- **Titres in HI test are well correlated with protection** (homologous antigen)

‘Replicating antigens’ (produced inside a host cell, MHC-1) induce antibodies and a T-cell response (cytotoxic T-cells)

- **Positive titres in HI test are well correlated with protection** (homologous antigen)
- **Negative HI titres less predictive**

Vaccines for AI



No live, attenuated AIV vaccines (not safe)

Inactivated vaccines (classical vaccines)

- **Complete virus: induces antibodies against all virus proteins (HA, NA, M, Np, etc)**

Subunit vaccines (HA protein),

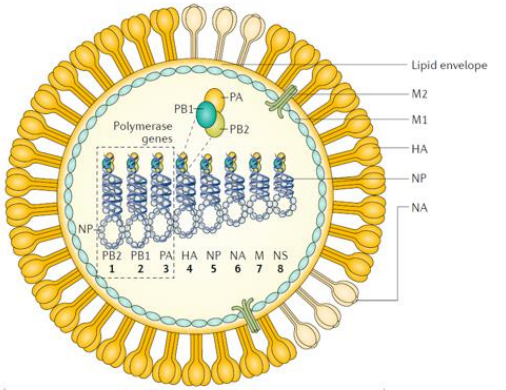
- **Selected protein of AIV**

Recombinant live vector vaccines,

- **Live vector vaccine (HVT, Fowl Pox,** NDV, ILTV, ADENO, Salmonella, Duck enteritis virus, Alphavirus etc**)**
- **Only part of AI virus (HA gene)**

mRNA, DNA (HA mRNA), 'expressed by cells'

DIVA response



Differentiating Infected from Vaccinated Animals

- Field infections must induce detectable levels of antibodies to a protein that is not present in the vaccine(s) that has/have been used
  - So, when antibodies against a protein of AIV that is not in the vaccine are detected: proof of field infection
- Detection of field strain itself (RT-PCR, virus isolation, antigen-test, …)
  - Non-replicating vaccines not detectable
  - Replicating vaccines: target is gene that is not in the vaccine (M-gene)
- Use test that can reliably detect these antibodies (or virus)

Present H5 vaccines, present DIVA options

- Vaccines
  - Inactivated complete virus
  - Subunit vaccine,
  - Live vectored vaccines (HVT, Pox, others),
  - mRNA, DNA, RNA particles, ……

Only antibody response against insert (e.g.) H5
Not against other proteins (M, Np, …..)

Find a suitable DIVA combination

- Tests
  - RT-PCR, virus isolation, staining, on-site, ELISA (general), ELISA (specific proteins), genotype specific ELISA, HI-test, AGPT

Conventional inactivated vaccines, general aspects

- Complete AIV virus as antigen: not only HA
- No replication, stimulates the antibody response very well, but no/hardly the cytotoxic T cell responses
  - **Systemic immunity, especially humoral**
- Long lasting protection
- Application in presence of MDA lowers humoral response
- No spreading, injection
- Suitable for boosting as well
- DIVA complicated

