University of Nottingham
UK | CHINA | MALAYSIA

Current Issues in Canine Vaccination

Steve Dunham

School of Veterinary Medicine and Surgery
University of Nottingham

University of Nottingham
UK | CHINA | MALAYSIA

Canine vaccination

- Principles of vaccination
- Canine vaccinations
  - Which diseases?
  - Recommendations?
  - Concerns?

Origins of Vaccination

Vaccination
vaccinus (Latin), relating to cows

Edward Jenner, 1796
– observed that milk maids did not develop smallpox

Hypothesised that this was due to prior infection with cowpox

Jenner vaccinated 8 year old James Phipps with cowpox

Then infected him with small pox

How do vaccines work?

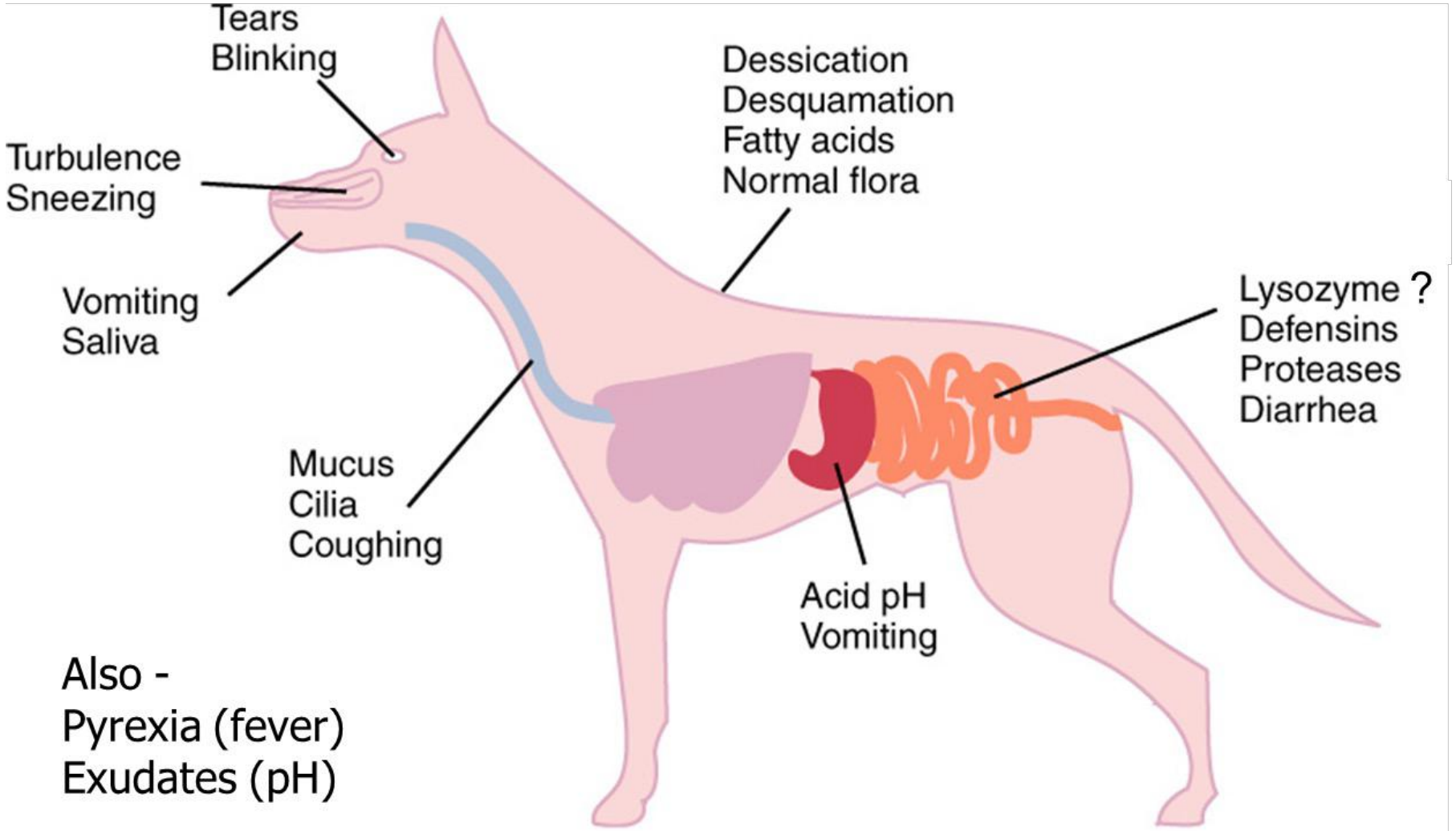
- Vaccination works by mimicking natural infection
  - Uses components from infectious organism
  - Causes an immune response like the real infection – without the associated disease
  - If an animal later encounters the real disease the body is able to produce a rapid protective immune response
  - Vaccines can be incredibly effective – e.g smallpox, rinderpest
  - Or not – e.g. HIV

How do vaccines work?

