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HIV & Hepatitis Education Prison Project

HEPP REPORT

HIV & HEPATITIS EDUCATION PRISON PROJECT

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INFECTIOUS DISEASES IN CORRECTIONS

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ABOUT HEPP

HEPP Report, a forum for correctional problem solving, targets correctional physicians, nurses, administrators, outreach workers, and case managers. Published monthly and distributed by email and fax, HEPP Report provides up-to-the moment information on HIV/AIDS, hepatitis, and other infectious diseases, as well as efficient ways to administer treatment in the correctional environment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education. HEPP Report is distributed to all members of the Society of Correctional Physicians (SCP) within the SCP publication, CorrDocs (www.corrdocs.org).

GASTROINTESTINAL COMPLICATIONS OF HIV DISEASE

Joseph Bick, MD, Chief Medical Officer, California Medical Facility, California Department of Corrections*

Diseases of the gastrointestinal tract are common among those who are HIV-infected. Sometimes the first clue that a previously undiagnosed inmate/patient is HIV-infected is the presence of an HIV-associated gastrointestinal condition. These conditions can lead to significant morbidity including pain, difficulty swallowing, diarrhea, and weight loss. Early diagnosis and treatment can substantially improve the lives of those who are afflicted by these conditions. Although identifying the specific etiology of a patient's symptoms can be challenging, a methodical approach can usually identify a treatable condition. This article focuses on some of the most common abnormalities of the gastrointestinal system that correctional health care providers are likely to encounter among their HIV-infected patients.

> "Although identifying the specific etiology of a patient's symptoms can be challenging, a methodical approach can usually identify a treatable condition."

Oral Lesions

The most common HIV-associated oral condition is candidiasis, or thrush. Thrush is usually found in those with advanced immunodeficiency, generally in patients with a CD4+ T cell count less than 300 cells/mm^3. Oral candidiasis is associated with progression to AIDS, and the presence of thrush in someone who is not known to be HIV infected should prompt a recommendation for HIV testing. Thrush most commonly appears as a white cheesy exudate that can be easily wiped off. Alternatively, thrush can present as erythema without exudates. The lesions are most commonly seen on the soft palate and tongue. Mild thrush can be treated with topical nystatin or clotrimazole troches. In more severe cases, oral fluconazole is highly effective. In cases of thrush caused by azole-resistant Candida, a higher dose of the azole can sometimes overcome resistance. If treatment with an azole drug is unsuccessful, a short course of either amphotericin swish and swallow or intravenous amphotericin is sometimes required. Candida can also cause angular cheilitis, or fissures located at the angle of the mouth. These lesions also occur in the setting of anemia or vitamin deficiency, but are more commonly due to Candida and typically respond promptly to oral azole therapy or even topical nizoral cream.

Oral hairy leukoplakia (OHL) generally presents as filamentous or hairy projections on the lateral borders of the tongue. The lesions are usually poorly demarcated and can have a flattened appearance. In contrast to thrush, the lesion of OHL cannot be brushed off. Thought to be due to Epstein-Barr virus, the lesions are asymptomatic and are generally of only cosmetic importance. OHL sometimes responds to acyclovir or valacyclovir, although probably the best treatment is HAART-induced immune reconstitution. As with thrush, OHL is highly predictive of HIV infection.

Aphthous ulcers are common and often severe in those who are HIV infected. Ulcers are traditionally classified as minor (≤10mm) or major (>10mm) in size, and can be single or multiple. The lesions are typically painful, well-demarcated ulcerations that can be either shallow or deep. Ulcers can be found on the buccal or labial mucosa, tongue, soft palate, or pharynx. Not uncommonly, the patient will have a tender adjacent submandibular node. Aphthous ulcers

Continued on page 2

WHAT'S INSIDE

Gastrointestinal Complications...
(continued from page 1)

are of unknown etiology. Some clinicians recommend treatment with topical suspensions of tetracycline with or without nystatin or hydrocortisone, while others recommend topical Kenalog® in Orabase, which is a paste that will stick to the wet surfaces of the mouth and form a protective film over the mouth ulcer. Minor aphthae usually heal without scarring in <10 days regardless of therapy. Perhaps the best approach is analgesics such as ibuprofen and, prior to meals, topical viscous lidocaine. Avoidance of acidic foods such as tomatoes and citrus is also useful while lesions are present. Major aphthae can be more painful and take longer to heal. Aphthae can also present in a herpetiform pattern, with multiple small ulcerative lesions. Oral lesions that do not heal within two weeks or those that are accompanied by systemic signs such as fever should be biopsied to rule out other etiologies such as deep fungal infection or malignancy. Single shallow painless ulcerations can be due to syphilis (condyloma lata), and should be screened for with a rapid plasma reagin (RPR) test.

Warts can be found on the lips or in the oral cavity and are typically painless. Caused by human papillomavirus, lesions can be either flat or cauliflower shaped and are often multiple in number. Lesions can be removed with a scalpel, by electrosurgery, laser ablation, or liquid nitrogen. If the lesion is flat and located on the tongue, consider other potential causes, such as syphilis.

Kaposi's sarcoma (KS) can be found anywhere in the GI tract. When found in the oral cavity, KS is most commonly red, blue, or purple in color and can be either macular or nodular. Lesions are most commonly found on the hard palate, but can also be seen on the gingiva or oropharynyx. The diagnosis is made by histologic examination of tissue obtained by biopsy. The most effective treatment is immune reconstitution by HAART, but in those for whom this is not possible intralesional chemotherapeutic agents such as vinblastine have been used.

