

ANTIBODY TITER TESTING

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In response to evolving canine and feline vaccination guidelines, veterinarians have expressed concern that some patients might be susceptible to infection if vaccines are not administered annually. These concerns prompted serologic testing to ensure that triennial vaccination of adult dogs and cats would provide a level of protective immunity no less than that derived from the administration of annual boosters. Today, several laboratories offer serologic panels that include antibody titers to selected antigens, particularly the core antigens, used in companion animal vaccines. This availability of serologic assessment for individual patients prompts questions concerning when to perform the tests as well as how to interpret the results. This issue of *Immunology Bulletin* addresses the role of postvaccinal serology (antibody titers) in dogs and cats.

What are antibody titers?

Serum antibody titers represent the relative concentration of circulating antibodies, usually IgG, to a particular antigen. It's important to note that although testing individual patients for antibody titers is becoming increasingly available, such testing does not provide a comprehensive assessment of immunity. Antibody titers represent only a portion of the overall immune response a patient can mount following exposure or infection. Most laboratories limit antibody testing to one or two classes of immunoglobulin: IgG and possibly IgM. Quantitative measures of cell-mediated immunity, although important in long-term immunity and recovery from infection, are not provided through commercial diagnostic laboratories.

A few facts should be considered when using antibody titers to assess vaccine response. First, with the exception of rabies titers, standardized laboratory methods for determining serum antibody concentration for vaccine antigens have not been established in the United States. Also, methods vary among laboratories—one may use virus neutralization assays to establish a titer for canine distemper (which is recommended), another may report results using less sensitive test methods, such as immunofluorescence assays. For an individual patient, results reported by one labora-

tory can differ substantially from those reported by another. Comparing test results between laboratories is not recommended.

Second, while all vaccines stimulate antibody responses, all antibodies are not protective. Leptospirosis titers, for example, are routinely used to establish exposure and infection to pathogenic serovars. Vaccine-induced titers for leptospirosis, however, are short-lived and poorly correlate with protection.

Third, laboratories offering vaccine antibody titers do not provide results for every vaccine antigen used. Only selected titers provide reliable information regarding protective immunity. For example, positive antibody titers to canine distemper virus (CDV), canine parvovirus (CPV), and feline parvovirus (FPV), also called panleukopenia virus, reliably reflect that a patient is capable of mounting a protective immune response if exposed. Some laboratories offer titers for other infections, such as canine adenovirus-1 (hepatitis), feline herpesvirus-1, and feline calicivirus. However, the significance of the results can be unclear.

Finally, a positive antibody titer in blood collected today is not predictive of the patient's titer tomorrow. Titers are only reflective of antibody levels on the day that serum was collected. Interpreting a positive titer to mean that the patient does not need to be vaccinated or retested for another year may be inappropriate.

What are the indications for performing antibody titers?

Veterinarians cite several reasons for performing antibody titers in individual patients. For example, owners who are particularly concerned about the potential for vaccine-induced injury may request titers in lieu of annual vaccination. Veterinarians who are reluctant to implement triennial vaccination recommendations for core vaccines may elect to submit serum for titers annually before administering a core vaccine.

In addition, it may be helpful on occasion to know whether an individual puppy or kitten failed to respond to the initial vaccine series (*i.e.*, maternal antibody interference). In such cases, it would be appropriate to submit serum a minimum of two weeks after administering the last vaccine in



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the initial series. A second indication is to assess antibody levels in a dog or cat that is considered to be at risk as a nonresponder. Historically, Doberman pinschers and Rottweilers were identified as breeds remaining susceptible to certain infections, especially parvovirus, despite having received appropriate vaccines. However, no vaccine can be expected to provide 100% protection to 100% of vaccinates.

Third, in patients with a history of having experienced a known or suspected adverse post-vaccinal reaction, performing an antibody titer may provide some assurance that the patient is immune if vaccination is deemed inappropriate. For example, any patient having experienced an acute-onset adverse event (*e.g.*, acute anaphylaxis) should not be subjected to vaccination when feasible. Also, antibody titer determination is indicated in any patient that has recovered from a serious immune-mediated disorder (*e.g.*, immune-mediated hemolytic anemia).

Does a positive titer correlate with protection from disease?

The reference range for antibody titers to specific antigens is established by the individual laboratory that performs the assay. In the case of the canine core antigens CDV and CPV and the feline core antigen FPV, a positive antibody titer is expected to correlate well with protective immunity. For several years, however, veterinarians have used—and continue to use—coronavirus antibody titers to establish FIP diagnoses. In the case of feline coronavirus, an antibody titer cannot prompt an FIP diagnosis nor does it correlate with immunity against developing FIP.

Does a negative titer correlate with susceptibility to disease?

Not necessarily—using antibody titers to decide that an individual patient requires vaccination can be problematic. While a positive titer to CDV, CPV, and FPV generally correlates with protection, a negative titer to these antigens does not necessarily correlate with susceptibility.^{1*} Immunoglobulin (antibody) is subject to catabolism. Over time, antibody titers may fall to levels below the threshold for detection. However, the B-lymphocyte, which produces the humoral immune response to specific antigens, has immunologic memory. Once activated by antigen,

clones of B-lymphocytes can be sustained for many years. These antibody-producing cells retain the ability to recognize discrete antigenic epitopes and can rapidly produce significant levels of antibody subsequent to re-exposure. In effect, the immunologic memory associated with B-lymphocytes serves to boost the patient's antibody level from nondetectable levels to protective levels in a matter of hours to days.²

A negative antibody titer for one of the core vaccines only reflects susceptibility to infection if the patient has never experienced infection, has never been vaccinated, or (rarely) failed to respond to previous vaccination.

Do all vaccines result in a comparable antibody response?

No. Bacterial vaccines (bacterins) typically induce a poorer immune response than viral vaccines. Killed vaccines generally induce a poorer antibody response than modified-live vaccines. Recombinant-vectored vaccines induce an immune response similar to that of modified-live vaccines.

Using defined portions of DNA isolated from pathogenic viruses, recombinant-vectored vaccines induce the expression of discrete immunogenic proteins in the absence of the infectious pathogen. The immune response is robust and typically includes both humoral immunity (antibody) and cell-mediated immunity. While some recombinant-vectored vaccines produce a significant level of antibody, inoculation of patients with discrete genes that encode protein antigens can result in lower antibody titers than those resulting from vaccines containing live, attenuated organisms. Animals vaccinated with a recombinant-vectored vaccine may normally have low to even undetectable titers yet still mount a sustained, protective immune response subsequent to exposure.

Conclusion

Whether a practitioner administers booster vaccines annually or triennially, there are few indications for routinely substituting antibody titers for vaccination. Differences in test methodologies and vaccine types and the ability of the individual patient to mount a protective immune response are significant variables in defining the value of antibody titers in assessing vaccination response.

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