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### Use of Cefotaxime and Metronidazole for Treating Cerebral Abscesses

SIR—In 1993, Sjölin et al. reported the cases of 15 patients with brain abscesses who were treated with cefotaxime and metronidazole and noted that cefotaxime had rarely been reported as a treatment for cerebral abscesses [1].

Since 1983, we have empirically used the combination of cefotaxime and metronidazole as the initial treatment for cerebral abscesses; this treatment has been based on the most likely focus of infection, the epidemiologic changes in the infections in our area and in our hospital [2], and our common sense antibiotic use policy [3].

In one study published in 1991 [4], we compared 35 adult patients with cerebral abscesses who received a standard treatment with 31 patients who were treated with cefotaxime and metronidazole. In the group treated with cefotaxime and metronidazole, there were higher rates of success and no significant differences in mortality or recurrences of abscesses, although there were fewer complications and there was lower mortality in the group treated with cefotaxime and metronidazole.

The total mortality in our study was 14%, whereas there were no deaths in the study by Sjölin et al. [1]; these differences in mortality were probably related to the fact that the patients had different types of disease and different types of complications. In our study, higher mortality was associated with an age of >40

years, an ultimately fatal underlying disease, an initial clinical status of critical illness, coma, or inadequate antibiotic treatment [4].

In the past several years we detected a rise in the incidence of infection due to group A streptococci that cannot be as effectively treated with cefotaxime and metronidazole as with penicillin G since the activity of cefotaxime against group A streptococci was lower than that against penicillin G; this rise may be due to the massive use of quinolones and third-generation cephalosporins for treating general infections. Thus, we believe that an individualized treatment approach and follow-up with serial CT scans is required in cases where penicillin or ampicillin plus chloramphenicol continue to be the antibiotics of choice for patients with cerebral abscesses.

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### Viral Antibodies in Chronic Fatigue Syndrome

SIR—In his article on viral antibodies in chronic fatigue syndrome (CFS), Manian [1] stated that patients with CFS frequently have elevated levels of IgG antibody to the viral capsid antigen (VCA) of Epstein-Barr virus, or elevated levels of antibody to coxsackievirus B1 or coxsackievirus B4. As Manian points out in his discussion, the outcome may have been biased by the fact that the serological tests of patients and controls were not performed concurrently. This is an important point, as we have found significant

differences in levels of IgG antibody to VCA and EA between patients with CFS and matched controls (IgG levels were elevated in patients with CFS), which disappeared after concurrent testing of the samples from patients with CFS and from controls (our unpublished observation).

Not only is concurrent testing of samples relevant, but concurrent collection of the serum samples is important as well. Enterovirus infections are subject to seasonal and geographic variation. This implies that serum samples from controls should be collected at the same time that those from patients are collected and that controls should be matched with the patients for domicile. When we followed such guidelines, we found no differences in levels of antibody to enteroviruses between patients with CFS and controls as well as no differences in levels of antibodies to coxsackie B viruses [2].

We also disagree with Manian's observation of elevated levels of CF antibody to coxsackieviruses. First, the CF antibody response to viruses that are closely antigenically related will not be type specific and may be affected by the "doctrine of original

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antigenic sin," thus actually revealing antibody to a childhood infection.

Furthermore, the statistical analyses applied in Manian's study do not seem appropriate. In the case of ordinal variables (as in immunofluorescence testing) and nonnormal distribution, nonparametric testing should have been applied.

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## Reply

SIR—We appreciate the comments of Swanink et al. regarding our recent article [1]. First, as we discussed in our article, we realize that concurrent serological testing of the case patients and controls would have been ideal. However, we are not sure why our results would necessarily be "biased" toward finding higher titers of antibody to certain viruses in the cases than in the controls when this was not done. Swanink et al.'s unpublished observation regarding the loss of significant differences in elevated levels of IgG antibody to Epstein-Barr virus capsid antigen (EBV VCA) and early antigen between patients with chronic fatigue syndrome and matched controls when concurrent testing was used is interesting. We look forward to their publication of these findings along with a possible explanation.

Second, we realize that enteroviral infection may be seasonal and subject to geographic variation. However, it is interesting that even though our controls were tested during two peak months (July and August) for enteroviral infection in the United States [2], as a group they did not have higher antibody titers against any of the enteroviruses tested when compared with the case patients. Because the case patients were tested throughout the year, any potential bias in comparing enteroviral antibody titers of these groups should have favored the finding of higher titers in the controls rather than in the case patients. However, when there was a significant difference in the enteroviral antibody titers between the case patients and controls, higher titers were always found in the case patients. We think that geographic variation may also help to explain the difference between our findings and those of Swanink and colleagues.

Third, Swanink et al. question the type specificity of CF antibody

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to enteroviruses. Although some cross-reaction may occur, it is interesting that of the 19 cases in which significant titers of antibody ( $\geq 1:8$ ) were found to at least 1 of the 10 coxsackie viruses tested (4 type A and 6 type B) in our study, the majority (68%) had concurrent significant antibody titers to only 4 or fewer viruses. Therefore, the degree of cross-reactivity, at least based on the findings in our study, did not appear to be inordinately high. Moreover, the problem with cross-reactivity should have equally affected the sera from the controls, since the same laboratory performed the tests. The statement regarding "the doctrine of original antigenic sin" is not fully correct, as CF (as opposed to neutralizing) antibodies to enteroviruses usually can be detected only for a few months after onset of infection [3].

Finally, concerning the statistical analysis, a *t* test was used for comparison of geometric means of antibody titers between the two groups. However, because of the possibility of a significant difference in the variances between the case patients and controls, we used the more conservative Welch's alternate *t*-test, which, as opposed to the standard *t*-test, does not assume equal variances [4]. Of note, significantly higher antibody titers to EBV VCA in the case patients vs. the controls were also found, even when the data was analyzed by a different method (Fisher's exact test).

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