The role of antibody titer testing in vaccination policy of dog and cat

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Introduction

Current vaccination guidelines recommend multiple vaccinations of pups and kittens before the age of 16-18 weeks, a booster vaccination between the age of 6 months and one year and subsequently 3 yearly revaccinations for the core vaccines. The core vaccines of dogs are those that protect against canine distemper virus (CDV), canine adenovirus-1 (CAV) and canine parvovirus-2 (CPV). The core vaccines of cats are those that protect against feline panleukopenia virus (FPV), feline herpes virus (FHV) and feline calicivirus (FCV). For FHV and FCV more frequent boosters are advised if a higher risk of infection can be expected like in shelters or catteries. The application of multiple vaccinations in the young animal takes into account the existence of interfering maternal antibodies. The interval between revaccinations in the adult animals is based on the knowledge of the minimal duration of immunity (DOI). However it is known that these animals might be protected for a much longer period. The 3 yearly revaccination interval is merely based on providing herd immunity. For the individual animal titer testing is an option to determine serological evidence of protection and to decide if vaccination can be postponed. To determine an antibody titer a serum sample can be send to a diagnostic laboratory or established in veterinary practice using in-practice test kits. In this presentation the properties of the available in-practice tests and the potential applications will be discussed.

Correlates of protection and gold standard tests.

The live core vaccines induce a humoral (antibodies) as well as a cellular immune response. Vaccination-challenge experiments have provided excellent data to show that there is a good correlation between a vaccine-induced antibody titer and protection against disease. This has been shown for the core vaccines against canine distemper virus (CDV), canine adenovirus-1 (CAV) and canine parvovirus-2 (CPV) in dogs and also rabies and feline parvovirus (FPV) in cats. For FCV mucosal IgA is a stronger correlate of protection but these are not routinely measured. For FHV cell-mediated immunity is more important for protection and can only be measured by more sophisticated laboratory methods.

The protective antibodies are directed against the surface proteins of the viruses and are able to prevent the infection of cells. These antibodies can be determined in diagnostic laboratories with a virus neutralization assay (VN-test) for CDV, CAV, CPV and FPV or a

haemagglutination inhibition assay (HI) for CPV and FPV. These tests are considered gold standard tests to determine the titer of protective antibodies in serum. The titer is determined by making several dilutions of the serum sample and defined as the reciprocal value of the highest dilution that prevents the infection of cells or the agglutination of red blood cells.

The in-practice testkits.

Currently two test kits , the Titerchek™ kit marketed by Zoetis and the Vaccicheck™ kit produced by Biogal laboratories are available for use in practice. So far the Vaccicheck kit is available and used in several countries. The test is ELISA based and has been validated against the gold standard assay. The test was shown to have an overall good sensitivity (detection of the samples that were positive by the gold standard assay) and specificity (detection of the samples that were negative in an gold standard assay) and therefore considered suitable for use in practice.

The kit contains a Comb, with attached antigens (CPV, CAV and CDV for dogs; FPV, FCV and FHV for cats) and control spots sufficient to perform triple test for 12 samples. The test is performed by adding a serum sample or whole blood to wells in the first row of a developing plate and subsequently by following several incubation and washing steps. The result can be read in 21 minutes by comparing the color tone of the test spots with the control spot. The color tone of the control spot coincides with the cut-off value for a positive result.

Applications of in-practice antibody testing

To control the antibody response in pups

After the initial series of vaccinations in the first months of life of the puppy or kitten the vaccine-derived protection can be determined by an in-practice test kit. If the last vaccination is given at 14-16 weeks a seropositive test result obtained at 18-20 weeks indicates that the animal has made an active immune response. At this age maternally derived antibodies (MDA) will not be present anymore in the majority of animals. If the last vaccine was given at an age of 16 weeks and protection shown at 20 weeks the WSAVA states that the 12 month booster may not be required and that animals could go straight to a triennial CORE vaccination program. There is not much data about the age at which the immune system is mature. Therefore it seems valid to advice yearly titer testing in these animals, particularly if the last vaccine was given before the age of 16 weeks. A puppy or kitten that is seronegative against one or more Core components at the age of 18-20 weeks should be revaccinated and tested again 3-4 weeks later. If the animal is still negative it should be considered a non-responder to the particular antigen and to be susceptible to infection an disease for life.

To test whether (re)vaccinaton is necessary.

The triennial Core vaccination is based on the minimal DOI. Since many vaccinated animals will have protective antibody titers for longer periods, sometimes lifelong, triennial serological testing can be performed as an alternative. This for CDV, CAV and CPV in dogs and FPV in cats. Since the correlation between antibodies and protection against FHV and FCV is less convincing revaccination, possibly annually, might still be considered.

For adult dogs and cats with an unknown vaccination history or an elapsed vaccination history a serological test might also be offered as an alternative to automatic revaccination.

The need for revaccination of animals that have previously experienced an serious adverse reaction should be carefully evaluated. This holds true for the Core and Non-Core products. For the Core vaccines this decision can be made based on the results of an in-practice antibody test.

To manage disease outbreaks in shelters

In the face of an outbreak of a disease caused by CDV, CAV, CPV in dogs or FPV in cats susceptible animals can be identified using the in-practice test. The advantage of such an approach is that protected seropositive animals can be separated from the low or negative responder animals. The seropositive animals need not to be vaccinated and might be adopted out. The seronegative animals should be isolated at least until the incubation periods of the diseases have passed. These animals might be retested before adopting out.

If possible animals could also be tested before admission into the shelter to determine if they are protected. If not the animals should be vaccinated and kept in strict isolation or preferably sent to foster homes to develop active immunity before entering the shelter

To determine the optimal age of vaccination in puppies and kittens

The first period of their life, puppies and kittens are protected through maternal antibodies (Mabs) which are obtained the first day of life from the mother via colostrum. These Mabs protect animals from infection but also interfere with immunization after vaccination. The level of Mabs will differ between litters and individual animals. Although in-practice tests could in principle be used to determine the time point at which interference is not expected anymore its use should be critically evaluated. Puppies and kittens need to be re-tested every 2-3 weeks since the optimal time point cannot be determined by just taken a single blood sample at an age of 6-8 weeks. Data on the score at which vaccination will lead to immunization are lacking. Also differences in performance of available vaccines in the presence of maternal antibodies can be expected.

In conclusion

Antibody titer testing can be a useful and reliable tool to determine if an animal has seroconverted after vaccination and to decide if the individual animal needs a revaccination at the time points proposed in the general vaccination guidelines. In vaccinated adult animals test can be done every 3 years. Since data on the role of aging of the immune system on the persistence of levels of protective antibodies are lacking yearly testing in older animals (dogs > 10 years and cats > 15 years) is advised. Titer testing is less practical for determining the optimal age of immunization of puppies and kittens in the face of decreasing maternal antibody titers.

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