

# Inclusion body hepatitis in chickens: from pathogenesis to vaccination

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**British Veterinary Poultry Association  
Spring meeting 2026**

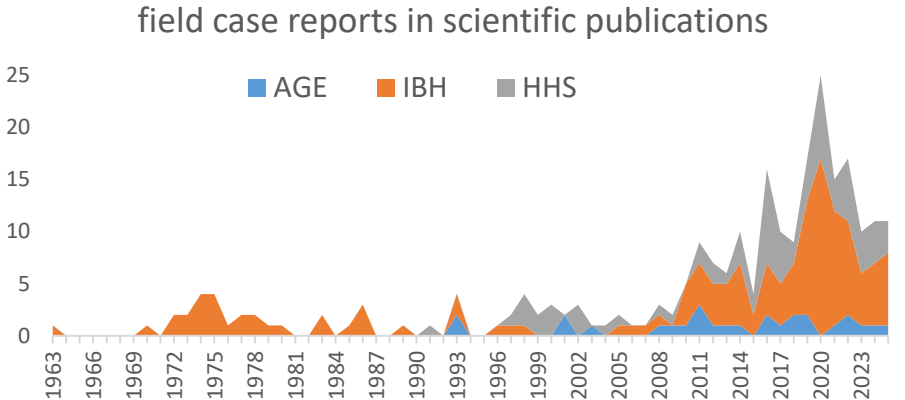
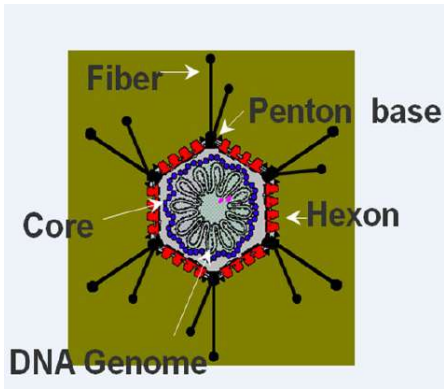
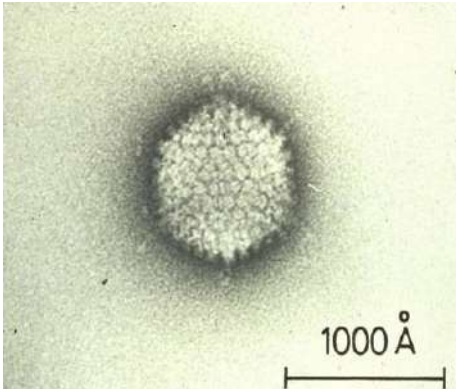
Clinic for Poultry Medicine  
Vetmeduni Vienna

Harrogate, UK  
26th March 2026



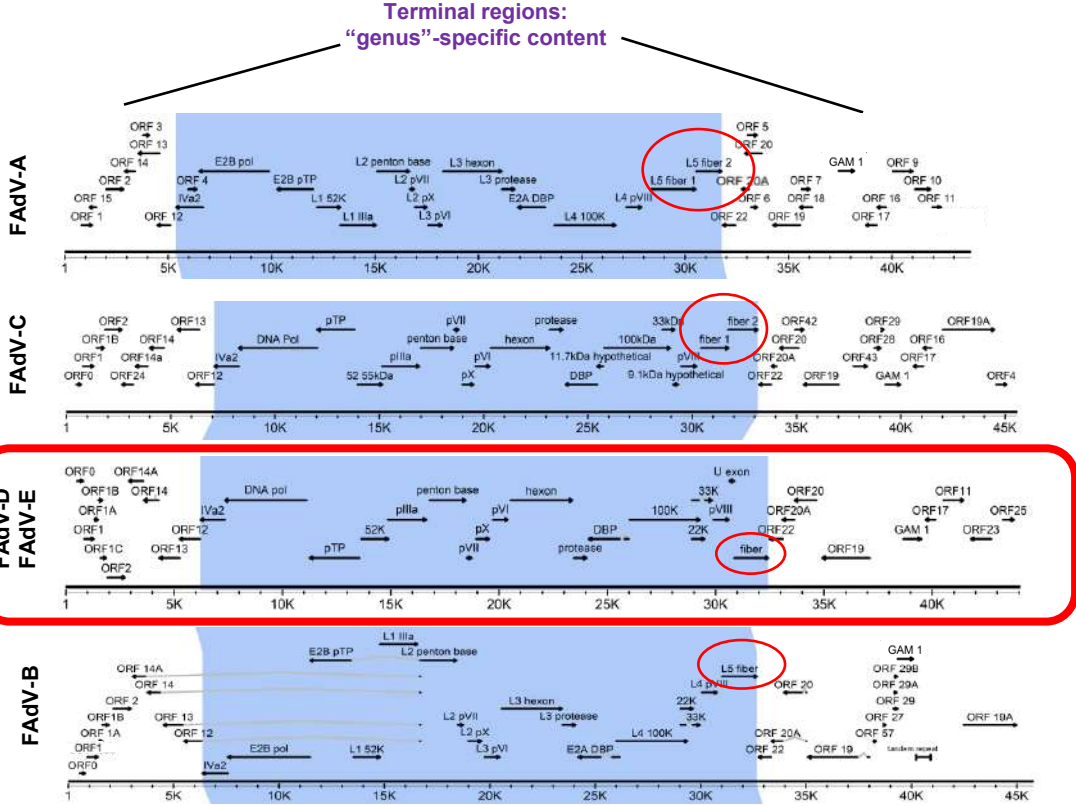
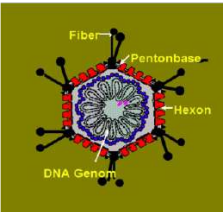
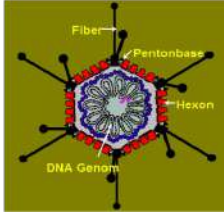
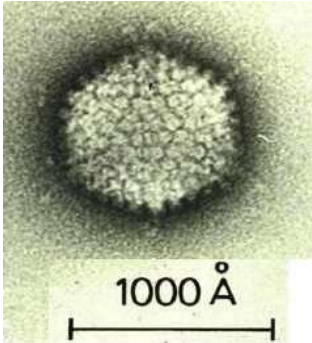
# introduction to FAdVs

- Fowl adenovirus (FAdV): family *Adenoviridae*, genus *Aviadenovirus* – icosahedral, non-enveloped dsDNA virus
- 3 diseases in poultry:
  - inclusion body hepatitis (IBH)
  - hepatitis-hydropericardium syndrome (HHS)
  - adenoviral gizzard erosion (AGE)



# morphology and genomes

FAdV genome: 43-45 kbp

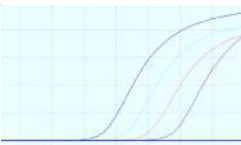
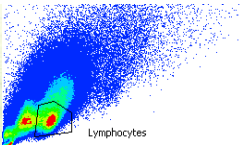
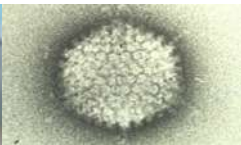
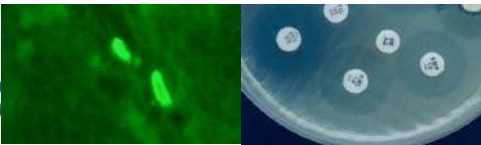


# Fowl adenoviruses - primary pathogens?

- **1963:** Helmboldt & Frazier: description of inclusion bodies in chicken livers with unknown significance
- **1973:** Fadly and Winterfield describe hepatitis in young chicks; “new agent: inclusion body hepatitis virus (IBHV)”
- **1973:** Winterfield et al.: hepatitis in young chickens induced by subcutaneous, intravenous and intraperitoneal injection of FAdV



- **1975:** Rosenberger et al.: Adenovirus isolates had no influence on aplastic anemia or gangrenous dermatitis
- **1976:** Fadly et al.: co-infection of adenovirus with infectious bursal disease virus (IBDV) is of importance for IBH
- **1986:** v. Bülow et al.: pathogenicity of certain avian adenoviruses increase after co-infection with chicken anemia virus (CAV)



