



# MMWR™

Morbidity and Mortality Weekly Report

**MMWR Dispatch**  
**Vol. 52 / September 18, 2003**

## Update: Detection of West Nile Virus in Blood Donations — United States, 2003

During the 2002 epidemic of West Nile virus (WNV) in the United States, a total of 23 persons were reported to have acquired WNV infection after receipt of blood components from 16 WNV-viremic blood donors (1), and an estimated 500 viremic donations might have been collected (B. Biggerstaff, Ph.D., CDC, personal communication, 2003). Because of the possibility of recurrent WNV epidemics in the United States, blood collection agencies (BCAs) recently implemented WNV nucleic acid–amplification tests (NATs) to screen all donations and quarantine and retrieve potentially infectious blood components. This report describes the performance of national blood donation screening during the WNV epidemic of 2003 and documents the first transfusion-associated WNV transmissions identified in 2003. Healthcare providers should report suspected cases of transfusion-associated WNV transmission to state health authorities; state health departments receiving such reports are encouraged to notify CDC.

### Surveillance and Testing Activities

Experimental screening tests were implemented to help identify viremic donations and prevent NAT-reactive blood components from entering the blood supply. WNV screening is performed using minipools (MPs) of six or 16 different donation samples depending on the manufacturer format. A reactive donation is identified when an index donation that is part of a reactive MP of plasma samples also is found to be reactive on individual donation testing (IDT). Donors are asked to participate in a follow-up study to confirm WNV infection, and the implicated donations and follow-up samples undergo confirmatory testing to determine if WNV is present. Blood components from donations that were not reactive in the MP or IDT screening test are released for transfusion, and all components made from IDT-reactive donations are discarded.

Several large BCAs that account for approximately 95% of the nation's civilian blood donations and 100% of the military donations provide weekly summaries of WNV screening data to CDC and the Food and Drug Administration (FDA)

that are used to evaluate the national screening effort. From late June to mid-September 2003, approximately 2.5 million donations were screened for WNV; 1,285 (0.05%) were initially reactive for WNV by using nucleic acid–amplification tests (NAT) implemented under FDA's investigational new drug (IND) mechanisms (2). Of these 1,285 donations, 601 (0.02% of the total donations) are considered presumptive viremic donations (PVDs) (i.e., a donation that is repeatedly reactive by the primary and/or alternate NAT assay or a primary NAT assay with a very high signal). Results of additional testing are pending for 209 initially reactive donations. For surveillance purposes, PVDs are reported by blood bank directors to state health departments with the results of testing; the date of the donation; and the donor's age, sex, and county of residence. The majority of states then provide this information to ArboNET, a cooperative surveillance project between CDC and 57 state and local health departments that monitors domestic arbovirus activities.

As of September 16, 2003, a total of 489 WNV-viremic blood donors have been reported to ArboNET. States reporting >50 PVDs to ArboNET include Colorado (154 donors), Nebraska (116), and South Dakota (56). During July 1–September 16, a total of 19 counties in four states (Colorado [five counties], Nebraska [10], South Dakota [two], and Wyoming [one]) reported at least five PVDs. Demographic information was available for 333 of these donors. The mean age was 45 years (range: 15–83 years); 181 (54%) were male. Dates of detection ranged from June 25 to September 12. Of these 333 persons, 296 (89%) remained asymptomatic after donation, 35 (11%) had WNV-associated fever, and two (0.7%) had WNV-associated meningoencephalitis.

To evaluate the sensitivity of the MP-NAT screening algorithm, a large BCA retested archived individual samples collected in regions with high MP-NAT yield rates that had tested nonreactive previously in MPs. Detection of samples reactive under IDT triggered immediate quarantine and retrieval to prevent transfusion of corresponding components. However, some associated components already had been transfused on the basis of nonreactive MP-NAT screening results before the

ID-NAT results were obtained. Additional WNV RNA and WNV-specific IgM antibody testing of the IDT-reactive donation specimens and follow-up donor samples were conducted to confirm reactivity. As part of standard operating procedures, blood component recipients are notified if these results indicated that the IDT-NAT reactivity was WNV-specific. As of September 16, two cases of confirmed transfusion-associated WNV transmission have been identified.

## Case Reports

**Case 1.** On July 29, a Texas man aged 48 years donated blood at a regional blood center. Initial WNV screening using a 16-donation sample MP-NAT was nonreactive, and the associated blood components were released for transfusion. On August 14, as part of the retrospective study, samples in this nonreactive MP were retested as individual samples. On retesting by IDT-NAT, the implicated donation was reactive. Previously issued components were recalled immediately by using standard operating procedures for withdrawal; the plasma was destroyed, and the platelets had not been transfused before expiration. The index donation sample was retested individually and found to be reactive; this was confirmed subsequently by using different NAT formats. Viral load testing is pending. The sample tested negative for WNV-specific IgM and IgG antibodies. On follow-up, the donor reported that he had not had any symptoms during the preceding month; a blood sample collected at 30 days after the index donation was ID-NAT nonreactive but positive for WNV-specific IgM and IgG antibody at a commercial laboratory, consistent with acute WNV infection and seroconversion.

