References


Reply

Sir—We thank Dr. White and colleagues for their interest in our article about paromomycin and the treatment of AIDS-related cryptosporidiosis [1]. We decided to present the as-treated analysis because, according to our interpretation of the data, there was no trend favoring treatment with paromomycin over administration of placebo. A P value of 0.23 from an intent-to-treat analysis represents an approximately 1 in 4 chance that a difference in efficacy does not actually exist. We did not consider this P value to be low enough to call it a trend.

The comments made by Dr. White and colleagues clearly point out the difficulty of conducting clinical research with enteric pathogens in immunocompromised hosts. Because coinfection with other pathogens is likely when AIDS-related cryptosporidiosis is present, our exclusion criteria included known coinfection at the time of enrollment with any of the following organisms: active cytomegalovirus (CMV colitis), Mycobacterium avium complex, Clostridium difficile, and Microsporidium. Giardia, Entamoeba, Isospora, Shigella, Salmonella, Yersinia, or Campylobacter species. Subsequent to enrollment, there were 3 patients in each arm of the study who had Microsporidium species detected in their stool. Evaluation of treatment failure encouraged investigation for coinfection but did not require it.

Biliary tract involvement is common in cases of cryptosporidiosis. Therefore, it would be quite difficult to exclude patients with biliary tract involvement in clinical trials of possible treatments. In addition, because biliary tract involvement is common, an agent deemed effective for AIDS-related cryptosporidiosis should be effective against all of the manifestations of the disease in the gastrointestinal tract.

Concurrent treatment with rifabutin, which might possibly prevent AIDS-related cryptosporidiosis, as has been recently shown [2], was allowed during the study, but treatment with macrolides was not allowed within 14 days of study entry or during the period when paromomycin was being administered. Changes to an antiretroviral therapy were allowed but seldom occurred. In addition, CD4 cell count showed no discernible effect on the outcome of treatment, because entry criteria required a CD4 cell count of <150 cells/mm³. In fact, the median CD4 count was <30 cells/mm³ for both the paromomycin and the placebo groups.

In reviewing our experience with AIDS-related cryptosporidiosis, what we found most interesting is the wide clinical variability of the disease in HIV-infected persons. The ability of the disease to resolve or improve without intervention in patients who were given placebo was remarkable and, in a study with no placebo control, could easily lead to the conclusion that a particular intervention did appear to be effective. We agree that there is still need for well-designed, placebo-controlled studies of any potential antimicrobial agent(s).

As Dr. White and colleagues imply, the best treatment for cryptosporidiosis in HIV-infected persons is highly active antiretroviral therapy [3]. Restoration of lost immune response has improved outcomes for a number of opportunistic infections, including cryptosporidiosis.

Ross G. Hewitt,1 Constantine T. Yiannoutsos,2 and Elizabeth S. Higgs3
1State University of New York at Buffalo, New York; 2Harvard University, Cambridge, Massachusetts; and 3National Institute of Allergy and Infectious Diseases, Bethesda, Maryland

References


Test ing of Urinary Escherichia coli Isolates for Shiga Toxin Production

Sir—We read with interest the recent letter by Wilson et al. [1] on the prevalence of Shiga toxin–producing Escherichia coli (STEC) among isolates from urine samples. Wilson et al. concluded that routine screening of E. coli isolates from urine...
samples for the production of Shiga toxins is not warranted. However, we believe that there are several reasons why this conclusion cannot be drawn from their study.

First, *E. coli* isolates that were present in urine samples were screened by Wilson et al. [1] for Shiga toxin production only if the isolates were sorbitol nonfermenting. The sorbitol-nonfermenting phenotype is specifically associated with the O157:H7 serotype of STEC; ≥50 other serotypes of STEC have been associated with disease in humans [2]. Therefore, use of this method as an initial screening tool will bias against isolation of non-O157:H7 STEC strains. The authors indicated that they used this method because most strains of STEC in the United States are of the O157:H7 serotype and thus are sorbitol nonfermenting. We disagree. Recent studies have revealed that a variety of STEC serotypes are associated with diarrheal disease in individuals in the United States [3, 4]. Estimates reported by the Centers for Disease Control and Prevention (Atlanta) in 1999 suggest that >100,000 cases of diarrhea caused by STEC occur in the United States each year; of these cases, one-third are of the non-O157:H7 serotype [5].

Furthermore, there is no reason to assume that hemolytic uremic syndrome (HUS) secondary to urinary tract infection (UTI) occurs exclusively after infection with the O157:H7 serotype. Although HUS appears to be a rare complication of UTI, there are published reports that link non-O157:H7 STEC with this phenomenon. Two recent case reports have described HUS in adults with UTI [6, 7]; both of the cases reported were due to non-O157:H7 STEC. In a recent literature review, 14 cases of HUS were reported to occur after STEC-associated UTI [8]. Only 6 of the 14 STEC isolates were serotyped; 5 of these 6 STEC isolates were of the non-O157:H7 serotype.

Although Wilson et al. [1] may be correct that routine screening of *E. coli* isolates from urine samples for the production of Shiga toxins is unwarranted, this conclusion cannot be drawn from the results of their study. We do agree that HUS rarely occurs after UTI. It is possible that STEC-associated UTI is rare, or it may be that HUS rarely occurs after STEC-associated UTI. Unfortunately, the authors’ study design did not permit evaluation of either of these possibilities. Until the true incidence of STEC-associated UTIs is known, it will be difficult to conclude how often HUS occurs after STEC-associated UTI and whether screening is warranted.

Recently, significant concerns have been raised that antibiotic treatment can increase expression of Shiga toxin by STEC [9] and that it can precipitate HUS in children with STEC-associated diarrhea [10]. One of the aforementioned case reports suggested that the use of a fluoroquinolone for the treatment of an elderly woman who had HUS and a case of UTI caused by nontypeable, Shiga toxin–producing *E. coli* may have worsened the patient’s clinical status [6]. These data indicate that knowing whether an *E. coli* isolate from a urine sample is an STEC may be advantageous in certain situations.

Until we know the answers to some of the fundamental questions about the overall prevalence of STEC in *E. coli* isolates from urinary samples and about the links between HUS and STEC-associated UTI, it would be premature to conclude that it is unnecessary to screen *E. coli* isolates from urine sample for the production of Shiga toxins.

**References**


Reprints or correspondence: Dr. David Acheson, Division of Geographic Medicine and Infectious Diseases, New England Medical Center, 750 Washington St., Boston, MA 02111 (Dacheson@Lifespan.org).

Clinical Infectious Diseases 2001;32:1517–8 © 2001 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2001/3210-0025$03.00

**Treatment of Foodborne Listeriosis**

Sir—In the third paragraph of the Treatment of Listeriosis section of Dr. Walter F. Schlech’s recent article, “Foodborne Listeriosis,” the author states, “Another regimen with precedence in the literature is the combination of trimethoprim-sulfamethoxazole (TMP-SMZ) and rifampin. A French study [36] has suggested that this regimen is superior to ampicillin and aminoglycoside therapy…” [1]. This