J HEALTH POPUL NUTR 2007 Dec;25(4):387-391
ISSN 1606-0997 | $ 5.00+0.20

EDITORIAL

Human Intestinal Parasites

Parasitic infections, caused by intestinal helminths and protozoan parasites, are among the most prevalent infections in humans in developing countries. In developed countries, protozoan parasites more commonly cause gastrointestinal infections compared to helminths. Intestinal parasites cause a significant morbidity and mortality in endemic countries.

Helminths are worms with many cells. Nematodes (roundworms), cestodes (tapeworms), and trematodes (flatworms) are among the most common helminths that inhabit the human gut. Usually, helminths cannot multiply in the human body. Protozoan parasites that have only one cell can multiply inside the human body. There are four species of intestinal helminthic parasites, also known as geohelminths and soil-transmitted helminths: *Ascaris lumbricoides* (roundworm), *Trichiuris trichiuria* (whipworm), *Ancylostoma duodenale*, and *Necator americanicus* (hookworms). These infections are most prevalent in tropical and subtropical regions of the developing world where adequate water and sanitation facilities are lacking (1,2). Recent estimates suggest that *A. lumbricoides* can infect over a billion, *T. trichiura* 795 million, and hookworms 740 million people (3). Other species of intestinal helminths are not widely prevalent. Intestinal helminths rarely cause death. Instead, the burden of disease is related to less mortality than to the chronic and insidious effects on health and nutritional status of the host (4,5). In addition to their health effects, intestinal helminth infections also impair physical and mental growth of children, thwart educational achievement, and hinder economic development (6,7).

The most common intestinal protozoan parasites are: *Giardia intestinalis*, *Entamoeba histolytica*, *Cyclospora cayetanenensis*, and *Cryptosporidium* spp. The diseases caused by these intestinal protozoan parasites are known as giardiasis, amoebiasis, cyclosporiasis, and cryptosporidiosis respectively, and they are associated with diarrhoea (8). *G. intestinalis* is the most prevalent parasitic cause of diarrhoea in the developed world, and this infection is also very common in developing countries. Amoebiasis is the third leading cause of death from parasitic diseases worldwide, with its greatest impact on the people of developing countries. The World Health Organization (WHO) estimates that approximately 50 million people worldwide suffer from invasive amoebic infection each year, resulting in 40-100 thousand deaths annually (9,10). Cryptosporidiosis is becoming most prevalent in both developed and developing countries among patients with AIDS and among children aged less than five years. Several outbreaks of diarrhoeal disease caused by *C. cayetanensis* have been reported during the last decade (11). Spread of these protozoan parasites in developing countries mostly occurs through faecal contamination as a result of poor sewage and poor quality of water. Food and water-borne outbreaks of these protozoan parasites have occurred, and the infectious cyst form of the parasites is relatively resistant to chlorine (12). Other species of protozoan parasites can also be found in the human gut, but they are not pathogenic, except *Microsporidia* sp.

In an article published in this issue of the Journal, Jacobsen *et al*. looked at the prevalence of intestinal parasites in young Quichua children in the highland or rural Ecuador (13). They have found a high prevalence of intestinal parasites, especially the intestinal protozoan parasites. They have used the traditional microscopic technique to diagnose intestinal parasitic infections. In total, 203 stool samples were examined from children aged 12-60 months and found that 85.7% of them had at least on parasite. The overall prevalence of intestinal protozoan parasites were: *E. histolytica*/*E. dispar* 57.1%, *Escherichia coli* 34.0%, G. *intestinalis* 21.1%, *C. parvum* 8.9%, and *C. mesnili* 1.7%, while the prevalence of intestinal helminthic parasites in this study were: *A. lumbricoides* 35.5%, *T. trichiura* 0.5 %, *H. diminuta* 1.0%, and *S. stercoralis* 0.7%. A recent study in Nicaragua in asymptomatic individuals found that 12.1% (58/480) were positive for *E. histolytica*/*E. dispar* by microscopy, but *E. histolytica* and *E. disapr* were positive by polymerase

Correspondence and reprint requests should be addressed to:
Dr. Rashidul Haque
Scientist and Head of Parasitology Laboratory
Laboratory Sciences Division
ICDDR,B
GPO Box 128, Dhaka 1000
Bangladesh
Email: rhaque@icddrb.org

chain reaction (PCR) only in three and four stool samples respectively among the microscopic positive samples (Unpublished data). This study proves again that the diagnosis of *E. histolytica*/*E. dispar* is neither sensitive nor specific when it is done by microscopy. To understand the real prevalence of *E. histolytica*-associated infection, a molecular method must be used for its diagnosis.

