

GASTROINTESTINAL COMPLICATIONS OF HIV

I. INTRODUCTION

RECOMMENDATIONS:

Clinicians should evaluate patients with GI complaints for non-HIV-related illness, non-GI-related illness, adverse effects of medications, possible opportunistic infections (OIs), and HIV-associated neoplasms.

Clinicians should not routinely dismiss GI complaints in HIV-infected pregnant women.

The estimated incidence of gastrointestinal (GI) complaints among HIV-infected patients varies between 30% and 90%. HIV-related disorders may affect all structures from the mouth to the anus. Oral and esophageal lesions, hepatobiliary disorders, and diarrhea are the most common. By direct involvement of GI organs and through food avoidance associated with GI symptoms, these processes can result in malabsorption, maldigestion, or decreased intake of nutrients, thus adding to the wasting and malnutrition associated with HIV/AIDS. For recommendations on oral health management, refer to *Oral Health Complications in the HIV-Infected Patient*.

In many patients with GI complaints, the cause may be elusive; therefore, diligence and perseverance are often required to establish the diagnosis. Nondiagnostic standard stool and blood tests may need to be repeated, followed by endoscopic evaluation with biopsy. During the course of a diagnostic evaluation, unusual opportunistic organisms are frequently identified, and common pathogens may be found in anatomic locations not usually associated with the pathogen. Unusual organisms should not be dismissed routinely as non-pathogens. Multiple pathogens may be found simultaneously; therefore, clinicians should be familiar with the many potential causes of GI diseases in HIV-infected patients. Diagnosis may be complicated by contributing factors, such as:

- Misidentification of non-pathogenic *Entamoeba* species and treating as pathogens
- Multiple concurrent GI disease processes, resulting in persistence of signs and symptoms despite adequate treatment of a single identified cause
- Adverse effects of multiple ARV medications
- Extraintestinal processes, such as pneumonia, which may be associated with diarrhea, or meningitis and central nervous system mass lesions, which may cause vomiting
- Non-HIV-related diseases that are appropriate to the patient's age, sex, and social habits

GI complaints should not be routinely dismissed in pregnant HIV-infected women. These symptoms should be carefully considered and investigated further if necessary.

II. GASTROINTESTINAL DISEASES AND SYNDROMES

A. Esophageal Disease

1. Diagnosis

Odynophagia and dysphagia with both liquids and solids are the symptoms most frequently associated with a variety of esophageal diseases (see Table 1). However, esophagitis may also cause esophageal spasm that mimics angina or occasionally causes hiccups. The patient's history may reveal potential causes of swallowing disturbances, such as medications or gastroesophageal reflux disease (GERD).

Physical examination may reveal OIs, such as pharyngeal candidiasis (thrush), herpes simplex virus (HSV), cytomegalovirus (CMV), or Kaposi's sarcoma (KS). Pharyngeal candidiasis suggests the possibility of esophageal candidiasis. Of note, the absence of oral thrush does not exclude the diagnosis of *Candida* esophagitis in patients without esophageal complaints. *Candida* esophagitis may occur at virtually any CD4 count, although it is most commonly seen in patients with CD4 counts <200 cells/mm³. HSV and CMV esophagitis are usually seen in patients with CD4 counts <100 cells/mm³. Because functional CD4 cell-mediated immunity may be incomplete, a patient's lowest, rather than current, CD4 count should be used to guide the relative risk for OIs in the early phase of immune reconstitution. It may take up to 1 year for immune reconstitution to occur.

Less commonly, aphthous ulcerations in the esophagus may be responsible for symptoms. Aphthous ulceration is diagnosed by exclusion. Other potential etiologies should be excluded before initiating steroids to treat aphthous ulcers.

Classification	Most Common Pathogen	Less Common Pathogens
Fungal	<i>Candida</i> species	<i>Histoplasma capsulatum</i> , <i>Pneumocystis carinii</i>
Viral	CMV, herpes simplex, Kaposi's sarcoma	Papillomavirus, HIV
Bacterial	Rarely seen	<i>Mycobacterium tuberculosis</i> , <i>Mycobacterium avium</i> complex (MAC), <i>Actinomyces</i> species
Protozoal	Rarely seen	<i>Cryptosporidia</i>
Neoplastic	Lymphoma	—
Miscellaneous	—	Aphthous ulcers, acid reflux, pill ulcers

2. Treatment

RECOMMENDATIONS:

Initial empiric therapy

Clinicians should prescribe an oral azole antifungal (fluconazole loading dose of 200 mg, followed by 100 to 200 mg/day) as initial empiric treatment for patients with suspected

esophagitis. If no improvement is seen after 7 to 10 days, diagnostic endoscopy should be performed.

