

Response to Aine Seavers' article "Three-year vaccination intervals: a different view from the parvo trenches of practice-land", *The Veterinarian* April 2010

In the spirit of "even-sided conversation", I wish to submit my perspective on the "vaccination debate" as a dog owner who has looked at the science behind the traditional vaccination protocols and the concept of immunisation.

Dr Seavers states: "...the current therapy [annual vaccination] works just fine."

My response: Vaccines are PROPHYLACTIC, not therapeutic, medicines. MLV vaccines are designed to mimic natural infection (without causing disease); they multiply in the body to elicit an antibody response (humoral immunity) and a memory response (cell-mediated immunity). This, I understand to be the basic principle of immunisation.

Dr Seavers states: *"...the three-year vaccine is ...not common in Germany and many vets in the UK...work out their own regime. That is a different picture from the one we are being told about by the WSAVA. THE VETS ON THE GROUND ARE NOT FOLLOWING WSAVA DICTUMS."*

My response: The Standing Commission on Vaccination (Vet) of the German Veterinary Association issued their updated vaccination policy in September 2007ⁱ (immediately after the WSAVA had presented their Guidelines at the August 2007 Annual Congress in Sydney); in the same spirit as the AAHA (2003 + 2006), the Association accepted the principle of vaccination, i.e. priming of the immune system, and recommends that vaccines (note: **not 3-year vaccines**) are not administered more frequently than every 3 years;

In the UK, the bulk of veterinary MLV vaccines for dogs have a 3 or 4-year label claimⁱⁱ; and

The WSAVA 2007 Guidelines very clearly state that they are not a standard of care but rather an educational tool for veterinarians, to alert them that sufficient evidence has been collected to justify the abandoning of the unscientific traditional revaccination protocols for small animal practice! Switzerland, the host of this year's WSAVA Annual Congress, published their extended interval vaccination recommendations in November 2008.

The WSAVA 2007 Guidelines are based on the AAHA 2006 update on the canine vaccination guidelines. The latter expressly state that

"Many other vaccine manufacturers [those who had not sought licensing of a 3-year vaccine] support their products as effective and protective when used in extended revaccination protocols. Furthermore, it is the opinion of the Task Force that vaccines against canine distemper virus (CDV), canine parvovirus (CPV), and canine adenovirus-2 (CAV-2) produced by major biologics manufacturers *all* produce excellent immune responses and can be soundly and reliably administered at the discretion of the clinician in

extended duration of immunity protocols. Discretionary administration indicates that all of these vaccines can be used in extended interval vaccination programs.”ⁱⁱⁱ

Richard Ford (2006)^{iv}, a member of the AAHA Canine Vaccine Task Force, explained that

“It’s important to note that the recommendations of the AAHA Canine Vaccine Task Force for triennial booster administration are based on data derived from vaccines that were on the market 5 years ago. Independent studies support the fact that extended durations of immunity (protection) against canine distemper, parvovirus, and adenovirus-2 are provided by all of the licensed (core) vaccines that were on the market between 2000 and 2003. **Any implication that a “3-year vaccine” must be used when adhering to current vaccination recommendations is wrong...and misrepresents the intent of the 2006 AAHA Canine Vaccine Guidelines...**the only significant change from the 2003 document [AAHA Canine Task Force: Canine Vaccination Guidelines, Recommendations and Supportive Literature] is new data supporting an extended (3 years or longer) duration of immunity derived from the recombinant canine distemper vaccine. **It is important to understand that the triennial booster recommendations in the 2006 Canine Vaccine Guidelines have been made without regard for a specific vaccine manufacturer, a specific vaccine, or any product sold as a “3-year” vaccine.**” (My emphasis)

Richard Ford (2003) answered the question “Why three-year intervals?”