Over the last several years, we have seen new approaches to the diagnosis, treatment, and prevention of intestinal protozoan parasites. However, the diagnosis and treatment of intestinal helminth infections have not been changed much, and the traditional microscopic method can be used for their diagnosis. Antigen-detection tests are now commercially available for the diagnosis of all three major intestinal protozoan parasites. Diagnosis of *E. histolytica* cannot be done any longer by microscopy, since this parasite is morphologically similar to the non-pathogenic parasite *E. dispar*. *E. histolytica*-specific antigen-detection test is now commercially available from TechLab, Blacksburg, Virginia, for the detection of *E. histolytica* antigen in stool specimens (14,15). In several studies, this *E. histolytica*-specific antigen-detection test has been used for the specific detection of *E. histolytica* (16,17). These studies have found that this antigen-detection test is sensitive and specific for the detection of *E. histolytica*. In a study in Bangladesh, *E. histolytica*-specific antigen-detection test identified *E. histolytica* in 50 of 1,164 asymptomatic preschool children aged 2-5 years (18). In a study in Nicaragua among patients with diarrhoea, where *E. histolytica*-specific test has been used, found that the prevalence of *E. histolytica* was 0.5% (19). In a study conducted in a cohort of Bangladeshi children found that the prevalence of *E. histolytica* in diarrhoeal stool samples was 8.0% (20). No studies that have been carried till date using *E. histolytica*-specific diagnostic test reported the prevalence of *E. histolytica* more than 10%. In addition to the antigen-detection test, several PCR-based tests specific for *E. histolytica* have been developed and used for specific detection of *E. histolytica* (21,22). Rapid diagnostic test for the detection of *E. histolytica* antigen in stool specimens has also been reported (23).

Diagnosis of giardiasis is best accomplished by detection of *Giardia* antigen in stool, since the classic microscopic examination is less sensitive and specific. A recent comparison of nine different antigen-detection tests demonstrated that all had high sensitivity and specificity, except one (24). *Giardia*-specific antigen-detection tests are now also commercially available from several diagnostic companies, and their performance is quite good, except a few. In addition to antigen-detection tests, PCR-based test for the detection of *G. intestinalis* has also been reported (25). The population genetics of *Giardia* are complex. However, a recent genetic linkage study has confirmed the distinct grouping of *Giardia* in two major types (26). These two main genotypes/assemblages of *G. intestinals* are commonly known as: assemblage A and assemblage B of *G. intestinalis*. Differentiation of these two assemblages of *G. intestinalis* can only be done by PCR-based tests. Findings of the largest case-control study conducted to date on the relationship between genotypes of *G. intestinalis* and symptoms of patients have been published (27). This study has shown that the *Giardia* assemblage A infection is associated with diarrhoea. In contrast, *Giardia* assemblage B infection is significantly associated with asymptomatic *Giardia*-associated infection, which was found to occur at a significantly higher rate (18.0%) as detected by the antigen-detection test (27). The PCR-based approach allowed resolution of infection to the genotype level and brought some clarity to the findings of asymptomatic giardiasis. Similar large-scale case-control studies need to be carried out in other continents to understand more on the association of *Giardia* assemblages with diarrhoea/dysentery.

