Vaccination in cats – vaccination recommendations in healthy and immunosuppressed cats

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Introduction
Vaccination is the most important measure to prevent infectious diseases in cats, especially those caused by viruses. In general, only healthy cats should be vaccinated. Thus, cats with acute diseases or short term immunosuppressive treatment should not be vaccinated, and vaccination should be postponed until recovery or after termination of the treatment course. In some situations, however, postponing vaccination would imply a significant risk for the cat, such as when entering a shelter environment with high infectious pressure, and in these specific situations vaccination might be necessary despite acute illness or poor general condition. In addition, some cats suffer life-long from a chronic disease and thus, vaccination cannot be postponed until recovery.

What is new in the vaccination of healthy cats?
Several international panels that have produced feline vaccination guidelines (American Association of Feline Practitioners, World Small Animal Veterinary Association, European Advisory Board on Cat Diseases) and recommend that an annual health examination be performed irrespective of whether vaccines are administered. It is generally accepted that healthy adult cats should be examined at least once per year. In the past, annual veterinary visits were structured around vaccinations as the primary focus. With the increasing body of knowledge about duration of immunity (DOI) from vaccinations, their potential adverse effects, and the increased awareness of pet owners about these issues, it is clear that vaccination can no longer justify the need for annual visits.

Vaccination is a medical procedure, and the decision to vaccinate should be based on a risk/benefit assessment for each cat and for each vaccine antigen. Vaccination can indeed be beneficial, but it is not innocuous, and the benefit of vaccinating an animal must be balanced against the risk of adverse events, likelihood of exposure, and severity of disease. In assessing the risk for an individual cat, information about the cat, the environment, and infectious agents to which the cat will be exposed need to be considered. Specifically, questions need to be asked that address the cat’s lifestyle as well as the lifestyle of any cats in the same household. Queries should also be posed regarding other sources of exposure, such as excursions outside the home, boarding, and travel.

Age is the most important element in assessing an individual's risk profile. Most infectious diseases are more prevalent in kittens, and kittens less than 6 months old are generally more susceptible to infection and disease than adult cats. Maternally derived antibodies (MDA) provide important protection for the kitten, but can interfere with, or neutralize, vaccines. As the level of MDA varies among individuals, the age at which a kitten can be able to respond to vaccination will vary, and in some cases can be 16 weeks of age or older. Stopping a vaccination course too early (when MDA are still interfering) is thought to be the single most common cause of vaccination failure in kittens.

What is the concept of Core versus non-core vaccines?
International guidelines groups have suggested which vaccines are considered core and non-core recognizing that antigens other than feline panleukopenia, herpesvirus-1 and calicivirus might not be required in all situations or in all countries. The specific circumstances in which non-core vaccines is appropriate vary considerably. Core vaccines are those recommended for all cats. International guideline groups recommend that feline panleukopenia (FPV), feline herpesvirus-1 (FHV-1) and feline calicivirus (FCV) vaccines fall into this category. Non-core vaccines should be administered to cats in specific risk categories on the basis of an individual risk/benefit assessment. Thus, rabies, feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), Chlamydia felis, Bordetella bronchiseptica, feline infectious peritonitis (FIP), and ringworm vaccines fall into this category.

What are general considerations in immunosuppressed cats?
Immunosuppression is a common condition in cats and can be caused by a variety of conditions, including congenital immunodeficiency, FIV or FeLV infection, tumours, tumour chemotherapy or radiation, glucocorticoids, cyclosporine, or other immunosuppressive drugs. For some of these conditions, affected cats will be severely immunocompromised; for others, such as FIV infection, the spectrum of disease severity due to disease stage will determine the degree to which the immune system is compromised. Some important points have to be considered when vaccinating immunocompromised cats, including (1) the safety of modified-live virus vaccines and the concern that
vaccines might regain their pathogenicity if the immune system is not working properly, (2) the question whether vaccines work at all in immunocompromised cats and whether duration of immunity after vaccination is shortened compared to that in healthy cats, (3) the concern that in some of these conditions, e.g., in cats with FIV infection or chronic kidney disease, vaccination and resulting immunostimulation might lead to a progression of the disease.

