

Vaccines for Humans and Animals

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ABIC - 2007

TYPES OF VACCINES

1. CONVENTIONAL

- Live
- Inactivated

2. GENETICALLY ENGINEERED

- Live
- Live chimeric
- Live replication defective
- Subunit
 - Monovalent vs. chimeric
 - Peptide
 - Plant based vaccines
- Polynucleotide

Models for Disease investigation

Surrogate models

Natural models



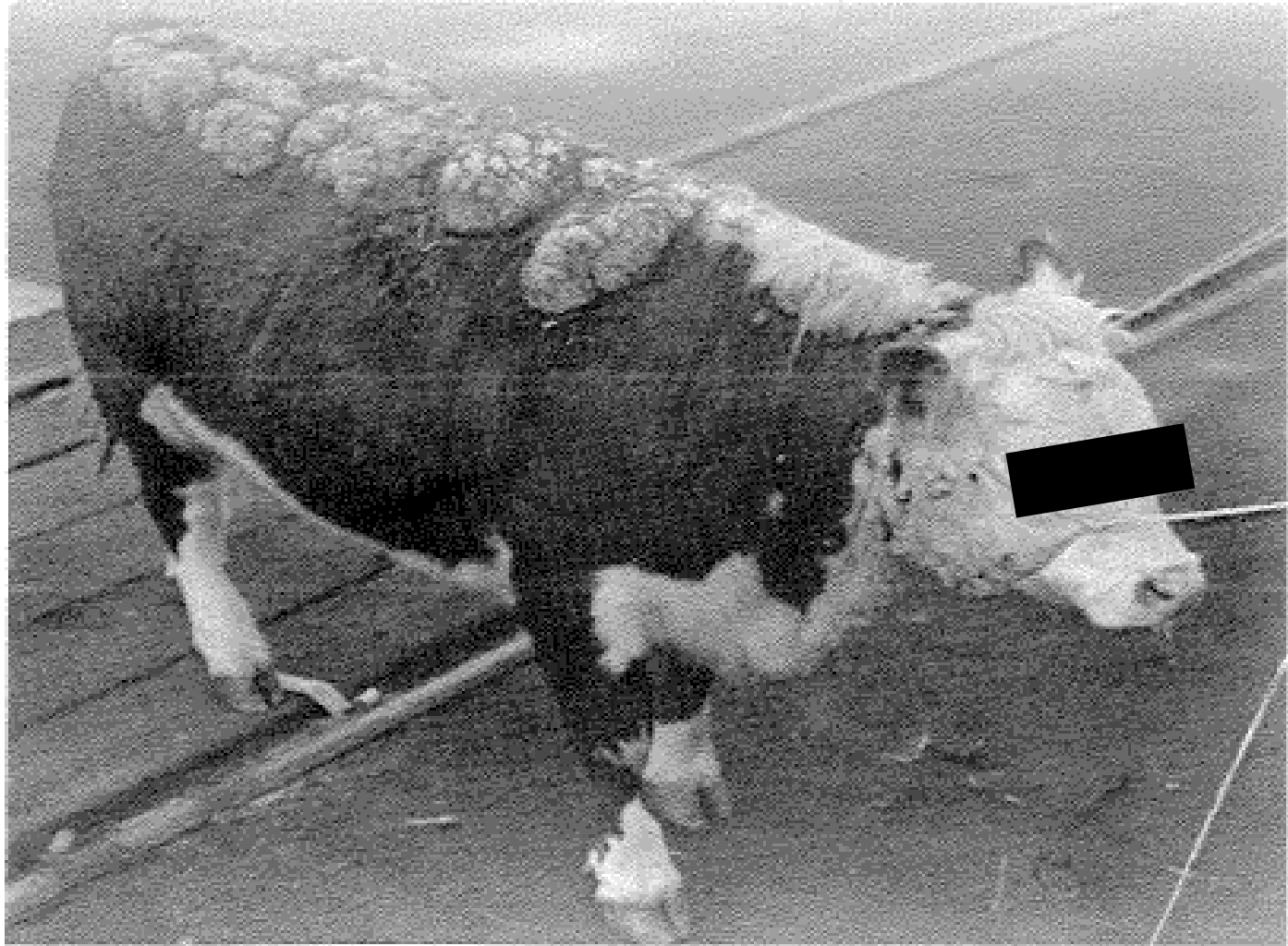
Are Animals perfect
Models of human disease?

Outline

- Papillomavirus
- Herpes virus
- Molecular adjuvants
 - bovine herpes virus
- Food safety vaccines