Diagnosis of cryptosporidiosis is also best accomplished by detection of *Cryptosporidium* spp. antigen in stool samples, since classic microscopic examination is less sensitive, and modified acid-fast staining is required. *Cryptosporidium* spp.-specific antigen-detection test has been used in several studies and has been found to be sensitive and specific compared to classic microscopic examination and PCR-based test (28,29). There are two main species of *Cryptosporidium* that infect humans: *C. hominis* (genotype I) and *C. parvum* (genotype II). The PCR-based test is required for differentiation of these two species of *Cryptosporidium* spp. (30). Both *C. hominis* and *C. parvum* have been found in humans. There are a few other species of *Cryptosporidium* that also can be found in humans (31-33). Rapid diagnostic tests for the detection of *G. lamblia* and *Cryptosporidium* spp. have also been reported (34,35). Multiplex PCR-based test for the detection of *E. histolytica*, *G. intestinalis*, and *Cryptosporidium* spp. has already been reported, and the development of multiplex antigen-detection test for these three common and pathogenic intestinal protozoan parasites is underway at TechLab, Blacksburg,

Virginia (36, Herbain J. Personal communication, 2007). These modern antigen-detection tests and PCR-based tests need to be used for understanding the actual prevalence and epidemiology of these protozoan parasites.

Soil-transmitted helminth infections are invariably more prevalent in the poorest sections of the populations in endemic areas of developing countries. The goal is to reduce morbidity from soil-transmitted helminth infections to such levels that these infections are no longer of public-health importance. An additional goal is to improve the developmental, functional and intellectual capacity of affected children (37). Highly-effective, safe single-dose drugs, such as albendazole, now available, can be dispensed through healthcare services, school health programmes, and community interventions directed at vulnerable groups (38). As these infections are endemic in poor communities, more permanent control will only be feasible where chemotherapy is supplemented by improved water supplies and sanitation, strengthened by sanitation education. In the long term, this type of permanent transmission control will only be possible with improved living conditions through economic development. Intestinal protozoa multiply rapidly in their hosts, and as there is a lack of effective vaccines, chemotherapy has been the only practised way to treat individuals and reduce transmission. The current treatment modalities for intestinal protozoan parasites include metronidazole, iodoquinol, diloxanide furoate, paromomycin, chloroquine, and trimethoprim-sulphamethoxazole (39). Nitazoxanide, a broad-spectrum anti-parasitic agent, was reported to be better than placebo for the treatment of cryptosporidiosis in a double-blind study performed in Mexico (40). Genomes of these three important protozoan parasites have already been published (41-43), and studies are underway to understand protective immunity to these protozoan parasites to develop vaccines for them.

REFERENCES

1. Savioli L, Albonico M. Soil-transmitted helminthiasis. *Nat Rev Microbiol* 2004;2:618-9.
2. Cappello M. Global health impact of soil-transmitted nematodes. *Pediatr Infect Dis J* 2004;23:663-4.
3. de Silva NR, Brooker S, Hotez PZ, Montresor A, Engles D, Savioli L. Soil-transmitted helminth infections: updating the global picture. *Trends Parasitol* 2003;19:547-51.
4. Stephenson LS, Latham MC, Ottesen EA. Malnutrition and parasitic helminth infections. *Parasitology* 2000;121:S23-38.
5. Stoltzfus RJ, Chway HM, Montresor A, Tielsch JM, Jape JK, Albonico M *et al*. Low dose daily supplementation improves iron status and appetite but not anemia, whereas quarterly anthelminthic treatment improves growth, appetite and anemia in Zanzibari preschool children. *J Nutr* 2004;134:348-56.
6. Drake LJ, Jukes MCH, Sternberg RJ, Bunday DAP. Geohelminth infections (ascariasis, trichiuriasis, and hookworm): cognitive and development impacts. *Sem Paediatr Infect Dis* 2000;11:245-51.
7. Guyatt HL. Do intestinal nematode affect productivity in adulthood. *Parasitol Today* 2000;16:153-8.
8. Davis AN, Haque R, Petri WA, Jr. Update on protozoan parasites of the intestine. *Curr Opin Gastroentrol* 2002;18:10-4.
9. World Health Organization. Amoebiasis. *WHO Weekly Epdemiol Rec* 1997;72:97-100.
10. Petri WA, Jr., Haque R, Lyerly D, Vines RR. Estimating the impact of amebiasis on health. *Parasitol Today* 2000;16:320-21.
11. Herwaldt BL. *Cyclospora cayetanensis*: review, focusing on the outbreaks of cyclosporiasis in the 1990s. *Clin Infect Dis* 2000;31:1040-57.
12. Okhuysen PC, White AC, Jr. Parasitic infections of the intestine. *Curr Opin Infect Dis* 1999;12:467-72.
13. Jacobsen KH, Ribeiro PS, Quist BK, Rydbeck BV. Prevalence of intestinal parasites in young Quichua children in the highlands of rural Ecuador. *J Health Popul Nutr* 2007;25:399-405.
14. Haque R, Huston CD, Hughes M, Houpt E, Petri WA, Jr. Amebiasis. *N Engl J Med* 2003;348:1565-73.
15. Haque R, Faruque AS, Hahn P, Lyerly DM, Petri WA, Jr. *Entamoeba histolytica* and *Entamoeba dispar* infection in children in Bangladesh. *J Infect Dis* 1997;175:734-6.
16. Evangelopoulos A, Legakis N, Vakalis N. Microscopy, PCR and ELISA applied to the epidemiology of amoebiasis in Greece. *Parasitol Int* 2001;50:185-9.
17. Silva MC, Monteiro Cdo S, Araújo Bdos A, Silva JV, Póvoa MM. [Determination of *Entamoeba histolytica* infection in patients from Greater Metropolitan Belém, Para, Brazil, by enzyme-linked immunosorbent assay (ELISA) for antigen detection]. *Cad Saude Publica* 2005;21:969-73.