# Fowl adenoviruses - primary pathogens!

- **1983:** Cook: oral experimental infection of 1-day-old chicks from SPF parents with various FAdV strains induces mortality and growth retardation
- **1989:** Christensen and Saifuddin: IBH in broiler flocks in New Zealand with no obvious co-infection
- **1991:** Erny et al.: field outbreaks of IBH in Australia can be reproduced following infection of chicks via the eye and nostril
- **2006:** Gomis et al.: clinical occurrence of IBH in Canada is independent of CAV and IBDV
- **2011:** Steer et al.: field data confirm that IBH in Australia in the absence of CAV and IBDV
- **2014:** Eregae et al.: no statistical association between flocks exposed to FAdV and co-infected with CAV or IBDV

# IBH: overview and pathology

FAdV-2, -11

*A. gallinae*/FAdV-D

FAdV-8a, -8b

*A. hepatitidis*/FAdV-E



**main host:** young broilers (up to 5 weeks old)

isolated from layers and breeders too



virus often isolated from healthy chickens

metabolic disease  
up to 30% mortality



immunosuppressive

FAdV-8b, 7 dpc

FAdV-8a, 5 dpc



**THYMUS**



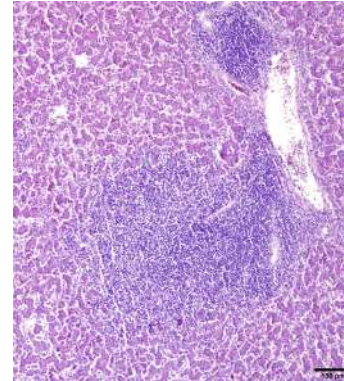
**BURSA OF FABRICIUS**



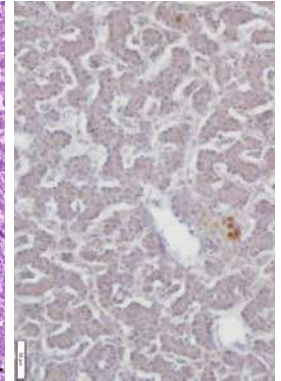
FAdV-11, 3 dpc  
(layer)



FAdV-8a, 7 dpc



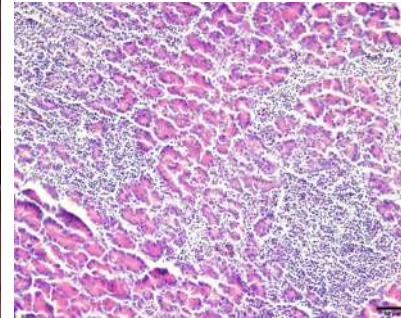
FAdV-8a, 3 dpc



FAdV-8a, 5 dpc



FAdV-8b, 3 dpc  
(layer)



FAdV-8a, 5 dpc



FAdV-8b, 5 dpc

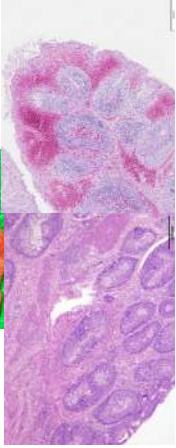
**MUSCLE**

## PANCREAS

experimental infection of SPF broilers/layers with FAdV-8b (13/18153), FAdV-8a (11-16629), or FAdV-11 (08-18926) i.m.,  $10^7$  TCID<sub>50</sub>/mL (0.5mL) 3 to 7 days post challenge (dpc)

# the importance of bursa of Fabricius

➤ intramuscular infection of 4-week-old SPF birds



Infection / treatment	no. birds	4 d.p.i.	7 d.p.i	17 d.p.i.
IBH-2 (FAdV-5; Tipton) + Cyclophosphamide	18	6/8*	4/4	0/6
IBHV	10	0/2	0/2	0/6
Cyclophosphamide	5	0/2	0/2	0/1
control	5	0/2	0/2	0/1

(Fadly et al., 1986)

