positive 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 \( \geq 6 \) 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.

Acknowledgment


Florian H. Pilsczek and Michael Augenbraun
Division of Infectious Diseases, State University of New York Downstate Medical Center, Brooklyn, New York

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.
[4]. Kassenborg et al. [1] state, “In our final multivariate model, we examined the following risk factors: eating chicken or turkey cooked at a commercial establishment, eating in a non–fast food restaurant, using antacids, and eating nonpoultry meat at home. Using this model, we found that eating chicken or turkey at a commercial establishment was the only risk factor that remained independently associated with illness” (p. S281). By contrast, when we examined the same data set using classification tree analysis (which allows all variables to be considered), we found that exposure to ground beef outside of the home and exposure to raw milk both appear to be significant risk factors for fluoroquinolone-resistant campylobacteriosis. If all variables are considered, chicken consumption as a whole and chicken consumption in commercial establishments have nonsignificant negative associations with fluoroquinolone-resistant campylobacteriosis, whereas chicken consumption as a whole (of all types and at all venues) is associated with a statistically significantly lower risk of campylobacteriosis.

In summary, the findings presented by Kassenborg et al. [1] appear to be highly sensitive to specific modeling choices. Different choices—or use of nonparametric methods, to avoid having to make such choices—lead to very different conclusions. The reported significant positive association between poultry consumption and domestically acquired fluoroquinolone-resistant Campylobacter infection appears to be an implication of the particular model used that disappears when less restrictive models are used.

Acknowledgment

Potential conflict of interest. L.A.C. has, in previous years, prepared comments on fluoroquinolone risk assessment for the US Food and Drug Administration’s Center for Veterinary Medicine and the Animal Health Institute. He testified in 2003 for Bayer Animal Health on enrofloxacin use and campylobacteriosis. None of these parties was involved in the writing of this letter.

Louis Anthony Cox, Jr.
Cox Associates, Denver, Colorado

References


Reprints or correspondence: Dr. Louis Anthony Cox, Jr., Cox Associates, 503 Franklin St., Denver, CO 80218 (tony@cox-associates.com).

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Reply to Cox

Sir—Amplifying comments he made previously [1], Cox [2] has provided an interesting critique of our analysis of the FoodNet Campylobacter case-control study data [3]. We agree that multivariable analysis of epidemiologic data is inherently selective from a large number of exposures and the nearly infinite number of model forms. We agree that choosing an appropriate model is an essential part of data analysis and interpretation [4]. We followed standard epidemiologic principles to analyze the largest reported case-control study of sporadic Campylobacter infections and found a consistent, strong, and robust association between domestically acquired fluoroquinolone-resistant Campylobacter infection and the eating of poultry (chicken and turkey) outside of the home [3].

We do not agree that classification and regression tree (C&R T) analysis is an appropriate analytic tool for our data. The purpose of our analysis was to estimate the contribution of several independent exposures (risk factors) on the main outcome (fluoroquinolone-resistant Campylobacter infection). The hierarchical nature of the C&R T models does not allow estimation of the net effects of individual risk factors on the main outcome [5]. Lemon et al. [5] caution that, in situations like those in our study, which was designed to determine risk factors for Campylobacter infection, C&R T analysis should “not be used as a substitute for proven regression techniques” (p. 179). Moreover, the repeated use of “all variables” in describing a reanalysis of our data [2] leads us to believe that the conclusions of this reanalysis may be the result of the “data dredging,” which Lemon et al. [5] specifically warn against in the application of C&R T.

Bayesian model averaging, which is distinct from C&R T, is an intriguing suggestion to account for uncertainty in our logistic model in a quite different fashion. As Viallefont et al. [6] discuss, when using Bayesian model averaging, the prior probability of the model form that was selected should take into account the available scientific knowledge. A Bayesian analysis of our data would use the large body of scientific evidence linking the use of fluoroquinolones (such as enrofloxacin) in poultry to the development of resistance in Campylobacter and the association between Campylobacter infection in humans and exposure to poultry to calculate a prior probability [7, 8]. Such an analysis would likely result in an even stronger measure of association between domestically acquired, fluoroquinolone-resistant Campylobacter infection in humans and eating chicken outside of the home.

Widespread use of the standards proposed by Bagley et al. [9] in the scientific literature would create greater transparency in describing what is done in multivariable analysis. Space limitations often limit such descriptions. Amplifying the description of the multivariable analysis in our study would not change the findings.

Readers interested in the legal context of this discussion, including the Administrative Law Judge’s initial decision to up-