[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

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### References

1. Kassenborg HD, Smith KE, Vugia DJ, et al. Fluoroquinolone-resistant *Campylobacter* infections: eating poultry outside of the home and foreign travel are risk factors. Emerging Infections Program FoodNet Working Group. Clin Infect Dis **2004**; 38(Suppl 3):S279–84.
2. Viallefont V, Raftery AE, Richardson S. Variable selection and Bayesian model averaging in case-control studies. Stat Med **2001**; 20:3215–30.
3. Bagley SC, White H, Golomb BA. Logistic regression in the medical literature: standards for use and reporting, with particular attention to one medical domain. J Clin Epidemiol **2001**; 54:979–85.
4. Lemon SC, Roy J, Clark MA, Friedmann PD, Rakowski W. Classification and regression tree analysis in public health: methodological review and comparison with logistic regression. Ann Behav Med **2003**; 26:172–81.

## 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&RT) 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 *Campy-lobacter* infection). The hierarchical nature of the C&RT 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&RT 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&RT.

Bayesian model averaging, which is distinct from C&RT, 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-

hold the US Food and Drug Administration's (FDA) proposed prohibition of fluoroquinolone use in poultry, are referred to FDA docket number 00N-1571 [1].

## Acknowledgment

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## References

1. Department of Health and Human Services. Expert witness testimony by Anthony Cox. Exhibit no. B1901. US Food and Drug Administration initial decision docket no. 00N-1571. Available at: http://www.fda.gov/ohrms/dockets/dailys/04/mar04/031604/00n-1571-idf0001-vol389.pdf. Accessed on 5 October 2004.
2. Cox A. Domestically acquired fluoroquinolone-resistant *Campylobacter* infection. Clin Infect Dis **2004**; 39:1399–400 (in this issue).
3. Kassenborg HD, Smith KE, Vugia DJ, et al. Fluoroquinolone-resistant *Campylobacter* infections: eating poultry outside the home and foreign travel are risk factors. Emerging Infections Program FoodNet Working Group. Clin Infect Dis **2004**; 38(Suppl 3):S279–84.
4. Breiman L. Statistical modeling: the two cultures. Statistical Science **2001**; 16:199–231.
5. Lemon SC, Roy J, Clark MA, Friedmann PD, Rakowski W. Classification and regression tree analysis in public health: methodological review and comparison with logistic regression. Ann Behav Med **2003**; 26:172–81.
6. Viallefont V, Raftery AE, Richardson S. Variable selection and Bayesian model averaging in case-control studies. Stat Med **2001**; 20:3215–30.
7. Friedman CR, Neimann J, Wegener HG, Tauxe R. Epidemiology of *Campylobacter jejuni* infections in the United States and other industrialized nations. In: Nachamkin I, Blaser M, eds. *Campylobacter*. Washington, DC: ASM Press, **2000**:121–39.
8. Smith K, Bender J, Osterholm M. Antimicrobial resistance in animals and relevance to human infections. In: Nachamkin I, Blaser M, eds. *Campylobacter*. Washington, DC: ASM Press, **2000**:483–95.
9. Bagley SC, White H, Golomb BA. Logistic regression in the medical literature: standards for use and reporting, with particular attention to one medical domain. J Clin Epidemiol **2001**; 54:979–85.

# Lack of Evidence That False-Positive *Aspergillus* Galactomannan Antigen Test Results Are Due to Treatment with Piperacillin-Tazobactam

Sɪʀ—Test results positive for circulating galactomannan (GM) in peripheral blood are a major criterion defining invasive aspergillosis [1]. Therefore, surveillance of patients with hematological malignancies who are at high risk for invasive aspergillosis by performing the GM assay on peripheral blood samples has become a standard method in many centers. Recent reports of false-positive results obtained with the Platelia *Aspergillus* GM ELISSA (Bio-Rad) in association with administration of piperacillin-tazobactam were published in *Clinical Infectious Diseases* and elsewhere [2, 3]. As a possible explanation, the investigators also reported on ELISA results positive for GM in most batches of piperacillin-tazobactam used during the study periods. We performed a study to survey the incidence of false-positive GM assay results associated with piperacillin-tazobactam therapy at our institution (Charité-Campus Benjamin Franklin; Berlin, Germany). From February 2003 through July 2003, we performed the *Platelia Aspergillus* GM assay twice weekly on peripheral blood samples obtained from neutropenic patients with hematological abnormalities who were receiving 13 different batches of piperacillin-tazobactam. Altogether, 40 neutropenic episodes (median duration, 14.3 days; range, 4–53 days) among 35 patients (median age, 51.6 years; range, 19–77 years) with acute leu-

kemia (18 patients), lymphoma (8 patients), myeloma (4 patients), or other diseases (5 patients) were evaluated. During piperacillin-tazobactam treatment (total duration, 254 days; median duration, 6.4 days), 96 GM assays were performed. Ninety-four GM assays had negative results, and only 2 had positive results (optical density indexes, 1.6 and 2.2). Because these GM-positive samples were obtained from a patient who died from proven pulmonary aspergillosis within a week after the first positive GM assay test results, they were considered to be true-positive results.

Although we performed our investigation during a time period similar to that of previous reports (i.e., early 2003), we found no evidence of false-positive GM assay results in association with piperacillin-tazobactam treatment. This casts some doubt on the hypothesis of Adam et al. [2] that false-positive GM test results caused by contamination of certain piperacillin-tazobactam batches are the result of a recent modification of the drug production process. Thus, further investigations are warranted to precisely determine the origin of false-positive results.

## Acknowledgment

**Olaf Penack, Stefan Schwartz, Eckhard Thiel, and Igor Wolfgang Blau**

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## References

1. Ascioglu S, Rex JH, de Pauw B, et al. Defining opportunistic invasive fungal infections in immunocompromised patients with cancer and hematopoietic stem cell transplants: an international consensus. Clin Infect Dis **2002**; 34: 7–14.
2. Adam O, Auperin A, Wilquin F, Bourhis JH, Gachot B, Chachaty E. Treatment with piperacillin-tazobactam and false-positive *Aspergillus* galactomannan antigen test results for patients with hematological malignancies. Clin Infect Dis **2004**; 38:917–20.
3. Sulahian A, Touratier S, Ribaud P. False positive test for *Aspergillus* antigenemia related to con-