Cryptosporidium, Enterocytozoon, and Cyclospora Infections in Pediatric and Adult Patients with Diarrhea in Tanzania

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Cryptosporidiosis, microsporidiosis, and cyclosporiasis were studied in four groups of Tanzanian inpatients: adults with AIDS-associated diarrhea, children with chronic diarrhea (of whom 23 of 59 were positive [$^+$] for human immunodeficiency virus [HIV]), children with acute diarrhea (of whom 15 of 55 were HIV$^+$), and HIV$^-$ control children without diarrhea. *Cryptosporidium* was identified in specimens from 6/86 adults, 5/59 children with chronic diarrhea (3/5, HIV$^+$), 7/55 children with acute diarrhea (0/7, HIV$^+$), and 0/20 control children. Among children with acute diarrhea, 7/7 with cryptosporidiosis were malnourished, compared with 10/48 without cryptosporidiosis ($P < .01$). *Enterocytozoon* was identified in specimens from 3/86 adults, 2/59 children with chronic diarrhea (1 HIV$^+$), 0/55 children with acute diarrhea, and 4/20 control children. All four controls were underweight ($P < .01$). *Cyclospora* was identified in specimens from one adult and one child with acute diarrhea (HIV$^-$). Thus, *Cryptosporidium* was the most frequent and *Cyclospora* the least frequent pathogen identified. *Cryptosporidium* and *Enterocytozoon* were associated with malnutrition. Asymptomatic fecal shedding of *Enterocytozoon* in otherwise healthy, HIV$^-$ children has not been described previously.

Numerous gastrointestinal pathogens have emerged in recent years, including three important types of protozoa: *Cryptosporidium, Cyclospora,* and microsporidial species. *Cryptosporidium* was first associated with human disease in 1976 [1], and reports of intractable diarrhea multiplied in association with the AIDS epidemic [2–5]. Subsequently, cryptosporidiosis was recognized to cause acute, self-limited diarrhea in immunocompetent hosts through transmission from farm animals or from person to person [6, 7]. Contaminated water supplies have caused large epidemics in the United States and United Kingdom, underscoring the public health importance of *Cryptosporidium* [7–12].

Acid-fast staining of feces to detect *Cryptosporidium* may have expedited recognition of *Cyclospora* [13]. First reported as an unknown coccidian in 1979 [14], this parasite was called a large *Cryptosporidium,* alga-like body, or cyanobacterium-like body from 1986 until 1993, when it was identified as *Cyclospora* [15]. Subsequent reports associated *Cyclospora* with acute, often relapsing diarrheal disease in children and adults, especially among travelers [16–19]. In the United States, epidemics during the summers of 1996 and 1997 incriminated imported fresh produce [20, 21]. Organisms similar in appearance have now been described as infecting patients with diarrheal illness throughout the western hemisphere, south and southeast Asia, and parts of Europe [13, 22]. Patients with HIV/AIDS may be disproportionately affected [17, 23, 24].

Although many genera of the family Microspora were known to be pathogens of invertebrate and vertebrate hosts, their role in human disease was not appreciated until the AIDS pandemic. Six new species of microsporidia in AIDS patients, causing a wide spectrum of diseases, have been described [25–29]. The most common presentation is chronic diarrhea and wasting [30]. Studies from Europe and the United States have revealed 6%–60% prevalence among such patients [29–31]. Approximately 90% of intestinal infections are caused by *Enterocytozoon bieneusi* [25, 26, 30]. However, little has been published on intestinal microsporidiosis in either children or adults in developing countries [32–37].

To describe the clinical epidemiology of these emerging pathogens in Africa, we investigated archived specimens from previous studies on diarrheal diseases [38, 39] and a new group of patients at the Muhimbili Medical Center, in Dar es Salaam, Tanzania. We related these protozoal infections to the clinical features and HIV status of children and adults hospitalized with diarrhea.

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Informed consent was obtained from the adult patients or from the parents/guardians of the pediatric patients. Guidelines for research involving human subjects of the U.S. Department of Health and Human Services, Duke University Medical Center, and Muhimbili University College of Health Sciences were observed in the conduct of this research.

