# Controversy and confusion: Revaccination of adult dogs and cats—An Update.

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## Introduction

Over the last 40–50 years companion animal vaccines have helped substantially to reduce the incidence of potentially fatal infectious diseases of dogs and cats (Appel 1999). Before the introduction of routine vaccination in the early 1960s, canine distemper was regularly encountered by veterinarians. Nowadays, it is extremely unusual to see a case in most developed, temperate countries. Similarly, when canine parvoviral enteritis first appeared in the late 1970s it caused severe disease and death in both puppies and adult dogs (Pollock and Carmichael 1979). Nowadays, parvoviral enteritis is seen much less frequently, and then almost invariably in young dogs that have been incompletely vaccinated. Infectious canine hepatitis and feline panleucopenia—two more diseases against which we routinely vaccinate—have also become very uncommon in many parts of the world. In large part, vaccination should be given the credit for reducing the incidence of these life-threatening companion animal diseases.

Why then, in recent years, have our companion animal vaccination protocols come in for so much scrutiny? Why have some leading veterinary associations and hospitals around the world decided to advocate and practice less frequent revaccination of adult dogs and cats (against some diseases) than some vaccine manufacturers still recommend? The answer to this question comes in two main parts, the first concerning the safety of companion animal vaccines and the second the duration of immunity induced by modern companion animal vaccines.

In this article, I shall aim to review arguments for and against regular, frequent revaccination of adult dogs and cats. At the end of the article, I shall offer some recommendations.

## Safety

Overall, modern companion animal vaccines seem to be remarkably safe. True, there have been occasional reports of adverse events (Sharp et al 1999; Harrus et al 2002; Evermann 2008), and even one unfortunate instance of bluetongue virus contamination of a vaccine batch that led to some canine fatalities (Akita et al 1994; Levings et al 1996), but these problems are few and far between. Some veterinarians passionately believe that a host of serious immune-mediated diseases (including hypothyroidism) can be blamed upon excessive use of vaccines, particularly live vaccines, but there is little or no objective evidence to support their arguments.

There is, however, one well-documented and often fatal adverse effect of feline vaccination, seen in a small minority of vaccinated cats, that has caused a huge furore.

In the early 1990s, veterinary pathologists at the University of Pennsylvania in Philadelphia, USA began to notice an alarming increase in the number of feline soft tissue sarcomas presented to their biopsy service (Hendrick and Goldschmidt 1991). Many of these ‘extra’ tumours were occurring in anatomical locations used for injection of vaccines and other substances. A few years earlier (in 1985/6), the first FeLV vaccine had been launched in America. In 1987, it had become a legal requirement that all cats in the State of Pennsylvania be vaccinated regularly against rabies. The University of Pennsylvania pathologists noticed aluminium particles in and near the tumours. Knowing that aluminium was used in many vaccine adjuvants, the pathologists hypothesised that the dramatic increase in the number of feline tumours they were seeing at these injection sites might somehow be related to recently altered vaccination practices (Hendrick et al 1992; Hendrick 1998).

Subsequently, large epidemiological surveys carried out in USA have confirmed an association between vaccination against both FeLV and rabies and development of injection-site sarcomas in cats (Kass et al 1993; Kass et al 2003; Kass 2004). A smaller study implicated killed, adjuvanted vaccines against panleucopenia and the feline respiratory viruses, herpesvirus and calicivirus (Lester et al 1996). There is scant evidence to suggest that modified live vaccines can induce sarcoma formation. In American studies, roughly 1-3 per 10,000 vaccinated cats were estimated to develop a tumour (Kirpensteijn 2006). Orange tabby cats may be more commonly affected than others, suggesting a genetic predisposition in some cats. It is thought that inflammation, most likely caused by vaccine adjuvant, precedes and predisposes to neoplastic transformation of fibroblasts at the injection site (Jelinek 2003). The more vaccines administered simultaneously, the higher the risk of cancer formation. It is not known for certain that annually repeated injections of adjuvant in the same anatomical location increase the risk of tumour formation at that site, but there are strong reasons to believe that this is the case.