**How should cats with congenital immunodeficiency disorders be vaccinated?**

Congenital (primary) immunodeficiency in cats has rarely been described. In human medicine, it is recommended that patients with primary immunodeficiency should receive all routine vaccines. Due to lack of data in cats, this recommendation should be followed in cats with congenital immunodeficiency as well.

**How should cats with feline immunodeficiency virus infection be vaccinated?**

Vaccination of FIV-infected cats is much in debate as is vaccination of HIV-infected people. FIV infection leads to progressive disruption of normal immune function. It has been proposed that cats with FIV infection should solely receive inactivated vaccines, if possible. Although there is no definitive scientific proof that FIV-infected cats are at increased risk from modified-live virus vaccines, inactivated vaccines are preferred, out of the concern that modified-live virus vaccines given to immunocompromised animals might regain pathogenicity. It has been reported that FIV-infected cats have developed illness with modified-live panleukopenia vaccine.

Efficacy of vaccination seems to depend on the stage of FIV infection. It has been shown that FIV-infected cats in an early stage of infection are able to mount appropriate levels of protective antibodies after vaccination, but responses can be impaired during the terminal phase of infection. One study investigated the effect of experimental primary-stage FIV infection on FCV vaccination and subsequent challenge. Although there was some level of protection through vaccination, clinical signs of acute FCV-associated disease were more widespread in the cats infected with FIV than in those which were not. FIV infection also prolonged shedding of FCV, with more FIV-infected cats becoming chronic carriers. There was also evidence of an impaired FCV-neutralizing antibody response in FIV-infected cats following FCV challenge. In another study, 15 cats experimentally infected with FIV and 15 FIV-negative control cats received a FeLV vaccine. High antibody titres developed after vaccination in both FIV-infected and FIV-negative cats. After challenge with FeLV, FIV-infected cats were protected as well as the non-FIV-infected cats. Thus, in this study at least in the early stage of FIV infection, the immune system was not markedly suppressed, and therefore, cats were successfully immunized. In a follow-up study, long-term protection of a FeLV vaccine was determined in 30 specified pathogen-free cats for over 3 years. Half of the cats had previously been infected with FIV, the other 15 cats served as non-infected controls. There was no difference in vaccine efficacy between FIV-infected and FIV-negative cats. After 3 years of observation, the FeLV-vaccinated FIV-infected cats had significantly higher survival rates as well as better clinical and laboratory parameters than the not-FeLV-vaccinated FIV-infected cats, thus indicating, that the FeLV vaccine was effective in these FIV-infected cats. In contrast, in a 5-year field study aimed to control FeLV infection by vaccination in a colony of 30 adult cats naturally exposed to FeLV, FeLV vaccination was effective in FIV-negative cats, but failed to protect FIV-infected cats against FeLV. Although results from experimental studies cannot necessarily predict outcome in naturally infected cats, it is clear that there are major differences in the response to vaccination depending on the immune status of the individual FIV-infected cat.

In addition to concerns about efficacy, there is debate about negative effects of vaccine-induced immunostimulation in FIV-infected cats, as immunostimulation could potentially lead to progression of FIV infection by altering the balance between the immune system and the virus. Although some studies even suggest that immunostimulation can help to stabilize CD4+ cell numbers, vaccination of chronically infected FIV-infected cats with a synthetic peptide on the other hand was associated with a decrease in the CD4/CD8 ratio. Stimulation of FIV-infected lymphocytes is known to promote FIV production in vitro, and in vivo, lymphocyte stimulation can increase the expression of cellular FIV receptors and increase virus production, a combination that could enhance progression of infection. Thus, vaccination and antigenic stimulation might potentially be disadvantageous with a potential trade-off of protection from infection for progression of FIV infection secondary to increased virus production. In conclusion, if adult FIV-infected cats that had been vaccinated previously, are kept strictly indoors, the risk of being infected with other pathogens is likely lower than the possible harmful effect of vaccination. Ideally, antibody levels, at least against FPV, should be determined and only in cats lacking protective antibodies vaccination should be considered. If antibody measurement is not possible, booster vaccinations in adult indoor-only cats, that have received previous vaccinations in their lives, are not recommended. If potential exposure to FPV, FHV, or...
FCV cannot be excluded, only core vaccines should be administered, and those, when available, in an inactivated form.

