Vaccination and antibody titre testing

Updated January, 2021

These Guidelines were drafted by Herman Egberink, Katrin Hartmann et al. in November 2020 and updated by Herman Egberink and Katrin Hartmann

Introduction

Vaccination guidelines, as published by the ABCD, aim to support the practitioner in making an informed decision about a vaccination schedule for an individual animal and/or group of animals. After primary vaccination re-vaccinations are recommended every 1-3 years for feline calicivirus (FCV) and feline herpesvirus (FHV), depending on the risk of infection, and every 3 years for feline panleukopenia virus. Vaccination intervals are based on the minimal duration of immunity (DOI) as determined in experimental vaccination-challenge studies performed by industry. However, individual differences exist at which age kittens can be vaccinated successfully (because of persistence of maternally derived antibodies) and how long vaccine-induced DOI lasts. In addition, vaccine-induced immunity in adult cats can be much longer than those DOI determined by industry challenge experiments. Moreover, cats might have undergone subclinical infection and might be protected life-long even without having received any vaccination. Additionally, individual immune reaction and subsequent duration of immunity might vary and depend on many different factors, such as age, nutritional status, concurrent subclinical infections etc. To achieve an optimal vaccination schedule for the individual animal and to avoid unnecessary vaccinations, antibody titre testing can be helpful. However, for the interpretation of antibody titres it is important to differentiate between actively or passively acquired antibodies. While titres of passively acquired antibodies, that generally only persist for weeks, allow a quantitative interpretation about the level of protection (“protective titre”), this is not the case for actively acquired ones. Following infection or vaccination the presence of antibodies indicates an acquired immunity, irrespective of the amount of antibodies.

Live vaccines induce a humoral (antibodies) as well as a cell-mediated immune response (CMI). The CMI plays an important role in the control of intracellular pathogens, such as viruses. However, vaccination-challenge experiments have provided excellent data to show that there is also a good correlation between the vaccine-induced antibody titre and protection against certain disease (Roth and Spickler, 2010). Antibody titre as a measure of immune status has been shown to be useful for the core vaccines against canine distemper virus (CDV), canine adenovirus (CAV)-1, canine parvovirus-2 (CPV), and rabies (Frymus et al., 2009; Killey et al., 2018) in dogs and against feline panleukopenia virus (FPV) and also rabies in cats. For rabies virus vaccination, however, national and regional legislation will determine recommendations for primary vaccinations and revaccinations, and thus, antibody testing is not performed routinely.

For FCV, the level of mucosal IgA is a stronger correlate of protection than blood antibody levels, however, the mucosal antibodies are not routinely measured (Sato et al., 2017). Also because of strain variation in the field the value of antibody testing in predicting protection is limited (Radford et al., 2009; Bergmann et al., 2019).

For FHV, CMI is more important for protection, however the cellular immune responses can only be measured by more sophisticated laboratory methods (Thiry et al., 2009), and serum antibody testing is also not useful to predict protection (Bergmann et al., 2020).

For FeLV, high levels of virus neutralizing antibodies can be detected in most cats that had overcome viraemia after field infection (but usually not after vaccination), indicating a role in protection, although cytotoxic T-lymphocytes also are very important (Flynn et al., 2002). Virus-neutralizing antibodies can be measured and are helpful, as positive cats are immune and do not need vaccination. However, this test is not widely available (except in the UK). Recently, a new FeLV antibody test came on the market in Europe. It is a point-of-care (POC) test (in-practice test) that measures antibodies to FeLV p15E (envelope transmembrane protein). Examination of different FeLV antigens to assess their diagnostic utility in a test for the detection of anti-FeLV antibodies in all exposed cats had found a recombinant preparation of FeLV p15E (envelope transmembrane protein) to be the most promising antigen for detecting antibodies (Boenzli et al., 2014). The value of this POC test to predict protection against new infection, however, still has to be evaluated as it is so far unknown how well the presence of anti-p15E antibodies correlates with protection from FeLV challenge.

Therefore, in this guideline only the role of the application of antibody titre testing in vaccination recommendations for FPV will be discussed.