Esophagitis in patients receiving antifungal therapy

When a patient receiving antifungal therapy presents with esophagitis, clinicians should assess for the following:

- a defect in drug absorption (common with itraconazole and ketoconazole)
- the development of resistance to the drug by the initial infecting fungus
- development of a fungal superinfection with a resistant strain
- development of a non-fungal etiology

When a patient receiving antifungal therapy presents with esophagitis, the clinician may prescribe increased doses of fluconazole (up to 800 mg/day); however, early endoscopy should also be strongly considered to establish the diagnosis in these cases.

CMV esophagitis

Clinicians should treat CMV esophagitis with oral valganciclovir or intravenously administered ganciclovir or foscarnet at induction doses for 3 to 6 weeks.

An ophthalmologic examination should be performed at the time of diagnosis to assess for the presence of concurrent CMV retinal disease.

The role of maintenance therapy for CMV esophagitis is currently not known, and relapse is common, even during maintenance therapy. Cidofovir, valganciclovir, and oral ganciclovir remain of unproven efficacy.

HSV esophagitis

Clinicians should treat mild or moderate HSV esophagitis orally for 2 weeks (if absorption is not an issue) with standard treatment doses of acyclovir, valacyclovir, or famciclovir.

Clinicians should treat severe HSV esophagitis with intravenously administered acyclovir for 2 weeks. Foscarnet should be used when acyclovir-resistant HSV is suspected.

Recurrent HSV esophagitis may be suppressed with maintenance dosing of oral acyclovir, valacyclovir, or famciclovir.

Gastroesophageal reflux disease

Clinicians should treat GERD primarily with proton pump inhibitors (omeprazole, lansoprazole), possibly in combination with pro-motility agents (metoclopramide).

Aphthous ulcers

Clinicians should use topical corticosteroids to manage aphthous ulcers; however, caution should be taken because steroid use may result in candidal overgrowth.

Steroids are the first-line therapy for aphthous ulcers. Thalidomide has been shown to be effective for the treatment of non-resolving aphthous ulcers in HIV-infected patients; however, there are serious documented teratogenic effects associated with thalidomide in pregnant women. Central nervous system toxicity and peripheral neuropathy may occur as well. Because of these potential side effects, thalidomide should only be used as second-line therapy. In adolescent and adult women capable of bearing children, thalidomide should only be used when the woman is known not to be pregnant and is using effective methods of birth control.

B. Gastric Disease

1. Diagnosis

RECOMMENDATIONS:

Clinicians should perform endoscopy in patients with recalcitrant symptoms or disease and/or acute events, such as hematemesis.

Clinicians should discuss with HIV-infected patients who are initiating ARV therapy the possible GI side effects associated with ARV medications. The patient should be informed that the duration of symptoms is generally limited to 2 weeks and that symptomatic treatment can be prescribed.

Diagnostic evaluation of patients with HIV-associated gastric disease is no different than that used in diagnosing peptic or duodenal ulcers or gastritis in non-HIV-infected populations. Although the full range of non-HIV-associated gastric disorders may be encountered in patients with HIV disease, opportunistic gastric processes may also be seen but are uncommon. The two most common infectious agents, CMV and Kaposi's sarcoma, are usually seen in the context of severe disseminated disease. CMV, like Kaposi's sarcoma, can cause episodes of hematemesis. Kaposi's sarcoma and antral lymphoma may cause gastric outlet obstruction and/or symptoms of early satiety.

Symptoms of dyspepsia or peptic ulcer disease should be thoroughly studied, including serology for *Helicobacter pylori* and/or endoscopy for urea test. If *H. pylori* infection is diagnosed, ARV medications may need to be stopped for the duration of *H. pylori* treatment to prevent drug-drug interactions.

The symptoms of nausea, vomiting, and general dyspepsia commonly occur in the early stages of ARV therapy. Zidovudine, didanosine, tenofovir, and the protease inhibitors (PIs) are the most common ARV drugs associated with GI side effects. In addition, other therapeutic agents may cause stomach upset, especially when the daily pill burden is high. Discussing the possible ARV medication side effects on the GI system before they arise, as well as their potential impact on adherence, is critical.

