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AN EVIDENCE-BASED APPROACH TO EMERGENCY MEDICINE

HIV-Related Illnesses: The Challenge Of ED Management

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CME Objectives

Upon completing this article, you should be able to:
1. assess a patient's risk of being infected with HIV, describe the importance of the CD4 count in determining the stage of infection, and evaluate the risk of infection with opportunistic pathogens;
2. describe the most common CNS, gastrointestinal, and respiratory complications of HIV-associated disease as well as their proper evaluation and treatment;
3. evaluate and manage the febrile AIDS patient; and
4. describe the most common side effects and toxicities of drugs used to treat HIV infection and AIDS.

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The triage note is innocuous enough—"fever for one week"—but when you walk into the room, you realize something else is going on. This young man is cachetic with thinning hair, and his spindly arms are crusted with an awful rash. As he speaks, you notice ominous white patches covering his tongue. His voice rasps, "Doc, can you help me? I think I have a virus."

PATIENTS infected with HIV present unique challenges for the emergency physician. Many are asymptomatic and are at no special risk for unusual diseases. However, those who progress to AIDS are susceptible to a wide range of opportunistic and traditional infections. Furthermore, even the therapies for HIV infection cause significant complications and morbidity.

Many of those infected with HIV are unaware of their serologic status. For this reason, *it is important to consider the possibility of HIV-related illness in anyone presenting with complaints suggestive of infection.* If a patient has known or suspected HIV infection, determining the degree of immunosuppression helps evaluate the risk of opportunistic disease.

HIV-infected patients may complain of vague constitutional symptoms, such as fever, weight loss, and fatigue. Others have complaints localized to a specific organ system—pulmonary, neurologic, abdominal, head and neck, dermatological, or psychiatric.[1] Lung and CNS infections are the most common illnesses identified in HIV-positive patients presenting to the ED.

Because AIDS-related infections frequently present atypically or with subtle findings, a high index of suspicion and an aggressive approach to diagnosis are crucial for successful management. Although AIDS-related infections often cannot be cured, many can be successfully treated in the short term and perhaps controlled in the long term using suppressive therapy.

The intimidating array of pathologies associated with HIV, as well as the dizzying pace of new developments, daunts many physicians. Fear not: This issue of *Emergency Medicine Practice* provides indispensable insight to the management of common HIV complications seen in the ED.

Epidemiology

The earliest known HIV infection was discovered in a stored blood plasma sample dating from 1959. The victim, from Leopoldville (now Kinshasa), in the Democratic Republic of Congo, puzzled local physicians with his symptoms. While they were unable to save him, they did save his blood—which decades later proved to harbor HIV.[2] Computer models suggest that the epidemic may have begun in central West Africa around 1930.[3] The early origins of human infection are shrouded in controversy; one theory suggests transmission of a simian AIDS virus via cuts on the hands of human hunters, while another suggests unsanitary immunization practices.[4,5]

The first report of AIDS in the United States involved five cases of unexplained immune deficiency in homosexual men in Los Angeles in June 1981. From there, the epidemic exploded; by the end of 2000, 774,467 Americans had met the case definition for the disease. In 2000, the Centers for Disease Control and Prevention estimated that 650,000-900,000 Americans are infected with HIV, and over 320,000 have AIDS.[6]

The dynamic of the epidemic has changed dramatically since the advent of highly active antiretroviral therapy (HAART), which uses protease inhibitors and other new agents in multi-drug regimens. Although the rate of new cases of HIV infection has remained steady, at 40,000 per year, the death rate has dropped significantly (a 50% decline in 1997 and 21% in 1998).[7,8] Yet for some segments of the population, especially Hispanics and African-Americans, the rates of infection are increasing. Heterosexual contact is the fastest-growing category of HIV transmission in the United States.

The local prevalence of HIV infection may vary widely, from nearly 0% in some rural locales to over 10% in some inner-city EDs, with an average of 0.56% for the U.S. population as a whole.[9,10] The prevalence of HIV in the ED is steadily growing. In one study, HIV-positive adults in an urban ED increased from 6.0% in 1988 to 11.4% by 1992.[11]

Pathophysiology And Natural History

The mechanism for immune destruction by HIV is complex and remains the focus of intense investigation. The virus gains entrance into the target cell after binding with the CD4 receptor and one of several chemokine receptors. Complex protein interactions fuse the viral capsule and the cell membrane.[12] The CD4+ T lymphocyte, also known as the T helper cell, is the primary target, but any cell expressing this receptor is susceptible to infection.

During the first 4-6 weeks of infection, the number of viral particles soars, and the virus disseminates throughout the circulation and lymphoid tissue. It is estimated that 55%-92% of patients experience the acute retroviral syndrome, a mononucleosis-like illness characterized by fever and generalized lymphadenopathy. Patients may also develop pharyngitis, rash, myalgias, headache, nausea, and diarrhea.[13,14]

As an immune response to the virus is generated, the viral load falls and a variable period of clinical latency ensues. During this stage, the CD4 count exceeds 500/mm^3. Opportunistic infections are rare, but patients may present with generalized lymphadenopathy or aseptic meningitis. The latency period may last 2-10 years or more, but despite the paucity of symptoms, levels of CD4+ cells decline. This depletion is due to both viral-mediated cell destruction and inhibition of normal T cell production.[15] Eventually, the loss of CD4+ cells and the resulting immunodeficiency permit infection from an opportunistic pathogen. At this stage of HIV infection—defined as AIDS—the viral load climbs steadily; in the absence of therapy, clinical decline is inexorable. Once this stage is reached, the median survival is 9-12 months if the patient remains untreated.[16,17]

"Fear and ignorance about AIDS can so weaken people's senses as to make them susceptible to an equally virulent threat: bigotry."
—"AIDS and the New Apartheid," editorial, New York Times, October 7, 1985.

Specific CD4 Levels

A patient with a CD4 count of 200-500/mm^3 may develop lymphadenopathy, oral candidiasis, idiopathic thrombocytopenic purpura, or hairy leukoplakia. This stage also predisposes the patient to more virulent pathogens, such as *M. tuberculosis* or *S. pneumoniae*.[18] Antiretroviral drugs are generally indicated for this degree of immunosuppression.