Understandably, the emerging association between vaccination of cats and occasional development of malignant neoplasia at injection sites caused widespread concern amongst practising veterinarians and American pet owners, even though only a small minority of cats were affected. It posed for the American veterinary profession a public relations challenge of colossal proportions. Many people, both veterinarians and pet owners, began to ask whether adult cats *and* dogs were perhaps being over-vaccinated. Eminent veterinary immunologists—who had argued for decades that annual revaccination was entirely without a sound scientific basis—suddenly found an eager, attentive audience. So did veterinarians with passionate anti-vaccine sentiments, but little or no data.

Eventually, a few excellent peer-reviewed publications appeared, strengthening the view that vaccines (both canine and feline) might not be quite as safe as had been hoped. For example, a relationship between vaccination and development of often-fatal canine immune-mediated haemolytic anaemia was identified (Duval and Giger 1996). This relationship was proved to be *temporal*, but not *causal*. Although unproven, a causal relationship is biologically plausible because in other species (*e.g.*, humans) certain vaccines have been convincingly shown to cause serious immune-mediated diseases in some recipients (Shoenfeld and Aron-Maor 2000). Many veterinarians are convinced that other, slightly less serious canine immune-mediated diseases (such as immune-mediated thrombocytopenia and polyarthritis) are sometimes linked, at least temporally, to vaccination. However, the evidence is less clear cut, and once again a causal relationship can only be inferred.

Although our vaccination protocols first came under scrutiny because of safety concerns, I believe that safety is no longer the central concern, the debate has moved on. At issue now, is whether or not veterinarians can justify their revaccination recommendations to inquisitive, well-informed client-owners of adult dogs and cats who would rather not repeatedly vaccinate their animals, if it is not entirely necessary.

## History of revaccination practices and statements from professional societies

Current recommendations concerning annual revaccination of dogs and cats date back to the late 1950s and early 1960s and are not soundly scientifically based. In one of the earliest studies, approximately 1/3 of puppies vaccinated with a modified-live distemper vaccine did not have a "protective" antibody titre when they were checked one year after initial vaccination. On this basis, it was recommended that dogs should be revaccinated annually as a safety measure. Forty years on, many immunologists argue that antibody titres are an indirect and often rather conservative measure of anti-viral immunity, since they tell us next to nothing about cellular immunity and memory B-cells. "Protective" distemper titre cut-off values tell us what amount of passively transferred maternal antibodies would be sufficient *on its own* to protect an unvaccinated puppy. The puppies used to develop the original revaccination guidelines were not challenged with virulent distemper virus, so it is not clear how well (or poorly) protected they would have been against distemper, one year after vaccination.

In 1961 another researcher was concerned that widespread vaccination of dogs against distemper might substantially reduce natural exposure and therefore natural boosting of immunity. He suggested that practitioners might choose to revaccinate adult animals whose immune status was in doubt. He did not make a blanket recommendation for annual booster injections, but felt that practitioners would be best placed to exercise discretion in deciding on the frequency (if any) of revaccination.

Nevertheless, routine annual revaccination of adult animals became the accepted norm in some countries during the 1960s and 1970s. In 1978 the American Veterinary Medical Association (AVMA) issued a set of guidelines on revaccination frequency based primarily on contemporary practices. An updated AVMA report in 1989 made no substantial alterations to the earlier recommendations. Annual revaccination was recommended for all vaccine components, with one exception. Because of its public health significance, *rabies* was treated differently. It was required that duration of immunity (DOI) be demonstrated for rabies virus vaccines. DOI studies showed that several rabies vaccines could provide solid immunity that lasted for at least 3 years so these vaccines were given triennially in some states.

