VACCINE-RELATED ISSUES

Today & Tomorrow for The DOG DETOX SUMMIT



The Picture of Optimal Health

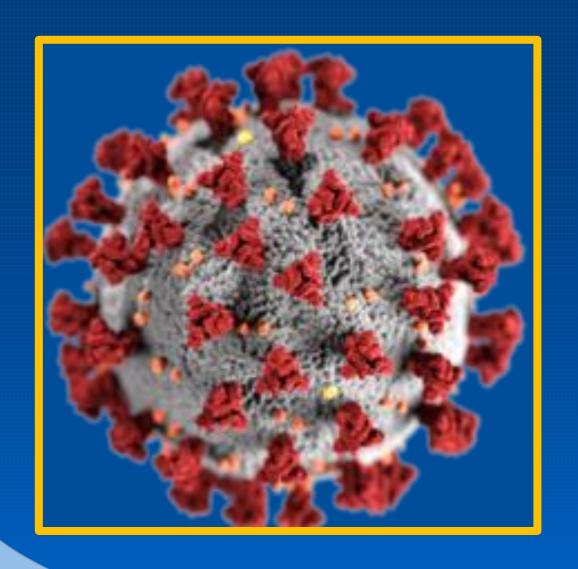


Pandemics -Spanish Flu 1918



Pandemics – Today in China





Coronavirus

Electron Microscopy (courtesy CDC)

Coronaviruses • • •

- belong to a large family of related viruses
- can infect and cause diseases of respiratory and gastrointestinal tracts
 of mammals and birds
- human strains first identified in 1960s, and caused common colds, which could lead to bronchitis and pneumonia
- zoonotic microbes that can jump between species and are transmitted between animals and people

Coronaviruses • • • (cont'd)

Intermediate Host required for zoonotic transmission



Horseshoe Bat



Pangolin (scaly anteater)



Dromedary Camel



Coronaviruses • • • (cont'd)

Intermediate Host required for zoonotic transmission



Civet Cat









Coronaviruses • • • (cont'd)

- **❖** Do <u>not</u> replicate readily in dogs, pigs, chickens or ducks
- ❖ Do grow readily in cats, Syrian hamsters, ferrets, and mink











Coronaviruses of Companion Animal Pets

- no current evidence had found that companion animals can be infected with SARS-CoV-2 or get COVID-19 disease
- no evidence that pet dogs or cats can infect other animals/ humans
- vaccinating dogs with commercial canine corona vaccines <u>cannot</u>
 provide cross-protection against SARS-CoV-2 and COVID-19 disease, as
 the enteric and respiratory canine corona viruses are different
- no vaccines are currently available for the respiratory coronavirus infection of dogs

Precautionary Measures for Safety

- ❖ If companion or other animals come in close contact with humans ill from or suspected of exposure to SARS-CoV-2 -----
- animals have no epidemiological role in this human disease, so only concern is when another zoonotic disease might be shared/ transferred between species
- common sense should prevail; people who have SARS-CoV-2 infection should limit close contact with other people, companion pets, and other animals
- SARS-CoV-2 aerosols survive a few hours in the air and a few days on surfaces

Precautionary Measures for Safety (cont'd)

- Social distancing -- leave 6 feet of space between people known or suspected of infection, avoid crowds in close quarters, and greet people by waving, nodding or bowing instead of hand shaking
- Importantly, wash hands in warm or cool soapy water or use a hand sanitizer for at least 20 seconds, and do not touch one's face (eyes, nose and mouth)
- Personal Protective Equipment (PPE) -- health care and food preparation workers, any exposure risk person or group, and anyone with an upper respiratory illness should wear a properly fitted face mask or face shield, gloves and gowns

Vaccine Hesitancy Amid SARS-CoV-2 and COVID -19

- Worldwide infection of SARS-CoV-2 and its disease, COVID-19, has focused health care professionals and society on the need for safe and effective vaccines
- Rapid development and mass production of mRNA, adenovirus vectored, and novel DNA vaccines against these mutating coronaviruses has been remarkable
- The goal is to vaccinate and protect a sufficient cohort (70% or more)
 of the world to achieve herd health
- With millions of doses of these vaccines given, the few reported adverse effects negate vaccine hesitancy and the naysayers concerned about long term neurodegenerative and other issues

