**DEVELOPING A PRACTICE VACCINATION SCHEDULE IN ACCORDANCE WITH WSAVA GUIDELINES**

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**COMPANION ANIMAL VACCINATION HISTORY**

Vaccination of dogs and cats to protect from infectious disease has been practised globally since the 1960s. In developed countries vaccination has proven highly successful in maintaining control of life-threatening viral diseases caused by canine distemper virus (CDV), canine adenovirus (CAV), canine parvovirus type 2 (CPV-2) and feline parvovirus (FPV). Vaccination has also had major impact in reducing morbidity and mortality associated with infections caused by feline calicivirus (FCV), feline herpesvirus (FHV), canine parainfluenza virus (CPi), feline leukaemia virus (FeLV), *Chylamydophila felis*, *Bordetella bronchiseptica* and *Leptospira interrogans* and new infectious disease vaccines continue to be developed (e.g. feline immunodeficiency virus [FIV], canine influenza virus [CIV]). In endemic areas, rabies virus vaccination of companion animals has major impact on the prevalence of this zoonotic infection in the human population. When used in co-ordinated control programmes vaccination has led to elimination of two infectious diseases globally – human smallpox (1979) and bovine rinderpest (2011). We are far from eradicating companion animal infections, which remain highly prevalent in developing countries and emerge as localized outbreaks in even the most developed nations.

 Although vaccination is now well entrenched in companion animal practice, as for many medical and surgical procedures, vaccination theory and practice continues to evolve. This presentation reviews companion animal vaccination in light of the 2015 revision of the WSAVA vaccination guidelines.

**WHAT HAS TRIGGERED CHANGE?**

There are striking parallels in recent changes in vaccination practice in human and veterinary medicine. Attention has focussed over the past two decades on issues related to the safety of human and companion animal vaccines. Within the veterinary profession the discussion over vaccine safety first emerged following the 1989 publication that suggested that some aggressive cutaneous sarcomas in cats might be related to vaccination. The feline injection site sarcoma (FISS) remains a serious problem in many countries today. In 1996 attention was focussed on the possibility that vaccination might trigger autoimmunity in dogs and initial reports of vaccine-associated immune-mediated haemolytic anaemia (IMHA) and thrombocytopenia extended to cases of polyarthritis or glomerulonephritis triggered by vaccination and the identification of autoantibodies specific for thyroid proteins in dogs and renal tubular epithelial cells in cats.

 In parallel with these observations has been the enormous media attention given to human adverse reactions post-vaccination; in particular the now refuted claims that childhood vaccination might be associated with autism and Crohn’s disease. New human vaccine scares continue to emerge with the introduction of new products (e.g. the human papilloma virus vaccine for cervical cancer and the potential association between narcolepsy and H1N1 influenza vaccination). The airing of these claims in the media and through the internet has led to inevitable parallels being drawn between human and companion animal adverse reactions. In many countries influential public lobby groups have become prominent in providing web-based opinion (and often misinformation) on companion animal vaccination – and it is all too common for these concerns to be raised in the consultation room. The phenomenon of internet ‘vaccinophobia’ is now being studied and recorded in the scientific literature.

 So are companion animal vaccines safe? The first fact to recognize is that no human or animal vaccine can be guaranteed 100% safe in any individual – but vaccines are very safe products with a low prevalence of associated adverse reactions. The high safety of vaccines is a reflection of the rigorous safety testing that must be undertaken before any product comes to market. It is difficult to put precise figures on the prevalence of adverse reactions to vaccines in dogs and cats. Some data are available from governmental pharmacovigalence schemes and the published scientific literature and when all reactions are considered (from common mild and transient illness to rare instances of death) the figure is somewhere between 0.61 to 38 reactions per 10,000 doses of vaccine (sold or administered, respectively) for dogs, and 0.21 to 51.6 reactions per 10,000 doses of vaccine (sold or administered, respectively) for cats.

 Even though adverse reactions are uncommon, best practice medicine should dictate that we make every effort to reduce further the prevalence of such reactions, for the benefit of companion animals and their owners.

**HOW HAS THE PROFESSION RESPONDED?**

The veterinary profession has responded in an appropriate and responsible manner to concerns over vaccine safety and the prevalence of adverse reactions. Expert groups have been established and these have produced information and guidelines to allow practitioners to develop and implement safer and more scientifically robust vaccination practices. Guidelines have been produced by the American Association of Feline Practitioners (1998, 2000, 2006 and 2013), the American Animal Hospital Association (2003, 2006, 2011 and 2017), the World Small Animal Veterinary Association (2007, 2010 and 2015) and the European Advisory Board on Cat Diseases (2006, 2013 and 2015). These various guidelines are essentially similar in their recommendations and those from the WSAVA have had greatest global impact. Many national veterinary associations have endorsed the WSAVA guidelines or used them to develop their own national recommendations.