- Vaccines provide “active” immunity by stimulating the body to make immune cells and antibody

- In contrast with “passive” immunity which involves the transfer of immunity from one animal to another
  - Most commonly from a mother to offspring across the placenta or in milk in the first few days after birth
  - **This is important when we are vaccinating puppies**

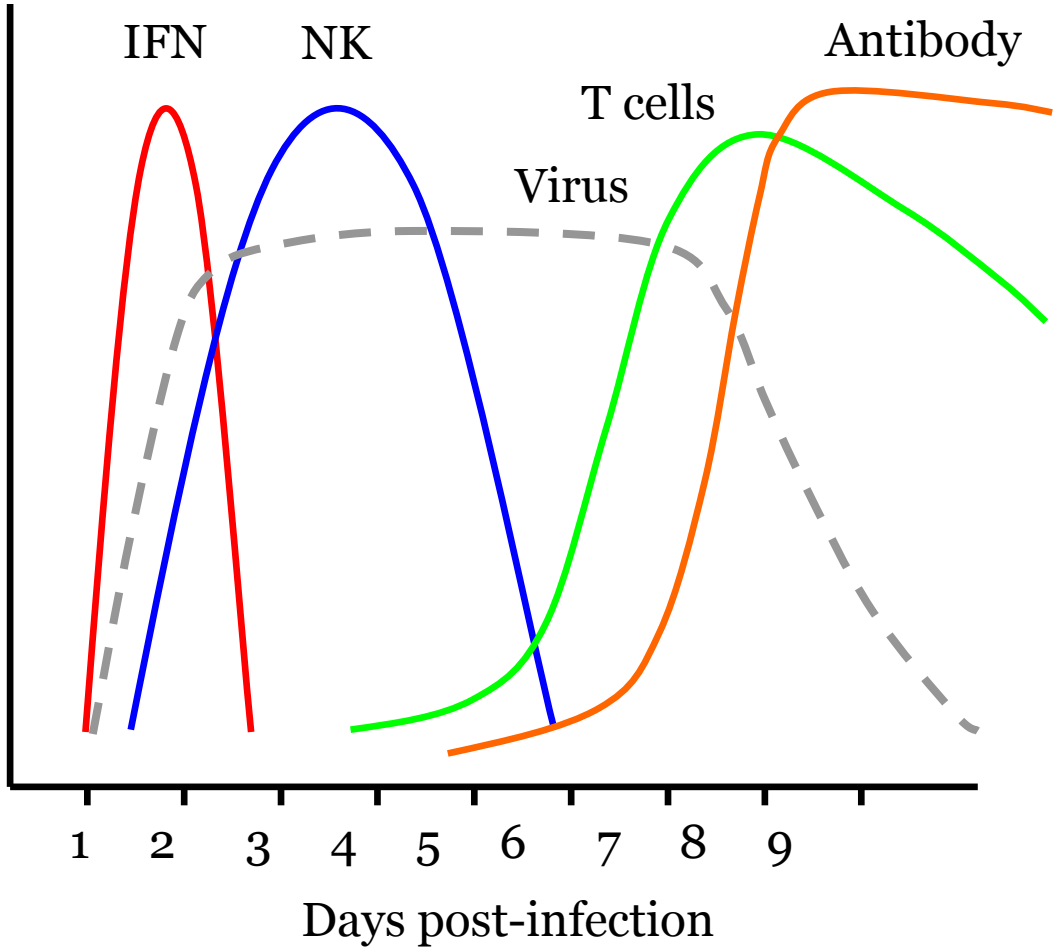
General barriers to infection



Overview of the Immune response

Innate responses

Cytokines, complement, NK cells. Contain virus replication until adaptive immunity develops.



Acquired responses

T cell responses

$CD8^+$ cells kill infected cells

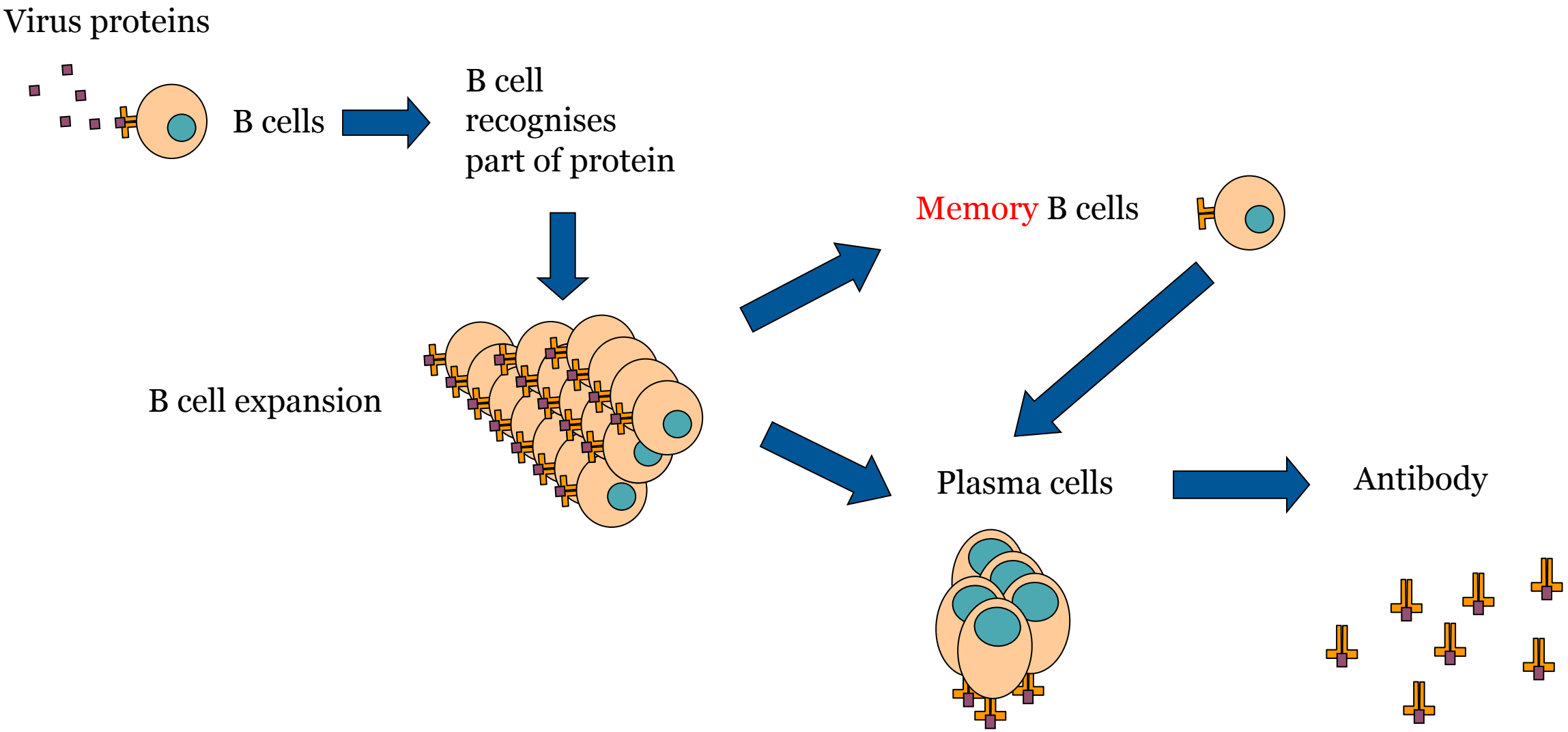
$CD4^+$ cells provide "help" for $CD8^+$ and B cells