Papillomavirus

- **Canine Papillomavirus**
- **Bovine Papillomavirus**



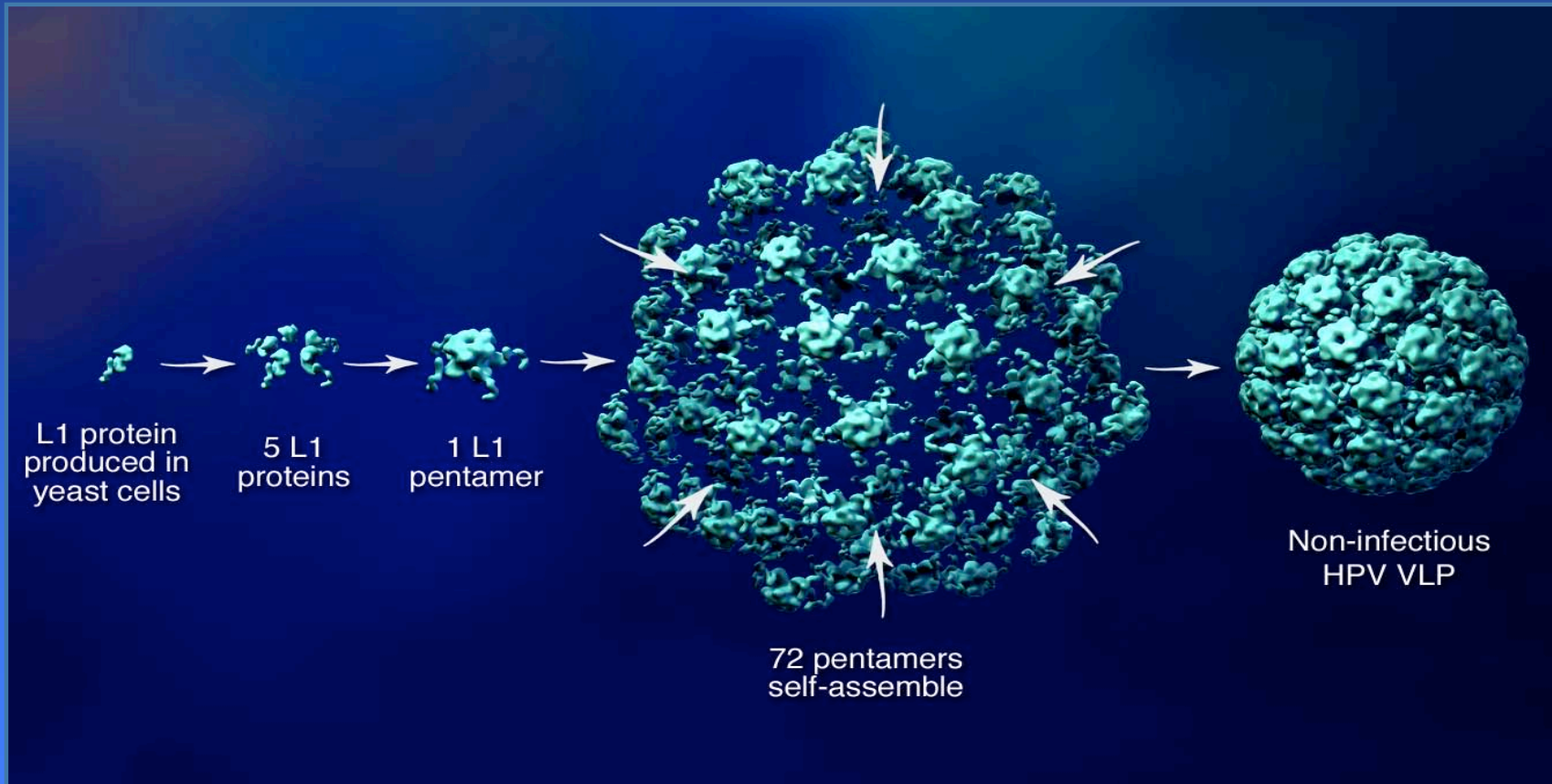
Canine Oral Papilloma Virus



Early vaccines

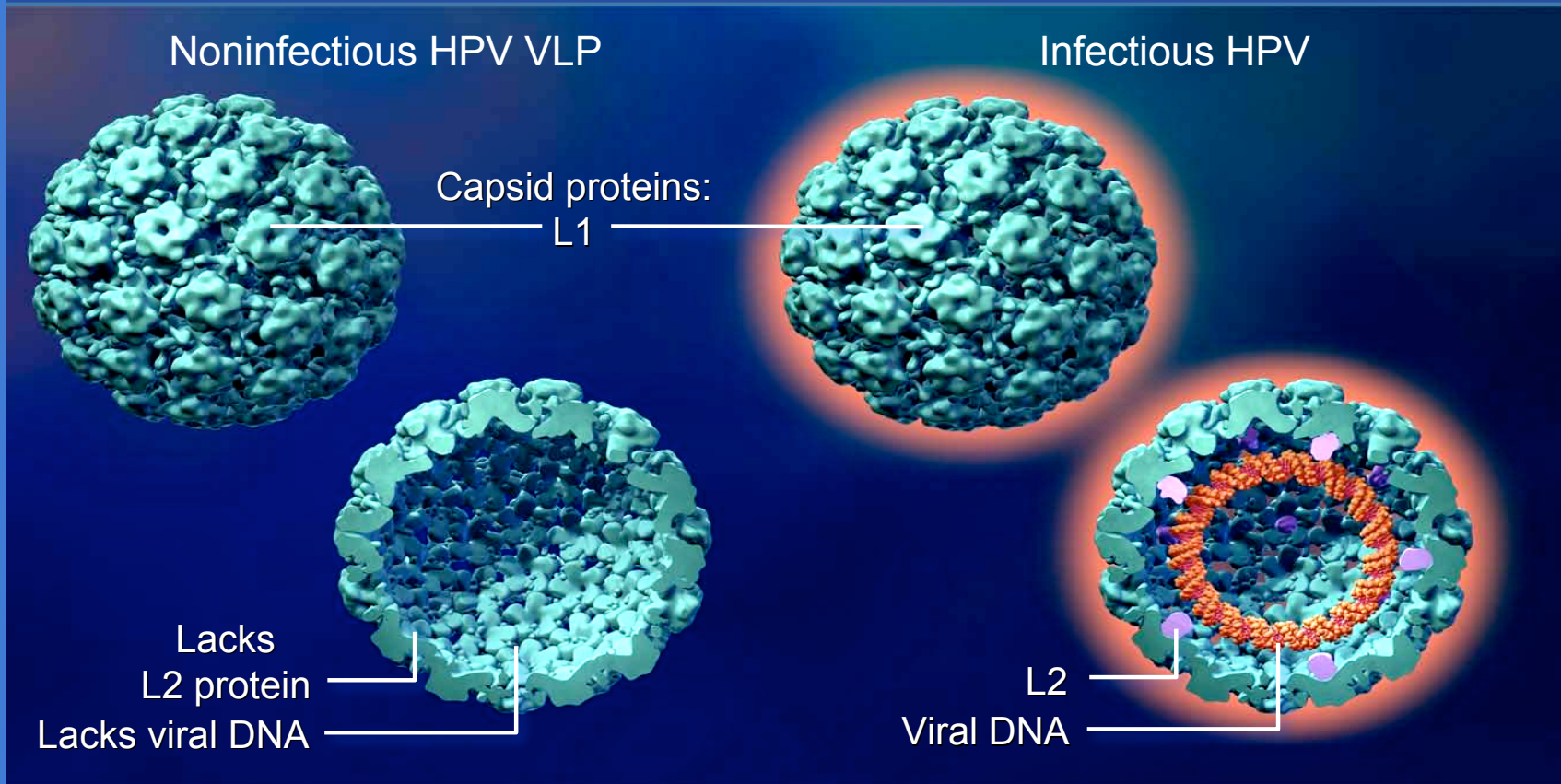
- Formalin fixed wart extract
- Autogenous vaccines

L1 Protein Self-Assembles Into VLPs¹⁻³



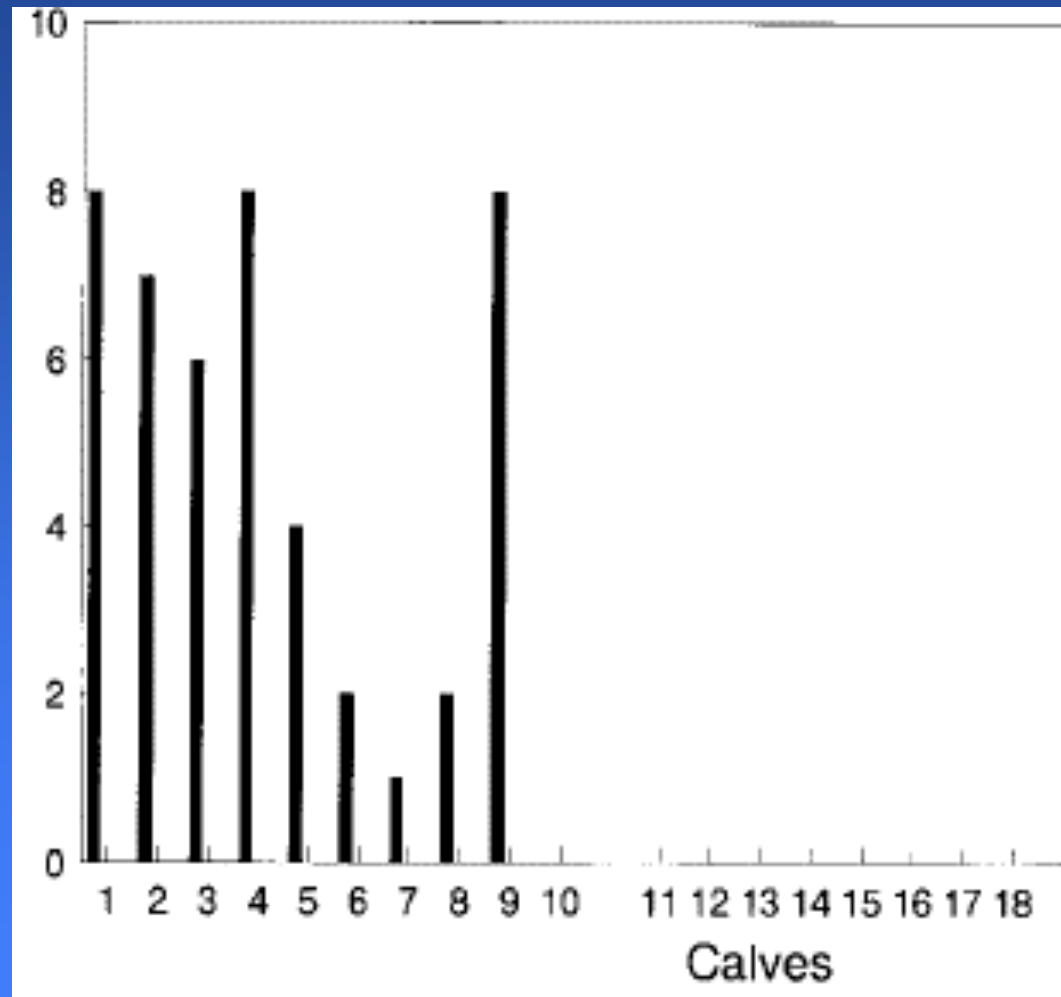
1. Berzofsky JA, et al. *J Clin Invest.* 2004;114:450–462.
2. Kirnbauer R, et al. *Proc Natl Acad Sci USA.* 1992;89:12180–12184.
3. Modis Y, et al. *EMBO J.* 2002;21:4754–4762.

L1 VLPs Mimic the Virion¹⁻⁴



1. Stanley M. *Vaccine*. 2006;24(Suppl 1):S16–22.
2. Berzofsky JA, et al. *J Clin Invest*. 2004;114:450–462.
3. Baker TS, et al. *Biophys J*. 1991;60:1445–1456.
4. Chen XS, et al. *Mol Cell*. 2000;5:557–567.

Protection of cattle with a VLP bovine papilloma vaccine

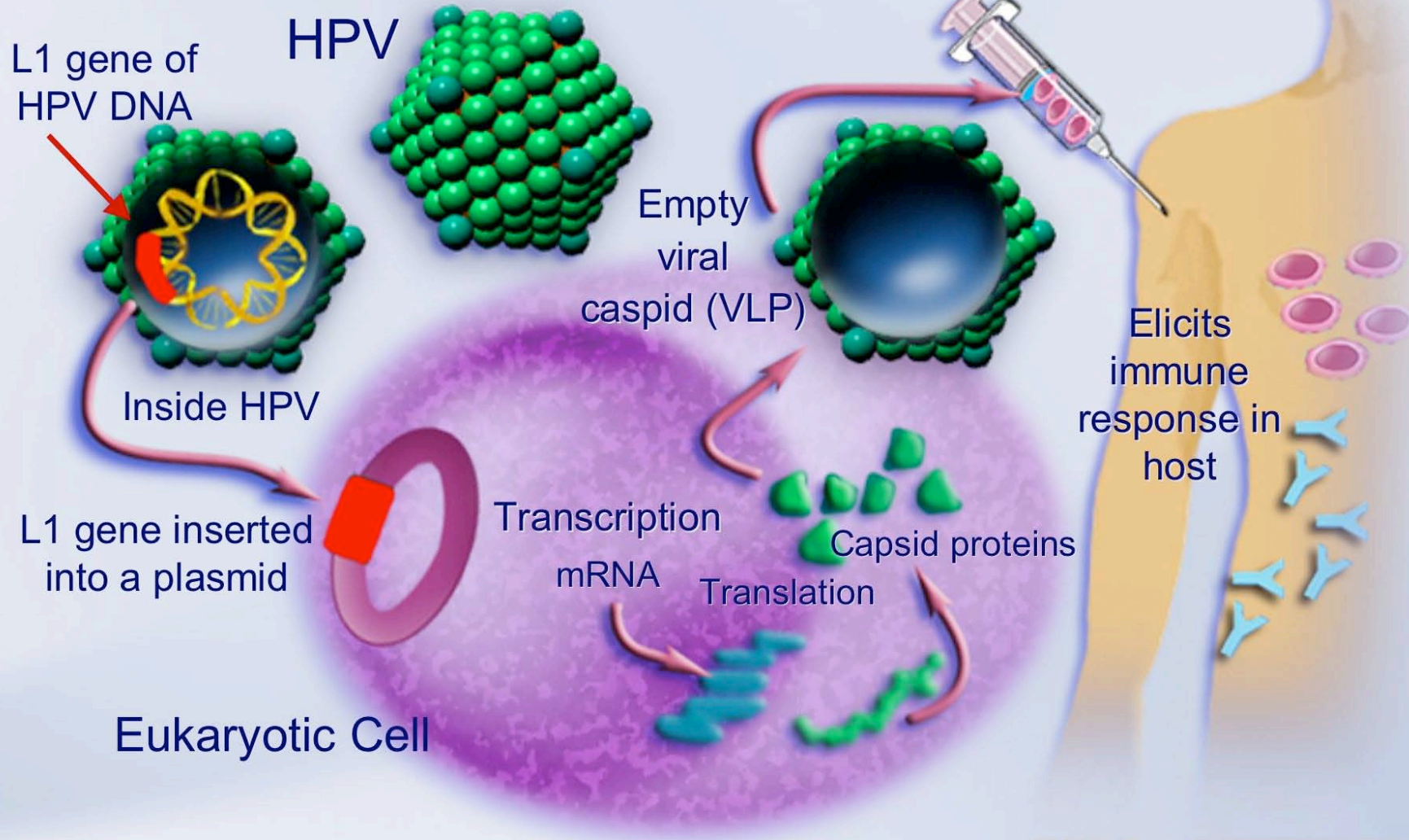


Vaccination of dogs against canine Papillomavirus

<u>Group</u>	<u>Vaccine</u>	<u>Number of dogs with warts</u>
1	Wart extract	0/7
2	PBS	7/7
3	Canine VLP (20 ug)	0/7
4	SDS denatured canine VLP	7/7
5	HPV-11 VLP	7/7