 There is often confusion over guidelines as in some instances they appear to conflict with recommendations given in the data sheets (or summary of product characteristics) that is the legal document that accompanies a vaccine. Put simply, guidelines are a reflection of current scientific thinking and offer advice to practitioners to help them use vaccines in the safest and most immunologically correct fashion. The advice given in guidelines is generally more current than that in data sheets, which for older products may not have been updated since initial licensure. Guidelines are not compulsory and have no legal standing. They may need to be adapted to local circumstances and are simply a tool for practitioners to use in developing a practice vaccination strategy. Where guideline recommendations do differ from those on data sheets (this is increasingly less common), then the application of guidelines recommendations (off-label use) should be done with informed client consent.

 The WSAVA guidelines are readily accessible from the WSAVA website, where you may also find a substantial information document written for pet owners and breeders and a series of single-page infectious disease fact sheets that are designed for use in the consultation room setting. What follows is a distillation of guideline recommendations given as 10 fundamental concepts in vaccinology.

1. **WE SHOULD VACCINATE MORE ANIMALS**

One of the major recommendations of the WSAVA guidelines is that as many animals as possible in a national or local population should be vaccinated. This comes from the concept of **herd immunity** which very simply states that where at least (for example) 75% of a population is vaccinated, it becomes very difficult for certain infectious agents to cause disease outbreaks in that population. There are clear examples of the importance of herd immunity in human and companion animal populations – where vaccination uptake has declined, allowing the re-emergence of previously controlled infections. It is best-practice medicine to ensure that as many dogs and cats in your practice area are vaccinated. Recent reports have suggested that one of the impacts of the current global economic recession has been reduced vaccination uptake by dog and cat owners – leading to concerns over the potential for disease outbreaks.

1. **VACCINES ARE CORE OR NON-CORE**

All vaccination guidelines categorize vaccines as **core** or **non-core**, which provides a framework for considering how these different products might best be used. Core vaccines are those which every dog or cat should receive to protect them from diseases that are life-threatening or that cause significant morbidity. Core canine vaccines for dogs are those that protect against CDV, CAV and CPV-2 and for cats FPV, FCV and FHV (and for both species, rabies in endemic areas). Non-core vaccines are those that are only required by some dogs and cats, where their lifestyle or geographical location puts them at risk of contracting disease.

1. **NON-CORE VACCINES SHOULD BE SELECTED ON BENEFIT-RISK ANALYSIS**

Which vaccines are non-core may therefore differ from country-to-country, from state-to-state or even town-to-town. Practitioners must assess available information on local disease prevalence and take into account the lifestyle of the individual animal when deciding on the use of non-core vaccines. This means a fundamental change in the delivery of vaccination, in which there is a move away from the ‘practice vaccination policy’ (the same protocol applied to every dog or cat that walks through the door) to ‘**individualized medicine**’ related to the needs of that individual animal.

1. **CONTRIBUTE TO DISEASE SURVEILLANCE**

In human medicine, informed decision on the use of non-core vaccines can be made on the basis of disease surveillance data that precisely maps where particular diseases are prevalent. Sadly, we lack such data in companion animal medicine, but there are some national voluntary disease reporting schemes that collate and publish disease distribution maps for the key canine and feline vaccine-preventable diseases. It should be beholden on all veterinarians to contribute information into these databases for the benefit of our animals and their owners.

1. **CORE VACCINES SHOULD BE GIVEN NO MORE FREQUENTLY THAN EVERY 3 YEARS**

This fundamental change is one of the key platforms of vaccination guidelines. When triennial revaccination of adult animals was first recommended, all vaccine products had a 1-year minimum licensed **duration of immunity** (DOI) and so this shift was regarded as contentious and treated with suspicion. A decade later, in the USA and Europe virtually all core canine MLV vaccine products and all FPV products had a 3-year minimum licensed DOI and triennial vaccination is now the norm. So what is DOI and how does it influence the choice of revaccination interval?

 DOI is simply the time after vaccination that an immune response (generally the presence of serum antibody to the vaccine antigens) can be detected. The DOI varies between different vaccines. Serum antibody titres decline relatively rapidly after vaccination with *Leptospira* or rabies, but persist after vaccination with MLV CDV, CAV, CPV-2 or FPV. A second term ‘**duration of protection**’ (DOP) is used to describe the time after vaccination that one can challenge an animal with a virulent organism without it developing disease (or pathology, or death depending on the claim for the vaccine). An animal may lack serum antibody, but still have effective cellular immunity and immunological memory and so be protected from disease. For FHV infection, cellular immunity provides a better correlate to protection than serum antibody. Similarly, for intranasally-administered CPi and *Bordetella* products, local mucosal antibody (particularly IgA antibody) is a more relevant correlate of protection than serum antibody concentration and mucosal immunity may also correlate better with protection against FCV. Although DOI and DOP are technically different terms, we often use DOI in reference to protection.