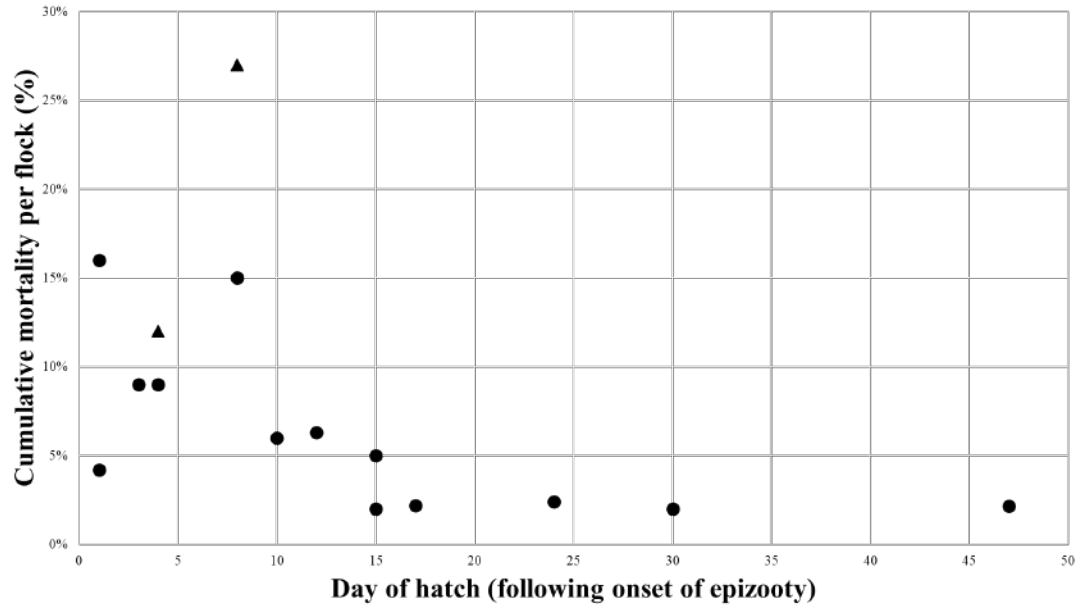
\*no. of birds with lesions/examined

# IBH/HHS - mortality – co-infections



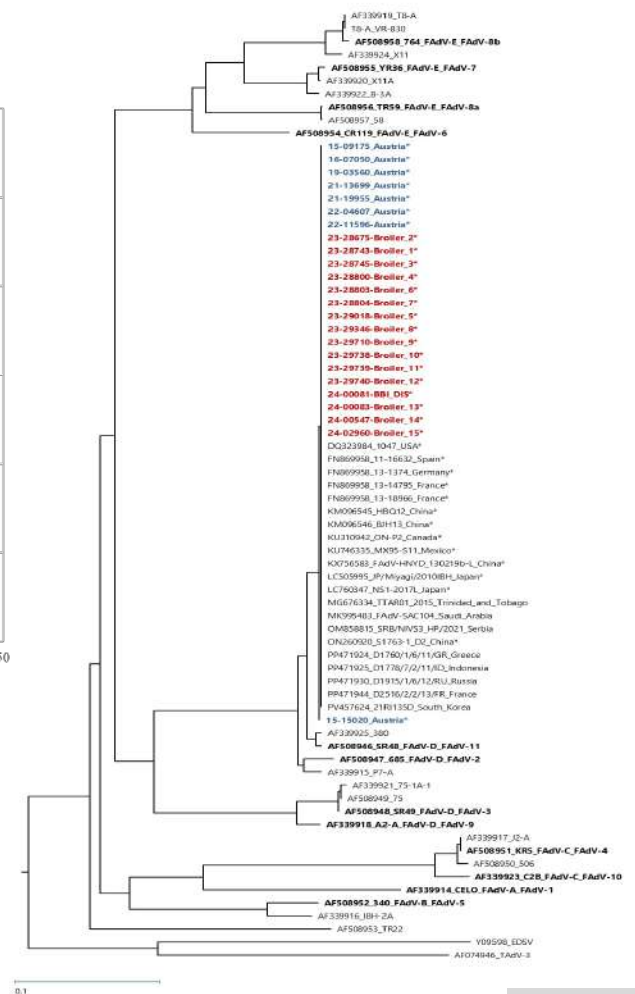
Case ID	Year	Province	Chicken type	Age (d)	% Mortality <sup>1</sup>	Clinical sign <sup>2</sup>		Virus detected by PCR or reverse-transcription PCR			
						IBH	HPS	FAdV <sup>3</sup> (type)	CIAV	IBDV <sup>4</sup> (type)	Others <sup>5</sup>
K07-01	2007	Chonbuk	Native	14	NR	+	+	4	+	-	-
K07-02	2007	Chonbuk	Native	45	15	+	+	4	+	-	-
K08-01	2008	Chonbuk	Native	29	21.50	+	+	4	+	-	-
K08-02	2008	Chonbuk	Layer	63	0.48	+	+	4	+	-	-
K08-03	2008	Ganwon	Broiler	16	11.50	+	+	4	+	-	-
K08-04	2008	Gyeonggi	Layer	28	NR	+	-	8b	+	(v)	-
K08-05	2008	Chungbuk	Broiler	13	2.80	+	-	8b	+	-	-
K08-06	2008	Chungnam	Broiler	10	2.50	+	-	8b	-	-	-
K08-07	2008	Chungnam	Broiler	12	9.50	+	-	8b	+	-	-
K08-08	2008	Chungnam	Broiler	13	3.20	+	-	8b	-	-	-
K08-09	2008	Chonbuk	Native	65	1.00	+	-	11	+	-	-
K08-10	2008	Chungnam	Broiler	17	0.60	+	-	11	-	-	-
K09-01	2009	Chonbuk	Broiler	16	NR	+	+	4	-	-	-
K09-02	2009	Chonbuk	Broiler	18	1.30	+	+	4	-	-	-
K09-03	2009	Chonbuk	Native	55	NR	+	+	4	+	-	-
K09-04	2009	Chonbuk	Broiler	9	14.50	+	+	4	-	-	-
K09-05	2009	Chonbuk	Broiler	13	4.20	+	+	4	-	-	-
K09-06	2009	Chonbuk	Broiler	27	55.00	+	+	4	+	-	-
K09-07	2009	Chonbuk	Broiler	25	NR	+	+	4	-	-	-
K09-08	2009	Chungbuk	Native	36	1.00	+	+	4	+	+	-
K09-09	2009	Ganwon	Broiler	14	20.00	+	+	4	-	+	-
K09-10	2009	Chungnam	Broiler	18	0.40	+	+	4	-	(v)	-
K09-11	2009	Chungnam	Native	50	0.80	+	+	4	+	+	-
K09-12	2009	Chonnam	Broiler	25	NR	+	-	8b	-	-	-
K09-13	2009	Chungnam	Broiler	10	2.00	+	-	8b	+	-	-
K09-14	2009	Chonbuk	Broiler	30	25.00	+	-	8b	-	+	-
K09-15	2009	Chonbuk	Broiler	19	NR	+	-	11	-	-	-
K09-16	2009	Chonbuk	Broiler	21	NR	+	-	11	-	-	-
K09-17	2009	Chonbuk	Broiler	22	NR	+	-	11	-	(v)	-
K09-18	2009	Chonbuk	Broiler	25	NR	+	-	11	+	-	-
K09-19	2009	Chungbuk	Broiler	25	8.60	+	-	11	+	-	-
K09-20	2009	Gyeonggi	Layer	23	15.00	+	-	11	-	+	-
K09-21	2009	Chonnam	Broiler	14	2.90	+	-	11	-	+	-
K09-22	2009	Chonnam	Broiler	23	<0.1	+	-	11	-	(v)	-
K09-23	2009	Chungnam	Broiler	22	<0.1	+	-	11	-	(v)	-
K09-24	2009	Chungnam	Broiler	25	<0.1	+	-	11	-	(v)	-
K10-01	2010	Chungbuk	Layer	112	<0.1	+	+	4	-	-	-
K10-02	2010	Chungnam	Broiler	19	NR	+	+	4	-	-	-
K10-03	2010	Chungnam	Broiler	20	NR	+	-	8b	-	-	-

# vertical transmission and co-infections



triangles represent flocks with concurrent IBDV infection

Grafi et al. (2026), Poultry,5:25



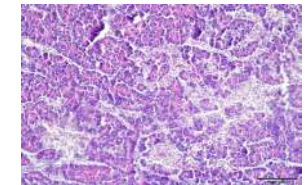
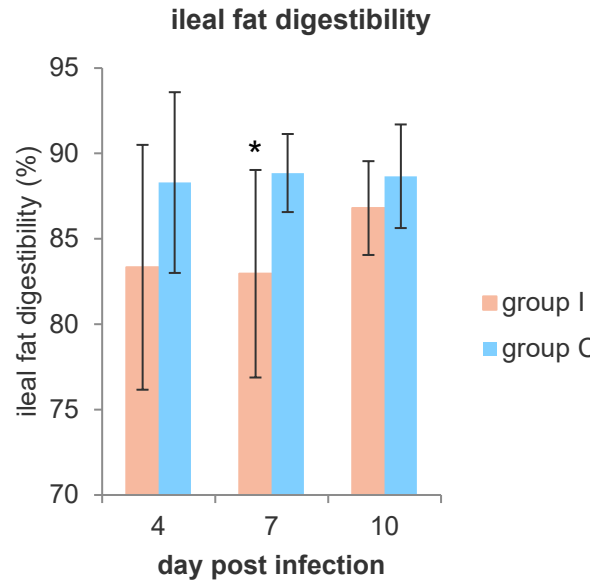
0.1  
 partial hexon gene (583 nt; loop-1 region)  
 Neighbor Joining (BJONJ) tree

Grafi et al. (2026), Poultry,5:25

# IBH subclinical induced hepato-pancreatitis

group	bird	age inoculation	route inoculation	virus isolate	virus dose/ml
I (infected)	20 SPF broilers	<b>21 days</b>	<b>oral</b>	13/18153 (FAdV-8b)	10 <sup>7</sup> TCID <sub>50</sub>
C (control)	20 SPF broilers	-	-	-	-

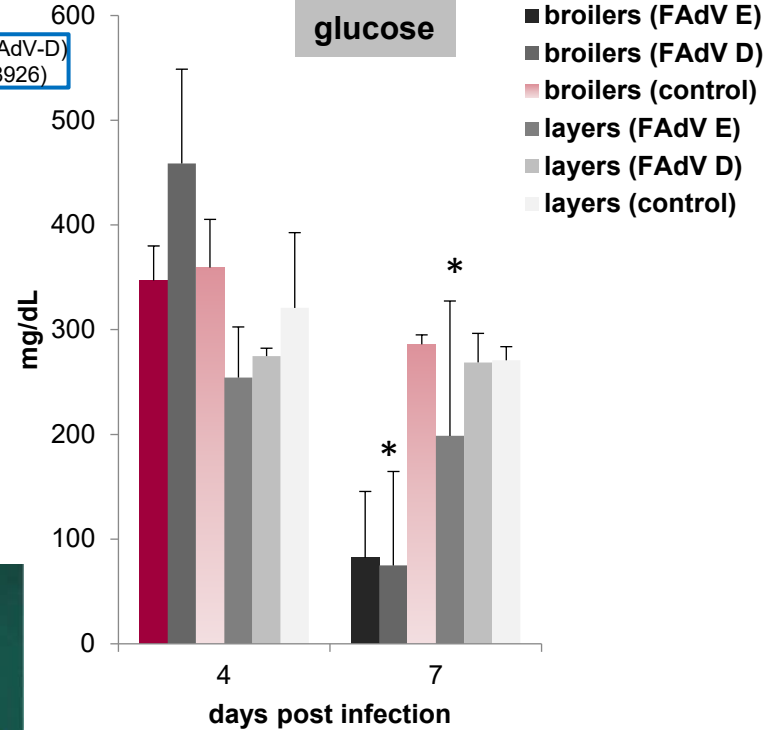
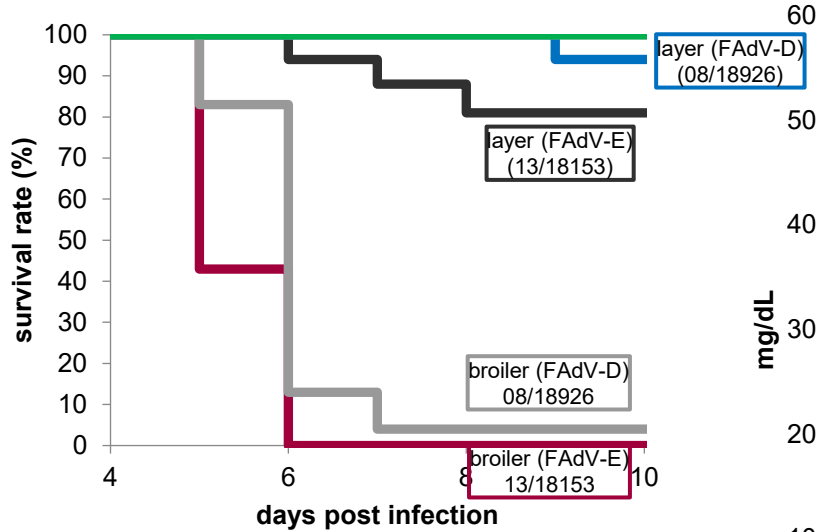
(Matos et al., 2018)