“That’s another embarrassing question. It’s **completely arbitrary**. I will say there is **no science behind the three-year recommendation...**We picked a compatible medium, and it corroborates and corresponds with what was recommended for the cat too...We have some level of consistency, but **there’s nothing magical about three years at all...**”^v

The same article reports that “Schultz agrees with Ford adding that he picked the **three-year interval** because he thought practitioners would be more likely to accept it. “I thought if the veterinarian understood that if a **killed rabies vaccine** could work for three years that they could surely understand that a modified-live distemper, adeno or parvo (vaccine) could work the three years, minimum...**Modified-live vaccines have a much longer duration of immunity than killed vaccines.**” (My emphasis)

Dr Seavers seems to have not only been thoroughly misguided on the appropriate use of immunobiological products in dogs, but she seems oblivious to the standard safety and efficacy testing prescribed by regulators in the U.K./Europe^{vi}, the U.S.A.^{vii}, and Australia^{viii}, for MLV canine core vaccines. All codes stipulate the use of Specific Pathogen Free (SPF) puppies for challenge testing (20 vaccinates/5 controls in the USP, and 5 vaccinates (efficacy)/2 vaccinates (safety) in the EuPh/BP), and a 14-day observation period after challenge. Furthermore, Dr Seavers, and others, might benefit from perusing the articles published by all major vaccine manufacturers on their respective studies of their commercially available vaccines in extended DOI trials^{ix-x-xi-xii}. These reports appeared in 2004 and 2005, i.e. immediately following the release of the 2003 AAHA Guidelines which were compiled without industry participation.

As a pet owner, I expect that the ‘professional’ has a sound knowledge of basic biological and immunological functions in the target species as well as the pharmacological properties of the medicines he/she administers; also, that he/she keeps abreast of new findings as may be published from time to time; the latter leads to ‘best practice’ and is commonly referred to as ‘evidence-based medicine’.

Portraying the ‘professional’ as an information-deprived by-stander and at the mercy of the vaccine manufacturers in the ‘vaccine debate’ is a cop-out:

- What would stop a true ‘professional’ from investigating whether current practices are, in fact, current best practice?
- Why would said ‘professional’ not have verified the origin of current vaccination protocols and questioned the ‘arguments’ leading to the blanket annual revaccination interval for dogs (and cats) some 50 years ago^{xiii}, then used their training in veterinary medicine, coupled with some common sense, and implement more appropriate health care for their dog (and cat) patients?
- Why would the ‘professional’ have embraced the ‘early finish vaccines’, when he/she knows that maternally derived antibodies are a major variable in the immunisation equation?

As a pet owner, having looked at the science, I ask why veterinary practitioners in Australia:

- Blindly follow the mantra by the vaccine manufacturers for the revaccination of previously and adequately vaccinated, thus immune adult dogs (a practice implemented in the 1950s), and ignore expert opinion and consensus published over the last few years especially?
- Risk vaccine-preventable disease, especially CPV, in juvenile dogs by following, what Marian Horzinek^{xiv} called the “misguided industry initiative” of early-finish vaccines, without verifying the immune status of puppies following the second puppy shot?
- Accept that 35–50% herd immunity amongst the Australian dog population is sufficient to control diseases like CPV? Why would they not place more emphasis on vaccinating a greater number of unvaccinated dogs, instead of unnecessarily revaccinating already immune dogs?
- Accept that the full complement of vaccine antigens is administered to every puppy presented for vaccination, when (a) the half-life of CDV/CAV and CPV MDA is so vastly different, and (b) adverse reaction potential increases as the number of antigens per injection goes up, especially in small dogs?^{xv-xvi} Have you made it clear to the vaccine manufacturers that you want to be able to target, say CPV, and ask for the – elsewhere available – monovalent vaccines to be made available to the profession in Australia?

Dr Seavers’ concern that “...**the dam’s maternal antibodies are alleged to be potentially so potent from the stronger vaccine...**” (my emphasis) seems to be unfounded. We recall that the so-called 3-year study reports by all major vaccine manufacturers were published within 12 to 18 months of the AAHA Guidelines (2003) being released; we recall Richard Ford’s and the AAHA (2006) assurances that the Guidelines were based on ‘traditional’ vaccines.

Having looked at the 'science' of 3-year vaccines, I found that there are two such products registered in Australia, i.e. Fort Dodge Duramune Adult (now distributed by Boehringer-Ingelheim after the Pfizer take-over of Wyeth and divestiture of the dog + cat vaccine range), and Intervet Nobivac.

My in-depth study of the Duramune Adult revealed that this vaccine was registered here in July 2005^{xvii}. Registration approval was granted as a REPACK of Protech (Duramune); the latter had received a 39-month DOI claim^{xviii} to facilitate, it would appear, the registration of the 'repack' product; the "new" product was so licensed although it did not meet the "identical in every respect"^{xix} criteria stipulated by the APVMA.