 Vaccine licensure requires that the manufacturer provides information on the **MINIMUM** duration of immunity of the vaccine. Traditionally this was for a 1-year period, which is why vaccines were licensed with a 1-year DOI. As stated above, most manufacturers have now provided further experimental data that support a **MINIMUM** duration of immunity of at least 3 (and sometimes 4) years. These new studies are generally done with the identical (or very similar) vaccines – it is not that some wonderful new product has been developed that provides longer-lasting immunity. MLV core vaccines with a 1-year licensed DOI have always been able to provide long-lived (and probably lifelong) immunity. For that reason, even in countries where core MLV vaccines still have only a 1-year licensed DOI, they can effectively be used in triennial programmes. Of course, where licensed products carry a 3-year DOI, it becomes ‘off-label’ to use them annually and such usage should only be with informed client consent.

 But if 3 years is the MINIMUM duration of immunity – what is the maximum? In reality, core MLV vaccines (CDV, CAV, CPV-2 and FPV) probably provide animals with lifelong immunity following appropriate puppy or kitten vaccination (see below). There are two forms of evidence that support a longer DOI than that currently accepted globally as minimum (3 years). The first is serological. The presence of virus neutralizing serum antibody is a strong ‘**correlate of protection**’ for CDV, CAV, CPV-2 and FPV and WSAVA guidelines indicate that the presence of antibody at any titre equates to a protective immune response and the presence of immunological memory. Numerous experimental and field studies have shown that animals vaccinated as pups or kittens (and not routinely as adults) remain seropositive for up to 14 years and Australian field data show protective titres in dogs last vaccinated >42 months previously (and up to 9 years previously). More importantly, there are **experimental challenge data** that show robust protection on challenge of dogs last vaccinated up to 9 years previously with core canine vaccines, and up to 7.5 years previously with core feline vaccines. Whether in future canine and feline vaccines will carry even longer licensed DOI depends upon whether manufacturers are able (financially and ethically) to make the large investment required to provide experimental challenge data.

1. **ENSURE PROTECTION OF PUPS AND KITTENS**

The reasoning behind the use of multiple core vaccines in primary vaccination of puppies and kittens is a fundamental immunological principle related to the blocking effects of **maternally-derived antibody** (MDA) against vaccine antigens. It is not possible to predict for any one animal when the ‘window of susceptibility’ (where there is no longer sufficient MDA to provide adequate protection, but still sufficient MDA to block endogenous response to vaccination) might lie. Veterinarians have become comfortable with vaccinating at 8 and 12 weeks assuming that MDA will have degraded in all pups and kittens by 12 weeks of age. New data suggest that higher-titre modified live virus core vaccines increase the concentration of MDA, which persists for a longer period. These data suggest that at 10 weeks of age, only 75% of pups are capable of responding to CPV vaccine and that at 12 weeks of age, only 90% of pups can respond. In some kittens, MDA has been shown to persist to up to 20 weeks of age. For this reason we now recommend that a third vaccination in the puppy and kitten series be given at 16 weeks or older, when all animals should be able to respond. Importantly, the puppy or kitten vaccination schedule must include either a 26 or 52 week fourth vaccine.

 The guidelines advice on puppy vaccination is at odds with the introduction of ‘early finish products’ that are designed to be given at 8 and 10 weeks of age to permit early socialization of puppies. Guidelines groups recognize the importance of early socialization for the behavioural development of young animals, but caution that there is an element of risk in this practice.

1. **ADULT ANIMALS MAY BE VACCINATED EVERY YEAR – BUT JUST NOT WITH EVERYTHING!**

There is a common misconception that guidelines advice is that animals may not be vaccinated every year and that this may therefore reduce veterinary visits and impact on practice income. In fact, in most situations, dogs and cats will still receive an annual vaccination – but just not with all components. This situation arises because most non-core vaccines retain a 1-year DOI and cannot be used effectively at intervals of greater than 1 year. So in reality, while an adult dog may only receive MLV CDV, CAV and CPV-2 every 3 years, in the intervening years the animal may receive non-core vaccines depending on that animal’s benefit–risk analysis (and providing that there are product ranges available that contain the appropriate monovalent or combination antigens). Although all three core feline MLV vaccine components (FPV, FCV and FHV) are recommended for triennial use in low risk adult cats, only the FPV component has a triennial license in some countries. One product has recently been licensed with a 3-year claim for FCV and FHV as well as FPV. It is recognized that the lifestyle of some cats (e.g. multicat households or frequent cattery visits) may increase the risk for upper respiratory tract infection and so benefit–risk analysis in these animals suggests that it is acceptable to give annual FCV and FHV vaccination (again providing that suitable product ranges exist). Whichever schedule is chosen, the important concept is that reduced numbers of vaccine antigens are being delivered to that animal overall, thereby increasing the margin of safety.