Asterisks indicate statistical significant difference when compared to the control group ( $P < 0.05$ )

Matos et al. (2018)

# SPF layers vs. broilers

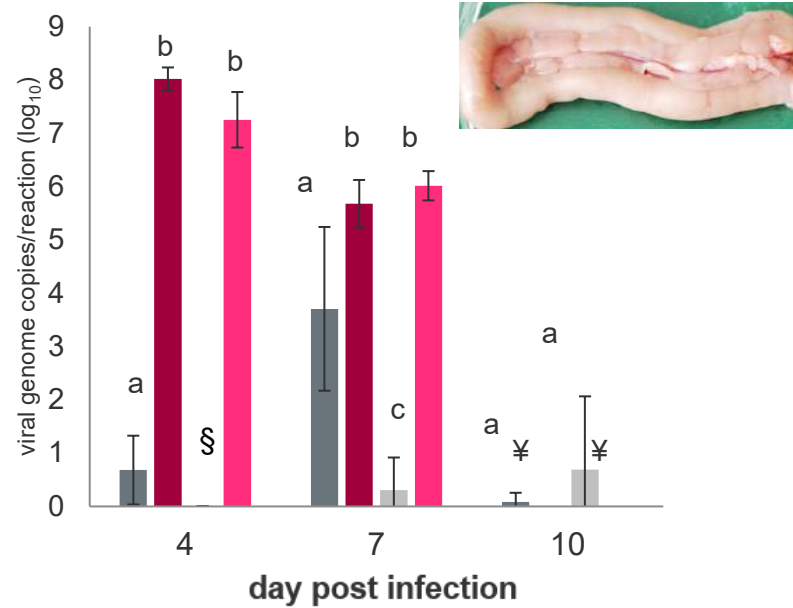
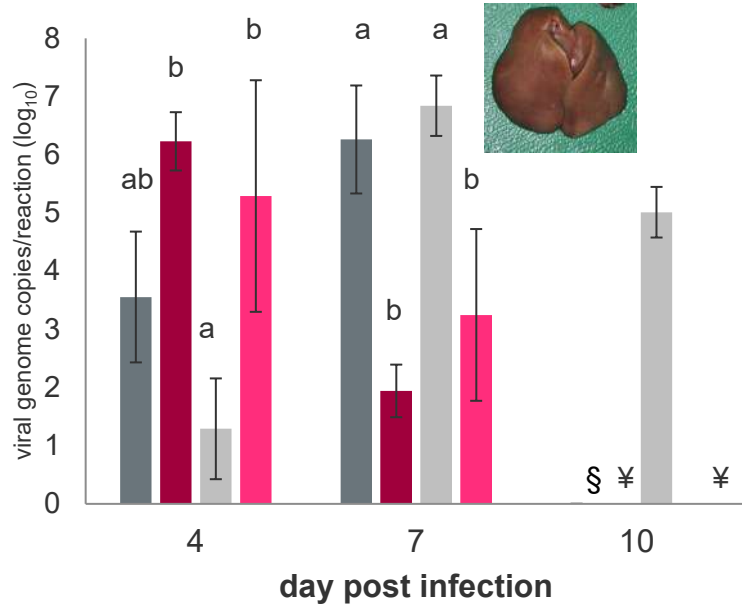


Asterisks indicate statistical significant difference when compared to the respective control group (P < 0.05)

Matos et al. (2016)

broiler (FAdV-11): 08/18926 7dpi

# viral load in liver and pancreas



- broilers (FAdV-E)
- broilers (FAdV-D)
- layers (FAdV-E)
- layers (FAdV-D)

Means with different lowercase letters at each time point are statistically different (P < 0.05)  
 ¥ not applicable; § no viral load was detected

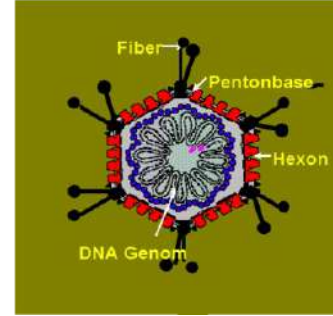
# pathogenesis

## horizontal transmission orofecal route



colonization of intestinal epithelium 12h p.i.,  
viremia from 24h p.i.  
(experimental, shown in SPF chickens, 2-day-old)  
(Saifuddin & Wilks, 1991)

## vertical transmission from breeder to egg (yolk & albumen)



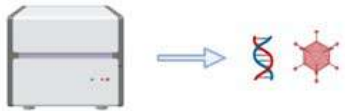
**fiber:** interact with CAR-like receptors of host cells

**penton base:** role in entering the host cells

**hexon:** most abundant and immunogenic capsid protein

# diagnosis

PCR & sequencing: typing via **hexon loop-1**



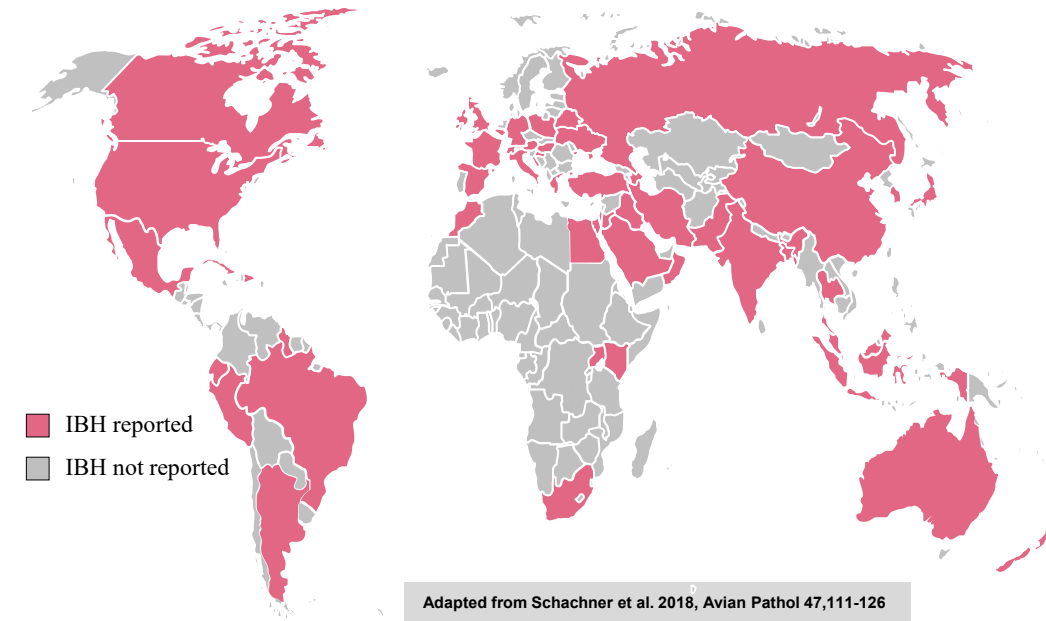
serotyping via virus neutralization test (VNT)