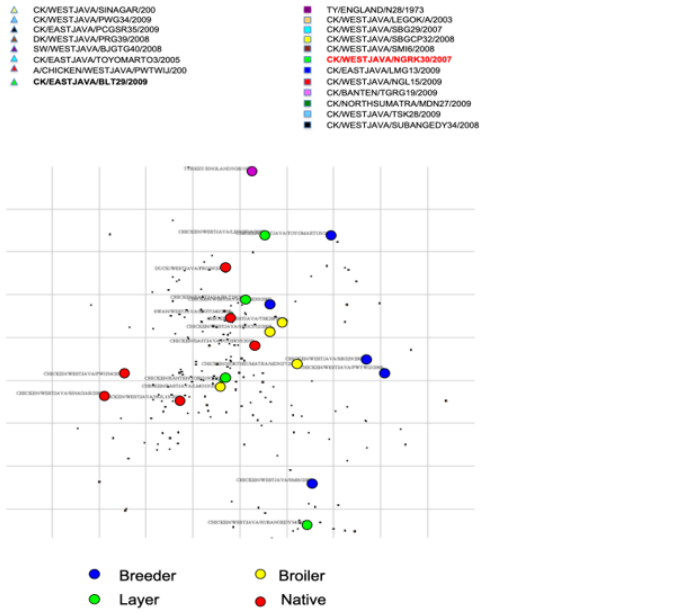


Figure N. Antigenic map of HPAI H5N1 viruses from industrial poultry in Indonesia. (Courtesy of Japfa Comfeed Indonesia and Erasmus MC: Ron Fouchier, Stefan van Vliet, I Wayan Wisaksana Yasa, and Teguh Prajitno). Antigenicity differs between red (unvaccinated kampong chickens) to (inappropriately) vaccinated breeder chickens where escape mutants (blue dots to the right) start to circulate. Need to use bivalent vaccines.

Draft Harder et al, in preparation

Duration of protection by inactivated vaccine

Table 1
Induction of homologous and heterologous AIV-specific HI titres (log_2) by vaccination in layer hens using inactivated adjuvanted whole A/duck/Potsdam/1402/86 (H5N2).

	Vaccination status	Number and proportion of hens with HI titre ≥5 log_2 and average HI titres against vaccine antigen (H5N2)			Number and proportion of hens with HI titre ≥5 log_2 and average HI titres against challenge antigen (H5N1)		
		n/m[a]	%	Xn	n/m	%	Xn
S1	NV	–	–				
S2	NV	1[b]/60	1.6				
	Vaccinated once	56/60	93.3	6.5	0/20	0	0.8
S3	NV	1[b]/60	1.6				
	BI	60/60	100	8.55	14/20	70	5
S4	NV	5[b]	8.3				
	BI	60/60	100	7.28	0/20	0	0
S5	NV	1[b]/60	1.6				
	BI	59/60	98.3	7.5	13/28	46.4	4.5
	RV1	60/60	100	9.12	16/20	80	6.35
S6	NV	4[b]/60	6.7				
	BI	55/60	91.7	6.06	12/20	60	4.9
	RV1	60/60	100	7.75	19/20	95	6.4
S7	NV	3[b]/60	5				
	BI	58/60	96.7	6.03	3/20	15	2.85
	RV1	60/60	100	7.53	17/20	85	5.45
	RV2	60/60	100	9.2	20/20	100	8.1
S8	NV	0	0				
	BI	15/31	48.4	3.32	0/31	0	0
	RV1	31/31	100	6.68	5/31	16.13	1.32
	RV2	27/28	96.4	7.36	15/28	53.57	4.64