Suzich et al. PNAS 97: 11533

HPV L1 Virus-Like-Particle (VLP) Vaccine Synthesis



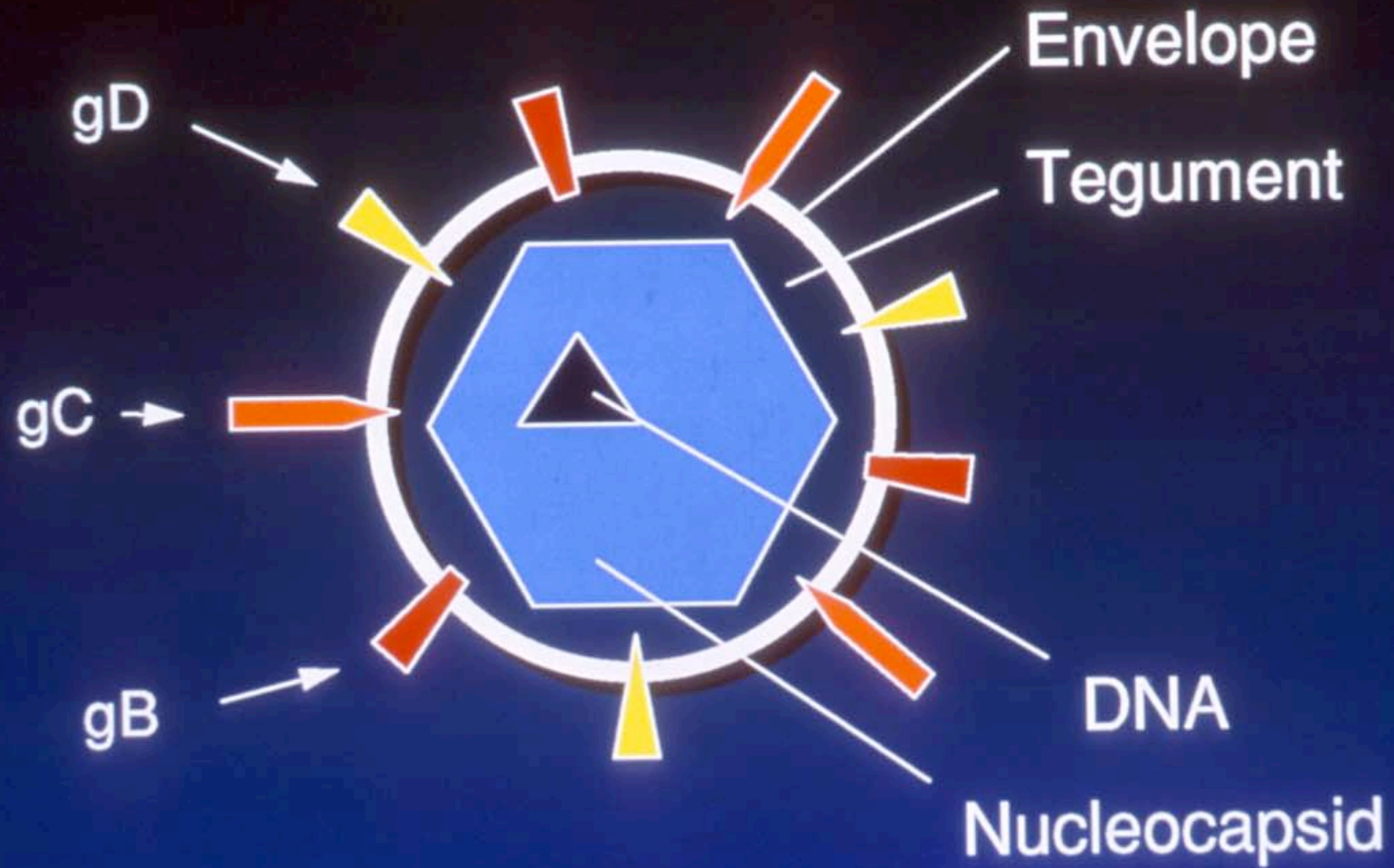
Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine: Cervical Cancer Vaccine

- HPV Types 6, 11, 16, 18¹
- Manufactured in *Saccharomyces cerevisiae*¹
- Proprietary aluminum adjuvant 225 µg per dose¹
- Each 0.5 mL injection volume contains HPV Types 6/11/16/18 (20/40/40/20 µg respectively)¹
- 0-, 2-, 6-month dosing regimen¹