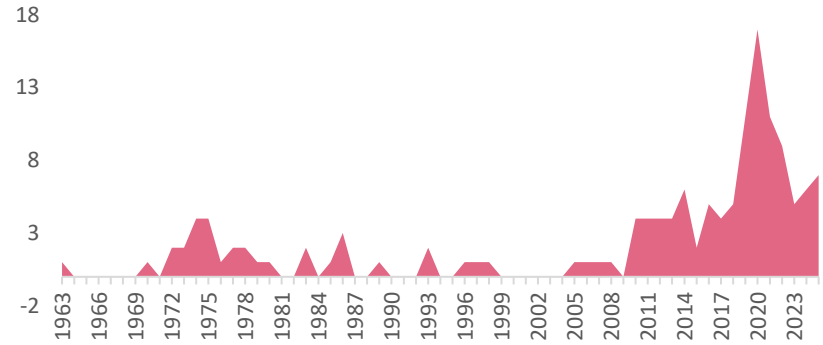
FAdV isolation & culture on egg/cell culture (liver cells)



# distribution in the field

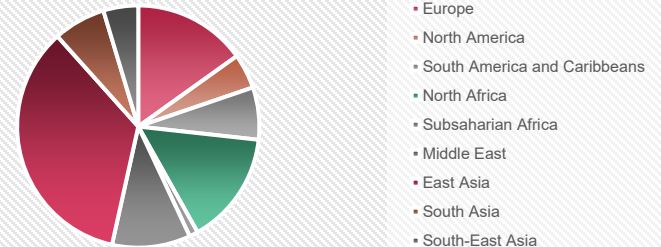


## field case reports in scientific publications



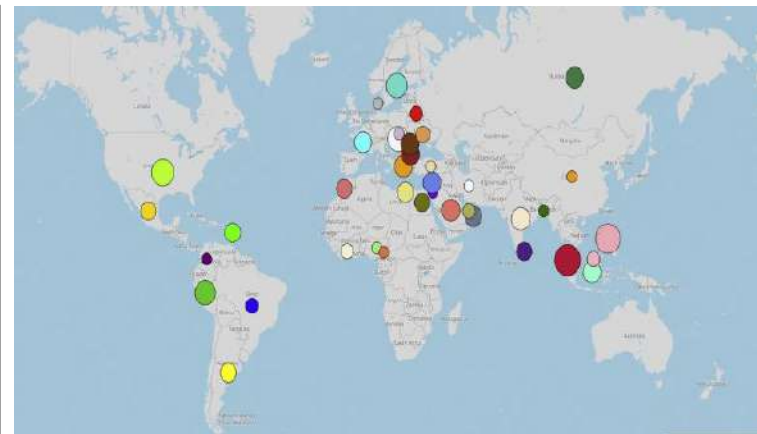
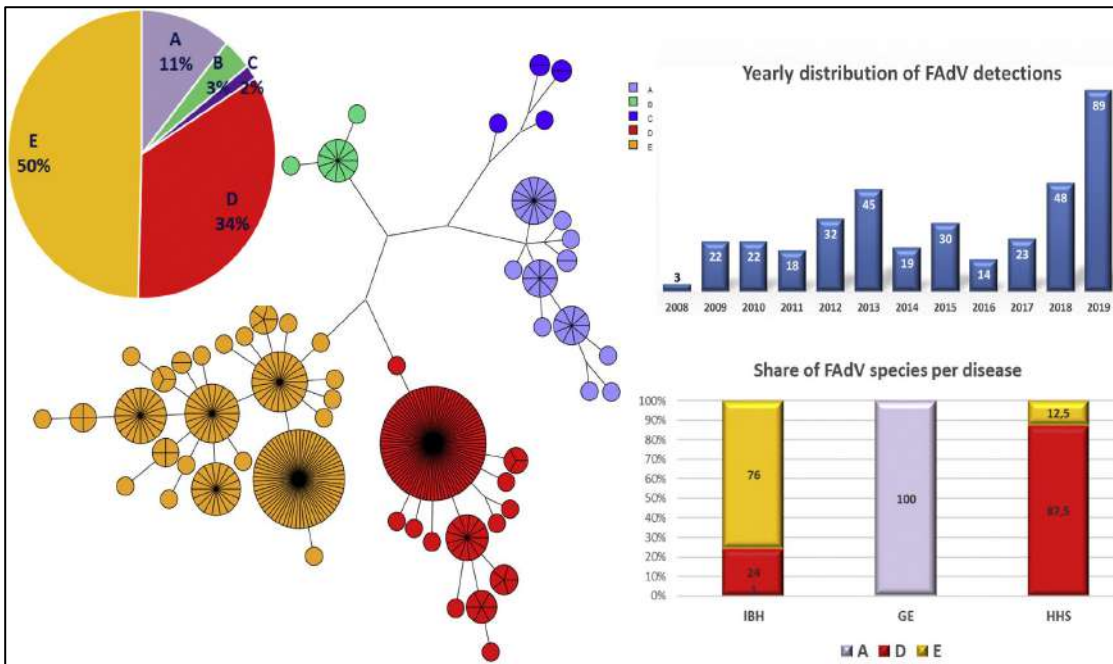
Adapted from Schachner et al. 2021, Avian Pathol 50,2-5

## field reports of IBH in chickens published in peer-reviewed journals from 2015 to 2025



- co-infections are possible
- circulation of non-pathogenic strains of FAdV-2, -8a, -8b, -11 common (e.g. reported in Columbia, El Salvador, Sweden...)
- data from many countries lacking

# FAdV (-diseases): 10 years global survey 2008 - 2019



the majority of detections not linked to FAdV-related diseases (82% FAdV-D, 72% FAdV-E)

most common isolates from “healthy” birds (subclinical infection?): FAdV-E (46%), -D (36%)

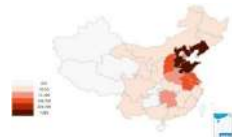
Kiss et al. 2021, Poult Sci 100,101052

maximum parsimony phylogenetic tree based on partial polymerase gene sequences, Advanced Cluster Analysis

# FAdV prevalence

## ■ 231 chicken flocks in Ontario, Canada (Eregae et al. 2014)

- Flock level prevalence during grow-out
- **FAdV (96.54%)**, CAV (77.06%) and IBDV (48.92%)
- 9613 samples from different farms



## ■ 9613 samples from different farms from 28 Chinese provinces; birds suspicious for IBH/HHS (Niu et al. 2022)

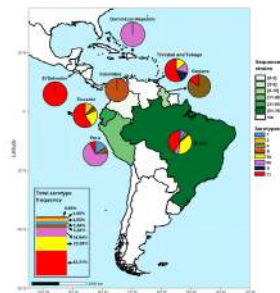
- LMH cells + PCR + sequencing – 2210 FAdV-positive
- **FAdV-1 (7.65%)**; **FAdV-2 (5.34%)**; FAdV-3 (2.04%) **FAdV-4 (38.24%)**; FAdV-5 (2.17%); FAdV-6 (0.32%); FAdV-7 (0.77%), FAdV-8a (**10.36%**); FAdV-8b (**11.58%**); FAdV-9 (0.5%); FAdV-10 (8.10%); FAdV-11 (12.67%)

## ■ 1920 samples from 7 Chinese provinces; birds clinically healthy (Zhuang et al. 2023)

- PCR + sequencing from cloacal swab samples
- chicken (13.27%); goose (2.5%); duck (0.48%) and pigeon (0.43%)

