

Summary:

WNV IgG avidity can help distinguish recent from past WNV infection. A low avidity index indicates, with 98% accuracy, that WNV exposure occurred within the previous 3-4 months.

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West Nile Virus (WNV) IgG Avidity: *An Indicator of Recent WNV Exposure*

BACKGROUND: Cases of West Nile Virus continue to occur in geographic regions that first experienced WNV infections in previous years. In these endemic areas, a laboratory test is needed to distinguish current season from prior season infection in a subset of patients with complicated medical histories and/or presentations. Unfortunately, WNV IgM is not useful for this application, since WNV IgM may persist for over a year, particularly in patients with WNV-related encephalitis. Likewise, WNV IgA detection is not a reliable indicator of recent infection, as WNV IgA persistence follows a pattern similar to that of WNV IgM. Scientists at Focus Diagnostics have thus investigated the potential utility of WNV IgG avidity to distinguish recent from past WNV exposure. Avidity, a measure of the strength with which IgG antibodies attach to antigen, matures with the length of time since infection. Typically, IgG produced early in infection exhibits low avidity, whereas IgG produced a few months later exhibits high avidity. Several studies have demonstrated the utility of IgG avidity as an indicator of time since infection with other pathogens, including Cytomegalovirus, Human Immunodeficiency Virus, and *Toxoplasma gondii*.

STUDY SAMPLES AND METHODS: WNV IgG avidity was evaluated using follow-up serum and plasma samples from blood donors who made a WNV RNA-positive (viremic) donation in 2003 or 2004. Because the WNV viremic period begins within a few days of infection and typically lasts for only 7-14 days, WNV RNA detection is an excellent indicator of very recent WNV infection. The WNV IgG avidity assay utilized the Focus Diagnostics WNV IgG ELISA kit and a modified procedure. A given sample (diluted 1:101) was added to duplicate microtiter wells, and after the serum incubation step, one well was washed with kit buffer, whereas the other well was washed with dissociating buffer (which causes low avidity IgG molecules to detach from the WNV antigen). Results were expressed as an Avidity Index (AI), calculated by dividing the absorbance of the well washed with dissociating buffer by the absorbance of the well washed with kit buffer.

RESULTS: We measured WNV IgG avidity in 348 follow-up samples collected from 170 viremic blood donors at various times after they made their RNA-positive donation. The results are shown in the accompanying figure. Two major observations were immediately clear from visual examination of the figure: (a) 95% (61/64) of samples collected more than 90 days after the RNA+ donation exhibited AI values >0.50 , and (b) 98% (189/192) of samples with AI values <0.50 were collected within 90 days of the RNA+ donation. An AI >0.50 was thus defined as high IgG avidity, and an AI <0.50 was defined as low IgG avidity. The surprising finding, evident in the figure, was that 33% (95/284) of follow-up samples collected within 90 days of the RNA+ donation exhibited high avidity. The reason for the very rapid maturation of WNV IgG avidity in some donors remains unclear; one hypothesis is that these donors had been previously exposed to another flavivirus, and produce high avidity WNV IgG as part of a memory immune response to common flavivirus antigens.

CONCLUSION: These findings indicate that WNV IgG avidity can be a useful laboratory tool for distinguishing current season from prior season infection, but the interpretation must be made with a clear appreciation of the assay's limitations. An AI <0.50 indicates with 98% accuracy that WNV infection occurred within the last 3 or 4 months; however, an AI >0.50 is not useful for estimating the time since WNV infection.