Back to Vaccine Basics

Background on Vaccine Issues

- Over 50 years ago, Prof. Ron Schultz and I were the only two people saying we were over-vaccinating pets. We were called irresponsible in public because others were unwilling to consider the idea that vaccines might not always be needed or safe
- Since then, people aren't shooting arrows at us now because our backs are full of them! Joking aside, we remain determined to educate about this topic

More Background

- Even today only about 40% of veterinarians are estimated to follow the current WSAVA, AVMA, AAHA, CVMA and BVA vaccine policy guidelines
- There is no such thing as an 'up to date' or 'due' vaccination
- Enlightened veterinarians now can offer separated vaccine components, rather than give them all together, since the published data show more adverse reactions when multiple vaccines are administered together

Key Points on Vaccine Issues

- Modern vaccine technology has afforded effective protection of companion animals against serious infectious diseases
- But, this advancement brings increased risk of adverse reactions (vaccinosis)
- Some are serious, chronically debilitating and even fatal
- Must balance this benefit: risk equation
- "Be wise and immunize, but immunize wisely!" (Dr. Ron Schultz)

Benefits of Vaccines

- More lives saved, more animal production safeguarded than any other medical advance
- Eradicated smallpox, & nearly all polio and measles in people
- First vaccines were against small pox, anthrax, and canine distemper
- Significantly reduced endemics of canine distemper, hepatitis and parvovirus, but not in wildlife reservoirs
- Significantly reduced endemic feline panleukopenia
- Eliminated rabies in Europe; eradicated Rinderpest in Africa,
 foot & mouth disease in Europe

Memory Cell Immunity

- Memory Cells are created by B and T lymphocytes that respond to an immune stimulus. These cells replicate when responding to an invading antigen; form clones that retain information about each prior exposure; and thereby generate immune memory
- The immune system thus mounts a faster and more powerful anamnestic response when it encounters the same antigen again – e.g. with viral exposures and vaccines
- The immune system capacity for memory generates immunity through vaccines, but can also trigger adverse events like autoimmune disorders and allergies/hypersensitivity

Vaccines & Immune Memory Cell Immunity

- Vaccination may not equate to immunization
- But, vaccinated and truly immunized animals should be fully protected from disease
- Immune memory cell immunity should persist life long
- Giving boosters to immunized animals is unwise, as it will introduce unnecessary antigen, adjuvant and preservatives

Sterilizing Immunity =

- An immune response that completely prevents and eliminates an infection
- Animals properly immunized against the clinically important viral diseases have sterilizing immunity that not only prevents clinical disease but also prevents infection. Only the presence of antibody can prevent infection
- An animal with a positive serum antibody test is protected from infection
- Vaccinating that animal would not cause a significant increase in antibody titer, but hypersensitivity to vaccine components (e.g. fetal bovine serum) may develop
- Furthermore, the animal doesn't need to be revaccinated and should not be revaccinated since the vaccine could cause an adverse reaction (hypersensitivity disorder)

Sterilizing Immunity (cont'd)

- But, not all vaccines produce sterilizing immunity
- Those that do include: distemper virus, adenovirus, and parvovirus in the dog, and panleukopenia virus in the cat.
- Examples of vaccines that produce non-sterile immunity would be leptospirosis, bordetella, canine influenza, rabies virus, and herpesvirus and calicivirus — the upper respiratory viruses of cats
- While non-sterile immunity may not protect the animal from infection, it should keep the infection from progressing to severe clinical disease

Summary on Vaccine Policy

- AAHA 2003 Current knowledge supports the statement that •••
 - "No vaccine is always safe, no vaccine is always protective and no vaccine is always indicated"
- "Misunderstanding, misinformation and the conservative nature of our profession have largely slowed adoption of protocols advocating decreased frequency of vaccination"

Summary on Vaccine Policy

* WSAVA 2015-2017

From the late Prof. Michael J. Day •••

- "Vaccination should be just one part of a holistic preventive healthcare program for pets that is most simply delivered within the framework of an annual health check consultation."
- "Vaccination is an act of veterinary science that should be considered as individualized medicine, tailored for the needs of the individual pet, and delivered as one part of a preventive medicine program in an annual health check visit."

