5º ENCUENTRO NANTA DE

PUESTA ALTERNATIVA

Miércoles
28 de mayo

Programa Layer Longevity

rliva

NANTA

Importancia de la inmunidad en recría ante el reto de ciclos largos

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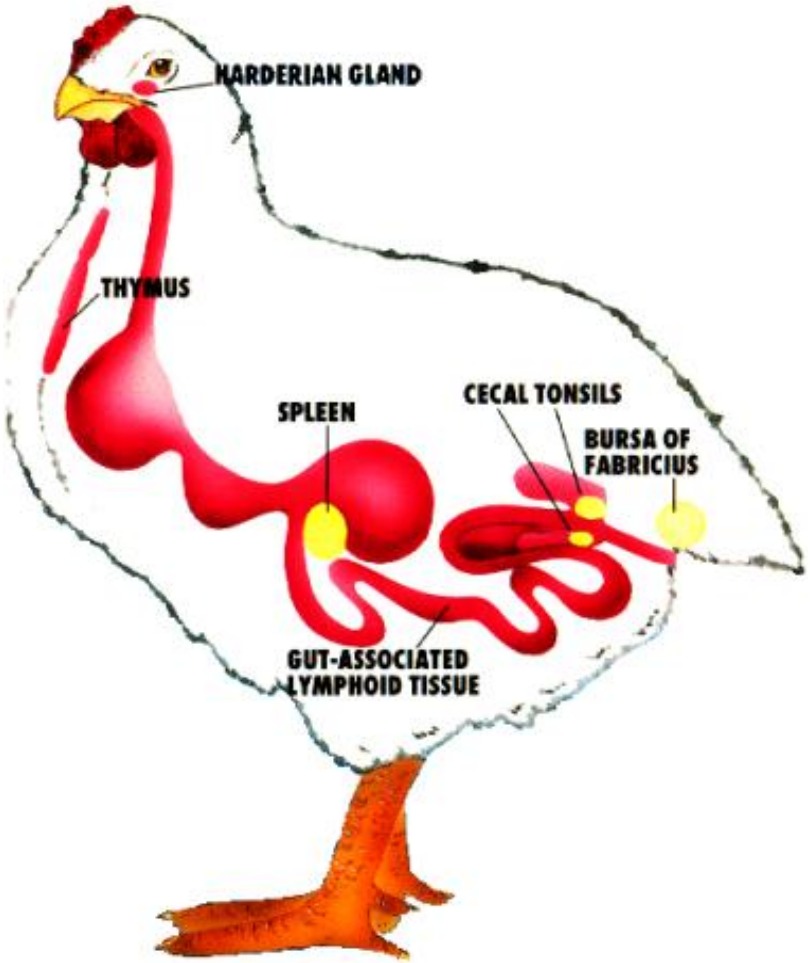
Veterinary Health Consultant - Poultry Friendly

Agenda

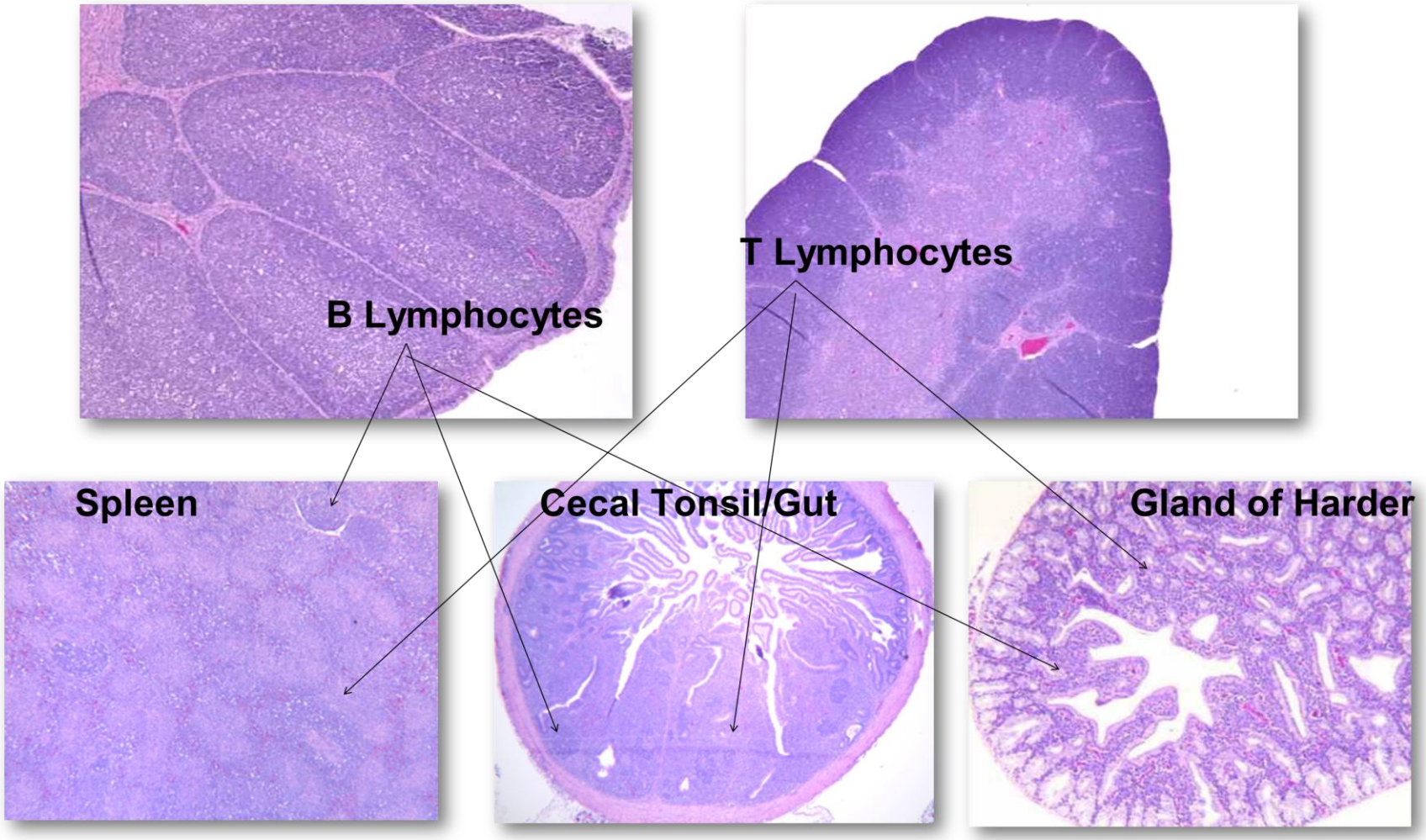
- The avian immune system and immunomodulation
- Immunosuppression
- Control of immunosuppressive infections
- Live IBD vs vector HVT-IBD vaccines
- Benefits of vector HVT vaccines

The Avian Immune System

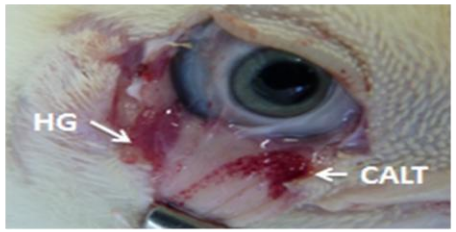


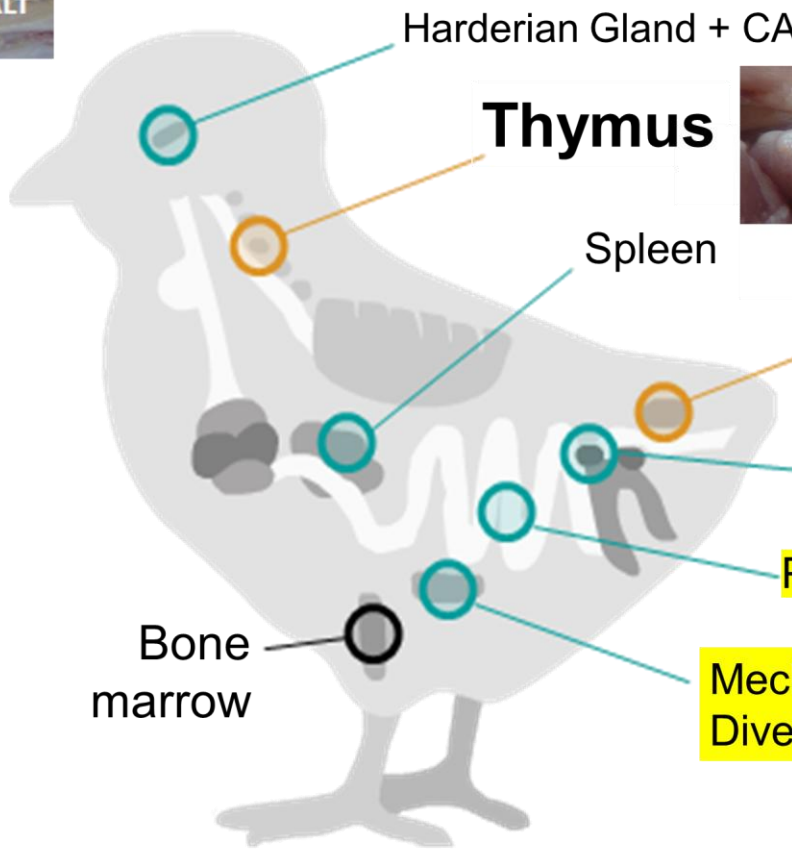
Bursa and Thymus: First 3-4 Weeks

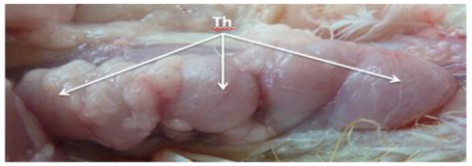
Primary Lymphoid Organs Seed Secondary Organs