Esophageal Lesions

Disease involving the esophagus is common in advanced HIV infection, and is most commonly due to Candida. Patients with candidal esophagitis usually have orpharyngeal involvement as well and present with dysphagia and odynophagia. In patients with a typical presentation, most clinicians empirically treat to cover Candida and reserve further evaluation for those who fail to respond. Oral fluconazole (200 mg on day one followed by 100 mg daily for two weeks) is usually highly effective, although azole resistance can be present at baseline or develop while on treatment. Intravenous fluconazole or low-dose amphotericin B (0.3mg/kg/day) can be used in patients who cannot swallow. Voriconazole may be effective in some cases of fluconazole resistant Candida. Caspofungin, an antifungal in the echinocandin class, has also shown clinical activity in some cases of azole-resistant candidal infections.

In cases of esophagitis that fail to respond to antifungal therapy, endoscopy with biopsy is required to rule out other etiologies such as herpes simplex virus, (HSV) cytomegalovirus, (CMV), malignancy, or aphthous ulcerations. Patients with CMV esophagitis commonly have systemic symptoms such as fever, nausea, emesis, diarrhea, abdominal pain, and weight loss. Biopsy reveals CMV infected cells with intranuclear inclusion bodies. CMV esophagitis can be treated intravenously with ganciclovir (5mg/kg q 12 hours for 14 days) or foscarnet (60mg/kg q 8 hours for 14 days). Ganciclovir can lead to myelosuppression, while foscarnet can cause renal insufficiency, electrolyte disturbances, and penile ulcerations.

Esophageal HSV can present with odynophgia, dysphagia, retrosternal pain, nausea, and emesis. Untreated patients can develop tracheoesophageal fistulas, necrosis, stricture, or hemorrhage. Biopsy demonstrates cytoplasmic inclusion bodies, ground glass appearance of nuclei, and multinucleated giant cells. HSV responds to intravenous acyclovir.

Major aphthae involving the esophagus can persist and be significantly debilitating. In some cases, systemic steroids or oral thalidomide is useful in hastening healing.

Diarrhea

Worldwide, diarrhea is the most common cause of morbidity and mortality among those who are HIV-infected. Diarrhea can be caused by bacterial, viral, or parasitic infections, or by a medication. In many cases, a careful search can identify a treatable etiology of the patient's diarrhea. There is little data specifically addressing the etiologies of diarrhea among the incarcerated. One would expect that the frequency of some pathogens would differ among those recently incarcerated as compared to those who have been institutionalized for an extended period of time. Likewise, the causes of diarrhea among foreign-born inmates and those who have traveled outside of the United States may differ from those who have never left the country.

The evaluation of a patient with diarrhea begins with a thorough history and physical examination. Patients may use the word diarrhea to describe anything from a rectal discharge, to occasional loose stools, to frequent large volume bowel movements. Additionally, acute self-limited diarrhea occurs frequently in otherwise healthy adults. Diarrhea that has been present for years with little if any weight loss is more likely to be due to irritable bowel, inflammatory bowel, or lactose intolerance than to an infectious etiology. In patients with advanced immunodeficiency, fever, and anemia, opportunistic infections such as those caused by Mycobacterium avium complex (MAC) and CMV must be considered. Medications or dietary changes are often an overlooked cause of changes in bowel frequency or consistency. In jails and prisons, regulated access to toilets and toilet paper can cause those who experience medication-induced diarrhea to adhere poorly to prescribed treatments. Drugs that commonly cause a change in bowel motility include laxatives, antacids, cardiac medications, some psychiatric medications, and antiretroviral agents such as ddI, ritonavir and nelfinavir. Antibiotics can alter intestinal flora and lead to loose stools.

In those who present with symptoms of greater than one-week duration associated with weight loss, fever, dehydration, or bloody stools, diagnostic studies are indicated. The intensity of the work-up is subject to debate, but most would agree that a stepwise approach is usually appropriate in those who are not critically ill. Generally, in HIV infected patients it is most appropriate to begin with evaluation of stool specimens for presence of ova, parasites, Clostridium difficile toxin, Salmonella, Shigella, Campylobacter, E. coli 0157 H7, Cryptosporidium, and Microsporidia. To increase the yield, it is recommended to send three separately collected specimens for ova and parasite analysis. If the patient is febrile, blood cultures for bacteria should be collected. In those with advanced immunodeficiency (CD4 <75/mm^3) blood cultures for mycobacteria are also indicated. If stool studies and blood cultures fail to identify an etiology, flexible sigmoidoscopy or colonoscopy with biopsy should be per-

Continued on page 4

Letter from the Editor

Dear Correctional Colleagues:

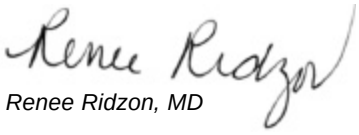
In this month's issue of HEPP, the lead article by Dr. Joseph Bick describes the most common HIV-related GI conditions, and how to diagnose and manage patients with these conditions. As Dr. Bick points out, the most important first step in the evaluation of GI complaints is a thorough history. The terms diarrhea, constipation and "stomach ache" denote different things to different people. Accordingly, clarifying what the patient means by his or her complaints is an important component to any evaluation. GI disease is common among persons with HIV infection. Luckily, most of the infectious causes are treatable and conditions not readily treated with antibiotics may respond to immune reconstitution with HAART.