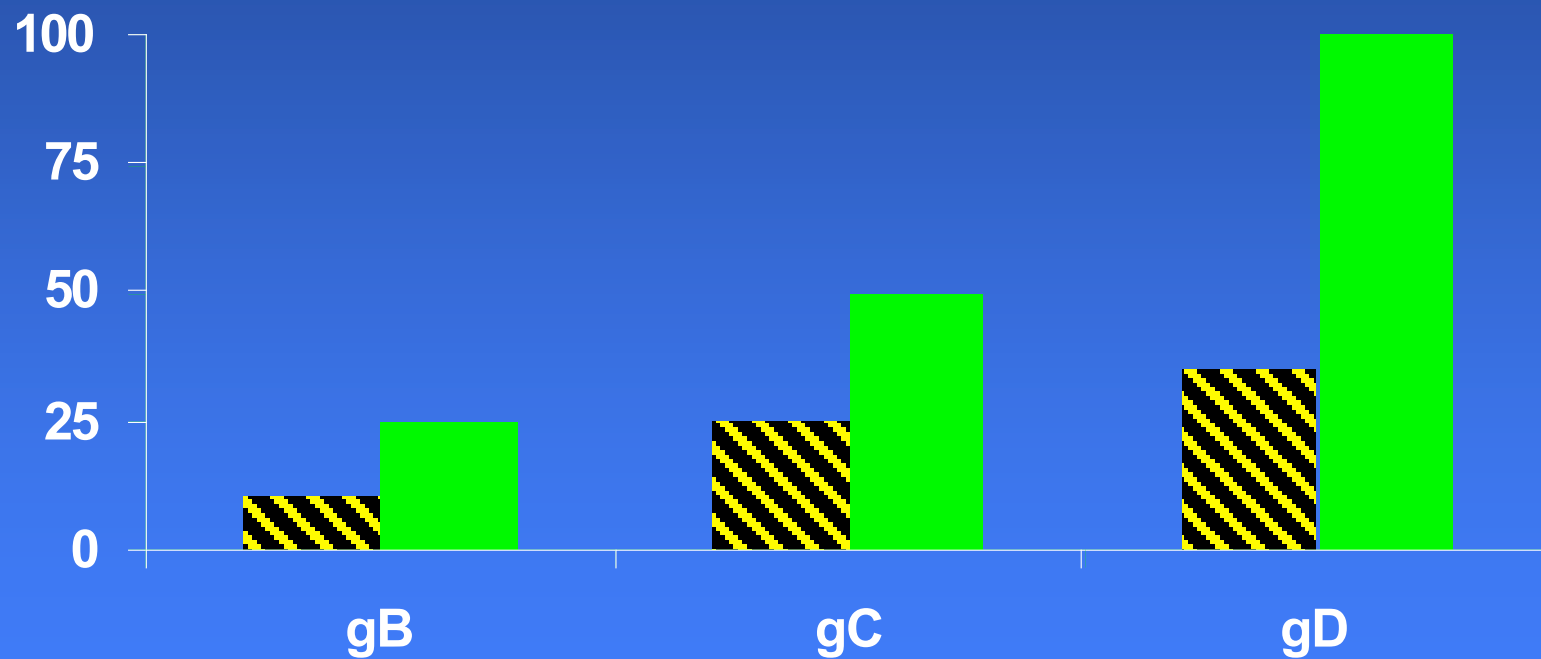


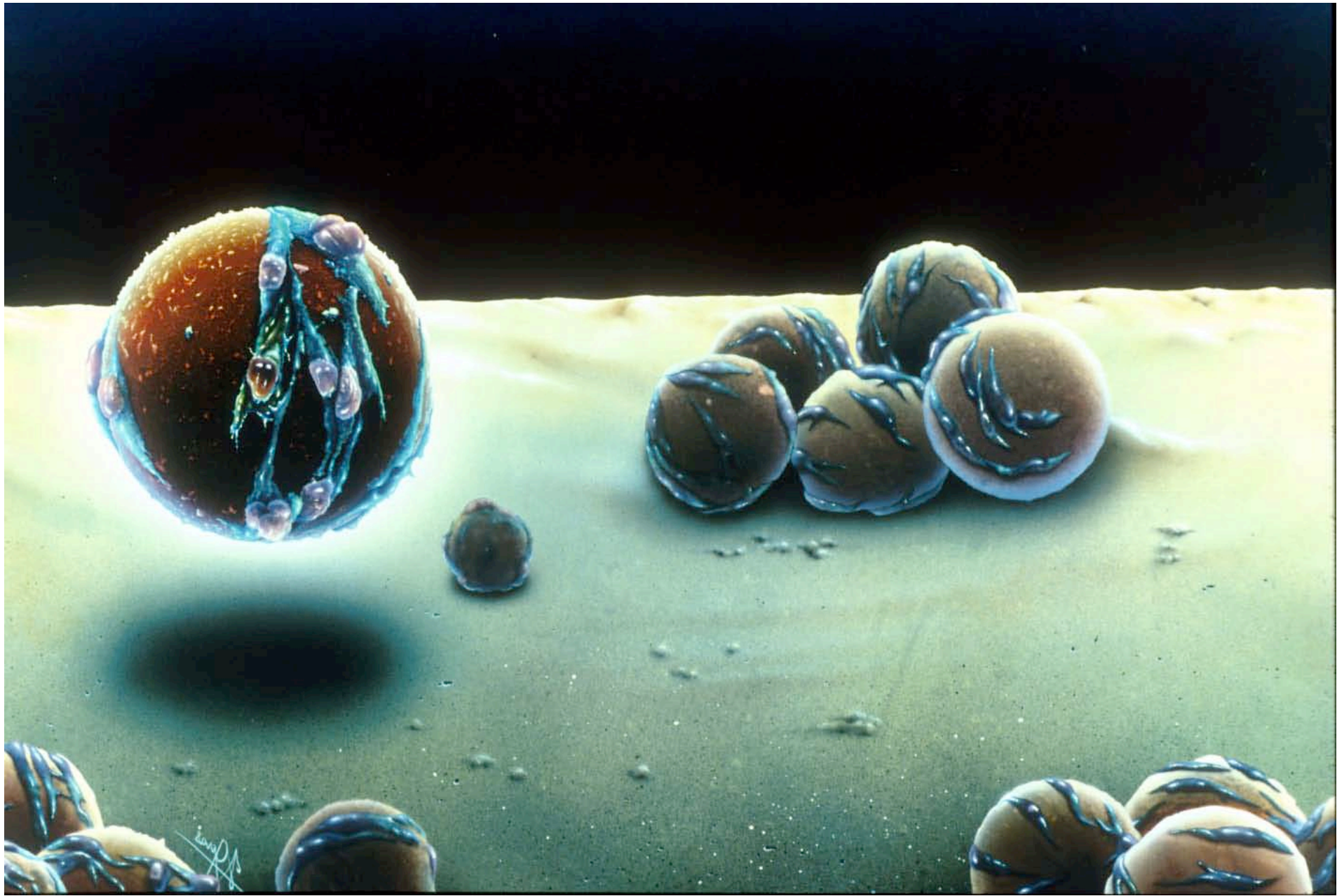
1. Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine Prescribing Information. Merck & Co., Inc., Whitehouse Station, NJ, USA.

BHV-1 virion

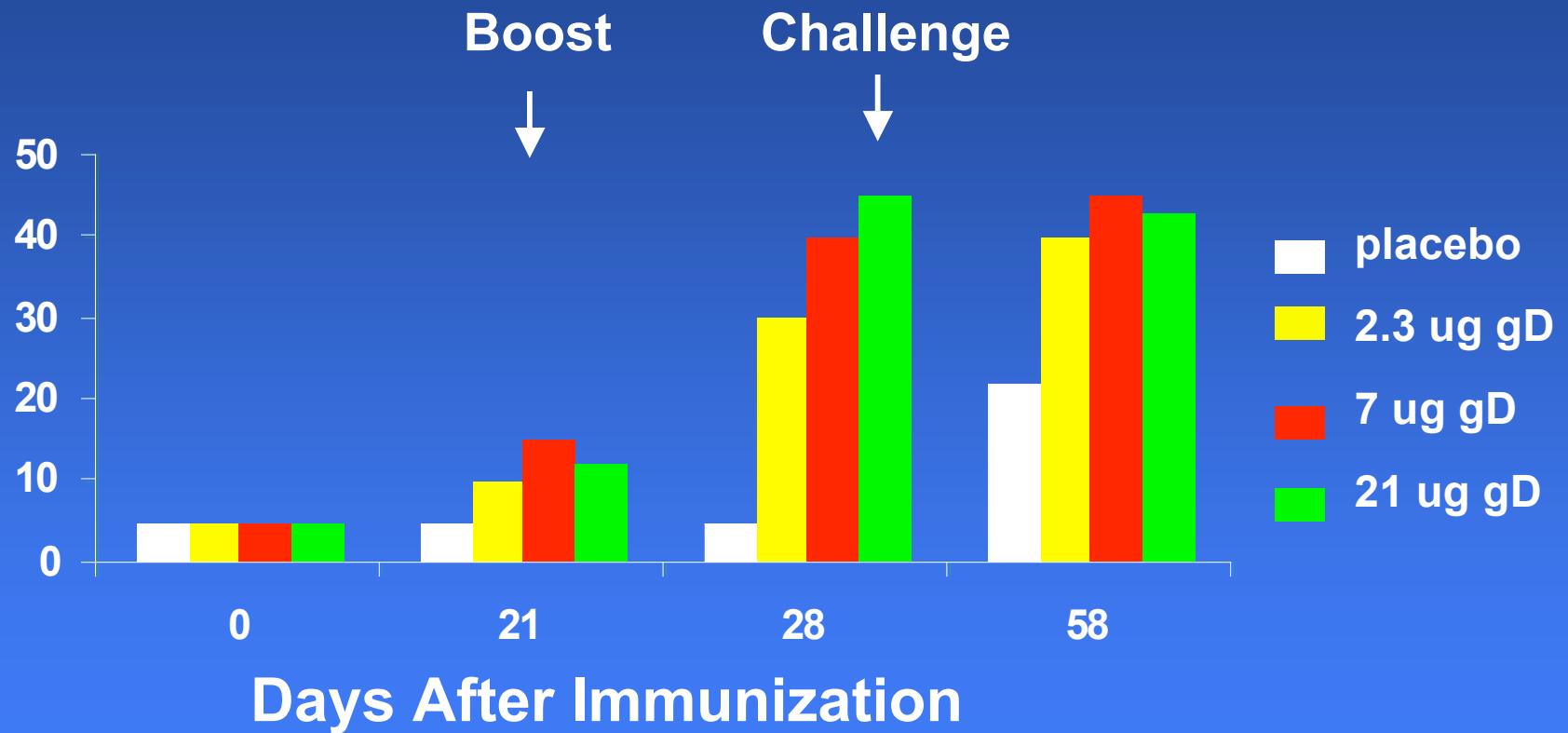


Induction of Neutralizing Antibody by BHV-1 Glycoproteins

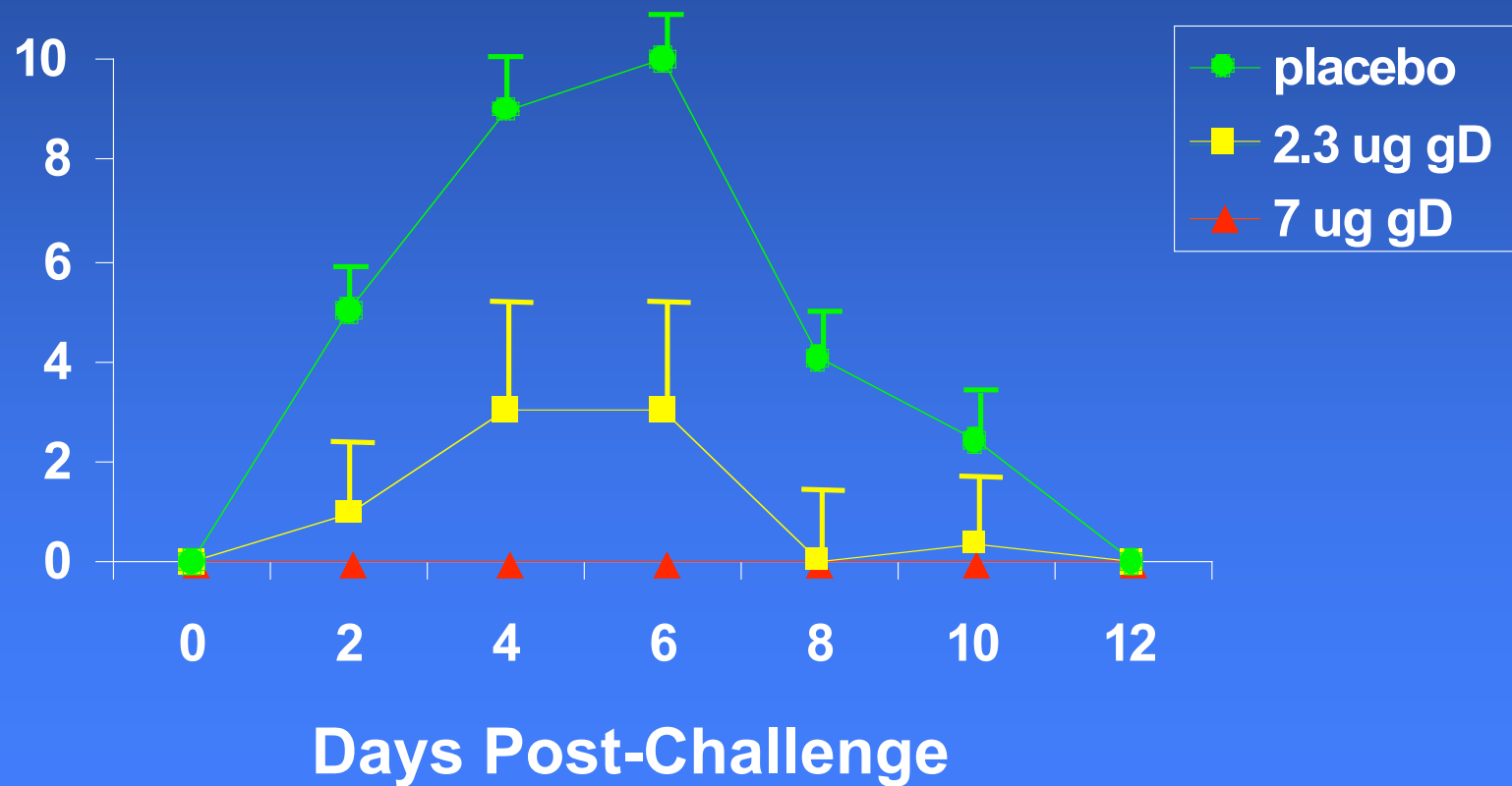




Dose Response to BHV-1 gD



Virus Shedding



Immune Defenses

Innate (hours)

.....