27w

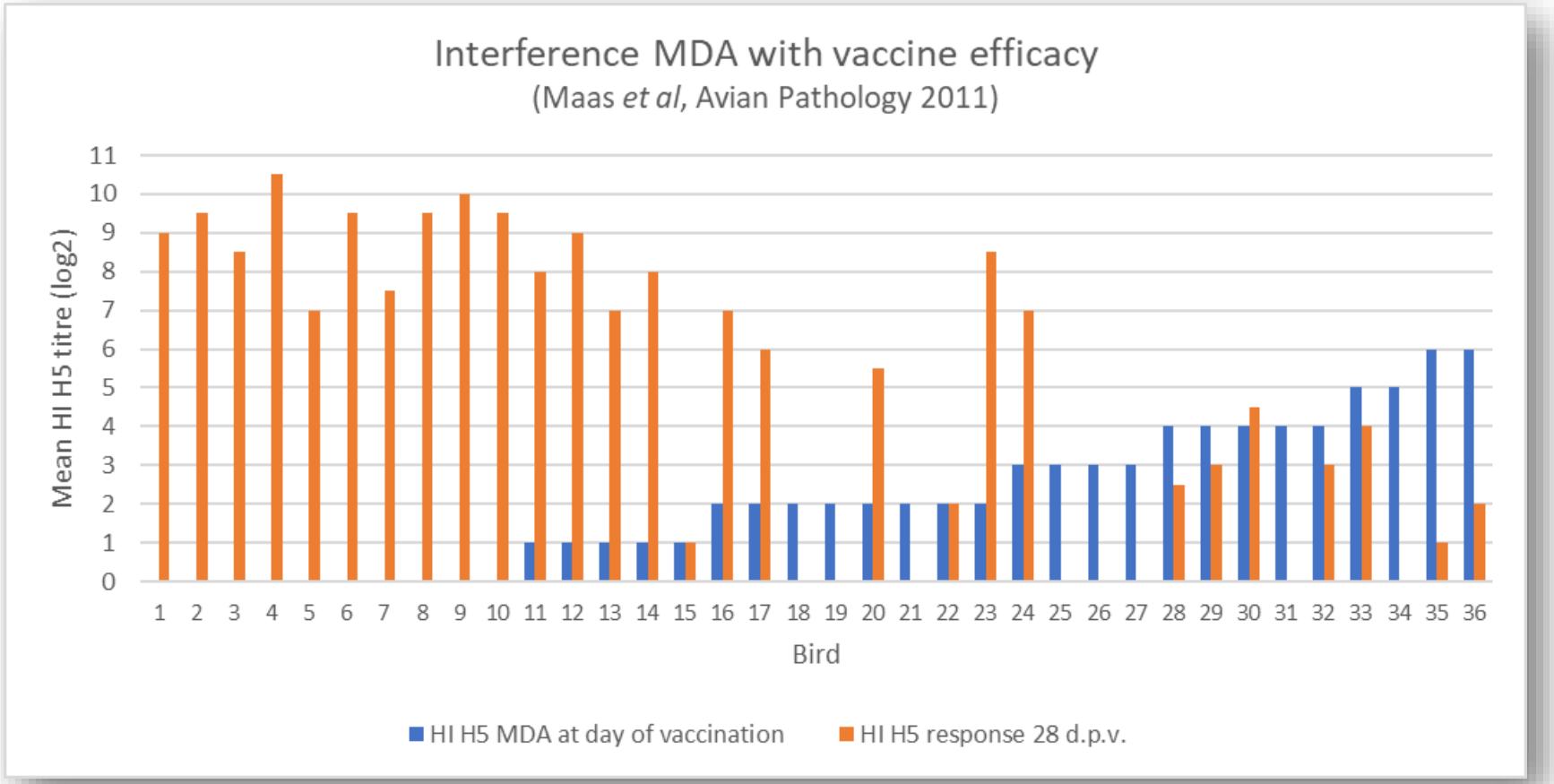
52w

100w

Utrecht University

Rudolf et al. Longitudinal 2 years field study of conventional vaccination against HPAI H5N1 in layer hens. Vaccine 2010-6832-6840

Effect of MDA against AIV at the age of vaccination



Low levels of MDA already interfere with (inactivated) vaccine efficacy

Utrecht University

Maas *et al*,, Maternal immunity against avian influenza H5N1 in chickens: lilited protection and interference with vaccine efficacy. Avian Pathology, 2011, 87-92

Subunit vaccines

As conventional vaccines:

- Vaccine with selected protein(s) as antigen(s)
- Proteins produced in insect cells (Baculovirus), bacteria (e.g. *E coli*)
  - Glycosylation of protein depending on host cell (insect (yes) or bacteria (no))
- DIVA supporting

Vectored live vaccines

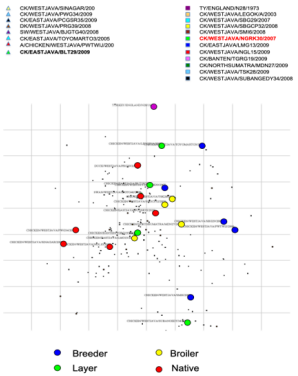
- Replication stimulates the immune response of all kind of cells (cytotoxic T cells, all T helper cells, B cells)
  - Systemic immunity
  - Local immunity (variable, mucosal replication?)
- Induce protection against the inserted gene (protein) and against vector
- Protection against vector decreases efficacy of vaccination
- DIVA possible

General aspects of HVT as vector

- B- and T-cell immunity against Marek's and against the insert
    - **Supports DIVA**
- Individual application (in ovo or s.c. at D0)
- Very long lasting replication (natural boosting), gradual rise in H5 antibody titres
- Low influence of MDA against vector and insert
- For chicken and turkey
    - **No spreading or shedding in chicken (miss is a miss)**
- No combining of HVT-vaccines unless proven otherwise
- Suitable as priming as well

HVT-H5 vaccine, broader protection?