A CD4 count less than 200/mm^3 leads to more advanced disease. It is important to identify patients in this category, because they are at much higher risk of opportunistic infections, including *Pneumocystis carinii* pneumonia (PCP), tuberculosis (TB), toxoplasmosis, cryptosporidiosis, isosporiasis, esophageal candidiasis, cryptococcosis, and histoplasmosis. Disseminated *Mycobacterium avium* complex (MAC) or cytomegalovirus (CMV) infection tend to occur in patients with CD4 counts of less than 50/mm^3.

Anyone who reports a previous opportunistic infection has, at some point, reached a critical CD4 nadir. Patients at this stage need both antiretroviral therapy and prophylaxis against opportunistic infections. An exception to this, however, is those who have experienced a successful immune reconstitution,

defined by a rise in their CD4 count to above 200 / mm^3. These patients will be continued on antiretroviral therapy but may stop taking PCP prophylaxis.[19]

Prehospital Care

The response of emergency medical service (EMS) units to a patient with HIV infection or AIDS should be no different than for an uninfected individual. Usually, the EMS personnel will be unaware of the patient's serologic status (as might the patients themselves). As with any healthcare situation, standard (previously called universal) precautions should be followed. EMS personnel should wear gloves and place a mask on patients with a cough when it is safe to do so. Very little literature has been published that directly addresses prehospital care of the HIV-infected patient.

ED Evaluation

History

One of the most valuable questions an emergency physician can ask when faced with a febrile patient with cough or constitutional symptoms is: "Have you ever been tested for the AIDS virus?" Up to 30% of HIV patients may not spontaneously disclose their serological status when seeking medical care.[20] On the other hand, many HIV-infected people in the United States are unaware of their serologic status. Unrecognized HIV infection is common in the ED, especially among women and the elderly.[21,22] Amazingly, a small percentage of patients claiming to have AIDS may, in fact, be HIV-negative. The deception may be engineered in order to receive preferential treatment in housing, disability payments, prescription drugs, or medical care.[23]

Factors associated with an increased risk of HIV infection include men who have sex with men, injection drug use, prostitution, heterosexual exposure to a partner at risk, and exposure to a blood product in the United States prior to 1985. Children born of mothers in such groups are also at risk. Because the number of people who fall into one or more of the high-risk groups is still a fairly small proportion of the general population, identification of risk factors remains important. However, as the epidemiology of HIV transmission continues to evolve and heterosexual transmission becomes more common, risk factor determination may become less useful.

Question patients about HIV risk factors if they present with complaints suggestive of infectious disease, especially respiratory illness, fever, headaches, diarrhea, and rashes. Possible risk factors among their sexual partners are germane. Although some patients may sometimes be hesitant to answer questions about such personal matters as sexuality and drug use, most will make an honest disclosure when questions are asked in a straightforward, nonjudgmental manner.[24]

If HIV infection is known or suspected, the next step is to estimate the stage of the disease. The expected complications of HIV infection vary depending on the phase of disease. (See **Table 1**.) Inquire about prior hospitalizations or complications. Any patient who reports a previous opportunistic infection has, at some point, had a CD4 count below 200 / mm^3.

In the evaluation of known seropositive patients, the CD4 count can provide valuable insight into the stage of HIV disease and the risk of opportunistic infection. Some patients may be able to report their latest CD4 count and when it was obtained. Those less medically sophisticated or lacking ready access to medical care may have no idea about their CD4 count. If the patient is receiving regular medical care, the list of medications may also suggest the stage of his or her disease.

Physical Examination

In addition to a careful and compassionate history, an appropriate physical examination is essential. The only study to address the sensitivity of the physical examination to detect HIV infection was conducted among infants.[25] However, cohort studies show that certain physical findings provide important clues to HIV-related infections.

Many patients in the advanced stages of AIDS can be detected with a "doorway diagnosis." Look to the general appearance of a patient for indications of advanced disease. Wasting (malnutrition) and lipodystrophy are the two major nutritional alterations in HIV, and temporal wasting and parietal hair loss are common.[26] Determine early during the encounter whether the patient is in respiratory distress.

Pay special attention to the oral examination. The finding of oral candidiasis or hairy leukoplakia in a patient with a fever suggests an HIV-related illness. Patients with oral lesions tend to have low CD4 counts and fast disease progression (especially when they remain untreated).[27,28] Thrush does not necessarily equal AIDS; other causes for oral candidiasis include out-of-control diabetes, recent antibiotic or inhaled steroid use, or chemotherapy.

Table 1. Staging Of HIV Disease.

Stage	Clinical appearance	CD4 Count
Acute	Mono-like syndrome	Normal
Early	Asymptomatic, or lymphadenopathy, aseptic meningitis, skin disease	> 500/mm^3
Middle	Asymptomatic, or lymphadenopathy, thrush, idiopathic thrombocytopenic purpura, hairy leukoplakia	200-500/mm^3
Late	Opportunistic infections, malignancy, dementia, wasting	< 200/mm^3

While the lung exam may reveal rales or other signs of pulmonary disease, *many patients with PCP pneumonia will have clear breath sounds.* In addition to traditional auscultation, there is another useful test known as auscultatory percussion. To perform this maneuver, place the diaphragm of the stethoscope on the posterior chest of the patient, and lightly tap the manubrium with the tip of the index or middle finger. Compare the sounds in opposite sides of the posterior chest, taking care that the stethoscope is placed in the same interspace on the right and left sides. Differences in the quality, pitch, duration, or intensity of breath sounds suggest lung pathology. In one study of HIV-positive patients, auscultatory percussion was more predictive (51.0%-69.6% sensitive) of chest x-ray abnormalities than standard percussion or traditional auscultation.[29] Still, the most reasonable approach to the HIV-positive patient with a pulmonary complaint is auscultation—then order a chest film regardless of the findings.

Other notable aspects of the physical exam include generalized lymphadenopathy, Kaposi's sarcoma (raised, purplish lesions), severe persistent dermatosis, and "track marks" from injection drug use. Seborrheic dermatitis, onychomycosis, herpes simplex, widespread scabies, alopecia, and rashes from systemic mycoses are common in HIV disease. Any underlying chronic dermatologic condition (psoriasis, seborrhea, eczema, etc.) may become exacerbated as immunosuppression progresses.

Both HIV and the medications used to treat it may cause neuropathy, manifested as sensory loss or abnormal reflexes.