When questioned about the major change in the DOI claim for the originally Australian designed (Webster 1991^{xx}) and made Protech, Raphael Zwijngenberg, then-Technical Services Manager of Fort Dodge Animal Health Australia explained that

"The Duramune Adult has to comply with higher viral titres compared to Protech Duramune for some fractions. Otherwise I agree they are very similar. Duramune Adult has got a 3-year claim though because a lot of work and effort went into this vaccine, and not Protech Duramune."^{xxi}

NOTE that the viral titres for CDV + CPV of both Protech Durmune and Duramune Adult were (and remain) the same, as per APVMA Gazette and the approved labels published on PUBCRIS database; only the CAV-2 titre in the Duramune Adult was (and remains) marginally higher compared with the Protech Duramune.

By December 2006, the Protech vaccine had been down-graded again, back to 12 months. The study documents for both vaccines, on which the APVMA approvals of variation (Protech Duramune) and registration (Duramune Adult) had been based, were released to me (with omissions) under the Freedom of Information Act. Both sets of study documents, leading to the products' registration by the APVMA, are IDENTICAL. The study of all 3 vaccine fractions in SPF puppies of the minimum age recommended for vaccination, and culminating in challenge exposure after 3 years of isolation, was carried out using a 1999 batch of DHPPi Duramune vaccine^{xxii}.

As for Nobivac, this vaccine is said to be the same as Canigen (Virbac); and the Summary of Product Characteristics (SPC) published on the U.K. regulator, Veterinary Medicines Directorate (VMD), website confirm that Nobivac is the same as Quantum (Schering-Plough, now part of the Intervet/Schering-Plough group) and Procyon Dog (also Schering-Plough)^{xxiii}, which, in turn is said to be repackaged and sold as Vanguard, marketed by Pfizer UK^{xxiv}.

Of interest in this context is that Canigen in the U.K. is authorized as a 3-year vaccine while the Australian registration still sports the 12-month claim. Furthermore, like many overseas formulations of C3 (DHP) vaccines, this product has higher viral titres than the Australian 'counterpart'; in fact, just about every MLV canine vaccine listed on the VMD Product Database seems to have higher antigen fractions than Australian registered products.

In their August 2005 newsletter, Virbac Australia alerted the profession to the dire outcomes of waning herd immunity, using the severe distemper outbreak in Finland during 1994/95 as an example; Dr Seavers also alludes to this outbreak, in her April 2010 contribution. What has not been acknowledged is that the vaccine coverage in Finland was very high (close to 100%) in the years leading up to the horrific outbreak. Investigations by the Finnish authorities squarely laid the blame for the outbreak at the feet of the market-leading vaccines; two products, enjoying 73% market share, were found to be non-immunogenic, leaving 'vaccinated' dogs unprotected^{xxv}. The non-immunogenic vaccines, coupled with a high percentage of young dogs, under the age of two years, amongst the population at that time, favoured the spread of distemper virus

amongst the vaccinated yet unprotected Finnish dog population. The offending vaccines were taken off the market early 1995. It sometimes helps to look at the whole story...

On the subject of titre testing and the strength of evidence, I would refer Dr Seavers, and Dr Kelman from Virbac, to the large-scale study by Twark & Dodds^{xxvi}. Somewhat closer to home, more than 50 % (or 30+ dogs) of the canine members of the dog sporting club I belong to have not been revaccinated for up to 7 years now; some dog had received the puppy series only, some had puppy shots and 1 booster at 12 months, and the majority had been vaccinated on a yearly basis for the first 4 to 6 years of their lives. These dogs range in age from 5 years to almost 14 years. All dogs have had their immune response verified by means of titre tests. None of the dogs has ever shown any signs of ill-health, including canine cough. The club's policy on proof of immune status was changed in 2004, after three middle-aged 'healthy' dogs had succumbed to immune-mediated disease the year before.

