of diagnostic tests, and it is appropriate to highlight its importance—particularly in the case of primary CNS lymphoma, which has decreased in prevalence since the advent of combination antiretroviral therapy [3–5].

Variability in nucleic acid amplification protocols between laboratories may result in varying levels of assay sensitivity. Our report aims, in part, to emphasize how EBV DNA PCR performs in a clinical setting that is commonly encountered in developed countries—specifically, in situations in which a commercial or commercially affiliated laboratory offers a novel diagnostic test for physicians in practice. These physicians often have no control over how the test is set up or performed. We believe our results have particular relevance for physicians practicing under such circumstances. We agree that, as for any nonstandardized test, the potential for variability should be carefully considered when EBV DNA PCR results are interpreted in the course of evaluation of patients with HIV infection and CNS disease.

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References


Confirmation of Results of Tests for West Nile Virus Infection in Organ Transplant Recipients

Sir—We refer to the recent article by Ravindra et al. [1], which describes 3 recipients of kidney or pancreas transplants who developed West Nile fever, 2 of whom had meningoencephalitis. We describe a renal transplant recipient who also developed West Nile fever with meningoencephalitis and who remained severely disabled after the development of infection. We also wish to point out the importance of confirming a positive result of an ELISA test with the plaque reduction neutralization test.

A 32-year-old man from Yemen who had received a renal transplant was admitted to the hospital in October 2003 with a 3-day history of fever, chills, and headache. He received immunosuppressive therapy that included prednisone, mycophenolate, and cyclosporine. The patient had no history of blood product transfusion since the time of his transplantation. At admission, the patient was lethargic and had a fever (temperature, 38.8°C), and he became encephalopathic, with a deteriorating level of consciousness that required ventilator support. Lumbar puncture was performed, and analysis of CSF samples revealed a WBC count of 110 cells/mm³ (23% polymorphs, 40% lymphocytes, 2% band form, and 22% monocytes), an RBC count of 15 cells/mm³, a protein level of 117 mg/dL, and a glucose level of 59 mg/dL. IgM Capture ELISA (PanBio) detected IgM antibody to West Nile virus in serum samples but not in CSF samples. The serum specimen was also IgG antibody negative. Testing of the serum samples with capture ELISA was repeated 4 weeks later, and the results were positive for both IgG and IgM antibody. An electroencephalogram showed severe slowing bilaterally and frontal sharp waves consistent with encephalopathy. A CT scan did not reveal any significant abnormality. Results of confirmatory testing with a plaque reduction neutralization test (performed at New York state Department of Health) were negative at admission and were strongly positive 4 weeks later.

Management of the patient’s illness involved supportive care. Immunosuppression was decreased by stopping treatment with mycophenolate and cyclosporine and by tapering the dose of prednisone. The patient required tracheotomy and receipt of long-term mechanical ventilation; his level of consciousness did not improve, and he died after 3 months.

In 2003 alone, 9858 cases of West Nile fever were reported across the United States, with a case-fatality rate of 2.6% [2]. Of the solid-organ transplant recipients with West Nile fever who were described in case reports, 8 of 9 had encephalitis, and 2 of the 8 died of the disease [1, 3]. Two of 3 patients in the report by Ravindra et al. [1] had encephalitis, and all recovered.

The patient whom we describe remained dependent on ventilatory support and did not recover consciousness for 3 months, at which time he died. This case emphasizes the serious consequences of West Nile fever, even if patients survive the illness [3].

West Nile virus infection is diagnosed by detection of IgM antibody to West Nile virus in serum or CSF samples by use of the IgM antibody capture ELISA as a sen-
sitive test. Of the patients with cases of West Nile virus identified in New York City in 1999 and 2000 and for whom a CSF sample was available, 95% had demonstrable IgM antibody (90% within 8 days of onset of symptoms) [4].

Residents in areas in which West Nile virus is endemic may have persistent IgM antibody from a previous infection that is unrelated to their current clinical illness, and, because most infected persons are asymptomatic and because IgM antibody may persist for ≥6 months, an increase in the West Nile virus–specific neutralizing antibody titer between serum samples obtained in the acute phase and serum samples obtained in the convalescent phase is confirmatory of acute infection [5].

Serum samples for which ELISA demonstrates positive results should also be tested by plaque reduction neutralization test, the most specific test for arthropod-borne flaviviruses, to determine the specificity of antibodies to West Nile virus [6]. False-positive results of ELISA can occur because of the presence of other flaviviruses, such as St. Louis encephalitis virus, Japanese encephalitis virus, yellow fever virus, and dengue fever virus [7].

The close antigenic relationships among the flaviviruses may cause persons who were recently vaccinated with yellow fever vaccine or Japanese encephalitis vaccine or persons who had been recently infected with a related flavivirus (e.g., St. Louis encephalitis fever or dengue fever) to have a positive result of a test for IgM antibody to West Nile virus [7, 8]. The patient from Yemen whom we describe had resided in the United States for many years and had no history of recent travel or of recent vaccinations, making infection with other flaviviruses less likely.

In conclusion, West Nile virus infection in solid-organ transplant recipients can cause severe disability, and diagnosis of West Nile virus infection made on the basis of results of ELISA for antibodies should be confirmed with a plaque reduction neutralization test—the most specific test to help distinguish positive results of ELISA or other assays (e.g., an indirect immunofluorescence assay or a hemagglutination inhibition assay) from false-positive results that are due to cross-reactions with other flaviviruses.

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References


Domestically Acquired Fluoroquinolone-Resistant Campylobacter Infection

Sir—In a recent article, Kassenborg et al. [1] reported that, “When patients with domestically acquired fluoroquinolone-resistant Campylobacter infection were compared with matched healthy control subjects in a multivariate analysis, those infected were 10 times more likely to have eaten chicken or turkey cooked at a commercial establishment (18 [55%] of 33 case patients vs. 7 [21%] of 33 controls; matched OR, 10.0; 95% CI, 1.3–78)…. This study provides additional evidence that poultry is an important source of domestically acquired fluoroquinolone-resistant Campylobacter infection” (p. S279).

The presented results are highly dependent on the specific model and variables selected, and they only achieve statistical significance if model uncertainty is improperly disregarded [2]. Our analysis of the same data reveals that the findings are highly sensitive to the subset of risk factors considered, the choice of variable-selection algorithms (e.g., forward vs. backward stepwise variable selection), the selection of a model form (e.g., logistic regression vs. nonparametric alternatives), and the treatment of missing data. The claimed 95% CI for the matched OR excludes 1 only because uncertainties have not been accounted for in these modeling choices [2]. Slight variations in modeling approach (e.g., using backward vs. forward stepwise variable selection vs. Bayesian model averaging) eliminate the claimed finding of a positive association between fluoroquinolone-resistant campylobacteriosis and poultry consumption. (Moreover, 55% is not usually considered “10 times more likely” than 21%. The matched OR of 10 is only a prediction from an unvalidated logistic regression model for which appropriate model diagnostics have not been presented [3], not an empirical finding.)

Nonparametric techniques, such as classification tree analysis, can help to avoid parametric model-selection biases.