**How should cats with feline leukemia virus infection be vaccinated?**

Cats with progressive FeLV are more severely immunocompromised than cats with FIV; they have suppressed cellular and humoral immunity, thus predisposing cats for just about any type of infection. Therefore, maintaining a good level of protection is considered very important. It has been shown that cats with progressive FeLV infection might not adequately respond to vaccination. When cats with FeLV infection were vaccinated with rabies vaccines, they were only protected for 6 months. This has been proven for rabies but is likely also true for other vaccine components as well. Thus, for good protection, vaccination with core vaccines (against FPV, FHV, and FCV) should be performed regularly, even if the cat is kept strictly indoors (this is different to FIV-infected cats). If an owner cannot be convinced to keep a FeLV-positive cat inside, rabies vaccinations should be given (in accordance with state and local regulations). Protection in a FeLV-infected cat after vaccination is not as complete and long-lasting as in a non-infected cat. Thus, either more frequent vaccinations (e.g., every 6 months) are recommended in FeLV-infected cats or measurement of antibodies to assure sufficient protection, e.g., against panleukopenia virus are recommended, especially if the cat is allowed to go outside.

**How should cats with tumours be vaccinated?**

Oncology patients can have immunosuppression for several reasons, including the cause of the tumour itself, e.g., if caused by FeLV infection, the debilitation, acquired disorders of antibody production and cell-mediated immunity caused by the tumour, and the drugs used to treat the tumour. In cats with tumour-associated disorders of antibody production, vaccination is very unlikely to be effective. Recommendations in human medicine state that vaccination should be maintained in humans with tumours, but in these patients no modified-live virus vaccines should be administered, because replication of the vaccine virus can be enhanced in severely immunocompromised persons.

A few studies in dogs demonstrated immunosuppression associated with various tumours, such as lymphoma or osteosarcoma and mammary carcinoma. Dogs with lymphoma or osteosarcoma had reduced T cells when compared to healthy dogs. A recent study demonstrated the immunosuppressive network present in dogs with mammary carcinoma; while the number of various T cell subpopulations was constant during tumour development, the number of regulatory T cells was significantly higher in tumour-bearing dogs than in healthy individuals as was the number of myeloid-derived suppressor cells. In one study, dogs with lymphoma or osteosarcoma were vaccinated and post-vaccination antibody titres were compared to those of a healthy control group. Although dogs with lymphoma or osteosarcoma appeared to be relatively T cell-deficient, antibody titres after vaccination were not significantly different to those of healthy controls. No studies have been performed in cats with tumours to demonstrate their ability to react to vaccination. However, a recent study assessed the prevalence of antibodies against FPV in 350 client-owned cats and identified factors that were associated with a lack of antibodies in cats. Factors, including information regarding signalment, origin, environment, lifestyle, housing conditions, health status, chronic diseases, glucocorticoid therapy, and vaccination status were analysed by a multivariable logistic regression analysis. Of the 350 cats, 103 (29.4%) had no antibodies against FPV, and among other factors, tumours were significantly associated with a lack of antibodies. Thus in cats with tumours, protection rate is not comparable to those of healthy cats. Antibody measurement, at least against FPV infection, would be a good possibility to confirm that protection is present. If antibody measurement is not an option, more frequent boosters than usually recommended (such as once yearly) should be considered in these cats. In cats with tumour-associated severe neutropenia or disorders of antibody production, vaccination should be postponed until tumour chemotherapy improved the condition.