Antibody

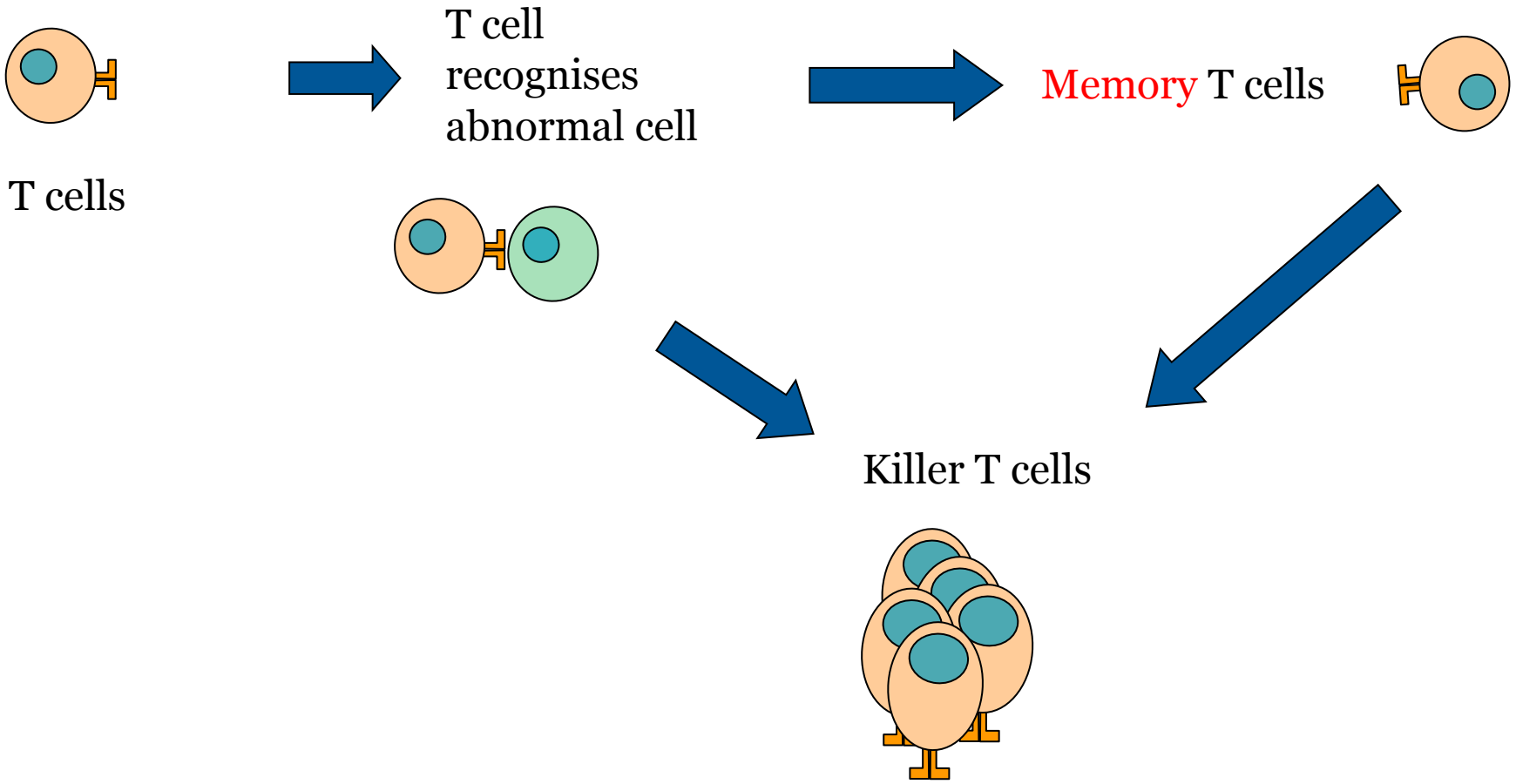
Restrict spread of infection

Prevent re-infection

Active immunity: Antibody



Active immunity: Cellular Responses



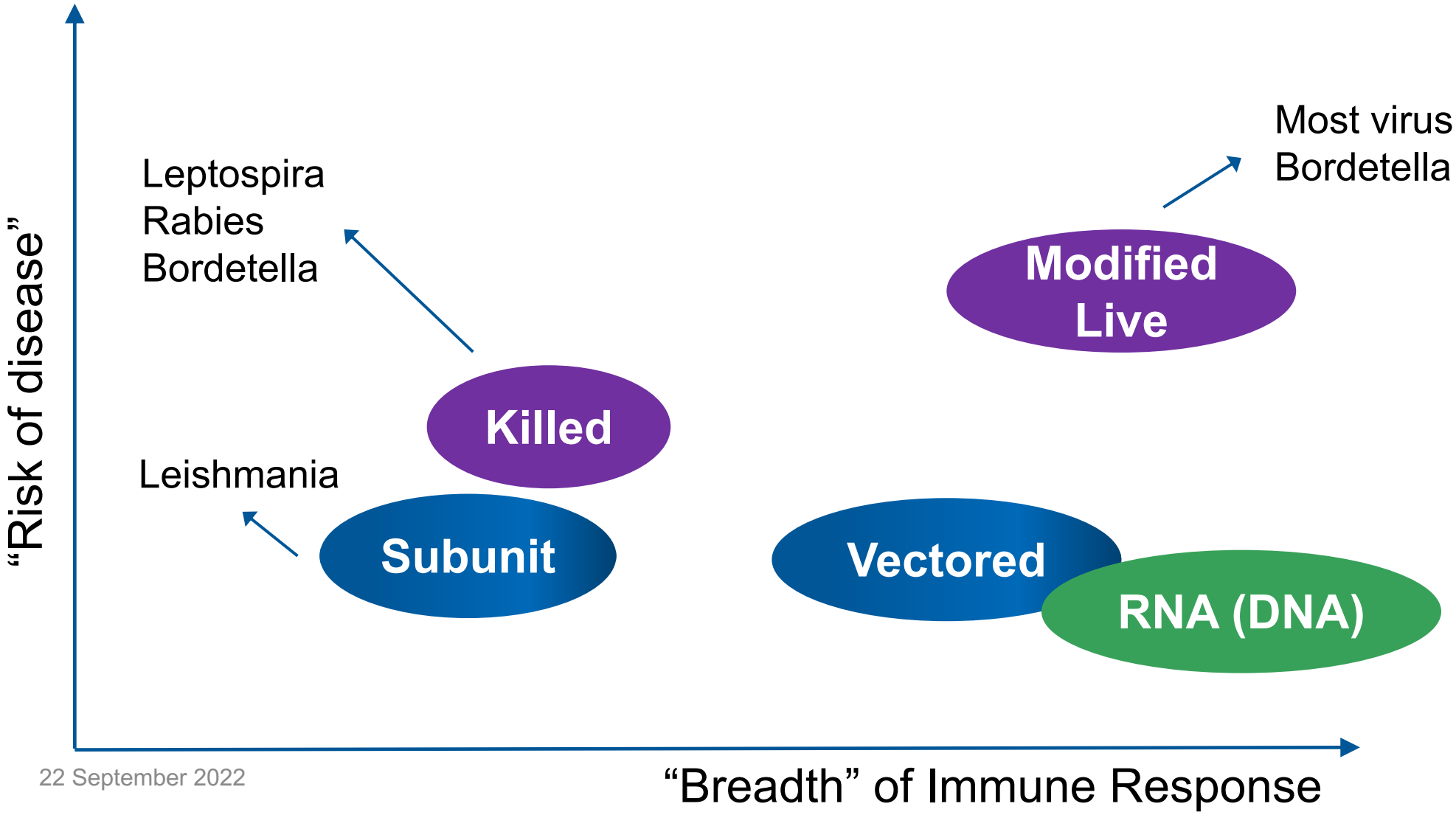
https://youtu.be/ntk8XsxVDio

The ideal vaccine would…

Generate an immune response that protects all vaccinated animals against challenge by the infectious agent under natural conditions of exposure and:

- be safe
- induce a long lasting immunity
- be commercially viable

Types of vaccine



University of Nottingham
UK | CHINA | MALAYSIA

What are we vaccinating dogs against?

Core Vaccines

Parvovirus
Distemper
Canine adenovirus

Leptospirosis

The British Small Animal Veterinary Association (BSAVA) recommends that, in the UK, core vaccines for dogs include leptospirosis.