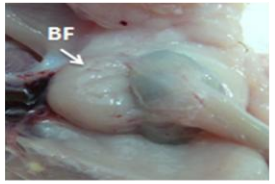


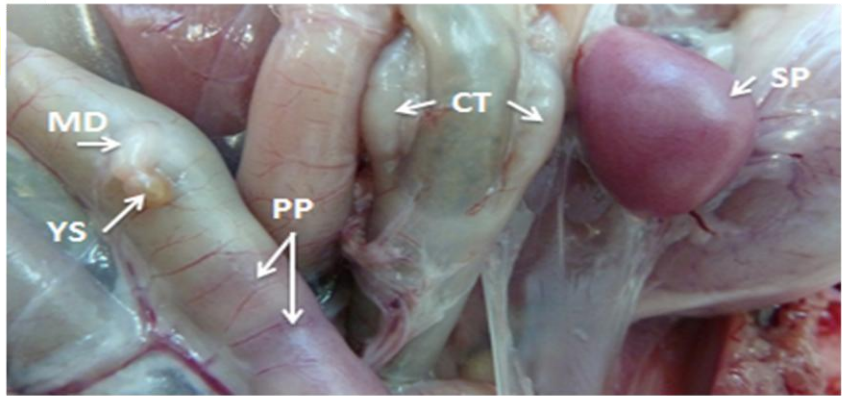
Avian Lymphoid Organs & Tissues







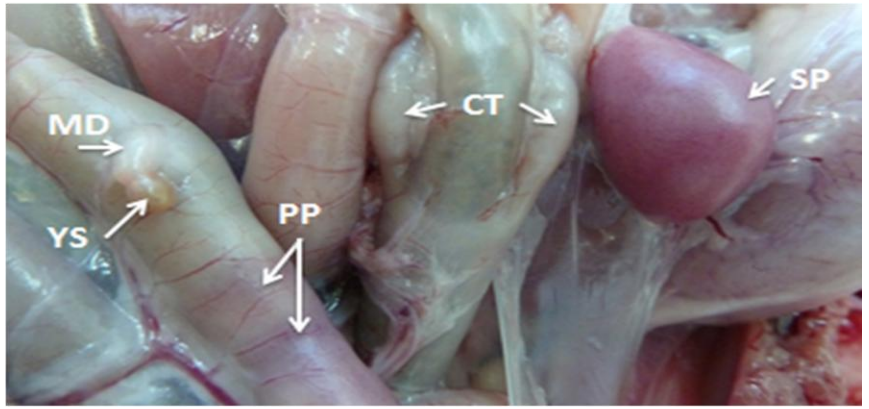




GALT = Gut Associated Lymphoid Tissues

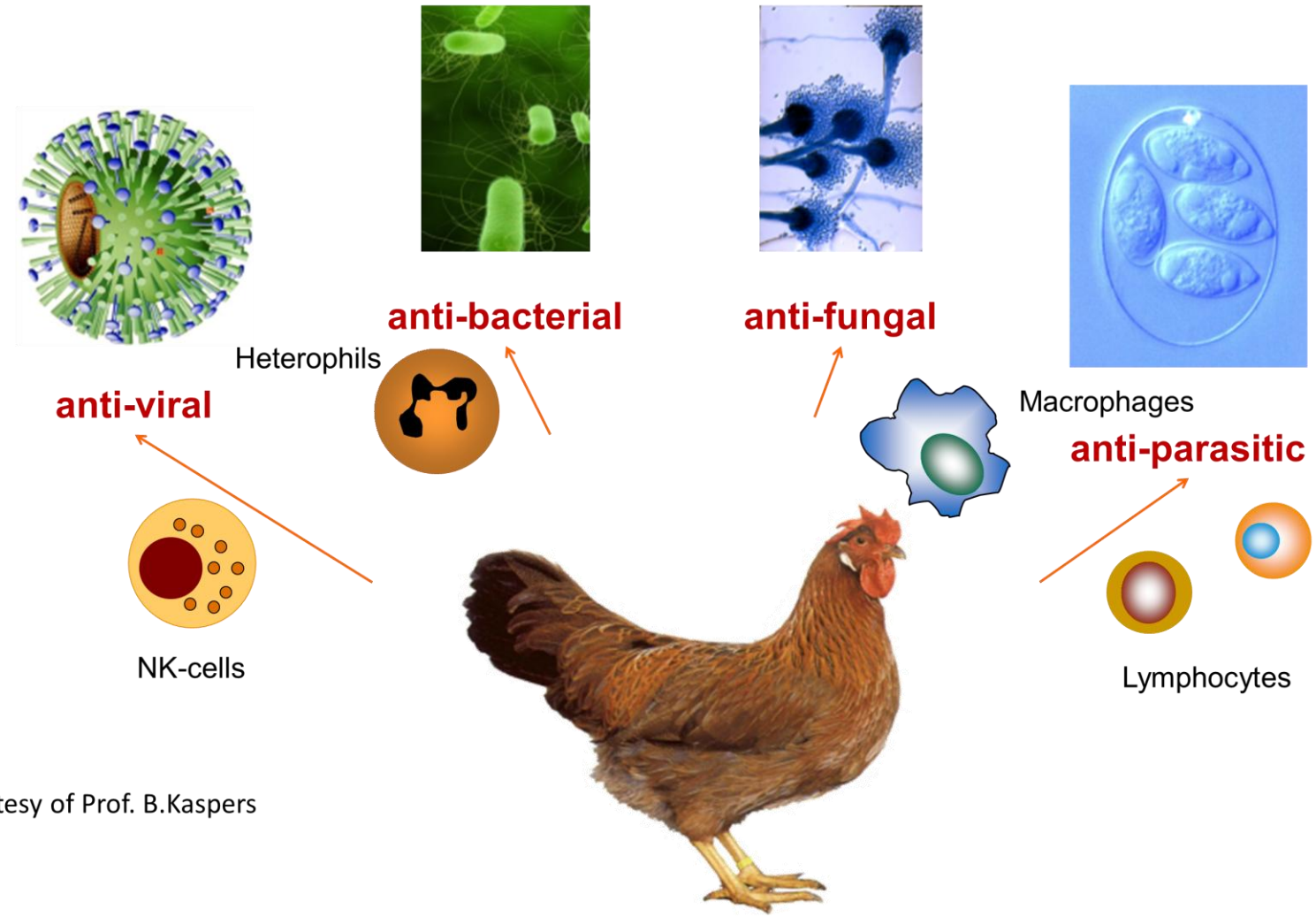
Gut Immune Compartments - GALT

- **GALT comprise more immune cells than any other tissue**
- Lymphoid aggregates located within the lamina propria of all Gut
- Lymphoid follicles in Proventriculus and Gizzard
- Meckel's diverticulum (MD)
- Peyer's petches (PP) throughout the Gut
- Cecal tonsils (CT)



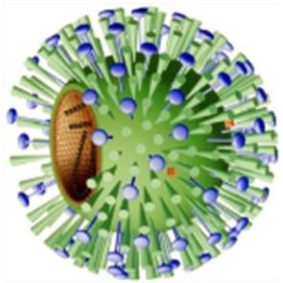
Avian Immunology – 2nd Edition

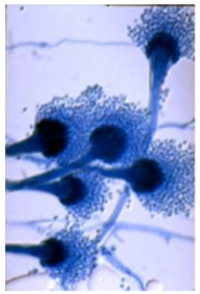
Cells of the Immune System

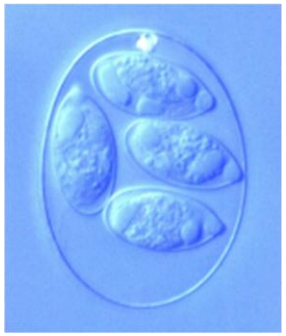


Courtesy of Prof. B.Kaspers

Soluble factors







anti-viral

anti-bacterial

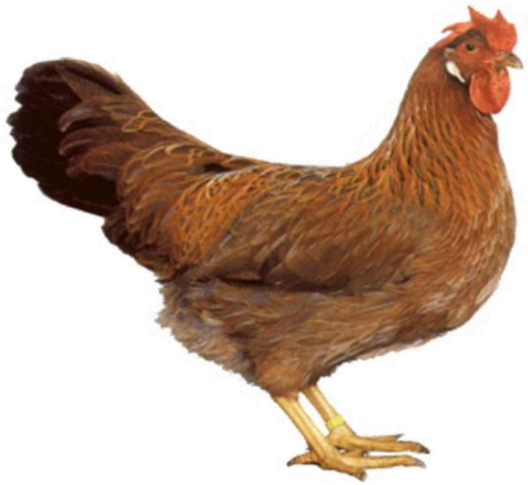
anti-fungal

anti-parasitic

anti- microbial peptides

Interferon

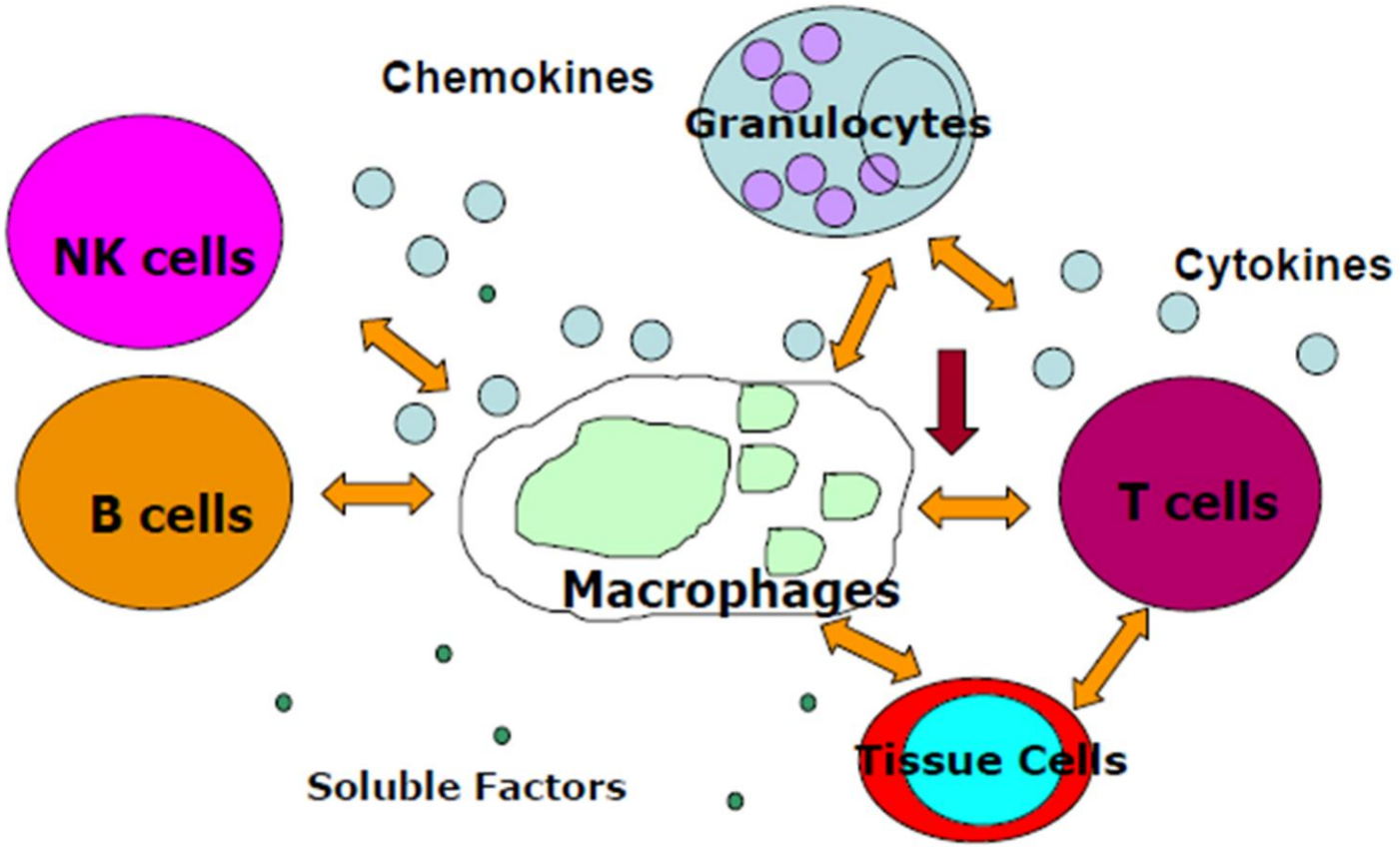
antibodies



Courtesy of Prof. B.Kaspers

The immune cell “orchestra”