**How should cats with immunosuppressive chronic diseases be vaccinated?**

There are a number of other diseases that can alter the immune system, such as diabetes, chronic kidney disease, and asplenia. In humans, these conditions increase the patient's risk for certain diseases, and thus, specific vaccines, such as particularly bacterial vaccines, are recommended for such patients. Frequently, the immune response of those patients to these antigens is not as good as that of immunocompetent persons, and more frequent boosters might be required. In humans, liver cirrhosis is also included in the guidelines as important immunosuppressive disease, which is a very rare condition in cats and thus, will not be further discussed in the present guideline.

**Diabetes mellitus** can alter the body's immune defences, therefore rendering the patient predisposed to infection. The reasons for this have not been completely explained but can involve abnormalities with cell-mediated immunity and abnormal phagocyte function as well as poor blood supply to various body tissues because of diabetic vascular disease. Thus, infections in animals with diabetes are more common and severe and can involve the skin, urinary tract, and other body sites, such as the gall bladder and liver. In diabetic cats, urinary
tract infections are the most common secondary infections. Although several in vitro tests of immunologic function are known to be abnormal among diabetic patients, these defects are likely of little clinical importance. In humans with longstanding diabetes, who often have cardiovascular, renal, and other end-organ dysfunctions, vaccinations, such as annual influenza vaccination are recommended. Patients receiving either insulin or oral antidiabetic agents responded normally to influenza vaccination without impairment of diabetic control. However, in human medicine, it is recommended to vaccinate adult diabetic patients as early as possible after their diagnosis. The immune function of a diabetic patient, however, is more severely compromised as long as the patient remains uncontrollably hyperglycemic. Thus, vaccinations should never be given to a cat with poorly controlled diabetes, and control of the diabetic situation should be achieved before vaccination. In cats, infections play an important role in inducing insulin resistance and by causing diabetic decompensation because of endogenous hypersecretion of stress hormones, such as cortisol. There are no data, however, whether vaccination could promote diabetic decompensation. Thus in conclusion, the recommendation would be to vaccinate diabetic cats according to the proposed guidelines for healthy cats, but postpone the vaccination in an uncontrolled diabetic case until control is achieved.

Chronic kidney disease can lead to an increased risk of infection with a variety of pathogens. An association between chronic kidney disease and reduced antibody development following vaccination has been described in humans. It has been shown, that the stage of the kidney disease and thus, the impairment of the glomerular filtration rates predicted ability to produce antibodies, since a rise of antibody titres after vaccination became increasingly unlikely as glomerular filtration rate decreased. Malnutrition in patients with chronic kidney disease was also suspected to be associated with an impaired immune response, and chronic uremia, directly or indirectly, was shown to alter immune cell function. Consequently, a generalized immunosuppression and decreased antibody development are expected in chronic kidney disease patients with secondary antibody responses being less affected than primary antibody responses. Thus, in humans immunisation strategies and especially vaccination with novel antigens should be formulated as early in the course of the chronic kidney disease as possible. No studies have been performed in cats with chronic kidney disease to demonstrate their ability to react to vaccination. However, a recent study assessed the prevalence of antibodies against FPV in cats in Southern Germany and identified factors that were associated with a lack of antibodies in 350 client-owned cats, and presence of chronic kidney diseases was significantly associated with a lack of antibodies. Thus in cats with chronic kidney disease, protection rate is not comparable to those of healthy cats.

There is another concern that has to be discussed when considering vaccination in cats with chronic kidney disease. Some studies suggested a risk association between chronic kidney disease and frequent vaccination in cats. As most of the cats with chronic kidney disease are of older age and likely have received vaccinations in the past, the risk for such a cat to acquire infectious diseases is considered low, and vaccination might not be necessary. Ideally, antibody levels at least against FPV should be determined and only cats lacking protective antibodies should be vaccinated. If antibody measurement is not possible, booster vaccination is not recommended if a cat with chronic kidney disease that has been vaccinated previously and is kept strictly indoors. If potential exposure to FPV, FHV, or FCV cannot be excluded, only intranasal vaccine should be given, if available.

