Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

GASTROINTESTINAL DISEASES IN AIDS 1052–5157/98 $8.00 + .00

DIAGNOSIS AND TREATMENT OF COLONIC DISEASE IN AIDS

Klaus E. Mönkemüller, MD, and C. Mel Wilcox, MD

Diseases of the gastrointestinal tract are among the most frequent complications of AIDS. In general, most opportunistic disorders are not seen until the CD4 lymphocyte count falls below 200 cells/μL. Infections are the most common cause of colonic disease, including both nonopportunistic (bacteria, protozoa) and opportunistic (viruses, mycobacteria, protozoa) causes. Abdominal pain, diarrhea, fever, bleeding, or peritonitis due to perforation may be the initial manifestations of colonic disease. Although the colon may be the only site of involvement of several infections, in general, these infectious disorders involve the colon as part of a generalized systemic process. Depending on the presentation, evaluation generally uncovers one or more enteric pathogens; however, in some HIV-infected patients with colonic symptomatology, no infectious agent can be identified. The authors discuss the three major clinical presentations of colonic disease in HIV-infected patients ([1] abdominal pain, [2] diarrhea, and [3] lower gastrointestinal bleeding [LGIB]), and review selected diagnostic and treatment issues of the most important etiologic agents.

ABDOMINAL PAIN

Abdominal pain is a common complaint among HIV-infected patients and frequently may be colonic in origin.[103] In most cases, a carefully performed history and physical examination in conjunction with the CD4 lymphocyte count narrows the differential diagnosis. The most common causes of abdominal pain in HIV-infected patients are listed as follows:

From the Division of Gastroenterology and Hepatology, University of Alabama, Birmingham, Alabama

Colonic
Colitis (infectious, neoplastic, idiopathic, drug-induced)
Neoplasm (non-Hodgkin's lymphoma, Kaposi's sarcoma [KS])
Inflammatory bowel disease (idiopathic, secondary to KS)
Toxic megacolon (cytomegalovirus [CMV] *Clostridium difficile, Cryptosporidium,* KS)
Colonic perforation (CMV, histoplasmosis, idiopathic, diverticula, neoplasm)
Diverticulitis
Irritable bowel syndrome
Noncolonic
Cholecystitis
infectious (CMV, *Isospora belli, Candida, Cryptosporidium,* Microsporidia)
gallstones
AIDS-cholangiopathy
Peptic ulcer disease
Pancreatitis
Pyelonephritis
Peritonitis
Ileal perforation
Gastroenteritis
Adrenal failure–adrenalitis
Nonulcer dyspepsisa
Gastroesophageal reflux disease
In female patients consider also
Pelvic inflammatory disease
Cervical cancer
Ectopic pregnancy

When evaluating abdominal pain in these patients, the main objective is first to rule out life-threatening complications such as viscous perforation,[51,91,101] appendicitis, intestinal obstruction,[107] and toxic megacolon.[39,65,66]

Abdominal radiographs are useful for the detection of free subdiaphragmatic air in the presence of viscus perforation, air-fluid levels in the presence of obstruction, and "thumbprinting" due to toxic megacolon or colitis. CT of the abdomen and pelvis should be performed in the ill-appearing patient with unexplained severe abdominal pain where it may demonstrate appendicitis, gangrenous cholecystitis, pancreatitis, and intra-abdominal abscess or lymphadenopathy. With severe colitis, CT often demonstrates focal or diffuse colonic wall thickening associated with pericolic and mesenteric inflammation.[5,37,102]

Therapy of abdominal pain should be directed to the underlying identified process(es). In most cases, the therapy is medical, but when indicated, an aggressive surgical approach is warranted because the surgical morbidity and mortality are acceptable in these patients.

LGIB

Clinically significant colonic bleeding is uncommon in HIV-infected patients.[68] It is important to recognize that diseases common in the nonim-

munocompromised host similarly occur in these patients including hemorrhoids, diverticulosis, and arteriovenous malformations.[113] Although a number of infectious agents have been reported to cause severe colitis and hemorrhage, the most common cause of LGIB in patients with AIDS is cytomegalovirus (CMV) colitis.[10, 39, 65, 101, 113] Other reported infectious causes of LGIB in these patients include histoplasmosis[7] *Mycobacterium avium* complex (MAC),[17, 62] *Isospora belli*,[3] *Bartonella henselae*,[54] and *Mycobacterium tuberculosis*.[48] Non-Hodgkin's lymphomas (NHL) may cause hemorrhage, perforation, or present with abdominal pain.[107] Although gastrointestinal Kaposi's sarcoma (KS) is usually asymptomatic,[85] massive gastrointestinal bleeding has been described,[71] usually in association with a large, friable, colonic mass or colitis.

The principles of initial management of LGIB are no different in the HIV-infected patient than in the immunocompetent host. Resuscitation with intravenous crystalloids and blood products should be dictated by the severity of bleeding as assessed by blood pressure, heart rate, stool color, and hematocrit. It is important to exclude any coagulopathy with the prothrombin time, disseminated intravascular coagulation profile, and platelet count. When evaluating an HIV-infected patient with LGIB, placement of a nasogastric tube is an important diagnostic step, especially if the bleeding is clinically significant, because hematochezia may be due to an upper gastrointestinal source.[113] An upper endoscopy should be performed if the NGT return is bloody or if there is clinical suspicion that the bleeding is from above the ligament of Treitz. Anorectal bleeding should be suspected when the blood loss is of small volume and associated with normal-colored stool. Careful inspection of the anorectal area should be performed before proceeding to colonoscopy. The most frequent etiologies of anorectal bleeding are hemorrhoids, fissures, and proctitis. Proctitis is suggested by the following symptoms: urgency, sense of incomplete evacuation, tenesmus, and dyskinesia. Anoscopy, rigid sigmoidoscopy, and flexible sigmoidoscopy are helpful when evaluating suspected proctitis. Colonoscopy is warranted when bleeding is significant and believed to originate from the proximal colon. If colonoscopy discloses no lesions and bleeding continues, localization should next be performed with a technetium 99m red cell scan or angiography, depending upon the rapidity of blood loss.

DIARRHEA

The most common manifestation of colonic disease in HIV-infected patients is diarrhea. The differential diagnosis of colonic diarrhea (colitis) is broad and the most important etiologic agents are discussed individually:

Bacterial
Shigella, Campylobacter, Salmonella
Clostridium difficile
MAC

M. tuberculosis
B. henselae
Aeromonas hydrophila
Rochalimae henselae
Viral
CMV
Herpes simplex virus
Adenovirus
Protozoa
Entamoeba histolytica
Isospara belli
Blastocystis hominis
Cryptosporidium
Microsporidia
Toxoplasma gondii
Fungi
Histoplasma capsulatum
Candida albicans
Cryptococcus neoformans
Pneumocystis carinii
Other
Inflammatory bowel disease
KS (herpesvirus 8)
Lymphoma
Acyclovir

The most common causes of colitis in HIV-infected patients are: CMV and enteric bacteria, such as *Shigella flexneri, Salmonella enteritidis, Campylobacter jejuni,* and *Clostridium difficile.* Protozoa; neoplasms, such as KS; and histoplasmosis are uncommon causes of colitis. Some medications can produce diarrhea; frank colitis is rare, but two case reports have proposed acyclovir as the cause of acute colitis in two HIV-infected patients.[80, 108]

When evaluating these patients, one must attempt to determine the site of origin of the diarrhea (i.e., enteritis or colitis), and the history alone is often helpful. For example, small bowel diarrhea (enteritis) is typically manifested as large volume (often > 2 L/d) watery stools, often associated with dehydration, electrolyte disturbances, and malabsorption. Abdominal pain, when present, is usually crampy and periumbilical in location. Symptoms, such as nausea, vomiting, bloating, distention, and borborygmi, are also commonly associated with small bowel diarrhea. In contrast, colitis is characterized by frequent, small-volume stools, that may contain mucus, pus, or blood, and is frequently accompanied by proctitis symptoms. In colitis abdominal pain is common and tends to be localized to the lower quadrants, more commonly the left. Physical examination is rarely diagnostic for the specific etiology of the diarrhea, but is extremely important in assessing the patient's general condition and hydration status.

