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WEST NILE VIRUS RNA DYNAMICS AND ANTIBODY EVOLUTION BASED ON FOLLOW-UP OF VIREMIC BLOOD DONORS

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Background:

Screening donors for West Nile virus (WNV) RNA using nucleic acid amplification technology (NAT) in 2003, led for the first time to detection of humans during the viremic, pre-seroconversion phase of infection. An understanding of the time course and dynamics of WNV RNA and serological markers following acute infection has important implications for donor screening and deferral policies, as well as for diagnosing WNV infection in clinical settings.

Methods:

Donations were screened for WNV by either Mini-Pool NAT (MP) with (16 units/pool) or individual donation NAT (ID-NAT) using the Gen-Probe/Chiron TMA assay. Index unit viral loads were determined using a target-capture/real-time PCR assay (Chiron Corporation) and IgM and IgG status using EIAs (Focus Technologies). NAT-reactive donors were offered enrollment into a follow-up study that included a symptom questionnaire at enrollment and sampling at weekly intervals, with follow-up ending when donors tested negative by ID-TMA and developed WNV IgM. Follow-up samples were tested for RNA by TMA and RT-PCR, as well as for IgM and IgG antibodies.

Results:

From July 1 through October 31, 2003, NAT screening of 681,567 donations yielded 220 confirmed viremic donations with 39 (18%) identified by ID-NAT and 181 (82%) identified by MP-NAT. Median viral load of confirmed positive donations was 2370 gEq/mL (range: <50 – 690,159); 43 (20%) confirmed viremic index donations tested IgM-reactive and 39 (18%) IgG-reactive. 182 (83%) of the confirmed positive donors enrolled into the follow-up protocol. The first follow-up specimen was obtained a median

of 9 days (mean 15 days) following the index viremic donation. Enrolled donors gave an average of 2.5 follow-up specimens (range: 1-8). Of the 140 IgM negative index donations, seroconversion occurred on the first f/u bleed in 113 (81%) cases and the second f/u bleed in 27 (19%) cases. The time to IgG SC following IgM SC averaged 3.7 (95%CI 2.6, 4.8) days. The time to loss of detectable RNA by ID-TMA averaged 7.9 (95%CI 6.2, 9.6) days after IgM SC and 4.1 (95% CI 2.3, 5.9) days after IgG SC.

Conclusions:

IgM and IgG seroconversion occur sequentially and consistently over the 2 weeks following viremic donations, supporting use of SC for donor confirmation and reinstatement, and for clinical diagnostic testing. However, low-level WNV RNA continued to be detectable by TMA for ~8 days following IgM and 4 days following IgG SC. The infectivity of transfusions with such low-level viremia post-SC is under investigation. We are also conducting further viral load analyses to estimate the duration and kinetic parameters of the RNA+ pre-SC phase.