Primary HIV Infection

Some believe it is important to diagnose acute retroviral syndrome because intervention with antiretroviral treatment during this stage may improve the long-term course of HIV infection. However, this improvement seems to be short-lived.[30,31]

As previously mentioned, 55%-92% of patients initially exposed to HIV experience the acute retroviral syndrome, a mononucleosis-like illness with fever and generalized lymphadenopathy. Patients with more severe symptoms at seroconversion have a faster disease progression.[32] Patients presenting with compatible symptoms may be questioned about HIV risk factors, and those with likely exposure should be tested or referred for testing. The HIV antibody test that is usually done to diagnose HIV infection is typically negative during the acute retroviral stage (the standard ELISA test requires a mean of 27 days following exposure to become positive).[33] Diagnosis at this stage would require testing for p24 antigen or detecting HIV viral RNA directly.

Not every patient with nonspecific viral symptoms warrants p24 testing. Which patients are at sufficiently high risk should be determined by the history and physical exam.

"AIDS was ... an illness in stages, a very long flight of steps that led assuredly to death, but whose every step represented a unique apprenticeship. It was a disease that gave death time to live and its victims time to die, time to discover time, and in the end to discover life."
—Hervé Guibert, French writer (1955–1991).
To the Friend Who Did Not Save My Life,
chapter 61, 1991.

Fever In HIV-Infected Patients

Fever is a common presenting complaint in HIV-infected patients, and it can be a diagnostic challenge for the emergency physician. The differential diagnosis of fever in HIV-infected patients is broad and includes potentially life-threatening infections.[34] (See **Table 2**.)

Fever is common in the seropositive patient. In one prospective study of 176 patients with advanced HIV, almost half had an episode of fever over a nine-month period, and a diagnosis was made in 83% of these. Lung infection accounted for more than 25%, while CNS infection accounted for more than 10%. Other common etiologies included disseminated MAC, line infection, sinusitis, and drug reaction. Among patients whose fever required more than two weeks to diagnose, the most common etiologies were lymphoma, *Mycobacterium avium*-intracellulare bacteremia, or PCP.[35]

Not all fever equals infection. HIV-positive patients with fever may be suffering from a drug reaction. Hyperthermia, tachycardia, and tachypnea may be manifestations of a variety of drug effects, including neuroleptic malignant or anticholinergic syndromes, serotonin crisis, malignant hyperthermia, heatstroke, and aspirin or sympathomimetic overdose. HIV infection is a known risk factor for neuroleptic malignant syndrome and should be considered in any seropositive patient who takes an implicated antipsychotic medication, especially if they present with fever and some combination of cogwheeling, diaphoresis, disorientation, or rigidity.[36] The antiretroviral drug abacavir (Ziagen) can cause a hypersensitivity reaction characterized by malaise, fever, and nausea, with or without vomiting. In such cases, the drug must be stopped and never restarted as fatal reactions may occur.[161]

Table 2. Common Etiologies Of Fever In AIDS Patients.

- *P. carinii* and other pneumonias
- Disseminated *M. avium* complex infection
- Lymphoma
- Infection of indwelling central lines
- Sinusitis
- Toxoplasmosis
- Cryptococcal meningitis
- Salmonellosis
- Tuberculosis
- Drug reactions
- Bacteremia/sepsis
- Cytomegalovirus

The history and physical examination provide important clues to the etiology of the fever. Determine how long or how often the patient has had fever. Prolonged fever is less likely to represent a treatable emergency. Ask regarding cough or shortness of breath. A new or worsening headache or neurological deficit in the HIV-positive patient with a low or unknown CD4 count suggests a CNS infection. Some constellation of nasal congestion / discharge, headache, or sinus tenderness may presage sinusitis, a common infection in the HIV-infected patient.[37] Most patients with significant intra-abdominal pathology will have both abdominal pain and tenderness. Back pain or tenderness in the HIV-infected patient may reflect endocarditis (especially in IV drug users), UTI, or a spinal infection or neoplasm.[38,39] Flank pain may also result from kidney stones, especially in those taking Indinavir. Patients with fever and extremity pain or tenderness may suffer pyomyositis[40] or, in the case of a painful joint, septic arthritis.

Laboratory Studies

History and physical examination supply the basis for additional diagnostic studies. Blood tests seem to be a reasonable response to fever in the AIDS patient, but the data are often slim. In particular, the value of the CBC in management of suspected or known HIV complications remains unknown. One study (published only in abstract form) showed that a high band count predicted positive blood cultures in HIV-positive patients.[41] If a CBC is drawn, recognize that HIV infection alone may induce eosinophilia.[42] Studies do show that neutropenia is strongly associated with risk of severe infections in those with end-stage AIDS[43] and in particular is linked to pseudomonal bacteremia.[44] One cohort study found that the rate of bacteremia due to *Escherichia coli, Klebsiella pneumoniae,* or *Pseudomonas aeruginosa* is increased eightfold when the absolute neutrophil count is less than or equal to 500 / mm^3. (However, in this study, the absolute neutrophil count was measured in a routine blood test the week *before* bacteremia developed, not during the acute event.)

Estimating The CD4 Count Using A CBC

The CD4 count is one of the best predictors of the risk for an opportunistic infection. However, obtaining a CD4 count within the time frame of an ED evaluation is generally not feasible. Fortunately, the absolute lymphocyte count (ALC) may represent a surrogate marker for the CD4 count.

The ALC can be calculated using data provided by the CBC and differential, like so:

ALC =
total white blood cell count X lymphocyte percentage

Two studies performed in a clinic (non-ED) setting showed a good correlation between the CD4 count and ALC.[45,46] On the other hand, these two studies are not necessarily applicable to the ED population, since all of the participants were tested during routine examinations, not while they were acutely ill. A third study, from Temple University, examined 807 blood samples where both a CD4 and a CBC with differential were ordered on HIV-positive patients.[47] In this retrospective investigation, CBCs were drawn in a variety of different settings, including clinics, inpatient wards, and EDs. While a single ALC threshold was neither sensitive nor specific for a low CD4 count, the investigators determined two valuable cut-offs of 1000 and 2000 cells / mm^3. An ALC less than 1000 cells / mm^3 was 91% predictive in identifying patients with CD4 counts less than 200 cells / mm^3 (sensitivity only 67%, but specificity 96%), while an ALC greater than 2000 cells / mm^3 was 95% predictive in identifying CD4 counts greater than 200 cells / mm^3. *The authors concluded that patients with ALCs greater than 2000 cells/mm^3 might be less susceptible to opportunistic infections, while those with ALCs less than 1000 cells/mm^3 are at higher risk.*[47] Unfortunately, these researchers had no access to clinical data and could not account for factors such as antiretroviral therapy or the presence of acute infection such as sepsis, pneumonia, or TB.