(simplified – Prof. S. Rautenschlein)



Immune Response

Infection or Vaccination

Penetration

Pathogen-Antigen

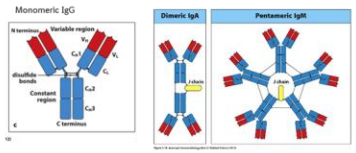
APC

T helper cells

T helper 1

T helper 2

B cell
humoral immune response

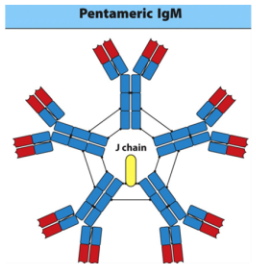


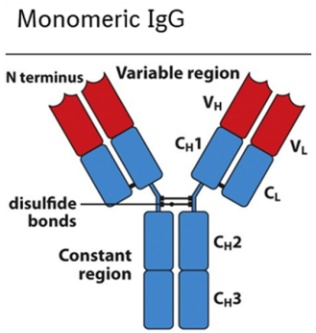
cytotoxic T cell
cellular immune response

immune memory

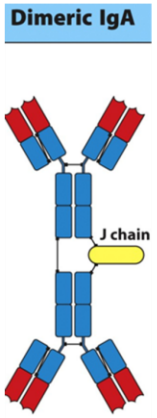
pathogen

Immunity

- **Humoral:**
  - **Systemic**: **IgM** 

and **IgY** 

  - **Local - mucosal**:
    - **IgA** produced locally in Gut, Respiratory tract, Conjunctiva
    - Transudation of **IgY** from blood



- **Cellular (cell-mediated): cytotoxic T lymphocytes**

Immunity

- **Infections mostly controlled by:**
  - **Cell-mediated immunity:** Marek's Disease, Pox, *Salmonella Gallinarum, etc.*
  - **Systemic immunity**: Gumboro D., Chicken Anemia, Encephalomyelitis, EDS, etc.
  - **Local - mucosal**: Mycoplasmas, Inf. Coryza,
  - **"Mixed"**: Newcastle D., Influenza, Inf. Bronchitis, ART, ILT, Salmonella, etc.

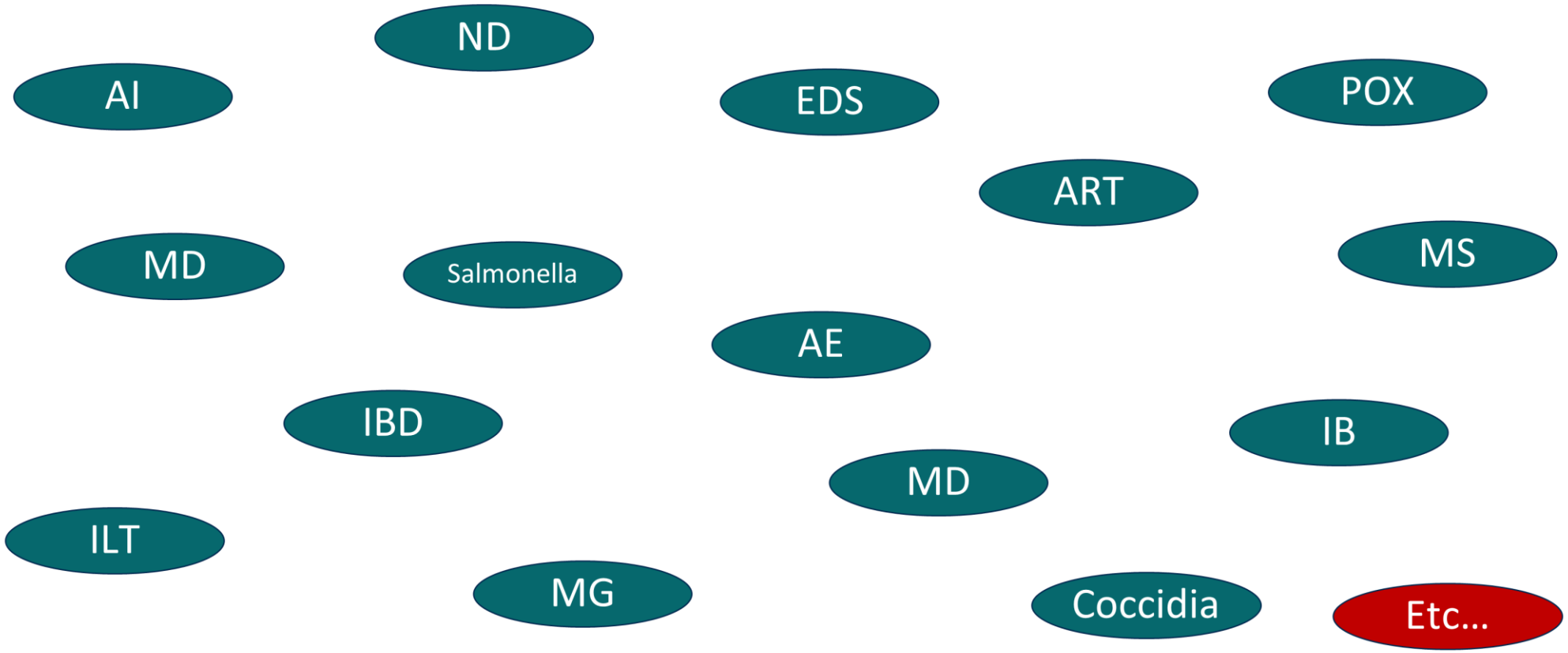
Key Role of Gut Immunity

- The gut is a major site of entry, development, passage and residence for many pathogenic and non-pathogenic microorganisms

- An effective immune capability in the gut is essential to combat many pathogenic microorganisms variously linked to this tissue

Avian Immunology – 3rd Edition

Exposure of Pullets' Immune System



Immune System in Pullets

- Development before sexual maturity
- Coincides with the rearing period
  - Numerous vaccinations scheduled within 15 weeks
  - Various possible natural infections
  - Impact on health and performance up to **more than 100 weeks**
- **Crucial to be “prepared” within 15-20 weeks of age**

Immunomodulation

- “Rebalancing of the Immune System, with some effector mechanisms increasing and other decreasing”.

Avian Immunology – 2nd Edition

Factors Modulating the Aviav Immune System

Type of regulation					
HORMONES		**PHISIOLOGICAL STATES**		**DIETARY EFFECTS**	

STRESS HORMONES	• Glucocorticoids
	• Adrenaline
	• Dopamine
		STRESS	• Temperature:
			  • Heat stress
			  • Cold stress
			• Air quality
			• Sanitation
			• Stocking density
				CRITICAL NUTRIENTS	Zinc, Essential AAs. Vitamins, Minerals

				IMMUNOMODULATORY NUTRIENTS	PUFA, Vit. A-D-E-C, Carotenoids, Phytonutrients
SEX HORMONES	• Androgens • Estrogens			**TOXIC SUBSTANCES**	Lead, Mercury, Pesticides, Mycotoxins
METABOLIC HORMONES	• Thyroxin • GH • Leptin			**MYCOTOXINS**	Aflatoxins, Ochratoxins, T-2, Fumonisin, DON
INTERACTIONS BETWEEN FACTORS!!!					

Avian Immunology – 2nd Edition

Immunosuppression

- “A state of temporary or permanent dysfunction of the immune response, resulting from damage to the immune system and leading to increased susceptibility to disease” (Dohms & Saif, 1984)
- Impairment of the normal immune response due to **infectious** and **non-infectious** causes
- A reduction of the activation or efficacy of the immune system

Consequences

- Deficient immune responses to infections and vaccinations
- Abnormal vaccination reactions
- Secondary infections (Bacteria, Coccidia, Fungi)
- Reduced performance
- Increased condemnation rate

Diseases Associated with Immunosuppression

- Respiratory diseases
- E.coli
- Stafylococcus
- Aspergillosis
- Coccidiosis
- Etc…

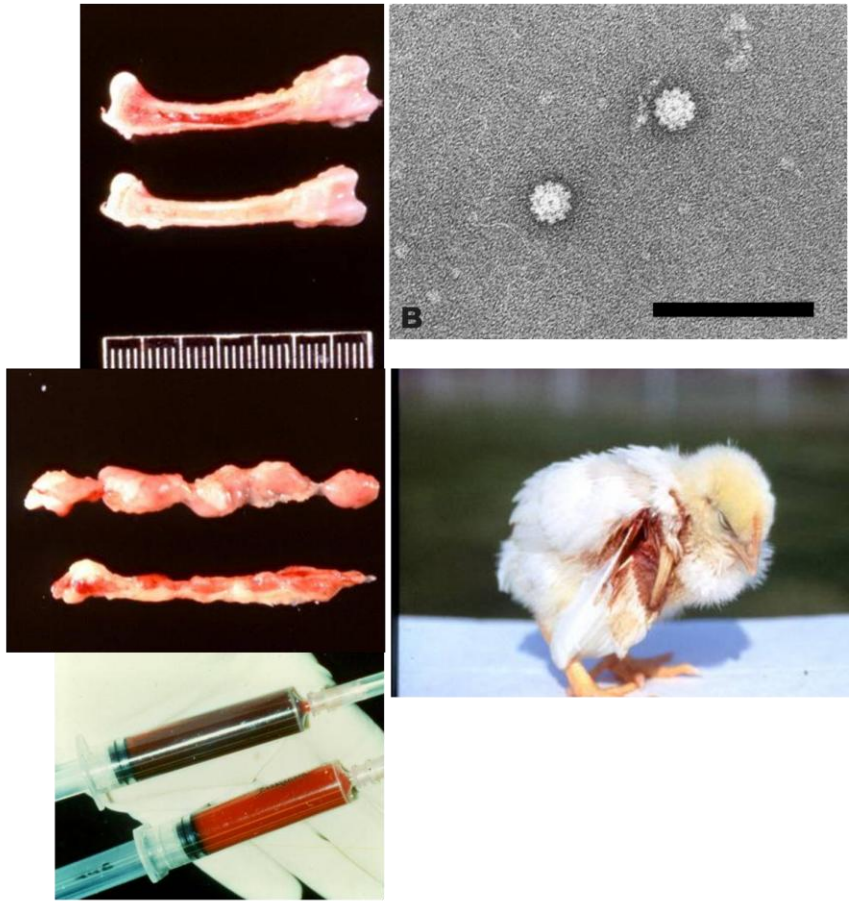
Agents Inducing Lymphoid Atrophy

ATROPHY (histology)			
TISSUE / AGENT	Bursa of Fabricius	Thymus	GALT
CIAV	+	+	+
MDV	+	+	+
IBDV	+	+	+
Reovirus	+	+	+
REV - ALV	+	+	+
NDV	+		+
Mycoplasma	+	+	+
Ammonia	+		+
Mycotoxins	+	+	+
Heat stress		+	+