It is perhaps a testament to the overall safety and efficacy of companion animal vaccines that these recommendations remained unaltered for so long. Undoubtedly the incidence of canine distemper, infectious canine hepatitis and feline panleucopenia have declined dramatically since the 1950s and, more recently, vaccination has played an important role in protecting dogs from parvoviral enteritis.

In July 1997 the first International Veterinary Vaccines and Diagnostics Conference was held in Madison, Wisconsin, USA. About 500 veterinarians and other scientists attended. Afterwards, several American veterinary schools promptly switched to a triennial schedule of revaccination for both dogs and cats against "core" viruses (infectious canine hepatitis, distemper and parvovirus for dogs; panleucopenia, herpesvirus and calicivirus for cats). About three years later, Massey University in New Zealand followed suit and the New Zealand Veterinary Association published guidelines for its members in line with the new Massey University position.

In 1998, 2000 and again in 2006 the American Association of Feline Practitioners (AAFP) issued guidelines suggesting that adult cats should be vaccinated triennially, rather than annually, against feline panleucopenia, feline herpesvirus and feline calicivirus (Richards et al 2006). They did so knowing their advice ran contrary to most vaccine manufacturers' label recommendations. These guidelines were based on a careful examination of *limited* available data on duration of immunity induced by modern feline vaccines.

In November 2002, the American Veterinary Medical Association (AVMA) published a report from its Council on Biologic and Therapeutic Agents concerning cat and dog vaccines (Klingborg et al 2002). In this report it was stated: "*There is increasing evidence that some vaccines provide immunity beyond 1 year. Unnecessary stimulation of the immune system does not result in enhanced disease resistance and may expose animals to unnecessary risks"*. The report also mentioned under individual disease monographs that revaccination intervals for adult dogs and cats can be extended beyond one year for vaccines against canine distemper, canine parvovirus, canine infectious hepatitis and feline panleucopenia. There is an updated set of vaccination principles (an AVMA policy) on the AVMA website (http://www.avma.org/issues/policy/vaccination_principles.asp).

In 2003, and again in 2006, the American Animal Hospital Association (AAHA) published reports encapsulating canine vaccine guidelines. These reports confronted the matter of revaccination intervals head-on and stated that revaccination every 3 years against canine distemper, hepatitis and parvovirus with modified live vaccines is considered protective, despite some manufacturer recommendations for annual revaccination (Paul et al 2006).

In April 1998 the Canadian Veterinary Medical Association (CVMA) published an article entitled "Vaccine protocol change deemed premature". In this article they stated their intention to abide by manufacturers' revaccination recommendations for the moment. This article spawned a critical commentary, describing the CVMA position statement as "ill considered". Subsequently CVMA announced its desire to harmonise its future revaccination recommendations with those of the AVMA.

Most recently, in 2008, the CVMA adopted a new position statement very much in line with the AAHA and AAFP guidelines (Vallee 2008).

In 2007 (in Sydney), and again in 2010, the World Small Animal Veterinary Association (WSAVA) launched and published guidelines very much in line with those of the AAHA and AAFP, but with greater consideration for the needs and concerns of veterinarians practicing in less developed countries (Day et al 2007, 2010).

Finally, in June 2009, the Board of the Australian Veterinary Association (AVA) ratified a new policy on canine and feline vaccination that is very much in line with the WSAVA guidelines.

Overall, my interpretation of these recommendations and position statements is that there is a clear and strengthening trend for large professional veterinary organisations to recommend or support less frequent revaccination of adult dogs and cats against some important diseases. Vaccine manufacturers have been taking careful note of these recommendations and many have already altered their label recommendations as a consequence.