The list of diagnostic tests to evaluate diarrhea in HIV-infected patients is extensive.

Stool
Cultures (*Salmonella, Shigella, Campylobacter*)
Toxin (*C. difficile*)
Ova and parasites (*E. histolytica*)
Stool stains
  Methylene blue (leukocytes)
  Modified Kinyoun acid-fast (*Cryptosporidium* and *I. belli*)
  Concentrated stool (zinc sulfate, Shether sucrose flotation) (Microsporidia)
Blood
Cultures (*Salmonella, Campylobacter*, MAC)
Antibodies (*E. histolytica*)
Tissue
Rectal biopsy
Colonic biopsy
  Biopsy stains
    Hematoxylin-eosin (CMV, HSV, tumors)
    Giemsa or methenamine silver (fungi)
    Methylene blue-azure II-basic fuchsin (Microsporidia)
    Fite (*Mycobacteria*)
    Electron microscopy (*Cryptosporidium*, adenovirus)
  Immunohistochemical stains (CMV))
Immunologic methods
In situ hybridization (CMV)
DNA amplification (CMV)
  Culture of tissue (colonic mucosal biopsy)
    CMV
    Herpes simplex virus
    Bacterial stool pathogens

Rarely, however, is it necessary to use more than a few of these tests. In general, the approach to the HIV-infected patient with suspected colitis should be stepwise, beginning with simple tests and gradually progressing to more invasive evaluation.[98] Routine blood tests may be useful to evaluate the impact of the diarrhea upon the host, such as hydration status and electrolyte disturbances. A markedly elevated white blood cell count suggests bacterial colitis or a complication, such as perforation or intra-abdominal abscess formation. Stool staining for fecal leukocytes with methylene blue is essential, and their presence suggests an inflammatory (colonic) origin, although their absence does not rule out colitis. Additional stool tests should include a modified acid-fast stain to evaluate for *Cryptosporidia* and other ova and parasites. Stool cultures for *Salmonella, Shigella,* and *Campylobacter* should be routinely submitted, as well as a *C. difficile* toxin screen. In the patient with distal colonic symptoms and diarrhea, proceeding to sigmoidoscopy is appropriate especially if stool studies are nondiagnostic. Colitis may be identified by flexible sigmoidoscopy; mucosal biopsies should be performed in severely immunocompromised patients to exclude CMV colitis.[11] The culture of colonic mucosal

biopsies for enteric bacterial pathogens may increase the diagnostic yield, but its effectiveness in routine clinical practice has not been proven. Barium enema plays no role in the evaluation of diarrhea or colitis in HIV-infected patients.

BACTERIAL COLITIS

Etiology

The spectrum of bacterial pathogens causing colitis in HIV-infected patients is similar to the normal host. The most frequently identified pathogens are *Campylobacter, Salmonella, Shigella,* and *C. difficle.*[77, 98, 99] *Yersinia enterocolitica, Staphylococcus aureus,* and *Aeromonas hydrophila*[91] have also been associated with severe enterocolitis in HIV-infected patients. The role of enteroadherent bacteria[64] and enteroadherent *Escherichia coli* as a cause of colitis and diarrhea is unknown.[74] There is one reported case of bloody diarrhea secondary to colonic bacillary angiomatosis (*B. henselae*).[54] Currently, the prevalence of these bacterial infections as causes of diarrhea is not well known, but may be low given the widespread use of trimethoprim-sulfamethoxazole for *Pneumocystis carinii* prophylaxis.

Clinical Manifestations

Although bacterial colitis can occur at any stage of immunodeficiency, unusual presentations of these bacterial diseases became apparent early in the AIDS epidemic where *Salmonella* sp[99] or *Campylobacter* sp bacteremia[77] were reported as initial manifestations of AIDS. In general, however, the clinical presentation of these organisms in AIDS is similar to immunocompetent patients. Bacterial colitis is typically manifested by an acute diarrheal illness (less than 2-weeks' duration). The diarrhea is usually watery, but may be bloody when the colitis is severe. *Salmonella* gastroenteritis may involve the upper gastrointestinal tract and present with watery diarrhea, abdominal pain, nausea, and vomiting. *Shigella* and *Campylobacter* manifest more commonly as dysentery with the classic colitis symptoms: mucopurulent, bloody diarrhea, tenesmus, and fever. Lower abdominal pain and fever may be prominent, but nausea and vomiting are uncommon. Physical findings include fever, tachycardia, and abdominal pain. Digital rectal examination may demonstrate frank blood or pus.

Laboratory Evaluation and Endoscopy

Blood or stool cultures are usually diagnostic and blood cultures may be positive when stool cultures are negative. The endoscopic appearance of bacterial colitis is similar regardless of the pathogen. Other causes of colitis including CMV and protozoa may appear similarly. The mucosa

appears edematous, friable, erythematous, or hemorrhagic. Occasionally, multiple ulcers and exudate may be seen. If the stool testing is negative, mucosal biopsy is mandatory. In the only reported case of colonic bacillary angiomatosis, the colonic mucosa was covered by reddish nodules with intervening ulcers.[54] Biopsy revealed chronic inflammation with thin-walled fibrovascular channels lined by endothelial cells.

Therapy

The antibiotic of choice for a presumed bacterial enterocolitis is trimethoprim-sulfamethoxazole, although ciprofloxacin (500 mg orally twice a day) is highly effective. As with normal hosts infected with these organisms, the duration of therapy should be 7 to 10 days. Clinical experience with HIV-infected patients suggests that infections with *Shigella* sp and *Campylobacter* sp can recur after successful treatment, can be more resistant to therapy, and require long-term suppressive antibiotic therapy.[98]

C. difficile Colitis

C. difficile colitis is an important cause of diarrhea in HIV-infected patients because of frequent exposure to antimicrobials and requirement for hospitalization, both factors that have been linked to *C. difficile* disease.[55] *C. difficile* colitis can also occur after the use of chemotherapeutic agents and antivirals, such as acyclovir.[22] Although nosocomial outbreaks of *C. difficile* tend to occur as an epidemic, outbreaks secondary to the same *C. difficile* strain have occurred at distant time periods,[6] probably due to the chronic carrier state.

Initial experience suggested that the clinical presentation of *C. difficile* colitis was different in the HIV-infected patient,[25] but prospective studies have shown that clinical presentation does not appear to be different in these patients as compared with nonimmunocompromised patients.[72] *C. difficile* can present fulminantly without diarrhea,[75,105] with clinical signs of peritonitis[79,105] or even ascites.

In the appropriate clinical setting the diagnosis of *C. difficile* is established by the detection of *C. difficile* toxin in the stool.[72] The presence of fecal leukocytes is common (60%), but may occasionally be absent despite the presence of colitis.[18] Plain films of the abdomen are usually nondiagnostic, although in severe cases megacolon or thumbprinting may be found.[18] Flexible sigmoidoscopy is warranted when the disease is suspected but stool toxin is negative. The characteristic endoscopic findings are multiple green-yellow pseudomembranes covering an edematous colonic mucosa. Occasionally, CT scanning in a patient with severe abdominal pain reveals a diffusely thickened colonic wall secondary to *C. difficile* colitis.

