Correspondence

Human Studies Provide Insight into the Pathogenesis, Immunology, and Treatment of Cryptosporidiosis

Sir—In their article about Cryptosporidium species, Leav et al. [1] provide a nice summary of data on the molecular biology of these parasites and findings from animal studies. However, there are also recent human studies on the pathogenesis, immunology, and treatment of infection with this organism that were not discussed in the article. For example, the section on pathogenesis states that the diarrhea is typically noninflammatory, although recent studies involving children in developing countries and volunteers with experimental infection have highlighted the role of host inflammation in pathogenesis [2–4]. The direct relationship between proinflammatory cytokines or IFN-γ that was postulated on the basis of findings from animal studies were not demonstrated in human studies [4, 5]. By contrast, recent studies suggest that neuropeptides may be key mediators of diarrhea [6].

The section on immune response focused on murine Cryptosporidium infection, in which IFN is a critical mediator of control of infection. By contrast, we have demonstrated that human infection seems to involve 2 distinct immune responses: a memory response associated with IFN-γ, but also a response in Cryptosporidium-naïve volunteers associated with IL-15 expression and activation of NK cells [7, 8].

Finally, the section on treatment should note that nitazoxanide was shown to be effective for treatment of cryptosporidiosis in 3 placebo-controlled trials, including 1 study that demonstrated improved survival rates among malnourished children [9]. It received approval from the US Food and Drug Administration for this indication in late 2002, and it is now widely available.

A. Clinton White, Jr.1, Prema Robinson,1 and Pablo C Okhuysen2

1Infectious Disease Section, Department of Medicine, and Departments of Molecular Virology and Microbiology and Immunology, Baylor College of Medicine, and 2Department of Medicine and School of Public Health, University of Texas Health Science Center, Houston, Texas

References

Reply

Sir—We appreciate the comments by White et al. [1] in response to our review on Cryptosporidium species [2]. We feel that our characterization of the diarrhea seen in human cryptosporidiosis as “typically noninflammatory” was correct, because fecal leukocytes are usually not detected. However, White et al. [1] correctly emphasize 2 recent studies (one of which was published after the submission of our review) that have demonstrated that cryptosporidiosis may be associated with mild inflammation in a subset of patients—namely, malnourished children from developing countries [3, 4]. One of these studies also reports that intestinal inflammation occurred in a small minority of adult volunteers experimentally infected with Cryptosporidium oocysts [4]. These studies correlate increased levels of several different stool cytokines and increased levels of fecal lactoferrin in children from developing countries with cryptosporidiosis. Lactoferrin level appears to be a reliable marker for intestinal inflammation in the absence of breast-feeding [5, 6]. Although the presence of different cytokines in the stool may indicate an inflammatory state in the intestine, the underlying mechanism for this phenomenon is unclear.

White et al. [1] also mention several important studies analyzing an experimental model of human cryptosporidiosis [7–10]. These studies were not directly...