- HPAI gene clade 2.2
- Average protection similar for clades 1, 2.1, 2.2, and 2.3



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- Role of T-cells?

Table 1. Compilation of protection results collected through various experiments conducted with the rHVT-H5 vaccine.

		Vaccination			Challenge					Protection against				
			MDA against		HPAIV					Mortality (%)		% Oropharyngeal shedders		
Location	Country	Type of chickens	HVT	AIV	Subtype	Strain	Clade	Route	Age	VACC	Control	When	VACC (%)	Control (%)	Reference
University of Maryland	United States	SPF	No	No	H5N1	A/CK/Vietnam/1203/2004	1	IN	4 wo	85	0	2 dpc	30	100	(Ceva Animal Health. Unpubl. data, 2012)
CODA CERVA	Belgium	COM BR	Yes	No	H5N1	A/Duck/Hungary/11804/2006	2.2	IN	2 wo	90	0	2 dpc	20	38	(3)
CODA CERVA	Belgium	COM BR	Yes	Yes (H5N2)	H5N1	A/Duck/Hungary/11804/2006	2.2	IN	2 wo	100	20	2 dpc	0	60	(3)
CODA CERVA	Belgium	COM BR	Yes	Yes (H5N2)	H5N1	A/Duck/Hungary/11804/2006	2.2	IN	3 wo	90	0	2 dpc	0	80	(3)
CODA CERVA	Belgium	SPF	No	No	H5N1	A/CK/Egypt/1709-1 VIR08/2007	2.2.1	ON	3 wo	100	0	3 dpc	80	100	(18)
CODA CERVA	Belgium	SPF	No	No	H5N1	A/CK/Egypt/1709-6/2008	2.2.1.1	ON	3 wo	100	0	3 dpc	100	100	(18)
CODA CERVA	Belgium	COM BR	Yes	No	H5N1	A/CK/Egypt/1709-6/2008	2.2.1.1	ON	4 wo	90	0	2 dpc	10	100	(16)
CODA CERVA	Belgium	COM BR	Yes	Yes (H5N1)	H5N1	A/CK/Egypt/1709-6/2008	2.2.1.1	ON	4 wo	100	0	2 dpc	10	90	(16)
CODA CERVA	Belgium	COM BR	Yes	Yes (H5N1)	H5N1	A/CK/Egypt/1709-1 VIR08/2007	2.2.1	ON	4 wo	90	0	2 dpc	100	100	(16)
CODA CERVA	Belgium	COM BR	Yes	Yes (H5N1)	H5N1	A/CK/Egypt/1709-6/2008	2.2.1.1	ON	4 wo	70	0	2 dpc	90	100	(16)
Bogor Agricultural University	Indonesia	COM BR	Yes	Yes (H5N1)	H5N1	A/CK/West Java Subang/29/2007	2.1.3	ON	4 wo	80	0	2 dpc	60–80	100	(19)
Bogor Agricultural University	Indonesia	COM BR	Yes	Yes (H5N1)	H5N1	A/CK/Puwakarta-Cilingga/142/2010	2.1.3	ON	4 wo	95	0	2 dpc	60–80	100	(19)
SEPRL	United States	SPF WL	No	No	H5N1	A/Whooper Swan/Mongolia/3/2005	2.2	IN	6 wo	100	0	2 dpc	13	100	(5)
SEPRL	United States	SPF BR	No	No	H5N1	A/CK/West Java Subang/29/2007	2.1.3	IN	4 wo	80	0	NT[A]	NT	NT	(5)
SEPRL	United States	SPF WL	No	No	H5N2	A/CK/Queretaro/14588/1995	—	IN	4 wo	95	0	NT	NT	NT	(5)
CODA CERVA	Belgium	SPF	No	No	H5N1	A/CK/Egypt/1709-6/2008	2.2.1.1	ON	4 wo	100	0	2 dpc	100	100	(17)
CODA CERVA	Belgium	SPF	No	No	H5N1	A/CK/Egypt/1709-6/2008	2.2.1.1	ON	8 wo	100	0	2 dpc	100	100	(17)
RLQP	Egypt	COM BR	Yes	Yes (H5N1)	H5N1	A/CK/Egypt/1709-6/2008	2.2.1.1	IN	4 wo	93	0	2 dpc	100	100	(9)
RLQP	Egypt	COM BR	Yes	Yes (H5N1)	H5N1	A/CK/Egypt-63/2010 "variant"	2.2.1.1	IN	5 wo	80	0	2 dpc	100	100	(9)
CODA CERVA	Belgium	SPF	No	No	H5N8	A/CK/Germany/2014	2.3.4.4	ON	4 wo	100	0	2 dpc	90	100	(20)
IZSVe	Italy	SPF	No	No	H5N1	A/CK/Bangladesh/11RS1 984-33/2011	2.3.2.1	ON	4 wo	100	0	2 dpc	10	All dead	(2)
RLQP	Egypt	COM LY WB	Yes	Yes (H5N1)	H5N1	A/CK/Egypt/128s/2012	2.2.1	ON	19 wo	73	0	3 dpc	0	100	(8)
RLQP	Egypt	COM LY BS	Yes	Yes (H5N1)	H5N1	A/CK/Egypt/128s/2012	2.2.1	ON	19 wo	60	0	3 dpc	7	100	(8)

