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WSAVA VACCINATION GUIDELINES

VACCINE SEROLOGY

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THE ROLE OF SEROLOGY IN VACCINATION DECISION MAKING

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Protection is the ability of a vaccine to prevent or reduce the effects of infectious disease (depending on the claim for the particular vaccine) when a vaccinated individual encounters virulent infectious agent. In regulatory terms, protection is defined in the context of a challenge experiment. For European vaccine licensing, 80% of vaccinated animals must be protected from disease, while 80% of controls must succumb to the infection. Correlates of protection may be used to indicate whether a vaccinated animal is likely to be protected from challenge with virulent pathogen. It is now well recognized that the presence of virus-specific serum antibody correlates strongly with protection from canine distemper virus (CDV), canine adenovirus (CAV), canine parvovirus (CPV) and feline parvovirus (FPV). In contrast, rabies serology is only used to determine whether vaccinated dogs or cats achieve a mandated antibody titre at a particular time post vaccination for the purposes of pet travel to certain countries.

Numerous studies have shown that dogs that were appropriately vaccinated as puppies (i.e. according to current guidelines) have persistence of protective serum antibody titres for long periods of time and up to the lifetime of the animal. The most recent of these studies shows that dogs last vaccinated up to 9 years previously have protective titres of serum antibody [1] and in an experimental setting; such antibody has been demonstrated up to 14 years after the last vaccination [2]. Similar studies clearly show persistence of serum antibody to FPV in vaccinated cats.

Serological Testing

Until recently, the only means of testing for serum antibody specific for vaccine antigens was to submit samples to a specialist diagnostic laboratory. The 'gold standard' tests for detection of antibody to CDV, CAV and rabies virus is the virus neutralization (VN) test and for CPV and FPV the haemagglutination inhibition test (HAI). Testing laboratories provide an antibody titre

and will suggest whether that titre is above a threshold that is considered 'protective'. The titre is defined as the reciprocal of the last serum dilution giving an unequivocally positive reaction in a serological test. Practitioners must remember that the titre indicates a range and is not a fixed number. For example a titre of 640 indicates that the serum sample contains antibody in a range not less than 320 and not more than 1280 in a doubling dilution series. Recently, in-house test kits have become available for the determination of the presence of protective concentrations of serum antibody against vaccine-preventable viral diseases of the dog and cat. The TitreChek™ test is produced by Synbiotics and marketed by Zoetis, while the VacciCheck™ test is produced by BioGal Laboratories. New test kits continue to emerge (e.g. Fastest™, Diagnostik Megacor, Austria). TitreChek determines whether a dog is protected against infection by CDV and CPV, while VacciCheck tests for protective antibody against CDV, CAV and CPV. A separate VacciCheck kit tests cats for the presence of serum antibody against FPV. In some countries the feline VacciCheck kit still includes feline calicivirus (FCV) and feline herpesvirus (FHV), but these antigens are being removed as the correlation between seropositivity and protection is less clear for these infectious agents. The kits are ELISA-based technologies, but while TitreChek uses a familiar microtitration plate format, the VacciCheck system uses an 'immunocomb' in which the reactions occur on spots impregnated into the teeth of a card-like comb and Fastest is a lateral flow procedure. TitreChek and VacciCheck kits have been validated against the gold standards, are simple to use in practice and provide a result within 20–30 minutes. Testing currently costs more than the price of a vaccine. Helpful instructional videos are available on-line (see Maddies Fund: <http://www.maddiesfund.org/maddies-laboratory.htm>) that work through the performance of each test kit. There are some variations between the two kits: for example both can be run with serum or plasma, but only the VacciCheck kit may be used with a whole blood sample. The 'read out' for the TitreChek system is a simple 'yes or no' (protected or not) answer, while VacciCheck provides a semiquantitative scoring system.

Both tests claim good sensitivity and specificity and there are now several published papers that independently evaluate the kits against gold standard tests. One study of the feline VacciCheck test examining antibody in shelter cats reports a sensitivity of only 49% but specificity of 99% for FPV [3], but another reports 78% and 89%, respectively [4]. In the same animals (in the first study) the sensitivity for FHV was 91% with 97% specificity and for FCV, the figures were 90% and 91%, respectively. The TitreChek kit was evaluated in a study of shelter dogs in Florida, giving a sensitivity of 98% for CPV (specificity 98%) and a sensitivity of 88% for CDV (specificity 95%) [5]. A further shelter study used

the TitreChek kit to evaluate seroconversion one and two weeks after vaccination in a population of proven seronegative dogs entering the shelter [6].

A new UK study has used VacciCheck to test serologically a population of 486 dogs visiting two large practice groups. These dogs were last vaccinated up to 124 months previously and the rates of protection were 96% for CDV, 97% for CAV and 98.5% for CPV-2 [7].

Although this current generation of test kits is a major advance, the ideal test would be rapid (i.e. 5 minutes within the period of a consultation), individual (rather than needing to be batched), cheap (cheaper than a vaccine) and able to give a simple yes/no (protected/not protected) answer.

Applications of In-house Testing

There are several applications of these test kits within the veterinary practice. The first of these is to determine whether puppies have appropriately responded to the primary course of core vaccination. According to current guidelines, the third dose of core vaccine should be administered at 16 weeks of age or older. Testing pups at 20 weeks of age will indicate those that are seropositive and therefore protected. Such pups may not require the fourth 26 week (or 52 week) vaccine. Seronegative pups are not protected and may be revaccinated and retested. Those that fail to respond after revaccination may be either 'low responders' or genetically-determined 'non-responders' that are incapable of making an immune response to that antigenic component of the vaccine. Such animals are estimated to be rare within the population, but there are higher risk breeds including the rottweiler that has a known predisposition to mounting less effective immune responses to CPV and rabies virus.

Another indication for serological testing is to determine the protective status (and therefore core vaccination requirements) of a newly adopted dog of unknown vaccination history or a dog which has not been revaccinated for some time. Seropositive dogs remain protected, while seronegative animals should be vaccinated.

When an animal has a history of an adverse event following vaccination, serological testing can be used to determine whether core revaccination is necessary for that animal. If vaccination is suspected as a trigger factor in an adverse event (e.g. an immune-mediated disease), then vaccination should be minimized in that animal in the future. As long as dogs remain seropositive for CDV, CAV and CPV they do not require revaccination. The use of non-core vaccines in such dogs should be considered carefully.

It is becoming increasingly popular for practices that have embraced the 'annual health check' concept to routinely offer serological testing in lieu of triennial core

revaccination. Clients are appreciative of this option and it makes greater medical sense to determine whether a core vaccine is required than to give a vaccine unnecessarily. Triennial 'titre testing' is adequate for adult animals, but current advice for geriatric patients (i.e. dogs > 10 years of age and cats >15 years old) would be to perform annual testing.

Finally, in-house serological testing has revolutionized the ability of the veterinarian to manage infectious disease outbreaks in animal shelters – particularly CDV, CPV or FPV outbreaks. Animals within the shelter are tested in order to identify seropositive and protected animals that should be housed together and separated from seronegative (susceptible) animals that will then be vaccinated. Seronegative and vaccinated animals should not be adopted out of the shelter until beyond the incubation period for the disease (2 weeks for CPV or FPV; 6 weeks for CDV) and they have seroconverted. Animals needing to enter the shelter should also be tested. Seropositive (protected) animals may enter and be housed with the seropositive residents, while seronegative animals should not enter the shelter and rather be fostered elsewhere.

Further Reading

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