Other Laboratory Tests

Because of the possibility of bacteremia with *S. pneumoniae, Salmonella* sp., or other organisms, some suggest that blood cultures be obtained in the febrile HIV patient. The utility of this approach is unknown. Blood cultures may be useful in diagnosing unsuspected MAC disease in those with low CD4 counts.[48] High-risk subgroups that may benefit most from blood cultures include those who appear toxic, injection drug users, those with signs of bacterial endocarditis (especially a new heart murmur), those with a central venous catheter, persons with very low CD4 counts (< 50 cells / mm^3), and patients with neutropenia and fever. One study showed that bacteremia in young HIV-infected children was associated with fever of 102.2˚F or greater, a WBC count of 15,000 cells / mm^3 or greater, and the presence of a central venous catheter.[49]

Dipstick or microscopic evaluation of the urine is indicated in patients with urinary symptoms or flank or lower abdominal pain. Because women in general have more UTIs than men, some emergency physicians regularly examine the urine in women with HIV who have no obvious source for their fever. However, routine urinalysis might also be valuable in the febrile *male* with advanced HIV disease. One study showed that HIV-infected men with CD4+ cell counts less than 200 x 10^6 / L are at increased risk for bacteriuria,[50] while another found that half of male AIDS patients with a UTI had no urinary symptoms.[51]

Radiographic Studies

Some authorities recommend chest radiography in all

febrile HIV-infected patients who have fever without a source. They argue that because the symptoms of PCP are often subtle in early stages, chest radiography may detect occult pneumonia.[52] (They further suggest that exercise pulse oximetry and serum LDH should be considered even if the patient lacks significant respiratory symptoms.[53])

Because CNS infection is a common etiology of fever, head computed tomography (CT) and lumbar puncture (LP) should be performed in AIDS patients with unexplained fever who complain of headache or neurologic symptoms. Neurological deficits or meningeal signs are not prerequisites for neuroimaging or LP, since HIV patients with focal lesions often lack focal findings, and cryptococcal meningitis typically presents without classic meningeal findings.[54,55] If the patient has nasal discharge or tenderness of the sinuses, consider CT scan of the sinuses in addition to head CT.

Echocardiography, once a slightly exotic test for the ED, is nowadays a reasonable intervention for the HIV-positive patient with a murmur (at least during daylight hours). A recent history of IV drug abuse significantly raises the likelihood of obtaining a positive study.[56,57]

Disposition

There are no robust studies that tell us which patients with HIV and fever require admission. It is generally accepted that those with unexplained fever who appear acutely ill should be admitted to the hospital for further work-up. Those who do not appear acutely ill can be sent home, provided that close follow-up can be arranged with a primary care provider. The primary care provider should review results of tests such as blood cultures for bacteria and MAC.

Respiratory Complaints

The lungs are the most common site of serious infection in patients with AIDS, and historically *P. carinii* has been the most common pathogen. Because of pneumocystis pneumonia prophylaxis, the disease appears to be occurring less frequently and at a more advanced stage of AIDS.[58] HIV-infected individuals are also at increased risk of bacterial pneumonia caused by *Streptococcus pneumoniae, H. influenzae*, and other bacteria.[59] *Mycobacterium tuberculosis* should be considered in all HIV-infected patients with pneumonia, and it often presents atypically in these patients. Fungi such as *Cryptococcus neoformans, Histoplasma capsulatum,* and *Coccidioides immitis* are less frequent culprits. Occasionally a malignancy such as Kaposi's sarcoma or lymphoma can be mistaken for pneumonia.[60]

Isolation Procedures

Although both risk factors for TB and symptoms of the disease are usually present, the opportunity to isolate TB-infected individuals is often missed at triage.[61] If a patient complaining of shortness of breath or cough and fever is believed (or known) to have HIV infection and / or a low CD4 count, the triage nurse should place him or her in respiratory isolation. Early isolation may protect both the ED staff and other patients from TB.[62] Many nosocomial outbreaks involve multidrug-resistant TB strains and result in very high mortality rates among those infected.[63,64] TB control measures such as respiratory isolation rooms, nonrecirculated air, and droplet shields reduce the spread of TB to ED personnel.[52]

History And Physical Exam

The evaluation of an HIV-infected patient with respiratory symptoms is similar to the evaluation of a patient from the general population. (See also "Clinical Pathway: Evaluation Of Respiratory Complaints In HIV / AIDS Patients" on page 14.) Aside from taking the "usual" history, consider the level of immune impairment, prior exposure to infectious agents, and the use of prophylactic therapy.

Emergency physicians should suspect *Pneumocystis carinii* whenever a patient who is at high risk of HIV infection presents with pneumonia. The classic presentation of PCP is subacute; patients complain of fatigue, fever, and malaise associated with dry cough. Dyspnea is common, especially with exertion. PCP is typically seen in those with CD4 counts less than 200 / mm^3, who may or may not have other markers of immunosuppression, such as Kaposi's sarcoma, lymphoma, oral candidiasis, weight loss, or dementia. Some present to the ED with progressive dyspnea, having been recently and unsuccessfully treated for bacterial pneumonia by their primary care physician.

Looking in the mouth may be more fruitful than auscultating the lungs in some patients with cough. The presence of oral candidiasis in any patient with dyspnea suggests PCP (odds ratio, 2.6).[53] Prophylactic therapy with trimethoprim-sulfamethoxazole (TMP-SMX) or dapsone does not rule out PCP infection, as about one-fifth of compliant patients will suffer breakthrough infections. Nearly one-third of those using aerosolized pentamidine will also develop disease.[65]

Another pathogen to consider is *Mycobacterium tuberculosis*. The incidence of TB in the United States rose by 18% between 1985 and 1992, largely because of the AIDS epidemic. (Fortunately, a comprehensive strengthening of control activities led to the lowest incidence in U.S. history by the year 2000.[66])

Not only are AIDS patients more likely to become infected with TB, their latent infections are also more likely to progress to active disease.[67] Whereas the risk of progression to active TB in a patient without immunosuppression is about 5%-10% over a lifetime, the risk for someone infected with HIV may be as high

as 8% *a year*.[68] Because *M. tuberculosis* is presumably more virulent than *P. carinii* or other opportunistic infections, it tends to occur at an earlier stage of HIV infection.[69]

The most common symptoms associated with pulmonary TB infection (chronic cough, hemoptysis, weight loss, and night sweats) may be absent or subtle in HIV infection.[70] Patients with active pulmonary TB frequently have multiple ED visits and often suffer non-pulmonary complaints.