Gardin *et al*. Experimental and Field Results Regarding Immunity Induced by a Recombinant Turkey Herpesvirus H5 Vector Vaccine Against H5N1 and Other H5 HPAI Virus Challenges, Avian Diseases 2016, 232-237

General aspects of Fowl Pox as vector

- B- and T-cell immunity against Fowl Pox and against the insert
  - Supports DIVA
- Individual application (in ovo or s.c. at D0 or later in non-FP challenged birds)
- Suitable as primer or boost
- Low influence of MDA, influence on insert?
- For chicken and ducks
  - No spreading or shedding in chicken and ducks (miss is a miss)
- HI response often low, often negative when heterologous H5 antigen is used
  - **Role of cell mediated immune response**

Fowl Pox vector, example

Table 1
Deduced hemagglutinin amino acid sequence similarity between the recombinant vaccine and highly pathogenic H5 avian influenza challenge viruses

Challenge virus strain	Abbreviation	Subtype	Hemagglutinin amino acid similarity with vaccine strain (%)
A/turkey/Ireland/83	TI/83	H5N8	100
A/turkey/England/91	TE/91	H5N1	94.2
A/tern/South Africa/61	TSA/61	H5N3	93.1
A/chicken/Scotland/59	CS/59	H5N1	92.0
A/human/Hong Kong/156/97	HK/97	H5N1	90.2
A/chicken/Queretaro/14588/95	CQ/95	H5N2	89.3
A/turkey/Ontario/77322/66	TO/66	H5N9	89.1
A/emu/Texas/39924/93	ET/93	H5N2	88.8
A/chicken/Pennsylvania/1370/83	CP/83	H5N2	87.3

Table 3
Virus isolation results and infectious titers from chickens vaccinated at 1 day of age with fowlpox (Vector-Control) or recombinant fowlpox-H5 avian influenze hemagglutinin gene (Vector-HA) vaccine and challenged 3 weeks later. Oropharyngeal and cloacal swabs were taken at peak of challenge virus shed

