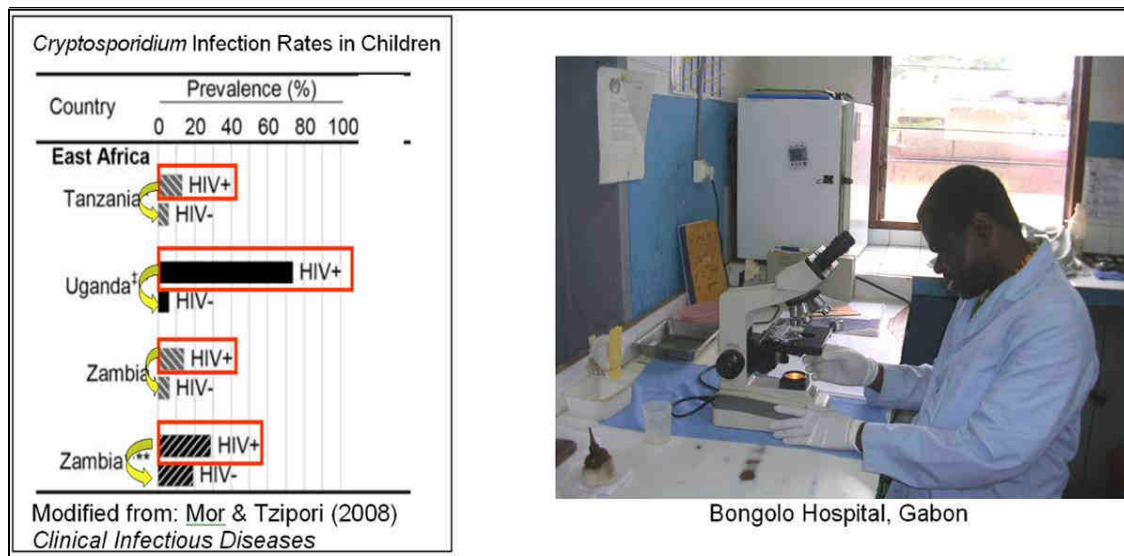


WATERBORNE PATHOGEN INFECTION RATES FOR PEOPLE LIVING WITH HIV/AIDS

A CAWST Literature Summary
November 2009 Edition

PART III – SUB-SAHARAN AFRICA





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cronyms

CAWST	Centre for Affordable Water and Sanitation Technology
HIV	Human Immunodeficiency Virus
AIDS	Acquired Immune Deficiency Syndrome
ART	antiretroviral treatment
PCR	polymerase chain reaction
CD4	cluster difference 4
CD	chronic diarrhea
UNICEF	United Nations International Children's Emergency Fund
WHO	World Health Organization
MIT	Massachusetts Institute of Technology

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Introduction

This document has been prepared for individuals working in either the fields of public health or water treatment, particularly those who work in resource-limited countries. There is increasing awareness that waterborne pathogens are an important cause of morbidity and mortality for people living with HIV/AIDS in resource-limited countries. This document focuses on pathogens that are commonly or sometimes waterborne. As noted in the journal *HIV Medicine*:

“Since the first reported case of HIV infection in 1981, many HIV-seropositive patients have died as a result of diarrhea induced by opportunistic protozoal infections: pathogens that would normally cause only a transient illness in immunocompetent individuals” (Miao and Gazzard).

The readers of this document are advised that the percent positive rates for different waterborne pathogens are likely higher than the infection rates summarized in this document as noted in the following from an article in *HIV Medicine*:

“Stool light microscopy and culture are highly specific but not particularly sensitive tests. Newer polymerase chain reaction (PCR) techniques are available, but these tests are costly and time-consuming and therefore not routinely available in hospital practice. The sensitivity of PCR techniques for both cryptosporidia and microsporidia may be much better than currently available techniques. Thus, some of the individuals formerly diagnosed with pathogen-negative diarrhoea may have been infected with these organisms” (Miao and Gazzard).

In a study conducted in the GHESKIO Centers in Haiti with the University of Virginia, Cornell University and the University of the Philippines, microscopy only detected *Cryptosporidium* oocysts in about 30% of the patients for which real-time PCR detected oocysts (Eyma et al.).

Besides the *Cryptosporidium* infection rates described in this document, the prolonged duration and severity of illness associated with Cryptosporidiosis and AIDS patients (Hunter and Nichols) is also important. In addition, higher waterborne pathogen infection rates in the community lead to increased quantities of pathogens that can potentially contaminate drinking water sources given the inadequate sanitation that exists in many resource-limited countries. In a study conducted by the University of Texas and Tufts University, total oocysts shed per person ranged from 5×10^6 to 1×10^{10} , the latter occurring in the volunteer with the longest episode of diarrhea and oocyst shedding (Chappell et al.). The same study found that the dose of *Cryptosporidium* oocysts high enough to infect 50% of the volunteers was estimated to be only 10 oocysts.

The reader should note the following relative to data contained in this document on relative to infection rates for *Entamoeba Histolytica*:

“Diagnosis of infection is complicated by the morphologically similar, but non-pathogenic, *E. dispar*. Microscopy is ineffective at distinguishing between the two species, and since the *E. dispar* infection-rate is 10-fold higher than that of *E. histolytica*, there is high incidence of misdiagnosis and treatment.” (Herbein et al.)

Because of the large volume of information provided in this document, colored lines have been added to make comparison of data in many of the tables easier.

References for Introduction Section

Chappell et al. “*Cryptosporidium Hominis*: Infectivity and Illness in Healthy Adults” Presented at ASTMH 2005 Annual Meeting

Eyma et al. “Improved diagnosis of Cryptosporidial and Microsporidial infections by PCR in patients with AIDS and diarrhea in Haiti” Presented at ASTHM Annual Meeting 2006

Herbein J, Buss S, Haque R., Ayeh-Kum³ P, Petri WA, Lyerly DM. “Evaluation of a rapid fecal diagnostic test for *Entamoeba histolytica* infection” *Am J Trop Med Hyg* 2004 Oct; 71(4 Suppl):12-30.

Hunter PR and Nichols G. “Epidemiology and Clinical Features of *Cryptosporidium* Infection in Immunocompromised Patients” *Clinical Microbiology Reviews*, 2002

Miao YM and Gazzard BG. “Management of protozoal diarrhoea in HIV disease” *HIV Medicine* 2000

SUB-SAHARAN AFRICA

Sub-Saharan Africa (General). Gilks CF. "Acute bacterial infections and HIV disease" *British Medical Bulletin* 1998,54 (No. 2): 383-393.

- "With high exposure, several *Enterobacteriaceae* are common causes of bacteraemia and septicaemia in adults with HTV infection in the tropics. The most important are the *Salmonellae*, as they are in temperate zones. In Africa, the non-typhi salmonellae (NTS), particularly *S. typhimurium* and to a lesser extent *S. enteritidis*, predominate."
- "NTS are only capable of regularly causing an enteric fever like illness with bacteraemia in immunosuppressed adults. Consistently, about 1 in 10 adults admitted to hospital with underlying HTV infection had NTS bacteraemia (Table 1), and mortality is high."

Table 1 Bacteraemia and fungaemia in HIV-positive adults admitted to hospital in Africa: a summary of cross-sectional studies from East, Central and West Africa

	Nairobi, 1988/89 (n = 95) ²⁸	Kigali, 1989 (n = 63) ³⁰	Abidjan, 1991 (n = 292) ³¹	Nairobi, 1992 (n = 144) ²⁹	Abidjan, 1995 (n = 199) ³²
Total with bacteraemia (%)	26.3	23.3	15.3	24.4	19.6
Non-typhi <i>Salmonellae</i> (%)	10.5	6.1	7.9	10.4	11.6
<i>Strep. pneumoniae</i> (%)	7.4	7.4	1.5*	10.4	2.0*
Mortality in patients bacteraemia (%)	58	NA	63	37	47
<i>C. neoformans</i> (%)	1.1	8.0**	2.5	0.7	0.0

NA, data not available; *significantly lower than other studies ($P < 0.001$); **significantly higher than other studies ($P < 0.001$).

- In developed countries "NTS bacteraemia is relatively rare, probably because of limited environmental exposure in communities that have good public health and hygiene. There are a variety of interlinked environmental and socio-economic reasons that explain the different features of HIV disease and AIDS in the tropics, especially the clinical spectrum and early death. In particular, this relates to the high background prevalence of acute bacterial and mycobacterial disease. Pathogen exposure in poor, overcrowded urban and rural settlements with inadequate sanitation and limited clean water is far higher than in the more affluent and better housed communities more typical of industrialized countries. The consequences for HIV-infected adults are hardly surprising: a far higher rate of acute bacterial and mycobacterial infection presenting relatively early in the course of progressive immunosuppression."

- “In Uganda, NTS bacteraemia is rare in adults with CD4 counts above 500, is seen at a rate of 5/1000 in adults with CD4 counts between 200-500, and occurs at a rate of about 75/1000 in adults with CD4 counts below 200. The commonest presentation is with an enteric fever-like illness. Blind therapy can be difficult because antibiotic resistance rates in NTS across Africa are high but variable. First line empirical therapy also depends on what is available and affordable. Mortality can be very high particularly when there is little awareness of the problem.”
- “Some acute bacterial infections, notably those caused by the pneumococcus and the non-typhi salmonellae, have not traditionally been considered as leading diseases in tropical medicine, despite their ubiquitous distribution and impact on health. The HIV/AIDS epidemic is forcing a re-evaluation of this position because of their importance in immunosuppressed adults, particularly where exposure is high and treatment relatively inadequate.”

Sub-Saharan Africa (General). Graham SM. “Salmonellosis in children in developing and developed countries and populations” *Current Opinion in Infectious Diseases* 2002, 15:507-512.

- “HIV infection is the major risk factor for invasive NTS (non-Typhoid *Salmonella*) disease in African adults, with the most recent large study from the region showing that 92% of 164 adults with NTS bacteraemia were HIV seropositive.”
- “However, very little is known regarding the source and transmission of NTS in developing countries. It is likely that animal-human transmission via the food chain is less responsible than is human-human transmission, with contaminated water an important vehicle in communities with poor hygiene and sanitation; this situation is similar to that with typhoid fever.”

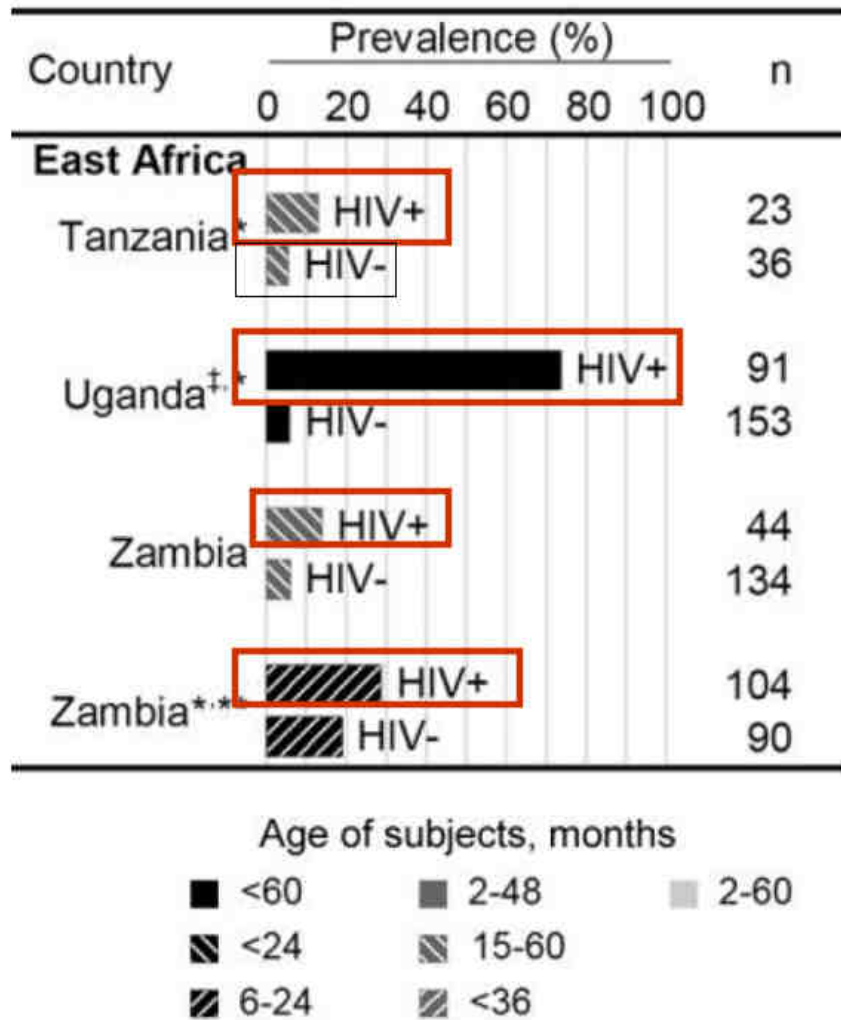
Sub-Saharan Africa (General). Kankwatira AM, Mwafulirwa GA, Gordon MA. “Non-typhoidal salmonella bacteraemia--an under-recognized feature of AIDS in African adults” *Trop Doct.* 2004 Oct;34(4):198-200.