Chest X-ray

Any patient with known or suspected HIV who presents to the ED with new respiratory symptoms deserves a chest film.

Although "classic" findings for each of the three major categories of HIV-related pneumonias (*P. carinii*, community-acquired bacterial pneumonia, and TB) may be absent, the chest x-ray is a logical first step. Recognize that the radiographic findings of pneumonia are highly variable in HIV disease. Some patients with infection may demonstrate single or multiple pulmonary nodules. In one study of 87 patients, opportunistic infections were the underlying etiology of pulmonary nodules in 57 patients; bacterial pneumonia in 30 patients; and TB in 14 patients.[71]

The classic chest x-ray finding in PCP involves a diffuse interstitial infiltrate. It typically appears as a bilateral interstitial pattern, which may is described as "granular," "reticular," or "ground glass."[72] Findings, however, vary widely and can include lobar or nodular infiltrates, hilar lymphadenopathy, spontaneous pneumothorax, cavitation, and, rarely, pleural effusions.[73] Apical infiltrates are often seen in patients taking prophylactic aerosolized pentamidine.[74] The chest film may also be normal, especially during early PCP.[75] *PCP cannot be reliably distinguished from bacterial pneumonia or TB based on symptoms or chest x-ray.*

While bacterial pneumonia often presents as a lobar infiltrate in the immunocompetent, it may exhibit atypical radiographic findings in the HIV-infected patient. In the immunosuppressed, traditional bacteria may produce diffuse interstitial infiltrates that are frequently misdiagnosed as PCP. In one review, 47% of cases of bacterial pneumonia in HIV-infected patients had chest x-ray findings indistinguishable from the "classic" appearance of PCP.[76]

Although apical cavitary lesions are traditionally associated with TB, pulmonary cavities are rare in AIDS patients with TB, particularly in those with more advanced immunosuppression. In one study of AIDS patients with TB, only 6% had "typical" chest x-ray findings. More common findings included hilar or mediastinal adenopathy or an infiltrate suggestive of pneumonia. About 35% of those with TB had no infiltrate, while 12% had a normal chest x-ray.[77]

Children with AIDS may demonstrate a dramatic finding on chest radiography consisting of diffuse ground-glass opacities known as lymphoid interstitial pneumonitis.

Laboratory Findings

Laboratory analysis can sometimes be helpful in HIV-infected patients with respiratory complaints, especially in patients suffering from PCP. In patients with pneumocystis, arterial blood gases (ABG) often demonstrate hypoxemia with a marked increase in the alveolar-arterial (A-a) oxygen gradient. Because the degree of hypoxia and the size of the A-a gradient have treatment implications (as described later), an ABG is useful in those suspected of PCP.

Pulse oximetry may be normal or near normal in PCP, especially early in the disease. Exercise-induced desaturation is much more predictive of PCP than resting hypoxemia (odds ratio, 4.88 vs 0.69; PPV, 77% vs 66%, respectively).[78] In one study of 45 AIDS patients with pneumonia, subjects were asked to pedal for two minutes on a stretcher bed. In patients with PCP, the SaO2 usually fell by 3% or more, but it increased slightly with exercise in those with non-PCP pneumonia. Sensitivity was 77% and specificity 91%.[79] While few EDs have bicycles mounted on stretchers, having the patient do jumping jacks or jog in place may be a suitable alternative.

Several studies have found that an elevated lactate dehydrogenase (LDH) level suggests pneumocystis pneumonia.[80,81] Although an elevated LDH in patients with dyspnea is a sensitive test, it is nonspecific (sensitivity 94% and specificity 78% for LDH > 220 IU/L).[82] A normal LDH level does not rule out the diagnosis of PCP, but it does make it unlikely (in one study, only 7% of 84 patients with PCP had normal LDH levels).[83]

The gold standard for diagnosis of pneumocystis pneumonia is demonstration of the organism by special stains of induced sputum or bronchoalveolar lavage. Because of the increased risk of TB in AIDS patients, sputum induction should not be done in the ED unless proper isolation facilities are available.

Treatment

Since the radiographic findings cannot reliably distinguish the pathogen in HIV-related pneumonia, how does an emergency physician determine therapy? While there may be clues in the patient's presentation and laboratory results that suggest a particular etiology, one safe approach is to address all of the most common pathogens (*Pneumocystis carinii*, community-acquired bacterial pneumonia, and TB) in each patient.

To a significant extent, treatment will depend on the severity of illness. Which begs the next question: "When should patients with suspected pneumocystis pneumonia be admitted?" Studies show that certain factors predict a poor outcome.[84-86] These include:

- increased LDH
- PO_2 less than 70 mmHg

- wide A-a gradient (usually associated with a low pCO_2)
- abnormal chest film
- previous admission for PCP
- rales on chest exam

Certain patients with these findings—especially those who appear toxic—and individuals who have persistent vomiting should be admitted to the hospital for further work-up. Those with unreliable follow-up should also be admitted. (See also the September 1999 issue of *Emergency Medicine Practice*, "Community-Acquired Pneumonia: Deciding Whom To Admit And Which Antibiotics To Use.") When opting for outpatient treatment, it is important to collaborate with the patient's primary care physician.

Oral Therapy

Although many patients who are diagnosed with pneumocystis pneumonia in the ED will require admission, some with mild illness can be managed as outpatients if close follow-up is available. Oral TMP-SMX is preferred for outpatient therapy; the usual dosage is two double-strength tablets given three times a day for small adults (or four times per day for larger individuals) for 21 days. Other oral treatment options include trimethoprim plus dapsone or clindamycin plus primaquine.[87]

Intravenous Therapy

For patients being admitted to the hospital, initiating therapy in the ED can help avoid delays that can occur if therapy is started after arrival on the ward. The drug of choice is intravenous TMP-SMX. The usual regimen is 15-20 mg/kg/d (based on the trimethoprim) in four divided doses, to be continued for 21 days. TMP-SMX is supplied in ampules containing 80 mg trimethoprim and 400 mg sulfamethoxazole, so for an average-sized adult, the dose is 3 amps every six hours. Potential side effects include rash (occurring in approximately 50% of AIDS patients), neutropenia, and anemia. If side effects are mild (including a mild rash), treatment can usually be continued. For less-severe rashes, diphenhydramine may provide relief.[88]

For patients who cannot tolerate TMP-SMX, intravenous (not aerosolized) pentamidine (4 mg/kg once daily) is regarded as the second-line choice.[89,90] Because it may cause hypotension during infusion, pentamidine should be given over the course of an hour. Monitor blood glucose levels, as pentamidine can result in hypoglycemia.[18] Because pentamidine is not active against bacteria, appropriate coverage for community-acquired pneumonia should be added until pneumocystis pneumonia is verified. Some experts prefer clindamycin 600 mg IV every eight hours, plus primaquine 15 mg base PO each day as a second-line agent because it has less toxicity than pentamidine. Other alternative treatment regimens for pneumocystis include trimethoprim plus dapsone, trimetrexate plus leucovorin, and atovaquone.