Challenge virus	Oropharyngeal swabs				Cloacal swabs			
	Vector-Control		Vector-HA		Vector Control		Vector-HA	
	(No. positive/total)	($\log_{10}$ EID_{50}/ml)	(No. positive/total)	($\log_{10}$ EID_{50}/ml)	(No. positive/total)	($\log_{10}$ EID_{50}/ml)	(No. positive/total)	($\log_{10}$ EID_{50}/ml)
TI/83	$9/9^{A}$	4.39^{a}	$0/10^{B}$	NI^{b}	$7/9^{A}$	2.24^{a}	$0/10^{B}$	NI^{b}
TE/91	$5/5^{A}$	5.22^{a}	$0/10^{B}$	NI^{b}	$5/5^{A}$	2.98^{a}	$0/10^{B}$	NI^{b}
TSA/61	$8/8^{A}$	4.07^{a}	$0/10^{B}$	NI^{b}	$8/8^{A}$	2.93^{a}	0.10^{B}	NI^{b}
CS/59	$9/10^{A}$	3.86^{a}	$1/10^{B}$	1.14^{b}	$9/10^{A}$	2.08^{a}	$2/10^{B}$	1.01^{b}
HK/97	$8/10^{A}$	4.00^{a}	$1/10^{B}$	1.10^{b}	$8/10^{A}$	3.00^{a}	$0/10^{B}$	NI^{b}
CQ/95	$10/10^{A}$	5.26^{a}	$9/10^{A}$	3.18^{a}	$8/10^{A}$	2.42^{a}	$1/10^{B}$	0.91^{b}
TO/66	$8/9^{A}$	4.43^{a}	$2/10^{B}$	1.07^{b}	$8/9^{A}$	2.52^{a}	$0/10^{B}$	NI^{b}
ET/93	$5/9^{A}$	3.17^{a}	$1/10^{B}$	1.42^{b}	$7/9^{A}$	1.91^{a}	$0/10^{B}$	NI^{b}
CP/83	$10/10^{A}$	6.40^{a}	$10/10^{A}$	4.56^{a}	$10/10^{A}$	3.88^{a}	$0/10^{B}$	NI^{b}
Total	72/80		24/90		70/80		3/90	

^{A,B} Different uppercase letters indicate significant difference ($P < 0.05$) between virus isolation of Vector-Control and Vector-HA groups using Fishers Exact Test.
^{a,b} Different lowercase letters indicate significant differences ($P < 0.05$) between titers of virus shed from Vector-Control and Vector-HA groups using Fishers Exact Test. NI = none isolated. For statistical purposes, all oropharyngeal and cloacal swabs from which virus was not isolated were given a numeric value of $10^{0.9}$ ELD_{50}/ml which represents the lowest detectable level of virus if the virus isolation procedure were modified to use four instead of three embryonating chicken eggs per sample.

Positive correlation between the sequence similarity of the HA and the ability to reduce virus titers shed from the oropharynx (r_s=0.78, P = 0.009)

Swayne et al,. Protection against diverse highly pathogenic H5 avian influenza viruses in chickens immunized with a recombinant fowl pox vaccine containing an H5 AI HA gene insert. Vaccine 2000, 1088-1095

Vector vaccines, other vectors

Newcastle Disease virus

Duck Enteritis Virus

- Herpes virus of ducks, replicates in chicken as well

Salmonella Gallinarum

Replication restricted Alphavirus with HA insert.

- Viral packaging in cell not completed (lacks several genes)
- Induces humoral and cell mediated immunity (‘replication in cell’)

etc

Others: mRNA, DNA, …

mRNA, cDNA of HA gene: expressed in cells

Chicken, turkey, duck, ….

Protection of White Leghorn chickens by U.S. emergency H5 vaccination against clade 2.3.4.4 H5N2 high pathogenicity avian influenza virus

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ABSTRACT

During December 2014–June 2015, the U.S. experienced a high pathogenicity avian influenza (HPAI) outbreak caused by clade 2.3.4.4 H5Nx Goose/Guangdong lineage viruses with devastating consequences for the poultry industry. Three vaccines, developed based on updating existing registered vaccines or currently licensed technologies, were evaluated for possible use: an inactivated reverse genetics H5N1 vaccine (rgH5N1) and an RNA particle vaccine (RP-H5), both containing the hemagglutinin gene of clade 2.3.4.4 strain, and a recombinant herpesvirus turkey vectored vaccine (rHVT-H5) containing the hemagglutinin gene of clade 2.2 strain. The efficacy of the three vaccines, alone or in combination, was assessed in White Leghorn chickens against clade 2.3.4.4 H5N2 HPAI virus challenge. In Study 1, single (rHVT-H5) and prime-boost (rHVT-H5 + rgH5N1 or rHVT-H5 + RP-H5) vaccination strategies protected chickens with high levels of protective immunity and significantly reduced virus shedding. In Study 2, single vaccination with either rgH5N1 or RP-H5 vaccines provided clinical protection in adult chickens and significantly reduced virus shedding. In Study 3, double rgH5N1 vaccination protected adult chickens from clinical signs and mortality when challenged 20 weeks post-boost, with high levels of long-lasting protective immunity and significantly reduced virus shedding. These studies support the use of genetically related vaccines, possibly in combination with a broad protective priming vaccine, for emergency vaccination programs against clade 2.3.4.4 H5Nx HPAI virus in young and adult layer chickens.