- “Non-typhoidal salmonella (NTS) infections are severe, invasive and recurrent in the HIV-infected adult, and NTS are the commonest cause of hospital admission with bacteraemia in sub-Saharan Africa. NTS bacteraemia typically presents in patients with HIV/AIDS once the CD4 count falls below 200 cells/microL. In-patient mortality is 35%-60%...Among survivors, 25%-45% may have single or multiple recurrences of NTS bacteraemia 1-6 months after the first illness, requiring retreatment. Diagnosis relies on blood culture, so in many areas this disease cannot be definitively diagnosed, and must be empirically treated.”

Sub-Saharan Africa (General). Mor SM and Tzipori S. “Cryptosporidiosis in Children in Sub-Saharan Africa: A Lingering Challenge” *Clinical Infectious Diseases* 2008; 47:915–21.

- “Hospital- and community-based studies in sub-Saharan Africa document a high prevalence of cryptosporidiosis in children aged 6–36 months, particularly among those who are malnourished or positive for human immunodeficiency virus (HIV) infection and during rainy seasons. This is despite advances in developed countries that have curbed the incidence of cryptosporidiosis in the general and HIV-positive populations.”
- “Among HIV-positive children with diarrhea, prevalence varies between 13.0% in Tanzania and 73.6% in Uganda. The astonishingly high prevalence in Uganda is due partly to the sensitive PCR-based assay used....”

Prevalence of cryptosporidiosis among children in sub-Saharan Africa



Sub-Saharan Africa (General). Morpeth SC, Ramadhani HO, Crump, JA. “Invasive Non-Typhi *Salmonella* Disease in Africa” *Clinical Infectious Diseases* 2009; 49:606–11.

- “Non-Typhi *Salmonella* (NTS) is among the 3 most common pathogens causing bacterial bloodstream infections in adults and children in sub-Saharan Africa.” Children and HIV–positive adults carry most of the burden of invasive disease, and mortality among these groups is high. This contrasts with developed countries, where NTS disease is usually a self-limited diarrhea, and mortality is lower. “Invasive NTS disease is endemic to rural and urban sub-Saharan Africa.”
- “Seasonal peaks of NTS disease occur with the rainy season among both adults and children, suggesting that environmental risk factors are important. Fecal organisms are found at the highest concentrations in drinking water sources in Africa at the onset of the wet season, and this may correspond to increased risk of waterborne NTS.”
- “NTS bacteremia is more common among HIV-infected individuals, and the association with HIV infection is strongest among adults. Recurrent NTS bacteremia is a World Health Organization (WHO) stage 4 defining condition. HIV infection is also a risk factor for bacteremia among children, including NTS bacteremia. HIV was associated with any bacteremia among children in Kilifi, Kenya (odds ratio, 3.22) and with NTS bacteremia (odds ratio, 3.21).”

Table 1. Risk Factors for Non-Typhi *Salmonella* Bacteremia in Africa

Risk factor category, risk factor	Grade of evidence ^a	
	Children aged <3 years	Older children and adults
Environment		
Food and water	B	B
Hospital-acquired infection	B	B
Direct and indirect animal contact	C	C
Transmission between humans	C	D
Host		
Age ^b	A	D
HIV infection	A	A
Malnutrition	A	...
Sickle cell disease	...	C
Malarial anemia	B	...
Schistosomiasis	...	D
Recent antimicrobial use	B	C

NOTE. An ellipsis (...) indicates lack of data. HIV, human immunodeficiency virus.

^a Levels of evidence were estimated from African studies included in this review and were classified according to the grades of the Oxford Centre for Evidence-based Medicine [20].

^b For older children and adults, the risk factor is old age.

Sub-Saharan Africa (General). Okeke IN, Aboderin OA, DK Byarugaba, Ojo KK, Opintan JA. "Growing Problem of Multidrug-Resistant Enteric Pathogens in Africa" *Emerging Infectious Diseases* Vol. 13, No. 11, November 2007

- "The effects of enteric infections in Africa are almost entirely driven by poor access to safe water and sanitation. Thus, once resistant pathogens emerge, they are easily spread. Providing safe water and sanitation to those who cannot afford these capital-intensive options and to public institutions such as schools, health centers, and markets is the single most important intervention for preventing outbreaks and sporadic cases of diarrheal disease, including those caused by resistant organisms. Interventions that affect disease prevalence attack resistance at the root of the problem and therefore have the greatest chance of success".
- "Safe water and sanitation, addressing the imbalance between antimicrobial drug supply and demand, and building realistic infrastructure for rational antimicrobial use are priority areas for resistance control that could address the short- and long-term disease effects on the poor."

Burundi. Kadende P, Nkurunziza T, Floch JJ, Mpfizi B, Laroche R, Ndabaneze E, Aubry P. "Infectious diarrhea in African acquired immunodeficiency syndrome (AIDS). Apropos of 100 patients studied in Bujumbura (Burundi)" *Med Trop (Mars)*. 1989 Apr-Jun;49(2):129-33.

- The study authors carried out a survey on 100 cases of AIDS at the Centre Hospitalier Universitaire de Kamenge, Bujumbura, Burundi.
- The waterborne pathogens most often found were *Isospora belli* 16.2% and *Cryptosporidium* 13.1%.

Cameroon. SARFATI C, BOURGEOIS A, MENOTTI J, LIEGEOIS F, OYOU-SOMO R, DELAPORTE E, DEROUIN F, NGOLE E, MOLINA JM. "PREVALENCE OF INTESTINAL PARASITES INCLUDING MICROSPORIDIA IN HUMAN IMMUNODEFICIENCY VIRUS–INFECTED ADULTS IN CAMEROON: A CROSS-SECTIONAL STUDY" *Am. J. Trop. Med. Hyg.*, 74(1), 2006, pp. 162–164.

- 154 HIV-positive patients in study.
 - *Cryptosporidium* – 6.5% with diarrhea, 2.8% of patients without diarrhea
 - Microsporidia – 6.5% with diarrhea, 4.6 % of patients without diarrhea
 - *Isospora belli* - 6.5% with diarrhea, 0 % of patients without diarrhea
-

Central African Republic. Gouandjika-Vasilache I, Akoua-Koffi C, Begaud E, Dosseh A. "No evidence of prolonged enterovirus excretion in HIV-seropositive patients" *Trop Med Int Health*. 2005 Aug; 10(8):743-7.

- "Mutations frequently occur in oral poliovirus vaccine (OPV) strains upon replication in the human intestine. These strains occasionally revert to being neurovirulent. The more prolonged the excretion of OPV, the higher the risk of reversion. We investigated whether HIV infection, which is very prevalent in the Central African Republic, causes prolonged excretion of enteroviruses and, in particular, of OPV strains in adults."
 - Studied 28 HIV-positive adults living with children who were immunized with OPV during national immunization days (NIDs). No poliovirus was isolated from any stool sample.
 - "Enteroviruses were not more frequently isolated from severely immunodeficient patients. Thus, HIV-infected adults do not appear to be at high risk of infection with OPV strains and the excretion of enteroviruses (and thus of polioviruses) does not seem to be prolonged in HIV-infected adults."
-

Central African Republic. Germani Y, Minssart P, Vohito M, Yassibanda S, Glaziou P, Hocquet D, Berthélémy P, Morvan J. "Etiologies of acute, persistent, and dysenteric diarrheas in adults in Bangui, Central African Republic, in relation to human immunodeficiency virus serostatus" *Am J Trop Med Hyg.* 1998 Dec;59(6):1008-14.

- Enteroaggregative *Escherichia coli* (EAaggEC) most frequently identified and *Cryptosporidium* the 2nd most common pathogen in HIV-positive patients with persistent diarrhea.
- HIV-negative patients without diarrhea (controls) had significant prevalence of *Cryptosporidium* (the highest of all pathogens) indicating a significant degree of asymptomatic individuals that could be a source of water contamination. *Cryptosporidium* associated with persistent diarrhea in HIV-positive patients but not in HIV-negative patients

Enteropathogen	Acute diarrheas n = 130 (%)		Dysenteries n = 23 (%)		Persistent diarrheas n = 137 (%)		Controls n = 140 (%)	
	HIV-positive n = 51 (39.2)	HIV-negative n = 79 (60.7)	HIV-positive n = 10 (43.4)	HIV-negative n = 13 (56.5)	HIV-positive n = 110 (80.3)	HIV-negative n = 27 (19.7)	HIV-positive n = 73 (52.1)	HIV-negative n = 67 (47.9)
<i>Salmonella</i> spp.	14 (27.4)	20 (25.3)	0	0	0	1 (3.7)	2 (2.7)	5 (7.4)
<i>Shigella</i> spp.	0	0	2 (20)*	5 (38.4)†	0	0	0	0
<i>Campylobacter</i> spp.	0	0	1 (10)‡	2 (15.3)‡	0	2 (7.4)	0	0
<i>Clostridium difficile</i>	1 (1.9)	0	0	0	1 (0.9)	1 (3.7)	0	0
Spirochetaceae	0	0	4 (40)	0	0	0	0	0
HEp2-adherent <i>Escherichia coli</i>								
Localized	0	0	0	0	2 (1.8)	0	0	0
Diffuse	0	0	0	0	9 (8.2)	0	1 (1.4)	3 (4.5)
Aggregative	1 (1.9)	0	0	0	14 (12.7)	0	0	0
Enterotoxigenic <i>E. coli</i>	2 (3.8)§	1 (1.3)¶	0	0	0	0	0	0
Enterohemorrhagic <i>E. coli</i>	0	2 (2.5)	0	0	0	0	0	0
<i>Entamoeba histolytica</i>	1 (1.9)	3 (3.8)	2 (20)	2 (15.3)	0	0	0	0
<i>Giardia lamblia</i>	0	3 (3.8)	0	0	1 (0.9)	0	0	0
<i>Schistosoma mansoni</i>	0	0	0	0	0	3 (11.1)	0	0
<i>Cryptosporidium</i> spp.	0	2 (2.5)	0	0	7 (6.4)	0	0	9 (13.4)
<i>Isoospora belli</i>	0	1 (1.3)	0	0	3 (2.7)	0	0	0
<i>Cyclospora cayentanensis</i>	0	2 (2.5)	0	0	5 (4.5)	0	0	0
<i>Microsporidium</i> spp.	0	0	0	0	6 (5.4)	0	0	0
<i>Blastocystis hominis</i>	0	0	0	0	4 (3.6)	0	0	0
<i>Strongyloides stercoralis</i>	0	0	0	0	2 (1.8)	0	0	0
Fungi	0	0	0	0	7 (6.4)	0	0	0
Multiple pathogens	9 (17.6)#	1 (1.3)#	1 (10)#	4 (30.8)#	7 (6.4)#	0	28 (38.4)	38 (56.7)
Total	28 (54.9)	35 (44.3)	10 (100)	13 (100)	68 (61.8)	7 (25.9)	31 (42.5)	55 (82.1)

Dem. Rep. of the Congo/Zaire (DRC). Colebunders R, Lusakumuni K, Nelson A M, Gigase P, Lebughe I, van Marck E, Kapita B, Francis H, Salaun J J, Quinn TC. “Persistent diarrhoea in Zairian AIDS patients: an endoscopic and histological study” *Gut* 1988; 29; 1687-1691.

- 42 patients were HIV-positive and had persistent diarrhea.
- *Cryptosporidium* was the intestinal parasite most often identified (30%)
- *Isospora belli* was found in 12% of the patients.

DRC. Keusch GT, DM Thea, M Kamenga, K Kakanda M Mbala, C Brown, F Davachi, “Persistent diarrhea associated with AIDS” *Acta Paediatrica* Volume 81 Issue s383, Pages 45 – 48 1992.

