Schizophrenia and Serological Methods for Diagnosis of Toxoplasmosis

Sir—Infection by the protozoan *Toxoplasma gondii* results in the formation of parasite cysts that persist throughout the life of the host in several tissues, mainly striated muscle and the brain. The size of the cysts (up to 200 microns in diameter) and their location in the brain raise the question of whether *Toxoplasma* infection has potential neurological consequences. This question was examined in a recent issue of *Clinical Infectious Diseases* by Yolken et al. [1]. After assuming that “humans can become infected with *T. gondii* cysts after ingesting cat feces” ([1], p. 842)—a mode of contamination for which the evidence is purely anecdotal—the authors found that individuals with a first episode of schizophrenia had significantly increased levels of anti-*Toxoplasma* antibodies, as compared with control subjects. This suggests that there is possibly a relationship between *Toxoplasma* infection and the occurrence of schizophrenia. We consider that such conclusions should be examined with extreme care, because the serological methods and statistical analysis used in the study have major limitations.

None of the laboratory methods described in the study are standard, so that the cutoff values of sensitivity and specificity for different antibody classes (IgG, IgA, and IgM) cannot be accurately defined. In addition, both the correspondence between the EIA optical density values and international units for IgG, and any defined standards for IgM or IgA are dramatically lacking. The results of Western blot analyses also appear very puzzling due to the low number of bands detected (4); usually, 10–15 bands are detected when standardized commercial blots (available in Europe) are used. The examples of Western blot reactions that readers are invited to view on the authors’ Web site are also intriguing: the only figure presented (which is poorly defined) shows a greater number of bands for a patient with recent toxoplasmosis than for a patient with schizophrenia. Therefore, on the basis of these results, it is not possible to clearly define the serological status of patients and control subjects or to differentiate between them by the date they were infected by *T. gondii*.

The statistical analysis used by Yolken and colleagues leads them to conclude there was a significant difference in the rate of seropositivity to *T. gondii* between patients and control subjects. This analysis is also subject to criticism, because of the possible inappropriate selection and small size of the control group. Surprisingly, the control group was smaller (n = 27) than the group of case patients (n = 38); recruitment of at least the same number of controls would be expected. Furthermore, using an arbitrary cutoff value for anti-*Toxoplasma* antibody levels, the authors report that reactivity to *T. gondii* was only 11% among control subjects. This rate is not consistent with the much higher prevalences (36%–54%) reported from other regions of Germany (where this study was performed) [2, 3, 4]. In addition, to take into account both uninfected and infected subjects in order to conclude that the case patients had “significantly” higher levels of antibodies to *T. gondii* than did the control subjects is nonsense.

Finally, although we do agree that experimental studies strongly suggest that *Toxoplasma* infection can induce behavioral changes in mice and rats, we think that extension of these findings to humans with severe psychiatric disorders needs more accurate and rigorous proofs that those presented in this article.

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References

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Reply

Sir—We thank Derouin et al. [1] for their interest in our research. The brief report format precluded the inclusion of details about our experimental approach and methods, and we welcome the opportunity to discuss them in this letter of reply.

The goal of our study was to compare the serum levels of *Toxoplasma* antibodies of different Ig classes for a group of individuals with recent-onset schizophrenia and levels for a group of well-characterized control individuals without evidence of psychiatric abnormalities. The goal of the study was not to determine the precise timing of *Toxoplasma* infections in the different study groups nor to compare the prevalence of infection in populations other than those we studied. For this reason, we chose to employ a microplate EIA format for the initial measurement of IgG-, IgM-, and IgA-class antibodies and to use Western blotting to confirm the specificity of the IgG and IgM class antibodies in samples that attained an arbitrary level of EIA reactivity. The materials used for the assays were obtained from reliable commercial sources and the specificities of both the EIA and Western blot reactions

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