Vaccinatie tegen AIV

Diverse types vaccins ‘beschikbaar’ met bewezen effectiviteit (experimenteel), DIVA geschikt, voor kip, kalkoen en eend

- **Effectiviteit onder veldomstandigheden kan lager zijn (zie ook andere pathogenen)**

Behoefte aan meer gegevens over de mate van reductie van de transmissie (dier-dier maar zeker ook onder veldomstandigheden van stal-stal, bedrijf-bedrijf) voor de nieuwe generaties vaccins

- **HAR titers erg behulpzaam voor evaluatie maar geven waarschijnlijk een onderschatting van de bescherming bij de ‘replicerende vaccins”**
- **R waardes tevens zeer informatief voor de eisen aan het aanslaan van de vaccins op koppelniveau**

Vaccins gelukkig ook te gebruiken in combinaties (verhoging, verlenging, verbreding bescherming, verdere verlaging R?)

Inzet van prime and boost lijkt (erg) verstandig voor langer levende dieren

- **Zie ook ervaringen buitenland**

DIVA vaccination programmes Layers, Parents, GP

Examples

- Hatchery (D0 or in-ovo) HVT-H5
- Hatchery HVT-H5, Week 8: Fowl Pox H5 vector (boost, wingweb)
- Hatchery HVT-H5, W14: Subunit H5 vector (boost, injection)
- Hatchery HVT-H5, W8: Fowl Pox H5 vector, (boost, wingweb), W14: Subunit H5 vector
- FP-H5, subunit as boost
- 2x subunit

Conclusie

Alleen vaccinatie tegen HPAI kan AI niet 100% voorkomen

Waardevolle toevoeging aan:

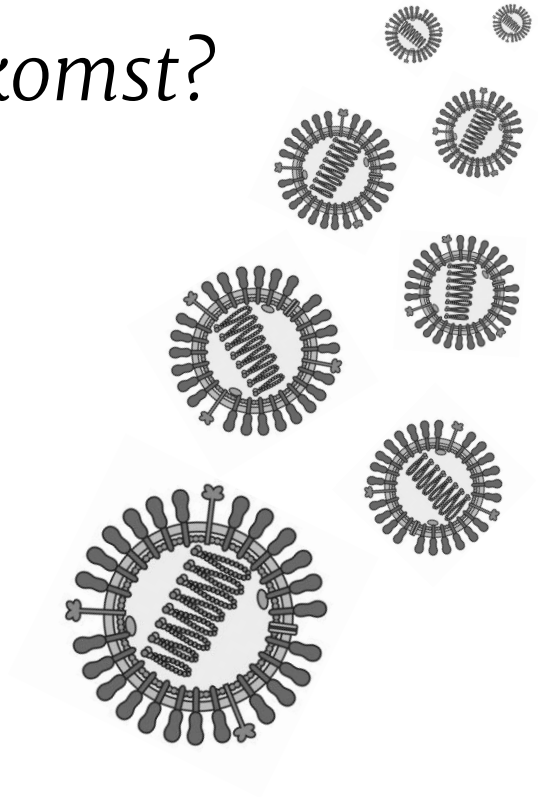
- biosecurity, Grondige schoonmaak/desinfectie
- surveillance and monitoring met geschikte diagnostiek
    - **Controle aanslaan vaccins**
    - **DIVA**
    - **Controleren evolutie veldstammen/doorbraken**

- Ruiming besmette koppels (anti verspreiding en evolutie, zoonotisch risico)