2. Treatment

RECOMMENDATIONS:

Because of the high incidence of diarrhea in HIV-infected patients, magnesium-containing antacids should be avoided, and aluminum- or bismuth-based antacids should be used.

Clinicians should prescribe short courses of the oral or suppository form of prochlorperazine or promethazine with or without metoclopramide for symptomatic relief of medication-associated nausea and vomiting.

Treatment of infectious gastric pathogens is the same as those outlined for esophageal disease (see Section A: *Esophageal Disease*). For moderate to severe or intractable vomiting ascribed to HAART, the more potent 5-hydroxytryptamine-3 (5-HT₃) receptor antagonists (e.g., ondansetron hydrochloride, dronabinol) may be required. Dronabinol is also helpful for nausea and anorexia.

Because of a poorly understood mechanism underlying hypochlorhydria, gastritis and peptic ulcer disease may respond better to a mucosal protective agent such as sucralfate than to histamine-2 blockers or proton pump inhibitors. Hypochlorhydria has not been fully demonstrated to be a significant effect of HIV disease. In addition, peptic ulcer disease occurring despite hypochlorhydria would be more likely to be infectious in etiology.

C. Liver Disease

1. Diagnosis

RECOMMENDATION:

When a patient has elevated serum transaminase, the clinician should assess for use of any possible hepatotoxic medications or alternative therapies (herbal therapies), alcohol abuse, and viral hepatitis.

Table 2 shows the hepatotoxicity of the available ARV drugs. For recommendations regarding hepatitis A, B, and C management, see [Viral Hepatitis](#).

TABLE 2		
HEPATOTOXICITY OF ANTIRETROVIRAL DRUGS		
Agent	Hepatotoxicity	Usual Time Frame
<i>Nucleoside Reverse Transcriptase Inhibitor (NRTI)</i>		
Abacavir (ABC)	Modest non-specific ALT, AST elevations	LFT elevations develop by 4th week
Didanosine (ddI)	Modest non-specific ALT, AST elevations; rare clinical hepatitis	LFT elevations develop by 4th week; fulminant hepatitis within 8 to 12 weeks
Emtricitabine (FTC)	Rare, except may cause LFT elevations when discontinued in HBV (similar to lamivudine)	—
Lamivudine (3TC)	Rare, except when discontinued in HBV (see text)	—
Stavudine (d4T)	Modest non-specific ALT, AST elevations; rare steatosis/lactic acidosis syndrome	LFT elevations develop by 4th week; fulminant hepatitis within 8 to 12 weeks and steatosis at generally >18 weeks
Tenofovir (TDF)	Rare, except may cause LFT elevations when discontinued in HBV (similar to lamivudine)	—
Zalcitabine (ddC)	Modest non-specific ALT, AST elevations	LFT elevations develop by 4th week
Zidovudine (ZDV)	Modest non-specific ALT, AST elevations; rare clinical hepatitis; rare steatosis/lactic acidosis syndrome	LFT elevations develop by 4th week; fulminant hepatitis within 8 to 12 weeks and steatosis at generally >18 weeks
<i>Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI)</i>		
Delavirdine (DLV)	Modest non-specific ALT, AST elevations	LFT elevations develop by 4th week
Efavirenz (EFV)	Rare	—
Nevirapine (NVP)	Modest non-specific ALT, AST elevations; common GGT elevations; rarely hepatitis	LFT and GGT elevations develop by 4th week; fulminant hepatitis within 12 weeks
<i>Protease Inhibitor (PI)</i>		
Amprenavir (APV)	Modest non-specific ALT, AST elevations	LFT elevations develop by 4th week
Atazanavir (ATV)	Rare; hyperbilirubinemia without abnormal LFTs common	Indirect bilirubin elevations develop by 6th week
Darunavir (DRV)	No data	—

Fos-Amprenavir (FPV)	Modest non-specific ALT, AST elevations	LFT elevations develop by 4th week
Indinavir (IDV)	Hyperbilirubinemia; hepatitis in the setting of chronic HBV or HCV (see text)	Indirect bilirubin elevations develop by 6th week
Lopinavir/r (LPV/r)	Modest non-specific ALT, AST and GGT elevations	LFT elevations develop by 4th week
Nelfinavir (NFV)	Rare	—
Ritonavir (RTV)	Modest non-specific ALT, AST elevations	LFT elevations develop by 4th week
Saquinavir (SQV)	Modest non-specific ALT, AST elevations	LFT elevations develop by 4th week
Tipranavir (TPV)	Modest non-specific ALT, AST and GGT elevations	LFT elevations develop by 4th week
<i>Fusion Inhibitor (FI)</i>		
Enfuvirtide (T-20)	Rare, non-specific ALT, AST elevations	—