We vaccinate, man and beast, with the aim to elicit a robust enough immune response to protect the body from future attacks by the pathogen(s) vaccinated against. The aim of vaccination is IMMUNISATION. Research has confirmed that "memory B...cells stimulated at the time of vaccination/infection [and MLV vaccines are designed to replicate in the body to mimic infection] ...continue to produce antibody to the core vaccines in the absence of overt antigenic stimulation for many years..."^{xxvii} Maruyama et al (2000) conclude that

"the antibody system is able to generate true memory cells, which are independent of persisting immunizing antigen and enable the animal to produce secondary, high-affinity antibody responses. Like many naïve B cells⁽¹⁷⁾, these cells are long-lived and act in concert with long-lived plasma cells secreting antibodies over extended periods of time^(20,21) and with memory T cells, for the maintenance of which antigen also does not seem to be required."^{xxviii}

I trust that this very small selection of texts and references will give the reader some idea as to the wealth of published research information, compiled by accomplished scientists and readily accessible by anybody interested in updating their knowledge on vaccines and on the canine (and feline) immune system, to move the profession towards evidence-based medicine.

The judicious vaccination and appropriate health care of your patients is much more than "an interesting topic of debate"^{xxix}. The profession must start acting in the best interest of their clients and patients if they are to salvage any credibility and integrity.

Beate Mies
Pet Owner + Advocate for the Judicious Use of Vaccines in Dogs

References + Endnotes:

ⁱ Bundesverband Praktizierender Tierärzte e.V., Fachgruppe Kleintierpraxis (FGK) "Deutsche Impfeempfehlungen für die Kleintierpraxis", with the support of Deutsche Gesellschaft für Kleintiermedizin (DGK-DVG) (German Association for Small Animal Medicine), and **with participation of the German vaccine manufacturers** (My emphasis)

ⁱⁱ Veterinary Medicines Directorate U.K. – Product Database

ⁱⁱⁱ American Animal Hospital Association – 2006 Update of Canine Vaccination Guidelines

^{iv} Richard B. Ford "2006 Canine & Feline Vaccination Guidelines *A Forum on Issues and Controversies*"

^v DVM (US magazine) – July 1, 2003 “Industry, profession questions AAHA vaccine guidelines; minor change made while confusion grows”, by Kathy Baumgardner

^{vi} British Pharmacopoeia/European Pharmacopoeia:

5.2.6 Safety Testing for Vaccines

5.2.7 Efficacy Testing for Vaccines

^{vii} USDA, Center for Veterinary Biologics, Code of Federal Regulations Title 9--Animals and Animal Products

CHAPTER I--ANIMAL AND PLANT HEALTH INSPECTION SERVICE, DEPARTMENT OF AGRICULTURE PART 113--
STANDARD REQUIREMENTS:

113.40 Dog safety tests

113.305 Canine Hepatitis and Adenovirus Type 2

113.306 Canine Distemper Virus

113.317 Parvovirus Vaccine

^{viii} APVMA Guidelines for Format and Data Requirements for Application to Register New Veterinary Immunobiologics in Australia ---- replaced by Guideline 49/Vet MORAG Vol. 4 (10 May 2006)

^{ix} Omar Y. Abdelmagid, Laurie Larson, Laurie Payne, Anna Tubbs, Terri Wasmoen, Ronald Schultz (Schering-Plough) "Evaluation of the Efficacy and Duration of Immunity of a Canine Combination Vaccine Against Virulent Parvovirus, Infectious Canine Hepatitis Virus, and Distemper Virus Experimental Challenges", *Veterinary Therapeutics, Vol. 5, No. 3, Fall 2004*

^x E Mouzin, Marianne J. Lorenzen, John D. Haworth, Vickie L. King (Pfizer Animal Health) "Duration of serologic response to five viral antigens in dogs", *JAVMA, Vol 224, No. 1, January 1, 2004*

^{xi} Michael Gill, Jay Srinivas, Igor Morozov, Janell Smith, Craig Anderson, Sherry Glover, Deborah Champ, Hsien-Jue Chu (Fort Dodge Animal Health): "Three-Year Duration of Immunity for Canine Distemper, Adenovirus, and Parvovirus After Vaccination with a Multivalent Canine Vaccine", *Intern J Appl Res Vet Med, Vol. 2, No. 4, 2004*

^{xii} Thomas C. Gore, Nallakannu Lakshmanan, Karen L. Duncan, Michael J. Coyne, Melissa A. Lum, Frank J. Sterner (Intervet Inc.) "Three-Year Duration of Immunity in Dogs Following Vaccination Against Canine Adenovirus Type-1, Canine Parvovirus, and Canine Distemper Virus", *Veterinary Therapeutics, Vol. 6, No. 1, Spring 2005:5-14*

^{xiii} Marian C. Horzinek “Vaccine use and disease prevalence in dogs and cats”, *Veterinary Microbiology 117 (2006) 2-8*

“Why has veterinary medicine adopted a practice that causes raised eyebrows in the biomedical environment, e.g. when talking to immunologists? The reason is largely historic: in the first years of vaccine development, the objective of maximum protection was thought to be achieved by maximum antigenic stimulation. At the time this seemed to be the right thing to do, with the newly developed, attenuated distemper and canine infectious hepatitis virus preparations. It became common practice in subsequent vaccine developments, including the parvovirus preparations, without asking why.”