## Why do some veterinarians frequently revaccinate adult dogs and cats against 'everything'?

At first glance, the answer to this question seems perfectly obvious: we do it because we believe it is the best way to provide and maintain strong protection against important infectious diseases to the animals under our care. Perhaps so, but what about the almost universal recommendation for *annual* revaccination against all sorts of infections? Given that immune responses to naturally-occurring infections vary a lot, it seems highly improbable that protection provided by chalk-and-cheese vaccines should, in so many cases, conveniently last for just over a year. In fact it's not just highly improbable, it's simply not the case. Regardless of their labelling, we know that many companion animal vaccines protect for far longer than a year while others, directed against more 'difficult' diseases, struggle to protect for a full year. A discrepancy between label revaccination recommendations and actual duration of induced immunity is possible because manufacturers have not been required to supply 'ultimate' duration of immunity data in order to get their products licensed. A vaccine that protects for longer than what is claimed on its label has, in the past, been viewed as a good thing. Indeed it is a good thing, but even better would be vaccines that have been proved to protect for considerably longer than a year and are accurately labelled with the *actual* duration of immunity they can be expected to provide in a large majority of recipients.

So the real reasons why some veterinarians revaccinate companion animals frequently (usually annually) against 'everything' are that:

1. It is still a label recommendation of many of the suppliers of vaccines. To deviate from their recommendations would constitute 'off label' use of vaccine and might lay the veterinary practice open to criticism (or litigation) if a vaccine used 'off label' failed to protect an individual animal. The practice's professional indemnity insurance might even be jeopardised by such off label use of vaccine.
2. It has become an accepted norm for conscientious owners. Many owners enjoy visiting their veterinarian for an annual revaccination and feel they are behaving as good pet-owning citizens by doing so.
3. It provides a convenient opportunity for the veterinarian to check carefully for any developing health problems that may be entirely unrelated to vaccination; for example, periodontal and heart diseases. It also provides a ready opportunity for the client to ask any questions they may have about the general health status of their animal, and to purchase various health-related products, for example, wormers and flea treatments; *and*
4. Kennel and cattery proprietors are, as yet, relatively uninformed about the duration of immunity induced by modern vaccines. Consequently, these proprietors have formulated their own rules and regulations, in some cases without much input from veterinary

professionals. Since many clients need to board their animals each year, they must get their animals vaccinated to abide by the rules of their preferred cattery or kennel.

To my mind, the second and third points above would be excellent reasons for continuing indefinitely the practice of regular revaccination of adult dogs and cats, regardless of DOI considerations, if **a)**. the vaccines were completely safe, and **b).** they were provided at no cost to the client. Since the vaccines we administer are neither completely safe nor provided for free, I think we need to be convinced that each vaccine we administer can be expected to do something *directly* beneficial for the recipient and, by extension, for the client who is paying for it. Unfortunately, there is strong and mounting evidence that most vaccines administered to adult dogs and cats serve no beneficial 'immunological' purpose whatsoever. It is this evidence that has led the AVMA, AAHA, CVMA, AAFP, NZVA and AVA to issue significantly revised guidelines in the recent past.

## "Core" and "non-core" vaccines

"Core" vaccines are defined as those that should be administered to every puppy or kitten, and should be used in adults in a manner that maintains robust protection for life (Levy et al 2008; Day et al 2010). Generally, to be designated as "core", a vaccine must provide strong protection against a life-threatening disease that is thought to pose a substantial risk to the population being vaccinated. A list of "core" vaccines identified by AVMA, AAHA, AAFP, CVMA and NZVA that is relevant to Australia comprises canine distemper, canine infectious hepatitis and canine parvovirus type 2 for dogs; and feline panleucopenia, feline herpesvirus 1 and feline calicivirus for cats. In some parts of Australia, it would be appropriate to add to this list of "core" vaccines. For example, in some wet regions, Leptospira vaccines for dogs can be considered "core".

"Non-core" vaccines are those that need not be administered to every animal because of one or more of the following:

- The diseases against which they protect are relatively mild;
- the animal has very little chance of exposure to the relevant infectious agent(s);
- the vaccine can cause serious adverse effects, making the risk-benefit ratio unattractive; and or
- there is insufficient scientific information to allow an informed decision about the need, efficacy or safety of the vaccine.