- Analysis of a study of 469 babies born to mothers with known HIV serostatus in Kinshasa, Zaire (now DRC), revealed progression of acute to persistent diarrhea was six times greater in HIV-positive compared to HIV-negative babies.
 - Progression of acute to persistent diarrhea was 3.5 times greater in HIV-negative babies born of HIV-positive mothers in comparison to HIV-negative babies with HIV-negative mothers.
 - HIV-positive babies were also at greater risk than HIV-negative babies to have recurrent episodes of diarrhea (RR = 2.3).
 - 50% of the deaths were due to acute or persistent diarrhea, and were strongly associated with HIV infection.
 - “Efforts to improve child survival in AIDS infected populations will need to address HIV infections in both mothers and infants.”
-

DRC/Zaire. Thea DM, St. Louis ME, Atido U, Kanjinga K, Kembo B, Matondo M, Tshiamala T, Kamenga C, Davachi F, Brown C, Rand WM and GT Keusch "A Prospective Study of Diarrhea and HIV-1 Infection among 429 Zairian Infants" *New England Journal of Medicine* Volume 329:1696-1702 December 2, 1993 Number 23

- In an update of the Keusch et al. 1992 study (see previous page), the England Medical Center, the CDC, the National Institute of Allergy and Infectious Diseases, Project SIDA and the Mama Yemo Hospital, Kinshasa studied 429 infants born to HIV-positive or HIV-negative mothers to determine the incidence of acute, recurrent (> or = 2 episodes), and persistent (> or = 14 days) diarrhea; outcome; and risk factors.
- Compared with HIV-negative infants, HIV-positive infants had higher incidence rates for acute diarrhea (170 vs. 100 episodes per 100 child-years, $P = 0.003$), recurrent diarrhea (21 vs. 11, $P = 0.12$), and persistent diarrhea (19 vs. 4, $P < 0.003$).
- Persistent diarrhea in 11 HIV-positive infants; all but 1 died. Persistent diarrhea occurred in 19 uninfected infants; all but 1 survived. Prevalence of pathogens was similar in two groups. Study found a relative risk of death of 6.1 in all infants if an episode of persistent diarrhea occurred during the study ($P = 0.03$).
- The incidence of persistent diarrhea in the uninfected infants of HIV-positive mothers was nearly double that in the uninfected infants of HIV-negative mothers (4.9 vs. 2.7 episodes per 100 child-years), and the risk increased if the mother died (relative hazard - 10.4).
- Authors conclusion - "In Zaire, infants with HIV infection have an 11-fold increased risk of death from diarrhea, largely persistent diarrhea, which is often preceded by recurrent episodes of acute diarrhea, malnutrition, or immunosuppression. Illness and death of the mother increase that risk, even among her uninfected infants".

CAUSE	ALL DEATHS DURING STUDY PERIOD*	DEATHS FROM 0-12 MO OF AGE			
		HIV INFECTED		UNINFECTED	
		no. (%)	no. (%)	no./1000 live births	no. (%)
Diarrhea	26 (36)	7 (37)	132	4 (31)	12
Acute	14 (19)	1 (5)	19	3 (23)	9
Persistent	12 (17)	6 (32)	113	1 (8)	3
Other	46 (64)	12 (63)	226	9 (69)	27
Total	72	19	358	13	39

*Includes children of indeterminate HIV status.

Table 1. Diarrhea-Related Deaths and HIV-1 Infection in 429 Zairian Infants

DRC/Zaire. Thea DM, Glass R, Grohmann GS, Perriens J, Ngoy B, Kapita B, Atido U, Mabaluku M, Keusch GT. "Prevalence of enteric viruses among hospital patients with AIDS in Kinshasa, Zaire" *Trans R Soc Trop Med Hyg.* 1993 May-Jun; 87(3):263-6.

- Samples from 17% of 198 consecutive adult admissions to Mama Yemo Hospital in Kinshasa.
 - "The prevalence of enteric viruses in stool specimens did not differ significantly between patients with and without HIV infection, and was not associated with acute or chronic diarrhoea, or constitutional symptoms. However, a trend ($P = 0.14$) towards greater frequency of virus in stools from patients in the lower 3 quintiles of the CD4/CD8 T cell ratio was seen. This trend approached statistical significance ($P = 0.07$) with stratification by HIV infection. Although we found no evidence in this population to support a major pathogenic role for these viruses alone in the enteropathy of AIDS, increased viral shedding was weakly associated with immunodeficiency."
 - 93% of all HIV-positive patients either had AIDS (stage IV) or advanced stage III disease. 49% of them died while in the hospital.
 - 17% of all adult patients studied were infected with at least 1 enteric virus, especially rotavirus.
 - Enteric viruses were isolated from both HIV-positive and HIV-negative patients (17% and 18%, respectively).
 - Chronic diarrhea was significantly associated with being HIV-positive.
 - "These findings suggest that enteric viruses were not a significant cause of diarrhea, but they were isolated somewhat more often in patients of advanced immunosuppression."
-

Ethiopia. Assefa S, Erko B, Medhin G, Assefa Z, Shimelis T. "Intestinal parasitic infections in relation to HIV/AIDS status, diarrhea and CD4 T-cell count" *BMC Infectious Diseases* 2009, 9:155.

Table 1: Distribution of different intestinal parasites among HIV positive and negative subjects, 2008

Type of parasite	HIV positive (N = 214) Number (%)	HIV-negative (N = 164) Number (%)
Helminths		
<i>A. lumbricoides</i>	26(12.2)	21(12.8)
<i>T. trichiura</i>	8(3.7)	13(7.9)
Hookworm species	7(3.3)	13(7.9)
<i>E. vermicularis</i>	2(0.9)	1(0.6)
<i>S. stercoralis</i>	27(12.6)	1(0.6)
<i>Taenia</i> species	3(1.4)	5(3.1)
<i>H. nana</i>	4(1.9)	1(0.6)
<i>S. mansoni</i>	4(1.9)	4(2.4)
Protozoa		
<i>E. histolytica/dispar</i>	53(24.8)	47(28.7)
<i>G. lamblia</i>	24(11.2)	12(7.3)
<i>I. belli</i>	26(12.2)	0
<i>Cryptosporidium</i> species	43(20.1)	0
<i>E. coli</i>	4(1.9)	3(1.8)

Table 5: Distribution of HIV-associated parasites in different categories of CD4 T-cell counts, Hawassa Referral Hospital, Ethiopia, 2008

CD4 T-cell count/ μ L	Total (%) examined	Positive (%) for any parasite	<i>S. stercoralis</i>	<i>I. belli</i>	<i>Cryptosporidium</i> species
< 200	61 (28.5)	51(83.6)	14 (23.0)	18 (29.5)	31(50.8)
200-349	58 (27.1)	35 (60.3)	4 (6.9)	1 (12.1)	7 (12.1)
350-499	46 (21.5)	20 (43.5)	3 (6.5)	1 (2.2)	4 (8.7)
\geq 500	49 (22.9)	22 (44.9)	6(12.2)	0	1(2.0)

Ethiopia. Awole M, Gebre-Selassie S, Kassa T, Kibru G “Prevalence of Intestinal Parasites in HIV-Infected adult Patients in Southwestern Ethiopia” *Ethiop J Health Dev* 2003, 17:71-78.

- *Cryptosporidium parvum* was detected in 11% of patients
 - *Isospora belli* – 7.4% of patients
 - *Cyclospora* – 3.7% of patients
-

Ethiopia. Endeshaw et al., “Intestinal Microsporidiosis in Diarrheal Patients Infected with Human Immunodeficiency Virus-1 in Addis Abada, Ethiopia” *Jpn. J. Infect. Dis.*, 2006 59, 306-310 .

- 16% positive for Microsporidia. Microsporidia found was mainly *Ecephaliozoan bieneusi* with some but much less *Ecephaliozoan intestinalis*.
-

Ethiopia. FISSEHA B, PETROS B, WOLDEMICHAEL T. “*Cryptosporidium* and other parasites in Ethiopian AIDS patients with chronic diarrhea” *East African medical journal* 1998, vol. 75, no2, pp. 100-101.

- Study included 246 AIDS patients with diarrhea in seven Addis Ababa hospitals.
 - Cryptosporidiosis was detected in 25.9% of the AIDS patients with diarrhea
 - Isosporiasis -1.4%
-

Ethiopia. Fontanet AL, Sahlu T, Rinke de Wit T, Messele T, Masho W, Woldemichael T, Yeneneh H, Coutinho RA. “Epidemiology of infections with intestinal parasites and human immunodeficiency virus (HIV) among sugar-estate residents in Ethiopia” *Ann Trop Med Parasitol.* 2000 Apr; 94(3):269-78.

- “Intestinal parasitic infections could play an important role in the progression of infection with human immunodeficiency virus (HIV), by further disturbing the immune system whilst it is already engaged in the fight against HIV.”
 - HIV and intestinal parasitic infections were investigated in 1,239 randomly selected individuals, and aged 15-54 years, living on a sugar estate in central Ethiopia.
 - The intestinal parasites identified in the study population were amoebic parasites (*Entamoeba histolytica/Enta. dispar*) - 24.6%, hookworms - 23.8%, *Ascaris lumbricoides* - 22.2%, *Trichuris trichiura* - 19.5%, *S. stercoralis* - 13.0%, *Giardia lamblia* - 3.0%
 - Amoebic parasites were found to be more common in the HIV-positive individuals than the HIV-negative individuals (43.7% v. 24.0%; P < 0.05).
-

Ethiopia. Mariam ZT, Abebe G, Mulu A. "Opportunistic and other intestinal parasitic infections in AIDS patients, HIV seropositive healthy carriers and HIV seronegative individuals in southwest Ethiopia" *East Afr J Public Health*. 2008 Dec; 5(3):169-73.

- A study at Jimma University Hospital, Mother Theresa Missionary Charity Centre, Medan Acts Projects and Mekdim HIV-positive persons and AIDS orphans' national association during 2004. *Cryptosporidium* was detected only in the stools of HIV-positive individuals (15.4%).
 - *Isospora* was detected also only in HIV-positive individuals (3.9%).
-

Ethiopia. Mengesha B. "Cryptosporidiosis among medical patients with the acquired immunodeficiency syndrome in Tikur Anbessa Teaching Hospital, Ethiopia" *East Afr Med J*. 1994 Jun; 71(6):376-8.

- Stool specimens, collected at random from 63 medical in-patients with AIDS, were analyzed for *Cryptosporidium* oocysts.
 - Using the modified Kinyoun acid-fast staining technique, 25 (39.7%) of the stool specimens were positive for *Cryptosporidium* oocysts.
-

Ethiopia. Tadesse and Kassu "Intestinal parasite isolates in AIDS patients with chronic diarrhea in Gondar Teaching Hospital, Northwest Ethiopia" *Ethiop Med J*. 2005 Apr; 43(2):93-6.

- Study of 70 AIDS patients with chronic diarrhea using Modified Acid-Fast staining method in Gondar Teaching Hospital between January and September 2000.
 - *Cryptosporidium* – 29% and *Strongyloides stercoralis* 17% were the most frequently isolated parasites in diarrheal specimens of AIDS patients, accounting for 80% of pathogens among positive specimens.
-

Gabon. BRETON J, KOMBILA M, OKOME-NKOU MOU M, RINDER H and THELLIER M. "Intestinal microsporidiosis among HIV-positive patients in Libreville (Gabon): *Enterocytozoon bienersi* isolates show a very high diversity of genotypes" *Journal of Eukaryotic Microbiology* Volume 52 Issue 2, Pages 28S - 34S Published Online: 6 Apr 2005

- 836 patients were screened for microsporidia by and confirmed by PCR. 27 cases of microsporidia (*E. bienersi*) infection were found, a prevalence of 2.7%. These patients were in the most severely immuno-depressed group, 84% had a CD4 < 200/mm³.

Gabon. Okome-Kouakou M, Bekale J, Kombila M. "Salmonellosis in HIV infection in a hospital setting in Gabon" *Med Trop (Mars)*. 1999;59(1):46-50.

- Records were studied of 2,759 HIV-positive patients and 441 HIV-negative patients hospitalized in the Infectious Disease Department of the Jeanne Ebori Foundation in Libreville, Gabon were studied to determine the incidence of *Salmonella* infection in HIV patients. The incidence of *Salmonella* infection was 13 per 100 patients in HIV-positive patients (76% of these non-Typhoid *Salmonella*) versus 5.4 per 100 patients in HIV-negative patients. The predominant serotypes in HIV-positive patients were *Salmonella typhimurium* and *Salmonella enteritidis*.
- "This study demonstrates the gravity of low-grade *Salmonella* infection in African HIV-positive patients."