CASE PRESENTATION OF WNV IgG AVIDITY: A 50 year-old female patient in South Dakota (where many cases of WNV occurred in 2003) is admitted to hospital with fever and altered mental status in September 2004. Suspecting WNV infection, the physician orders WNV serologic tests. Both WNV IgM and WNV IgG are positive, but the WNV IgM index is only 2.15. Noting that the relatively low WNV IgM index value is more typical of past versus recent infection, the physician orders a WNV IgG avidity test to assess time since infection. The physician knows that, if the patient's WNV infection occurred within the last 3 or 4 months, there is roughly a 70%

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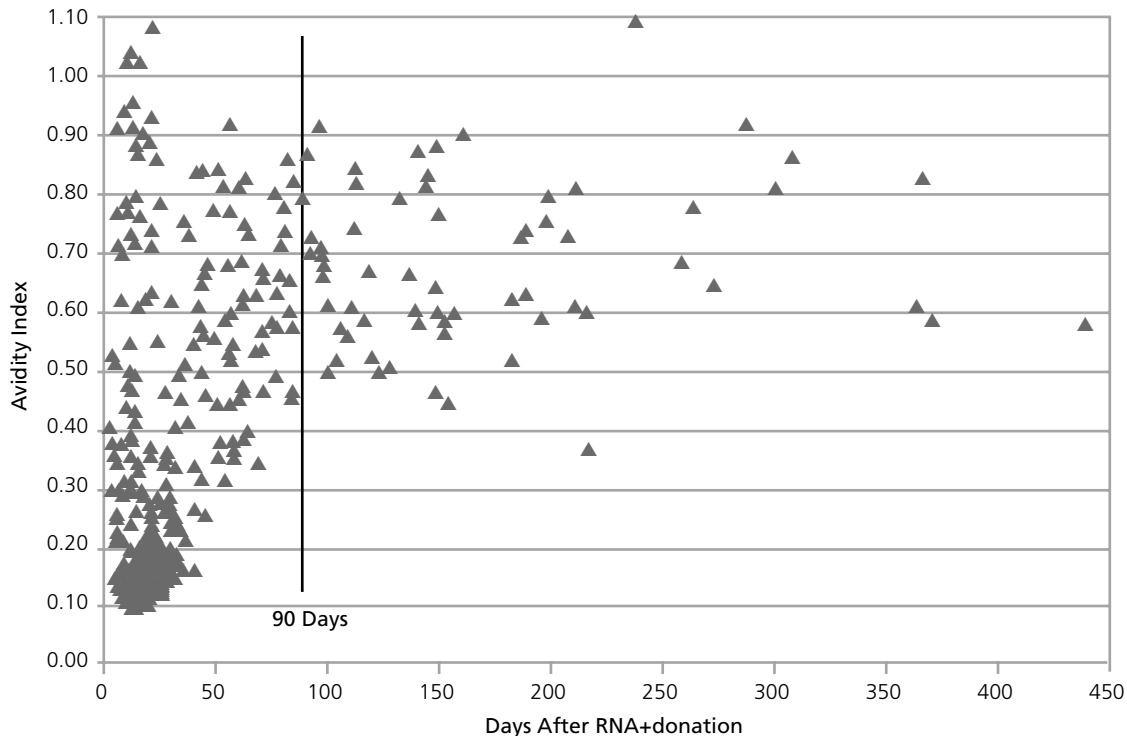
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Continued from Front

chance that the AI will be low; if the result is indeed "low avidity", then he can safely assume (based on 98% accuracy of a low avidity result) that the patient became infected during the last 3-4 months. However, if the result is "high avidity", then he cannot tell when the patient was exposed to WNV. The reported avidity result is indeed low (AI=0.24), indicating recent WNV infection. The

physician accepted the reasonable odds that a WNV IgM+IgG+ patient recently infected with WNV will show low IgG avidity, and indeed obtained a low avidity result that clearly supports a diagnosis of recent WNV infection. Armed with this information, the physician can now design an appropriate management course for the patient.

WNV IgG avidity of follow-up samples from RNA+ blood donors



Listing of Related Assays

For complete specimen information and CPT Code(s), view our Reference Laboratory test listing on our website at www.focusdx.com.

Code #	Test Description
42601	West Nile Virus IgG Avidity, ELISA

To send specimens or obtain additional information, please contact our Client Services Department at

800 445 4032

For technical assistance, contact Focus Diagnostics' Scientific Director of Immunology.



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