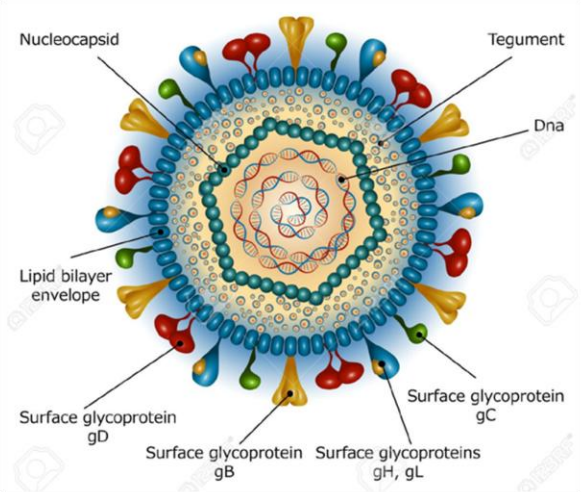
CIAV Immunosuppression

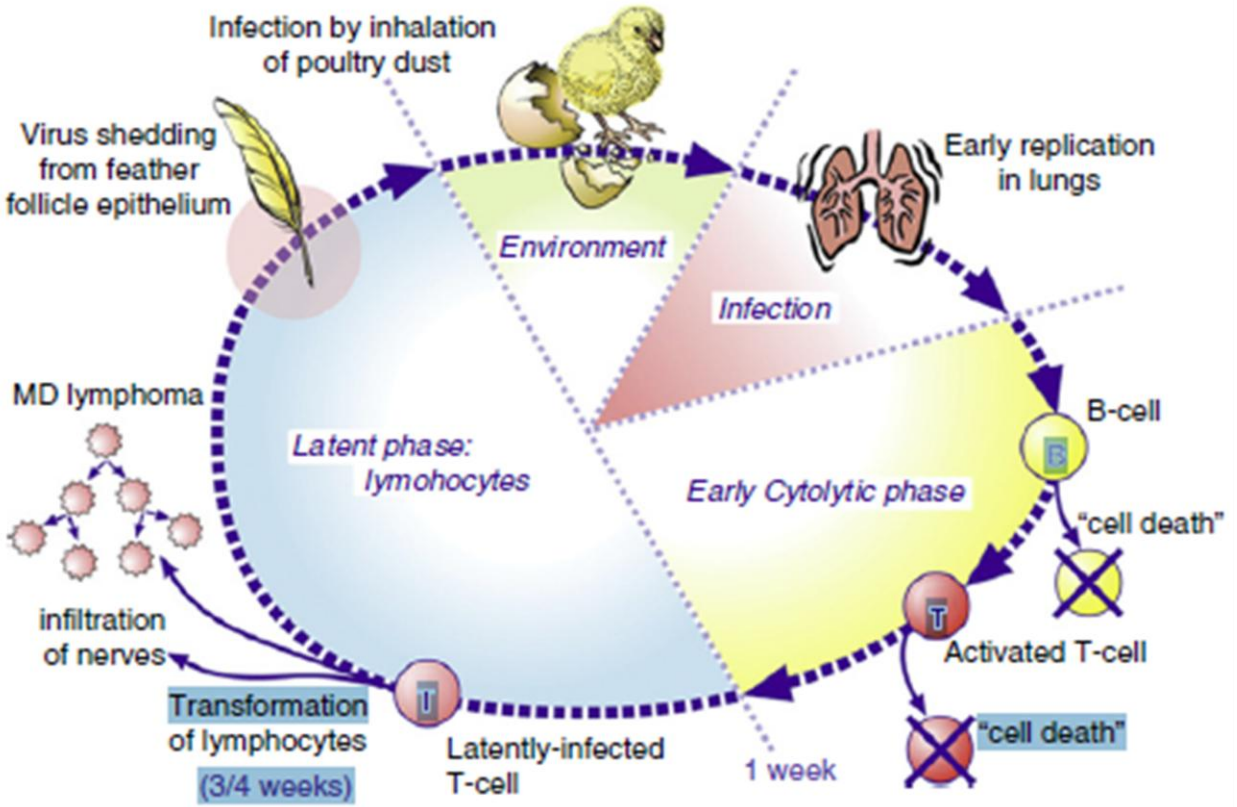
In young chickens lacking Maternal Abs:

- Infection of hemocytoblasts
- Bone marrow atrophy
- Depletion of T lymphocytes
- Decline in red cells and thrombocytes

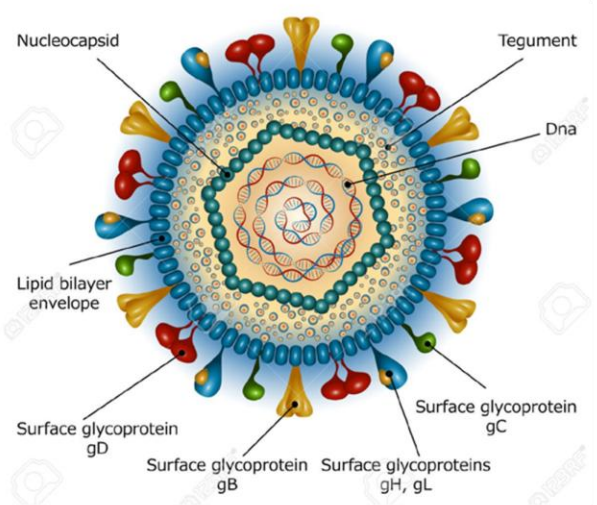


MDV Pathogenesis





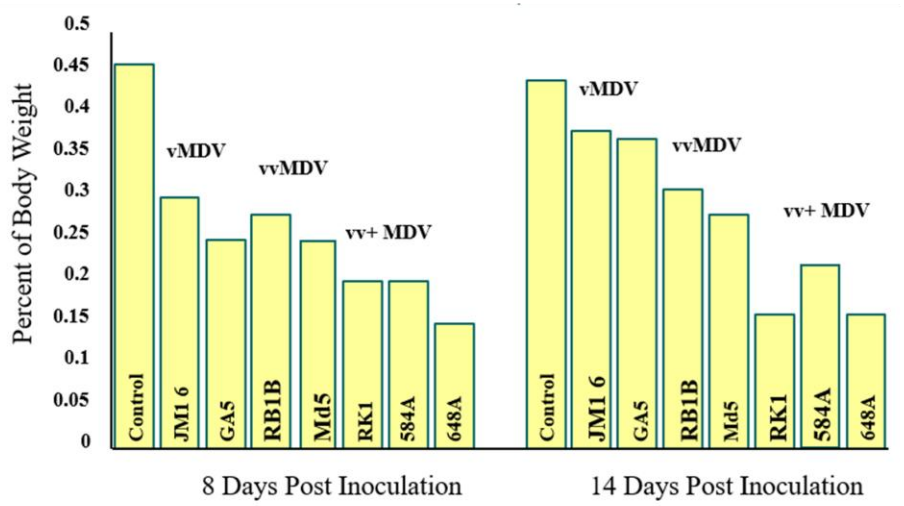
MDV impact on the Immune System

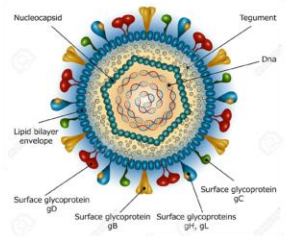


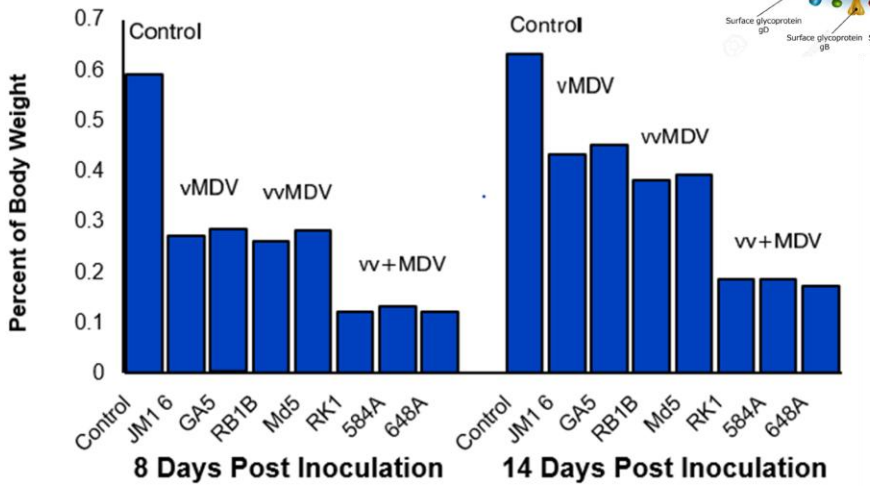
- Lymphoid organ atrophy in acute MD in chicks
- Immunosuppression

MDV impact on the Immune System

- Transient acute cytolytic atrophy in lymphoid organs:

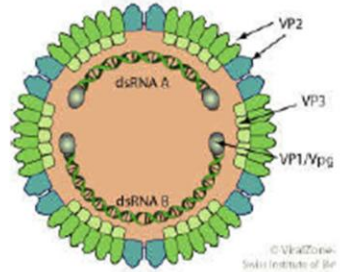






B.W. Calnek et al.