WSAVA classify this as non-core but recognise this differs between countries and regions

What are we vaccinating against?

Non-Core Vaccines

Bordetella bronchiseptica Kennel cough
Canine parainfluenza-3

Rabies (where dogs travel to/from UK)

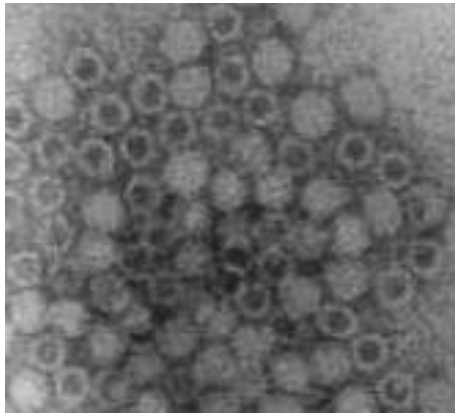
Other: Leishmania, canine herpesvirus, (Lyme Disease)

University of Nottingham
UK | CHINA | MALAYSIA

Canine Parvovirus

Key Features

- Small DNA virus
- Infect and kill actively replicating cells
  1. Fading Puppies
  2. Myocarditis in neonatal puppies (uncommon)
  3. Bone marrow → Depressed white blood cell counts
  4. Intestine → Enteritis → Vomiting & Diarrhoea
  5. Gut immune tissues → Immunosupression