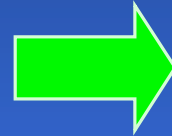
Adaptive (days)

Threat Detection



Pattern Recognition Receptor

- TLRs
- Mannose receptors
- Scavenger receptors
- NODs, etc.



Cytokines
Chemokines

- IFN
- TNF
- IL-12, etc.



Non-specific killing

- Local inflammation
- Host defence peptides
- Recruitment of cells

Activate

Modulate
Th1 vs. Th2

T + B cells

Antibody

CMI

Memory

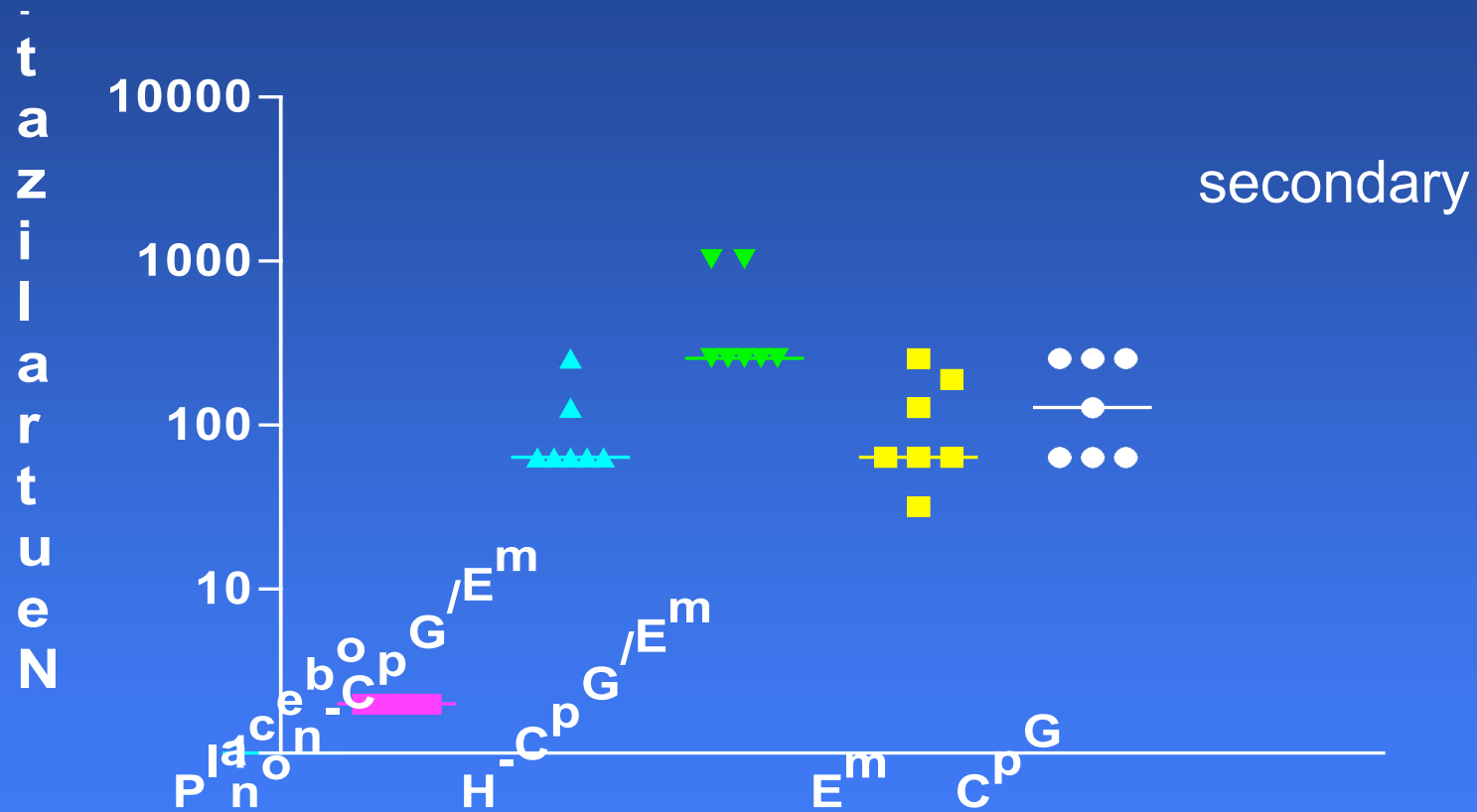


Allergy

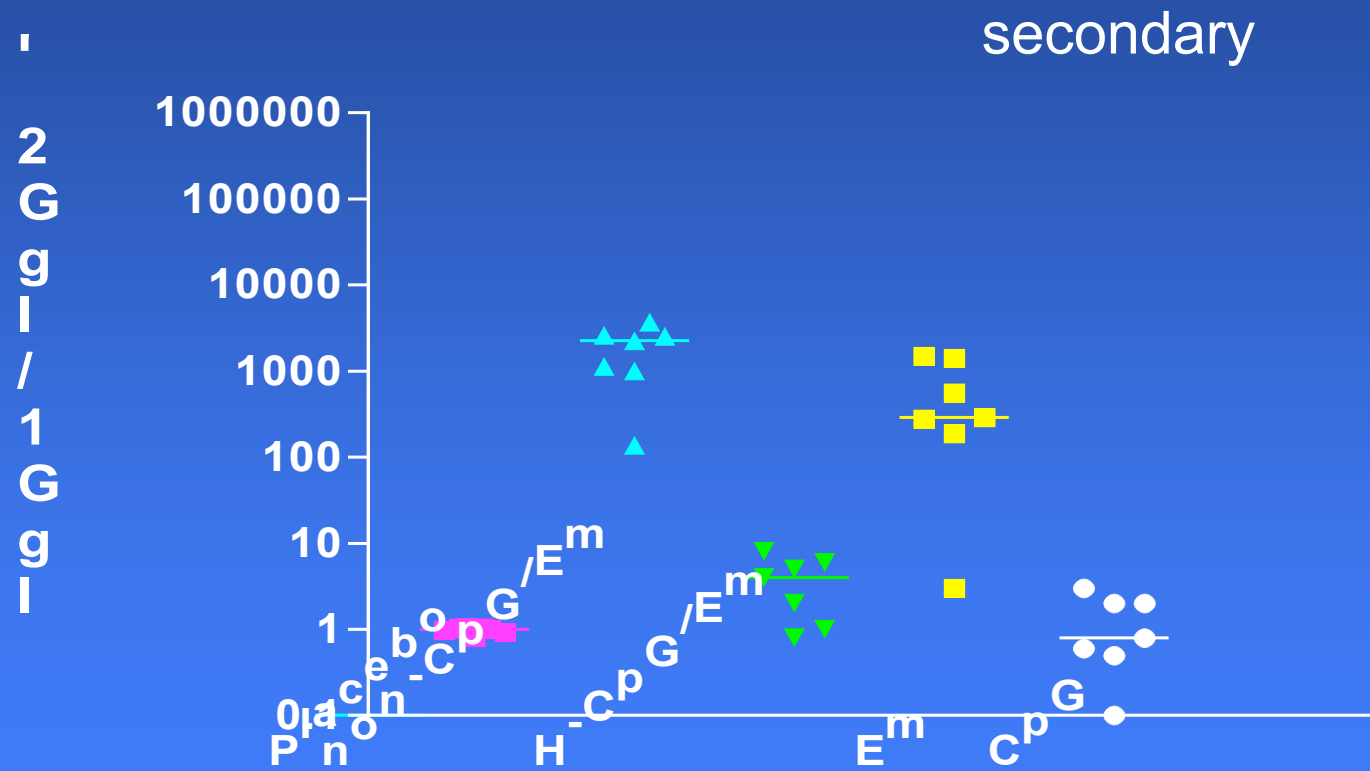
Asthma

CpG Adjuvant Effects in Cattle