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Patients and Methods

Four groups of inpatients at Muhimbili Medical Center were included. The first was consecutive adults with AIDS who were admitted because of diarrhea (≥3 loose or watery bowel movements per day) of at least 30 days' duration, weight loss, and fever, who participated in a treatment trial for their diarrhea-wasting syndrome [39]. The second group was consecutive children aged 15–60 months with chronic diarrhea who were admitted to a specialized pediatric diarrhea ward over a period of 6 months [38]. Chronic diarrhea was defined as diarrhea occurring for more than one-half of the days in the preceding month. The third group was consecutive children aged 15–60 months admitted to the pediatric surgery ward for acute trauma or elective surgery with no history of diarrhea in the previous 3 months, selected as controls for the preceding group. These three groups have been described in greater detail [38, 39], but the major findings presented here have not been published previously. The fourth group was consecutive children (any age) with acute diarrhea (lasting <2 weeks in total) admitted to the same diarrhea ward over a period of 2 months. This group has not been previously described.

Each patient had a standardized clinical evaluation and provided a fresh stool specimen upon admission. For the pediatric patients, a second specimen was obtained after 48 hours. HIV serology by ELISA was performed for all patients, and results were confirmed by western blotting or, in a few cases, by a second, different ELISA. For the adult patients, the complete blood cell count, total bilirubin level, and serum level of aspartate aminotransferase were determined routinely.

Portions of each stool were emulsified in 3×-volume 10% formalin and in 3×-volume polyvinyl alcohol. Formalin specimens were concentrated by the formalin–ethyl acetate procedure [40], and some was reserved for analysis of unconcentrated specimens. All slides were examined without knowledge of the patient's age or HIV status by at least two investigators and one technician. For detection of *Cryptosporidium,* thin smears of the concentrate were prepared with Kinyoun and auramine-rhodamine stains (Difco, Detroit) and direct fluorescent monoclonal antibodies (Merifluor; Meridian Diagnostics, Cincinnati), according to the manufacturers' instructions. Slides were scanned at 400× magnification, and suspected cysts were confirmed under oil immersion. Polyvinyl alcohol–prepared specimens were stained by the Wheatley trichrome method (Difco) [40].

For microsporidial spores, thin smears of unconcentrated stool-formalin suspension were stained with use of Weber's modified trichrome method as described [41]. Slides were examined by the scanning of 100 oil-immersion fields (1,000× magnification). All positive or questionable slides, plus a random sample of negative slides, were sent to a highly experienced research laboratory and reexamined to confirm the species with use of these criteria: spores were sized 1–3 μm, stained pink to red, were ovoid, and contained a distinctive equatorial belt–like stripe. Species identity was confirmed by transmission electron microscopy (TEM). For TEM, stool was fixed in glutaraldehyde, osmium tetroxide, and uranyl acetate. After dehydration, it was embedded in resin, and ultrathin sections were poststained with uranyl acetate and lead citrate. Sections were examined for thick-walled round to ovoid eukaryotic organisms 1–3 μm in length with characteristic polar bodies.

For *Cyclospora,* wet mounts of concentrated and unconcentrated feces were examined for oocysts by phase-contrast microscopy. Second, fixed smears were stained with a modified acid-fast procedure and examined by light microscopy. Third, unstained smears were examined with ultraviolet fluorescence microscopy at 365 nm for autofluorescent oocysts.

All results from a given subject were pooled to determine the net intestinal parasitic infection of that subject. Subjects with these parasites were compared to each other and to those without intestinal parasites in terms of clinical features and HIV status. Statistical comparisons of categorical data used the χ^2 test or Fisher's exact test. Continuous data were compared with the Wilcoxon rank-sum test.

Results

The 4 groups comprised 55 children with acute diarrhea (median age, 13.5 months; range, 3–108 months; 55% male); 59 children with chronic diarrhea (median age, 21 months; range, 15–51 months; 47% male); 20 control children with no diarrhea (median age, 22.5 months; range, 15–51 months; 55% male); and 86 adults with AIDS and chronic diarrhea (median age, 31 years; range, 18–61 years; 62% male).

Children with Acute Diarrhea

Seven (13%) of the 55 children with acute diarrhea (table 1) had *Cryptosporidium,* none had microsporidia, and one (2%) had *Cyclospora* in fecal specimens. Fifteen were HIV-positive, but eight of the 15 were aged <1 year so their antibodies to HIV may have been maternal. None of the patients infected with *Cryptosporidium* were HIV-positive ($P > .05$). One *Cyclospora*-infected patient was HIV-negative.