Testing for FPV antibodies

Results of some experimental and field studies in FPV vaccination indicate a much longer period of persistence of antibodies than 3 years; in some animals even lifelong antibody persistence has been demonstrated (Scott and Geissinger, 1999; Mouzin et al., 2004). In this regard the 3-yearly booster interval, as recommended in current guidelines for FPV, is merely intended to sustain herd immunity. For the individual animal, an antibody titre can be determined to decide whether a (re)-vaccination is needed. To measure the antibody titre, a serum sample can be sent to a diagnostic laboratory or POC tests can be used in the veterinary practice.

Gold standard tests

Vaccine induced immunity is based on the induction of antibodies and cellular immune responses through the activation of B and T cells and the formation of memory cells. The antibodies that protect against infection are directed against the surface proteins of the viruses and are able to prevent the infection of cells. These antibodies are particularly important for the prevention of systemic infections like FPV. The level of protective antibodies against FPV can be determined in diagnostic laboratories with a virus neutralization assay (VN-test) or a haemagglutination inhibition assay (HI). These tests are considered gold standard methods to determine the titer of protective antibodies in serum.

The antibody titre is determined by making serial dilutions of the serum sample which are added to a standard amount of virus. After certain time of incubation, the virus-antibody mixture is inoculated onto cell cultures or added to red blood cells. The titre is defined as the reciprocal value of the highest dilution that prevents the infection of cells or the agglutination of red blood cells.

Point-of-care test kits

Different POC tests are available for practice. The tests are ELISA- or immuno-migration-based, and results of some of the tests have been validated against the gold standard assay (Mende et al., 2014). In one of these tests (Feline®, Biogal laboratories) antibodies against FPV, FCV and FHV are detected, and with one kit a maximum of 12 feline samples can be investigated at once. The result can be read in 21 minutes by comparing the colour tone of the test spots with the control spot which gives a semi-quantitative result. Data on sensitivity and specificity of this test have been provided by the commercial company (Biogal laboratories) that produces the test and additionally were published in two other independent studies. The test kit was reported to have 99% specificity and 49% sensitivity in a study in shelter cats (DiGangi et al., 2011). Mende et al. (2014) reported the results of a study after the test had been slightly modified and of which the sensitivity was improved. In this study the test had 89% specificity and 79% sensitivity when compared with a HI titer at a cut-off value of 20, as a titre of ≥20 in adult cats that have been vaccinated or have overcome an active infection is considered protective (Lappin et al., 2002). In another study, cats were considered to be protected against FPV if they had a HI titer of ≥40 (Mouzin et al., 2004). At a cut-off point of 1:40, the specificity of the assay was determined at 86% and sensitivity at 83%. For the purpose of this test, specificity is the most important parameter since it determines the percentage of negative tests that are correctly identified as negative, and thus the number of false positive results that can be expected. Cats with a false positive test result will not receive a booster vaccination and will potentially remain unprotected. The specificity is considered acceptable assuming a titer of ≥20 as being protective. Especially if the test is used in cats belonging to a population with an expected high prevalence of antibody-positive animals, the positive predictive value is high, and the test can be considered suitable for use in veterinary practice (Mende et al., 2014), for example in adult cats with a known vaccination history.

New tests that have recently come on the market that only detect antibodies against FPV (and not FCV and FHV), are based on an immunochromatographic principle, and generally deliver qualitative (protected or not) results in a shorter period of time. They have not been evaluated in independent studies so far.

Applications of POC antibody testing against FPV

To measure the antibody response in kittens following vaccination

After the initial series of vaccinations in the first months of life of the kitten, vaccine-induced protection can be determined by POC tests. If the last vaccination is usually given around the age of 12-16 weeks, a positive test result in an antibody test obtained at the age of 20 weeks indicates that the animal has made an active immune response. At this age maternally derived antibodies (MDA) are expected to have waned to very low or undetectable titres in the majority of animals (Addie et al., 1998). If the last vaccine was given at an age of 16 weeks and protection was shown at 20 weeks, the WSAVA vaccination guidelines state that the 12-month

booster might not be required and that animals could go straight to a triennial FPV vaccination program (Day et al., 2016). There are not much data about the age at which the immune system matures and if the quality of the induced immune response at 16 weeks is as good as in adult animals. Therefore, it seems valid to advise yearly titre testing in these animals, particularly if the last vaccine was given before the age of 16 weeks. A kitten that is negative for FPV antibodies at the age of 20 weeks should be revaccinated and tested again 3-4 weeks later to determine if antibodies have developed. If the animal is still negative, the kitten is most likely a non-responder to the particular antigen and might be susceptible to infection and disease for life (Day et al., 2016).