IBDV Immunosuppression



- Primarily directed against **B**-lymphocytes → death / depletion
- 3 - 8 weeks → B cell proliferation at maximum level in the Bursa
- Humoral immunity specifically depressed

Control of Immunosuppressive Infections

- Immunosuppressive infections mainly affect the first weeks of chickens' life

- Vaccinations are concentrated during the first 15-20 weeks

- Production cycles keep getting longer

Control of Immunosuppressive Infections

- **Vaccination:**
  - CIA
  - MD
  - IBD
- **Maternal derived antibodies:**
  - CIA
  - IBD

CIAV Vaccination

- Live attenuated vaccines in Breeders:

A. 1 dose at 10-12 weeks

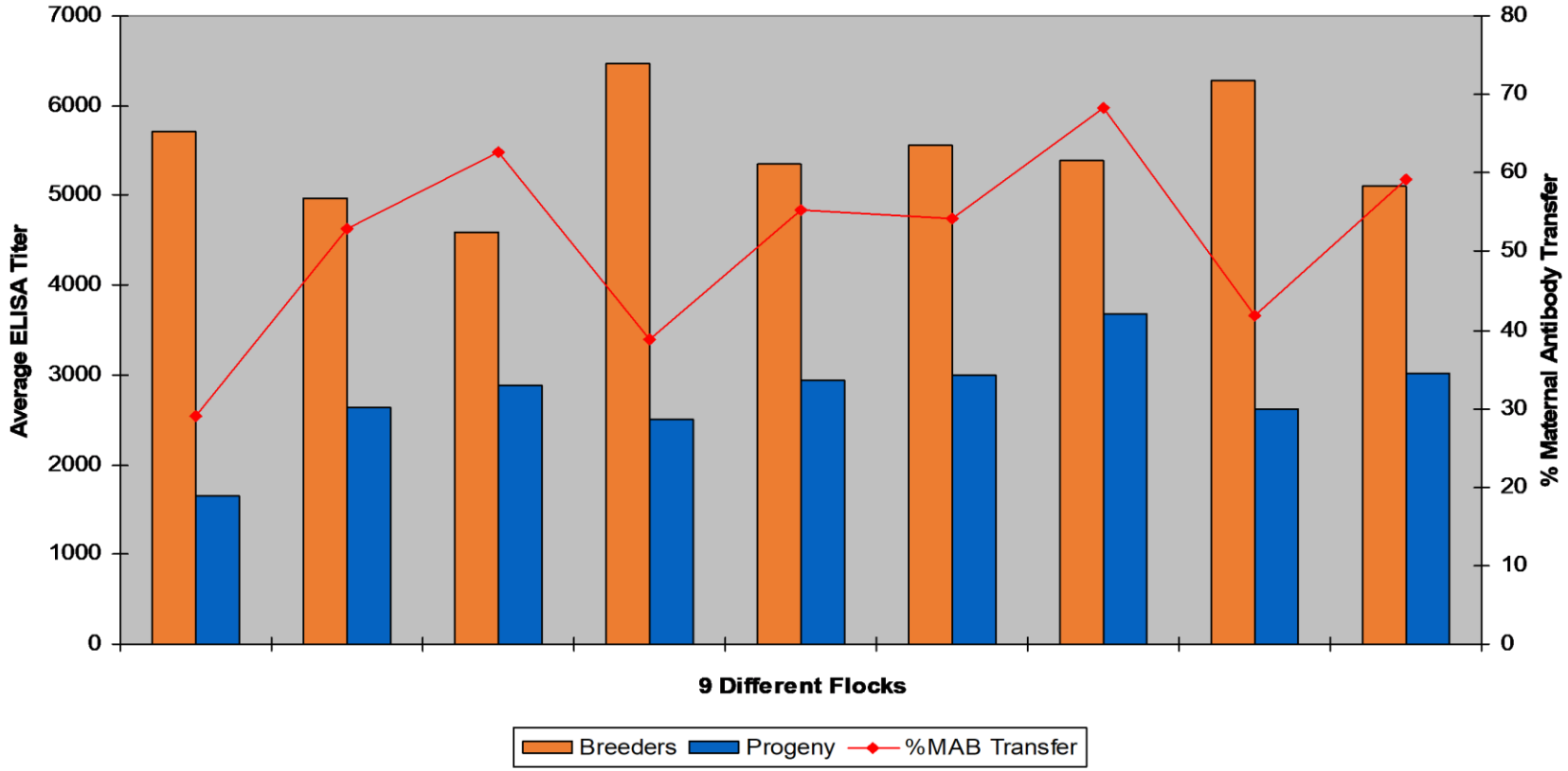
B. 1 dose at 6-7 weeks + 1 dose at 10-12 weeks

→ **ANTIBODIES**:

- In **breeders**: stop vertical transmission
- In **progeny**: MDA protect from virus challenge

CIAV Serology

MAB Transfer - Average Titers for Broiler Breeders and Progeny



MDV Vaccination

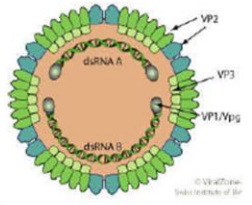
- Modified live vaccines
- Strongly cell-associated → liquid nitrogen storage
- Serotypes: 1 or 2 or 3 or combinations
- Hatchery *in-ovo* or s.c. injection

IBDV Vaccination

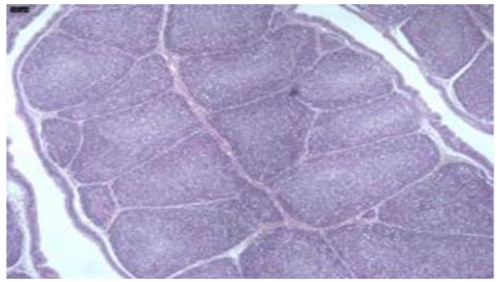
- Live attenuated vaccines:
  I. “Classic”
  II. Immunocomplex
- Recombinant vector HVT-IBD vaccines
- Inactivated vaccines

Live Iinfectious Bursal Disease
vs
Vector HVT-IBD Vaccines

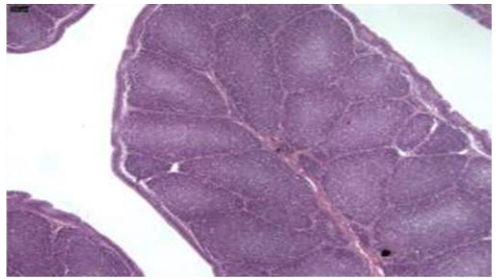
Live IBD Vaccines - Drawbacks



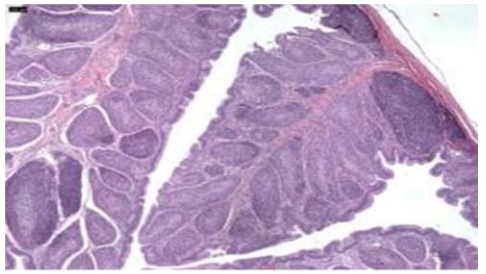
- Interference from MDA → delayed protection
- Possible in vivo **MUTATIONS** and **REASSORTMENTS** with field IBDVs
- **Replication in B lymphocytes → immunosuppression**



Unvaccinated Controls



vHVT-IBD



Live IBD Int. plus

Effect of a live IBD vaccine on *S.Enteritidis* infected chickens

Vaccine 35 (2017) 3682–3689

Contents lists available at ScienceDirect

Vaccine

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

Effect of infectious bursal disease (IBD) vaccine on *Salmonella* Enteritidis infected chickens

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Effect of a live IBD vaccine on *S.Enteritidis* infected chickens

White Hy-Line commercial pullets

- G.1: Negative controls
- G.2: **IBD Int. Plus vaccine** at 12 days
- G.3: **IBD Int. Plus vaccine** at 12 days + ***S.Enteritidis*** at 13 days
- G.4: ***S.Enteritidis*** at 13 days

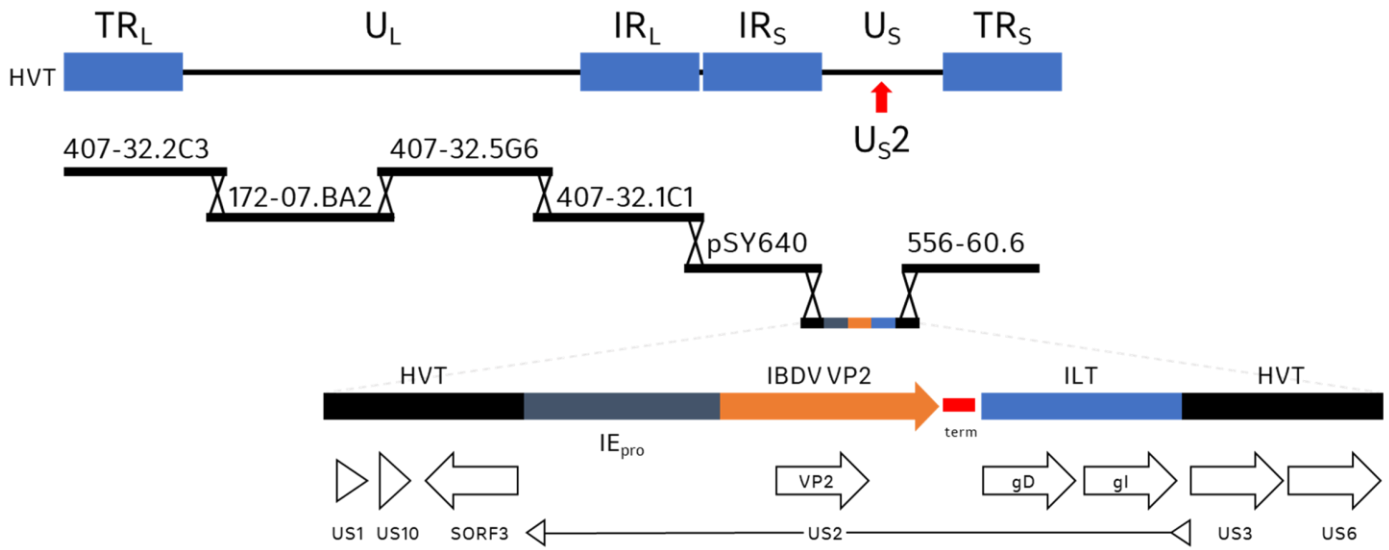
Results

S.E. + live IBD vaccine vs S.E.