Ghana. Adjei A, Lartey M, Adiku TK, Rodrigues O, Renner L, Sifah E, Mensah JD, Akanmori B, Otchere J, Bentum BK, Bosompem KM. "*Cryptosporidium* oocysts in Ghanaian AIDS patients with diarrhoea." *East Afr Med J*. 2003 Jul; 80(7):369-72.

- Study of HIV/AIDS patients with diarrhoea over a nine month period at Korle-Bu Teaching Hospital and Korle-Bu Polyclinic Accra, Ghana.
- *Cryptosporidium parvum* in six (28.6%) of HIV/AIDS and 10 (37.0%) of the HIV-negative patients, respectively.
- *Salmonella* spp. - 9.5% and *Strongyloides stercoralis* - 4.8%

Guinea-Bissau. Lebbad, M, 2001 "Intestinal parasites in HIV-2 associated AIDS cases with chronic diarrhoea in Guinea-Bissau" *ACTA TROPICA* 2001 80, 1, p. 45 – 49.

- 52 adult patients with chronic diarrhoea of which 37 were HIV-positive and fulfilling the clinical criteria of AIDS were screened for parasitic infections.
- *Cryptosporidium parvum* – 25%
- *Isospora belli* - 11%
- Microsporidia – 11%

Kenya. Batchelor BIF, Kimari JN, Brndle R J. "Microbiology of HIV Associated Bacteraemia and Diarrhoea in Adults from Nairobi, Kenya" *Epidemiology and Infection*, 1996, Vol. 117, No. 1 pp. 139-144.

- For bacterial pathogens in stools, *Salmonella* and *Shigella* were much more common in HIV-positive than HIV-negative patients (see "Table 3" below).
- For parasites/protozoan pathogens, *Cryptosporidium*, *Ascaris* and *Entamoeba histolytica* and hookworm were significantly higher in HIV-positive patients.

Table 3. Stool isolates by HIV status. Some stools had more than one bacterial pathogen isolated

Isolates	Number of positive events	
	HIV Negative	HIV Positive
Bacteria		
<i>Salmonella typhimurium</i> *	3	40
<i>Salmonella havana</i>	0	2
<i>Salmonella enteritidis</i>	1	1
<i>Salmonella typhi</i>	0	2
<i>Salmonella braenderup</i>	1	1
Other <i>Salmonella</i> spp. (1 each)	1	12
<i>Shigella flexneri</i> *	9	49
<i>Shigella sonnei</i>	3	15
<i>Shigella boydii</i>	1	15
<i>Shigella dysenteriae</i>	1	5
<i>Campylobacter coli</i> †	0	3
<i>Campylobacter jejuni</i>	0	4
Ova, cysts, parasites		
<i>Strongyloides</i> sp.‡	0	3
<i>Ascaris lumbricoides</i>	6	21
<i>Schistosoma mansoni</i>	2	6
<i>Tricuris trichiura</i>	2	12
Hookworm	12	61
<i>Taenia</i> spp.	0	3
<i>Entamoeba histolytica</i>	0	14
<i>Giardia lamblia</i>	2	3
<i>Cryptosporidium parvum</i> §	0	45

Kenya. Berkley JA et al. "Bacteremia among Children Admitted to a Rural Hospital in Kenya" *N Engl J Med* 2005;352:39-47.

- "Each year in sub-Saharan Africa, 4.6 million children die before reaching the age of five years, and the vast majority of these deaths are not fully investigated. Most health facilities lack the resources for doing microbiologic studies, so the data on invasive bacterial infections are very limited. However, there are almost no estimates of incidence, mortality, or hospital burden for the majority of pathogenic bacterial species. Most data are from a few urban referral centers, with very little recent data from the rural areas where most people in sub-Saharan Africa live. Thus, the impact of childhood bacteremia is largely unknown. We aimed to establish a complete description of community-acquired bacteremia among children admitted to a rural Kenyan district hospital by investigating all acute admissions, without selection."
- "Between August 1998 and July 2002, we cultured blood on admission from 19,339 inpatients and calculated the incidence of bacteremia on the basis of the population served by the hospital."

Table 4. Odds Ratio for Community-Acquired Bacteremia in Children with Malnutrition and Those with HIV Infection.

Pathogen	Odds Ratio (95% Confidence Interval)*	
	Malnutrition	HIV Infection†
None‡	1.00	1.00
Any organism	2.02 (1.65–2.47)	3.22 (2.34–4.44)
<i>Streptococcus pneumoniae</i>	1.85 (1.36–2.52)	5.84 (3.98–8.56)
<i>Staphylococcus aureus</i>	1.31 (0.76–2.26)	1.93 (0.87–4.27)
Group A streptococci	3.28 (1.75–6.15)	2.24 (0.82–6.14)
Group B streptococci§	1.15 (0.45–3.00)	—
Nontyphoidal salmonella species	1.68 (1.15–2.44)	3.21 (1.95–5.28)
<i>Haemophilus influenzae</i>	1.16 (0.75–1.79)	2.97 (1.71–5.17)
<i>Escherichia coli</i>	4.73 (3.15–7.10)	2.24 (1.19–4.22)

Kenya. Gilks CF, Brindle RJ, Otieno LS, Simani PM, Newnham RS, Bhatt SM, Lule GN, Okelo GB, Watkins WM, Waiyaki PG, et al. "Life-threatening bacteraemia in HIV-1 seropositive adults admitted to hospital in Nairobi, Kenya." *Lancet* 1990 Oct 6;336(8719):877-8.

- During 6 months, 506 consecutive adult emergency admissions to hospital in Nairobi were enrolled in a study of bacteraemia and HIV infection. 19% were HIV-1 antibody positive.
- Significantly more HIV-positive than HIV-negative patients had bacteraemia (26% vs 6%). The predominant organisms isolated from the seropositive patients were *Salmonella typhimurium* and *Streptococcus pneumoniae*. Mortality was higher in the HIV-positive than in the HIV-negative bacteraemic patients.
- The findings suggested that *Salmonella* bacteria are important causes of morbidity and mortality in HIV-positive individuals in Africa.

Kenya. Mwachari C, Batchelor BI, Paul J, Waiyaki PG, Gilks CF. "Chronic diarrhoea among HIV-infected adult patients in Nairobi, Kenya" *J Infect.* 1998 Jul; 37(1):48-53

- Samples from 75 consecutive HIV-seropositive patients with chronic diarrhoea admitted to a Nairobi hospital were analyzed. The most common pathogens follow. :
- *Cryptosporidium* sp. - 17%
- *Salmonella typhimurium* - 13%
- Detection of *Cryptosporidium* was the single most significant predictor of death (RR = 5.2, P<0.05).

Malawi. Cranendonk RJ, Kodde CJ, Chipeta D, Zijlstra, EE, Sluiter, JF. "*Cryptosporidium parvum* and *Isospora belli* infections among patients with and without diarrhoea" *East African Medical Journal*, 2003 Aug; 80(8):398-401.

- 204 HIV-positive patients admitted to Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi. •
- Conclusion – "*Cryptosporidium parvum* and *Isospora belli* infections are a significant cause of diarrhoea among medical in-patients at QECH".

Mali. Alfa Cisse O, Ouattara A, Thellier M, Accoceberry I, Biligui S, Minta D, Doumbo O, Desportes-Livage I, Thera MA, Danis M, Detry A. "Evaluation of an immunofluorescent-antibody test using monoclonal antibodies directed against *Enterocytozoon bieneusi* and *Encephalitozoon intestinalis* for diagnosis of intestinal microsporidiosis in Bamako (Mali)." *J Clin Microbiol.* 2002 May; 40(5):1715-8.

- A 2-month study was carried out in Mali to evaluate an immunofluorescent-antibody test (IFAT) using monoclonal probes specific for Microsporidia (*Enterocytozoon bieneusi* or *Encephalitozoon intestinalis*).
- Microsporidia were detected in stools from 8 of 61 patients (13.1%) seropositive for HIV. A single species, *E. bieneusi*, was identified.
- "Since the introduction of highly active antiretroviral therapy, intestinal microsporidiosis has been less frequently reported in Europe and the United States. In developing countries, however, an increase in the impact of microsporidiosis is to be expected due to the rapid expansion of AIDS."

Mali. Diarra SB. "Prevalence of opportunistic parasitics among HIV patients hospitalized in Bamako: Study of 70 cases one year 200-2001" *Int Conf AIDS.* 2002 Jul 7-12;14.

- October 2000 at October 2001 in Bamako, Mali, 70 patients; a total of 29 deaths (41%).
- The incidence of *Cryptosporidium* - 30%, *Isospora belli* - 9%; Microsporidia - 34%
- The survival time was 190 days +/- after the first episode.
- Diarrhea and weight loss adversely affect immune function by increasing vulnerability to opportunistic parasites.

Mali. Konate A, Minta D, Diarra M, Dolo A, Dembele M, Diarra B, Maiga MY, Traore HA, Doumbo O. "Intestinal parasitosis during AIDS diarrhoea" *Bull Soc Pathol Exot.* 2005 Apr; 98(1):33-5.

- Study was from October 2000 to November 2001 at Toure Hospital in Bamako (Mali), concerning HIV-positive patients suffering from diarrhea.
 - *Cryptosporidium parvum* - 20%,
 - Microsporidia - 11.5%
 - *Isospora belli* - 8.5%
 - "Death within the first two weeks seems more important in case of infection by *Cryptosporidium parvum*."
-

Mali. Maiga I, Doumbo O, Dembele M, Traoré H, Desportes-Livage I, Hilmarisdottir I, Giboyau E, Maiga L, Kassambara L, el Fakhry Y, Datry A, Gentilini M, Pichard E. "Human intestinal microsporidiosis in Bamako (Mali): the presence of *Enterocytozoon bieneusi* in HIV seropositive patients" *Sante* 1997 Jul- Aug;7(4):257-62.

- A study was conducted between 1993 and 1996 in Bamako, Mali to determine the rate of occurrence of microsporidia in 88 patients. Most (80%) had chronic diarrhea associated with weight loss and 87.5% were HIV-positive.
- Intestinal microsporidia were detected in 32% of the patients infected with HIV-1, HIV-2, or co-infected with both strains. Microsporidiosis was also diagnosed in 3 of 11 HIV-negative individuals (27%).
- "These results suggest that microsporidia are common pathogens in HIV-positive patients in Bamako. Cases of microsporidiosis have been reported for the first time in HIV-2-infected patients. The proportion of women microsporidiosis patients is higher in Mali than in industrialized countries. The presence of microsporidia in HIV-negative patients suggests that these parasites may be an underestimated cause of enteritis in developing countries".

Mali. Minta D, Dembele M, Dolo A, Sidibe AT, Diakite A, Ouattara A, Sidibe AF, Thera MA, Pichard E, Traore HA, Doumbo O; "Parasitosis in HIV - infected people in the national hospital service of internal medicine and infectious diseases. Bamako – Mali" *Int Conf AIDS*. 2004 Jul 11-16; 15: abstract no. B12383.

- In 2002, 205 patients in services of internal medicine and infectious diseases of National Hospital of Point G of Bamako.
- *Entamoeba histolytica* represented 18% of cases.
- *Cryptosporidium* sp (13.3%), *Isospora belli* (5%) and microsporidiosis (3%).
- The rate of HIV-positive patients was 53.3% with a percentage of death of 27%.
- "Even with introduction of antiretroviral therapy, we reported that HIV is responsible of a high number of deaths (81%). Drugs prescribed are expensive or not well supported by patients."

Mozambique. von Seidlein et al. "Is HIV infection associated with an increased risk for cholera? Findings from a case-control study in Mozambique" *Tropical Medicine and International Health* 2008 Volume 13 no 5 pp 683–688.

- In a high risk area for cholera 23% of cholera cases were HIV-positive versus a 15% HIV-positive rate for non-cholera controls.

Niger and Vietnam. Espern A, Morio F, Miegerville M, Illa, H, Abdoulaye M, Meyssonnier, V, Adehossi, E, Lejeune, A, Cam, PD et al. "Molecular study of microsporidiosis due to *Enterocytozoon bieneusi* and *Encephalitozoon intestinalis* among human immunodeficiency virus-infected patients from two geographical areas: Niamey, Niger, and Hanoi, Vietnam" *J Clin Microbiol* 2007 45, 2999–3002.