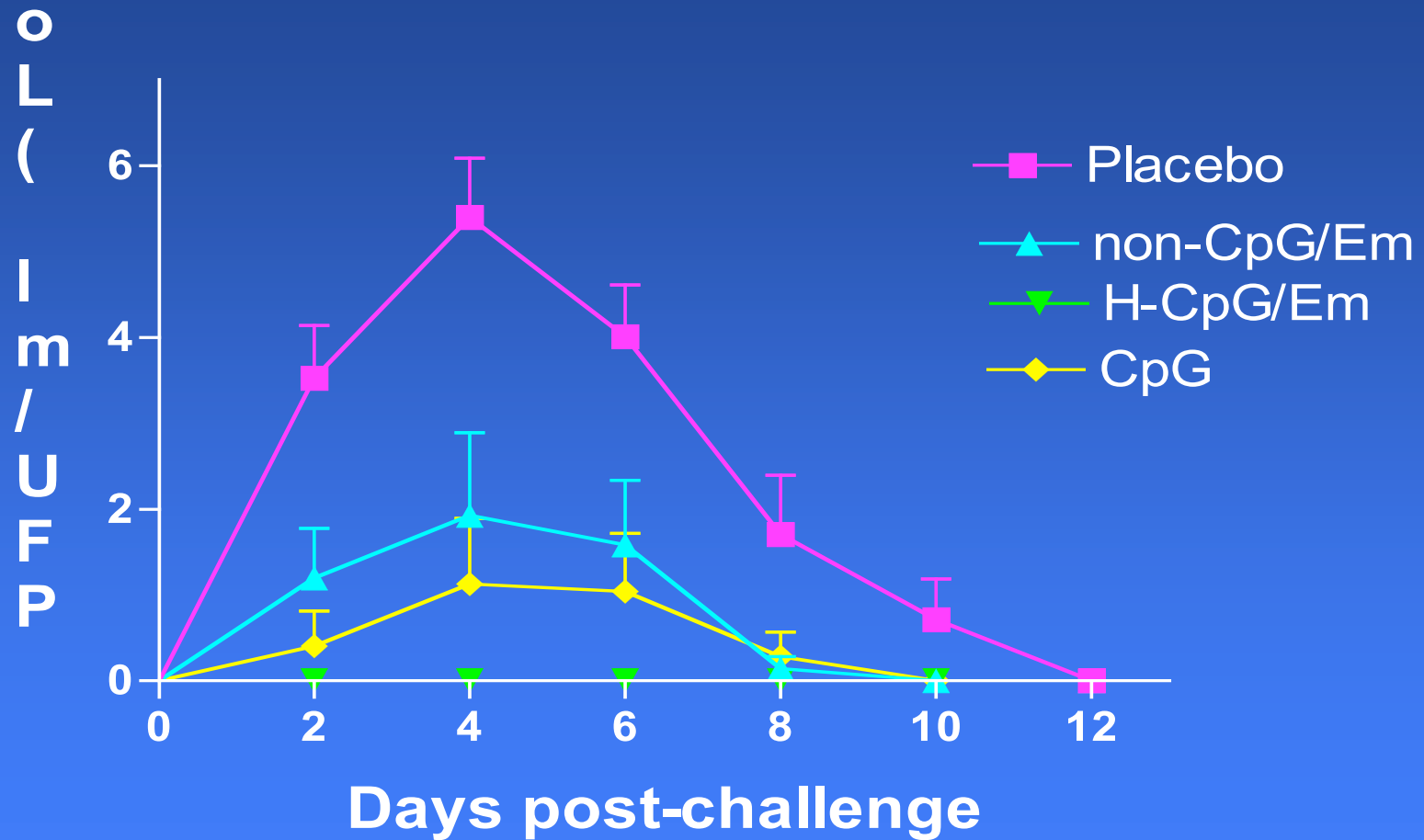
BHV-1 SN Antibody Responses



BHV-1 Antibody Ratios

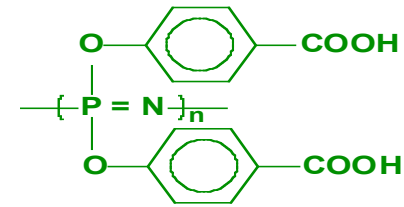


BHV-1 Shedding Following Challenge

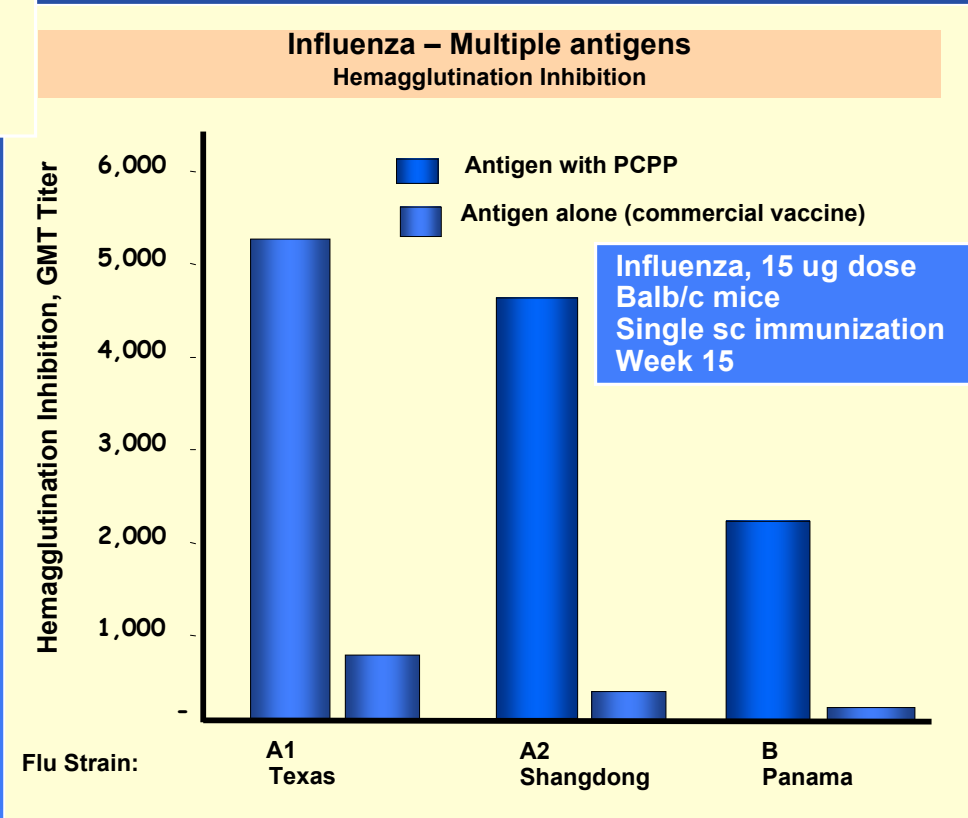
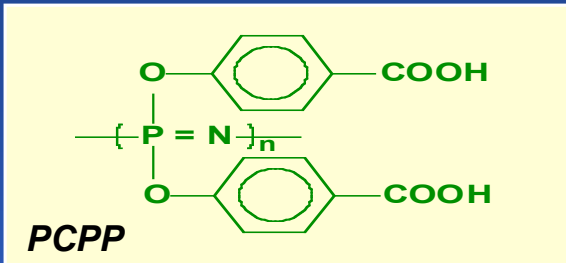


Polyphosphazenes – A Novel Delivery Molecule

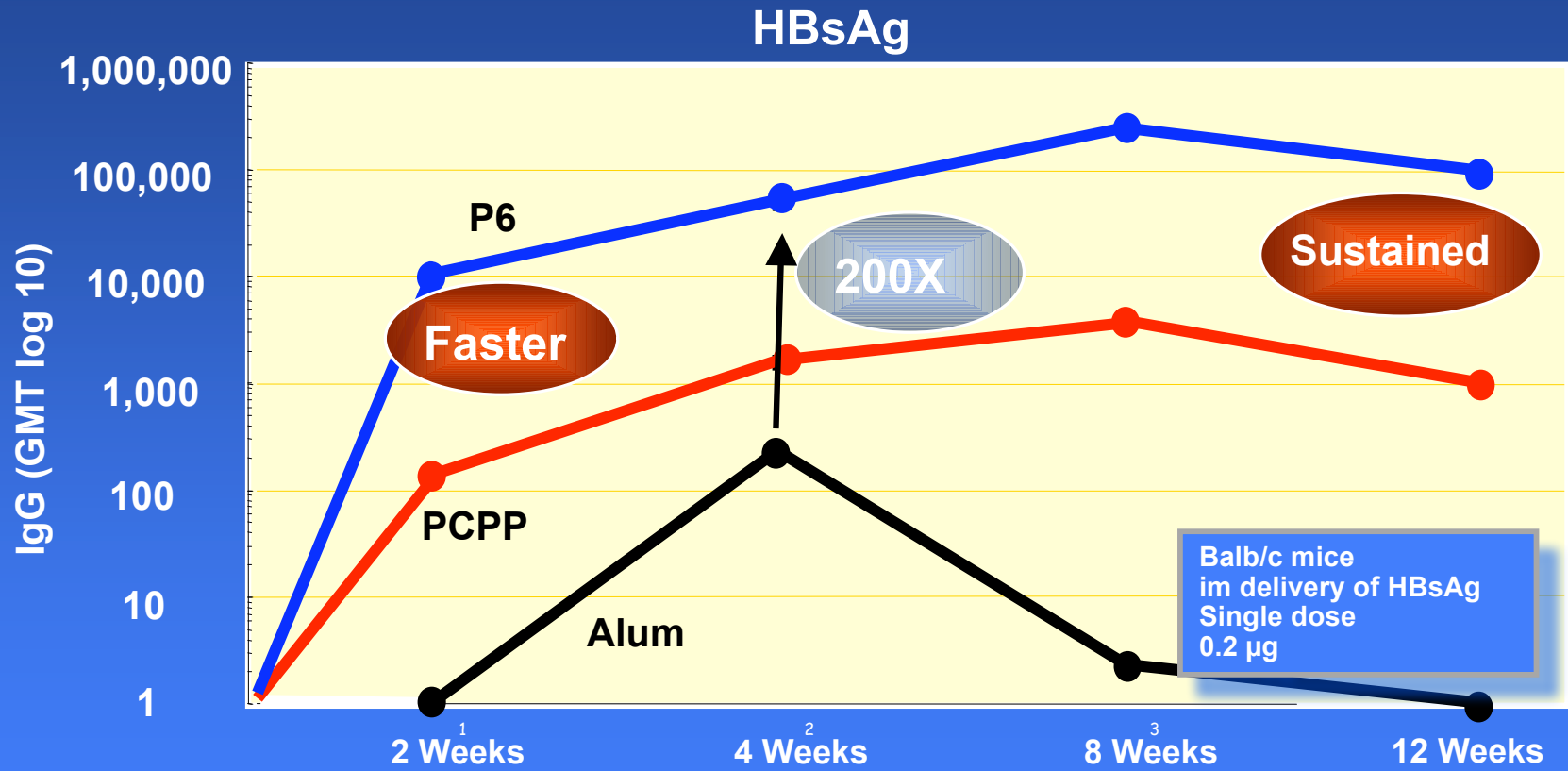
- Active with a range of antigens in animals and humans
- Active in soluble and microsphere form
- Long lasting immune responses
- Safe and well tolerated in humans