Infections are the etiology for many of the HIV-related GI disturbances. As Dr. Bethany Weaver illustrates in this month's case study, the causative organisms can be myriad. In crowded congregate settings such as correctional facilities, food-related outbreaks are relatively more common. Any potential clustering of illness in such a setting should raise suspicions of an outbreak and appropriate investigation and control measures should take place. While those with HIV infection may not be at increased risk of acquiring pathogens that cause most foodborne illnesses such as Salmonella or Campylobacter, consequences of such an outbreak can be more severe in an immunocompromised host.

In Part II of the highlights from the Eleventh Annual Conference on Retroviruses and Opportunistic Infections (CROI) held in San Francisco. Dr. Rick Altice reports on two therapeutic trials that examined use of once-daily dosing of ritonavir-boosted PI-containing regimens of highly effective ART. Simplifying regimens to once-daily dosing will be an important step toward improved patient adherence that could potentially lead to improved outcomes and decreased development of viral resistance. With the continued development of medications with longer half lives and pharmacoenhancement with drug combinations, hopefully more once-daily regimens will soon be a available.

We strive to present topics that our readers find useful and interesting and pertinent to correctional settings. If you have an idea of a topic you think should be addressed in HEPP Report, we welcome your thoughts or suggestions.

Sincerely,



Renee Ridzon, MD

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Faculty Disclosure

In accordance with the Accreditation Council for Continuing Medical Education Standards for Commercial Support, the faculty for this activity have been asked to complete Conflict of Interest Disclosure forms. Disclosures are listed at the end of articles. All of the individual medications discussed in this newsletter are approved for treatment of HIV and hepatitis unless otherwise indicated. For the treatment of HIV and hepatitis infection, many physicians opt to use combination antiretroviral therapy which is not addressed by the FDA.

Gastrointestinal Complications...
(continued from page 2)

formed. Biopsy specimens should be cultured for Salmonella, Shigella, Campylobacter, mycobacteria, CMV, and HSV. Histologic evaluation should include staining for mycobacteria, fungi, protozoans, and viral inclusions.

Bacterial causes of diarrhea
In non-incarcerated HIV-infected persons in the U.S., the most common bacterial causes of diarrhea are Salmonella, C. difficile, MAC, Shigella, and Campylobacter. The overall incidence of bacterial colitis has been reduced in this country by the widespread use of trimethoprim/sulfamethoxazole (TMP/FMX) for Pneumocystis prophylaxis.

Fever is more commonly seen in Salmonella infection than in other bacterial cause of diarrhea. Blood in the stool suggest Shigella or Campylobacter rather than Salmonella. Among those infected with HIV, Salmonella is more likely to lead to bacteremic disease and to relapse after treatment. Predictors of relapse include septicemia and low CD4 lymphocyte counts. Salmonella can be treated with TMP/FMX, a quinolone, or azithromycin. Among those with CD4 counts less than 50 cells/mm^3 who have experienced relapsed infection with Salmonella, ongoing maintenance therapy with ciprofloxacin should be considered. If bacterial colitis is suspected, medications that decrease bowel motility such as diphenoxylate, loperamide, paregoric, and tincture of opiates should be avoided because they have been associated with the development of toxic megacolon or prolongation of infection. Clustering of cases of bacterial diarrhea caused by Salmonella, Shigella, or E. Coli 0157H7 may indicate a food borne outbreak or person-to-person transmission and should lead to an investigation.

Infection with C. difficile can lead to diarrhea in patients with AIDS. Both receiving antibiotics and being hospitalized are associated with an increased risk for C. difficile infection. Diagnosis can be made by the detection of C. difficile toxin in stool. The first line treatment is oral metronidazole at a dose of 500 mg by mouth 3X/day for 10-14 days. Because of the concern for encouraging the development of resistant organisms, oral vancomycin should be reserved for only those patients who fail to respond to metronidazole.

Disease due to MAC is uncommon among those who have a CD4 lymphocyte count of >100/mm^3 and those who are taking macrolide prophylaxis. Among those with severe immunosuppression, disseminated MAC can cause diarrhea with fever, sweats, anemia, neutropenia, weight loss, and hepatosplenomegaly. Stool or blood cultures for acid-fast bacilli (AFB) can confirm the diagnosis. While culture of the organism from a tissue specimen is the gold standard for diagnosis, endoscopic biopsy showing foamy macrophages and acid-fast organisms can be used as evidence of infection as well. Cultures are necessary to differentiate MAC from tuberculosis. Treatment with combinations of medications including rifampin or rifabutin, ethambutol, ciprofloxacin, amikacin, and clarithromycin or azithromycin have been used with some success. Ultimately, the only long-term effective strategy for controlling MAC disease relies on immune restoration with HAART.

> **"**Worldwide, diarrhea is the most common cause of morbidity and mortality among those who are HIV-infected.**"**

Parasitic causes of diarrhea
Common parasitic causes of diarrhea include Cryptosporidium, Microsporidium and Entamoeba histolytica. Cryptosporidium parvum is found worldwide in drinking water that has been contaminated by fecal cysts from grazing animals. Water that is drawn from wells is less likely to be affected. Heat and chlorine are not effective against Cryptosporidia. Illness due to Cryptosporidium can last for months in those who are HIV-infected, leading to dehydration, electrolyte abnormalities and wasting. Treatment of Cryptospridium is only of marginal benefit. The non-absorbable aminoglycoside paromomycin is most commonly used for treatment in this country.