Asplenia can increase the risk for infectious diseases, but is rare in cats and mainly occurs after iatrogenic removal of the spleen. Asplenic cats’ protection rate might not be comparable to those of healthy cats. Antibody measurement, at least against FPV infection, would be an option to confirm if protection if present. If antibody measurement is not an option, more frequent boosters than usually recommended (such as once yearly) should be considered in these cats. When elective splenectomy is planned, vaccination should precede surgery by at least 2 weeks, if possible.

How should cats be vaccinated that receive immunosuppressive therapy?

Immunosuppressive drugs, such as glucocorticoids, cyclosporine, or tumour chemotherapeutics, are commonly used in cats with various diseases. If used short-term, vaccination can be postponed until after the treatment, but some cats require long-term therapy.

Glucocorticoid treatment is used for many clinical conditions that require long-term glucocorticoid treatment, and the degree of immunosuppression depends on the glucocorticoid dosage used. The exact amount of systemic glucocorticoids and the duration of their administration needed to suppress the immune system in an otherwise healthy cat are not well defined. The immunosuppressive effects of steroid treatment vary, but many clinicians consider a dose equivalent to either 2 mg/kg prednisolone as sufficiently immunosuppressive to raise concern about the safety of immunisation with modified live-virus vaccines. Glucocorticoids used in lower (but greater than physiologic) doses also might reduce the immune...
response to vaccines. In human medicine, glucocorticoid therapy usually does not contraindicate administration of vaccines (not even with modified-live virus vaccines) when glucocorticoid therapy is short-term (less than 2 weeks); low to moderate dose; long-term alternate-day treatment with short-acting preparations; maintenance physiologic doses (such as replacement therapy in patients with Addison’s disease); or administered topically (skin or eyes), by aerosol, or by intra-articular, bursal, or tendon injection. One study investigated the effect of oral prednisolone on vaccination against canine distemper virus in Beagle puppies and found that doses of 1 mg/kg and 10 mg/kg over a period of 21 days had no effect on the response to vaccination. No prospective studies have been performed in cats. However, a recent study assessed the prevalence of antibodies against FPV in cats in Southern Germany and identified factors that were associated with a lack of antibodies in 350 client-owned cats. In this study, glucocorticoid treatment was significantly associated with a lack of antibodies, and cats receiving glucocorticoids for 11 weeks and longer were particularly at risk. In conclusion, if possible veterinarians should wait at least 3 months after discontinuation of glucocorticoid therapy before administering vaccines, especially modified-live virus vaccines, to cats who have received high-dose, systemic steroids for more than 2 weeks. If continuous long-term glucocorticoid therapy is necessary, vaccinations schedules should be maintained, but inactivated vaccines should be applied, if available.

Cyclosporine treatment is used more and more commonly in cats, such as for feline hypersensitivity dermatitis or autoimmune diseases. Cyclosporine can interfere with cell-mediated immunity, thus compromising the host defence system against infectious agents, such as intracellular parasites. One study investigated the immunosuppressive effect of cyclosporine on the ability of cats to mount an immune response following vaccination. Thirty-two healthy, immunocompetent adult cats (16 cats/group) were treated with either cyclosporine for 56 days at a dose of 24 mg/kg once daily (more than 3 times the therapeutic dose) or sham-dosed. Prior to treatment, cats had an adequate antibody response to primary vaccination against FPV, FHV, FCV, FeLV, and rabies. Booster vaccination against FPV, FHV, FCV, FeLV and rabies or novel vaccination against FIV were administered 28 days after initiation of treatment with cyclosporine. There were delays/reductions in antibody response to FHV, FeLV, and rabies in treated cats; however, adequate protection was achieved in response to all booster vaccinations. Following primary vaccination with FIV, however, control cats showed a response, but treated cats showed no antibody production. Thus, adult cats treated with high-dose cyclosporine were able to achieve adequate protection following booster vaccination, while in contrast, cats failed to mount a humoral response to a novel vaccination. This suggests that memory B-cell immune responses remain intact during high-dose cyclosporine administration in cats, but that primary immune responses are impaired. Thus, booster vaccination can be given to cats receiving cyclosporine, but novel vaccinations should be applied before cyclosporine treatment is initiated, if possible.