- Virus is hardy: transmitted by faecal/oral route and on food bowls etc (can survive for months in environment)
  - NB bleach diluted 1:30 is effective at killing CPV
- Vaccines are live attenuated

Parvovirus symptoms as 'horrendous' outbreak kills puppy in Nottingham

Owners are being urged to watch out for a parvovirus outbreak amongst dogs

NEWS By Robbie Purves
16:42, 13 SEP 2022 | UPDATED 17:44, 13 SEP 2022

Canine parvovirus is incredibly contagious (Image: Getty Images/500px)

Canine Adenovirus

Key Features

CAV-1

- Acute severe liver infection
- Vomiting, diarrhoea, abdominal pain, may be fatal
- Can lead to more chronic disease (jaundice)
- “Blue Eye”

CAV-2

- Kennel cough (with other infectious agents)
- Typical “hacking” cough
- Vaccines are live attenuated CAV-2

Canine Distemper Virus

Key Features

- Virus related to measles
- Young dogs especially susceptible
- Transmitted by direct contact
- Pyrexia, depression
- Ocular and nasal discharge
- Cough
- Vomiting, diarrhoea
- Hyperkeratosis of nose/pads (“hardpad”)
- Live attenuated vaccine

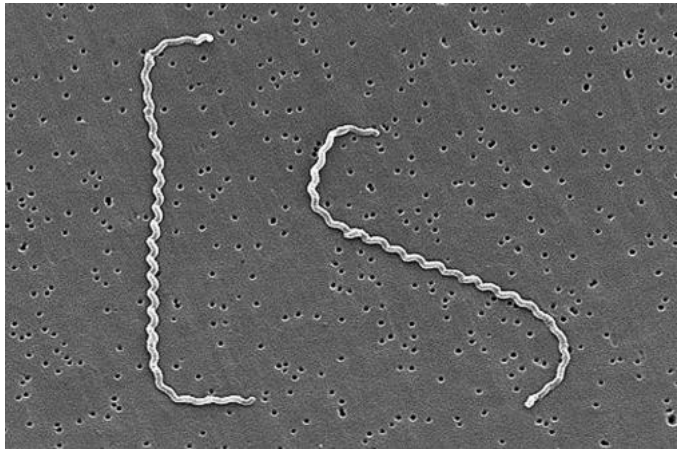
Outcome

- May recover with supportive treatment
- May develop neurological signs (seizures etc) – typically with be fatal

Canine Leptospirosis

Key Features

- Bacterial infection (*Leptospira interogans*)
- *L. canicola* and *L. icterohaemorrhagia*
- *L. grippotyphosa*, *L. bratislava (Australis)* [and *L. Pomona*]
- Bacteria spread through urine, carried by rodents especially and can survive in water for many months



- Range of clinical signs depend on “type”
- Acute kidney failure, hepatitis and pulmonary haemorrhage
- L2 vs L4 vaccines (killed bacterial vaccines)

Vaccination “protocols”

- Vary depending on the manufacturer’s recommendations
- Minimum age 6 – 8 weeks
- Boost 3 – 4 weeks later

- Vaccinate at 1 year of age

- Boost every 1 – 3 years

WSAVA Guidelines

- Vaccinate pups at 8-9 wk with core vaccines, again 3-4 wk later, **third vaccination at 14-16 wk**
- All dogs receive a booster at 12 months
- Booster vaccines every three years or longer

- Non-core vaccines (Leptospirosis) should ideally be administered after core vaccines in puppies
- Non-core vaccines (Leptospirosis, other) when used, require yearly boosters

Onset of immunity

Killed vaccines

- Minimum of two doses, two weeks apart plus 1 wk

Live vaccines

- In the absence of maternal antibody: 1 – 7d
- CDV: 1-2d
- CPV: 3d
- CAV: 7d

A small proportion of animals will not respond adequately to vaccination due to genetic factors (non-responders)

Onset of immunity

Kennel Cough (*Bordetella*)

- Nasal vacc: 5 days
- Injectable: 1 month

Vaccine “Failures”