Additional Antibiotics

In addition to *Pneumocystis carinii*, AIDS patients are at increased risk of pneumonia caused by typical pathogens, especially *S. pneumoniae*. Because TMP-SMX has activity against the most common bacterial pathogens, some use it as the sole agent for AIDS patients with pneumonia of mild-to-moderate severity. Others believe it prudent to broaden antimicrobial coverage. Because of increasing resistance to TMP-SMX among *S. pneumoniae* (10.7% of all strains nationwide, as of 1997-1998),[91] many physicians add an additional drug such as a third-generation cephalosporin or a quinolone for those with moderate-to-severe pneumonia.

Insufficient evidence exists regarding the need for "atypical organism" coverage in patients with HIV-related infections. However, in one recent study of community-acquired pneumonia, *P. carinii*, *M. tuberculosis*, *S. pneumoniae*, and *M. pneumoniae* were the most common etiologic agents in HIV-positive patients.[92] A macrolide or a third-generation quinolone would have been a useful addition in this population. The addition of an antibiotic with anti-pseudomonal activity may be valuable in those with advanced immunosuppression, as *Pseudomonas* pneumonia occurs in those with end-stage disease.

While it is important to consider TB in the ED in order to order respiratory isolation precautions, it is usually not critical to begin treatment of TB in the ED. Consider empirical treatment of TB for those patients with chest x-ray findings strongly suggestive of TB (i.e., apical infiltrates with adenopathy). TB in HIV patients is typically treated with the same drugs as in non-HIV infected patients. However, rifabutin is often substituted for rifampin to avoid drug interactions in patients taking protease inhibitors.[93]

Steroids

Steroids should be used as adjunctive therapy for those with more severe PCP. Prednisone will reduce the incidence of respiratory failure and mortality in an important subgroup of patients—those with a PaO_2 less than 70 mmHg or an A-a gradient greater than 35 mmHg.[94]

When indicated, begin prednisone at a dose of 40 mg orally twice a day, the first dose given 15-30 minutes prior to the antibiotic. Taper the dosage over a 21-day course of therapy. If the patient is later shown to have bacterial pneumonia or TB, the steroids can be stopped without causing any serious adverse consequences.

Central Nervous System Complaints

After lung infections, CNS infections are the next most common site of serious infections in HIV-infected

persons presenting to the ED. It is estimated that 40%-70% of HIV patients will develop a symptomatic neurological disorder over the course of their lifetime.[95]

Toxoplasmosis is the most common CNS infection, occurring in approximately 3%-10% of United States AIDS patients.[54,96] Immigrants from Africa, Latin America, and Haiti are 3-4 times more likely to develop CNS toxoplasmosis than American-born patients with AIDS.[97]

Cryptococcal meningitis is also very common, developing in up to 10% of patients.[55] Others with AIDS may suffer from CNS TB, lymphoma, or fungal infections such as *C. immitis* and *H. capsulatum*. Viral infections usually involve CMV and herpes simplex virus. Additional CNS diseases include progressive multifocal leukoencephalopathy and syphilis.

HIV itself can produce a progressive dementia with brain atrophy.[98] Patients demonstrate cognitive abnormalities affecting attention, memory, and information processing.[99]

Drug toxicity should also be considered in the differential diagnosis of altered mental status in the AIDS patient; many antiretrovirals and other antimicrobials are associated with altered mental status, weakness, or other neurologic complaints. Efavirenz, in particular, is associated with dizziness and confusion.

History And Physical Exam

While fulminant presentations of meningitis occur, many CNS infections in HIV-infected patients are indolent, and the presenting symptoms and signs may be subtle.

Fever and headache are often the only presenting symptoms in AIDS patients with CNS toxoplasmosis (each occurring in about half of cases). It is not uncommon for the neurological exam to be normal in AIDS-related toxoplasmosis, despite the sometimes-dramatic mass lesions seen on head CT. Altered mental status is found in only about 60% of patients, seizures in about 30%, and focal deficits in about 60%.[100]

As with toxoplasmosis, cryptococcal meningitis may present with only fever and nonspecific constitutional symptoms such as nausea and malaise. *Nuchal rigidity and other meningeal signs are often absent.* Cryptococcal meningitis is associated with a headache in the vast majority of patients (75%-90%).[101,102] Other findings include vomiting (42%), altered mentation (28%), stiff neck (22%), photophobia (18%), focal deficits (6%), or seizures (4%). Unlike bacterial meningitis, cryptococcal meningitis tends to develop slowly, and the patient's complaints may be relatively mild.[103]

Another important CNS infection to consider in patients with AIDS is CMV retinitis. This presents as painless loss of vision, usually in end-stage AIDS patients.[101] The characteristic retinal lesions have central pallor with surrounding hemorrhage (the fundus being imaginatively referred to as a cheese-and-tomato pizza). Lesions usually develop peripherally (yielding lateral field cuts) and progress inward toward the macula, and may eventually result in blindness. In early retinitis, patients may complain of floaters or blind spots, and the lesions may be difficult to identify on funduscopic examination. Therefore, even when the retina appears normal on funduscopic exam, any HIV-positive patient with complaints suggestive of CMV retinitis should be referred to see an ophthalmologist within 1-2 days.