Before administering antimicrobrial therapy, it is important to stop the offending antibiotic or other predisposing factor(s) for *C. difficile* infec-

tion. Metronidazole, which can be administered either orally or intravenously, represents first-line therapy. Vancomycin should be reserved for those patients with contraindication to or failure of metronidazole or when the disease is life threatening; this agent is only effective when administered orally. One study reported that *C. difficile* isolates from HIV-infected patients belonged to serogroup C,[6] which had been previously reported to be resistant to antimicrobial therapy. To date, however, clinical resistance to therapy has not been a major problem with clinical cure obtained in essentially all patients. The relapse rate appears to be similar in HIV-infected as compared with uninfected patients.[72] If the patient has acute abdomen from fulminant *C. difficile* colitis, a laparotomy is necessary.[75, 79]

VIRAL COLITIS

CMV

Epidemiology

CMV is one of the most common opportunistic infections in patients with AIDS. Greater than 90% of homosexual patients with AIDS have serologic evidence of CMV infection. CMV disease occurs late in the course of HIV infection when immunodeficiency is severe (CD4 lymphocyte count $< 100/mm^3$).[35, 40, 41, 87] Among patients with AIDS and diarrhea (colitis or enteritis), CMV has been identified in mucosal biopsies in as many as 45% of cases.[98] The most common organs involved by CMV are the retina and the gastrointestinal tract, particularly the colon and esophagus.[56, 90, 98]

Clinical Presentation

Colonic CMV-infection typically presents with chronic watery diarrhea, abdominal pain, wasting, anorexia, fever, and weight loss.[56, 69] When the distal colorectum is involved, symptoms of dysentery and proctitis may be reported. Gastrointestinal bleeding without diarrhea may be the initial manifestation and result from either severe colitis or isolated well-circumscribed ulcers.[37, 102] Perforation has been reported to occur most often with disease located between the distal ileum and the splenic flexure.[65] Toxic megacolon[84, 103] and colonic stricture have also been described as complications.[30] Physical findings are nonspecific, and primarily reflect CMV-related complications, such as dehydration, acute abdomen, or gastrointestinal bleeding.

Endoscopy

The endoscopic features of CMV disease are variable. The spectrum varies from normal and minimal erythema and mucosal edema to a hem-

orrhagic pancolitis.[90] Occasionally, submucosal petechial hemorrhages (Fig. 1) or ulcerations with normal intervening mucosa resembling Crohn's disease may be seen (Fig. 2). The colitis may be patchy in as many as 41% of cases and involve only the right colon or cecum in 18% to 44%.[23, 35] Tumor or polypoid-like mass lesions have also been observed.

Diagnosis

Serologic studies for CMV antibody are not diagnostically helpful in AIDS given the high positivity rate in these patients. Stool tests are negative unless there are coinfections; fecal leukocytes are variably present. Abdominal radiographs are nonspecific but may suggest colitis when colonic dilation and thumbprinting of the mucosa are observed. CT may reveal circumferential thickening of the wall of the colon with inflammatory infiltration of the mesentery.[102] The main diagnostic tool for the identification of CMV colitis is endoscopy with mucosal biopsies. Given that disease is often distally located, sigmoidoscopy with biopsy is often sufficient.[23, 35] The diagnosis of CMV disease is established pathologically by the identification of viral cytopathic effect (large mononuclear, endothelial, epithelial, or smooth muscle cells containing intranuclear or cytoplasmic inclusions with surrounding inflammation[27, 98] in gastrointestinal mucosal biopsies on routine hematoxylin-eosin stains). Immunohistochemical stains of mucosal biopsies may be required to confirm the infection, but in most cases, its use does not offer greater advantage over conventional light microscopy; viral cultures of biopsy specimens are less sensitive and

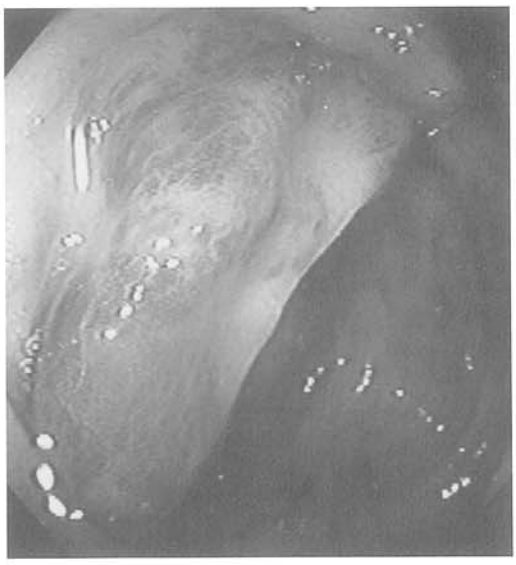

Figure 1. Cytomegalovirus colitis. Marked mucosal edema with characteristic subepithelial hemorrhages.

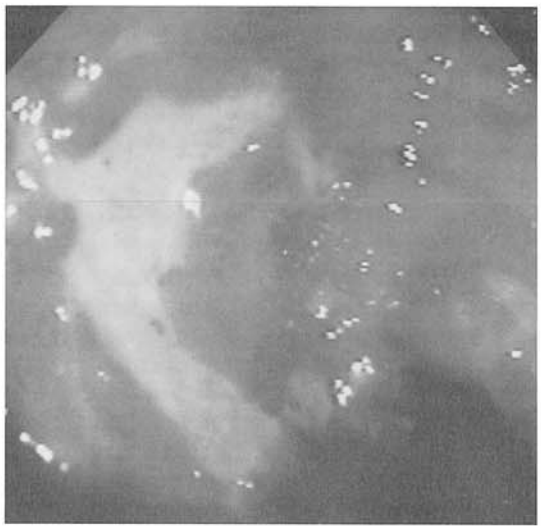

Figure 2. Cytomegalovirus colitis. Large serpiginous ulcer associated with multiple smaller ulcers with skip areas of normal-appearing mucosa resembling Crohn's disease.

specific than mucosal biopsies because contamination of the specimen with blood can give a false-positive result.[44]

Therapy

The natural history of CMV colitis is variable. In untreated patients, it usually has a chronic course characterized by progressive diarrhea and weight loss, although occasionally there is spontaneous remission of symptoms and histologic abnormalities. Unlike CMV retinitis, for which there is strong evidence supporting induction therapy followed by lifelong maintenance therapy,[26, 56] the optimal duration of therapy and need for maintenance for CMV colitis are undefined.[33, 114] Treatment of gastrointestinal CMV disease is limited to intravenous therapy with ganciclovir and foscarnet.[11, 12, 31, 32, 35, 87] Cidofovir, the newest agent available, has been reported only in patients with retinal disease,[88] but is effective in our experience for gastrointestinal disease.

A number of open-label trials of ganciclovir for HIV-infected patients with gastrointestinal CMV disease have demonstrated clinical improvement in approximately 75% of patients.[32, 56] Open-label trials of foscarnet have yielded comparable results.[11, 12] The only placebo-controlled trial of ganciclovir in AIDS-associated CMV colitis found no clinically significant differences, probably because the treatment period was only for 2 weeks.[32] A randomized trial comparing ganciclovir with foscarnet in 48 AIDS patients with gastrointestinal CMV disease found similar clinical efficacy (73%) regardless of the location of disease (esophagus versus colon) with endoscopic improvement documented in over 80% of patients.[12] Time to

progression of disease was also similar (13 to 16 weeks) despite the use of maintenance therapy. Side effects occurred in half the patients in each group. The management of the patient with bowel perforation or massive hematochezia not responding to medical therapy is surgical.[37, 111]

The use of either ganciclovir or foscarnet for CMV disease in AIDS should be based on the experience of the physician as well as the differing toxicities of each agent. Our current policy for the therapy of gastrointestinal CMV disease is to administer intravenous ganciclovir assuming there are no major contraindications to this agent, such as pancytopenia. The usual induction dose is 10 to 15 mg/kg administered twice a day or three times a day for 3 to 4 weeks. The response to therapy is judged by several parameters, which include improvement in symptoms and endoscopic findings. Ophthalmologic examination is mandatory in all patients at the time of diagnosis to exclude retinal disease. If retinal disease is absent and a complete symptomatic and endoscopic response is documented following induction therapy, we stop therapy and observe for recurrent symptoms.[114] The relapse rate for colonic disease is 30% to 50%.[12] Endoscopic re-examination following therapy is important for those patients with persistent symptoms. When there is relapse, lifelong once-daily maintenance intravenous administration is appropriate.

As many as 32% of patients with gastrointestinal CMV disease do not tolerate ganciclovir due to toxicities or ineffectiveness due to low serum levels or drug resistance.[26] For these patients, foscarnet is usually effective.[33] The recommended dosing schedule is 90 mg/kg intravenously twice a day for 14 to 21 days.