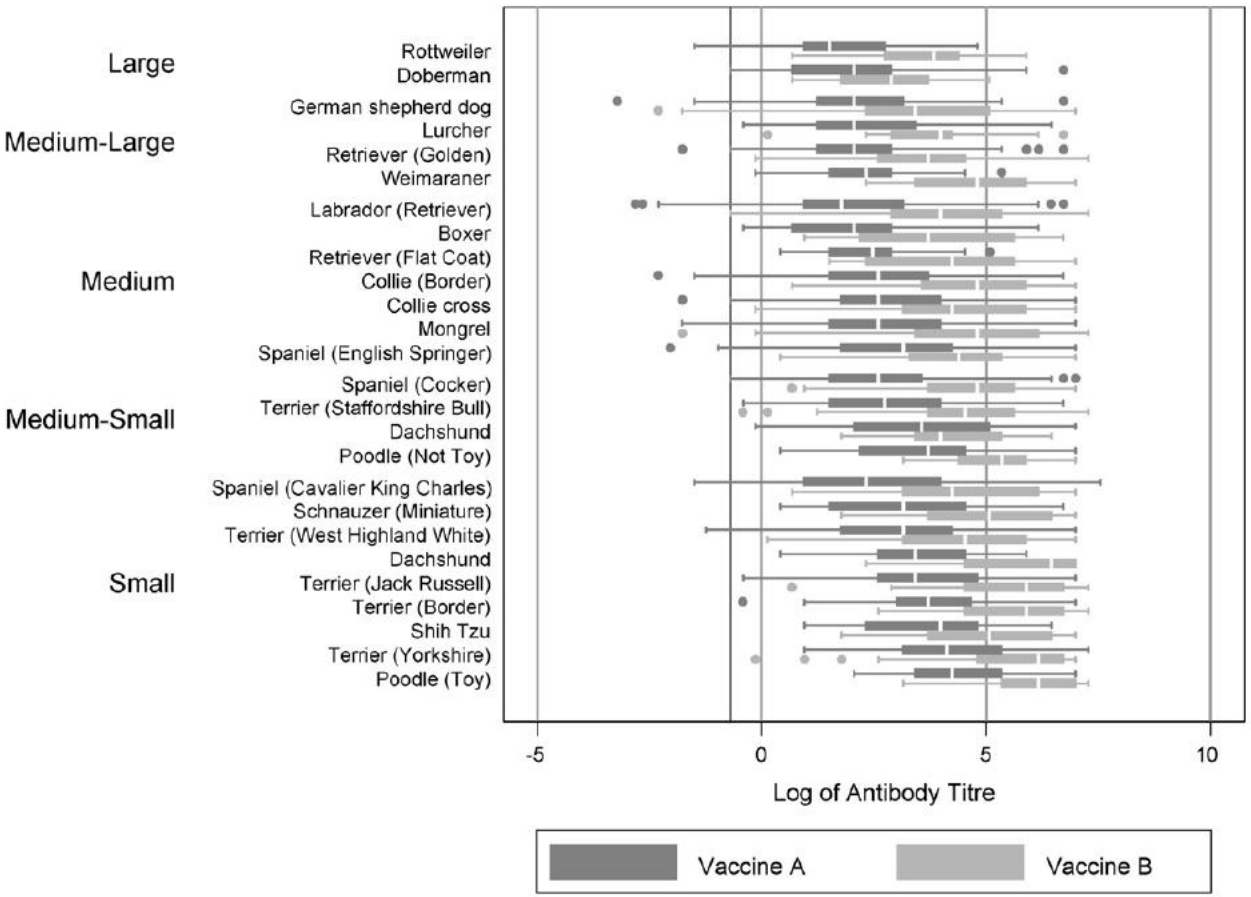
The majority of dogs respond well to vaccination and are protected against life threatening diseases.

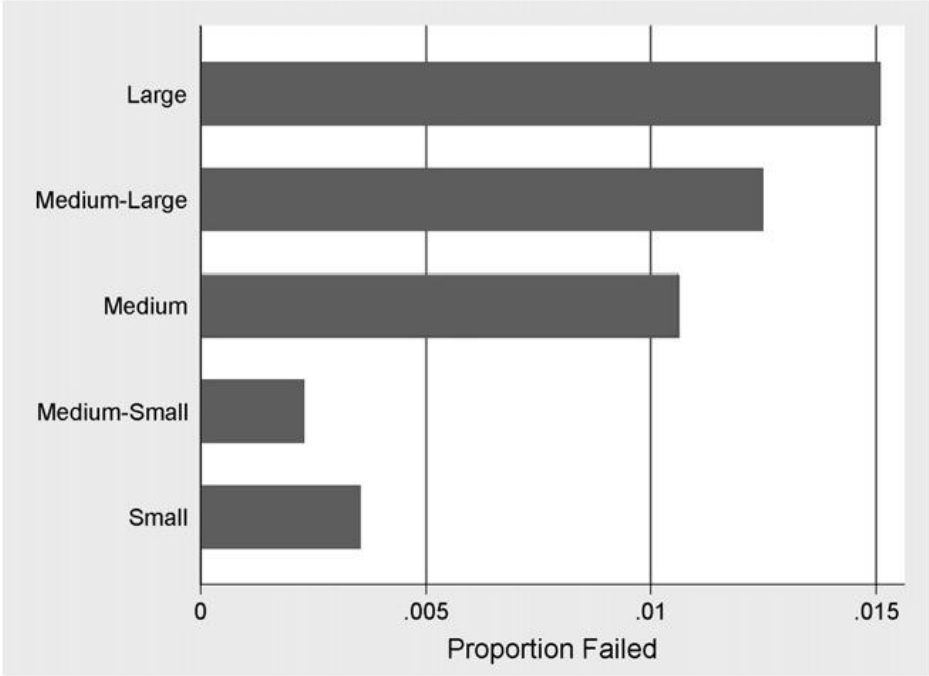
- some vaccines are less effective
- vaccines may have been improperly stored/batch issues
- improper administration?!

- genetic factors?
- interference by maternal antibody

Response to vaccination

- Larger dogs responded less well to rabies vaccination
  - Kennedy LJ et al. (2007) Vaccine 25:8500-8507

