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## Prevalence of Acute Enteric Viral Pathogens in Acquired Immunodeficiency Syndrome Patients With Diarrhea

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**Diarrhea due to enteric pathogens is an important complication of advanced human immunodeficiency virus infection. Whereas numerous bacterial and parasitic agents have been implicated, the role of pathogenic enteric viruses is less clear. Stools from 153 human immunodeficiency virus seropositive men were tested by electrophoresis, enzyme-linked immunosorbent assay, and immune electron microscopy for the presence of rotaviruses (group A and non-group A), adenoviruses, and Norwalk agent. Virus was detected in 9% of the patients with acquired immunodeficiency syndrome, 3% of the patients with acquired immunodeficiency syndrome-related complex, and none of the seropositive men without these diagnoses. Virus detection was not more likely in stool from patients with diarrhea.**

The immunosuppressive sequelae of human immunodeficiency virus (HIV) infection include opportunistic infections and cancer (1). Persistent diarrhea and wasting are important and relatively common gastrointestinal illnesses in patients with acquired immunodeficiency syndrome (AIDS) and AIDS-related complex (ARC) (2). A variety of bacterial and parasitic pathogens have been linked to diarrheal illness in patients infected with HIV. These pathogens include agents frequently responsible for diarrhea in HIV-seronegative homosexuals such as *Shigella*, *Salmonella*, *Campylobacter*, *Giardia lamblia*, *Entamoeba histolytica*, and others that are perhaps more common in AIDS, such as *Cryptosporidium*, *Isospora belli*, *Mycobacterium avium-intracellulare*, and cytomegalovirus (3,4). Despite extensive investigation, however, an enteric pathogen

cannot be identified in some HIV-infected patients with diarrhea (5,6). Human immunodeficiency virus infection itself has been suggested as important in these cases (7).

During the past two decades a variety of viral agents, including group A and non-group A rotaviruses, enteric adenoviruses, Norwalk and Snow Mountain agents, astroviruses, caliciviruses, and enteric coronaviruses have been implicated in both endemic and epidemic acute diarrheal disease (8,9). To determine whether enteric viral infections contribute to diarrhea in HIV-infected patients, we tested stool samples from AIDS and ARC patients for the presence of virus particles, virus antigens, and viral nucleic acids.

Specimens were obtained from a large study of enteric infections in gay men in Baltimore and from AIDS and ARC patients not part of investigational protocols in New York City (6). Stool samples from 102 AIDS patients (77 with diarrhea at the time of collection), 38 ARC patients (19 with diarrhea at the time of collection), and 13 HIV-seropositive gay men with diarrhea but without a diagnosis of AIDS or ARC were received frozen on dry ice and stored at  $-70^{\circ}\text{C}$  until used. After thawing, a 10% suspension of feces in phosphate-buffered saline with 0.1% sodium azide was made. The samples were tested by (a) polyacrylamide gel electrophoresis followed by

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*Abbreviations used in this paper:* AIDS, acquired immunodeficiency syndrome; ARC, AIDS-related complex; HIV, human immunodeficiency virus.

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Table 1. Prevalence of Viral Pathogens

Diagnosis	AIDS		ARC		HIV + serology
	+	-	+	-	+
Diarrhea Patient (n)	77	25	19	19	13
Small round viruses	3	0	0	0	0
Conventional adenovirus	4	2	1	0	0
Enteric adeno/rotavirus (A and non A)	0	0	0	0	0
Total virus	7	2	1	0	0

AIDS, acquired immunodeficiency syndrome; ARC, AIDS-related complex; HIV, human immunodeficiency virus.

silver staining using rotavirus ribonucleic acid and adenovirus deoxyribonucleic acid controls (10); (b) enzyme-linked immunosorbent assay for adenovirus, enteric adenovirus, and rotavirus (11,12); and (c) immune electron microscopy following incubation of the sample with pooled human  $\gamma$ -globulin and anti-Norwalk serum (13).

We found evidence of enteric virus excretion in 9% (9 of 102) of the stools from patients with AIDS, 3% (1 of 38) of those with ARC, and none from the HIV-seropositive gay men (0 of 13) (Table 1). Small round particles were seen by immune electron microscopy in three samples and adenovirus was detected by enzyme-linked immunosorbent assay in six samples from the AIDS group and in the single positive ARC patient. The adenoviruses detected did not belong to groups 40 or 41, which have previously been associated with human diarrheal disease (14). Virus detection did not correlate with the presence or absence of diarrhea at the time of sample collection.

Although virus detection was more likely to occur in the AIDS group (9% vs. 3%,  $\chi^2 = 4.40$ ,  $p < 0.05$ ), the agents we sought do not appear to be important causes of diarrhea in the HIV-infected patients studied. Rather, our results suggest that the increasingly severe immunocompromise implied by progression of an HIV-infected person to ARC and then AIDS can include clinically silent enteric viral opportunists as well as the clinically apparent bacterial, parasitic, and viral infections. As these viral enteric pathogens were not found frequently in our AIDS or ARC patients with diarrhea, possible alternative etiologies for such cases include the other known enteric viruses, HIV infection itself, or currently unknown pathogens.

Although AIDS patients are clearly at increased risk for symptomatic infection with a number of enteric pathogens, we did not find that this increased susceptibility extends to rotaviruses, adenoviruses, or Norwalk agent. Cunningham et al. (15) have recently found an increased likelihood of rotavirus and adenovirus isolation from AIDS and ARC patients compared with asymptomatic HIV-seroposi-

tive men in Australia. Whereas we both noted that rates of virus detection for symptomatic HIV-infected men with or without diarrhea were similar, Cunningham et al. found a much higher frequency of virus infection in AIDS and ARC patients (50%–54%) and in asymptomatic HIV-seropositive men (16%). Neither we nor Smith et al. (5) found rotavirus in any AIDS patients. The basis of this apparent geographic variation in the enteric viral infections of AIDS patients is unclear and merits further investigation.

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