Herpes Simplex Virus

In contrast to other immunocompromised patients, herpes simplex virus (HSV) is an uncommon gastrointestinal pathogen in HIV-infected patients. In addition, HSV is a rare colonic pathogen because this virus infects almost exclusively squamous mucosa. HSV may reactivate when immunodeficiency worsens or can be acquired by receptive anorectal intercourse. The most common colonic manifestation of HSV in HIV-infected patients is distal proctitis. Herpes proctitis is characterized by rectal pain, tenesmus, and frequent mucosanguineous discharge, which may be misinterpreted as diarrhea. If the disease extends to the proximal colon, proctocolitis with hematochezia and diarrhea may occur.[98] Diffuse HSV colitis has been reported in other immunosuppressed patients (kidney and bone marrow transplant),[1, 82] but not in HIV-infected patients. On endoscopy, herpetic lesions appear as superficial aphthous ulcers surrounded by a red halo in most patients, but may vary from small vesicles to large ulcers; when severe, a diffuse hemorrhagic mucosa may be observed. Histologic identification of intranuclear (Cowdry type A) inclusions in cells within the lesion in mucosal biopsy specimens is the most useful method to confirm the infection. Biopsies should be obtained at the edge of the ulcers, in contrast to CMV, which is most readily identified from

the ulcer crater. Cytology, culture, and in situ hybridization also appear to be reliable techniques. For the patient with mild to moderate disease, oral administration of acyclovir, 15 to 30 mg/kg/d, is effective,[92, 114, 115] with the usual dose being 400 mg orally five times a day for 2 weeks. Intravenous administration should be given when the patient has not responded to high-dose oral therapy. Ganciclovir, valacyclovir, and famciclovir are also highly effective against HSV. Several studies have confirmed the safety and efficacy of foscarnet (40 mg/kg every 12 hours) in the treatment of this disease, as well as supported utility of this agent as a maintenance therapy by delaying recurrences. Long-term oral therapy is often necessary to maintain a remission.[40]

Adenovirus

Adenovirus is an uncommon gastrointestinal pathogen in HIV-infected patients. Two reports suggest that among HIV-infected patients with diarrhea in the United States, stool excretion of adenovirus is no more common than in patients without diarrhea.[61, 69] Despite the clear demonstration of the virus in intestinal tissue in 7.4% of HIV-infected patients with chronic diarrhea, a causal relationship between pathologic changes and diarrhea has not been well established.[57] In contrast, 23% of Australian HIV-infected patients with diarrhea were reported to excrete adenovirus compared with 5.4% of asymptomatic patients.[28] Pathologically, a chronic nonspecific inflammation that surrounds epithelial cells (especially goblet cells) containing large, amphophilic intranuclear inclusions, which fill the nucleus, are highly suggestive of the disease; cytoplasmic inclusions are not seen.[57] Immunoperoxide staining for adenovirus is sensitive and specific,[73] with electron microscopy the most specific. The most common symptoms are chronic, watery, nonbloody, nonmucoid diarrhea accompanied by weight loss. On endoscopy, the mucosa appears edematous, with small discrete, raised, erythematous lesions. There is no known therapy for adenovirus colitis.

Other Viral Diseases

A number of other viral pathogens have been reported to involve the gastrointestinal tract in patients with AIDS.[95] Rotavirus has been linked to both acute and chronic diarrhea.[28] Several unusual viruses have been identified in HIV-infected patients with chronic diarrhea including astrovirus, picobirna virus, and coronavirus.[47, 61] Although the true incidence of these viruses as gastrointestinal pathogens is unknown, it is probably low and there is no effective therapy.

PROTOZOA

Among the protozoa, the only pathogen that consistently infects the colon is *Entamoeba histolytica.* Despite a high frequency of stool carriage

in asymptomatic and symptomatic homosexual men,[4, 15] amebic dysentery[84, 100] or invasive amebic disease (ameboma or liver abscess) has been rarely reported in HIV-infected patients,[59] even in developing countries. Stool carriage of ameba in HIV-infected patients is not only limited to nonpathogenic strains of ameba, such as *Entamoeba dispar, Entamoeba hartmanni* and *Entamoeba coli,* but also to nonpathogenic *E. histolytica.*[15] In most studies, symptomatic patients with diarrhea in whom ameba were identified had other copathogens, suggesting that a search for other intestinal pathogens is appropriate in a symptomatic HIV-infected patient with diarrhea and amebic cysts in the stool. Furthermore, despite clearance of these protozoa from the stool, treatment has not been reliably shown to cure diarrhea in these patients.

There are several case reports of possible colitis secondary to *Dientamoeba fragilis* or *Blastocystis hominis.*[14, 19, 117] Large studies have not found a high prevalence of these protozoa in AIDS patients with diarrhea.[2] Albrecht et al[2] studied 262 HIV-infected patients and reported that although the stool carriage of *B. hominis* increased as the degree of immunodeficiency worsened, an association with clinical symptoms (diarrhea, colitis) was difficult to establish.

Although *Cryptosporidia,* Microsporidia, and *I. belli* are frequent causes of diarrhea in these patients, they uncommonly involve the colon.[3, 24, 43] These parasites are associated with chronic, water diarrhea; abdominal pain; and weight loss (small bowel diarrhea). The illness is more severe in patients with marked immunosuppression, and is self-limited if the T4 cell count is normal.[38] In a study of duodenal, ileal, and colonic biopsies, *Cryptosporidia* were detected in 53% of colonic biopsies,[46] thus showing that this method is more sensitive than stool examination with acid-fast or immunologic stains. For this reason, in the HIV-infected patient with diarrhea undergoing colonoscopy, mucosal biopsies should be performed to exclude these pathogens. Although many therapies have been used to treat this parasite, the most effective agent currently available is paromomycin. The incidence of these infections may be decreasing because of better prophylaxis[40] and use of combination antiretroviral therapy.

There is one reported case of *Toxoplasma* colitis.[86] The patient presented with diarrhea, the diagnosis was established by mucosal biopsy, and the response to conventional therapy (pyrimethamine) was appropriate. *Schistosoma* has also been reported as a cause of colitis in an HIV-infected individual.[36] The true incidence and significance of these protozoal pathogens as cause of colitis in HIV-infected patients remains to be determined. *Giardia lamblia* has not been reported as a colonic pathogen in immunocompetent or immunosuppressed persons; thus, fever and bloody stools (colitis) are not associated with this infection. Giardiasis has also no increased prevalence in HIV-infected patients, and the clinical presentation, diagnostic methods, and treatment are similar to HIV-seronegative patients.

MYCOBACTERIA

MAC is a common pathogen in AIDS patients with advanced immunosuppression, where an incidence of 39% has been described when the

CD4 count remains less than $10/mm^3$.[50] MAC has rarely been reported to involve the colon, and the small intestine is the most common site of luminal gastrointestinal involvement.[45] The most common manifestations of colonic MAC infection are chronic diarrhea and abdominal pain, although coexistent small bowel disease may result in intestinal malabsorption. Frank colitis[81] and hematochezia,[18] which may be massive,[62] are both uncommon. Positive blood cultures and bone marrow biopsy establish the diagnosis of disseminated MAC, but do not prove active gastrointestinal involvement. Likewise, the presence of a positive stool culture suggests, but does not prove, gastrointestinal involvement; stool culture positivity is, however, a marker for subsequent disseminated disease.[20] It has been clearly established that a macrolide- (e.g., clarithromycin) containing multidrug regimen is superior to a non–macrolide-containing regimen for initial therapy of MAC disease.[96]

Although *M. tuberculosis* often presents in an atypical fashion in patients with AIDS, gastrointestinal involvement remains rare, especially in developed countries.[67] Reported clinical presentations of colonic tuberculosis in HIV-infected patients include massive LGIB,[48] colitis, and ileocolonic pseudotumor.[67] On endoscopy, the lesions vary from small ulcers with normal intervening mucosa, frank strictures, or tumorlike lesions. The diagnosis of gastrointestinal tuberculosis is best established by mucosal biopsy and acid-fast stain and culture (Löwenstein-Jensen).[78] Multidrug regimens are effective for *M. tuberculosis* with microbiologic and clinical cure seen at 9 months provided drug resistance is not present[78]; therefore, long-term therapy is unnecessary.