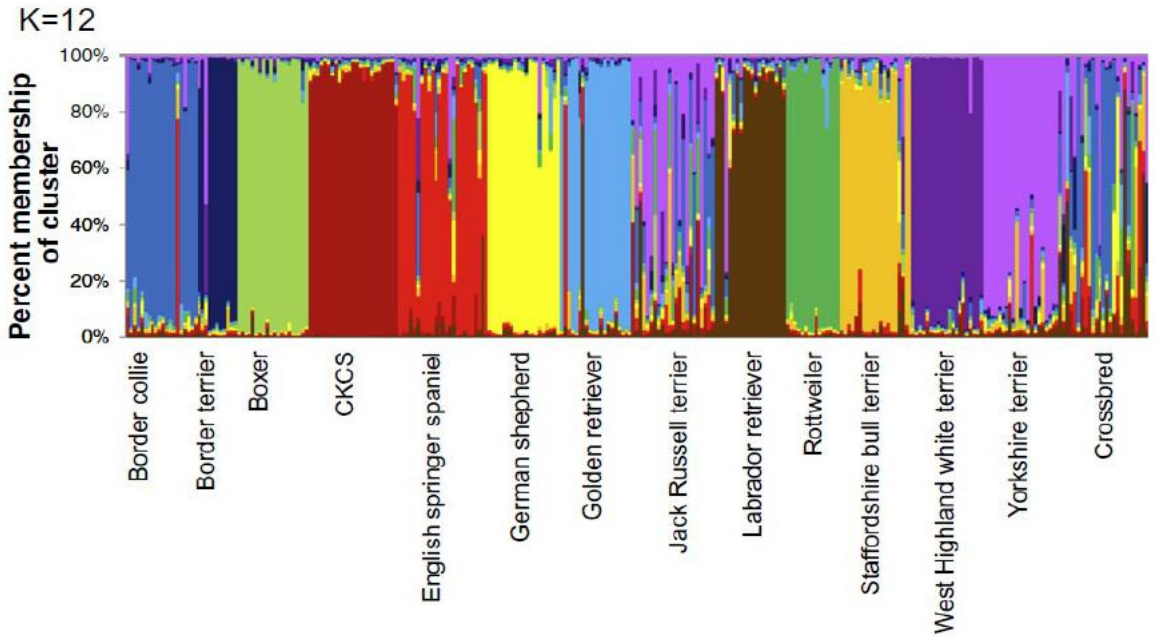




University of Nottingham
UK | CHINA | MALAYSIA

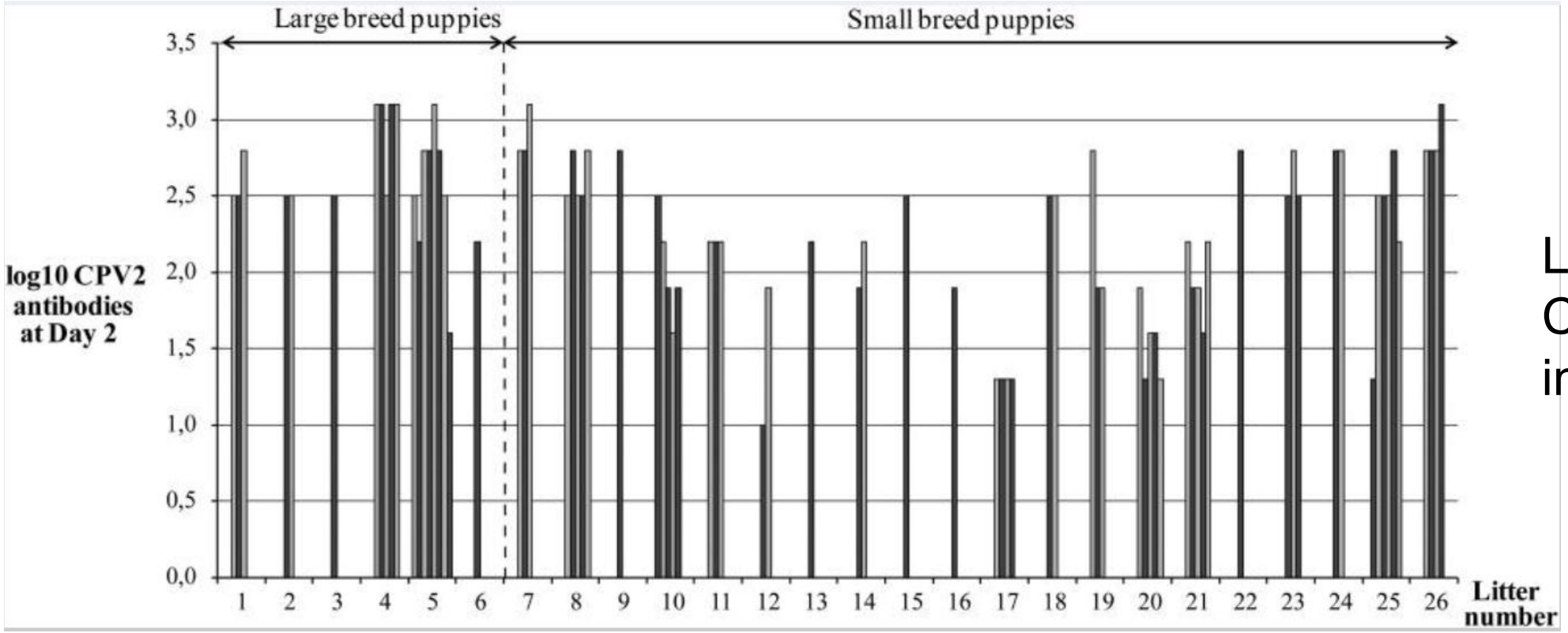
Canine genetics

- Genetic variability can be very different from breed to breed
  - Mellanby RJ et al. (2013) Vet J 196: 1392-97
- Likely to be highly restricted for BMD



Importance of maternal antibody

Puppies acquire antibody from their dam in colostrum up to 24hr after birth



Level of anti-CPV antibodies in puppies

Mila H, Grellet A, Desario C, et al. Protection against canine parvovirus type 2 infection in puppies by colostrum-derived antibodies. *J Nutr Sci*. 2014;3:e54. Published 2014 Nov 13. Link to Paper

Importance of maternal antibody

Half life of antibody (in blood) is 10-13 days

Proportion of puppies protected from CPV2 infection (HI ≥ 1:80) depending on MDA level at 2 d of age

	Age of puppies ~~(weeks)~~ days!								
	2	**7**	**14**	**21**	**28**	**35**	**42**	**49**	**56**
Group A	21/34 (62)	14/30 (47)	5/26 (19)	0/26 (0)	0/25 (0)	0/25 (0)	0/25 (0)	0/25 (0)	0/25 (0)
Group B	45/45 (100)	44/44 (100)	41/44 (93)	34/44 (77)	24/42 (57)	10/44 (23)	9/44 (20)	2/44 (5)	0/43 (0)
P-value for each period of time	<0·001	<0·001	<0·001	<0·001	<0·001	0·011	0·021	0·531	–

n_i/n = number of puppies protected in the category considered/total number of puppies in the category (%).