Diagnostic Testing

Consider scanning the head of any AIDS patient with any new CNS-related symptoms, including headache. One study examined which neurologic signs or symptoms predict new focal lesions on head CT in HIV-infected patients. In this study of 110 HIV-infected patients, the presence of any one of the following variables was 100% sensitive for a new focal lesion and would have resulted in a 37% reduction in the number of head CTs ordered in the ED:[104]

- new seizure
- depressed or altered orientation
- headache, different in quality than usual
- prolonged headache (≥ 3 days)

Another retrospective study looked at HIV-infected patients complaining of headache to identify those at low risk for intracranial mass lesion. In this report, those without focal neurological signs, altered mental status, seizure, or decreased CD4 lymphocytes were unlikely to have intracranial mass lesions.[105] Other reviews confirm that a low CD4 count (≤ 200 / mm^3) is an important risk factor for a positive CT scan in HIV-positive patients presenting with uncomplicated headache (i.e., no altered mental status, meningeal signs, neurologic findings, or symptoms of subarachnoid hemorrhage).[106]

While some hospitals routinely use contrast in the CT evaluation of an HIV patient with headache or neurological symptoms, others rely on non-contrast scans. In one study, for every positive enhanced scan in an HIV-infected patient, the unenhanced scan was abnormal, suggesting that intravenous contrast may be unnecessary in the ED setting.[107] Typically, the CT scan shows multiple lesions (which will enhance if contrast is given). Magnetic resonance imaging is slightly more sensitive than CT scanning and may be indicated in patients strongly suspected of having toxoplasmosis despite a non-diagnostic CT.

Approximately 20% of patients with toxoplasmosis will have a single lesion.[108] Although other etiologies such as lymphoma should be considered when a solitary lesion is found, it is common practice to treat these patients empirically for toxoplasmosis and consider biopsy later if they fail to respond to treatment. Toxoplasma antibody titers are usually unavailable within the time frame of an ED

evaluation, but more importantly are insensitive to CNS toxoplasmosis.[109]

After a CT scan has ruled out intracranial mass lesions, LP is indicated for immunosuppressed patients with any new CNS-related symptoms. (See also "Clinical Pathway: Evaluation Of CNS Complaints In HIV/AIDS Patients" on page 15.) Perform an LP in patients with CD4 counts below 200/mm^3 who appear nontoxic but complain of headache or altered mental status.

When performing the LP, measure the opening pressure when feasible. An elevated opening pressure is a common finding in cryptococcal meningitis, occuring in about 70% of cases. Fluid should be sent for cell count (including differential), protein, glucose, India ink stain, and cerebrospinal fluid (CSF) cryptococcal antigen. In addition to routine bacterial cultures, fungal and mycobacterial cultures should also be performed. Because of the higher incidence of neurosyphilis in HIV-infected people, order a CSF VDRL.

In AIDS-related cryptococcal meningitis, the CSF may appear normal or nearly normal on standard studies; glucose is less than 40 mg/dL in only 24%, protein is greater than 45 mg/dL in only 55%, the WBC count exceeds 20/mm^3 in only 21%, and the polymorphonuclear cell count is above 10% in only 16%.[101] India-ink stains reveal the fungus in approximately three-fourths of patients, but a CSF cryptococcal antigen test has over 90% sensitivity and may be the only indication of cryptococcal meningitis. A serum cryptococcal antigen is less sensitive than CSF cryptococcal antigen for the diagnosis of meningitis.[101]

Treatment

Most CNS infections in HIV-infected persons follow an indolent course, and treatment can await a diagnosis based on CT scan and LP. If a patient presents with a fulminant illness suggestive of acute bacterial meningitis, treat empirically before sending the patient to CT.

Patients with presumed toxoplasmosis should be admitted and treated with pyrimethamine and sulfadiazine, or pyrimethamine and clindamycin for those with sulfa allergies.[64] Because this infection usually progresses slowly, starting therapy immediately in the ED is not critical. Steroids should be given if significant surrounding edema is found.[110] Because toxoplasmosis in an AIDS patient cannot be cured, lifelong secondary prophylaxis is required.

Therapy for cryptococcal meningitis is usually initiated with IV amphotericin B on an inpatient basis, followed by prolonged oral fluconazole.[111-113] Complications, such as headache, nausea, and vomiting, may be reduced by removing CSF from those with an elevated opening pressure.[114] If symptoms are minimal and CSF parameters are acceptable (i.e., WBC < 20/mm^3, cryptococcal antigen < 1:1024), some physicians opt for outpatient management with oral fluconazole.[115] Close follow-up and consultation with the primary care physician are essential if outpatient management is to be considered.

Patients with normal CSF chemistries and a negative India-ink stain who do not appear toxic and have a normal mental status can be sent home if follow-up can be arranged. Should the cryptococcal antigen test come back positive, a delay of a few days should not have a serious impact on outcome.

Like pneumocystis pneumonia and toxoplasmosis, cryptococcosis frequently recurs and thus requires secondary prophylaxis with fluconazole. If an immunosuppressed AIDS patient with a history of cryptococcal meningitis stops taking fluconazole, it is highly likely that the disease will relapse.[116]

Patients with retinal lesions characteristic of CMV retinitis should be admitted to the hospital for a two- to three-week course of therapy with IV ganciclovir or foscarnet. Oral val-ganciclovir recently became available for induction therapy. Cidofovir is another antiviral drug that is used in some cases. These therapies have similar efficacy, but different resistance patterns and side-effect profiles.[117] Lifelong maintenance therapy is usually required to prevent relapses, but it can be stopped if the immune system is reconstituted with HAART. Some patients can be controlled with oral ganciclovir maintenance or ganciclovir ocular implants, but those with aggressive disease may require IV maintenance therapy through a central catheter.[118]

"The AIDS epidemic has rolled back a big rotting log and revealed all the squirming life underneath it, since it involves, all at once, the main themes of our existence: sex, death, power, money, love, hate, disease, and panic. No American phenomenon has been so compelling since the Vietnam War."
—Edmund White, AIDS: An American Epidemic.

Abdominal Complaints

In addition to respiratory and neurologic problems, abdominal complaints often prompt AIDS patients to seek immediate care, diarrhea and dysphagia being the most common causes.

Patients with esophagitis usually complain of pain and difficulty swallowing. *Candida albicans* is most often responsible for esophagitis in AIDS patients, causing about 60%-75% of cases.[119] Other etiologies include CMV and herpes simplex virus. The antiretroviral drug ddC can produce esophageal ulcers, and some patients with HIV have idiopathic esophageal ulcers that respond to steroids.[120] Those using topical solutions for oral candidiasis, such as clotrimazole troches or nystatin suspensions, may not have visible evidence of oral or pharyngeal thrush but still have esophageal disease; topical solutions are effective for oral candidiasis but not for esophageal infection.