Liver disease is common among HIV-infected patients. Frequently asymptomatic, it may be identified by elevations of either serum transaminases (i.e., AST or ALT) or alkaline phosphatase and gamma-glutamyltranspeptidase (GGTP) levels. A satisfactory marker of hepatic fibrosis or fibrogenesis other than needle biopsy is not yet available, particularly for early-to-mid-stage disease. Abdominal imaging studies (CT scan, MRI, or ultrasound) may help assess advanced cirrhosis, portal hypertension, peri-portal disease (schistosomiasis), echinococcal disease, and hepatocellular carcinoma.

Alkaline phosphatase and GGTP elevations are indicative of intrahepatic or cholestatic disease. The most common causes of cholestatic disease include disseminated mycobacterial, fungal, or protozoal infections; drug-induced hepatotoxicity; and biliary tract disorders. In addition to the classic viral hepatitis, hepatobiliary pathogens encountered in the setting of HIV infection include HSV, tuberculosis, *Bartonella*, and histoplasmosis, as well as ascending cholangitis caused by OIs, such as CMV, MAC, *Cryptosporidium*, and microsporidia ascending from the gut via the common bile duct. When treating a patient with advanced immunosuppression, clinicians should conduct a thorough search for the offending organism(s). In the setting of HIV disease, organisms that are generally regarded as of little clinical significance should not be routinely dismissed as non-pathogenic. Serum lactate also should be considered as a cause of increased serum liver enzymes.

Although the benefits of HAART are readily apparent, use of these complex regimens has multiplied the risk of potential medication interactions and hepatotoxicity. The potential for such

toxicity is exacerbated by the presence of acute or chronic viral hepatitis, ethanol use/abuse, and hepatic steatosis.

2. Treatment

RECOMMENDATIONS:

The clinician should avoid using any potentially hepatotoxic non-essential drugs in the setting of new or worsening abnormal serum liver enzyme levels.

When one of the HAART agents is suspected as the cause for the hepatotoxicity, the clinician should substitute an equally potent agent. If the clinical situation does not permit the initiation of an alternative agent, the discontinuation of *all* the components of the HAART regimen is recommended. Therapy with the alternative HAART regimen should be initiated after the abnormal laboratory values have returned to the patient's baseline values.

Clinicians should initiate standard treatment for pathogens found in the liver, such as fungi and mycobacteria.

Treatment for liver disease should be directed to the suspected or specific pathogen. Standard treatment for pathogens found in the liver, such as fungi and mycobacteria, should be initiated; however, suboptimal outcomes, even after multiple and prolonged regimens, are not uncommon. Treatment of an offending organism may be further complicated by the overlapping toxicities of the regimen with the patient's underlying liver function and HAART. If a component of the patient's HAART regimen must be discontinued and a suitably potent ARV agent cannot be substituted, then all components of the HAART regimen should be discontinued temporarily to prevent the development of HIV resistance. HAART should be restarted after the abnormal laboratory values have returned to the patient's baseline values. An alternative HAART regimen may be necessary.

Asymptomatic and clinically insignificant hyperbilirubinemia (total bilirubin > 2.5 mg/dL) may occur with the use of indinavir and atazanavir therapy. Indinavir has been implicated as a rare cause of significant symptomatic hepatitis (elevated total bilirubin with a greater than 5-fold increase in serum transaminase levels) when given to patients with preexisting chronic viral hepatitis. These patients should be observed closely after the initiation of indinavir therapy. A full discussion of the viral hepatitis and their treatment in the context of HIV infection is provided in [Viral Hepatitis](#).

D. Diarrhea

1. Diagnosis

RECOMMENDATIONS:

Clinicians should assess the following in HIV-infected patients with diarrhea:

- **a careful dietary history, including lactose and fat intake**
- **medication history to assess whether diarrhea is medication-induced**

- travel history
- alcohol use
- sexual activity
- weight loss

Clinicians should perform endoscopy in the setting of moderate to severe diarrhea if stool studies for pathogens are negative and medication is not a suspected etiology.