HI titre ≤1:160 (13 <1:80)

HI titre > 1:160

University of Nottingham
UK | CHINA | MALAYSIA

Value of Titre Testing?

- In puppies
  - After final (third?) vaccine to ensure immunity is adequate
  - If not positive then re-vaccinate puppy
  - Consider possibility that pup is a non-responder

- In adults
  - Positive titre against CPV, CAV or CDV indicates vaccination not required
  - Negative titre does not necessarily mean dog is not immune but to be safe a booster is often recommended

University of Nottingham
UK | CHINA | MALAYSIA

Concerns with vaccination?

University of Nottingham
UK | CHINA | MALAYSIA

Concerns with vaccination?

- Of 2743 adverse events reported by VMD in 2013 in dogs, 206 were associated with use of a live vaccine, 177 with a mixed vaccine
- 118 of these were anaphylaxis (rapid allergic reaction)
- But over 8 million dogs in the UK owned as pets

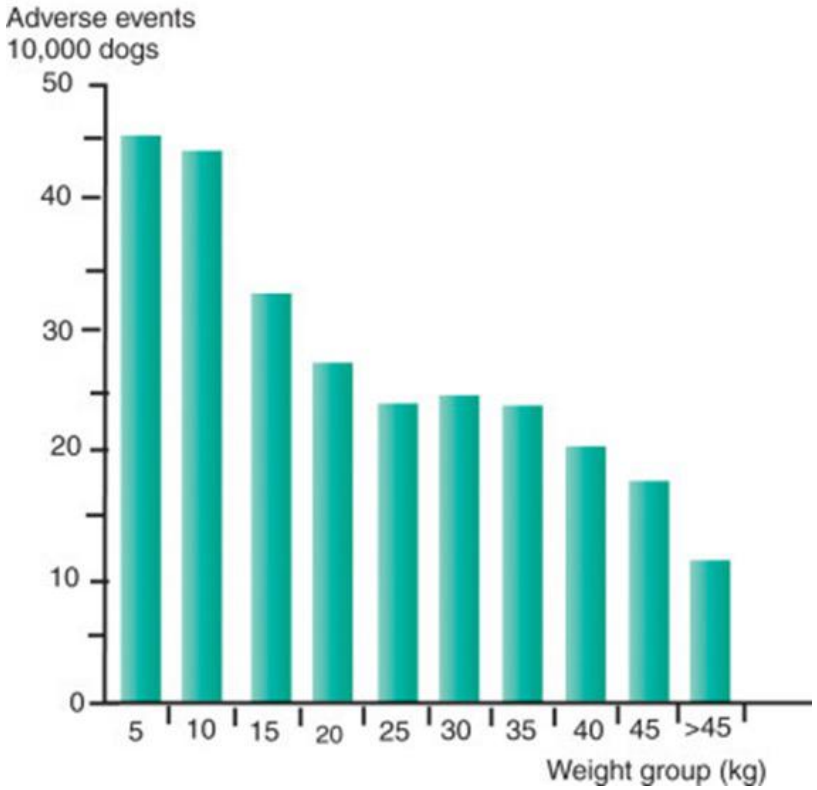
- Anaphylaxis more likely with killed vaccines

Concerns with vaccination?

Clinical Sign	Disorder type	Incidence Rate per 100,000 doses sold
Lethargy	Systemic	3.4
Emesis	Digestive tract	2.3
Hyperthermia	Systemic	1.7
Allergic oedema	Immune system	1.5
Injection site oedema	Application site	1.5
Anorexia	Systemic	1.3
Diarrhoea	Digestive tract	1.1
Injection site infection	Application site	1.1
Pale mucous membrane	Systemic	1.0
Injection site pain	Application site	0.8
Anaphylaxis	Immune system	0.8
Cough	Respiratory tract	0.7
Malaise	Systemic	0.7
Injection site reaction NOS*	Application site	0.7
Vocalisation	Behavioural	0.5
Lack of efficacy	Systemic	0.5
Loss of consciousness	Neurological	0.5
Ataxia	Neurological	0.5
Pruritus	Skin	0.4
Tachypnoea	Respiratory tract	0.4

*NOS – Not otherwise specified – i.e. not fully described

VMD position paper



Adverse consequences of vaccination - PMC (nih.gov)

University of Nottingham
UK | CHINA | MALAYSIA

Concerns with vaccination?

- Risk of autoimmune disease?
  - Vaccine-associated immune-mediated hemolytic anemia in the dog
    - Duval and Gieger JVIM 1996
  - IMHA more frequent in dogs within 30d of vaccination?

University of Nottingham
UK | CHINA | MALAYSIA

Leptospira vaccine safety?

- Least safe of the commonly used vaccines – BUT still relatively few adverse reactions

  > "In other words, the VMD has received fewer than 2 adverse reactions for L2, and fewer than 6 for L4, for every 10,000 doses sold." VMD

- Least effective of the commonly used vaccines
- Less duration of immunity
- Risk of immunological reactions is higher in toy breeds
- L2 vs L4??
- Decision to vaccinate based on risk to dog

University of Nottingham
UK | CHINA | MALAYSIA

Q & A