Examples of non-core vaccines are those against feline chlamydophilosis, feline dermatophytes, canine and feline bordetellosis, canine and feline giardiasis, canine and feline coronaviruses and canine Lyme borreliosis. Many of these vaccines are not currently available in Australia. In addition, the commercially-available vaccine against feline immunodeficiency virus has been designated "non-core" in most of the published reports and guidelines. This designation is based upon uncertainties about efficacy and concerns about the challenge of distinguishing cats vaccinated with this vaccine from those naturally infected by FIV (Hosie and Beatty 2007). The vaccine is not being sold in Europe and is not selling particularly well in North America. In experiments conducted by the vaccine's inventor, it protected American cats against two strains of FIV. The vaccine failed to protect Scottish cats against a highly pathogenic Scottish strain of FIV (Dunham et al 2006). Further intensive study of this vaccine, including field trials, is warranted.

## "Long-lasting" and "short-lasting" vaccines

Modified live versions of some of the "core" vaccines mentioned above (canine distemper, hepatitis and parvovirus for dogs; panleucopenia for cats) are almost universally accepted to provide very long lasting protection, for well over 3 years, and possibly for life. This assumes that vaccine has been properly transported, stored and administered to a healthy animal and that, in puppies and kittens,

interfering maternal antibodies have waned sufficiently so that the animal can be successfully immunized by the vaccine.

Vaccines against the feline respiratory viruses (herpesvirus and calicivirus) provide relatively poor protection, but one expertly-conducted study has shown that substantial levels of protection can persist for at least 7.5 years (Scott and Geissinger 1997, 1999). It is not necessarily the case that a poor vaccine can be improved by administering it more frequently. For example, a major problem with feline calicivirus vaccines is that the strain in the vaccine (usually it is just one) may not cross-protect against the prevalent strains in a particular recipient's home neighbourhood (Pedersen et al 2000). More frequent vaccination against the wrong strain will provide little or no benefit.

It is generally held that available vaccines against leptospirosis, bordetellosis and feline chlamydophilosis induce relatively short-lived immunity, in some cases for less than a full year. The duration of immunity provided by canine parainfluenza virus vaccines has proved more difficult to determine precisely but may be shorter than 3 years. If protection against these infections is considered necessary for a particular patient, then revaccination every 6-12 months, or shortly before periods of high risk, is recommended.

Many Australian dogs and cats receive only long-lasting "core" vaccines. If, in the future, all manufacturers' label recommendations change to recommend much longer revaccination intervals, there is the potential that some animals will not be examined at practices every year because their owners will not be 'triggered' to bring them in by the need for revaccination. Annual visits to the veterinarian are easy to remember. Biennial, triennial or even less frequent revaccination recommendations may be confusing and difficult for clients to remember. Clients may be more easily lost to follow-up by practices. Understandably, some veterinarians find these prospects very worrying and are concerned that there will be a consequent overall decline in the quality of health enjoyed by pets and working dogs.

To combat these potential adverse effects, practices should vigorously market the professional skills of their veterinary staff and—if they are persuaded it provides a tangible health benefit to their patients—promote to their clients the advantages of frequent (for example, annual) health checks of each animal. Underplaying the importance of vaccination and emphasising the potential benefits of a thorough, expert clinical examination and professional consultation would seem sensible, even if changes to revaccination practices are not contemplated by practice staff in the immediate future.