Vaccine Adjuvants

- Act to accelerate, prolong, or enhance antigen-specific immune responses
- Added into vaccines to enhance their immunogenicity, but this increases risk of autoimmune and inflammatory adverse events following vaccination
- Killed, inactivated vaccines containing adjuvants make up about 15% of veterinary biologicals used, but have been associated with 85% of the post-vaccination reactions
- Adjuvants have been used safely in human and veterinary medicine for decades, but there is increasing worldwide concern about the safety of using thimerosal (mercury) and aluminum

Vaccine Non-Responders

- Genetic trait; do not breed them
- They will remain susceptible to the disease life long
- Rate = 1:1000 for CPV (parvovirus)
 - Especially Black Labradors and Akitas
- Rate = 1: 5000 for CDV (distemper virus)
 - Especially Greyhounds
- Rate = zero for CAV (hepatitis, adenovirus)
- Rate = unknown for cats

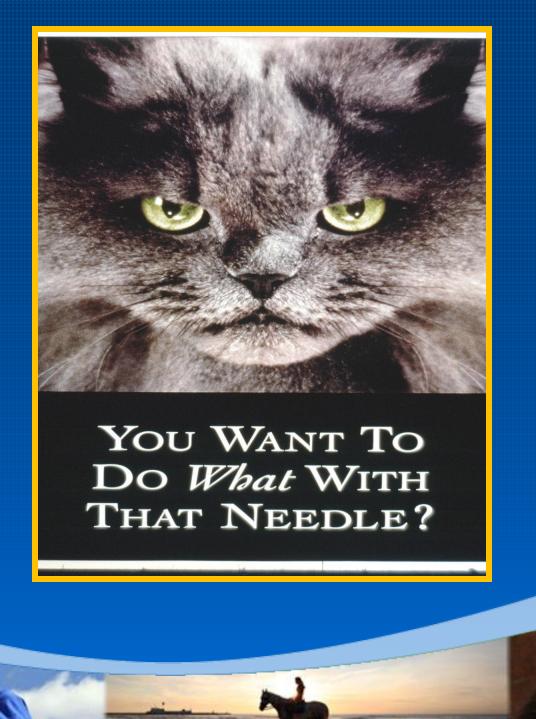
Adverse Vaccine Events = Vaccinosis

- How and Why do they occur ?
- Millions of people, pets and livestock vaccinated annually
- Reactions relatively rare --- about 3-5 events per 100 vaccines given
- Affects those genetically predisposed
- Can be acute, sub-acute, and delayed for 30-45 days
- New data links reactions to integrity and function of gut microbiome
- Heavy metal exposure from vaccines is an emerging concern for humans, pets and livestock. Aluminum and mercury found in brains of autistics, and from vaccine adjuvants that cross the blood –brain barrier after injection, then persist life-long.

More on Heavy Metals and Vaccinosis

- Vaccines containing aluminum are commonly used in sheep herd management and have been found to cause the ASIA syndrome
- Studies from Spain evaluated sheep divided into 3 groups: control, aluminum adjuvant only and aluminum adjuvanted vaccine. 16 inoculations were given to the groups over an 11-month period
- Results showed behavioral changes, aggression, stereotypic and excitatory responses, compulsive eating, and reduced sociability in both the adjuvant alone and adjuvanted vaccine groups but not in the controls
- Changes were more pronounced in the vaccinated group; some began after only 7 inoculations

[Pinczowski, et al. Pharm Res, Nov 3, 2018; doi.org/10/10.1016/j. phrs.2018.10.019]