Before retrospective testing and recall of blood components, packed red blood cells from this implicated donation had been transfused into a Texas man aged 71 years who had undergone aortic graft surgery on the preceding day; an additional four components from MP-NAT negative donations (all determined to be IDT-NAT nonreactive) were transfused the same day. At the time of transfusion, the patient was in poor health and had sepsis. Fever and signs of encephalitis compatible with WNV infection were identified on the third day after transfusion; WNV infection in the recipient was documented by the development of WNV-specific IgM and neutralizing antibody by the 11th day after the transfusion of the implicated component. In addition, NAT of the recipient's serum from the second, seventh, and 11th days after transfusion all indicated the presence of WNV RNA. As of September 16, the patient was recovering.

**Case 2.** On August 4, a Nebraska man aged 80 years received 27 blood components following cardiac surgery, including packed red blood cells (from eight donors), platelets (12 donors), and fresh frozen plasma (six donors). The patient was discharged on August 14. On August 17 (13 days after transfusions), he had mental confusion followed by fever, and he was rehospitalized with a diagnosis of encephalitis. Serum and cerebrospinal fluid collected on August 20 were positive for WNV IgM by capture ELISA. As of September 16, the patient was recovering.

All of the 26 persons who donated the blood products received by this patient were residents of southeast Nebraska who donated locally: six in February 2003 and 20 from late July to early August. At the time of donation, serum from these 20 donors was screened for WNV using MPs of six donors; all MPs containing these donations were nonreactive. The six donations collected during February 2003 were collected before the institution of WNV testing in the United States and were not screened for WNV.

The Nebraska Health and Human Services System identified samples of the original donations from the 20 persons who donated from late July to early August, 2003. These 20 samples were tested by NAT at three different laboratories; one sample tested reactive or equivocal in all three laboratories. A convalescent serum sample was obtained from the implicated donor 45 days after the initial donation. Serum from the initial donation did not contain WNV-specific IgM antibody; however, the convalescent serum sample did contain antibody, demonstrating seroconversion. Other components from this donor were quarantined on reporting of WNV infection in the index patient; no other components from this donation were transfused.

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**Editorial Note:** Nearly all human WNV infections result from mosquito bites; however, transfusion-associated WNV transmission resulted in a small number of WNV infections in 2002 (1). Implementation of national blood donor screening for WNV in 2003 has reduced this risk substantially by removing hundreds of units of potentially infectious blood donated by asymptomatic donors. WNV titers in infectious blood components have been documented as low as 0.8 plaque-forming units/mL during the 2002 investigations (1) and are lower than the titers seen in other screened blood-borne viral pathogens such as human immunodeficiency virus or hepatitis C virus. Despite these low levels, all of the infectious components identified in the 2002 investigations would have been detected by using the current investigational assays in a MP-NAT format. The two cases of transfusion-associated WNV transmission reported here illustrate that potentially infectious units can escape detection due to very low viremia or other possible mechanisms; for this reason, the risk for transmission has not been eliminated.

Because MP screening might not detect low-level viremic donations, a large BCA initiated the retrospective testing study of MP-NAT nonreactive samples as individual samples to determine the frequency of blood with low-level WN viremia in blood banks serving regions experiencing a large number of mosquito-borne human infections. The findings of this study suggest the need to develop more sensitive screening NATs for use in MP testing; if BCA screening capacity allows, replacing MP screening with IDT screening might be considered in areas experiencing a high number of infections among donors. Although individual unit testing of the nation's blood supply is not feasible because of logistics, space, and resource constraints, IDT is being implemented in selected blood banks serving Kansas, Nebraska, North Dakota, Oklahoma, and South Dakota.

Cases of WNV illness associated with transfusions might be identified during local health department investigations of

patients with reported WNV disease (1). History of blood donation or transfusion during the 4 weeks before illness onset is cause for investigation to identify possible transfusion-associated transmission of WNV. Other suspected cases might be identified by investigation of recipients of MP nonreactive donations that have been tested separately and found to be viremic at levels below detection by current MP-NAT format. During 2003, to assist BCAs, federal agencies, and state health departments in assessing the residual risk for transfusion, FDA and CDC have worked with state and local health departments to conduct surveillance to detect possible transfusion-associated WNV transmission so appropriate and timely measures can be taken to maintain the safety of the nation's blood supply. Health-care providers should continue to investigate WNV illness in persons who have received blood transfusions (3) and report suspected cases of transfusion-associated WNV transmission to state health authorities. State health departments receiving such reports are encouraged to notify CDC through ArboNET as part of the national surveillance of human WNV infection.

#### Acknowledgments:

P Ericson, L Sieg, D Michels, MD, Community Blood Bank; S Rademacher, MD, Consultants In Infectious Disease, Lincoln; B Beecham, Nebraska Health and Human Svcs. J Brown, DVM, RS Lanciotti, PhD, A Lambert, A Noga, Div of Vector-Borne Infectious Diseases, CDC.

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