To test whether (re)vaccination for FPV is necessary

The triennial vaccination for FPV is based on the minimal DOI. Since many vaccinated animals will have protective antibody titres for longer periods, sometimes lifelong, triennial antibody testing can be performed as an alternative for routine booster vaccination. Re-vaccinations were shown not to be beneficial especially in cats with a high titre and are therefore unnecessary (Bergmann et al., 2018). For adult cats with an unknown vaccination history, or an elapsed vaccination history, an antibody test might also be offered as an alternative to routine revaccination for FPV. However, this requires that monovalent FPV vaccines are available which is not the case in all countries.

Especially in animals that have previously experienced a serious adverse reaction, the need for revaccination should be carefully evaluated. This holds true for the Core and Non-Core vaccines. For the FPV vaccines this decision can be made based on the results of an POC antibody test. Another situation in which necessity of vaccination should be determined by antibody measurement is in cats with immunocompromisation (see ABCD guidelines on Vaccination of immunocompromised cats).

To manage FPV infection and disease outbreaks in shelters

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

In the face of an outbreak of disease caused by parvoviruses in cats, susceptible animals can be identified using the POC antibody test and could then be immediately vaccinated. The advantage of such an approach is that protected antibody-positive animals can be separated from the low or negative responder animals. Antibody-positive animals do not need to be vaccinated. The antibody-negative animals should be vaccinated and isolated, at least until the incubation period of the disease has passed (on average 2-7 days). These animals should be retested before adopting out. In countries where available, passive immunization of these unprotected cats also might be a short-term option.

To determine the optimal age of vaccination in kittens

During the first period of their lives, kittens are protected through MDAs, which for the most part are obtained on the first day of life from the mother via the colostrum. These MDAs protect animals from infection but also interfere with immunization after vaccination (Addie et al., 1998). The level of MDAs will differ between litters and

individual animals within litters depending on the antibody levels in the colostrum of the queens and the amount of colostrum ingested. Although POC tests could in principle be used to determine the time point at which interfering maternal antibodies have waned, its use in this situation should be, however, critically evaluated. Kittens would need to be re-tested every 2-3 weeks with POC tests since the optimal time point might not be determined by just taking a single blood sample at an age of 6-8 weeks. It is recognized that repeated blood sampling of young kittens in this way can be difficult and potentially stressful for the kittens, as well as costly, precluding routine adoption of this suggestion.

Data on the score or levels of MDAs at which vaccination will lead to active immunization are lacking. Also, differences in the performance of available vaccines in the presence of MDAs can be expected. Where titre testing is being used to decide upon the optimal age of first vaccination, a real titre, as produced by diagnostic laboratories, is preferable to a POC test on grounds of increased precision of the result. Based on the antibody titre of the queen, and the average half-life of maternal antibodies (9.5 days for FPV MDA), an estimate of the age of first vaccination can be calculated, bearing in mind that individual kittens in a litter will suckle different amounts of colostrum.

In conclusion

Antibody titre testing against FPV can be a useful and reliable tool to determine if a cat has developed antibodies after vaccination, and to decide if the individual animal needs revaccination at the time proposed in the general vaccination guidelines. In vaccinated adult animals, titre testing can be done yearly as part of the annual health check appointment which could also include a complete blood count, serum biochemistry and urinalysis at least in mature cats. Since data on the role of ageing of the immune system on the persistence of levels of antibodies are lacking, yearly testing in old animals (cats > 15 years) is strongly advised. Titre testing with POC tests is less suitable for determining the optimal age of immunization of kittens in the face of decreasing maternal antibody titres for reasons described above.

Acknowledgement

ABCD Europe gratefully acknowledges the support of Boehringer Ingelheim (the founding sponsor of the ABCD) and Virbac.