- "In this study, we found a major difference between the results of microscopic examination and PCR. Of the 270 samples analyzed, 83 were positive by microscopy using Uvitex 2B. Finally, only 28 of the 83 (32.7%) were positive by real-time PCR either for *E. bieneusi* or *E. intestinalis*".
- "Several reasons could explain this difference. First, the microscopic examination of microsporidian spores is quite difficult and highly dependent on the expertise of the examiner). Furthermore, fluorescence-based methods like the Uvitex 2B method are known to increase sensitivity but could lead to false-positive results due to small fungi or some artifact material that may fluoresce. Hence, Uvitex 2B is suitable for screening but requires confirmation with a method like the molecular method."

TABLE 1. Results of microscopy, real-time PCR, and genotyping for the 270 stool specimens analyzed

Assay and species or genotype identified	No. of stool samples positive from ^a :	
	Niamey (n = 228)	Hanoi (n = 42)
UV-light microscopy	62	21
PCR	24	4
<i>E. bieneusi</i>	24	3
<i>E. intestinalis</i>	0	1

Nigeria. Adesiji YO, Lawal RO, Taiwo SS, Fayemiwo SA, Adeyeba O A. "CRYPTOSPORIDIOSIS IN HIV INFECTED PATIENTS WITH DIARRHOEA IN OSUN STATE SOUTHWESTERN NIGERIA" *European Journal of General Medicine* Vol. 4, No. 3, 2007, pp. 119-122.

- "Contrary to a previous report of apparent rarity of *Cryptosporidium* infections in certain parts of Nigeria, this study revealed a high prevalence of this parasitosis among HIV infected patients in Southwestern Nigeria."
- "The *Cryptosporidium* prevalence rate of 52.7% reported among these diarrhoea patients is similar to rates reported from other African countries indicating that cryptosporidiosis is an important opportunistic parasitic disease causing diarrhoea among HIV infected patients in Nigeria. This is especially so as this parasite was detected in stool samples of only HIV infected patients and this further highlights the association between immunodepression and cryptosporidiosis."

Table 3. Distribution of parasites isolated from stool of patients with diarrhoea in 3 health institutions in Southwestern Nigeria

Parasite types	HIV-infected (n:100)	HIV-negative (n:50)	Total (%) (n:150)
<i>Cryptosporidium</i>	79	0	79 (52.7)
<i>Ascaris</i>	9	8	17 (11.3)
Hookworm	2	3	5 (3.3)
<i>Trichuris</i>	1	2	3 (2)
<i>Entamoeba</i>	6	9	15 (10)
Total	97	22	119 (79.3)

Fisher Exact OR=41.152, 95%CI=11.467-147.68, P<0.0001

$\chi^2=0.8002$, df=3, P=0.8494 (Minus *Cryptosporidium* prevalence)

Nigeria. Alakpa GE, Clarke SC and Fagbenro-Beyioku AF. "*Cyclospora cayetanensis* infection in Lagos, Nigeria" *Clinical Microbiology and Infection* Volume 9 Issue 7, Pages 731 – 733.

- A total of 1,109 stool samples were submitted to the microbiology and parasitology Departments of 7 hospitals in Lagos, Nigeria between March 1999 and April 2000. All samples were screened for the presence of *Cyclospora* oocysts.
- 11 of 1,109 samples were positive for *Cyclospora*. 10/11 patients with Cyclosporiasis had diarrhea. 7 of the 11 Cyclosporiasis patients were HIV-positive.

Nigeria. Ibrahim K, Ikeh EL, Malu AO, Okeke EN, Damen JG: "Intestinal Parasitosis in Human Immunodeficiency Virus (HIV) Infected Adults with Chronic Diarrhoea At Jos University Teaching Hospital, Nigeria" *The Internet Journal of Parasitic Diseases*. 2007. Volume 2 Number 1.

Prevalence of Intestinal Parasites in HIV-Infected Adult Patients (n = 101) with Chronic Diarrhoea at Jos University Teaching Hospital, Nigeria.

Parasite	No. Isolated	Relative %
<i>Cryptosporidium parvum</i>	17	16.83
<i>Enterocytozoon bienersi/</i> <i>Encephalitozoon intestinalis</i>	09	8.91
<i>Cyclospora cayentanensis</i>	02	1.98
<i>Isoospora belli</i>	01	0.99
<i>Entamoeba histolytica</i>	10	9.90
<i>Giardia lamblia</i>	02	1.98
Hookworm	11	10.89
<i>Trichuris trichiura</i>	06	5.94
<i>Ascaris lumbricoides</i>	03	2.97
<i>Strongyloides stercoralis</i>	02	1.98
<i>Schistosoma mansoni</i>	04	3.96
<i>Dicrocoelium dendriticum</i>	05	4.95
Polyparasitism	14	13.86
<i>Candida species</i>	10	9.90

Nigeria. Keshinro IB, Musa BO. "Cellular immunity and diarrhoeal disease Keshinro amongst patients infected with the human immunodeficiency viruses 1 and 2 in Zaria, Nigeria" *Niger J Med.* 2003 Jan-Mar;12(1):22-6.

- The mean duration of diarrhea was 20.7 weeks.
- *Giardia lamblia* was the most common waterborne pathogen - 25% of the 40 patients.
- *Isospora belli* was isolated in 3 of the patients (7.5%) but in none of the controls.
- *Salmonella* spp. - 12.5%,
- *Entamoeba histolytica* - 7.5%,
- *Shigella* spp. - 5%.
- No pathogens were identified in seventeen cases (42.5%). No statistically significant difference was established in the stool microbiological findings of the cases and controls. No statistically significant relationship was established between stool microbiological findings and cellular immunity in the patients ($P > 0.05$).
- It was concluded that the organisms associated with diarrhea in the HIV-infected patients were similar to those found in HIV-seronegative patients with diarrhea, and that there is no correlation between the degree of immunodeficiency and the etiology of diarrhea. However it was unclear whether *Cryptosporidium* was analyzed for since no results were reported for it, which may have changed this conclusion.

Nigeria. Omalu I, Duhlinska D, Anyanwu G, Pam V, Omalu PI. "Seroprevalence of Microsporidiosis in Immunocompromised Patients in Kano-Nigeria" *The Internet Journal of Parasitic Diseases* 2007. Volume 1 Number 2.

- Stool samples were examined for microsporidial spores.
- 14/192 (7.29%) of HIV/AIDS patients had microsporidia, comprising *Enterocytozoon bieneusi* - 57% of positive samples, *Encephalitozoon intestinalis* - 36% of positive samples and mixed infection of both 1/14 (7.14%)
- 0 of 50 of HIV-negative patients were positive for Microsporidia.

Nigeria. Ogunsola FT, Arewa DG, Akinsete IE, Oduyebo OO, Akanmu AS, Odugbemi TO. "Aetiology Of Bacteraemia Among Adult Aids Patients Attending Lagos University Teaching Hospital (LUTH), Lagos, Nigeria" *Niger Postgrad Med J.* 2009 Sep;16(3):186-92.

- Blood samples from 67 consecutive patients with AIDS attending the Lagos University Teaching Hospital were cultured. Twenty-two (33%) of the 67 AIDS patients were culture positive. Non-typhoidal *Salmonella* spp (45.5%) were the most common aetiological agent of bacteraemia among AIDS patients.

Rwanda. Clerinx J, Bogaerts J, Taelman H, Habyarimana JB, Nyirabareja A, Ngendahayo P, Van de Perre P. "Chronic diarrhea among adults in Kigali, Rwanda: association with bacterial enteropathogens, rectocolonic inflammation, and human immunodeficiency virus infection" *Clin Infect Dis.* 1995 Nov;21(5):1282-4.

- 100 patients with chronic diarrhea were seen in the Department of Internal Medicine at the Centre Hospitalier de Kigali, Rwanda. HIV-1 antibodies were detected in 82 (94%) of 87 patients tested.
- Enteropathogenic bacteria were isolated from 39% of the patients.
- *Shigella* species (22 of 100 patients tested)
- Non-typhi *Salmonella* (11 of 100)
- *Aeromonas* species (5 of 60)
- *Campylobacter* species (4 of 60).
- "Chronic diarrhea, as seen in a hospital setting in a region highly endemic for HIV-1 infection, is strongly associated with HIV-1 infection, with rectocolonic inflammation, and with infection due to enteropathogenic bacteria".

Rwanda. Lepage L et al. "Bacteraemia as Predictor of HIV Infection in African Children" *Acta Paediatrica* Volume 78 Issue 5, Pages 763 – 766 Published Online: 21 Jan 2008

- Study to determine if bacteraemia is a marker of HIV infection among ambulatory and hospitalized Rwandese children. All children presenting at the Department of Paediatrics of the Centre Hospitalier de Kigali and who had their blood cultured during a two-month period were eligible for the study. 135 children were included in the study.
 - No association was found between bacteraemia and HIV seropositivity when all the children were considered. However, among patients less than 2 years old, bacteraemic subjects were more frequently ($p \leq 0.05$) patients who were HIV-positive than those HIV-negative.
 - Conclusion - "Our study shows that in young children in Central Africa, the presence of bacteraemia may be an important marker of HIV seropositivity."
-

Rwanda. Taelman H, Rugimbanya P, Kagame A, Suermond G, Horemans D, Mugabekazi J, Clerinx J; "Case-control etiological study of chronic diarrhea among HIV infected adults in Rwanda" *Int Conf AIDS*. 1998; 12:541-2 (abstract no. 32105).

- All adult HIV-infected patients with chronic diarrhea (CD) (defined as ≥ 2 loose stools/day for ≥ 21 days) admitted to the Centre Hospitalier de Kigali between 01-01-97 and 31-08-97 were included in the study except those who had taken antimicrobial drugs during the week preceding their admission. Patients were screened on 3 different stool samples for parasites (trophozoites, ova, cysts) and on 2 different stool samples for bacterial enteropathogens according to approved culture protocols.
- Controls were chosen among HIV-infected patients without CD seen during the study period and stratified according to the WHO stages of HIV infection established among the HIV-positive patients with CD.
- 54 patients presented with CD during the study period, of whom 50 (93%) were HIV-positive.

Prevalence of the infectious agents identified among the CD group and the control group and their statistical significance were the following:

- *Cryptosporidium* sp (24% vs 8%; $P = 0.035$),
- *Isospora belli* (18% vs 0; $P = 0.03$),
- *Giardia lamblia* (20% vs 12%; $P = 0.25$),
- *Entamoeba histolytica* (8% vs 0; $P = 0.12$),
- Helminths (10% vs 2%; $P = 0.44$), *Shigella* sp (15% vs 2%; $P = 0.03$),
- *Salmonella* sp (13% vs 2%; $p = 0.06$).
- *Campylobacter* sp (5% vs 0; $P = 0.5$).

CONCLUSIONS:

1. *Cryptosporidium* and *Isospora belli* were the predominant causes of CD;
2. Bacterial enteropathogens are significantly associated with CD and at a much higher prevalence than in other African countries.

Senegal. Dieng T, Ndir O, Diallo S, Coll-Seck AM, Dieng Y. "Prevalence of *Cryptosporidium* sp and *Isospora belli* in patients with acquired immunodeficiency syndrome (AIDS) in Dakar (Senegal)" *Dakar Med*. 1994;39(2):121-4.

- 72 patients with AIDS, having diarrhoea and admitted in the Unit of Infectious Diseases, Fann Hospital from 1989 to 1991 were investigated for *Cryptosporidium* sp. and *Isospora belli*.
- Results - *Isospora belli* (15.3%) and *Cryptosporidium* sp (13.9%)

Senegal. Gassama A, Sow PS, Fall F, Camara P, Guèye-N'diaye A, Seng R, Samb B, M'Boup S, Aïdara-Kane A. "Ordinary and opportunistic enteropathogens associated with diarrhea in Senegalese adults in relation to human immunodeficiency virus serostatus" *International Journal of Infectious Diseases* Volume 5, Issue 4, 2001, Pages 192-198.