Patients with cryptosporidiosis (median age, 9 months) tended to be younger than patients without cryptosporidiosis (median age, 16 months; $P = .4$) and patients with no parasites (median age, 23 months; $P = .07$). Gastrointestinal manifestations differed between the groups. All children with cryptosporidiosis, vs. 20 of 48 children without cryptosporidiosis, were vomiting ($P = .004$). Similarly, severe dehydration was more frequent among children with cryptosporidiosis (4 of 7) than among children without such infection (9 of 48; $P = .05$). The frequency, duration, and character of diarrheal stools were comparable. There were no significant associations with domestic animals, developmental milestones (crawling or walking), or the type or location of domestic toilets or water supply.

Nutritional status was poor. Seventeen had kwashiorkor and/or marasmus [42]. Twenty-one were stunted (height-for-

Table 1. Characteristics of patients infected with *Cryptosporidium, Enterocytozoon,* and *Cyclospora* in three pediatric study groups: children with chronic diarrhea, children with acute diarrhea, and control children without diarrhea.

Characteristic, per group	Total no. of patients	No. of patients infected with		
		Cryptosporidium	*Enterocytozoon*	*Cyclospora*
No. of patients				
Acute	55	7	0	1
Chronic	59	5	2	0
Control	20	0	4	0
HIV-positive				
Acute	15*	0	NA	0
Chronic	23	3	1	NA
Control	0[†]	NA	0	NA
Frequency of diarrhea (bm/d)				
Acute				
3–5	33	3	NA	0
6–9	19	2	NA	1
>10	3	1	NA	0
Chronic				
3–5	29	1	0	NA
6–9	20	3	2	NA
>10	10	1	0	NA
Bloody diarrhea				
Acute	14	1	NA	1
Chronic	18	3	0	NA
Vomiting				
Acute	27	7[‡]	NA	0
Chronic	28	3	1	NA
Breast-feeding				
Acute	34	4	NA	0
Chronic	9	1	0	NA
Control	9	NA	0	NA
Fecal leukocytes				
Acute	46	6	NA	1
Chronic	46	3	2	NA
Control	3	NA	1	NA
Malnutrition[§]				
Acute				
Normal	6	0	NA	1
Underweight	31	5	NA	0
Severe	17	2	NA	0
Chronic				
Normal	5	1	0	NA
Underweight	11	1	0	NA
Severe	43	3	2	NA
Control				
Normal	14	NA	0	NA
Underweight	6	NA	4[‖]	NA
Severe	0	NA	0	NA
Mortality				
Acute	11	2	NA	0
Chronic	17	2	0	NA
Control	0	NA	0	NA
Length of stay in days: median (range)				
Acute	4 (1–18)	10 (2–18)[#]	NA	17
Chronic	7 (2–20)	7 (3–12)	5.5 (3–8)	NA
Control	NA	NA	NA	NA

NOTE. bm/d = bowel movements per day; NA = not applicable.

* HIV serology data available for 51 patients.

[†] Compared with acute and chronic diarrhea groups, $P = .002$.

[‡] Compared with patients without cryptosporidiosis, $P = .004$.

[§] Defined according to the Welcome Working Party classification [41]. Severe malnutrition includes kwashiorkor and marasmus.

[‖] Among controls, compared with those with normal weight, $P = .003$.

[#] Compared with those without cryptosporidiosis, $P = .03$.

age Z score [HAZ], < -2.0) and 18 were wasted (weight-for-height Z score [WHZ], < -2.0) [43, 44]. All seven cases of cryptosporidiosis involved malnourished children. The child with cyclospora infection was neither stunted (HAZ, 0.05) nor wasted (WHZ, −1.4). Ongoing breast-feeding did not appear to protect against these parasites, malnutrition, or death.

Mortality was high: 11 (20%) of 55 died in the hospital, with no differences in the parasite subgroups. Length of stay, however, was significantly longer in the cryptosporidiosis group (median, 10 days; range, 2–18 days) than in the rest of the sample (median, 4 days; range, 1–17 days; $P = .03$). The patient with cyclosporiasis stayed 17 days.