18. Haque R, Ali IM, Sack RB, Farr BM, Ramakrishnan G, Petri WA, Jr. Amebiasis and mucosal IgA antibody against the *Entamoeba histolytica* adherence lectin in Bangladeshi children. *J Infect Dis* 2001;183:1787-93.

19. Leiva B, Lebbad M, Winiecka-Krusnell J, Altamirano I, Tellez A, Linder E. Overdiagnosis of *Entamoeba histolytica* and *Entamoeba dispar* in Nicaragua: a microscopic, triage parasite panel and PCR study. *Arch Med Res* 2006;37:529-34.

20. Haque R, Mondal D, Kirkpatrick BD, Akther S, Farr BM, Sack RB *et al*. Epidemiologic and clinical characteristics of acute diarrhea with emphasis on *Entamoeba histolytica* infections in preschool children in an urban slum of Dhaka, Bangladesh. *Am J Trop Med Hyg* 2003;69:398-405.

21. Haque R, Ali IK, Akther S, Petri WA, Jr. Comparison of PCR, isoenzyme analysis, and antigen detection for diagnosis of *Entamoeba histolytica* infection. *J Clin Microbiol* 1998;36:449-52.

22. Roy S, Kabir M, Mondal D, Ali IK, Petri WA, Jr., Haque R. Real-time-PCR assay for diagnosis of *Entamoeba histolytica* infection. *J Clin Micrbiol* 2005;43:2168-72.

23. Leo M, Haque R, Kabir M, Roy S, Lahlou RM, Mondal D *et al*. Evaluation of *Entamoeba histolytica* antigen and antibody point-of-care tests for the rapid diagnosis of amebiasis. *J Clin Microbiol* 2006;44:4569-71.

24. Aldeen WE, Carroll K, Robison A, Morrison M, Hale D. Comparison of nine commercially available enzyme-linked immunosorbent assays for detection of *Giardia lamblia* in fecal specimens. *J Clin Microbiol* 1998;36:1338-40.

25. Ng CT, Gilchrist CA, Lane A, Roy S, Haque R, Houpt ER. Multiplex real-time PCR assay using Scorpion probes and DNA capture for genotype-specific detection of *Giardia lamblia* on fecal samples. *J Clin Microbiol* 2005;43:1256-60.

26. Le Blancq SM, Adam RD. Structural basis of karyotype heterogeneity in *Giardia lamblia*. *Mol Biochem Parasitol* 1998;97:199-208.

27. Haque R, Roy S, Kabir M, Stroup SE, Mondal D, Houpt ER. *Giardia* assemblage A infection and diarrhea in Bangladesh. *J Infect Dis* 2005;192:2171-3.