Microsporidia species are spore-forming parasites that can cause a wide variety of clinical syndromes among those who are HIV-infected. The microsporidial organisms Enterocytozoon bieneusi and Encephalitozoon intestinalis can cause diarrhea and wasting, and albendazole can be effective for treatment.

In most cases, E. histolytica is a colonizer and does not cause symptoms; however, some strains of E. histolytica can lead to cramping, abdominal pain, painful bowel movements, and bloody stools. E. histolytica is diagnosed by stool examination or blood serology. Treatment for symptomatic disease (i.e. invasive disease) is metronidazole 750mg 3X/day for 10 days. There is disagreement as to the benefit of treating those who are asymptomatic but have been demonstrated to pass cysts. If the goal is to eradicate cysts from the intestinal lumen, the recommended treatment is iodoquinol 650mg 3X/day for three weeks.

Giardia lamblia is an enteric protozoan with a worldwide distribution that causes acute and chronic diarrhea throughout the world. Giardiasis can be transmitted through water and person-to-person by the fecal-oral route. Most of those who ingest Giardia cysts will not become infected. Of those who are infected, some will become asymptomatic cyst passers while others will develop diarrhea. Symptoms can include cramps, diarrhea, bloating, flatulence, and weight loss. Giardia is diagnosed by the detection of cysts or trophozoites in the stool by direct examination or antigen assay. Treatment is generally metronidazole at a dose of 250 mg 3X/day for five days.

Viral causes of diarrhea
Diarrhea due to rotavirus or other viral agents is relatively common but is usually self-limited. In most cases these illnesses are of short duration and require no specific diagnostic or therapeutic intervention other than oral fluids and over-the-counter antimotility agents.

In those with advanced immunosuppression (typically CD4 counts of <50/mm^3) CMV can lead to colitis, but since the introduction of HAART, the incidence of active CMV disease has fallen dramatically in the U.S. Diagnosis is usually made by flexible sigmoidoscopy or colonoscopy. CMV can lead to areas of erythema, ulceration, and hemorrhage. Histologic examination of biopsy specimens reveals intranuclear inclusion bodies in infected epithelial, endothelial, or smooth muscle cells.

Acute treatment of CMV colitis is ganciclovir IV 10-15mg/kg/day in two to three divided doses. Foscarnet is also effective at a dose of 180 mg/kg/day IV in two or three divided doses. In the absence of immune restoration, active disease commonly recurs. In the event of relapse, retreatment followed by daily maintenance therapy is indicated. The only long term

Continued on page 5

Gastrointestinal Complications...
(continued from page 4)

effective treatment for CMV is HAART-induced immune restoration.

Fungal causes of diarrhea
Disseminated fungal diseases are uncommon causes of diarrhea in those who are HIV-infected. Histoplasmosis can involve the gastrointestinal tract, leading to diarrhea, fever, pain, and weight loss. Diagnosis can be made by the detection of intracellular budding yeast in colonic biopsy specimens. The histoplasmosis urinary antigen is very useful for diagnosing this infection and for monitoring therapy. Initial therapy of disseminated histoplasmosis is generally amphotericin B, followed by maintenance with either amphotericin B or itraconazole. Maintenance must be continued lifelong, unless HAART leads to significant sustained immune reconstitution.

Anorectal Disease
Anorectal disease is very common among those who are HIV-infected. Oftentimes patients will not divulge that they have anorectal symptoms or lesions. Clinicians should routinely ask patients about anorectal symptoms, and periodically perform a visual inspection of the external anal area.

Herpes Simplex Virus
Both HSV1 and 2 commonly cause anorectal disease. HSV infection can also lead to urinary symptoms, impotence, and sacral paresthesias. In HIV-infected patients who present with perianal ulcerative lesions or fissures, the most common cause is HSV. Patients should be treated with oral acyclovir or valacyclovir for ten to fourteen days. Lesions that fail to respond should be cultured for HSV, and if positive, sent for susceptibility testing. Lesions that are acyclovir resistant can be effectively treated with intravenous foscarnet. Relapses are quite common but can be decreased in frequency by the use of suppressive therapy with acyclovir at a dose of 200-400mg 2X/day.

Gonorrhea, syphilis, and chlamydia
Patients who are infected with Neisseria gonorrhoeae and/or Chlamydia trachomatis can present with symptoms that include anal discharge, pain, tenesmus, and bleeding. Cultures of rectal swabs and urine ligase chain reaction (LCR) for Gonorrhea or Chlamydia infection can be useful in making the diagnosis. Ceftriaxone 250mg IM for one dose, followed by either doxycycline 100mg 2X/day for seven days or azithromycin 1200 mg for one dose is recommended for both anorectal gonorrhea and chlamydia. Syphilis can also cause painful or painless ulcers of the anal mucosa or rectum. The diagnosis is usually made clinically in conjunction with a serum RPR test.

Condyloma
Warts, caused by human papillomaviruses, (HPV) are commonly found in the perianal area. Lesions can be either flat or cauliflower-shaped, are usually multiple and asymptomatic but can cause itching or bleeding. Small warts can spontaneously resolve, and removing visible warts does not reliably eradicate the causative virus. HPV can frequently be isolated from individuals who have no visible lesions. Regardless of the type of treatment, warts commonly recur. Some strains of HPV are associated with anal cancer, and biopsy should be performed in those with extensive lesions and patients who do not respond to therapy. Data have been presented this past year concerning the development of therapeutic and preventive vaccines for HPV. These vaccines hold great promise for reducing the risk for anal and genital lesions and most importantly for decreasing the likelihood of cervical and anal carcinoma. Although beyond the scope of this article, there is a growing body of literature that discusses the potential role of anal pap smears in the early diagnosis of malignancy. Some of the most commonly used treatments for warts are outlined in Table 1.