Children with Chronic Diarrhea

These 59 children (table 1) included 5 (9%) with cryptosporidiosis, 2 (3%) with microsporidiosis, and none with cyclosporiasis. Since these children were aged at least 15 months, their HIV testing results indicated true infection; 23 (39%) were HIV-positive, including 3 of 5 children with cryptosporidiosis and 1 of 2 with microsporidiosis.

The abdomen was normal in all 7 patients with these parasites but abnormal in 30 (58%) of 52 without parasites ($P < .001$); abdominal distension was most common (15 of 30). The diarrhea itself did not differ between the groups. Again, there was no association between these parasites and domestic toilet facilities, water supply, animals, or development.

Nutritional status was extremely poor. Forty-three (73%) had kwashiorkor and/or marasmus [42]. Thirty-nine (66%) were stunted (HAZ, < -2.0) and 37 (63%) were wasted (WHZ, < -2.0). Four of five patients with cryptosporidiosis and both patients with microsporidiosis were malnourished.

Length of stay did not differ for the children with parasites or the rest of the group. Mortality was higher than in the acute diarrhea group: 17 (29%) of the patients died in the hospital, including 2 of 5 with cryptosporidiosis.

Control Children Without Diarrhea

The 20 children in this group (table 1) were admitted with trauma (11), benign tumors (3), and 6 other isolated surgical problems (1 each). Clinical findings were restricted to the condition necessitating admission. All 20 children were HIV-negative.

The most noteworthy finding in four of these children were microsporidial spores in their stool, despite the absence of any gastrointestinal symptoms over the preceding 3 months. *Cryptosporidium* and *Cyclospora* were not identified.

While there was no severe malnutrition in this group, six of 20 were underweight [42]. Five were stunted (HAZ, < -2.0) and one was wasted (WHZ, < -2.0), indicating chronic and acute malnutrition, respectively. All four children with microsporidiosis were underweight, vs. only two of the others ($P = .003$).

Adult Patients

Of 86 adults with AIDS-related chronic diarrhea (table 2), 6 (7%) had cryptosporidiosis, 3 (3%) had microsporidiosis, and 1 (1%) had cyclosporiasis. TEM confirmed the microsporidial spores as *E. bieneusi* (figure 1). The patient infected with *Cyclospora* also had *Isospora belli* in the stool specimen.

Patients had multiple previous and concurrent medical problems consistent with late-stage HIV infection, chiefly pneumonia, tuberculosis, oral candidiasis, and skin infections. These infections occurred proportionally among patients with intestinal protozoa. Diarrhea was less frequent among those with cryptosporidiosis (median, 2.0 bowel movements per day after admission) than among the remainder of the patients (median, 3.5 bowel movements per day; $P = .04$). Abdominal tenderness was common (49 of 86). Hepatosplenomegaly was noted in 14 patients (18%), including one with microsporidiosis, but none with cryptosporidiosis or cyclosporiasis.

Patients with cryptosporidiosis had lower neutrophil counts (median, 1,596/μL; range, 875–1,870/μL) than the rest of the patients (median, 2,457/μL; range, 1,106–6,132/μL; $P = .003$).

Discussion

This report describes three emerging gastrointestinal protozoa in four inpatient groups in urban east Africa, where they have been studied little. *Cryptosporidium* has been described in several African studies but not in parallel cohorts of children with acute and chronic diarrhea and asymptomatic controls. A study in the mid-1980s revealed cryptosporidiosis in 48% of adults with enteropathic AIDS in Kinshasa, Zaire [45]. These early results were widely quoted as representative of Africa, fostering the fallacy that 52 nations and 540 million people were homogeneous in this respect. Combining three sensitive and specific techniques [46–49], we identified *Cryptosporidium* in 13% of children with acute diarrhea and 8% of children with chronic diarrhea but in no controls. The lack of association with HIV infection may have been due to the prevalence of malnutrition among these patients [50].