In the immunocompromised individuals the more frequent pathogens were:

- Enteroaggregative *E. coli* (19.6%),
- Microsporidia (9.4%)
- *Cryptosporidium* (8.2%)
- Rotavirus (8.2%)
- *Shigella* (7.6%)
- *E. histolytica* (5.1%)
- *Isospora belli* (4.4%)

South Africa. Johnson S, Crewe-Brown H, Dini L, Freaun J, Perovic O, Vardas E, Hendson W. "Differences in Enteropathogens between HIV positive and negative children in Soweto, South Africa" *Int Conf AIDS*. 2000 Jul 9-14; 13: abstract no. MoPpB1090

- "Over 30% of all pediatric admissions in Soweto are due to HIV-related illnesses. Of these diarrhoea remains one of the most common and serious." Study included 181 children admitted to Chris Hani Baragwanath Hospital over a 14 month period. Of the 176 children with an HIV result, 17.6% were classified as HIV-positive.
- The most common pathogen was rotavirus, found in the stool of 36% of HIV-negative and 15% of HIV-positive children ($p = 0.06$).
- Pathogenic *E. coli* was found in the stool of 7% of both groups.
- *Cryptosporidium parvum* occurred in 17% of HIV-positive and 14% of HIV-negative children. HIV-positive children were more likely to have had prolonged diarrhea (16.1% vs 5.9%, $p = 0.07$).
- HIV-positive children were five times more likely to have a prolonged hospital stay (OR = 5.11).
- Conclusion: HIV-positive children with diarrhea have a similar spectrum of pathogens in their stool compared with HIV-negative children. Despite this, they have a worse outcome, and should be investigated and managed aggressively.

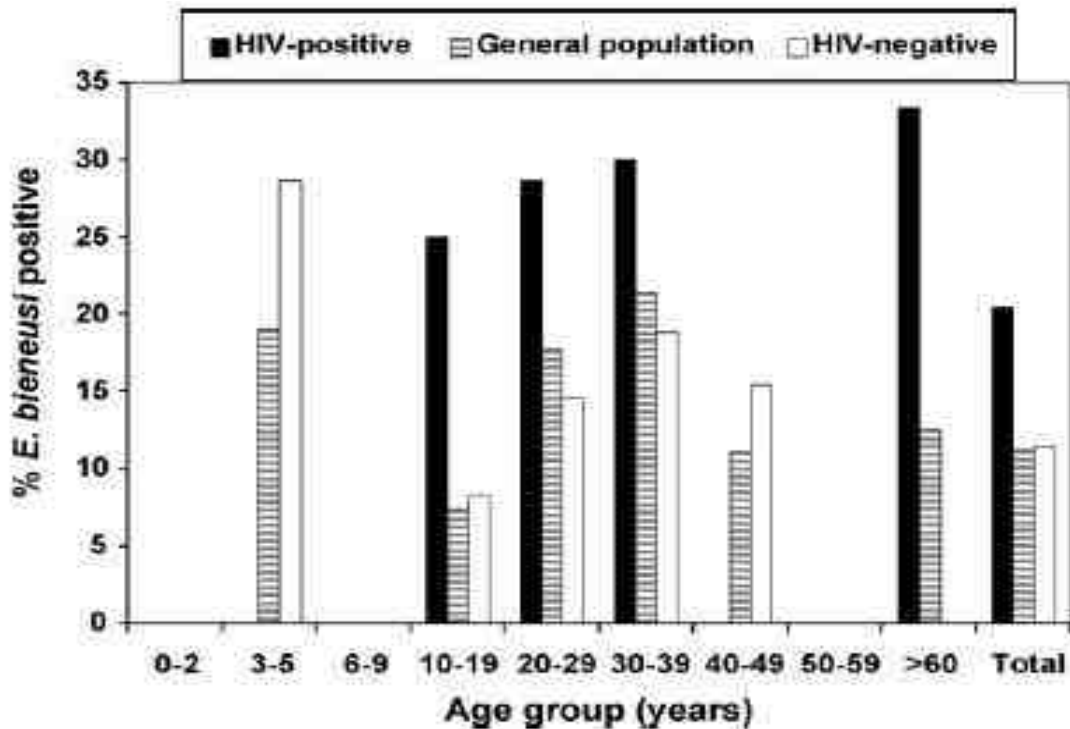
South Africa. Mtandu R, Kellerman R, Sooka A, Quan V, Meiring S, Govender N. "The impact of HIV on clinical-microbiologic features and mortality among patients with invasive nontyphoidal salmonella infection in South Africa". AIDS 2008 - XVII International AIDS Conference: Abstract no. WEPE0126

- Study goal – "To determine the impact of HIV on clinical-microbiologic features and mortality of invasive nontyphoidal *Salmonella* (NTS) infection among patients admitted in hospitals at 10 surveillance sites around South Africa, between 2003 and 2006."
- A total of 1 398 patients with NTS and known HIV-serostatus were analyzed.
- 82.26% of patients were HIV-positive.
- HIV-positive patients were 3.90 times more likely to have recurrence of invasive non-Typhoid *Salmonella* than HIV-negative patients.

South Africa. Samie A, Bessong PO, Obi CL, Sevilleja JE, Stroup S, Houpt E, Guerrant RL. "*Cryptosporidium* species: preliminary descriptions of the prevalence and genotype distribution among school children and hospital patients in the Venda region, Limpopo Province, South Africa" *Exp Parasitol.* 2006 Dec; 114(4):314-22. Epub 2006 Jun 27

- PCR was used for initial screening to detect positive samples.
 - From a total of 244 stool samples tested, 18% had *Cryptosporidium* with 28.6% of two to five year olds positive for *Cryptosporidium*.
 - *Cryptosporidium* was detected in 12.5% of the 31 HIV-positive individuals. *C. hominis* (82%) was more common than *C. parvum* (18%).
-

South Africa. Samie A, Obi C.L, Tzipori S, Weiss LM, Guerrant RL, “Microsporidiosis in South Africa: PCR detection in stool samples of HIV-positive and HIV-negative individuals and school children in Vhembe district, Limpopo Province” *Transactions of the Royal Society of Tropical Medicine and Hygiene* (2007) 101, 547—554.



- Study only analyzed for microsporidia.
- Microsporidia (*Enterocytozoon bienewsi*) was significantly associated ($P = 0.039$) with diarrhea in HIV-positive patients (21.6%) compared to HIV-negative individuals (9%).
- “In the HIV-positive group, *E. bienewsi* was found only in diarrheal samples indicating the possible involvement of these organisms in the production of diarrhea in immunocompromised hosts.”

Tanzania. Atzori C, Bruno A, Chichino G, Cevini C, Bernuzzi AM, Gatti S, Comolli G, Scaglia M. “HIV-1 and parasitic infections in rural Tanzania” *Ann Trop Med Parasitol.* 1993 Dec;87(6):585-93

- A sample of 300 adults was selected at random from patients, from the rural area of Malenga Makali, Tanzania, who were attending a dispensary because they had diarrhea of at least 2 weeks duration.
- Intestinal infections with *Cryptosporidium parvum* and *Isospora belli* were virtually restricted to HIV-positive individuals who had had diarrhea for a relatively long time.

Tanzania. Blomberg B, Mwakagile DS, Urassa WK, Maselle SY, Mashurano M, Digranes A, Harthug S, Langeland N. "Surveillance of antimicrobial resistance at a tertiary hospital in Tanzania" *BMC Public Health* 2004; 4: 45.

- "Bloodstream infection is a common cause of hospitalization, morbidity and death in children. Bloodstream infection and malaria are practically indistinguishable by clinical examination, and available WHO guidelines for managing childhood illnesses fail to identify up to half of the cases of bloodstream infections. A recent study from Kenya found that bloodstream infection caused one quarter of all deaths of children in the hospital, outnumbering malaria deaths. Bloodstream infection was less common than malaria, but caused more deaths. While malaria can be treated with highly effective, inexpensive and widely available quinine, treatment of bacterial and fungal bloodstream infection is compromised by antimicrobial resistance and unavailability of expensive second-line antibacterial and systemic antifungal drugs."
- Study assessed the incidence of bloodstream infection and risk factors for fatal outcome in 1,828 consecutive admissions of children aged zero to seven years with signs of systemic infection. Blood was obtained for culture, malaria microscopy, HIV antibody test and, when necessary, HIV PCR.
- The incidence of laboratory-confirmed bloodstream infection was 13.9% (255/1828) of admissions, despite two thirds of the study population having received antimicrobial therapy prior to blood culture.
- One third (34.9%) of the children with laboratory-confirmed bloodstream infection died. The mortality rate from non-Typhoid *Salmonella* bloodstream infection (36.4%) was almost double that of from malaria (20.2%).

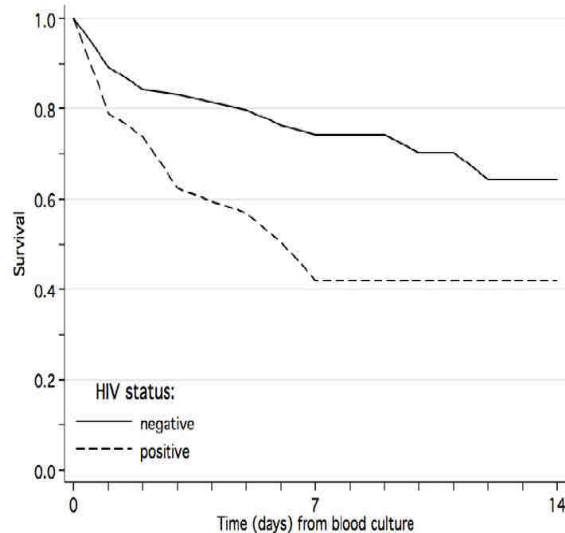


Figure 5
Impact of HIV co-infection on survival from laboratory-confirmed bloodstream infection.

Tanzania. CEGIELSKI J P, ORTEGA YR, MCKEE S, MADDEN J F. et al. "Cryptosporidium, enterocytozoon, cyclospora infections in pediatric and adult patients with diarrhea in Tanzania" *Clin Infect Dis.* 1999 Feb; 28(2):314.

- Study of 86 AIDS patients with chronic diarrhea.
- *Cryptosporidium* – 6/86
- Microsporidia – 3/86
- *Cyclospora* – 1/86.

Tanzania. Cegielski JP, Msengi AE, Miller SE. "Enteric viruses associated with HIV infection in Tanzanian children with chronic diarrhea" *Pediatr AIDS HIV Infect.* 1994 Oct; 5(5):296-9.

- Study's goal was to determine whether specific viruses are associated with HIV infection in Tanzanian children with chronic diarrhea using electron microscopy. Consecutively admitted HIV-positive and HIV-negative children with chronic diarrhea, and controls without diarrhea, aged 15 months to 5 year at major national teaching hospital in Dar es Salaam, Tanzania.
- Small round structured viruses (SRSV) were more frequent in HIV-positive than HIV-negative children with chronic diarrhea (4 of 21 vs. 1 of 32, prevalence ratio = 6.09).
- Rotavirus and coronavirus-like particles (CVLP) were not associated with HIV infection.
- "SRSV may be associated with HIV infection in Tanzanian children with chronic diarrhea. Larger, confirmatory studies are needed."

Tanzania. Gomez Morales MA, Atzori C, Ludovisi A, Rossi P, Scaglia M, Pozio E. "Opportunistic and non-opportunistic parasites in HIV-positive and negative patients with diarrhoea in Tanzania" *Trop Med Parasitol.* 1995 Jun; 46(2)

- *Cryptosporidium parvum*, *Isospora belli* and *Strongyloides stercoralis* prevalence was higher in HIV-positive than in HIV-negative patients ($P < 0.01$).
 - The prevalence of *Entamoeba histolytica* was higher in HIV-negative 25.1% than in HIV-positive patients 12.5%.
-

Tanzania. HOUP T ER, BUSHEN OY, SAM NE, KOHLI A, ASGHARPOUR A, NG CT, CALFEE DP, GUERRANT RL, MARO V, and OLE-NGUYAINE S, AND SHAO JF, "SHORT REPORT: ASYMPTOMATIC *CRYPTOSPORIDIUM HOMINIS* INFECTION AMONG HUMAN IMMUNODEFICIENCY VIRUS-INFECTED PATIENTS IN TANZANIA" *Am. J. Trop. Med. Hyg.*, 73(3), 2005, pp. 520–522.