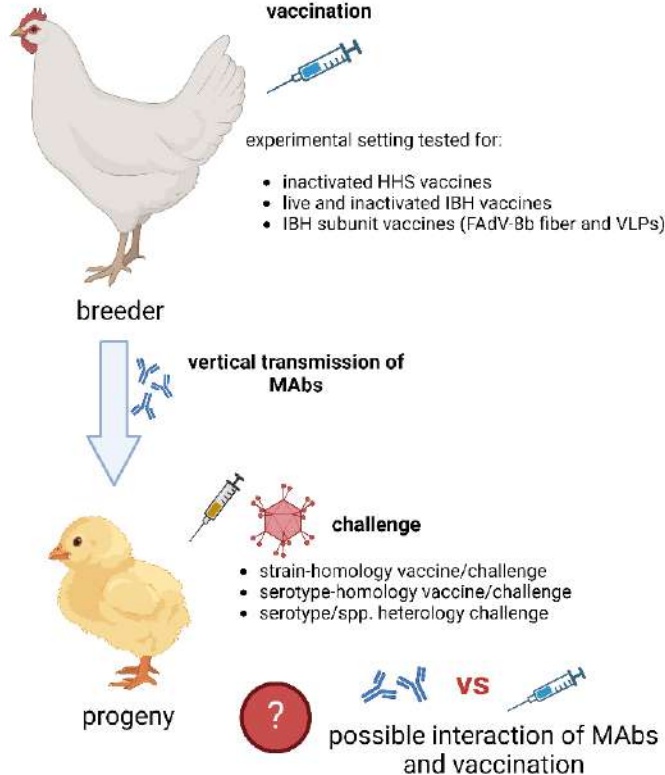
## ■ 1171 samples from different farms from 14 Brazilian states (birds suspicious for FAdV diseases); 62 samples from 34 farms in Central and South America (Chacón et al. 2026)

- qPCR + sequencing from pooled tissue samples (Brazil) or FTA cards (other Central/South American countries)
- prevalence in Brazil: broiler (21.26%); layer (14.75%); breeder (7.71%)
- FAdV-1, FAdV-2, FAdV-4, FAdV-6, FAdV-8a, FAdV-8b, FAdV-11 in Brazil; FAdV-8b and FAdV-11 in Peru; FAdV-6 in Colombia; FAdV-4 and FAdV-11 in Guyana; FAdV-11 in El Salvador

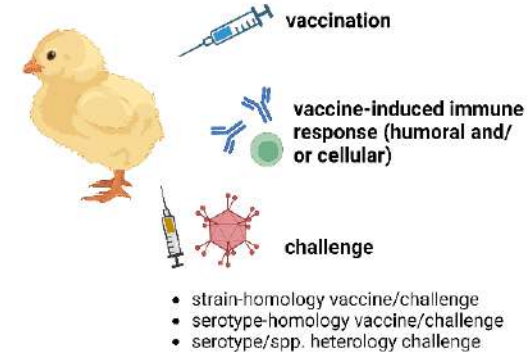


# FAdV vaccines

## VERTICAL PROTECTION



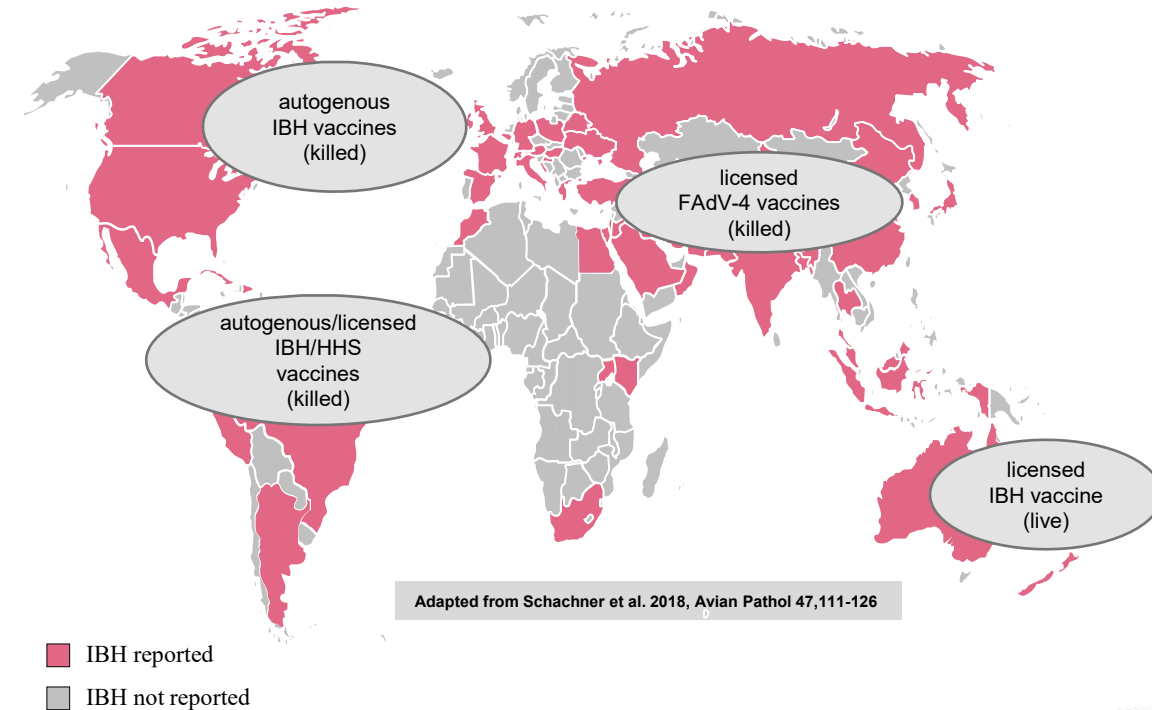
## HORIZONTAL PROTECTION



## TYPES OF FAdV VACCINES

- live virus (attenuated/apathogenic strains)
- inactivated whole virus
- subunit vaccines (recombinant capsid proteins, VLPs)
- recombinant whole virus with modified capsid proteins (live or inactivated)
- vector vaccines: FAdV backbone (expressing IBDV VP2)
- vector vaccines: viral/bacterial/yeast backbone (NDV, *L. lactis*, *E. faecalis*, *S. cerevisiae* expressing FAdV capsid proteins)

# available vaccines and impact in the field



diverse & evolving field situation:

-) mixed infections

-) shift to outbreaks from different serotypes after field vaccination

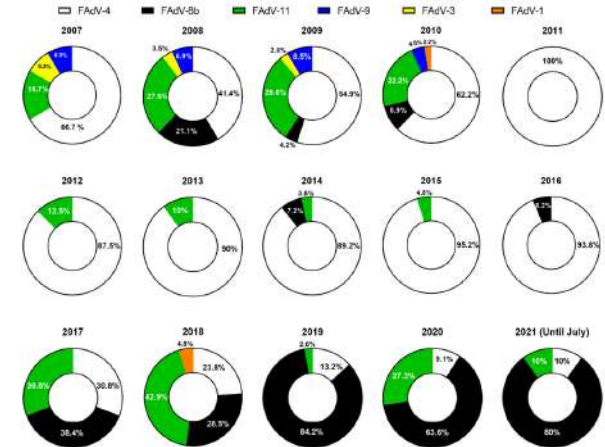


Figure 1. Proportion of reported cases for each FAdV serotype in South Korea from 2007 to 2021. Data are based on published literature [45,55,58-60] and unpublished data (Supplementary Materials).

# effect of vaccination



- breeders vaccinated at 12 and 18 weeks of age with a commercial inactivated formulation (i.m.); samples from progenies from 2 consecutive cycles

Table 2. Distribution of positive flocks for FAdV based on vaccination status, location, code, production cycle, and age.