FUNGI

Histoplasmosis

To date, fewer than 40 cases of gastrointestinal histoplasmosis have been reported in AIDS patients, usually occurring in the setting of disseminated disease. Gastrointestinal involvement occurs in about 5% of patients with disseminated disease.[112] Occasionally, the gastrointestinal tract is the first site of involvement, with the colon being the most common site (80%).[5, 112] The most frequent symptoms of gastrointestinal histoplasmosis are fever, diarrhea, weight loss, and abdominal pain, which occur in over half of all cases.[5, 49, 112] Vomiting and diarrhea are noted in approximately 25% of cases of progressive disseminated histoplasmosis. Less common presentations of colonic disease include a colonic mass lesion,[53] ulcerative colitis,[83] hematochezia,[7] obstruction, or an acute abdomen secondary to perforation.[51] The radiologic features of colonic histoplasmosis were described by Balthazar et al.[5] Barium enema disclosed segmental "apple core" lesions resembling carcinoma. CT examination revealed circumferential thickening of the wall of the colon with adjacent lymphadenopathy of mixed attenuation.[5] The endoscopic appearance of colonic histoplasmosis is that of a single segmental or constricting mass mimicking

a neoplasm, but multiple ulcerations with skip areas suggestive of Crohn's disease,[21, 42] infectious colitis, or diffuse ulcerative colitis[83] have been described. Rarely, erythema and edema, intestinal polyposis,[49] or pseudopolyps[21] have been reported. The diagnosis is established by identifying the fungus by tissue stains (periodic acid–Schiff, Giemsa) and culture. The documentation of systemic infection by chest roentgenogram, blood or bone marrow cultures, and detection of histoplasma polysaccharide antigen in serum are also helpful. Amphotericin B is the drug of choice and the recommended dosing is the same as for disseminated histoplasmosis.[112]

Other Fungi

To date, only 32 cases of gastrointestinal cryptococcosis in patients with AIDS have been reported, all of which occurred in the setting of disseminated disease. To our knowledge, there are only three reported cases of colonic cryptococcosis, which were identified at autopsy, and none of these cases had gastrointestinal manifestations.[109] Amphotericin B is the treatment of choice, and oral fluconazole and itraconazole are effective prophylactic agents for systemic cryptococcosis. There is one reported case of *Candida* colitis[58] and four cases of *P. carinii* colitis.[8, 89, 93] Two patients with *P. carinii* suffered from bowel perforation.[93] The patients with colitis not complicated by perforation responded to standard medical therapy (trimethoprim-sulfamethoxazole).[8, 89]

NEOPLASMS

Gastrointestinal involvement by KS is common, occurring in up to 50% of HIV-infected patients with cutaneous disease, and is the most common colonic neoplasm in AIDS. The colonic manifestations are variable, but in general most patients are asymptomatic; chronic diarrhea, LGIB,[71, 106] obstruction, perforation, toxic megacolon,[9] and colitis[76, 94, 110] have been described. The colitis has clinical and radiographic findings that closely resemble those of chronic inflammatory bowel disease, including loss of haustral pattern and segmental or diffuse fine mucosal ulcerations.[110] Endoscopically, colonic KS is characterized by discrete submucosal nodules with an intense red color (Fig. 3).[85] Mucosal biopsies may fail to identify this tumor, which characteristically is submucosal in location.

NHL can also involve the colon. These lesions are typically large, resulting in abdominal pain or obstruction.[107] Night sweats, weight loss, splenomegaly, and lymphadenopathy are often present. In HIV-infected patients, gastrointestinal NHL is usually an aggressive disease with survival in the range of 6 months. Multiple chemotherapeutic regimens have been used to treat HIV-associated gastrointestinal lymphomas, although the prognosis remains poor. The presence of obstruction or perforation warrants an exploratory laparotomy. Colonic adenocarcinoma has also been reported in these patients and therapy is similar to the nonimmunocompromised host.

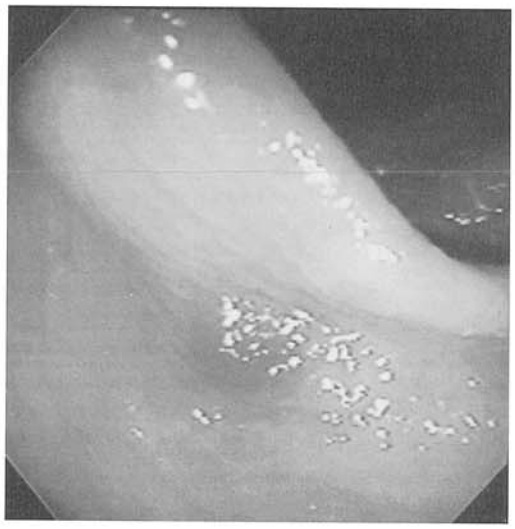

Figure 3. Kaposi's sarcoma. Subtle submucosal nodule in the transverse colon in a patient with extensive cutaneous Kaposi's sarcoma.

MISCELLANEOUS CONDITIONS

Toxic Megacolon

In patients with HIV-infection, toxic megacolon has been reported as a consequence of infections with CMV,[84] *C. difficile*,[75] *Cryptosporidium*,[24] or due to KS-associated colitis.[9, 110] It is noteworthy that most patients with HIV-infection and toxic megacolon were receiving antimotility drugs at the time of diagnosis, suggesting that caution is warranted when using these drugs in patients with diarrhea. In many patients, toxic megacolon is treated surgically, although associated with a high mortality in HIV-infected patients. Medical therapy has been proposed as an alternative to emergency colectomy, particularly for critically ill patients.

Typhlitis

Typhlitis, also refered to as *necrotizing enterocolitis* or *neutropenic enterocolitis*,[29] is an acute transmural inflammation of the cecum, most commonly occurring in cancer patients with neutropenia. This disease results most likely from chemotherapy-induced mucosal damage, stasis, and overgrowth of bacteria, resulting ultimately in mucosal inflammation and ischemia. In the cases of typhlitis described in HIV-infected patients, neutropenia has not been invariably present.[104] The classic findings of typhlitis on CT include a thickened cecal wall with inflammatory changes surrounding the serosa.[29] In the only case of HIV-related typhlitis that

was confirmed at laparotomy, a thick fibrinopurulent material was noted covering the cecum and hepatic flexure.[60] Treatment of this condition is supportive, with antibiotics and surgical resection of the cecum.

Inflammatory Bowel Disease in AIDS

Given the immunopathogenesis of inflammatory bowel disease, ulcerative colitis or Crohn's disease might be unexpected in these immunosuppressed patients. Interestingly, remission of Crohn's disease and ulcerative colitis following HIV-infection has been reported, and the improvement in symptoms was correlated with a decline in the CD4 lymphocyte count.[118] In contrast, other studies have not shown an attenuation of disease with progressive immunodeficiency.[70] Hing et al[52] reported on six HIV-infected patients with chronic diarrhea who were followed-up for 4 years and who had a chronic colitis similar to inflammatory bowel disease as documented by repeated biopsy examinations. These authors suggested that this form of colitis may represent a new entity related to HIV-infection. Sturgess et al[100] reported on a patient who developed ulcerative colitis and toxic megacolon after amebic dysentery. This patient responded to corticosteroids and mesalazine.

Pneumatosis Intestinalis

The significance of pneumatosis intestinalis in adults with AIDS is unknown. It is a late-stage phenomenon in adult patients with AIDS that characteristically involves the cecum or right colon. It has been reported in association with *C. difficile*, CMV, *Cryptosporidia*, and MAC.[16] In HIV-infected patients with pneumatosis intestinalis, even the presence of necrotic epithelium and pneumoperitoneum does not necessarily constitute a surgical emergency or is a sign of impending bowel necrosis; a benign prognosis is usual and conservative management is appropriate.[97, 116]

Idiopathic Colonic Ulcer

Like the esophagus, ulcerations have been observed in the colon that have no specific etiology. These patients usually have advanced immunodeficiency and present with fever, abdominal pain, weight loss, and gastrointestinal bleeding. Perforation has been noted. On colonoscopy, the appearance of the ulcers is identical to CMV disease, although endoscopic colitis is absent (Fig. 4). The diagnosis of idiopathic colonic ulcer can only be made after other potential etiologies have been excluded. In contrast to idiopathic esophageal ulcer, little is known about the diagnosis and management of idiopathic colonic ulcers.