TABLE 1: Commonly Used Treatments for Warts

Treatment	How Administered	Frequency	Side Effects	Comments
Bichloroacetic acid (BCA) or trichloroacetic acid (TCA).	By clinician, solution applied in several thin coats to wart(s). Dries as a white "frost"	Q 1-2 weeks, up to 6 applications	burning	Don't reapply if the area is not healed from prior treatment.
Podophyllin 10% to 25% resin	By clinician, small amount applied to each wart, air dry	Q week until warts are gone	pain, ulceration, scarring	Wash off several hours after application to decrease toxicity and systemic absorption.
Podofilox 0.5% gel or solution	By patient, applied with an applicator/ swab to visible warts	BID for 3 consecutive days each week	pain redness,	No need to wash off. Not for use in pregnancy
Imiquimod 5%	By patient, applied in thin film to warts at bedtime.	Three times weekly for up to 16 weeks.	pain, or ulceration	Wash off in morning.
alpha-interferon	By clinician, intralesional injection	Depends upon response	fever, myalgia, flu-like symptoms	Not for use in pregnancy
surgical excision	By clinician, with scalpel, scissors, laser, or electrocautery	Once	pain, infection	Requires local or general anesthesia
cryotherapy	By clinician, warts are frozen with liquid nitrogen	Q 1-2 weeks for 3-6 treatments	pain, blistering, scarring	Most effective with several freeze-thaw cycles for 10-25 seconds per freeze

Disclosures:
**Nothing to disclose.*

CASE STUDY: Diarrhea in a Patient with AIDS

Bethany Weaver, D.O., M.P.H., Acting Instructor of Medicine, University of Washington Center for AIDS & STD Research (CFAR) and Northwest Correctional Medicine Education Program.*

***CASE:** A 43-year-old male inmate with stage C3 HIV/AIDS presents with loose, watery stools, abdominal cramping, sweats, fevers, poor appetite (2 months) and 15 lbs weight loss. He is taking Combivir one tablet bid and Nelfinavir 1000mg tid, and trimethoprim/sulfamethoxazole for secondary pneumocystis carinii pneumonia (PCP) prophylaxis. He reports good adherence, with an undetectable viral load and a CD4 count of 100 cells/mm^3. He was diagnosed with HIV and PCP when he entered the U.S. from Mexico one year ago, at which time he had a CD4 count of 2 cells/mm^3 and "high" HIV-1 viral load. He is an injecting drug user and has sex only with men. He reports unprotected sex with two anonymous partners two to three months ago when he traveled to Mexico. He weighs 130 lbs and is afebrile with normal blood pressure, genital and neurologic exam. His pharynx was without thrush; there was no scleral jaundice, some temporal wasting, no rash, abdominal tenderness, organomegaly, lymphadenopathy, or peripheral edema.*

Q: What is the differential diagnosis?
A: Opportunistic pathogens such as disseminated Mycobacterium avium complex (MAC), PCP, and cytomegalovirus (CMV), should be considered, though PCP does not typically cause GI disease. He is also at risk for Entamoeba histolytica, Dientamoeba fragilis, Blastocystis hominis, Giardia lamblia, Campylobacter jejuni, Shigella spp, Salmonella spp, C. difficile, syphilis and herpes simplex virus. Because of recent travel to Mexico, Escherichia coli, Vibrio parahaemolyticus, Yersinia spp, rotaviruses, and Norwalk-like viruses are also in the differential. Additionally, this inmate could have diarrhea and wasting from HIV itself. It is not likely that Nelfinavir is causing his diahhrea as he tolerated this drug for nine to ten months and only recently developed diarrhea. Though the Nelfinavir may not be the cause of the diarrhea, it may be aggravating it.

Q: What tests should you perform/order?
A: Stool samples should be sent for for WBCs, to help differentiate inflammatory from non-inflammatory causes of diarrhea (history of watery as opposed to bloody diarrhea suggests non-inflammatory). Stool samples should also be sent for culture for enteric pathogens, smear for ova and parasites, Giardia antigen, Clostridium difficile toxins A and B, and acid-fast bacilli (AFB) smear and culture. Tests for ova and parasites, C.difficile toxins, and smears for AFB should be repeated twice, as it often takes multiple evaluations before some of these pathogens are detected. Blood should be sent for AFB culture and routine bacterial culture. If there is no temporal association of the onset of diarrhea with antiretroviral therapy and the stool and blood studies are negative, the next step in the evaluation is a colonoscopy. The highest yield for colonoscopy is typically in patients with fever, weight loss, and a CD4 count of fewer than 200 cells/mm^3.

Concentrated exam of the stool showed many cysts of Giardia lamblia and Entamoeba histolytica. This diagnosis should be reported to the local public health department. Many Entamoeba coli cysts, many Endolimax nana cysts, and moderate Iodamoeba butschlii cysts were also seen. On auramine stain, moderate cryptosporidia were detected.