- Higher mortality rate → **10%** vs **2.5%**
- Lower anti-SE Ab titres (IgA) in Sera and Gut
- Higher SE fecal shedding and organ colonization
- Lower B/BW ratio → **1.3** vs **3.9**
- Higher bursa lesion score → **3.0** vs **0.0**

vHVT-IBD Vaccines

- Construction:
  - **Vector** – HVT
  - **IBDV insert** – **VP2** gene
  - **Other inserts: ND / ILT / AI**



vHVT-IBD Vaccines - Advantages

- No interference from MDA → earlier protection
- No risks of IBDV mutations or reassortments
- **No depletion of B lymphocytes → immune system preserved**
- **Marek's Disease protection**

Commercial Pullets

AVIAN PATHOLOGY, 2016
VOL. 45, NO. 1, 114–125
http://dx.doi.org/10.1080/03079457.2015.1127891

Taylor & Francis
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ORIGINAL ARTICLE

Comparison of infectious bursal disease live vaccines and a HVT-IBD vector vaccine and their effects on the immune system of commercial layer pullets

Francesco Prandini[a], Birgid Simon[b], Arne Jung[c], Manfred Pöppel[d], Stéphane Lemiere[e] and Silke Rautenschlein[c]

vHVT-IBD vs live IBD vaccines

Age - days	CONTROLS	vHVT-IBD	Intermediate	Intermediate Plus
1	Rispens H120 ND live	**vHVT-IBD** Rispens H120 ND live	Rispens H120 ND live	Rispens H120 ND live
14	Live IB variant	Live IB variant	Live IB variant	Live IB variant
21	ND live	ND live	ND live	ND live
28			**IBD Int.**	**IBD Int. plus**
42	Inactivated IB-ND-EDS	Inactivated IB-ND-EDS	Inactivated IB-ND-EDS	Inactivated IB-ND-EDS

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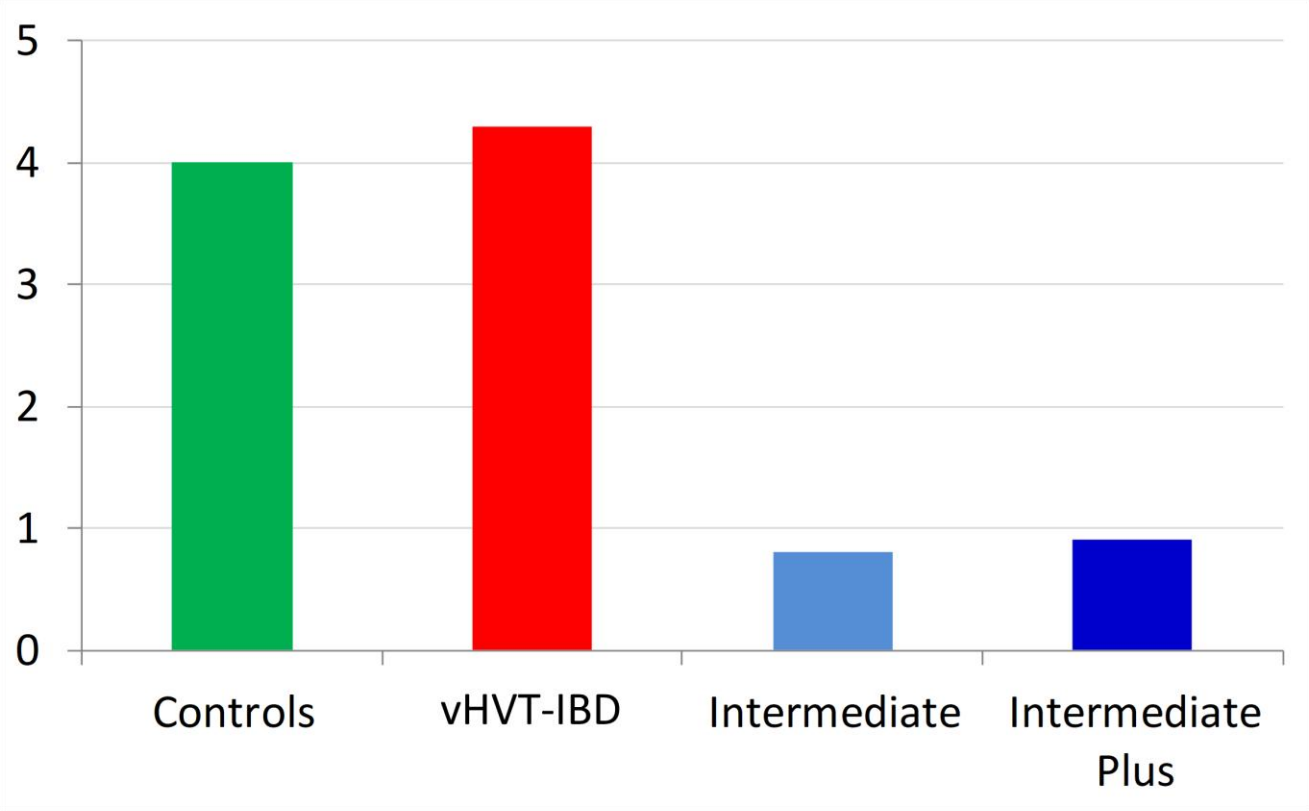
Results

Bursa / body weight ratio post live IBD vaccination

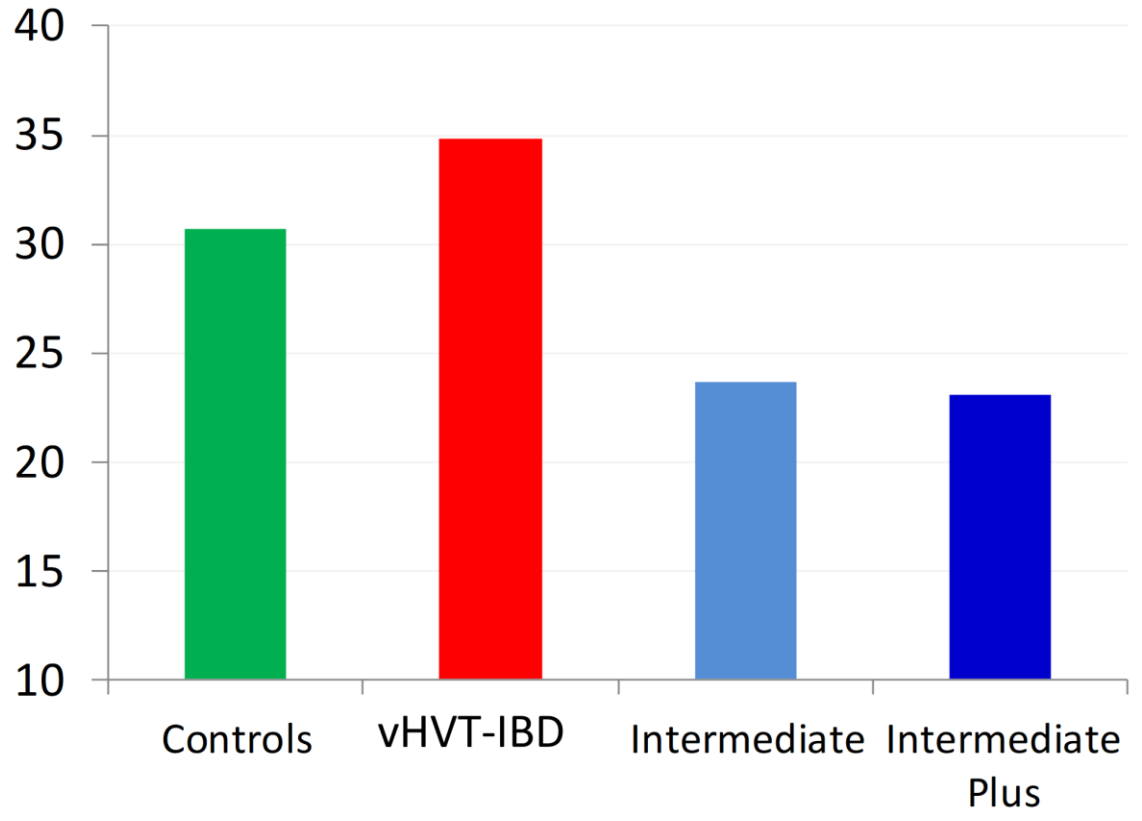


vHVT-IBD vaccine

Live IBD int. vaccine

Results

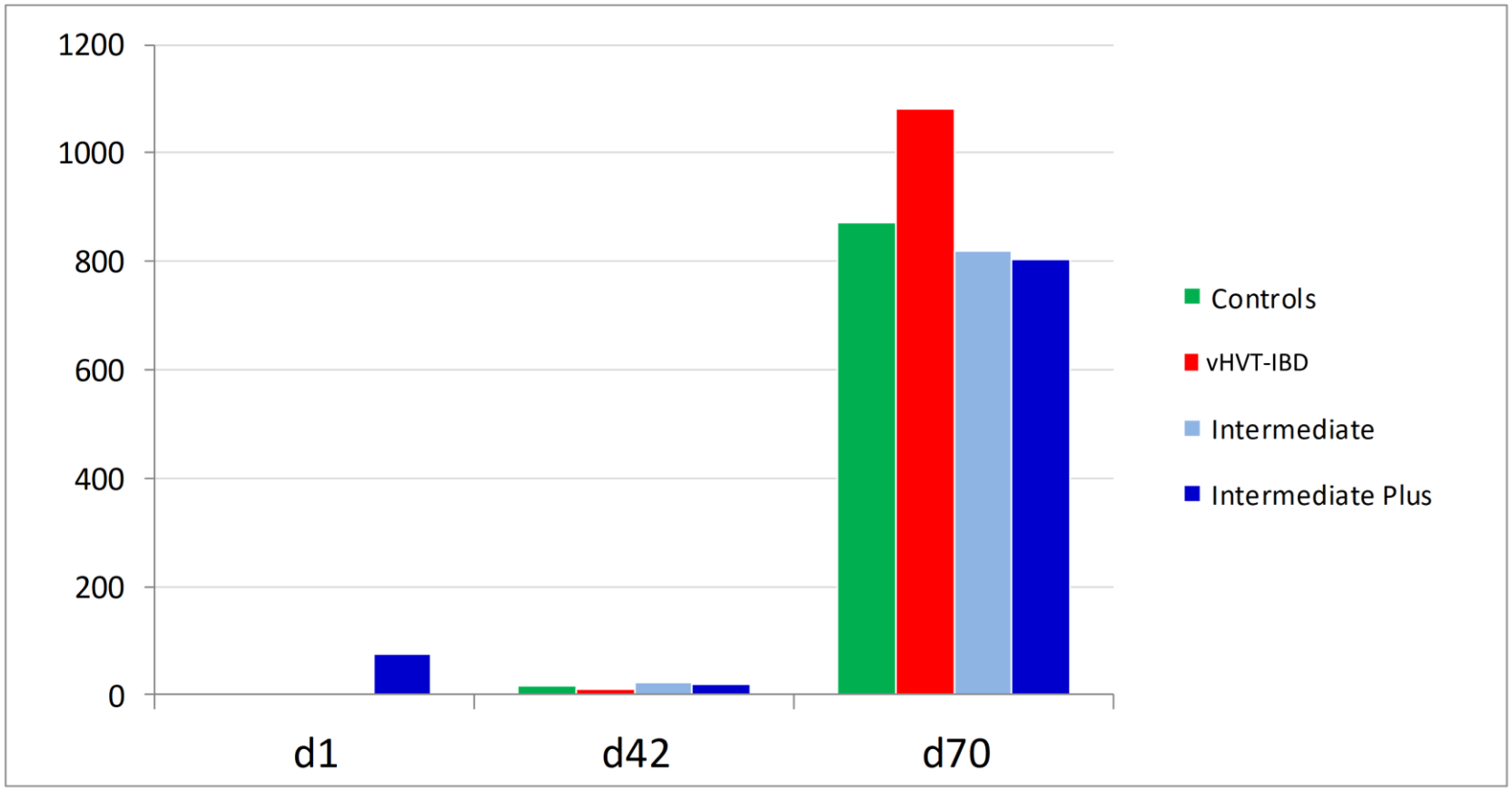
% B lymphocytes / total lymphocytes in the peripheral blood 13 days post-vaccination with live IBD vaccines