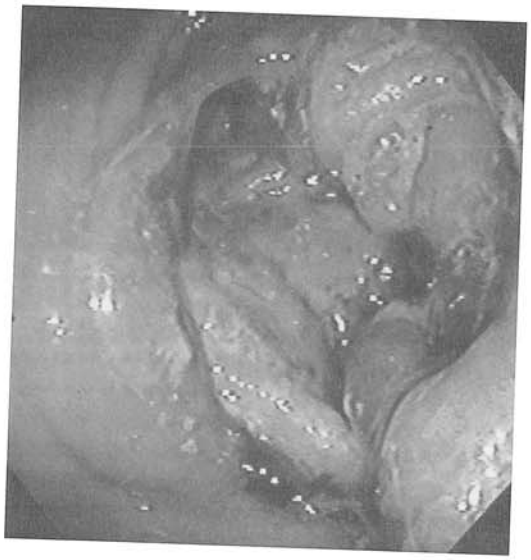

Figure 4. Idiopathic colonic ulcer. Large, well-circumscribed ulcer occupying the cecal pole.

Intussusception

Intussusception is uncommon in young adults, but its frequency has apparently increased since the beginning of the AIDS epidemic. Recurrent crampy abdominal pain is the typical presentation. Causes of intussusception include colonic infections, neoplasms, and lymphoid hyperplasia. The best method to diagnose intussusception is abdominal CT. Treatment is aimed at reduction of the intussusception and may be accomplished with a therapeutic barium enema.

References

1. Adler M, Goldman M, Liesnard C, et al: Diffuse herpes simplex colitis in a kidney transplant recipient treated with acyclovir. Transplantation 43:919, 1987
2. Albrecht H, Stellbrink HJ, Koperski K, et al: *Blastocystis hominis* in human immunodeficiency virus-related diarrhea. Scand J Gastroenterol 30:909, 1995
3. Alfandri S, Ajana F, Senneville E, et al: Hemorrhagic ulcerative colitis due to *Isospora belli* in AIDS. Int J STD AIDS 6:216, 1995
4. Allason-Jones E, Mindel A, Sargeaunt P, et al: *Entamoeba histolytica* as a commensal intestinal parasite in homosexual men. N Engl J Med 315:353, 1986
5. Balthazar EJ, Megibow AJ, Barry M, et al: Histoplasmosis of the colon in patients with AIDS: Imaging findings in four cases. AJR Am J Roentgenol 161:585, 1993
6. Barbut F, Depitre C, Delmee, et al: Comparison of enterotoxin production, cytoxin production, serogrouping, and antimicrobial susceptibilities of *Clostridium difficile* strains isolated from AIDS and human immunodeficiency virus-negative patients. J Clin Microbiol 31:740, 1993

7. Becherer PR, Sokol-Anderson M, Joist, et al: Gastrointestinal histoplasmosis presenting as hematochezia in human immunodeficiency virus-infected hemophilic patients. Am J Hematol 47:229, 1994
8. Bellomo AR, Perlman DC, Kaminsky DL, et al: *Pneumocystis* colitis in a patient with the acquired immunodeficiency syndrome. Am J Gastroenterol 87:759, 1992
9. Biggs BA, Crowe SM, Lucas CR, et al: AIDS related Kaposi's sarcoma presenting as ulcerative colitis and complicated by toxic megacolon. Gut 28:1302, 1987
10. Bini EJ, Gamagaris Z, Falkenstein DB: Lower gastrointestinal hemorrhage in 312 HIV-infected patients: Etiology and clinical outcome. Am J Gastroenterol 92:1670, 1997
11. Blanshard C: Treatment of HIV-related cytomegalovirus disease of the gastrointestinal tract with foscarnet. J Acquir Immune Defic Syndr Hum Retrovirol 5:S25, 1992
12. Blanshard C, Benhamou Y, Dohin E, et al: Treatment of AIDS-associated gastrointestinal cytomegalovirus infection with foscarnet and ganciclovir: A randomized comparison. J Infect Dis 172:622, 1995
13. Blanshard C, Francis N, Gazzard BG: Investigation of chronic diarrhoea in acquired immunodeficiency syndrome: A prospective study in 155 patients. Gut 39:824, 1996
14. Boreham RE, Benson S, Stenzel DJ, et al: *Blastocystis hominis* infection. Lancet 348:272, 1996
15. Burchard GD, Hufert FT, Mirelman D: Characterization of 20 *Entamoeba histolytica* strains isolated from patients with HIV infection. Infection 19:164, 1991
16. Burton EM, Mercado-Deane MG, Patel K: Pneumatosis intestinalis in a child with AIDS and pseudomembranous colitis. Pediatr Radiol 24:609, 1994
17. Cappell MS, Gupta A: Gastrointestinal hemorrhage due to gastrointestinal *Mycobacterium avium intracellulare* or esophageal candidiasis in patients with the acquired immunodeficiency syndrome. Am J Gastroenterol 87:224, 1992
18. Cappell MS, Philogene C: *Clostridium difficile* infection is a treatable cause of diarrhea in patients with advanced human immunodeficiency virus infection: A study of seven consecutive patients admitted from 1986 to 1992 to a University teaching hospital. Am J Gastroenterol 88:891, 1993
19. Carrascosa M, Martinez J, Pérez-Castrillón JL: Hemorrhagic proctosigmoiditis and *Blastocystis hominis* infection. Ann Intern Med 124:278, 1996
20. Chin DP, Hopewell PC, Yajko DM, et al: *Mycobacterium avium* complex in the respiratory or gastrointestinal tract and the risk of *M. avium* complex bacteremia in patients with human immunodeficiency virus infection. J Infect Dis 169:289, 1994
21. Clarkston WK, Bonacini M, Peterson I: Colitis due to *Histoplasma capsulatum* in the acquired immune deficiency syndrome. Am J Gastroenterol 86:913, 1991
22. Colarian J: *Clostridium difficile* colitis following antiviral therapy in the acquired immunodeficiency syndrome. Am J Med 84:1081, 1988
23. Combes R, Vallot T, Marche C, et al: Diagnostic de colite a cytomegalovirus au cours du SIDA. Valeur comparative de la coloscopie totale et de la rectosigmoidoscopie (a propos de 24 cas). Presse Med 24:572, 1995
24. Connolly GM, Gazzard BG: Toxic megacolon in cryptosporidiosis. Postgrad Med J 63:1103, 1987
25. Cozart JC, Kalangi SS, Clench MH, et al: *Clostridium difficile* diarrhea in patients with AIDS versus non-AIDS controls. J Clin Gastroenterol 16:192, 1993
26. Crumpacker CS: Ganciclovir. N Engl J Med 335:721, 1996
27. Culpepper-Morgan JP, Kotler DP, Scholes JV, et al: Evaluation of diagnostic criteria for mucosal cytomegalic inclusion disease in the acquired immune deficiency syndrome. Am J Gastroenterol 82:1264, 1987
28. Cunningham AL, Grohman GS, Harkness J, et al: Gastrointestinal viral infections in homosexual men who were symptomatic and seropositive for human immunodeficiency virus. J Infect Dis 258:386, 1988
29. Cutrona AF, Blinkhorn RJ, Crass J, et al: Probable neutropenic enterocolitis in patients with AIDS. Rev Infect Dis 13:828, 1991
30. De la Prieta R, Montejo M, Aguirrebengoa K, et al: Colitis por citomegalovirus que simula una neoplasia en paciente con infección por HIV. Enferm Infecc Microbiol Clin 12:341, 1994
31. Dieterich DT, Chachoua A, Lafleur F, et al: Ganciclovir treatment of gastrointestinal infections caused by cytomegalovirus in patients with AIDS. Rev Infect Dis 10:532, 1988