A first generation molecule, PCPP, has a potent and sustained immune response



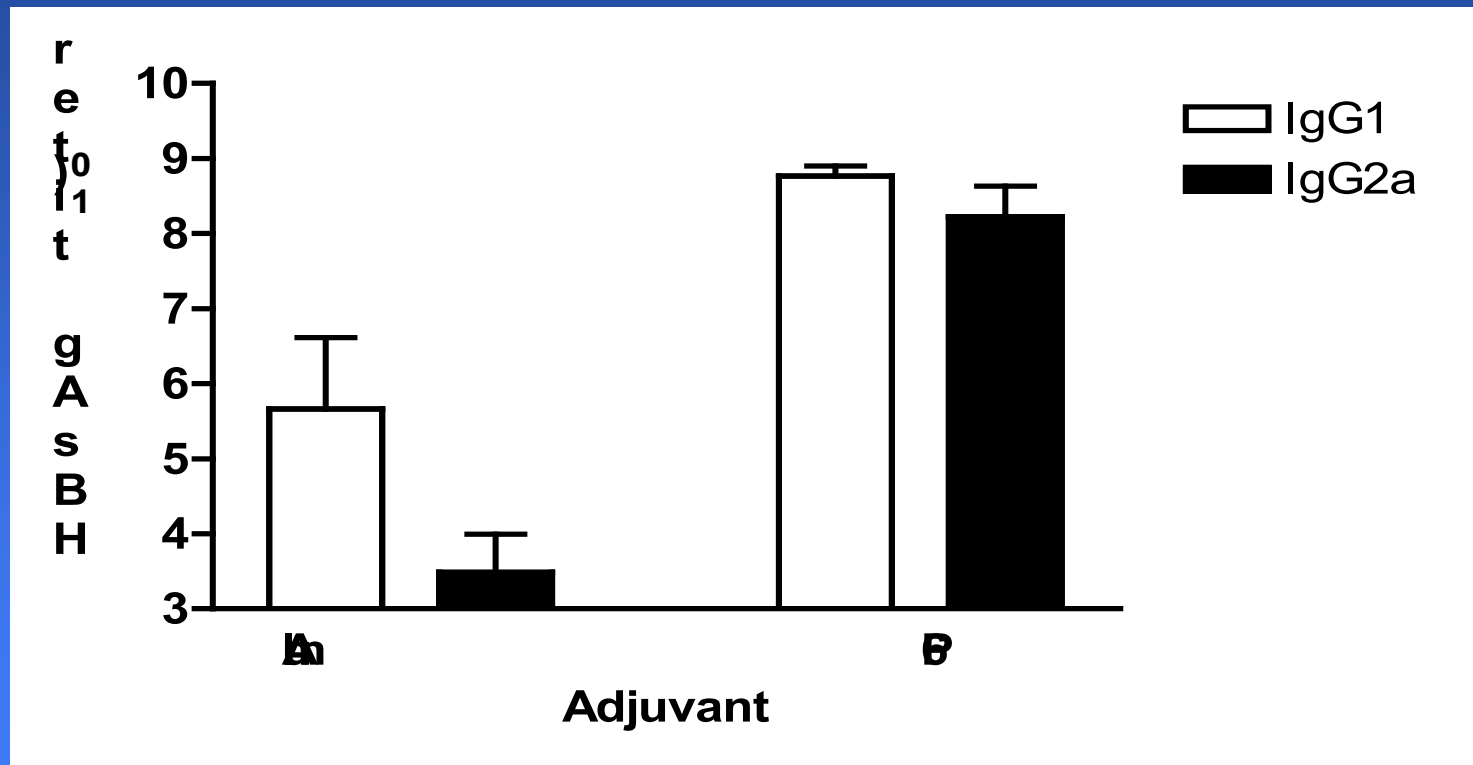
Second Generation Molecules: Faster Kinetics and Sustained Response



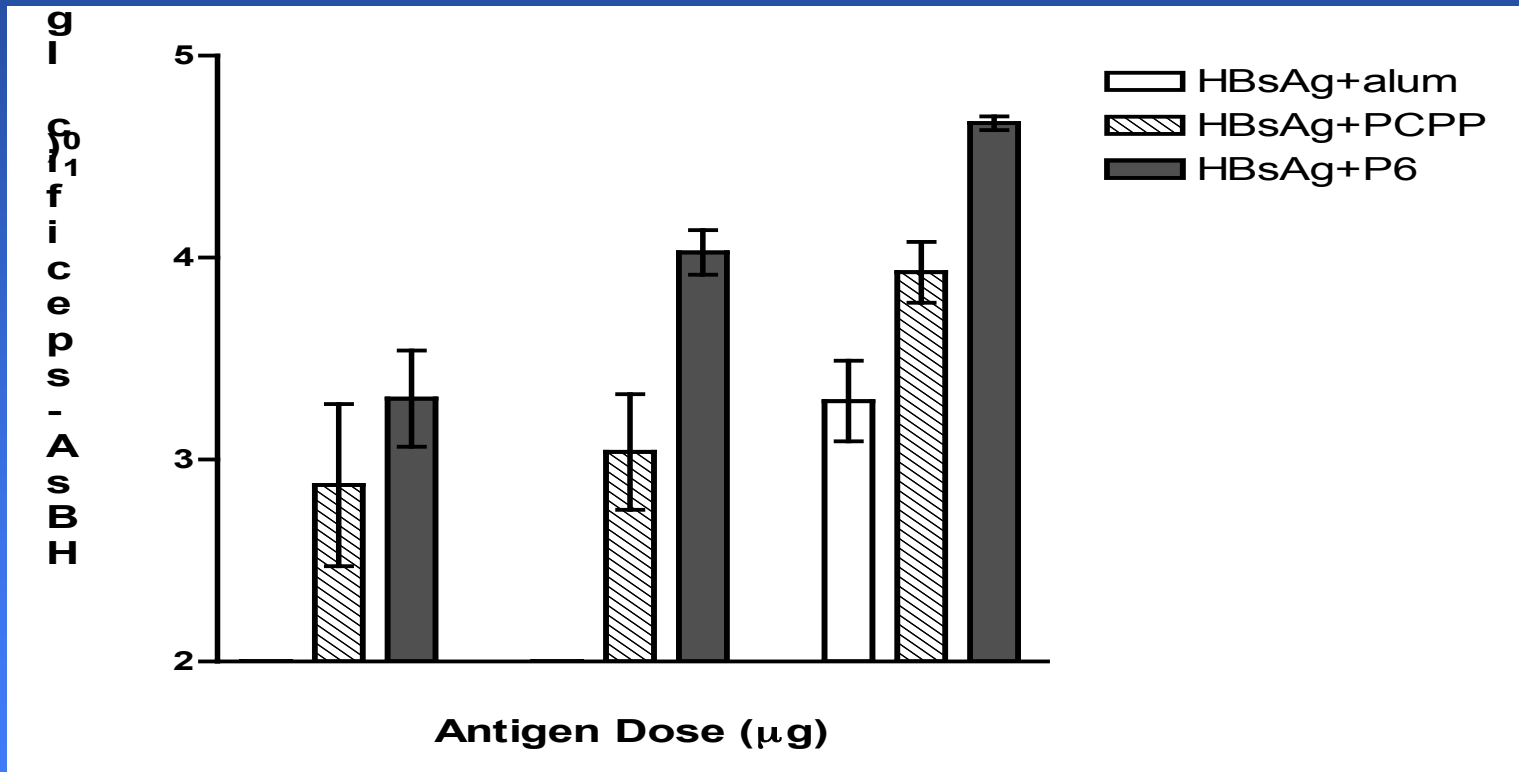
.....Response continues at 8 weeks

Note: ~3,000 highest with alum vs $1.3 \times (10)^6 = 430x$ with P6

Polyphosphazenes enhance a balanced Th1/Th2 response (12 weeks)