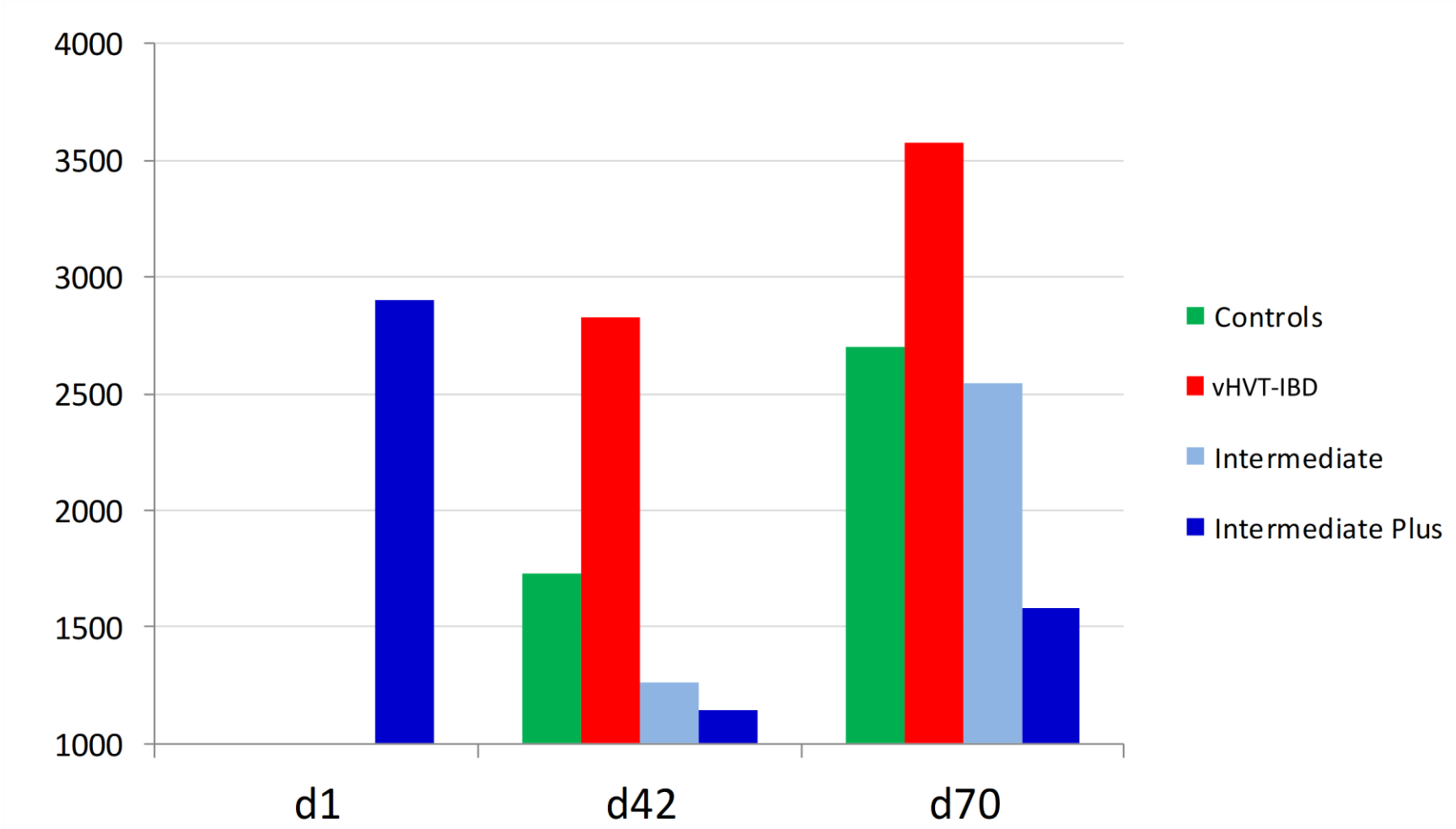
*Indicates significant differences to the other groups ($p < 0.05$)

Results

Mean HI ND antibody levels



Mean ELISA IB antibody levels



Benefits of Vector HVT Vaccines

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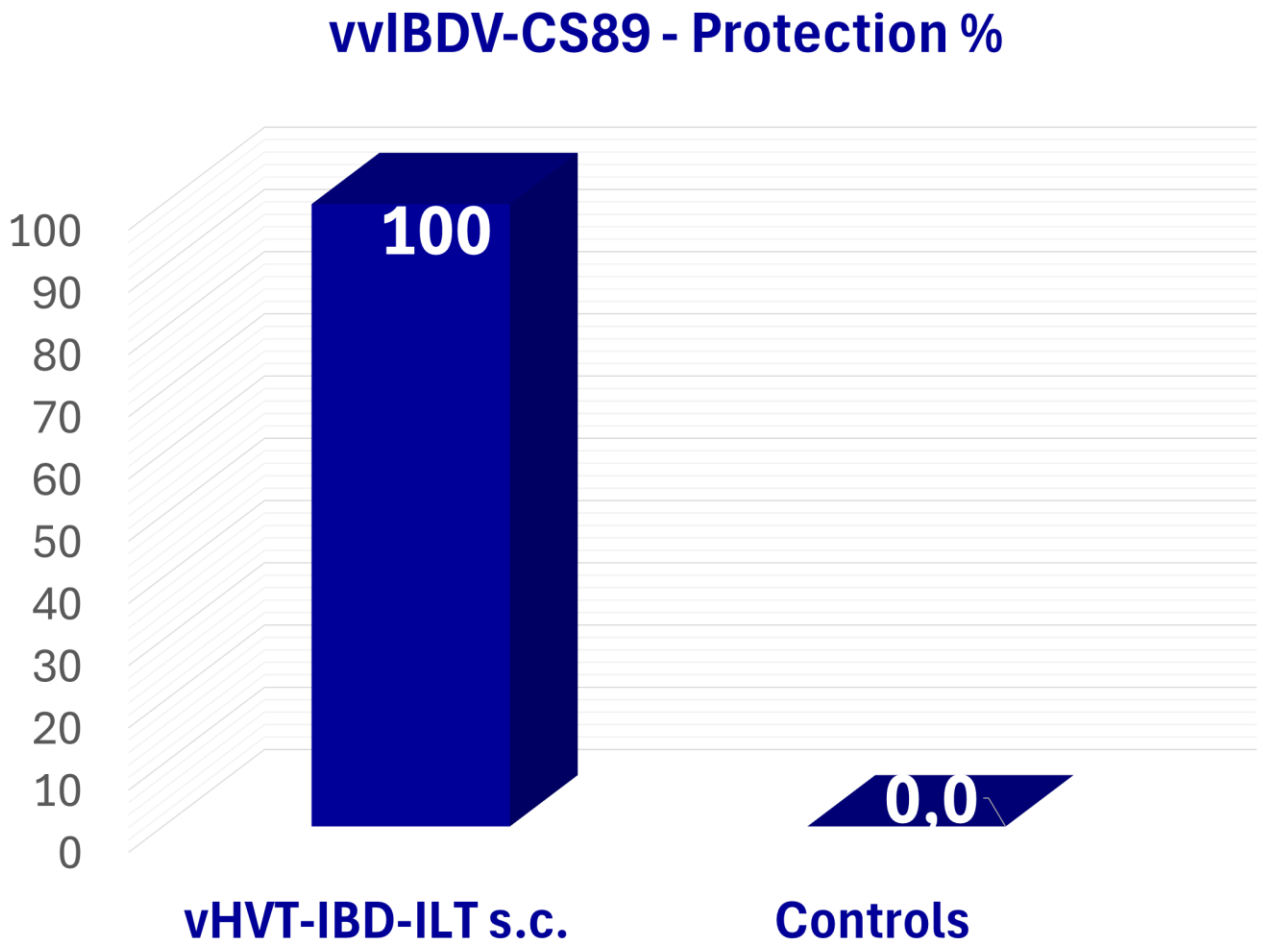
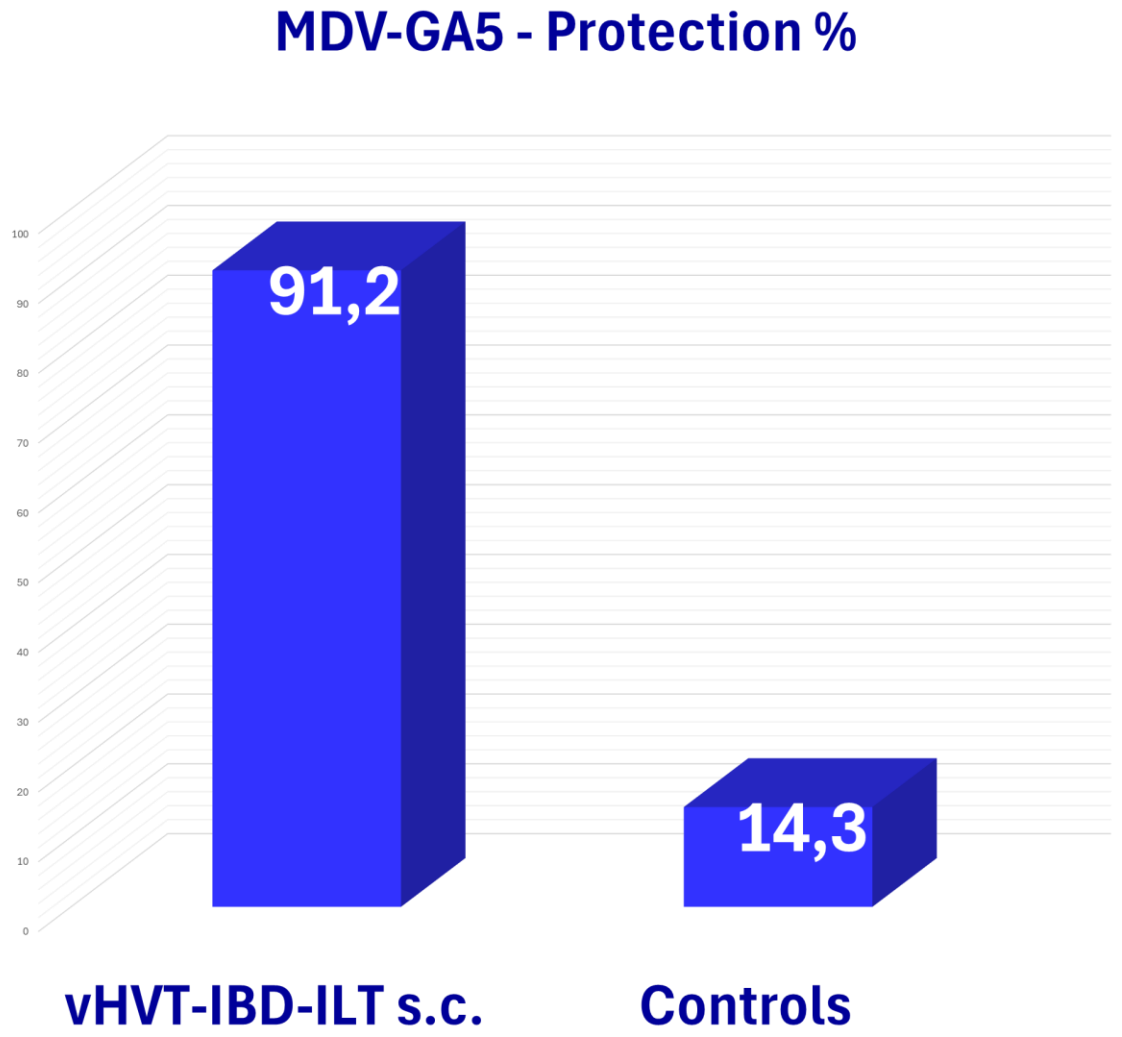
vHVT-IBD-ILT - Efficacy IBD