Clinical features of the human immunodeficiency virus-infected study population (n = 127) Kilimanjaro, Tanzania

Feature	
Age, years (median, range)	35 (18–65)
Sex (M:F)	47:80
<i>Cryptosporidium</i> infection	22 (17%)
CD4 cell count (median/ μ L)	179
Symptoms of ≥ 3 liquid stools/day	61 (48%); median duration = 1 month

Comparison of *Cryptosporidium hominis* versus *C. parvum* infection*

	<i>C. hominis</i>	<i>C. parvum</i>
Total	15 (71%)	6 (29%)
Association with symptoms	6/61 (10%)	5/61 (8%)
Duration of symptoms (months)	4 [†]	0.3 [†]
Association with asymptomatic infection	9/66 [‡] (14%)	1/66 [‡] (2%)
CD4 cell count	55 [§]	256 [§]

- "The most important new findings in this study are the high rate of asymptomatic *C. hominis* infection in this population and the apparent preferential association of *C. hominis* infection with a low CD4 cell count. The 17% rate of asymptomatic *Cryptosporidium* carriage in this study is higher than the 1–5% asymptomatic rate previously reported in AIDS inpatients from many developing world sites. The high rate was not due to our use of a PCR-based assay (since 9 of 10 asymptomatic patients were also IF positive) and is surprising given the low CD4 cell count of this asymptomatic group (128/L), since other studies have suggested that chronic symptoms are the norm in this CD4 range. We believe there may be an under appreciation of asymptomatic *Cryptosporidium* infection, at least in this region of Africa..."
- *Cryptosporidium* infection was a marker for HIV infection, 22 of 127 HIV-positive patients were infected with *Cryptosporidium* versus 0 of 29 HIV-negative patients (P = 0.01).

Tanzania. Mmbaga BT, Kinabo GD, Swai M, Shao J, Mchele J, Henderikx M, Hout E, Tolboom J, Schimana W. "Prevalence of *Cryptosporidium* infection and related risk factors in children with or without diarrhoea in northern part of Tanzania" 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention Abstract no. TUPEB135

- Children aged 5 months to 13 years old attending Kilimanjaro Christian Medical Centre (KCMC) and Mawenzi regional hospital in Moshi, Kilimanjaro in Tanzania were enrolled from September 2005 – March 2006. Single stool specimen was collected from inpatient children with diarrhoea irrespective of their HIV status and from HIV-positive children whether they had diarrhea or not. If the HIV status was not known, HIV serology was performed using two rapid tests for antibody or polymerase chain reaction (PCR) for HIV-1 RNA was used for infants less than 18 months of age.
- The methods used for detection of *Cryptosporidium* were modified acid-fast stain (mAFS), ELISA and PCR.
- A total of 300 specimens were collected from 300 children, including 180 children who presented with diarrhea and 120 HIV-positive children (with or without diarrhea). Out of 300 specimens, 217 were from children with diarrhea: 192 had acute diarrhoea (27 HIV-positive) and 25 had chronic diarrhea (10 HIV-positive).
- Overall, out of 300 stool samples, *Cryptosporidium* was detected in 40 (13.3%).
- Acute diarrhea - 13% of samples collected from children with acute diarrhea were positive for *Cryptosporidium*.
- Persistent diarrhea - 32.0% of children with persistent diarrhea had *Cryptosporidium* (50% of children with persistent diarrhea and *Cryptosporidium* were HIV-positive). *Cryptosporidium* infection was statistically significantly present in children with persistent diarrhea ($p=0.013$).
- 7.2% of specimens collected from HIV-positive children without diarrhea showed *Cryptosporidium*.
- Watery diarrhoea and drinking unboiled water were statistically significantly associated with *Cryptosporidium* infection ($p=0.0001$ and $p=0.0001$ respectively).
- HIV infection, severe dehydration and malnutrition were predictors of death ($P=0.001$ each).
- Other intestinal pathogens identified included *Giardia* 5% and *Strongyloides* 0.3%.

Conclusions: *Cryptosporidium* infection was common in both HIV-positive and HIV-negative children. *Cryptosporidium* leads to persistent diarrhea in HIV infected children.

Tanzania. TARIMO DS, KILLEWO JZJ, MINJAS JN, MSAMANGA GI. "Prevalence of intestinal parasites in adult patients with enteropathic AIDS in North-Eastern Tanzania" *East African medical journal* 1996, vol. 73, n°6, pp. 397-399.

- A total of 352 patients were recruited of whom 45% had chronic diarrhea
- 62.6% of the patients with intestinal parasites had chronic diarrhea.
- The types of parasites detected were *Cryptosporidium*, *Isospora belli*, *Strongyloides stercoralis*, *Schistosoma mansoni*, *Trichuris trichiura*, *Ascaris lumbricoides*, hookworm and *Entamoeba histolytica*.
- The prevalence of intestinal parasites was significantly higher in patients with chronic diarrhea than in those without ($P < 0.05$).
- "*Cryptosporidium* and *Isospora belli* were only detected in patients with chronic diarrhoea and were thus the most likely cause of the diarrhoea."

Uganda. Brink AK, Mahé C, Watera C, Lugada E, Gilks C, Whitworth J, French N. "Diarrhea, CD4 counts and enteric infections in a community-based cohort of HIV-infected adults in Uganda." *J Infect.* 2002 Aug; 45(2):99-106.

- *Cryptosporidium parvum* infection alone was associated with low CD4 counts.
- Diarrhea was common and most strongly associated with low CD4 counts.
- Bacteria were frequently found, even in stools from asymptomatic individuals.

Uganda. Lindström I, Kaddu-Mulindwa DH, Kironde F, Lindh J. "Prevalence of latent and reactivated *Toxoplasma gondii* parasites in HIV-patients from Uganda" *Acta Trop.* 2006 Dec; 100(3):218-22. Epub 2006 Dec 8.

- "Untreated *Toxoplasma gondii*-infections are often fatal in AIDS-patients. Many African countries struck hard by HIV/AIDS exhibit a high seroprevalence of *T. gondii*, but the rate of reactivated parasites among African HIV-patients has never previously been determined."
 - IgG and PCR was used to analyze blood samples from 130 HIV-positive patients in Uganda. Anti-T. *Gondii* antibodies were detected in 54% of the patients while 23% had parasites in the blood, which indicates active infection.
 - "This study emphasizes the high prevalence of toxoplasmosis among Ugandan HIV patients...."
-

Uganda. Lule JR, Mermin J, Malamba S, Ransom R, Hughes P, Downing R, Kizito F, Wafula W, Nakanjako D, Kigozi A, Quick R; "Pathogens associated with diarrhea among persons with and without HIV in rural Uganda" *Int Conf AIDS*. 2002 Jul 7-12; 14: abstract no. ThPeC7468.

- Persons with HIV and their household members were enrolled in a household-based, water quality improvement project. On weekly home visits data on diarrhea, defined as >3 loose or watery stools in the past 24 hours, and stool specimens from participants with diarrhea were collected. Stool samples were examined for pathogenic bacteria by culture and parasites by light microscopy.
 - **RESULTS:** 452 participants (53% HIV-positive). Recovery rates of *Shigella* were higher in HIV-positive - 0.18/per year observation (PYO) compared to 0.05/PYO in HIV-negative participants (RR=3.9), *Aeromonas*, 0.12/PYO in HIV-positive compared to 0.05/PYO in HIV-negative (RR=2.7). No difference was observed for *Campylobacter* and *Salmonella*.
 - The rates of *Cryptosporidium* were 0.18/PYO in HIV-positive compared to 0.06/PYO in HIV-negative (RR=3.0, 95% CI=1.3-7.6), and the rates for *Strongyloides Stercoralis* were 0.45/PYO in HIV-positive compared to 0.21/PYO in HIV-negative (RR=2.1).
 - **Conclusion:** "In this study of persons with diarrhea, those with HIV infection had higher recovery rates of bacterial and parasitic pathogens and higher rates of *Shigella*, *Aeromonas*, *Cryptosporidium* and *Strongyloides* than persons without HIV." Concluded that these organisms should be considered when managing people with HIV who present with diarrhea.
-

Uganda. Musiime V, Kalyesubula I, Kaddu-Mulindwa D, Byarugaba J. "Enteric Bacterial Pathogens in HIV-Infected Children With Acute Diarrhea in Mulago Referral and Teaching Hospital, Kampala, Uganda" *Journal of the International Association of Physicians in AIDS Care* (2009) Vol. 8, No. 3, 185-190.

Table 1. Enteric Bacterial Pathogens in Children at Mulago, Kampala Uganda With Acute Diarrhea by HIV Status

Pathogens	HIV-Infected Children, N = 9 (%)	HIV-Negative Children, N = 38 (%)	OR (95% CI)	P Value
EPEC	4 (44.4)	13 (34.2)	1.30 (0.28-5.87)	.473
ETEC	0 (0)	9 (23.7)	0.00 (0.00-3.06)	.179
EIEC	0 (0)	1 (2.63)	0.00 (0.00-83.0)	.812
EHEC	2 (22.2)	1 (2.63)	8.44 (0.51-265)	.117
<i>Salmonella</i> spp	2 (22.2)	9 (23.7)	0.94 (0.12-6.09)	.655
<i>Shigella</i> spp	1 (11.1)	5 (13.2)	0.84 (invalid)	.684
Total	9	38		

Abbreviations: CI, confidence interval; EHEC, enterohemorrhagic *Escherichia coli*; EIEC, enteroinvasive *E coli*; EPEC, enteropathogenic *E coli*; ETEC, enterotoxigenic *E coli*; OR, odds ratio; spp, subspecies.

- The overall prevalence of enteric bacterial pathogens in HIV-positive children was 19% (9 of 47) and prevalence in the HIV-negative children was 27% (38 of 143).
- The study found that severely malnourished children more likely to be HIV-positive than the well nourished children, 36.8% and 12.6% respectively (P <.001).
- The study revealed high rates of resistance to cotrimoxazole, a drug recommended in many countries as the first-line drug for treatment of acute diarrhea where antibiotics are required. This drug is also widely used for prophylaxis of infections in HIV-positive children.

Uganda. Nsubuga BM, Todd J, Van der Paal L, Mugisha J, Atuhumuza E, Tabuga P, Hughes P, Maher D, Grosskurth H. "Septicaemia in a population-based HIV clinical cohort in rural Uganda, 1996 - 2007: incidence, aetiology, antimicrobial drug resistance and impact of antiretroviral therapy" AIDS 2008 - XVII International AIDS Conference: Abstract no. WEPE0126

- "Septicaemia commonly causes morbidity and mortality in HIV-infected persons. Methods: Between April 1996 and December 2007, members of a prospective clinical cohort in rural southwest Uganda with fever above 38°C but without malaria parasites had blood taken for culture and antimicrobial drug resistance testing. We calculated septicaemia incidence in HIV-uninfected, and HIV-infected patients on ART, and not on ART, and examined antimicrobial resistance patterns." 759 participants were included.
- The commonest isolates were *Streptococcus pneumoniae* (SPN, n=68) and Non typhoid *Salmonella* (NTS, n=42).
- "All the NTS isolates were susceptible to ciprofloxacin, while 75% were resistant to cotrimoxazole and 67% resistant to chloramphenicol."
- Conclusions: "Septicaemia incidence was higher in HIV-infected than HIV-uninfected participants, remained high after HIV-infected patients started ART, and only declined after the first year on ART, consistent with slow immune recovery. Determining the long-term impact of ART on HIV-related septicaemia requires longer follow-up."

Uganda. SARFATI C, BOURGEOIS A, MENOTTI J, LIEGEOIS F et al. "PREVALENCE OF INTESTINAL PARASITES INCLUDING MICROSPORIDIA IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTED ADULTS IN CAMEROON: A CROSS-SECTIONAL STUDY" *Am. J. Trop. Med. Hyg.*, 74(1), 2006, pp. 162–164.

- "The results of our study should therefore prompt physicians caring for HIV-infected patients in Cameroon to request stool examination and specific tests for microsporidia, *Cryptosporidium*, and *Isospora belli*, especially in patients with low CD4 cell counts."

Opportunistic protozoa (OP) identified in 154 human immunodeficiency virus-infected adults in Yaounde, Cameroon

	No. of patients (%) [*]	No. of patients (%) without diarrhea	No. of patients (%) with diarrhea
Total	154	108 (70)	46/154 (30)
Patients with OP	15 (9.7)	7/108 (6.4)	8/46 (17.3)
<i>Cryptosporidia</i>	6 (3.8)	3/108 (2.8)	3/46 (6.5)
<i>Microsporidia</i>	8 (5.2)	5/108 (4.6)	3/46 (6.5)
<i>Isospora belli</i>	3 (2)	0/108 (0)	3/46 (6.5)

* One patient can have more than one pathogen.