32. Dieterich DT, Kotler DP, Busch DF, et al: Ganciclovir treatment of cytomegalovirus colitis in AIDS: A randomized, double-blind, placebo-controlled multicenter study. J Infect Dis 167:278, 1993
33. Dieterich DT, Poles MA, Dicker M, et al: Foscarnet treatment of cytomegalovirus gastrointestinal infections in acquired immunodeficiency syndrome patients who have failed ganciclovir induction. Am J Gastroenterol 88:542, 1993
34. Dieterich DT, Poles MA, Lew EA, et al: Concurrent use of ganciclovir and foscarnet to treat cytomegalovirus infection in AIDS patients. J Infect Dis 167:1184, 1993
35. Dieterich DT, Rahmin M: Cytomegalovirus colitis in AIDS: Presentation in 44 patients and a review of the literature. J Acquir Immune Def Syndr Hum Retrovirol 1:S29, 1991
36. Dionisio D, Vivarelli A, Di Lollo S, et al: Proctocolite da *Schistosoma mansoni* in AIDS. Studio clinico ed immunoistochimico di un caso. Recenti Prog Med 82:385, 1991
37. Escudero-Fabre A, Cummings O, Kirklin JK, et al: Cytomegalovirus colitis presenting as hematochezia and requiring resection. Arch Surg 127:102, 1992
38. Flanagan T, Whalen C, Turner J, et al: Cryptosporidium infection and CD4 counts. Ann Intern Med 116:840, 1992
39. Frank D, Raicht RF: Intestinal perforation associated with cytomegalovirus infection in patients with acquired immunodeficiency syndrome. Am J Gastroenterol 79:201, 1984
40. Gallant JE, Moore RD, Chaisson RE: Prophylaxis for opportunistic infections in patients with HIV infection. Ann Intern Med 120:932, 1994
41. Gallant JE, Moore RD, Richman DD, et al: Incidence and natural history of cytomegalovirus disease in patients with advanced human immunodeficiency virus disease treated with zidovudine. J Infect Dis 166:1223, 1992
42. Gonzalez Keelan CG, Imbert M: Colonic histoplasmosis simulating Crohn's disease in a patient with AIDS: Case report and review of the literature. Bol Asoc Med P R 80:248, 1988
43. Goodgame RW: Understanding intestinal spore-forming protozoa: *Cryptosporidia,* microsporidia, *Isospora,* and *Cyclospora.* Ann Intern Med 124:429, 1996
44. Goodgame RW, Genta RM, Estrada R, et al: Frequency of positive tests for cytomegalovirus in AIDS patients: Endoscopic lesions compared with normal mucosa. Am J Gastroenterol 88:338, 1993
45. Gray JR, Rabeneck L: Atypical mycobacterial infection of the gastrointestinal tract in AIDS patients. Am J Gastroenterol 84:1521, 1989
46. Greenberg PD, Cello JP: Diagnosis of *Cryptosporidium parvum* in patients with severe diarrhea and AIDS. Dig Dis Sci 41:2286, 1996
47. Grohmann GS, Glass RI, Pereira HG, et al: Enteric viruses and diarrhea in HIV-infected patients. N Engl J Med 329:14, 1993
48. Gutberlet H, Rösch W: Primäre Darmtuberkulose bei AIDS. Z Gastroenterol 30:869, 1992
49. Halline AG, Maldonado-Lutomirsky, Ryoo JW, et al: Colonic histoplasmosis in AIDS: Unusual endoscopic findings in two cases. Gastrointest Endosc 45:199, 1997
50. Havlik JA, Horsburgh CR, Metchock B, et al: Disseminated *Mycobacterium avium* complex infection: Clinical identification and epidemiologic trends. J Infect Dis 165:577, 1992
51. Heneghan SJ, Li J, Petrossian E, et al: Intestinal perforation from gastrointestinal histoplasmosis in acquired immunodeficiency syndrome: A case report and review of the literature. Arch Surg 128:464, 1993
52. Hing MC, Goldschmidt C, Mathijs JM, et al: Chronic colitis associated with human immunodeficiency virus infection. Med J Aust 156:683, 1992
53. Hofman P, Mainguene C, Huerre M, et al: Pseudotumor colique a *Histoplasma capsulatum* au cors du SIDA. Diagnostic morphologique et immunohistochimique d'une lesion isolee. Arch Anat Cytol Pathol 43:140, 1995
54. Huh YB, Rose S, Schoen RE, et al: Colonic bacillary angiomatosis. Ann Intern Med 124:735, 1996
55. Hutin Y, Molina JM, Casin I, et al: Risk factors for *Clostridium difficile*-associated diarrhoea in HIV-infected patients. AIDS 7:1441, 1993
56. Jacobson MA, O'Donnell JJ, Porteous D, et al: Retinal and gastrointestinal disease due to cytomegalovirus in patients with the acquired immune deficiency syndrome: Prevalence, natural history, and response to ganciclovir therapy. Q J Med 67:473, 1988
57. Janoff EN, Orenstein JM, Manischewitz JF, et al: Adenovirus colitis in the acquired immunodeficiency syndrome. Gastroenterology 100:976, 1991

58. Jayagopal S, Cervia JS: Colitis due to *Candida albicans* in a patient with AIDS. Clin Infect Dis 15:555, 1992
59. Jessurun J, Barron-Rodriguez LP, Fernandez-Tinoco G, et al: The prevalence of invasive amebiasis is not increased in patients with AIDS. AIDS 6:307, 1992
60. Jumper C, Weems JJ, Lettau LA: Typhlitis and HIV. Ann Intern Med 117:698, 1992
61. Kaljot KT, Ling JP, Gold JWM, et al: Prevalence of acute enteric viral pathogens in acquired immunodeficiency syndrome patients with diarrhea. Gastroenterology 97:1031, 1989
62. Keller C, Kirkpatrick S, Lee K, et al: Disseminated *Mycobacterium avium* complex presenting as hematochezia in an infant with rapidly progressive acquired immunodeficiency syndrome. Pediatr Infect Dis J 15:713, 1996
63. Knapp AB, Horst DA, Eliopoulos G, et al: Widespread cytomegalovirus gastroenteritis in a patient with acquired immunodeficiency. Gastroenterology 85:1399, 1983
64. Kotler DP, Orenstein JM: Chronic diarrhea and malabsorption associated with enteropathogenic bacterial infection in a patient with AIDS. Ann Intern Med 119:127, 1993
65. Kram HB, Shoemaker WC: Intestinal perforation due to cytomegalovirus infection in patients with AIDS. Dis Colon Rectum 33:1037, 1990
66. Kyriazis AP, Mitra SK: Multiple cytomegalovirus-related intestinal perforations in patients with acquired immunodeficiency syndrome: Report of two cases and review of the literature. Arch Pathol Lab Med 116:496, 1992
67. Lanjewar DN, Anand BS, Genta R, et al: Major differences in the spectrum of gastrointestinal infections associated with AIDS in India versus the West: An autopsy study. Clin Infect Dis 23:482, 1996
68. LaRaja RD, Rothenberg RE, Odom JW, et al: The incidence of intraabdominal surgery in acquired immunodeficiency syndrome: A statistical review of 904 patients. Surgery 105:175, 1989
69. Laughon BE, Druckman DA, Vernon A, et al: Prevalence of enteric pathogens in homosexual men with and without acquired immunodeficiency syndrome. Gastroenterology 94:984, 1988
70. Lautenbach E, Lichtenstein GR: Human immunodeficiency virus infection and Crohn's disease: The role of the CD4 cell in inflammatory bowel disease. J Clin Gastroenterol 25:456, 1997
71. Lew EA, Dietrich DT: Severe hemorrhage caused by gastrointestinal Kaposi's syndrome in patients with the acquired immunodeficiency syndrome: Treatment with endoscopic injection sclerotherapy. Am J Gastroenterol 87:1471, 1992
72. Lu SS, Schwartz JM, Simon DM, et al: *Clostridium difficile*-associated diarrhea in patients with HIV positivity and AIDS: A prospective controlled study. Am J Gastroenterol 89:1226, 1994
73. Maddox A, Francis N, Moss J, et al: Adenovirus infection of the large bowel in HIV positive patients. J Clin Pathol 45:684, 1992
74. Mayer HB, Wanke CA: Enteroaggregative *Escherichia coli* as a possible cause of diarrhea in an HIV-infected patient. N Engl J Med 332:273, 1995
75. Medich DS, Lee KK, Simmons RL, et al: Laparotomy for fulminant pseudomembranous colitis. Arch Surg 127:847, 1992
76. Meltzer SJ, Rotterdam HZ, Korelitz BI: Kaposi's sarcoma occurring in association with ulcerative colitis. Am J Gastroenterol 82:378, 1987
77. Molina JM, Casin I, Hausfater P, et al: *Campylobacter* infections in HIV-infected patients: Clinical and bacteriological features. AIDS 9:881, 1995
78. Mönkemüller KE, Lewis JB Jr: Massive rectal bleeding from colonic tuberculosis. Am J Gastroenterol 91:1439, 1996
79. Morris JB, Zollinger RM Jr, Stellato TA: Role of surgery in antibiotic-induced pseudomembranous enterocolitis. Am J Surg 160:5335, 1990
80. Moshkovitz M, Konikoff FM, Arber N, et al: Acyclovir-associated colitis. Am J Gastroenterol 88:2110, 1993
81. Müller A, Munch R, Meyenberger C, et al: Diagnostische Schwierigkeiten bei der infektiösen Kolitis im Rahmen der HIV-Krankheit. Schweiz Med Wochenschr 122:201, 1992
82. Naik HR, Chandrasekar PH: Herpes simplex virus (HSV) colitis in a bone marrow transplant recipient. Bone Marrow Transplant 17:285, 1996

