Letters to the Editor

Pathogenicity of *Blastocystis hominis*

The letter of J. E. Rosenblatt (6) refutes some published work affirming *Blastocystis hominis* to be an important agent of intestinal disease in humans. The superb and well-controlled study by Kain et al. is one example of a plethora of sound studies (2). The proportion of affirmative literature on *B. hominis* pathogenicity to the "anti" literature is approximately 20:1. The two most quoted "anti" articles are basically flawed. A complete bibliography can be found in an upcoming review by me (11).

Unfortunately, the scant criticism in the literature of work on the pathogenicity of this protozoan is based on speculation rather than credible data. I submit that ". . . speculation concerning its pathogenicity," as stated by Dr. Rosenblatt, might more accurately be stated ". . . speculation concerning its nonpathogenicity." Dr. Rosenblatt states: "Some patients with diarrhea have the organism in their stool and some do not; some asymptomatic patients have it in their stool and some do not." What a beautiful description of the presence of *Entamoeba histolytica*!

In response to Dr. Rosenblatt's numbered critiques: (i) "Koch's postulates have never been satisfied. . . ." To invoke Koch's postulates in this area is unnecessary. At least a dozen articles describing *B. hominis* epidemics in soldiers and institutions and familial outbreaks, in which transmission followed by symptomatic infection is described, are available.

(ii) "No pathogenic evidence of or immunologic response to 'infection' has been demonstrated in humans. . . ." There are many descriptions of gastrointestinal pathology (1–3, 7–10). Immunological aspects are essentially unstudied. Eosinocytosis is frequent.

(iii) "No mechanisms of pathogenicity, such as toxin elaboration, attachment to intestinal mucosa, or invasiveness, in humans have been described. . . ." Here, again, purified-toxin studies have not been reported to date. Employing the isolated ileal segment technique in the rabbit, injection of purified fractions from *B. hominis* cultures elicits strongly positive fluid response (12). Attachment to or invasion of intestinal mucosa is not a requirement for pathogenicity (as, for example, with *Cryptosporidium parvum* and *Giardia lamblia*). However, mucosal invasion in *B. hominis* infections in gnotobiotic guinea pigs has been recorded (5). As for the requirement for bacterial cohorts for pathogenesis, this is true also of *E. histolytica*, and this has been in the literature for 35 years (4).

(iv) Dr. Rosenblatt states that "no antimicrobial agent which is uniquely active against *B. hominis* has been shown to reliably eradicate both the organism and the diarrhea. . . ." Emetine is very effective against blastocystosis but must be used in the hospital because of possible toxicity. The arsenicals Stovarsol (acetarsone) and Narsonal are also very effective and are approved for use. References to use of the various drugs are too numerous to list here. In recent years, metronidazole has been used most and is usually effective, although there is indication of resistant strains of *B. hominis*. Trimethoprim-sulfamethoxazole is effective, and Floraquin (diiodohydroxyquinoline) is moderately effective.

(v) "There has never been a point-source outbreak of gastroenteritis in which epidemiologic evidence suggested that *B. hominis* was the cause." Dr. Rosenblatt seems to believe that all intestinal protozoa must fit the mold of some archetypical pathogen. Unfortunately, there is no such model against which all others are measured. Diversity is the hallmark of pathogenic protozoa. But there will probably be "point-source" outbreaks reported as more studies are done. The many military and institutional outbreaks reported had a source, even though it was too convoluted to discern.

One might comment that the Comte de Buffon and John Needham have been dead for over 200 years, and Felix Pouchet for over 100 years, but their spirit lives on.

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Author's Reply

I do not believe the disagreement over the scientific evidence for the pathogenicity of *Blastocystis hominis* will be settled in the letters section, and I am reluctant to contribute further to this dispute. However, having been given the opportunity to respond to Dr. Zierdt's letter, I will do so. Of course, those interested in this area will recognize that Dr. Zierdt has long been a proponent of the pathogenicity of *B. hominis* theory. I am simply a detached observer

trying to view the question in a scientifically objective way. I am neither in favor of nor against this organism actually being a pathogen.