Clinicians should perform colonoscopy in patients with bloody diarrhea or diarrhea with tenesmus when bacterial stool cultures are negative, obtaining multiple biopsies from both abnormal and normal-appearing segments of bowel. Pathologists should be specifically instructed to seek organisms listed in Table 3.

Clinicians should perform distal duodenal biopsy in patients with large volume diarrhea (>2L/24hr) of suspected small bowel origin. If microsporidia is suspected, electron microscopy or PCR should be used to confirm and identify the microsporidia.

Clinicians should include invasive enteric disease (bacterial, viral) or disseminated mycobacterial infection in the differential diagnosis in patients who present with fever and diarrhea.

TABLE 3 EVALUATION OF DIARRHEA BASED ON CD4 COUNT		
CD4 Count	Common Pathogens	Method of Identification
<100 cells/mm ³	<i>Cryptosporidium</i>	Antigen assay or modified Kinyoun stain
	Microsporidia	Trichrome stain
	<i>Enterocytozoon bienewisi</i>	Biopsy with Giemsa stain or electron microscopy
	<i>Septata intestinalis</i>	Biopsy with Giemsa stain or electron microscopy
	<i>Cyclospora</i>	No fecal leukocytes, AFB smear of stool for oocytes
	<i>Isospora</i>	No fecal leukocytes, AFB smear of stool for oocytes
	CMV	Biopsy demonstrating intranuclear inclusion bodies
	MAC	Blood culture
	<i>Histoplasma capsulatum</i>	Blood culture and urine antigen assay
	<i>Giardia</i>	Antigen assay and/or stool examination for ova and parasites

<200 cells/mm ³	Common bacterial pathogens: <i>Salmonella</i> <i>Shigella</i> species <i>Campylobacter jejuni</i> <i>Giardia</i>	Fecal leukocytes, and stool and blood cultures Fecal leukocytes, stool cultures Fecal leukocytes, stool cultures Antigen assay and/or stool examination for ova and parasites
Any CD4	<i>Clostridium difficile</i>	Fecal leukocytes, antigen assay for toxin a and b

* Usually part of disseminated infection.

Diarrhea is a prevalent complaint among HIV-infected patients. It is defined as >250 mL of stool per day. The primary process may occur in the large or small intestine, or both. Attempting to localize the source based on specific characteristics of the diarrhea may allow the clinician to narrow the list of potential pathogens (see Table 4), select appropriate diagnostic studies, and prescribe the most effective therapy.

<p>Characteristics of Large Bowel Diarrhea</p> <ul style="list-style-type: none"> • Small, frequent bowel movements with tenesmus • Sense of incomplete evacuation • Blood that may or may not be present in the stool <p>Characteristics of Small Bowel Diarrhea</p> <ul style="list-style-type: none"> • Particularly symptomatic at night • Large volume, watery bowel movements • Increase throughout the day

Clinicians should perform distal duodenal biopsy in patients with large volume diarrhea (>2L/24hr) of suspected small bowel origin. If microsporidia is suspected, electron microscopy or PCR should be used to confirm and identify the microsporidia. If the results of small bowel biopsy are negative, the possibility of pancreatic insufficiency should be considered and quantitative or qualitative stool testing for fecal fat after a 100-gram fat challenge should be performed.

Most patients with diarrhea will have a specific pathologic process or infection identified by use of readily available studies, including endoscopy with biopsies when necessary. If initial stool studies are negative, the tests may be repeated. If repeated stool studies are negative, an empiric trial of metronidazole may be given for 1 to 2 weeks before endoscopy is performed. If the

patient's stool examination is positive for fecal leukocytes, a colonic pathogen is more likely. *Clostridium difficile* diarrhea is common in HIV-infected patients, sometimes even in the absence of antibiotic therapy. The routine use of loperamide for symptomatic treatment should be avoided in HIV-infected patients until *C difficile* is excluded by obtaining stool *C difficile* toxin assay.

Another common cause of diarrhea in HIV-infected patients is the use of ARV agents. Although all ARVs may be associated with diarrhea, the class of drugs most likely to cause diarrhea is the PIs, especially nelfinavir, amprenavir, and any ritonavir-enhanced regimen. The titration of over-the-counter psyllium products may offer symptomatic relief for the PI-induced diarrhea and may obviate the need for prescription agents.