'Core' Vaccines *
Dog Cat

Distemper

Feline Parvovirus

Adenovirus

Herpesvirus

Parvovirus

Calicivirus

Rabies

Rabies

* Vaccines that every dog and cat should have

Maternal Immunity & Protection

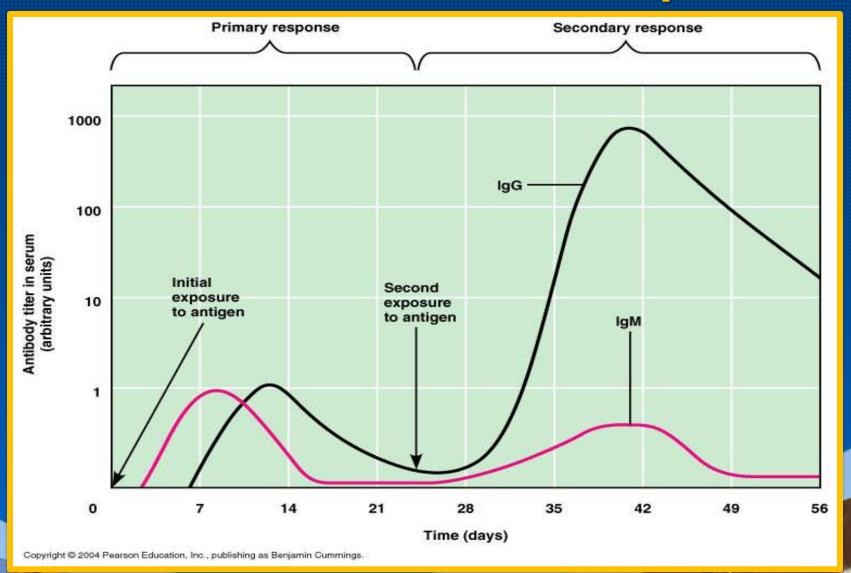
Milk Replacer

- Feeding milk replacer proteins instead of natural colostrum will coat bowel of newborns and shut down absorption of antibodies needed for protection from disease
- Give FFP (Fresh-Frozen Plasma) immediately to orphan or weak pups to get passive immunity; then add milk replacer

Vaccine Timing

- Last puppy vaccine at 16-18 weeks for protection
- Last kitten vaccine at 12-14 weeks for protection

Anamnestic Immune Response



Vaccine Dosage

Body Mass

- Same dose intended for toy and giant breeds
- Mhy \$
- MLV vaccines --immunogenic principle not based on body mass
- Killed inactivated vaccines -- should be adjusted for body mass
- Minimum/optimum doses for protection ?
- Excess antigen present

Vaccine Dosage (cont'd)

Neonate & Infant Children

- Urgent need to remove heavy metals, like aluminum and mercury, from infant vaccines
- Currently, neonates receive 17 times more aluminum from vaccines than allowed if doses were adjusted for body weight
- Body weight is ignored in human vaccines, as they use these heavy metals to enhance immune efficacy
- Experts now urge that aluminum and mercury not be given in vaccines until after brain maturation (6-7 months of age but preferably 12 months)
- Alternatives are <u>calcium phosphate</u> and <u>zinc</u>

[Weiler & Ricketson, J Trace Elements in Med and Biol. 48: 67-73, 2018; Ivanovski et al. ibid, 51:138-140, 2019]

Half-Dose CDV & CPV Vaccine Study in Small Breed Adult Dogs

W. Jean Dodds, DVM [JAHVMA, vol. 41; 12-21, winter 2015]

- Small breed adult dogs, between 3-9 years of age, were studied.
- Dogs were healthy and had no vaccines for at least 3 years.
- Purpose was to determine if just half-dose of bivalent CDV & CPV vaccine elicited protective serum antibody titer responses.
- Titer levels compared 1 & 6 months later vs pre-vaccine titers.
- Half-dose vaccine resulted in sustained protective serum antibody titers for all dogs studied.

Vaccine Dosage (cont'd)

Age

Optimal age for response

12 wks + for puppies

10 wks for kittens

Same for all breeds and sizes?

- Earliest age for safety
 6 wks for puppies and kittens
- Effective age varies
- Blocking effects of maternal immunity

When to Vaccinate Puppies? Which Vaccines are Needed? What About Socialization?

- Should receive MLV or recombinant "Core" vaccines (canine distemper and parvovirus) preferably either at 9-10 and 14-16 weeks of age (minimum protocol), or, at 9, 12 and 16-18 weeks
- Rabies vaccines are all adjuvanted killed products and are given as required by law, <u>preferably always given separately from other vaccines</u>, and as late as legally allowed e.g. 20-24 weeks of age. Thimerosal (mercury) free rabies vaccines are preferred and safer

More on Puppy Vaccines

- Other vaccines including hepatitis are optional, depending on circumstances and local disease risk
- Leptospirosis vaccines protect against only 4 serovars of the organism and are second to rabies vaccines in risk of hypersensitivity and other adverse effects. Use only if endemic
- Three or more days after the last round of puppy vaccines, they
 can be out and about to be socialized. Between 10-14 weeks
 of age, socialization can take place in the back yard or at
 puppy training classes with known friends and healthy dogs
- Until fully vaccinated, puppies should not walk on unfamiliar or public grounds; they can be carried about, if need to travel