To support his cause, Dr. Zierdt states that there is a 20:1 preponderance of affirmative literature as compared to "anti" literature concerning pathogenicity. Does he mean that we should base scientific credibility on the quantity of papers written on a subject as opposed to the quality and significance of the content? He also says that ". . . the two most quoted 'anti' papers are basically flawed," without citing the references or indicating how they are flawed.

The second paragraph of Dr. Zierdt's letter seems to suggest that we should assume that *B. hominis* is a pathogen until it is proven not to be one. Somehow, I always thought that in science things should be the other way around. Since we live in a "sea" of microorganisms, most of which are nonpathogenic for humans, the presence of one of them in our flora should not be equated with pathogenicity. The reference to *Entamoeba histolytica* is inappropriate since that organism is a well-established pathogen (4) and has been shown to exist in both pathogenic and nonpathogenic forms (5).

Dr. Zierdt states that fulfillment of Koch's postulates is unnecessary without telling us why. Have they been shown to be invalid? He also refers to "at least a dozen articles describing epidemics . . ." without providing the references or any other specific information.

I have reviewed the articles cited by Dr. Zierdt as providing evidence of gastrointestinal pathology except number 10, which is from the Polish literature and not accessible.

Reference 1 indicates that no relevant pathology was found in the four patients who underwent endoscopy.

Reference 2 indicates that of 14 patients who had *B. hominis* infection only, none had an abnormal endoscopy and 13 had normal tissue biopsies; 1 showed mild inflammation, but no organisms were present.

References 3, 7, and 9 consist of single case histories associating the presence of *B. hominis* with rectal ulcers, colitis, and ileitis, respectively. Two patients seemed to respond to metronidazole. While there may be a cause-and-effect relationship here, the absence of full microorganism stool workups and the lack of long-term follow-up information on the patients, as well as the dissimilar nature of the lesions in the three patients, leave room for doubt. Perhaps these patients had inflammatory bowel diseases, such as regional enteritis or ulcerative colitis. Moreover, it is very unlikely that the disease in these three patients is representative of the gastroenteritis present in the relatively large number of patients whose stools contain *B. hominis* when examined in the routine clinical parasitology laboratory.

Reference 5 provides no information on gastrointestinal pathology in humans and indicates that when germfree guinea pigs were given *B. hominis*, infection occurred only in those that also received a bacterial inoculum. Those that received *B. hominis* only were not infected. Even if one accepts the concept of pathogenicity of *B. hominis* only when it is given together with bacterial cohorts to germfree guinea pigs, this is a far cry from pathogenicity in the human intestine. Dr. Zierdt's reference to the requirement for bacterial cohorts for pathogenesis of *E. histolytica* is not completely accurate. Although amebic virulence, as determined by in vitro assays, is stimulated by association with bacteria, axenically grown trophozoites are capable alone of virulence (1). I do not believe that this same capability has been demonstrated for *B. hominis*.

I am eager to see the as-yet-unpublished results of *B. hominis* and the rabbit ileal loop assay to which Dr. Zierdt refers in his paragraph iii. I am puzzled by his comments on giardia and cryptosporidium, since both have been shown to attach to the intestinal epithelium (2, 3).

As I stated in my original letter, perhaps *B. hominis* will someday be demonstrated to be pathogenic for humans. I certainly have nothing against it being a pathogen. It just has yet to be proven adequately. By the way, there are two more articles which can be thrown on the "anti" pile (6, 7).

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Genetic Heterogeneity in Strains of *Pseudomonas aeruginosa* from Patients with Cystic Fibrosis

The article by Hjelm et al. (2) contains interesting observations. However, we question the authors' interpretation of data published previously by our group and others regarding the number of strains of *Pseudomonas aeruginosa* present in patients with cystic fibrosis (CF) and the genetic events related to the changes in the restriction patterns reported by Hjelm et al. in their studies.

The authors state: "Ogle et al. . . . and Pasloske et al. . . ., using separate DNA probes to test restriction fragment length polymorphisms (RFLPs) within serial isolates of *P. aeruginosa* from cystic fibrosis patients, demonstrate that cystic fibrosis patients are infected by only one strain of *P. aeruginosa*, which displays many different phenotypes." Although CF patients are usually infected with only one