Furthermore, we found *Cryptosporidium* in 7% of adult AIDS patients with chronic diarrhea, though the frequency would likely have been higher had we examined more than one specimen per patient in the adult group. Estimates of the increase in yield of protozoa from additional specimens vary from 10% to 15% [51]. In rural Tanzania, *Cryptosporidium* was found in 20% of AIDS patients with diarrhea but in none without diarrhea [52]. At Kenyatta Hospital in Nairobi, Kenya, *Cryptosporidium* was identified in 4% of stool samples submitted for routine microscopy, primarily from children aged <5 years [53].

A community-based study in rural Kenya showed *Cryptosporidium* in 4% of children with diarrhea but in none without diarrhea [54]. In North America and Western Europe, *Cryptosporidium* was identified in 1%–3% of patients with diarrhea,

Table 2. Frequency of infection due to *Cryptosporidium, Enterocytozoon,* and *Cyclospora* species and associated characteristics in Tanzanian adults with AIDS and chronic diarrhea.

Characteristic	Total no. of patients	No. of patients infected with		
		Cryptosporidium	*Enterocytozoan*	*Cyclospora*
No. of patients	86	6	3	1*
Frequency of diarrhea (bm/d)				
≤3	43	5	2	1
>4	43	1[†]	1	0
Vital signs on admission				
Temperature of >38°C	14	2	1	0
Pulse rate of >100	50	4	2	0
Weight in kg, mean (SD)	44.5 (8.9)	42.2 (9.2)	53.3 (20.8)	34.0
Laboratory values: median (range)				
Hemoglobin (g/dL)	8.8 (2.2–14.6)	8.9 (4.4–10.4)	7.1 (6.6–8.2)	9.4
Leukocytes (cells/μL)	3,400 (1,250–8,400)	2,800 (1,250–3,600)[‡]	3,450 (2,900–5,000)	6,000
Granulocytes (cells/μL)	2,368 (875–6,132)	1,596 (875–1,870)[§]	2,291 (2,242–4,600)	2,880
Lymphocytes (cells/μL)	840 (0–2,820)	916 (187–1,353)	580 (300–1,035)	2,820
Total bilirubin (μmol/L)	8.0 (3–64)	11.0 (5–13)	20 (7–21)	8.0
Aspartate aminotransferase (U/L)	50.0 (20–99)	57.0 (44–80)	99 (55–99)[‖]	45.0
Comorbidity				
Malaria	34	3	1	1
Pneumonia/bronchitis	15	2	1	0
Tuberculosis	15	2	0	0
Oral candidiasis	5	1	0	1
Skin infection(s)/exanthem(s)**	6	0	0	0

NOTE. bm/d = bowel movements per day.
* Patient also had *Isospora belli* in stool specimen.
[†] Compared with patients without cryptosporidiosis, $P = .04$.
[‡] Compared with patients without cryptosporidiosis, $P = .07$.
[§] Compared with patients without cryptosporidiosis, $P = .003$.
[‖] Compared with patients without microsporidiosis, $P = .06$.
** Includes prurigo nodularis, herpes zoster, multiple cutaneous abscesses, and unidentified rashes.

excluding those in known outbreaks, and in 5%–10% of patients with diarrhea in Asia and Africa [6, 55–57]. Among HIV-infected patients with diarrhea in the United States and Europe, 11%–21% excrete *Cryptosporidium* [2, 58], while in Africa, a 12%–48% prevalence has been reported [45, 59, 60]. Thus, in a second consecutive study (cf. [38]), cryptosporidiosis in Dar es Salaam was at the low end of the prevalence range reported for Africa.

Clinically, the distinctive findings were vomiting and dehydration among children with acute diarrhea who had cryptosporidiosis. This is consistent with the pathology of cryptosporidiosis, which affects the duodenum and upper jejunum as well as the ileum and colon [56]. In addition, these patients were hospitalized more than twice as long as the complementary group, underscoring the potential severity of cryptosporidiosis. Fecal leukocytes were common among these patients, including those with cryptosporidiosis, in contrast to other reports [61]. This finding and the frequency of fecal blood (28%) suggest that some patients may have been coinfected with other pathogens. However, we did not look for other pathogens in this study. Because of this and the limited sample size, we cannot draw firm conclusions regarding the pathogenicity of these three protozoa in our patients. Lack of protection from breast-feeding is consistent with findings from investigations with a primate model [62].