Kennel Cough & Flu Vaccines

- Oral/Intranasal Bordetella releases interferon, which impairs growth of other respiratory viruses (parainfluenza, adenovirus - 2, influenza) [Oral preferred as it doesn't spray around the face of pet and those nearby]
- Injectable Bordetella vaccine does not release interferon
- Hypersensitivity reactions with intranasal vaccine
- Kennel cough vaccines not 100% effective. Needed?
- Influenza (vaccine needed?)
- Produces fever whereas kennel cough does not. When combined with Streptococcus, 2-3% can die

More on Canine Influenza

Best way to clinically distinguish canine influenza from kennel cough:

- Kennel Cough typically does not produce a fever unless it subsequently leads to pneumonia in debilitated dogs
- Canine Flu usually presents as a fever with a cough in the early stages. For mild fever (102-103 ° F) no treatment is needed. If above 104 ° F, then secondary pneumonia can result and should be treated promptly with antibiotics and supportive care.
- We do not routinely give canine influenza vaccines to <u>healthy</u> pups or adult dogs.
- Even though canine flu viruses (H3N2 and H3N8) are highly contagious

Hormonal State During Vaccination

Avoid Vaccination

- Period just before estrus (30 days)
- During estrus
- Pregnancy
- Lactation

Vaccination, Exposure & Protection

CDV (distemper virus)

- Vaccinates immediately protected, if exposed simultaneously
- MLV CDV does not shed appreciably

CPV (parvovirus)

- Vaccinates protected after 48-72 hrs; exposed pups get sick
- MLV CPV sheds from post-vaccine days 3-14; exposure risk
- Shed vaccine CPV not seen on Idexx SNAP, but present on CPV PCR of feces for 2 weeks

Periodicity of Booster Vaccinations

- No evidence that annual boosters are necessary
- Need to lengthen interval (every 3-7 years or more for healthy adults)
- Geriatric animals vaccinated only with caution
- Monitor serum antibody titers instead
 - Protection is indicated by a positive titer result
 - Any measurable antibody level shows protection

Alternatives to Current Vaccine Practices

- Measure serum antibody titers
- Avoid unnecessary vaccines or over-vaccinating
- Caution vaccinating sick or febrile animals
- Tailor specific minimal vaccine protocol for dogs/cats breeds or families at risk for adverse reactions
- Start vaccination series later (9-10 wks, dog; 8 wks cat)
- Alert caregiver to watch puppy/kitten behavior and health after boosters
- Avoid revaccination of those with prior adverse events

Available Vaccine Titers for Dogs

- Distemper Virus
- Parvovirus
- Adenovirus 2 (hepatitis)
- Bordetella
- Leptospirosis
- Lyme disease
- Corona Virus [not recommended]
- Rabies Virus (RFFIT: non export)

Vaccine Titer (Serum Antibody) Testing

- Assesses the immunologic status of animals against common, clinically important infectious diseases
- Determines if vaccine boosters are required or advisable
- Once animal's titer stabilizes it should remain constant for many years
- Protection is indicated by a positive titer result
- Any measurable antibody level shows protection
 - Titers sustained unless animal has medical problem such as cancer or receives high/prolonged doses of immunosuppressive drugs
- Viral vaccines prompt an immune response that lasts much longer than that elicited by classic antigen
- Clinicians often do not distinguish between these two kinds of responses

Options & Solutions

Education, Education, Education

- Understand duration of vaccinal immunity
- Accept potential for adverse events
- Recognize adverse events rather than dismiss or deny them
- Inform clients of issues and encourage options
- Offer titers for 'core' vaccines triennially/more often
- Explain optional vaccines may not be needed

Vaccine Conclusions for Canines*

Factors increasing risk of adverse events 3 days after vaccination:

- Young adult age
- Small-breed size
- Neutering
- Multiple vaccines given per visit
- These risks should be communicated to clients

* from Moore et al, JAVMA 227:1102–1108, 2005













































The Thimerosol (Mercury)-Free Rabies Vaccine



Rabies Challenge Study Update

- Rabies remains a serious and usually fatal disease in many countries, despite the absence in North America of documented cases of rabies in vaccinated, truly immunized dogs and cats for 2 decades
- While most pet dogs are vaccinated for rabies, fewer cats have historically been vaccinated until recent laws have required it
- The Rabies Challenge Fund research studies are now completed; the live rabies challenge phase results showed 80% survival at 5 years. [The formal study paper was published in the April 2020 issue of Canadian Journal of Veterinary Research]

Footprints in the Sand