1. **MINIMIZE USE OF ADJUVANTED VACCINES IN CATS**

Although it is now clear that FISS may be linked to a wide range of injectable products, there is still evidence that the local inflammatory response that precedes neoplastic transformation may be more intense in the presence of adjuvant. Non-adjuvanted feline vaccines should be used where available. Advice varies on the optimum site of vaccination for cats and the distal limbs, lateral abdomen and distal tail are all suggested. At very least vaccines should not be administered into the scruff and the site of administration should be rotated (and recorded) on each occasion.

1. **USE SEROLOGICAL TESTING TO AID DECISION MAKING**

Until recently, determining whether an animal had serum antibody specific for vaccine antigens required sending a blood sample to a specialist diagnostic laboratory for virus neutralization (CDV, CAV, FCV, FHV) or haemagglutination inhibition (CPV-2, FPV) testing. Simple in-house test kits are now available that can determine the presence of serum antibody to CDV and CPV-2 (e.g. Synbiotics TiterchekTM) or to CDV, CAV and CPV-2 (e.g. Biogal VaccicheckTM) or to FPV (e.g. Biogal Feline VaccicheckTM). There are multiple uses for such kits in a vaccination programme to assist with decision making on vaccination and to reduce vaccine load in an individual animal. Such kits are now well-entrenched as part of the practice laboratory in the USA and are becoming popular in Europe; including within corporate practice groups. Informed pet owners may on occasion request serological testing instead of routine revaccination.

 The canine kits may be used to determine whether a pup has responded to primary vaccination by testing at 20 weeks of age. This is particularly relevant for some low-responder breeds (e.g. rottweilers) where alternative strategies might be implemented on the basis of the test result. Serological testing may also be invaluable in determining whether an animal that has previously suffered an adverse reaction to vaccination (e.g. a dog with vaccine-associated IMHA) requires revaccination that may trigger a further episode of disease.

 Serology may be used to determine the best vaccination protocol for an adult dog with ‘lapsed’ vaccination or of unknown vaccination history. A seropositive adult dog does not require core vaccination and may move to a triennial revaccination programme. A seronegative adult dog should only require a single dose of core MLV vaccine with triennial boosters. For non-core vaccines, two doses and then annual boosters are required.

 In the context of the annual health check (see below), serology may be used routinely at the time of the annual veterinary visit in order to determine vaccine requirements for the coming year. The aim of this is simply to avoid unnecessary revaccination and minimize the risk of adverse reactions.

 Serological testing also has a valuable role to play in shelter outbreaks of infectious disease (e.g. CDV, CPV and FPV). Testing can rapidly determine which animals within a shelter are protected and which are susceptible and similarly determine which animals might safely enter a shelter during an outbreak. Testing avoids the need to destroy all animals in the shelter as might previously have occurred.

1. **VACCINATION SHOULD BE DELIVERED AS PART OF AN ANNUAL HEALTH CHECK PROGRAMME**

 All of the above concepts are enshrined in the ‘**annual health check**’. The annual health check programme was developed in the USA and is becoming increasingly popular in Europe. The annual health check is a new means of marketing and promoting veterinary services. There is a move away from using vaccination as the primary reason for an annual veterinary visit, towards a professional consultation that considers equally all aspects of the health and well-being of the animal. The use of ‘annual booster’ terminology and reminder cards should be replaced by reminders to visit for the annual health check. Vaccination becomes just one part of a discussion between the veterinarian and client. Decisions about vaccination are made on the basis of the lifestyle of the individual (individualized medicine) and are reviewed annually, perhaps with the aid of serological testing. There is no longer a ‘one size fits all’ vaccination regime. The prominence of vaccination might also be reduced in invoicing – the client should not be paying for the vaccine or vaccination *per se*, but for the professional consultation. The vaccine is often provided at cost price (or even for free) in many programmes where the professional fee is the top line. None of this threatens practice income – it is the presentation and marketing that changes – and where used appropriately, practice income may actually benefit. Put simply, this is preventive healthcare for pets; and many practices and corporate groups have now introduced effective preventive healthcare packages for their clients.

**FURTHER READING**

The 2015 WSAVA Vaccination Guidelines, Disease Fact Sheets and the 2015 WSAVA Vaccination Guidelines for Owners and Breeders of Dogs and Cats are all available from the Vaccination Guidelines Group area of the WSAVA website:

http://www.wsava.org/guidelines/vaccination-guidelines

Day MJ (2017) Small animal vaccination: a guide for UK vets. *In Practice*, **39**, 110-118. [also available from the WSAVA website]