## Recommendations offered to veterinary practices

1. Develop a practice policy dealing with all relevant aspects of companion animal vaccination. For example, decide what you think are your "core" and "non-core" vaccines. If the policy is sufficiently complicated, write it down clearly and keep it with your other written operating procedures. Make sure everyone in the practice knows and 'buys into' the policy. Clients should then receive consistent advice from any practice staff member they may consult.
2. Make sure front line staff members understand and are ready to explain why the practice has adopted its particular policy. All should be ready to answer questions from clients about alternative approaches, which other local practices may have adopted. Know some of the advantages and disadvantages of the alternative approaches.
3. If you decide to use vaccines "off-label" (*e.g.*, more or less often than the manufacturer recommends) make sure you obtain informed consent from clients before doing so.
4. Follow closely guidelines on the storage and use of companion animal vaccines. Check all batches of vaccines as they arrive with the courier. Return to sender any vaccines (especially modified live ones) that do not arrive at the required temperature (usually 2-8°C). Do not be embarrassed about this, it is essential that vaccines be handled properly to maintain their efficacy. Ensure you keep vaccines in a serviceable refrigerator that maintains your vaccines within the required temperature range. Only reconstitute vaccines immediately prior to use.

5. Vets in the practice should no longer inject vaccines into the interscapular furrow of cats. It is one of the worst possible places in which to detect and from which to resect a sarcoma. Commonly-used modified live vaccines against feline herpesvirus, calicivirus and panleucopenia are better administered subcutaneously over one or other of the scapulae; *i.e.*, a few centimetres lateral to the dorsal mid-line. It is easier to see and deal with any post-vaccinal lump that may arise in this location. This advice is offered even though the risk of a non-adjuvanted modified live vaccine causing a sarcoma is considered to be much lower than with use of adjuvanted vaccines.

6. Adjuvanted feline vaccines (killed or subunit) have the potential to cause injection site reactions and, in rare cases, sarcomas. The risk of sarcoma formation is fairly low (~1-3 per 10,000 vaccinates in countries where it has been studied). This is considered high enough to justify special precautions when using adjuvanted vaccines. Adjuvanted vaccines should be injected subcutaneously, as distally as possible, in one of the hind legs. In practice, this usually means just proximal to the stifle. If both FeLV *and* adjuvanted FHCP and or FIV vaccines are used in the practice, the FeLV vaccine should be injected into the left hind leg and the adjuvanted FHCP or FIV vaccine into the right hind leg. If FeLV and modified live FHCP vaccines are used, the FeLV vaccination site should be alternated between the left and right hind legs from year to year, to avoid repeatedly depositing adjuvant in the same anatomical location.

7. Owners should be instructed to watch and feel for development of lumps >1cm diameter at injection sites. Lumps form rather commonly after vaccination, the vast majority are of little or no concern, decreasing in size with the passage of time. However, a post-vaccinal lump >1cm diameter that persists for more than 3 months is of serious concern and should be biopsied. Incisional or needle (*i.e.*, Trucut®) biopsy, rather than an attempt at complete excision is recommended. These tumours can be very difficult to excise completely and if the first surgery is unsuccessful, the overall prognosis for the cat is worsened.

## Recommendations offered to kennels / catteries

1. In collaboration with your chosen veterinary advisor(s), develop a well-reasoned, science-based policy concerning your revaccination requirements. Take your time and do it properly. For example, make time to discuss your draft policy document with local veterinary practitioners. Once it has been formulated, make sure that all kennel / cattery employees understand and apply the policy consistently.

2. When examining a vaccination certificate, check that the animal has been vaccinated against the necessary diseases. Then check to see how far into the future the veterinarian says the animal should be protected against these diseases. In a world of changing revaccination recommendations, this is the most important information on the vaccination certificate. Nowadays, vaccine manufacturers do not all make the same duration of immunity claims. This situation is likely to become even more complicated in future. Trust what the veterinarian writes on the certificate about protection into the future.

3. Avoid setting your own hard-and-fast rules about when the animal must have received its last injection(s). Your rules might contradict vaccine manufacturers' instructions or local veterinary practice science-based policies. Such rules might also require your clients' animals to receive unnecessary ‘extra’ vaccinations, which are not entirely without risk.

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