Q: What treatment(s) should you offer this inmate? Are there drug-drug interactions to consider?
A: Endolimax nana, Entamoeba coli, and Iodamoeba butschlii are nonpathogenic commensals and as such require no treatment. They are however markers of exposure to human feces and are often found in patients who are also infected with pathogenic organisms. Giardia and Entamoeba histolytica can cause invasive disease and should generally be treated.

The drug of choice for giardiasis is metronidazole 250 mg tid for 7 days, which also has activity against E. histolytica. Unfortunately, there are no reliable therapies for Cryptosporidiosis, though paromomycin or nitazoxanide may have activity and offer benefit. Supportive care with hydration and nutrition, as well as institution of an effective antiretroviral regimen, are crucial aspects of care since improvement in the immune system often helps eradicate the infection. In immunocompetent hosts, cryptosporidiosis is usually self-limited. It may be in this inmate's best interest to change his medications to a more potent antiretroviral regimen in an effort to improve his T cell response and minimize his gastrointestinal side effects. If the regimen is not changed, the dose of Nelfinavir should be changed to 1250mg po bid as this dose is easier to take and is associated with fewer loose stools compared to the tid dose. There are no known drug-drug interactions between metronidazole, paromomycin, or nitazoxanide and the antiretrovirals he is currently taking. There is a drug-drug interaction between the oral solution form of the protease inhibitor amprenavir and metronidazole. This is not true for the capsule formulation of amprenavir.

Q: What infection-control measures should you recommend?
A: To minimize secondary transmission to others via fecal-oral spread, it is important to educate the inmate and staff on good hand-washing skills, particularly before and after meals and use of the restroom. He should be excluded from any kitchen work until his diarrhea has resolved and his stool is cleared of all organisms.

Disclosures:
**Stockholder: Pfizer*

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References continued on page 7

SPOTLIGHT: Keys to Successful HIV Management in Corrections-

Knowing the patient and the prison/jail environment

Joseph Paris, MD, CCHP Georgia Department of Corrections*

A university-based ID consultant familiar with prisoners and detainees is puzzled. After initial success, the patient, a 29 year-old Haitian male, now has a viral load of 185,000. In accented English, the patient states that he has taken all his medications. A quick check of three months of Medication Administration Records shows that all his antiretrovirals (ARVs) are given under Directly Observed Therapy (DOT), and that fewer than three percent of doses were missed.

When first seen by the consultant, the case had seemed simple. The prisoner said that his injecting drug use started a decade ago, and that he had never taken antiretroviral therapy before. The prison family practitioner had obtained a positive HIV antibody, a CD4 count of 20, and a viral load of 15,000. The consultant recommended Didanosine (ddI) EC, Atazanavir, and Lamivudine (3TC). For the first two months, the patient's viral load was undetectable and his CD4 count was rising. However, four months into the therapy, viral loads were increasing. The consultant ordered a genotype, which showed the presence of mutations K65R, I50L, and M184V, suggesting that all three drugs were failing. What went wrong?

The consultant had the foresight to call the referring prison practitioner to discuss this patient's circumstances, and a number of facts emerged. Although both the consultant and primary care doctor had educated the patient on the need to take the ddI EC one hour before breakfast, and the Atazanavir during the meal, the patient found it too difficult to comply with these instructions in the correctional setting. In his segregation unit, breakfast was at 4:30 a.m. on weekdays and 6:00 a.m. on Saturdays and Sundays. ART and other DOT medications were administered cell by cell by a nurse who began most days at 6:00 a.m. and finished at 8:00 a.m. or later. Depending on which end of the wing the nurse started, this inmate may receive his ART as early as 6:00 a.m. or as late as 8:00 a.m. The inmate had decided to take all his medications together, usually after breakfast. To compound the problem, he had a chronically upset stomach and resorted to purchasing variable amounts of antacids from the Commissary. As a result, antacids and the Didanosine EC buffering were inactivating the Atazanavir. A valuable opportunity to stabilize the patient with his first regimen had been lost.

> **"** It used to be said that, in ART, the best medication regimen is the one that the patient will take. The newer version now reads: the best medication regimen is the one that the patient will take at the right time.**"**

This case illustrates two points: the well known necessity to time certain ART with regard to meals, and the challenges of so doing in the correctional environment. To succeed, both consultants and primary care givers need to understand the totality of the patient circumstances and proceed accordingly. The National Institutes of Health has published guidelines entitled *Use of Antiretroviral Agents in HIV-infected Adults and Adolescents*. These guidelines available at www.aidsinfo.nih.gov provide useful information concerning drug-drug interactions and antiretroviral medications that are no longer recommended for the treatment of HIV-infected patients. Practitioners should question patients extensively concerning the variability of pill calls, DOT lines and meals. In some cases, it may not be prudent to prescribe drugs with strict meal timing requirements. In other situations, a light snack may be provided so the inmate can time his meal to scheduled ART accordingly. Finally, even in DOT systems, it may be necessary to make an exception for certain medications to be self-administered, so as to permit the proper timing with respect to food. Open lines of communication with patients on ART are a necessity. It used to be said that, in ART, the best medication regimen is the one that the patient will take. The newer version now reads: the best medication regimen is the one that the patient will take at the right time.

Disclosures:
**Nothing to disclose.*

CASE STUDY: DIARRHEA IN PATIENTS WITH AIDS...