Tenesmus or proctitis may occur as part of the infectious diarrheal symptom complex, hemorrhoids, or more commonly as the result of an infection with an STI (herpes simplex, HPV, syphilis). More information about STI-related symptoms can be found in *Atypical Presentations of STIs and Anal Dysplasia*.

TABLE 4 POSSIBLE HIV-RELATED ETIOLOGIC AGENTS OF DIARRHEA IN HIV-INFECTED PATIENTS		
Small Intestine	Large Intestine	Miscellaneous
<i>Cryptosporidium</i>	CMV	Drugs
Microsporidia	<i>Cryptosporidium</i>	Alcohol
<i>Isospora belli</i>	MAC	Lactose intolerance
MAC	<i>Shigella</i>	Pancreatic insufficiency
<i>Salmonella</i> species	<i>Clostridium difficile</i>	
<i>Campylobacter</i> species	<i>Campylobacter jejuni</i>	
<i>Giardia lamblia</i>	<i>Histoplasma capsulatum</i>	
	Adenovirus	
	Herpes simplex (rare)	
	<i>Pneumocystis carinii</i> (rare)	

2. Treatment

RECOMMENDATIONS:

Clinicians should provide symptomatic treatment for all patients with diarrhea to prevent volume depletion and wasting and to maximize comfort and functional status (see Table 5).

Clinicians should counsel patients with diarrhea about the effects of diet, advocating a low-fat, lactose-free diet if these are found to be etiologic.

Clinicians should treat parasitic and bacterial pathogens with standard regimens.

Clinicians should treat CMV colitis with intravenous ganciclovir, valganciclovir, or foscarnet for 3 to 6 weeks with induction doses. Maintenance therapy remains controversial but should be used in the setting of a low CD4 count (<100 cells/mm³). An ophthalmologic examination should be performed at the time of diagnosis to assess for the presence of concurrent CMV retinal disease.

TABLE 5 SYMPTOMATIC TREATMENT FOR PATIENTS WITH DIARRHEA		
Agent	Dose	Indications
Loperamide	2-4 mg 4x/day	Moderate to severe ARV-related diarrhea; should only be used after bacterial or amoebic etiology has been excluded
Diphenoxylate	2 tablets 4x/day	Moderate to severe ARV-related diarrhea; should only be used after bacterial or amoebic etiology has been excluded
Paregoric	30 mL po every 4h	Moderate to severe ARV-related diarrhea; should only be used after bacterial or amoebic etiology has been excluded
Deodorized tincture of opium	10 to 20 drops po every 3 to 4h	Moderate to severe ARV-related diarrhea; should only be used after bacterial or amoebic etiology has been excluded
Bismuth subsalicylate		Mild, non-infectious diarrhea
Aluminum antacids		Mild, non-infectious diarrhea
Cholestyramine		Mild, non-infectious diarrhea
Fiber supplement		Mild, non-infectious diarrhea
Calcium carbonate pills*		ARV-related diarrhea
Glutamine supplementation*		ARV-related diarrhea

*Anecdotal noted to be useful for ARV-related diarrhea.

Relapse of parasitic and bacterial pathogens is common, and maintenance therapy may be required, especially when accompanied by low CD4 counts (see *Infectious Complications Associated With HIV Infection*). The role of maintenance therapy for CMV infection is currently not known and relapse is common, even during maintenance therapy. Cidofovir, valganciclovir, and oral ganciclovir remain of unproven efficacy.

Octreotide 100 to 500 µg administered subcutaneously or intravenously every 8 hours has been advocated for treatment of diarrhea, especially in severe situations not responsive to oral agents. However, the efficacy of this agent is largely untested in controlled trials.

E. Biliary Disease

1. Diagnosis

RECOMMENDATIONS:

Clinicians should perform an abdominal ultrasound to establish a diagnosis of biliary disease.

Clinicians should confirm acalculous cholecystitis by hepatoiminodiacetic acid (HIDA) scan.

If stool tests and radiologic studies are unrevealing, clinicians should perform an endoscopic evaluation of the biliary tree and small bowel with or without biopsies to identify the pathogen.

The signs and symptoms of biliary disease do not differ between HIV-infected and non-HIV-infected patients except jaundice is less common in patients with HIV. Right upper quadrant or epigastric pain, fever, and cholestasis are presenting symptoms in >90% of patients. Nausea and/or vomiting occur in approximately 50% of patients with biliary disease, but pruritus is rare.