28. Zhu G, Marchewka MJ, Ennis JG, Keithly JS. Direct isolation of DNA from patient stools for polymerase chain reaction detection of *Cryptosporidium parvum*. *J Infect Dis* 1998;177:1443-6.

29. Weitzel T, Dittrich S, Möhl I, Adusu E, Jelinek T. Evaluation of seven commercial antigen detection tests for *Giardia* and *Cryptosporidium* in stool samples. *Clin Microbiol Infect* 2006;12:656-9.

30. Garcia LS, Shimizu RY. Evaluation of nine immunoassay kits (enzyme immunoassay and direct fluorescence) for detection of *Giardia lamblia* and *Cryptosporidium parvum* in human fecal specimens. *J Clin Microbiol* 1997;35:1526-9.

31. Chalmers RM, Ferguson C, Cacciò S, Gasser RB, Abs EL-Osta YG, Heijnen L *et al*. Direct comparison of selected methods for genetic categorisation of *Cryptosporidium parvum* and *Cryptosporidium* hominis species. *Int J Parasitol* 2005;35:397-410.

32. Matos O, Alves M, Xiao L, Cama V, Antunes F. *Cryptosporidium* felis and *C. meleagridis* in persons with HIV, Portugal. *Emerg Infect Dis* 2004;10:2256-7.

33. Stroup SE, Roy S, Mechele J, Maro V, Ntabaguzi S, Siddique A *et al*. Real-time PCR detection and speciation of *Cryptosporidium* infection using Scorpion probes. *J Med Microbiol* 2006;55:1217-22.

34. Garcia LS, Shimizu RY, Novak S, Carroll M, Chan F. Commercial assay for detection of *Giardia lamblia* and *Cryptosporidium parvum* antigens in human fecal specimens by rapid solid-phase qualitative immunochromatography. *J Clin Microbiol* 2003;41:209-12.

35. Regnath T, Klemm T, Ignatius R. Rapid and accurate detection of *Giardia lamblia* and *Cryptosporidium* spp. antigens in human fecal specimens by new commercially available qualitative immunochromatographic assays. *Eur J Clin Microbiol Infect Dis* 2006;25:807-9.

36. Haque R, Roy S, Siddique A, Mondal U, Rahman SM, Mondal D *et al*. Multiplex real-time PCR assay for detection of *Entamoeba histolytica*, *Giardia intestinalis*, and *Cryptospordium* spp. *Am J Trop Med Hyg* 2007;76:713-7.

37. Bundy DA, Wong MS, Lewis LL, Horton J. Control of geohelminths by delivery of targeted chemotherapy through schools. *Trans R Soc Trop Med Hyg* 1990;84:115-20.

38. World Health Organization. Prevention and control of schistosomiasis and soil-transmitted helminthiasis; report of a WHO expert committee. Geneva: World Health Organization, 2002. 63 p. (WHO technical report series no. 912).

39. Gupta YK, Gupta M, Aneja S, Kohli K. Current drug therapy of protozoal diarrhoea. *Indian J Pediatr* 2004;71:55-8.

40. Rossignol JF, Hidalgo H, Feregrino M, Higuera F, Gomez WH, Romero JL *et al*. A double-'blind' placebo-controlled study of nitazoxanide in the treatment of cryptosporidial diarrhoea in AIDS patients

in Mexico. *Trans R Soc Trop Med Hyg* 1998;92:663-6.

41. Loftus B, Anderson I, Davies R, Alsmark UC, Samuelson J, Amedeo P *et al*. The genome of protist parasite *Entamoeba histolytica*. *Nature* 2005;433:865-8.
42. Xu P, Widmer G, Wang Y, Ozaki LS, Alves JM, Serrano MG *et al*. The genome of *Cryptosporidium hominis*. *Nature* 2004;431:1107-12.
43. Morrison HG, McArthur AG, Gillin FD, Aley SB, Adam RD, Olsen GJ *et al*. Genomic minimalism in the early diverging intestinal parasites *Giardia lamblia*. *Science* 2007;317:1921-6.

Rashidul Haque

Scientist and Head of Parasitology Laboratory
Laboratory Sciences Division
ICDDR,B
GPO Box 128, Dhaka 1000
Bangladesh
Email: rhaque@icddrb.org