(continued from page 6)

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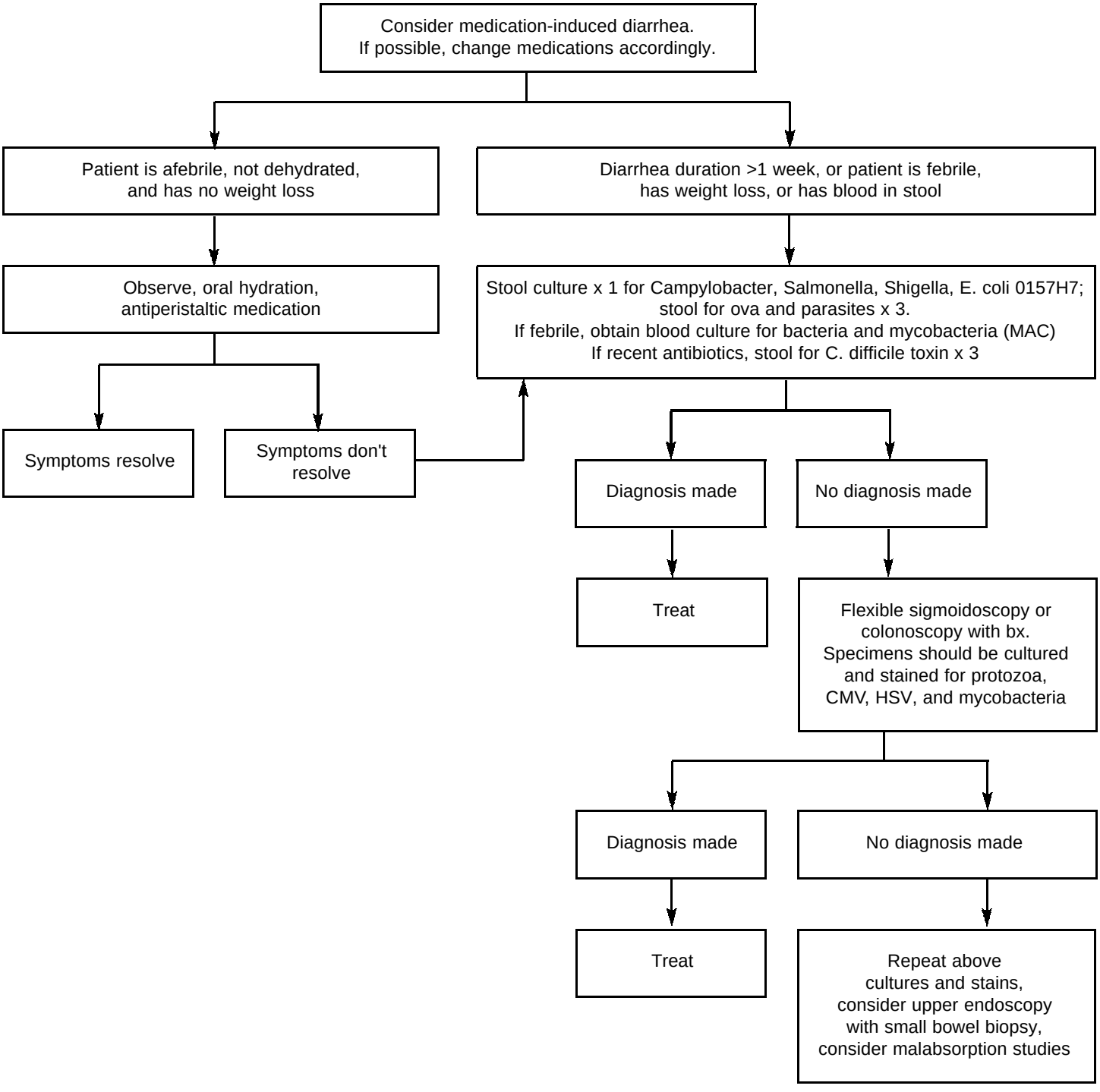
Parasites and Parasitologic Resources of the Ohio State University www.bioscy.ohio-state.edu/~parasite/

HEPPIGRAM: Evaluation of Diarrhea in Patients with HIV

Joseph Bick, MD, Chief Medical Officer, California Medical Facility, California Department of Corrections

Diarrhea is defined as loose, watery stools occurring more than three times in one day. The average adult has a bout of diarrhea four times per year. It is a common problem that usually lasts a day or two and goes away on its own without any special treatment. Prolonged diarrhea can be due to a variety of pathogens as outlined in the HEPPigram below.

Keep in mind that patients may use the word diarrhea to describe anything from an upset stomach, to occasional watery stools, to frequent voluminous bowel movements. Sometimes, patients may require observation to allow objective documentation of symptoms. Reliably obtaining stool specimens in the correctional setting can be challenging and may require a brief stay in the infirmary.