Vaccination status	Code	First cycle			Second cycle		
		1 day	14 days	28 days	1 day	14 days	28 days
Vaccinated flocks	VF1	—	—	—	—	—	—
	VF2	—	—	—	—	—	—
	VF3	—	L + CS	L + CS	—	—	—
	VF4	—	—	—	—	—	—
	VF5	—	CS	L + CS	—	L + CS	L + CS
	VF6	—	—	—	—	—	—
	VF7	—	—	—	—	—	—
	VF8	—	—	—	—	—	—
	VF9	—	—	—	—	—	—
	VF10	—	—	—	—	—	—
	VF11	—	—	—	—	—	—
	VF12	—	—	—	—	—	—
	VF13	—	—	—	—	L + CS	L + CS
	VF14	—	—	—	—	—	—
	VF15	—	—	—	—	—	—
	VF16	—	—	—	—	—	—
	VF17	—	—	—	—	—	—
	VF18	—	—	—	—	—	—
	VF19	—	—	—	—	—	—
	VF20	—	—	—	—	—	—
Rate of positive L samples (%)		0	1/20 (5)	2/20 (10)	0	2/20 (10)	2/20 (10)
Rate of positive CS samples (%)		0	2/20 (10)	2/20 (10)	0	2/20 (10)	2/20 (10)
Nonvaccinated flocks	NVF1	—	—	—	—	—	—
	NVF2	—	L + CS	L + CS	—	—	—
	NVF3	—	—	L + CS	—	L + CS	L + CS
	NVF4	—	CS	L	—	—	—
	NVF5	—	L + CS	L + CS	—	L + CS	L + CS
	NVF6	—	—	—	—	—	—
	NVF7	—	—	—	—	—	—
	NVF8	—	L + CS	L + CS	—	L + CS	L + CS
	NVF9	—	CS	L + CS	—	—	—
	NVF10	—	—	—	—	—	—
	NVF11	—	L + CS	L + CS	—	—	L
	NVF12	—	L + CS	L + CS	—	L + CS	L + CS
	NVF13	—	—	—	—	—	—
	NVF14	—	—	—	—	L + CS	L + CS
	NVF15	—	—	—	—	—	—
	NVF16	—	L + CS	L + CS	—	L + CS	L + CS
	NVF17	—	—	—	—	—	—
	NVF18	—	—	—	—	L + CS	L
	NVF19	—	L + CS	L	—	CS	L + CS
	NVF20	—	—	—	—	—	—
Rate of positive L samples (%)		0	7/20 (35)	10/20 (50)	0	8/20 (40)	10/20 (50)
Rate of positive CS samples (%)		0	9/20 (45)	8/20 (40)	0	9/20 (45)	8/20 (40)

L=liver  
CS=cloacal swab

vaccinated

non-vaccinated

# experimental vaccines

## live vaccines

- apathogenic strains
- attenuation (ex. via cell culture or embryo-adaptation)

first published with FAdV-E formulations, spray-vaccination of apathogenic strains  
(Pallister et al., 1993)

### dual serotype formulations:

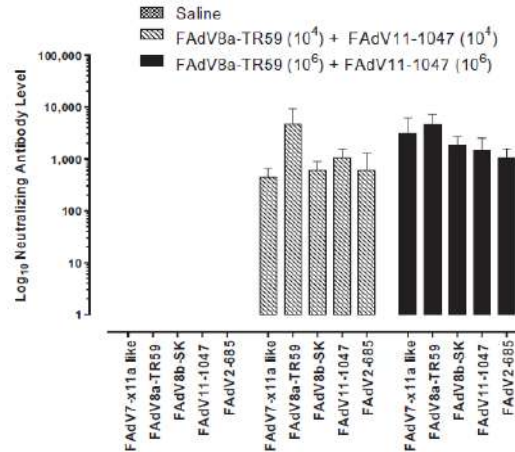
FAdV-8a + -11 (orally) ✓ vertical protection

### progeny challenge



FAdV-2  
FAdV-7  
FAdV-8a  
FAdV-8b  
FAdV-11

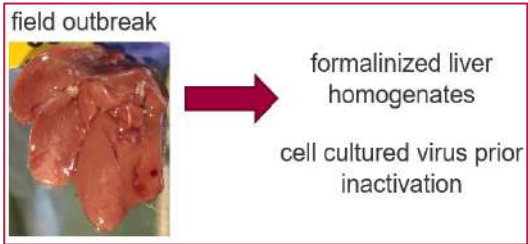
(Popowich et al., 2018)



protection  
associated with high  
level of systemic  
nAbs

Fig. 4. Neutralizing antibodies against FAdVs of broiler progenies at 0 d of age for serotypes FAdV7-x11a like, FAdV8a-TR59, FAdV8b-SK, FAdV11-1047 and FAdV2-685.

# killed vaccines



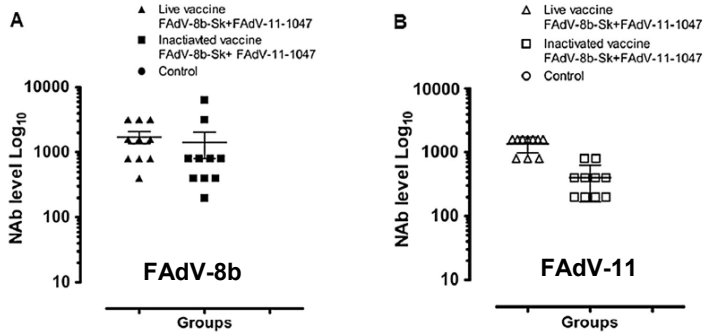
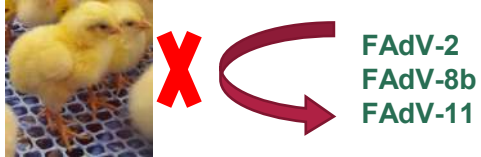
first IBH vaccines (concept borrowed from HHS)  
(Kaur et al., 1997)

!! diverse aetiology: problem of **cross-protection**

## dual serotype formulation:

FAdV-8b + -11  
(Alvarado et al., 2007; Gupta et al., 2018) vertical protection

### progeny challenge



nAbs

Gupta et al. 2018, Vaccine 36,744-750

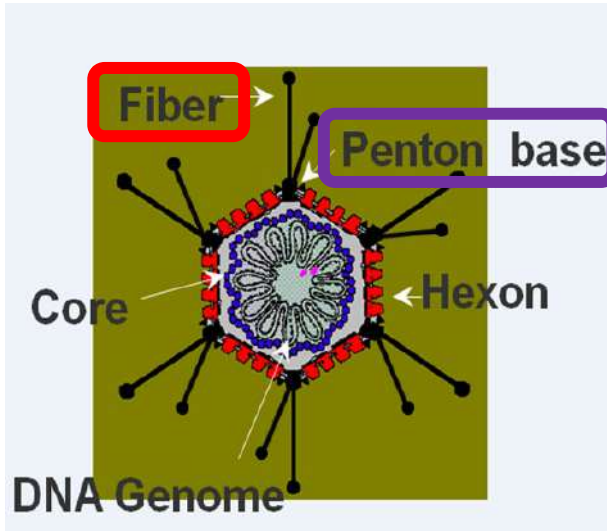
**cross-protection reports:** FAdV-8a vaccine vs. -11 challenge (few birds with cross-reacting nAbs)  
(Steer-Cope et al., 2019)

## Expanding protective spectrum with recombinant vaccines:

nAbs no nAbs

FAdV-4 w/ FAdV-8b fiber (killed) → grants homologous protection **but not** heterologous vs. FAdV-8a  
(Lu et al., 2022)

## subunit vaccines: concept



**Based on recombinant FAdV-D or -E capsid proteins**

expressed mainly via *E. coli* or baculovirus systems

studies on experimental FAdV subunit vaccines:

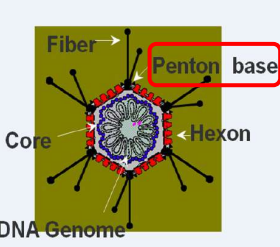
**major structural proteins**

- **fiber (fib)**
- **penton base (Pb)**
- hexon

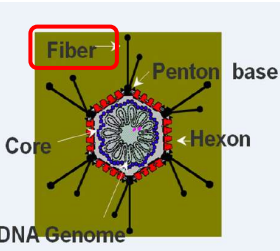
**others**

- chimeric proteins
- virus-like particles (VLPs)

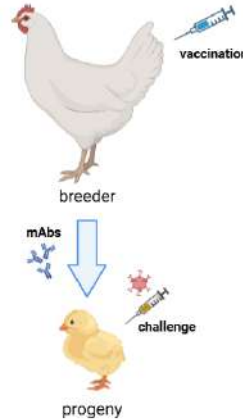
# subunit vaccines: penton base and fiber



- FAdV-E Pb granted **no protection** vs. FAdV-8b (*De Luca et al., 2023*)
- booster vaccination needed to elicit ELISA Abs, no nAbs
- no information on cellular immunity