Tumour chemotherapy commonly inhibits cell division, and when this occurs, the B and T cells are often times destroyed, thus impairing the body’s ability to produce antibodies and to allow for cell-mediated immune protection. In dogs, chemotherapy has been documented to have no effect on pre-existing antibody titres. A prospective study determined the association between tumour chemotherapy and serum canine distemper virus (CDV), canine parvovirus (CPV), and rabies virus antibody titres in tumour-bearing dogs, including 21 client-owned dogs with various malignancies and 16 with lymphoma. No significant changes were detected in CDV, CPV, and rabies virus titres following chemotherapy in tumour-bearing dogs. Thus, established immunity to CDV, CPV, and rabies virus from previous vaccination was not significantly compromised by standard chemotherapy. Another prospective study evaluated the effects of 2 common chemotherapy protocols on T and B cell numbers and humoral immune responses to de novo vaccination in 21 dogs with tumours (12 with lymphoma, 9 with osteosarcoma) comparing effects of doxorubicin versus multi-drug chemotherapy. Doxorubicin treatment did not cause a significant decrease in T or B cell numbers, whereas treatment with combination chemotherapy caused a significant and persistent decrease in B cell numbers. Antibody titres after vaccination were not significantly different between control and chemotherapy-receiving dogs. These findings suggest that chemotherapy might have less impact on T cell numbers and ability to mount antibody responses in dogs with tumours than was previously anticipated and that administration of chemotherapy does not preclude administration of vaccines. Although there are no data in cats; however, in cats in which tumour chemotherapy or immunosuppressive therapy is considered, ideally vaccination should precede the initiation of chemotherapy or immunosuppression by greater than or equal to 2 weeks. Vaccination during chemotherapy therapy should be avoided because antibody responses are suboptimal. Patients vaccinated while on immunosuppressive therapy or in the 2 weeks before starting therapy should be considered unimmunised and should be revaccinated at least 3 months after discontinuation of chemotherapy.
How should geriatric cats be vaccinated?
Several immunological differences have been demonstrated in some studies in geriatric cats when compared to younger adult cats. In humans, specific guidelines for elderly people (generally > 60 years of age) exist, and increased vulnerability to infection of the elderly makes them a particularly important target population for vaccination. In cats, so far no studies have been published on the response of geriatric cats to vaccination, however, there are no data that would support the idea of infectious diseases being more common in senior or geriatric cats, and the incidence of infectious diseases preventable by vaccination in senior and geriatric cat is generally considered low. On the other hand, it is also not known, whether vaccine boosters could worsen a pro-inflammatory state in a senior or geriatric cat, and thus, reducing number of booster vaccinations would seem appropriate. In addition, many senior or geriatric cats are diagnosed with chronic inflammatory or immune-mediated diseases, such as chronic gingivitis or periodontal disease, chronic kidney disease, inflammatory bowel disease, inflammatory liver disease, or pancreatitis. Duration of immunity (DOI) studies have shown long-term immunity against FPV, FHV, and FCV, and experimental studies have shown that immunity persists for years showing that immunological memory to core vaccines is adequate as well as the immunological response to boosters. Based on these studies and expert opinion, healthy geriatric cats properly vaccinated should receive boosters at recommended intervals based on published guidelines and following assessment of individual risk. On the other hand, there is some evidence that older cats might not respond efficiently to novel antigens that are administered for the first time. This has been shown with rabies vaccine in dogs but could be presumed for any other antigen. Older dogs vaccinated for the first time against rabies showed lower antibody levels compared to younger dogs, in general having difficulties to reach titres above 0.5 UI/ml. Thus, based on this study, if healthy senior or geriatric cats that need to be vaccinated against a novel pathogen for the first time (travelling, moving, changing life style), even if the regular vaccination schedule consists in one injection (e.g., rabies), a single dose should not be considered enough to ensure a proper immunisation, and a second dose is recommended in these animals.

References

Other references can be provided by the author on request.