Many pathogens causing opportunistic biliary disease can be isolated from the stool; therefore, obtaining stool specimens may assist in establishing a probable diagnosis. Elevations in alkaline phosphatase and GGTP are suggestive of cholestatic disease. Common causes of cholestatic disease include disseminated mycobacterial infections, HIV cholangiopathy, and other OIs (*Cryptosporidium* and microsporidia) that affect the biliary tract; traditional biliary tract disease would include gallstones, acalculous cholecystitis, and cholangitis. Abdominal ultrasound is a sensitive (at least 75%) procedure for diagnosing gallbladder disease. Acalculous cholecystitis is a common finding on ultrasound and should be confirmed by hepatoiminodiacetic acid (HIDA) scan. The etiologic organisms of cholecystitis are similar to those that cause cholangitis, and the two processes often co-exist.

Endoscopic retrograde cholangiopancreatography (ERCP) may be required as an adjunct to ultrasound in diagnosing bile duct pathology. Bacterial septic cholangitis may complicate ERCP or occur superimposed on cholecystitis because of other causes. The latter is seen in advanced HIV infection when CD4 counts are <100 cells/mm³. If papillary stenosis is present, sphincterotomy may reduce pain, but serum liver enzyme elevations often persist post-sphincterotomy. The most common opportunistic pathogens implicated in cholangitis are *Cryptosporidium* (biliary involvement in up to 20% of intestinal infections), CMV, and microsporidia, especially *Enterocytozoon bienersi*. Rare causes include *Isospora*, MAC, lymphoma, and Kaposi's sarcoma. In addition, medications used to treat HIV or associated OIs may produce a cholestatic hepatitis (e.g., efavirenz, nevirapine, and clarithromycin) or steatohepatitis (e.g., NRTIs).

2. Treatment

RECOMMENDATIONS:

Clinicians should treat the underlying pathogen(s) isolated from the biliary tract or stool.

Clinicians should treat jaundice and pruritus with ursodeoxycholic acid and symptomatic treatments such as doxepin. Pain should be treated when indicated.

Clinicians should use appropriate antimicrobial therapy with or without cholecystectomy to treat acalculous cholecystitis.

Treatment of biliary disease should be aimed at the underlying pathogen. Pain should be treated when indicated, and narcotics may be used if necessary.

F. Pancreatic Disease

1. Diagnosis

RECOMMENDATIONS:

Clinicians should obtain serum lipase levels in patients suspected of having acute pancreatitis; serum lactate levels should also be obtained to exclude lactic acidosis.

Clinicians should obtain abdominal ultrasound or CT scans both to delineate possible non-infectious etiologies or complications of pancreatitis, such as perforating gastric ulcers or pancreatic pseudocyst, as well as to follow the degree of inflammation and response to treatment over time. ERCP should be reserved for the evaluation of ductal lesions.

Although abdominal discomfort may be vague or mild during early pancreatitis, the characteristic steady, boring epigastric pain of acute pancreatitis with its radiation to the back and the associated signs and symptoms of nausea, vomiting, and abdominal distension should be expected as frequently in the HIV-infected population as in the non-HIV-infected population.

The usual causes of pancreatitis are alcohol and pancreatotoxic medications. Pentamidine, trimethoprim-sulfamethoxazole, dideoxyinosine, dideoxycytidine, stavudine, hydroxyurea, megestrol acetate, and octreotide have all been reported as pancreatotoxins.

Hypertriglyceridemia, either as a result of HIV infection or as a common consequence of PI therapy, is another inciting cause of pancreatitis. Opportunistic pathogens also may be associated with the development of pancreatitis. Biopsy is usually not an option in pancreatic disease; therefore, ascribing an infectious etiology, other than through blood culture isolation of CMV, mycobacteria, or fungi, usually will require supporting clinical evidence of end-organ disease elsewhere. The most common infectious etiology in an autopsy series was CMV, followed by *Cryptococcus* and toxoplasmosis.

2. Treatment

RECOMMENDATIONS:

Clinicians should provide vigorous intravenous hydration and pain control for patients with severe pancreatitis. These patients should be kept NPO.

The clinician should discontinue the use of all known or suspected pancreatotoxic agents. If one ARV agent is to be discontinued and another ARV agent cannot be expediently substituted to maintain effective HAART, then all ARV agents should be withheld to circumvent the development of resistance.

If an infectious etiology is present or suspected, the clinician should initiate appropriate antimicrobial therapy.

FURTHER READING

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