^{xiv} M. C. Horzinek “Vaccination Protocols for Companion Animals: The Veterinarian’s Perspective”, *J. Comp. Path. 2010, Vol. 142, S129eS132*

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- ^{xv} Novak, W. 2007. Predicting the “unpredictable” vaccine reactions. Proceeding of the NAVC North American Veterinary Conference. Jan. 13-27, 2007, Orlando, Florida
- ^{xvi} Moore, G.E., Guptill, L.F., Ward, M.P., Glickman, N.W., Faunt, K.K., Lewis, H.B., Glickman, L.T. 2005. Adverse events diagnosed within three days of vaccine administration in dogs. *JAVMA*. Vol. 227, No. 7, October 1, 2005. 1102-1108
- ^{xvii} Gazette APVMA 9, 6 September 2005 Page 12; 3. Veterinary Products based on Existing Active Constituents (Date of Registration: 25 July 2005)
- ^{xviii} Gazette APVMA 6, 7 June 2005; VARIATIONS (Date of Variation: 4 April 2005)
- ^{xix} Beate Mies, Letter to the Editor/*The Veterinarian* magazine, March 2006
- ^{xx} Cyanamid Websters COMMUNIQUÉ/Technical Update T002 May 1996 “Canine Parvovirus Protection with Protech Vaccines”: 4th generation: Websters launch Australia’s first and world second 12 week vaccines against Parvovirus – PROTECH Canine vaccine
- “The patented vaccine strain Passage 69 (P69)...A derivative of CPV-2 K3i strain isolated from a virulent case of parvovirus was obtained from James Cook University, Townsville, Australia...”
European Patent 0 485 463 B1/Application No. 90911906.7/Date of filing: 08.08.90
- ^{xxi} Letter from Raphael Zwijnenberg, Technical Services Manager/Veterinary Ethical Division, Fort Dodge Australia P/L dated March 2, 2006
- ^{xxii} Document B569-04-001R/Report Title: “Evaluation of Three-Year Duration of Immunity Duramune DAPPi+LC Vaccine in Six-Week-Old Puppies against Canine [Distemper], [Parvovirus] [and Hepatitis] Virus Challenge; Report dates June 14, 2004 [CDV], June 17, 2004 [CPV], June 21, 2004 [CAV-2]”; Batch Number: Duramune 8 (P85) DA2P+PV L#362056 + CvK/LCI L#1460-56-03Sept1999
- ^{xxiii} Marlies Böhm “Current vaccination strategies in dogs and cats”, *In Practice – January 2009*
- ^{xxiiii} Summary of Product Characteristics – Procyon Dog DA₂PPI/L; Vm 00201/4199; 09.09.2005
- ^{xxiv} Marlies Böhm “Current vaccination strategies in dogs and cats”, *In Practice – January 2009*
- ^{xxv} U. Rikula, L. Nuotio, L. Sihvonen “Canine distemper virus neutralising antibodies in vaccinated dogs”, *The Veterinary Record, November 18, 2000*
- ^{xxvi} Lisa Twark and W. Jean Dodds “Clinical use of serum parvovirus and distemper virus antibody titers for determining revaccination strategies in healthy dogs”, *JAVMA, Vol 217, No. 7, October 1, 2000*
- ^{xxvii} Ronald D. Schultz “Duration of immunity for canine and feline vaccines: A review”, *Veterinary Microbiology 117 (2006) 75-79*
- ^{xxviii} Mitsuo Maruyama, Kong-Peng Lam & Klaus Rajewsky “Memory B-cell persistence is independent of persisting immunizing antigen”, *Nature, Vol 407, 5 October 2000*
- ^{xxix} Mark Kelman, Virbac Animal Health “Vaccination frequency – formulating protocols”, *The Veterinarian, September 2009*