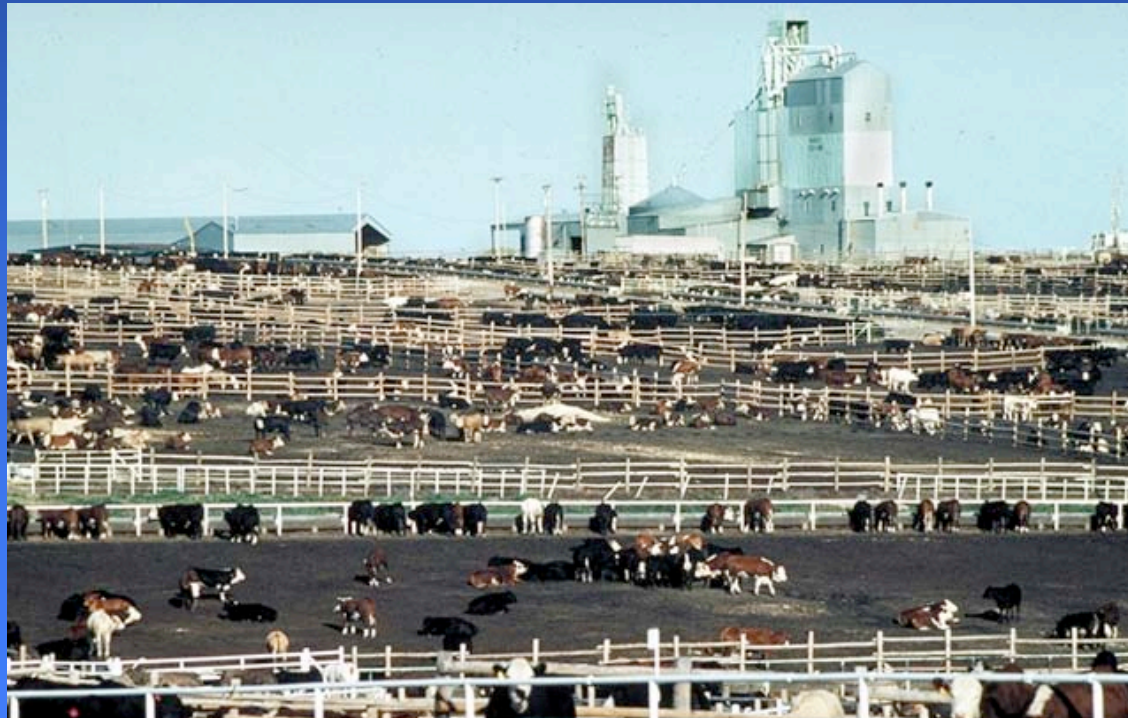
Polyphosphazenes dramatically reduces dose of antigen



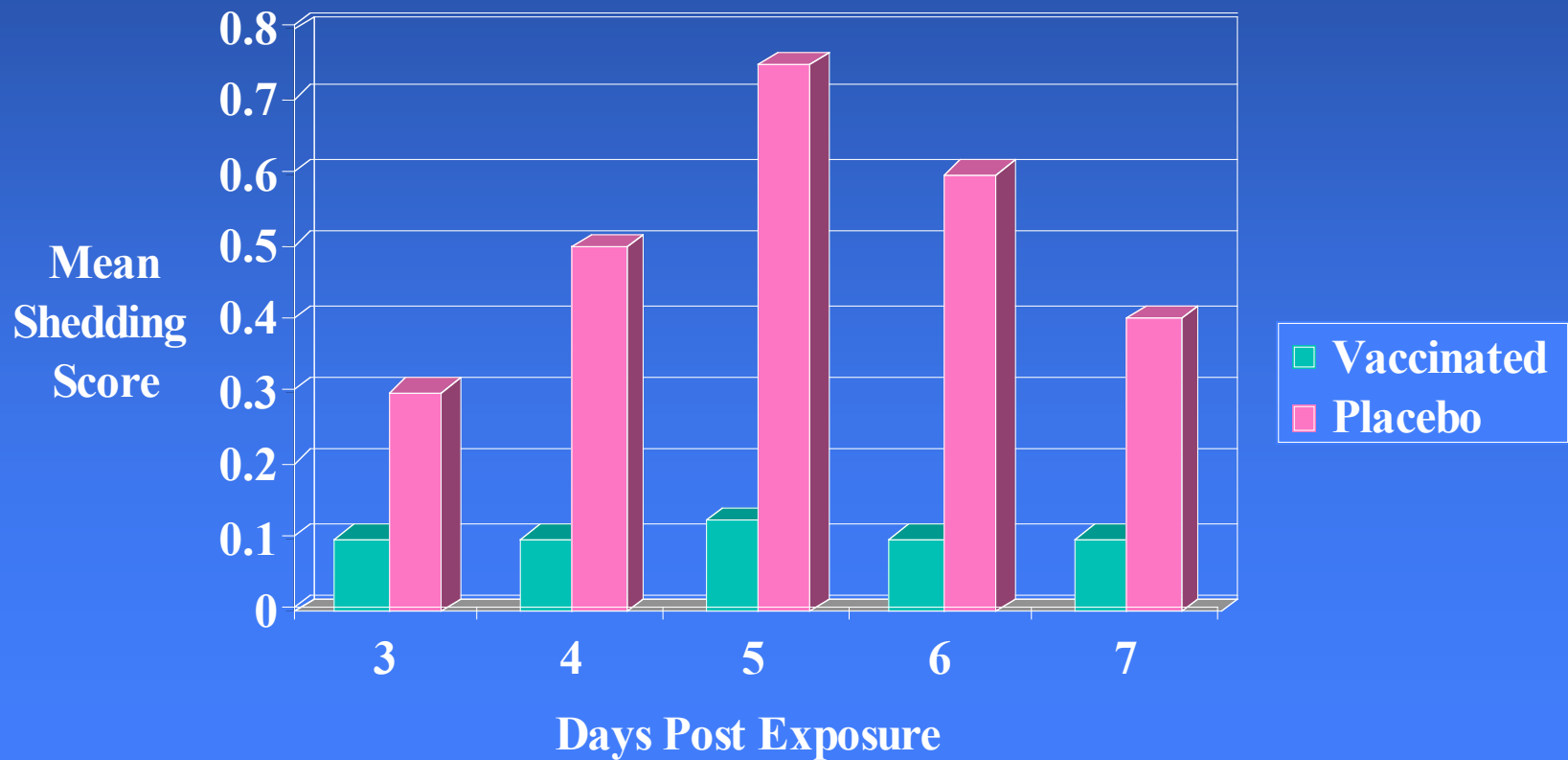
Food Safety vs. Production Vaccines

- May not cause any production losses
- Who will drive their use?
- Who pays?

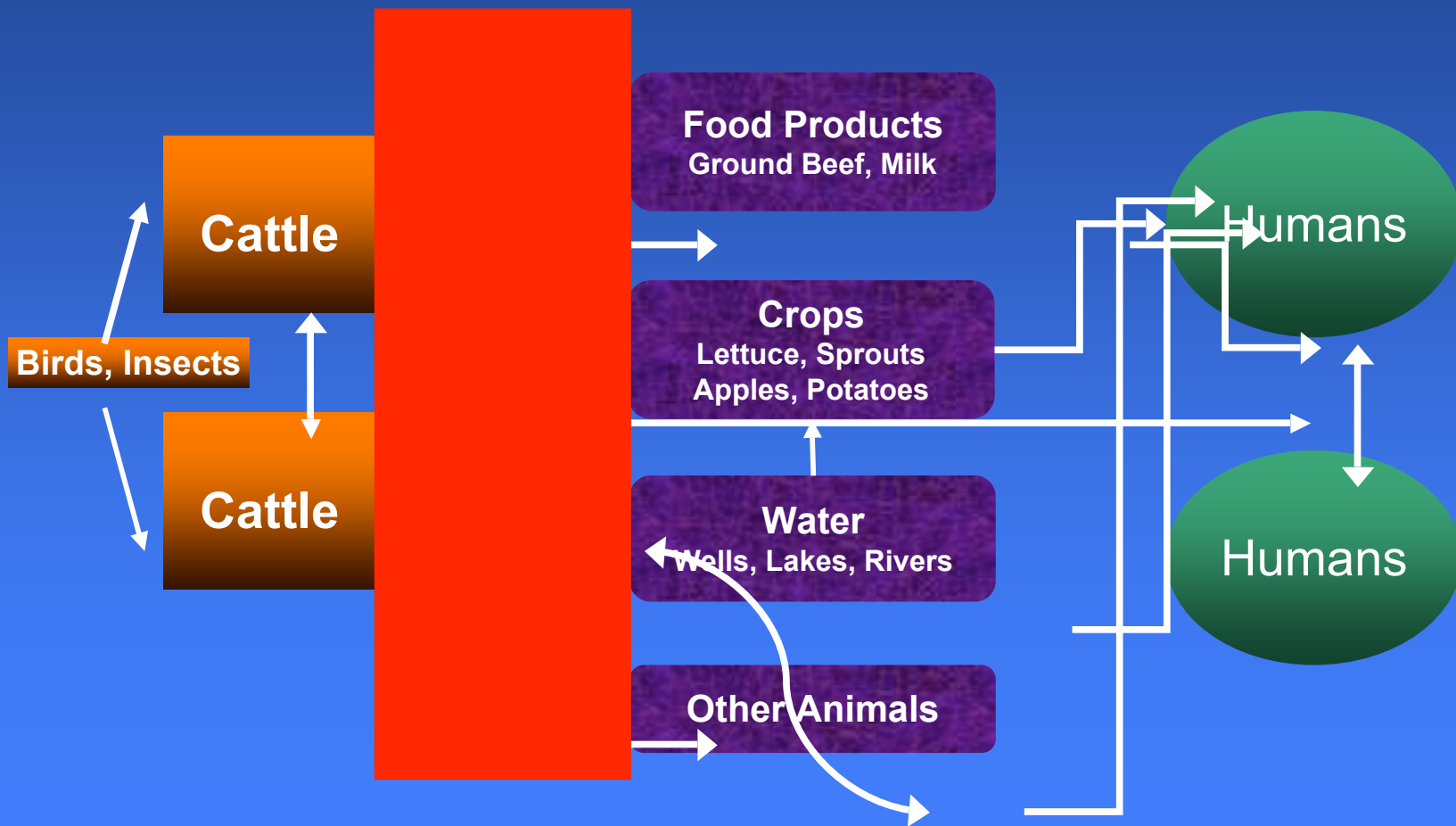
**Cattle populations are widely recognized
as an important reservoir
of *Escherichia coli* O157:H7**



Protective Capacity of EHEC Vaccine



Transmission of *E. coli* O157:H7



Summary

- **It is relatively easy to identify protective antigens from most pathogens**
- **Novel molecular adjuvants are being developed to enhance vaccine efficacy**
- **Formulations will be the key to vaccine coverage**
- **Food safety concerns will become more important in the future**