References

ABCD Guidelines on Vaccination of immunocompromised cats. http://www.abcdcatsvets.org/vaccination-of-immunocompromised-cats/

Addie DD, Toth S, Thompson H, Greenwood N, Jarrett O (1998): Detection of feline parvovirus in dying pedigree kittens. Vet Rec 142, 353-356.

Bergmann M, Schwertler S, Reese S, Speck S, Truyen U, Hartmann K (2018): Antibody response to feline panleukopenia virus vaccination in healthy adult cats. J Feline Med Surg 20(12), 1087–1093.

Bergmann M, Speck S, Rieger A, Truyen U, Hartmann K (2019): Antibody response to feline calicivirus vaccination in healthy adult cats. Viruses 11, e702.

Bergmann M, Speck S, Rieger A, Truyen U, Hartmann K (2020): Antibody response to feline herpesvirus-1 vaccination in healthy adult cats. J Feline Med Surg (Epub ahead of print).

Boenzli E, Hadorn M, Hartnack S, Huder J, Hofmann-Lehmann R and Lutz H (2014): Detection of antibodies to the feline leukemia virus (FeLV) transmembrane protein p15E: an alternative approach for serological FeLV detection based on antibodies to p15E. J Clin Microbiol 52, 2046-2052.

Day MJ, Horzinek MC, Schultz RD, Squires RA (2016): WSAVA Guidelines for the vaccination of dogs and cats. J Small Anim Pract 57, E1-E45.

DiGangi BA, Gray LK, Levy JK, et al (2011): Detection of protective antibody titers against feline panleukopenia virus, feline herpesvirus-1, and feline calicivirus in shelter cats using a point-of-care ELISA. J Feline Med Surg 13, 912-918.

Flynn JN, Dunham SP, Watson V, Jarrett O (2002): Longitudinal analysis of feline leukemia virus-specific cytotoxic T lymphocytes: Correlation with recovery from infection. J Virol 76 (5), 2306-2315.

Frymus T, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Gruffydd-Jones T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Radford AD, Thiry E, Truyen U, Horzinek MC (2009): Feline rabies. ABCD guidelines on prevention and management. J Feline Med Surg 11 (7), 585-593.

Killey R, Mynors C, Pearce R, Nell A, Prentis A, Day MJ (2018): Long-lived immunity to canine core vaccine antigens in UK dogs as assessed by an in-practice test kit. J Small Anim Pract 59 (1), 27-31.

Lappin MR, Andrews J, Simpson D, et al (2002): Use of serologic tests to predict resistance to feline herpesvirus 1, feline calicivirus, and feline parvovirus infection in cats. J Am Vet Med Assoc 220, 38–42.

Mende K, Stuetzer B, Truyen U, Hartmann K (2014): Evaluation of an in-house dot enzyme-linked immunosorbent assay to detect antibodies against feline panleukopenia virus. J Feline Med Surg 16(10), 805-811.

Mouzin DE, Lorenzen MJ, Haworth JD, King VL (2004): Duration of serologic response to three viral antigens in cats. J Am Vet Med Assoc 224(1), 61-66.

Radford AD, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Frymus T, Gruffydd-Jones T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Thiry E, Truyen U, Horzinek MC (2009): Feline calicivirus infection. ABCD guidelines on prevention and management. J Feline Med Surg 11 (7), 556-564.

Roth J, Spickler A (2010): Duration of immunity induced by companion animal vaccines. Animal Health Research Reviews 11(2), 165-190. doi:10.1017/S1466252310000150

Sato H, Sehata G, Okada N, Iwamoto K, Masubuchi K, Kainuma R, Noda T, Igarashi T, Sawada T, Noro T, Oishi E (2017): Intranasal immunization with inactivated feline calicivirus particles confers robust protection against homologous virus and suppression against heterologous virus in cats. J Gen Virol 98 (7), 1730-1738.

Scott FW, Geissinger CM (1999): Long-term immunity in cats vaccinated with an inactivated trivalent vaccine. Am J Vet Res 60, 652–658.

Thiry E, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Frymus T, Gruffydd-Jones T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Radford AD, Truyen U, Horzinek MC (2009): Feline herpesvirus infection. ABCD guidelines on prevention and management. J Feline Med Surg 11 (7), 547-555.

Source

http://www.abcdcatsvets.org/vaccination-and-antibody-titre-testing/