Uganda. Tumwine JK, Kekitiinwa A, Bakeera-Kitaka S, Ndeezi G, Downing R, Feng X, Akiyoshi DE, Tzipori S. "Cryptosporidiosis and Microsporidiosis in Ugandan Children with Persistent Diarrhea with and Without Concurrent Infection with the Human Immunodeficiency Virus" *Am. J. Trop. Med. Hyg.* 73(5) 2005pp. 921-925.

- Microsporidia: for HIV-positive children – 77%, for HIV-negative children – 7%
- *Cryptosporidium*: HIV-positive children - 74%, HIV-negative children - 6%

Zambia. Amadi B, Kelly P, Mwiya M, Mulwazi E, Sianongo S, Changwe F, Thomson M, Hachungula J, Watuka A, Walker-Smith J, Chintu C. "Intestinal and systemic infection, HIV, and mortality in Zambian children with persistent diarrhea and malnutrition" *J Pediatr Gastroenterol Nutr.* 2001 May; 32(5):550-4.

- Study included 200 children (6-24 months old) from the malnutrition ward of University Teaching Hospital in Lusaka, Zambia.
- *Cryptosporidium parvum* (26%) and non-typhoid *Salmonella* spp (18%) were NOT significantly more common in HIV-positive than in HIV-negative children.
- Of the 200 children, 39 (19.5%) died within 28 days; cryptosporidiosis and marasmus were the only independent predictors of death.

Zambia. Chintu C, Zumla A, Luo N, Mathewson J, Perera C, Ngwenya B; "Acute and chronic diarrhea (AD, CD) in HIV-1 infected patients, Lusaka, Zambia and Houston, Texas, 1992" *Int Conf AIDS.* 1993 Jun 6-11; 9(1):64 (abstract no. WS-B21-4).

- Of 56 pediatric patients studied in Zambia, 30 had acute diarrhea (AD) and 26 had chronic diarrhea (CD). Eight patients with AD (27%) and 10 with CD (38%) were HIV-positive. Of 77 adult patients studied 31 had AD and 46 CD. 20 patients with AD (65%) and 44 with CD (96%) were HIV-positive.
- The enteric pathogens most commonly identified in the HIV-positive patients were: *Shigella*; *Salmonella*; *Isospora*; *Cryptosporidium* and *Giardia*.

Zambia. Chintu C, Luo C, Baboo S, Khumalo-Ngwenya B, Mathewson J, DuPont HL, Zumla A. "Intestinal Parasites in HIV-seropositive Zambian Children with Diarrhoea" *Journal of Tropical Pediatrics* 1995 41(3):149-152.

- The commonest parasites identified were *Ascaris* and *Cryptosporidium*.
 - *Cryptosporidium* spp. was isolated from 14 per cent of HIV-positive children, while 6 per cent of HIV-negative children had the parasite (p=0.01).
-

Zambia. Conlon CP, Pinching AJ, Perera CU, Moody A, Luo NP, Lucas SB. "HIV-related enteropathy in Zambia: a clinical, microbiological, and histological study" *Am J Trop Med Hyg.* 1990 Jan; 42(1):83-8.

For HIV-positive patients with a history of chronic diarrhea, most common pathogens:

- *Cryptosporidium* (32%)
- *Isospora belli* (16%)

Zambia. Kelly P, Davies SE, Mandanda B, Veitch A, McPhail G, Zulu I, Drobniowski F, Fuchs D, Summerbell C, Luo NP, Pobe JO and Farthing MJG, "Enteropathy in Zambians with HIV related diarrhoea: regression modelling of potential determinants of mucosal damage" *Gut* 1997;41;811-816.

TABLE 3 *Intestinal infection in 56 patients with HIV related diarrhoea in Lusaka*

<i>Pathogen</i>	<i>Number (%)</i>
Microsporidia ^a	20 (34)
<i>Isospora belli</i>	14 (24)
<i>Cryptosporidium parvum</i>	12 (21)
<i>Blastocystis hominis</i> ^b	6 (10)
<i>Strongyloides stercoralis</i>	3 (5)
<i>Giardia intestinalis</i>	1 (1)
<i>Mycobacterium tuberculosis</i>	4 (7)
<i>M avium</i> complex	2 (3)
Negative	12 (21)

^a Species identified by electron microscopy in seven of these: five *Enterocytozoon bieneusi*, two *Septata intestinalis*.

^b The status of *B hominis* as a pathogen is controversial.

- "HIV infection is commonly accompanied by persistent diarrhoea and severe weight loss; this syndrome has been referred to as "slim disease" in sub-Saharan Africa. The aetiology of diarrhoea has not been clearly defined, but the protozoal enteropathogens found in African patients infected with HIV almost certainly play a part."

- “As protozoa were found in the majority (79%) of the patients in this study, who had quite advanced HIV disease; it is distinctly possible that multiple infections were more common than was apparent given the insensitivity of most microscopic detection techniques.”
- “*Cryptosporidium parvum* is known to damage the mucosa in immunocompetent children and it would be surprising if it had no such effect in the immunodeficient.”
- “Stool cultures for *salmonellae*, *shigellae*, and *Campylobacter* spp. were not undertaken, nor were virological examinations of stool. However, no viral particles were seen by electron microscopic examination of the biopsy specimens, and other studies have indicated that viral infections do not play a major role in this syndrome.”

Zambia. Kelly P, Todd J, Sianongo S, Mwansa J, Sinsungwe H, Katubulushi M, Farthing M and Feldman R. “Susceptibility to intestinal infection and diarrhoea in Zambian adults in relation to HIV status and CD4 count” *BMC Gastroenterol.* 2009;9:7.

Frequency of intestinal infection for select pathogens in relation to recalled diarrhea

Organism	Frequency (%) in months when <u>diarrhea reported</u> n=408	Frequency(%) in months when <u>diarrhoea not reported</u> n= 3790
<i>Cryptosporidium parvum</i>	2.7	1.0
<i>Isospora belli</i>	1.7	0.3
Microsporidia	0.7	0.1
<i>Giardia intestinalis</i>	1.7	1.2
<i>Blastocystis hominis</i>	7.6	6.6
<i>Entamoeba histolytica</i>	0	0.3
<i>Ascaris lumbricoides</i>	16.7	15.4
Hookworm	3.4	2.9
<i>Strongyloides stercoralis</i>	0.3	0.3
<i>Schistosoma mansoni</i>	0.5	0.4
<i>Trichuris trichiura</i>	0	0.2
<i>Salmonella</i> spp.	1.3	1.3
<i>Shigella</i> spp.	0.5	0.3
<i>Vibrio cholerae</i>	0.5	0.1

- *Cryptosporidium*, *Isospora* and Microsporidia significantly higher in HIV/AIDS patients with diarrhea than without, a likely cause(s) of diarrhea in this study

Organism	HIV		P	HIV positive	
	HIV+ n = 1313	HIV- n = 2981		CD4 < 200 cells/ μ l	CD4 > 200 cells/ μ l
<i>Cryptosporidium parvum</i>	2.7	0.6	< 0.001	25	6
<i>I. belli</i>	1.0	0.2	0.002	8	1
<i>A. lumbricoides</i>	13.1	17.4	< 0.001	48	72
<i>S. stercoralis</i>	0	0.5	0.008	-	-

Zambia. Kaonga K, Kangende B "Prevalence and consequences of *Cryptosporidium* oocysts in drinking water" *Int Conf AIDS*. 1998; 12: 540 (abstract no. 31226).

- 72% (23 of 32) of HIV-positive adults with and *Cryptosporidium* had chronic diarrhea of more than 1 month.
- In all the HIV-negative 20 children, 60% (12 of 20) below the age of 2 years had mild diarrhea for not more than 8 days, while those above 2 years were asymptomatic.
- Study appeared to demonstrate the impact of *Cryptosporidium* on chronic diarrhea for people living with HIV/AIDS.

Zambia. Khumalo-Ngwenya et al. "Gut parasites in HIV-seropositive Zambian adults with diarrhoea" *East Afr Med J*. 1994 Jun; 71(6):379-83.

- *Cryptosporidium* was detected in 4.7% HIV-positive adults in one clinic and in 4% in another clinic. *Isospora* were detected in 6% of HIV-positive patients in once clinic and 9% in the other clinic.
- *Isospora belli* and *Cryptosporidium* spp were seen only in the HIV-positive group.
- Study found a statistically significant difference between parasite detection rate of *Isospora* and *Cryptosporidium* in HIV-positive patients with chronic diarrhea compared to asymptomatic HIV-positive individuals.

Zambia. Nchito et al. "Cryptosporidiosis in Urban Zambian Children: An Analysis of Risk factors" *Am. J. Trop. Med. Hyg.* 59(3) pp. 435-437.

- *Cryptosporidium* infection rate in children was 18%, breastfeeding was not associated with reduced *Cryptosporidium* risk.

Zambia. Zulu I, Kelly P, Mwansa J, Veitch A, Farthing M. "Contrasting Incidence of *Clostridium Difficile* and other enteropathogens in AIDS patients in London and Lusaka" *Transactions of the Royal Society of Tropical Medicine and Hygiene* (2000) 94,167-168.

Table. Prevalence of enteropathogens in AIDS-related diarrhoea in London and Lusaka

Organism	London (n = 126)	Lusaka (n = 68)	P
<i>Clostridium difficile</i>	14 (11%)	0	0.003
<i>Giardia intestinalis</i>	4 (3%)	0	NS
<i>Salmonella</i> spp.	0	3 (4%)	NS
<i>Shigella</i> spp.	0	5 (7%)	NS
<i>Cryptosporidium parvum</i>	8 (6%)	4 (6%)	NS
Microsporidia	8 (6%)	11 (16%)	0.05
<i>Isospora belli</i>	0	25 (37%)	<0.001

P calculated by Fisher's exact test; NS, not significant (i.e., $P > 0.05$).

Zimbabwe. GUMBO T, SARBAH S, GANGAIDZO IT, ORTEGA Y, STERLING CR, CARVILLE A, TZIPORI S, WIEST PM. "Intestinal parasites in patients with diarrhea and human immunodeficiency virus infection in Zimbabwe" *AIDS: Volume 13(7)* 7 May 1999 pp 819-821.

- Microsporidia (*E. bienersi*) was identified in 18% of samples but when samples were examined using PCR 51% of stools were positive for *E. bienersi*.
- *Cryptosporidium parvum* - 9%
- *Isospora belli* and *Giardia lamblia* were each detected in 2%
- *Ascaris lumbricoides* and *Schistosoma mansoni* were each found in 1% of specimens examined.
- *Cyclospora* was not detected in 82 samples examined.

Zimbabwe. Gwavava C, Chihota VN, Gangaidzo IT, Gumbo T. "Dysentery in patients infected with human immunodeficiency virus in Zimbabwe: an emerging role for *Schistosoma mansoni* and *Escherichia coli* O157?" *Ann Trop Med Parasitol.* 2001 Jul; 95(5):509-13.

Study compared the pathogens associated with bloody diarrhoea.

- *Shigella* 45% *Shigella dysenteriae* type-1 occurred more often in the HIV-negative individuals than HIV-positive individuals (P = 0.02).
- *Schistosoma mansoni* - 16%
- *Escherichia coli* H7:O157 - 8%
- *Campylobacter jejunii* - 5%
- There was no evidence of *Salmonella* or *Entamoeba histolytica* infection.

Zimbabwe. Pithie AD, Malin AS, Robertson VJ. "*Salmonella* and *shigella* bacteraemia in Zimbabwe" *Cent Afr J Med.* 1993 Jun;39(6):110-2.

- Study included review of cases of patients with enterobacteriaceae bacteraemia admitted to Parirenyatwa Hospital, Harare.
- "In patients with HIV infection, non-typhoidal salmonellae are a recognized cause of bacteraemia. "
- Non-typhoidal *Salmonella* bacteraemia as compared with typhoid fever was significantly more common in HIV-positive patients than in HIV-negative patients ($p < 0.01$).
- "3 out of 11 patients (27%) with typhoid died, while 11 out of 27 patients (40.7%) with nontyphi bacteremia died."

Zimbabwe. van Gool T, Luderhoff E, Nathoo KJ, Kiire CF, Dankert J, Mason PR. "High prevalence of *Enterocytozoon bieneusi* infections among HIV-positive individuals with persistent diarrhoea in Harare, Zimbabwe" *Trans R Soc Trop Med Hyg.* 1995 Sep-Oct; 89(5):478-80.

- Microsporidia (*E. bieneusi*) were identified in specimens 10% of patients (for whom HIV infection was indicated by serology and/or clinical signs) and 0% of HIV-negative patients.
 - Microsporidia were not detected in samples from any child.
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