

Rabies Serology – Vaccine Titer Response

What is measured?

Rabies virus neutralizing antibodies (RVNA) are antibodies with the ability to neutralize rabies virus and prevent the virus from infecting cells. The testing we perform does not measure the amount of rabies specific antibodies but the neutralizing activity of the antibodies present in the serum. In the test, serum (the non-cellular portion of blood) is first diluted in a diluent (e.g. 1 part serum in 4 parts diluent). Further dilutions are performed, each of which contain less and less serum. These serum dilutions are mixed with a standard amount of live rabies virus and incubated. Whatever RVNA is present will neutralize the virus. Next, some tissue culture cells are added and the serum/virus/cells are incubated together. Whatever rabies virus is left (i.e., that which has not been neutralized by the antibody in serum), will infect the cells and this can be seen under the microscope through the use of specific staining. Calculation of the endpoint titer is made from the percent of virus infected cells observed on the slide.

What does the result mean?

The result of this test can be expressed in two ways: as a RVNA endpoint titer (e.g., 1:5) or as a value for RVNA potency (e.g., 0.5 IU). The IU stands for international unit and is calculated from the titer by comparing it against the titer of a standard reference serum. If there is no RVNA present in the serum it will not neutralize the virus and the titer will be LESS THAN 1:5 (i.e. the 1:5 diluted serum did not prevent the virus from infecting the cells). RVNA antibody will neutralize rabies virus to an “endpoint titer” – to a specific dilution where the virus is neutralized. For example, if there is a little RVNA in the serum low dilutions (e.g. 1:5 or 1:25) will neutralize the virus, but higher dilutions will not. In contrast, if there is a lot of antibody in the serum the virus will be neutralized by high dilutions of the serum (e.g. 1:500 or 1:1400) and not infect the cells. Therefore the further the serum can be diluted and still neutralize virus, the more RVNA in the serum. In summary, the bigger the denominator in the reported titer, the more antibody in the blood sample (e.g., a titer of 1:125 has more antibody than a titer of 1:5 because it still neutralized at a much higher dilution).

What does the level of RVNA mean?

A detectable RVNA titer means that there is evidence of a humoral immune response to the rabies virus. The test does not differentiate whether the immune response is to rabies virus exposure or to rabies vaccination. Nor is there an established level of protection. Though titer levels are evidence of an immune response to the rabies virus, they are not directly correlated with the degree of protection. This is because there are other immunological factors which are involved in the protection from rabies infection. An overview of rabies challenge studies indicates RVNA levels predict survival on more a qualitative rather than quantitative basis [1]. Whether an animal requires a rabies booster vaccination is not determined by the level of RVNA in the serum, but by local regulations. As stated in the compendium of animals rabies protection and control report by the CDC, RVNA levels are not to be used in place of current vaccination for either management of rabies exposure or for determination of booster vaccinations for animals [2].

References

1. Aubert MF. Practical significance of rabies antibodies in cats and dogs. Rev Sci Tech 1992;11:735-60.
2. Centers for Disease Control and Prevention. Compendium of animal rabies prevention and control., National Association of State Public Health Veterinarians, Inc.(NASPHV), 2008.