Microsporidia, generally *E. bieneusi,* cause up to 70% of otherwise unexplained cases of chronic diarrhea involving patients with AIDS and low CD4 cell counts [61]. The modified trichrome stain for stool and duodenal aspirates provides a useful means of screening clinical specimens [41]. However, detecting fecal protozoa depends on both the intensity of the infection and the sensitivity of the diagnostic tests. Thus, we examined two specimens per patient (when possible) and multiple slides per specimen, and we used multiple techniques for each specimen. Nonetheless, the single light microscopic technique for microsporidial spores may have been relatively less sensitive than the combined techniques for *Cryptosporidium* and *Cyclospora.* Compared with TEM, the sensitivity and specificity of the three methods used for the detection of microsporidial spores were as follows: 100% and 82.8% for modified

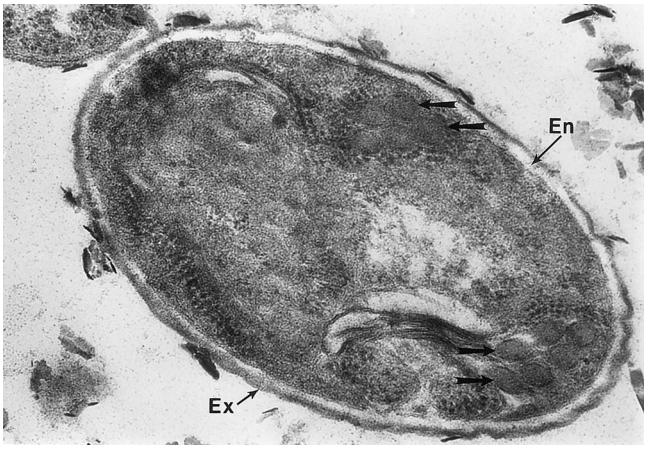

Figure 1. Transmission electron micrograph of a microsporidial spore from a formalin-fixed stool specimen from a Tanzanian adult with AIDS and chronic diarrhea. This spore measures 1.55 μ in length, has an electron-dense exospore (Ex), electron-lucent endospore (En), and an inner and outer layer of coiled polar tubules (*arrows*). These features are diagnostic of *Enterocytozoon bieneusi.* (Original magnification, × 34,000; electron micrograph courtesy of Dr. Sara Miller.)

trichrome staining, 100% and 77.4% for calcofluor chitin staining, and 83.3% and 96% for indirect immunofluorescent staining [63]. The lower limit of detection was about 50 organisms per μL of stool and required examining up to 100 oil-immersion fields. Stool concentration did not help sensitivity [41].

Scant data are available on intestinal microsporidiosis in HIV-infected African adults [32–37], and little is known about microsporidial infections in children worldwide. In Zimbabwe, *E. bieneusi* spores were identified in stool from 10% of adults with known or suspected HIV infection and diarrhea but in no children with diarrhea, regardless of HIV infection. *Enterocytozoon* was identified by light microscopy in 7% of duodenal and jejunal biopsy specimens from HIV-infected persons in Uganda and Zambia [37]. Among HIV-infected patients with diarrhea in Zambia, TEM of duodenal biopsies and light microscopy of stools revealed *Encephalitozoon* (*Septata*) *intestinalis* in 3% but no enterocytozoon infections [36]. Another Zambian study identified microsporidia by light microscopy in 23% of adults with HIV-associated chronic diarrhea [35].

Only two reports from Africa describing pediatric microsporidiosis have been published. In rural Zambia, a 7-month-old HIV-negative boy was identified as having *E. bieneusi* infection [32]. He had a good nutritional status, no history of diarrhea, and no other intestinal pathogens, and he was negative for microsporidia 9 months later. In an outpatient clinic in Niger, 1% of children with diarrhea and 0.5% without diarrhea had *E. bieneusi* infection [64]. These children were not tested for HIV. *E. bieneusi* was identified in 7% of HIV-infected adults with <50 CD4 cells/μL in the same clinic.