- SPF
- **vHVT-IBD-ILT** *s.c.*
- vvIBDV-CS89
- Challenge 3 WPV



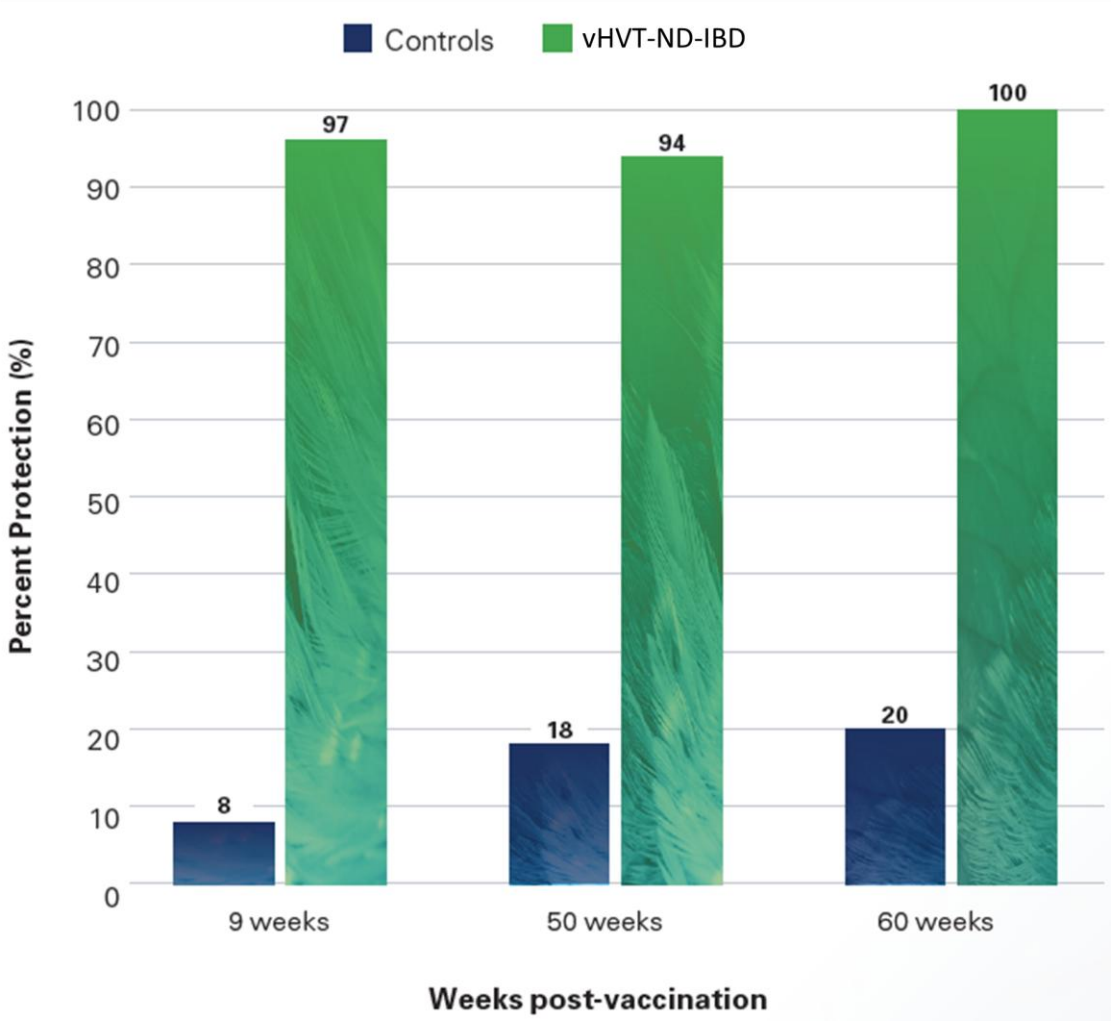
vHVT-IBD-ILT - Efficacy MD

- SPF
- **vHVT-IBD-ILT** *s.c.*
- MDV-GA5
- Challenge 5 DOA



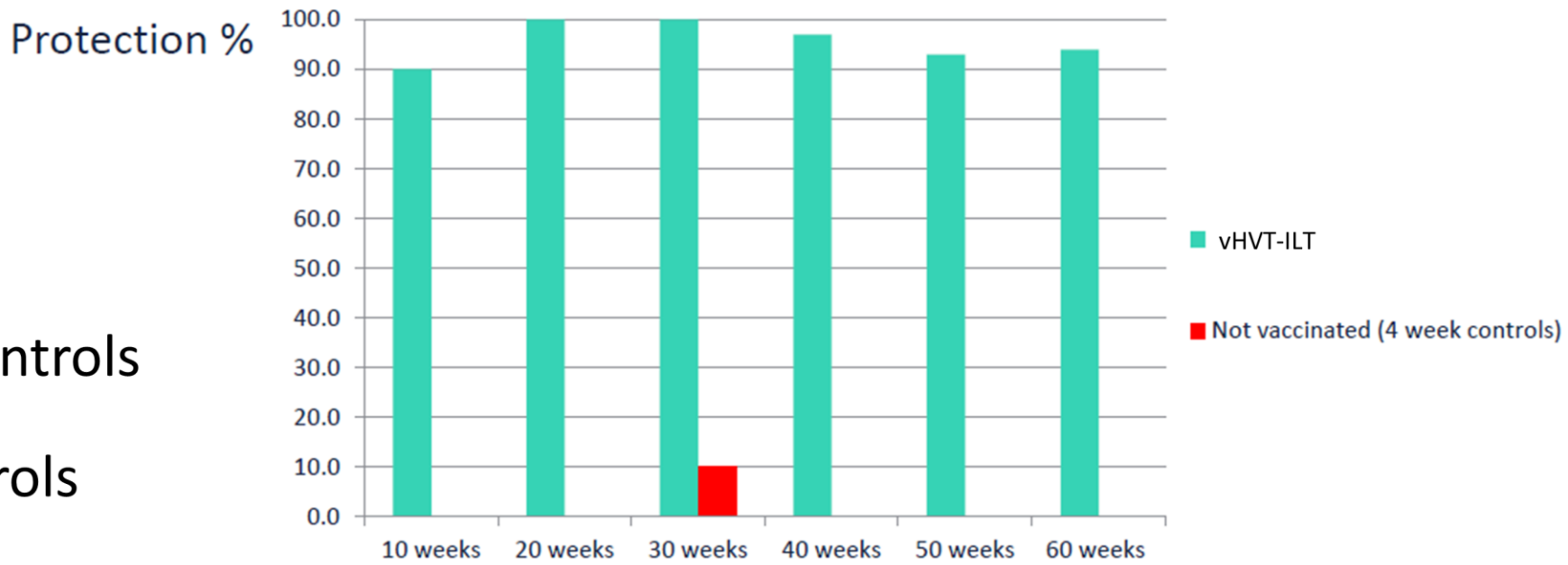
Duration of Immunity - ND

- SPF chickens
- **vHVT-ND-IBD + Rispens** *s.c.*
- NDV Texas GB (10_4EID50) i.m.
- 14 days observation



Duration of Immunity - ILT

- SPF chickens
- **vHVT-ILT** *s.c.*
- ILTV LT 07-03
- Age-matched controls
- 4 week old controls



HVT Accelerates Maturation of Chicken Embryo Immune Responses

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In Ovo Vaccination with Turkey Herpesvirus Hastens Maturation of Chicken Embryo Immune Responses in Specific-Pathogen-Free Chickens

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Vector HVT Vaccines - Key Benefits

- No interference from MDA
- No damage to the immune system
- Multiple protection
- Avoiding or minimizing the use of corresponding live vaccines
- Life-long duration of immunity
- Fitting management of long production cycles

Conclusions

- The immune system is essential to health and performance
- Several infections and other factors can negatively impact it
- Its preservation must begin with parents
- Vector HVT vaccines bring multiple benefits

Gracias