83. Naveau S, Roulot D, Cartier I, et al: Colite ulcereuse a "*Histoplasma capsulatum*" chez un patient atteint d'un syndrome d'immunodepression acquise (SIDA). Gastroenterol Clin Biol 10:760, 1986
84. Ohnishi K, Murata M, Okuzawa E: Symptomatic amebic colitis in a Japanese homosexual AIDS patient. Intern Med 33:120, 1994
84. Orloff JJ, Saito R, Lasky S, et al: Toxic megacolon in cytomegalovirus colitis. Am J Gastroenterol 84:794, 1989
85. Parente F, Cernushi M, Orlando G, et al: Kaposi's sarcoma and AIDS: Frequency of gastrointestinal involvement and its effect on survival. A prospective study in a heterogeneous population. Scand J Gastroenterol 26:1007, 1991
86. Pauwels A, Meyohas MC, Eliaszewics M, et al: Toxoplasma colitis in the acquired immunodeficiency syndrome. Am J Gastroenterol 87:518, 1992
87. Peters BS, Beck EJ, Anderson S, et al: Cytomegalovirus infection in AIDS: Patterns of disease, response to therapy and trends in survival. J Infect 23:129, 1991
88. Polis MA, Spooner KM, Baird BF, et al: Anticytomegaloviral activity and safety of cidofovir in patients with human immunodeficiency virus infection and cytomegalovirus viruria. Antimicrob Agents Chemother 39:882, 1995
89. Raviglione MC: Extrapulmonary pneumocystosis: The first 50 cases. Rev Infect Dis 12:1127, 1990
90. Rene E, Marche C, Regnier B, et al: Intestinal infections in patients with acquired immunodeficiency syndrome: A prospective study in 132 patients. Dig Dis Sci 34:773, 1989
91. Roberts IM, Parenti DM, Albert MB: *Aeromonas hydrophila*-associated colitis in a male homosexual. Arch Intern Med 147:1502, 1987
92. Rompalo AM, Mertz GJ, Davis LG, et al: Oral acyclovir for treatment of first episode herpes simplex virus proctitis. JAMA 259:2879, 1988
93. Rosenberg AS, Telzak E, Koll B, et al: *Pneumocystis carinii* associated with bowel perforation in two AIDS patients [abstract]. *In* Eighth International Conference on AIDS/Third STD World Congress. Amsterdam, 1992, p B140
94. Roth JA, Schell S, Panzarino S, et al: Visceral Kaposi's sarcoma presenting as colitis. Am J Surg Pathol 2:209, 1978
95. Schmidt W, Schneider T, Heise W, et al: Stool viruses, coinfections, and diarrhea in HIV-infected patients. J Acquir Immune Defic Syndr Hum Retroviol 13:33, 1996
96. Shafran SD, Singer J, Zarowny DP, et al: A comparison of two regimens for the treatment of *Mycobacterium avium* complex bacteremia in AIDS: Rifabutin, ethambutol, and clarithroymcin versus rifampin, ethambutol, clofazimine, and ciprofloxacin. N Engl J Med 335:377, 1996
97. Sivit CJ, Josephs SH, Taylor GA, et al: Pneumatosis intestinalis in children with AIDS. AJR Am J Roentgenol 155:133, 1990
98. Smith PD, Lane HC, Gill VJ, et al: Intestinal infections in patients with the acquired immunodeficiency syndrome (AIDS): Etiology and response to therapy. Ann Intern Med 108:328, 1988
99. Smith PD, Macher AM, Bookman MA, et al: *Salmonella typhimurium* enteritis and bacteremia in the acquired immunodeficiency syndrome. Ann Intern Med 102:207, 1985
100. Sturgess I, Greenfield SM, Teare J, et al: Ulcerative colitis developing after amoebic dysentery in a hemophiliac patient with AIDS. Gut 33:408, 1992
101. Tatum ET, Sun PC, Cohn DI: Cytomegalovirus vasculitis and colon perforation in a patient with the acquired immunodeficiency syndrome. Pathology 21:235, 1989
102. Teixidor HS, Honig CL, Norsoph E, et al: Cytomegalovirus infection of the alimentary canal: Radiologic findings with pathologic correlation. Radiology 163:317, 1987
103. Thuluvath PJ, Connolly GM, Forbes A, et al: Abdominal pain in HIV infection. Q J Med 78:275, 1991
104. Till M, Lee N, Soper WD, Murphy RL: Typhlitis in patients with HIV-1 infection. Ann Intern Med 116:998, 1992
105. Triadfilopoulos G, Hallstone AE: Acute abdomen as the first presentation of pseudomembranous colitis. Gastroentrology 101:685, 1991
106. Wang CYE, Schroeter AL, et al: Acquired immunodeficiency syndrome-related Kaposi's sarcoma. Mayo Clin Proc 70:869, 1995

107. Wang CYE, Snow JL, Su WPD: Lymphoma associated with human immunodeficiency virus infection. Mayo Clin Proc 70:665, 1995
108. Wardle TD, Finnerty JP, Swale V, et al: Acyclovir-induced colitis. Aliment Pharmacol Ther 11:415, 1997
109. Washington K, Gottfried MR, Wilson ML: Gastrointestinal cryptococcosis. Mod Pathol 4:707, 1991
110. Weber JN, Carmichael DJ, Boylston A, et al: Kaposi's sarcoma of the bowel presenting as apparent ulcerative colitis. Gut 26:295, 1985
111. Wexner SD, Smithy WB, Trillo C, et al: Emergency colectomy for cytomegalovirus ileocolitis in patients with the acquired immunodeficiency syndrome. Dis Colon Rectum 31:755, 1988
112. Wheat LJ, Connolly-Stringfeld PA, Baker RL, et al: Disseminated histoplasmosis in the acquired immunodeficiency syndrome: Clinical findings, diagnosis and treatment, and review of the literature. Medicine 69:361, 1990
113. Wilcox CM, Chalasani N: Etiology and outcome of lower gastrointestinal bleeding in patients with AIDS. Am J Gastroenterol, in press
114. Wilcox CM, Mönkemüller KE: Review: The therapy of gastrointestinal infections in acquired immunodeficiency syndrome. Aliment Pharmacol Ther 11:425, 1997
115. Wilcox CM, Schwartz DA, Clark WS: Causes, response to therapy, and long-term outcome of esophageal ulcer in patients with human immunodeficiency virus infection. Ann Intern Med 122:143, 1995
116. Wood BJ, Kumar PN, Cooper C, et al: Pneumatosis intestinalis in adults with AIDS: Clinical significance and imaging findings AJR Am J Roentgenol 165:1387, 1995
117. Yarze JC: Hemorrhagic proctosigmoiditis and *Blastocystis hominis*. Ann Intern Med 125:860, 1996
118. Yoshida EM, Chan NH, Herrick RA, et al: Human immunodeficiency virus infection, the acquired immunodeficiency syndrome, and inflammatory bowel disease. J Clin Gastroenterol 23:24, 1996

Address reprint requests to

C. Mel Wilcox, MD
Division of Gastroenterology and Hepatology
UAB Station
University of Alabama at Birmingham
Birmingham, AL 35294–0007

e-mail: mel_wilcox@gasmac.dom.uab.edu