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Inside News

CROI Update Part II:

Continued from HEPP Report, March 2004

Rick Altice, MD, Director, HIV in Prison Program, Yale University AIDS Program*

Comparison of Two Boosted PIs in Heavily ART-experienced patients

BMS-045 is a randomized controlled trial of the once-daily boosted atazanavir (ATV/r) vs. twice-daily boosted lopinavir (LPV/r). A third arm with the dual PI combination of ATV+SQV was also used, but for a number of reasons, was clearly inferior to either of the arms. Eligibility for this study included having failed at least two ART regimens and at least one regimen from two different classes. All subjects were given tenofovir + another NRTI after the first two weeks of the boosted PI. Patients were similarly matched on demographic characteristics, prior AIDS (28%), median VL on HAART (4.45 log) and CD4 (~300) and prior type and duration of HAART use (prior PI use ~2.5 years). With regard to 48 week outcomes, both arms resulted in similar reductions in VL (~1.9 log), increases in CD4 (~120 cell/mL) and using an intent-to-treat analysis (ITT), VL<400 (56%) and VL<50 (~39%). Efficacy was dependent on the number of PI mutations present at baseline and similar between the two groups. Subjects who had fewer than four major PI mutations were more likely to have a virological response compared to those with four or more mutations. Unlike previous studies with LPV/r, however, the investigators did not analyze whether a similar break point of six mutations portended a better outcome between the two comparison arms. Withdrawal due to adverse events in both groups was low (5%), however compared to LPV/r, there was less diarrhea (3% vs. 11%) and more jaundice (6% vs. 0%) in the ATV/r arm. In the ATV/r arm, the proportion of subjects who experienced bilirubin >2.5 mg/dl and >5.0 mg/dl was 39% and 9%, respectively. No patient withdrew from the study for hyperbilirubinemia and was not associated with changes in hepatic transaminases. Use of antidiarrheal agents was significantly less in the ATV/r (6%) arm compared to the LPV/r (24%) arm. Anxiously awaited was whether boosted ATV would continue to maintain a lipid benefit in subjects. Compared to LPV/r, ATV/r resulted in lower mean changes in cholesterol (-8% vs. +6%) and triglycerides (-4% vs. +30%) even after censoring data for those who started lipid-lowering agents. Clinically, the ATV/r group was less likely to initiate lipid-lowering therapy than the LPV/r group (8% vs. 19%). In summary, once-daily ATV/r has similar efficacy to the standard twice-daily LPV/r in heavily pre-treated subjects with drug-associated clinical diarrhea and hyperlipidemia. ATV/r does, however, result in increased bilirubin levels that is not associated with liver toxicity.

Standard LPV/r Dosing vs. Once-Daily Treatment

In a study of 190 ART-naïve patients, randomized in a 3:2 schema and who received the NRTI backbone of once-daily emtricitibine (FTC) + tenofovir (TDF), subjects received either once-daily (six Kaletra all at once) or twice-daily (three Kaletra twice daily) LPV/r. The subjects had similar background characteristics, including mean baseline CD4 = 216 (45% with CD4 <200) and VL=4.8 log (~65,000 copies/mL). Both groups had an impressive increase in CD4 (~185) and VL was assessed using ITT and as-treated (AT) approaches. Compared to the standard twice-daily therapy, the proportion with a VL<50 at 48 weeks in the once-daily arm was 70% vs. 64% using ITT and 90% vs. 85% using AT analysis, respectively (no significant differences). Though total discontinuations for the study was no different between groups (19% vs. 25%), it was higher than found in other studies of Kaletra. Discontinuation due to adverse side effects, however, was higher in the once-daily group (12% vs. 5%); diarrhea was also significantly greater in the once-daily group (16% vs. 5%). Mean triglyceride changes did not differ between the groups (+82 mg/dL vs. +76 mg/dL). In sum, this provides supportive data for the use of once-daily LPV/r in ART naïve subjects for up to 48 weeks, particularly at a time when simplified regimens are preferred in correctional settings.

Disclosures:

**Consultant and Speaker's Bureau: Agouron, Abbott, BMX, Boehringer Ingleheim, DuPont,*

Resources

General Information on diarrhea:
http://digestive.niddk.nih.gov/ddiseases/pubs/diarrhea/index.htm#whatis

Information on diarrhea associated with HIV:
www.aids.org/factSheets/554-Diarrhea.html

The CDC's 2002 treatment guidelines for genital warts and other STDs:
www.cdc.gov/std/treatment

Guidelines for Using Antiretroviral Agents Among HIV-Infected Adults and Adolescents:
www.cdc.gov/mmwr/preview/mmwrhtml/rr5107a1.htm

Recommendations and tables on HIV:
www.hivguidelines.org/public_html/center/clinical-guidelines/adult_hiv_guidelines/supplemental_pages/other/pdf/gastro-recandtab.pdf

Self-Assessment Test for Continuing Medical Education Credit

Brown Medical School designates this educational activity for 1 hour in category 1 credit toward the AMA Physician's Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through October 31, 2004. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. Most mild cases of thrush can be treated effectively with:
   a) intravenous amphotericin
   b) oral fluconazole
   c) nystatin or clotrimazole
   d) oral azole

2. A patient who presents with odynophgia, retrosternal pain, nausea, emesis and tracheoesophageal fistula most likely has:
   a) candida esphogitis
   b) esophageal herpes simplex virus
   c) cytomegalovirus (CMV)
   d) none of the above

3. Drugs that commonly cause a change in bowel motility include:
   a) psychiatric medications
   b) some antiretroviral and cardiac medications
   c) antacids
   d) all of the above

4. In an HIV-infected patient who presents with diarrhea that lasts for more than one week, it is recommended to send three separately collected specimens for ova and parasite analysis.
   a) True
   b) False

5. Bacteremic disease in those with HIV infection is most likely a result of:
   a) Salmonella infection
   b) Shigella infection
   c) Campylobacter infection
   d) Mycobacterium avium complex (MAC)
   e) Areomonas infection

6. An effective, long-term strategy for controlling MAC, CMV, and histoplasmosis is:
   a) amphtericin B or itraconazole
   b) foscarnet
   c) immune reconstitution
   d) none of the above

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