We identified *Enterocytozoon* spores in 2 (3%) of the children with chronic diarrhea (1 HIV^+, 1 HIV^-) but in no children with acute diarrhea. Three percent of the adults had enterocytozoon infection. Thus, microsporidia may not be as prevalent in Tanzania as in some developed countries. The most striking finding was *Enterocytozoon* spores in four control children with no history of gastrointestinal symptoms. All 4 were underweight, vs. 2 of 16 control children without microsporidia, suggesting a possible association with undernutrition. Intestinal microsporidiosis is a well-documented cause of malnutrition and wasting in adults with AIDS [25, 26], and asymptomatic infections with *E. bieneusi* have been described as occurring in HIV-infected adults [65]. This report confirms the occurrence of intestinal microsporidiosis in HIV-negative children without diarrhea and suggests that these agents may not be pathogenic in all cases or that acquired immunity may result in asymptomatic carriage. Similar findings have been noted with respect to *Cyclospora* in areas of high endemicity.

Cyclospora is the most recently described of these three parasites. The first probable report of *Cyclospora,* from Papua New Guinea in 1979, went largely unnoticed [14]. Studies from 1986 to 1993 reported protozoa that were likely *Cyclospora* but were not identified as such (reviewed in [13]), until Ortega and colleagues established the genus as *Cyclospora* and proposed the species name *cayetanensis* [15]. Worldwide, similar organisms have now been described as occurring in persons with protracted diarrheal illness [13, 24, 66].

Cyclospora caused several outbreaks of diarrhea in North America in 1996–1997, advancing our understanding of the transmission and incubation of cyclosporiasis [20, 21]. More detailed information came from studies in Nepal, Peru, and Haiti [16, 18, 23, 67], but little was known about *Cyclospora* in Africa. *Cyclospora* commonly caused chronic or relapsing diarrhea (>11%) in travelers and nonnative residents of Nepal that was associated with consumption of untreated water during the hot, rainy season [16]. In Nepal, *Cyclospora* was found in 5% of symptomatic children and 2% of asymptomatic children aged >18 months but in no children aged <18 months [68]. In a longitudinal study in the slums of Lima, Peru, 9% of children developed fecal cyclosporiasis, but only one-third of those had diarrhea [15]. A cross-sectional survey in Lima detected *Cyclospora* in 1.1% of children (1.6% of those aged <8 years; 0.3% of those aged >8 years), again with strong seasonal variation [18]. Again, only one-third of these children were symptomatic at some point during oocyst excretion. Diarrhea tended to be mild and short-lived. For comparison, adults were all negative for *Cyclospora.*

In a prospective study of Haitian AIDS patients with chronic diarrhea, 11% were positive for *Cyclospora,* vs. none of the controls [23]. Clinical features were not distinctive, but treatment with trimethoprim-sulfamethoxazole stopped the diarrhea in 1–5 days and terminated oocyst excretion. In addition, two placebo-controlled trials of trimethoprim-sulfamethoxazole demonstrated its efficacy for cyclosporiasis [18, 69]. Histologically, AIDS patients infected with *Cyclospora* may have higher parasite densities than immunocompetent individuals [23, 24].

In contrast, *Cyclospora* was identified in only 1 of our 86 adult AIDS patients, 1 of the 55 children with acute diarrhea, and no children with chronic diarrhea or asymptomatic con-

trols. While geographic variation is expected, seasonality may be a factor because our study did not span the long rainy season. In addition, use of trimethoprim-sulfamethoxazole before admission may have decreased the prevalence of *Cyclospora.* Most of the pediatric patients had received anti-infective drugs before admission; trimethoprim-sulfamethoxazole was specifically identified in 20 cases. In patients with AIDS in Lima, <1% of individuals who presented with diarrhea were infected with *Cyclospora,* possibly because of the frequent use of trimethoprim-sulfamethoxazole for *Pneumocystis carinii* prophylaxis, while the higher prevalence of *Cyclospora* in the Haitian study may be due to the infrequent use of trimethoprim-sulfamethoxazole in these patients [23].

In conclusion, *Cryptosporidium* is an important diarrheal parasite in Dar es Salaam in adults with AIDS, though at lower prevalence than reported elsewhere in Africa. It is also an important pathogen in children with both acute and chronic diarrhea and is not confined to HIV-infected children. *Enterocytozoon* was detected in four control children without diarrhea, suggesting asymptomatic carriage. Both cryptosporidiosis and microsporidiosis were associated with malnutrition. Only two patients with *Cyclospora* were identified, though *Cyclospora* may have been more frequent in the rainy season and in the absence of prior treatment.

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