Utrecht University

GD

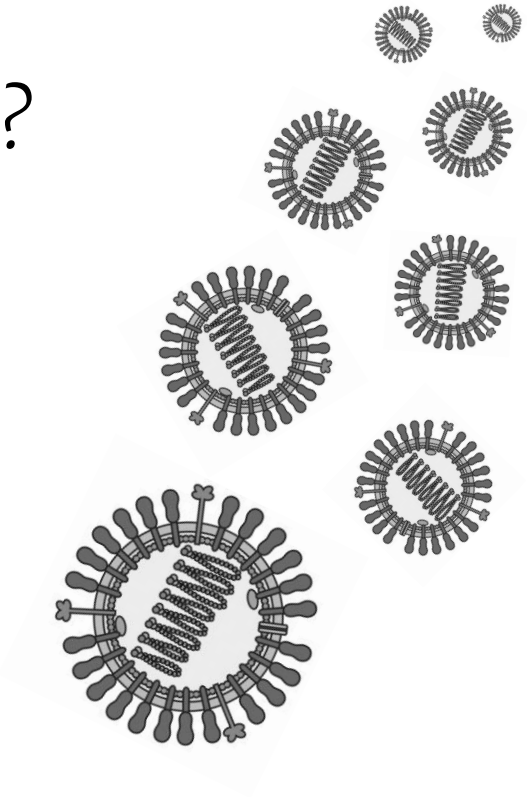
Zijn vaccins de oplossing voor de toekomst?



Flint et al., 2015. Principles of virology 4th edition

Met HPAI endemisch in de natuur:

Is er toekomst zonder vaccinatie?



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Vaccination against AIV

International Alliance for Biological Standardization

Paris, France

October 25 - 26, 2022

IABS Meeting on High Pathogenicity Avian Influenza Vaccination Strategies to prevent and control HPAI : Removing unnecessary barriers for usage

Since October 2020, H5Nx 2.3.4.4b lineage of HPAI has spread across Europe, Middle East, Africa and Asia and is a threat to spread into North America. The uncontrolled spread of these viruses through wild aquatic bird migration is of utmost concern and ongoing climate changes contribute to a wider seasonal migration pattern. In addition, the keeping of poultry in free range systems has reduced physical separation of poultry and wild birds increasing risk of HPAI introduction into poultry. Thus, maintaining avian influenza freedom in poultry and preventing zoonotic infections are an increase challenge.

Vaccination can be a useful tool for prevention and control, but its use is prohibited or severely restricted in many countries worldwide. Wider use of avian influenza vaccination would increase sustainable poultry production, improve animal welfare, reduce economic damage, reduce human infections, and contribute to consumers and animal welfare acceptance of control programs.

A harmonised vaccination strategy with updated vaccine strains and innovative vaccine technologies, combined with appropriate diagnostics, surveillance, and disease management, can offer a better approach than stamping-out alone.

This workshop is intended to discuss how to reduce barriers for broader use of vaccination in avian influenza prevention and control strategy.

The workshop will be an open-discussion forum with participation by a wide variety of stakeholders (OIE, WHO, OFFLU, FAO, WTO, governments, breeding companies, animal welfare, human health, consumers, retailers, scientists, etc).

Register here

SCAN ME

Venue :

OIE
12, rue de Prony
75017 - Paris
France

Scientific Committee :

- David Swayne, USDA, USA – Chair
- Gounalan Pavade, OIE, FR
- Sjaak de Wit, GD Deventer, European College of Poultry Veterinary Science, Netherlands
- Madhur Dhingra, FAO, Italy
- Sophie Von Dobschuetz, FAO, Italy
- Richard Webby, WHO, USA
- Les Sims, Consultant veterinarian in Asia, Australia
- Marisa Peyre, CIRAD, France
- Connie Schmellik-Sandage, USDA, USA
- Ian Brown, APHA+ OFFLU, UK
- David Zeman, AAVLD, USA
- Timm Harder, FLI, Germany

Removing unnecessary barriers for usage

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Negative DIVA results means free status

Utrecht University

Dank voor uw aandacht