host cellular immune response among HTLV-I carriers. In data published elsewhere, we documented subclinical immunosuppression on the basis of the association of HTLV-I infection with reduced response to the tuberculin-purified protein derivative (PPD) recall antigen [3, 4]. In vitro studies suggest that the nonresponsiveness to PPD in these HTLV-I carriers may be related to a lack of IFN-γ production [5]. Other investigators reported evidence of altered cellular immune function in asymptomatic HTLV-I carriers [6, 7].

Unpublished data from the Miyazaki Cohort Study indicate a possible negative interaction between HTLV-I and HCV with respect to abnormal levels of alanine aminotransferase (ALT), with the prevalence of elevated ALT levels being lower in coinfected subjects than in subjects with HCV infection alone. Other researchers in Japan reported a similar effect of coinfection on ALT levels [8]. We postulate that coinfection with HTLV-I could reduce the acute immune-mediated damage to HCV-infected hepatocytes and the release of ALT while at the same time enhancing the persistence of HCV infection and the subsequent risk of liver disease development. However, HCV infection itself could cause liver cancer without the induction of chronic hepatitis, as has been observed in transgenic mice [9]. In addition, we found that HCV coinfection increased the association of HTLV-I with diminished PPD response, although HCV seropositivity itself was not related to the lack of PPD reactivity [10]. As suggested by Dr. Casseb [1], it also is possible that increased cytokine levels play a role in HCV-associated disease progression in HTLV-I carriers. Woitas et al. [11] noted an increased induction of IL-2 and IFN-γ among patients with HCV and human immunodeficiency virus infections but not among patients with HCV alone.

The effect of HTLV-I infection on host immunity in general and on HCV-specific immune response is likely a complicated one. It seems clear that HTLV-I induces dysregulation of cellular immune function. However, to characterize this effect as either immunosuppressive or immune stimulatory, with respect to the natural history of HCV coinfection, may be overly simplistic.

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Waterborne Outbreak of Microsporidiosis

To the Editor—Cotte et al. [1] claim to describe the first documented outbreak of microsporidiosis linked to drinking water. However, before accepting this outbreak as truly being linked to water, we should examine the evidence on which they base their conclusion.

In the United States (USA) and United Kingdom (UK), waterborne outbreaks are ranked depending on the strength of evidence implicating water [2, 3]. Both systems rely on an analysis of both epidemiologic and water quality data to determine the strength of association. In the USA, outbreaks are ranked I (adequate epidemiologic data on exposed and nonexposed persons with relative risk or odds ratio >2 or P < .05 and adequate evidence of water quality failure) to IV (limited epidemiologic data and inadequate evidence of water quality failure). In the UK, outbreaks are categorized into strongly, probably, and possibly associated with water. An outbreak is classified as possibly associated with water if “there is evidence of a water quality failure and/or water treatment problem of relevance but outbreak pathogen is not detected in water” or if “descriptive epidemiology

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suggests that the outbreak is water related and excludes obvious alternate explanations. For an outbreak to be classified as being probably or strongly associated, there must be these factors and/or detection of the pathogen in the water and/or an analytical (case-control or cohort) study demonstrating an association.

Turning to the report by Cotte et al. [1], the outbreak was detected during a 1993–1996 study of microsporidia in stool. There was a marked increase in the proportion of stools positive for microsporidia from June to September 1995, termed the outbreak period. This increase immediately followed a change in technique to increase the sensitivity of the method. The authors did no analytical epidemiologic study (case-control or cohort study). Furthermore, no adequate descriptive epidemiologic study was done, for case patients were not interviewed about possible risk factors, and virtually no information was obtained on case patients not known to be human immunodeficiency virus positive.

During the study, some 4822 water samples from the Lyon distribution systems were examined; there was only 1 coliform failure, which occurred outside the outbreak period. There were 6 samples positive for fecal streptococci, only 1 of which was taken during the outbreak period. No other evidence of water treatment failure was presented.

It appears that the authors based their conclusion regarding a waterborne outbreak solely on the finding that most of the residents lived in the area supplied by one distribution system. No other geographically localized possibility for the outbreak was considered by the investigators.

In the UK, the findings presented would be insufficient for this outbreak to be associated with water, even at the lowest level of possibly associated. In the USA, the outbreak would at best be classified as strength of association IV. Although a waterborne hypothesis is certainly plausible, this outbreak cannot be said to be waterborne on the basis of the evidence presented.

Outbreaks provide unequalled opportunities to study the epidemiology of infectious disease. The results of outbreak investigations often have significant public health, legal, and policy impacts. When making conclusions about the possible causes of outbreaks, epidemiologists must be careful not to draw conclusions that are not fully supported by the available data.

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Reply

To the Editor—We read with interest the comments by Hunter [1] regarding the lack of a real case-control or cohort study design. We agree with this comment, since it was a direct consequence of the retrospective collection of data in our study [2]. However, exhaustive data collection during the study period allowed the study population to be considered as a historical cohort. Regarding criteria for the classification of waterborne outbreaks, they share some limitations for protozoal infections. Markers for fecal contamination have been previously demonstrated to be inappropriate following a cryptosporidiosis outbreak, as was the case in our study. There is also a lack of a reliable, standardized, and routine method to demonstrate the presence of microsporidia in water. Thus, microsporidiosis would never meet the criteria to be considered a cause of a waterborne outbreak, according to these classifications. There is now a large body of evidence for the association of microsporidiosis with water. Since microsporidiosis in immunocompetent persons spontaneously resolves in a few weeks, it appears to be a minor public health problem. However, previous experience in cryptosporidiosis outbreaks demonstrated that even a self-limiting disease may have large medical and economic implications. The aim of our study was to organize and describe previously unreported data. In light of these observations, there is a need for a prospective study regarding the epidemiology of microsporidiosis and its relation with water.

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