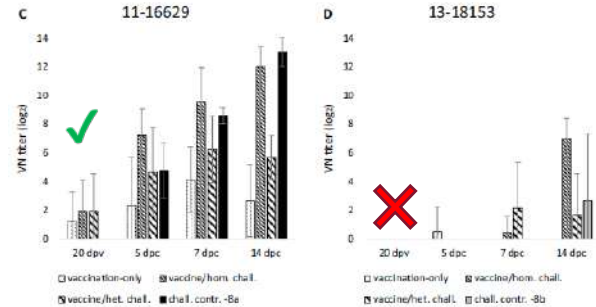


- FAdV-8b fiber was able to grant **vertical** protection vs. FAdV-8b chall. through transmission of maternal antibodies (mAbs) (*Gupta et al., 2017*) ✓



- cellular immunity: systemic increase of CD4<sup>+</sup>:CD8<sup>+</sup> after booster

- FAdV-8a fiber was able to protect chickens against FAdV-8a chall. **but not -8b**
- serotype-specific nAbs development (*De Luca et al., 2020*)



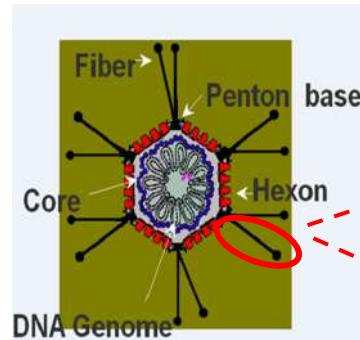
De Luca et al. 2020, Vet Res 51:143

protection from IBH depends on serotype-specific nAbs

# subunit vaccines: chimeric fibers

## recombinant **chimeric fibers (crecFib)** proteins

- **limit number of antigens in the vaccine**
- **basic idea:**
  - retain full-length fiber
  - engineer sequence replacement between 2 distinct types



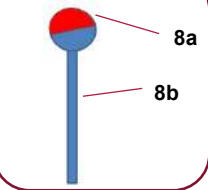
FAdV-8a fib



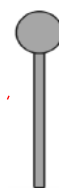
FAdV-8b fib



crecFib-8b/8a



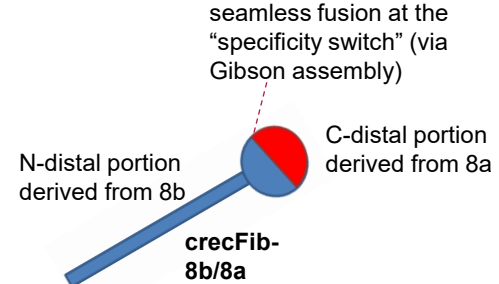
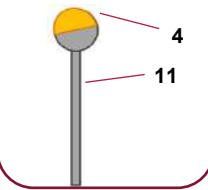
FAdV-4 fib-2



FAdV-11 fib



crecFib-4/11

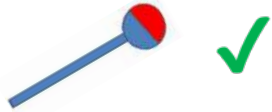


merging epitopes from different **serotypes**

merging epitopes from different **species**

# subunit vaccines: chimeric fibers

## crecFib-8b/8a

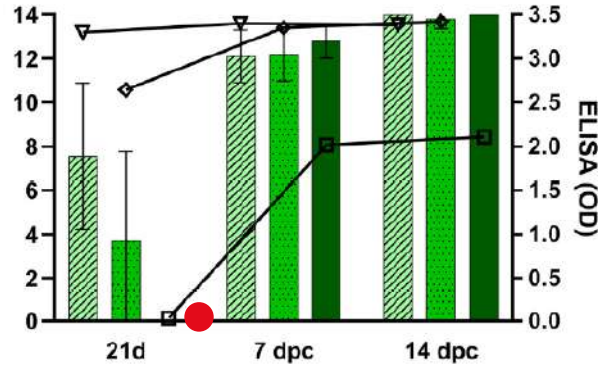


protection from IBH  
by FAdV-8a and -8b

(Schachner et al., 2022)



Abs vs. FAdV-8b

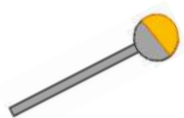


✓ ELISA Abs

✓ nAbs

W<sup>8b/8a</sup>C<sup>8b</sup>
 V<sup>8b/8a</sup>C<sup>8b</sup>
 C<sup>8b</sup>  
 ELISA W<sup>8b/8a</sup>C<sup>8b</sup>
 ELISA V<sup>8b/8a</sup>C<sup>8b</sup>
 ELISA C<sup>8b</sup>

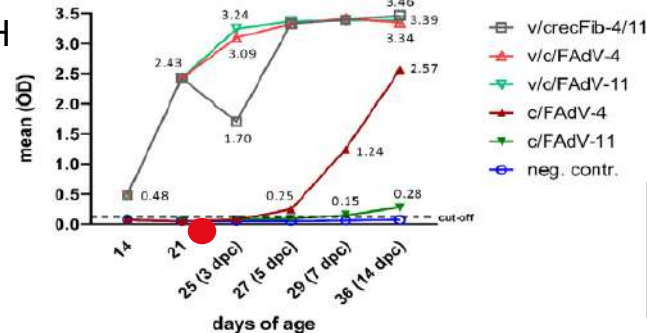
## crecFib-4/11



protection from HHS and IBH  
by FAdV-4 and -11

(De Luca et al., 2022)

crecFib-4/11 ELISA

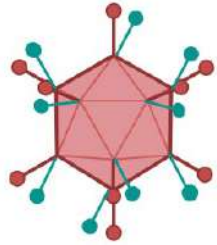


✓ ELISA Abs

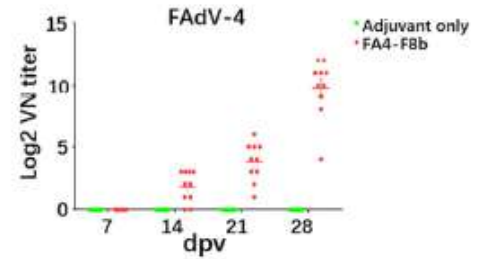
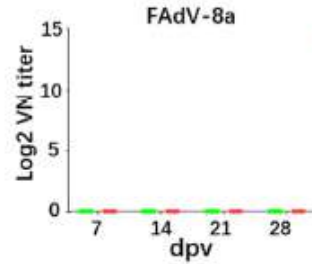
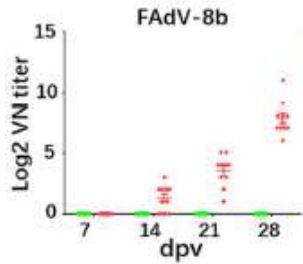
✗ no nAbs

further investigations  
needed to clarify  
mechanisms for protection

# recombinant FAdV vaccines incorporating subunits from different FAdV species/serotypes



- FAdV-4 expressing fiber from either FAdV-8a or -8b, or even -8b + -11 (live or inactivated) (Lu et al., 2022; 2023; Wang et al., 2022; Song et al., 2023; Yang et al. 2026)
- induction of serotype-specific nAbs → no protection from non-included serotypes
- ELISA Abs ✓



## summary

- IBH is caused by FAdV-D (serotypes 2 & 11) and -E (serotypes 8a & 8b)
- it is a metabolic disease that primarily targets liver, pancreas, spleen, kidneys and lymphoid organs
- immunosuppression is caused by affection of thymus and bursa of Fabricius
- transmission can be both horizontal (orofecal) and vertical
- the major capsid proteins are involved in the receptor interaction (fiber) and entry (penton base) in the host cells
- the virus can be isolated from cloacal swabs and infected target organs in egg/cell culture; typing is commonly performed by PCR and sequencing of the hexon gene (loop-1 region)
- IBH-causing FAdVs have been isolated worldwide; however, the availability of licensed vaccines is limited
- live, inactivated and subunit experimental vaccines have been described as efficacious against IBH, both in a horizontal and vertical setting
- among subunit formulations, fiber vaccines have been proven protective, albeit the protection is serotype specific (due to the development of specific nAbs)
- chimeric fiber constructs can be used to expand the protective spectrum and include diverse serotypes/species of disease-causing FAdVs

# vetmeduni

## THANK YOU FOR YOUR ATTENTION!

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### Clinic for Poultry