Abdominal pain in AIDS patients can be due to a wide variety of etiologies, including CMV colitis, lymphoma, appendicitis, MAC infection, pancreatitis, and AIDS cholangiopathy.[121-123] AIDS cholangiopathy typically presents with right upper quadrant pain and fever in patients with advanced AIDS (CD4 < 50/mm^3). Because of shared routes of transmission, hepatitis B and C frequently complicate HIV.[124] Remember that some abdominal culprits may be unrelated to the patient's immune suppression, such as peptic ulcer disease, hernias, gastroenteritis, ectopic pregnancy, and the like. Opportunistic infections can cause perforation and obstruction. CMV of the gastrointestinal tract may lead to fecal peritonitis.[122]

Diarrhea is often a debilitating problem for AIDS patients; nearly all have it at some point during their illness. AIDS-related diarrhea is difficult to treat. The cause is often obscure, and even when pathogens are identified, they may be resistant to therapy.[125]

Bacterial pathogens such as *Salmonella*, *Shigella*, and *Campylobacter* can lead to acute-onset diarrhea. AIDS patients are at particular risk of recurrent *Salmonella* bacteremia.[126] Indolent, chronic diarrhea is more likely the result of parasitic, mycobacterial, or viral infection, including *Giardia lamblia*, *Cryptosporidium parvum*, and *Isospora belli*; CMV

Continued on page 16

Cost-Effective Strategies For Patients With HIV/AIDS

1. Base the intensity of the work-up on the degree of immunosuppression.

If a patient has a normal or near-normal CD4 count, he or she might not need a chest film for a simple cough or a CT scan/LP for a routine headache. Searching the laboratory computer for a recent CD4 count may prevent wasting time and money in fruitless investigations. An absolute lymphocyte count above 2000/mm^3 suggests that the CD4 count is above 200/mm^3.

HIV-positive patients with a CD4 count of 500/mm^3 or more are not at risk for opportunistic infections. Those with a CD4 count between 200/mm^3 and 500/mm^3 may be slightly more susceptible to tuberculosis and oral thrush but not PCP, *Cryptococcus*, toxoplasmosis, or disseminated MAC. If the patient has a recent CD4 count above the "dangerous range," medical evaluation can proceed without special concern for unusual organisms.

Caveat: Many patients do not know their CD4 count. Others may have had a low or normal count several months ago, which may have dipped below 200/mm^3 in the ensuing time interval. When in doubt, assume the patient is at risk for opportunistic infections.

2. Consider outpatient therapy for well-appearing patients with PCP.

Not every patient with PCP requires hospitalization. Patients at low risk for complications who appear well and are not hypoxic may be discharged on appropriate oral medication.

Caveat: Patients who are discharged must have reassuring chest films, relatively low LDH levels, and an acceptable pulse oximetry reading. They should be reliable, demonstrate that they can tolerate fluids, and have early follow-up arranged.

3. Limit laboratory testing for PCP.

In some hospitals, the diagnosis of PCP is made only after demonstration of the organism on induced sputum or bronchiolar lavage. In other centers, a clinical picture alone is adequate to initiate therapy. In one cost analysis, the use of exercise saturation measurements (using a desaturation of three points during exercise) was one of the most sensitive and economical approaches to the diagnosis of PCP.[159] The addition of an LDH measurement may be helpful.

Caveat: Patients who appear acutely ill or toxic, those with atypical presentations, and individuals with unusual findings on chest radiography may require more extensive microbiologic investigations. Be liberal in applying a PPD to HIV-infected patients with pulmonary complaints, especially if they are not admitted to the hospital. (Of course, do not order a PPD if they have had a history of TB.)

4. Limit the LP/CT pathway to patients who are likely to have CNS disease.

A low CD4 count in association with a new or different headache is a worrisome finding.

One study showed that HIV-infected patients were at low risk for a mass lesion if they had no focal neurologic signs or alteration of mental status, no history of seizures, and a CD4+ cell count of 200/mm^3 or higher (or a total lymphocyte count above 2000/mm^3 if CD4+ cell counts were not available).[105] Another study showed that no case of an opportunistic meningitis occurred in a patient with a CD4 count greater than 200/mm^3.[160]

Caveat: Certain presentations mandate the CT/LP pathway. These include focal neurological findings, altered mental status without an obvious cause (such as hypoglycemia), and new-onset seizures. If the patient complains of a new headache and the CD4 count is below 200/mm^3 or unknown, CT followed by LP is indicated. Any patient who appears toxic without a source or who has meningeal signs needs a CT and LP regardless of the CD4 count. ▲

Clinical Pathway: Evaluation Of The HIV-Positive Patient Who Has Fever Without A Source*

- CD4 count above 200/mm^3
- Absolute lymphocyte count above 2000/mm^3 (need to calculate using CBC with differential)

Yes → Evaluate as if patient has no immune suppression. (Class I-II for CD4 > 200/mm^3; Class III for ALC > 2000/mm^3)

↓

Obtain chest x-ray:
- If cough, dyspnea on exertion, or pulmonary signs (Class I-II)
- Routine chest-x-ray for all febrile patients (Class III)

↓

Obtain urinalysis:
- if back pain, urinary symptoms, or female (Class II)
- Routine UA for all febrile patients (Class III)

↓

Obtain blood cultures:
- if high risk for bacteremia (Class II)
  - high band count
  - new murmur
  - appearing malnourished
  - IV drug use
  - central venous catheter
  - CD4 count < 50/mm^3
- if not at high risk for bacteremia (Class III)

↓

- New or different headache than usual?
- Headache lasting more than three days?
- Focal neurologic deficit?
- Altered mental status?
- New-onset seizure?

Yes → Head CT followed by LP if negative (Class I-II)

↓ No

Go to top of next page

* Give antibiotics emergently if signs of toxicity or sepsis—*before* obtaining diagnostic studies. (May draw blood cultures if done expediently.)

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: Evaluation Of The HIV-Positive Patient Who Has Fever Without A Source (continued)

New-onset diarrhea? — Yes → Stool cultures (Class III)

↓ No

New-onset murmur or murmur not known to be old? — Yes →
- Stat or next-day echocardiogram (Class III)
- Blood cultures (Class II)

↓ No

Search for non-infectious cause of fever (Class II-III)
- Neuroleptic malignant syndrome
- Anticholinergic toxicity
- Serotonin crisis
- Malignant hyperthermia
- Heatstroke
- Aspirin overdose
- Sympathomimetic overdose
- Drug fever

↓

- Toxic-appearing?
- Persistent vomiting?
- Follow-up unlikely?

Yes →
- Admit (Class I-II)
- Give antibiotics if ill-appearing (ceftriaxone 50 mg/kg IV)

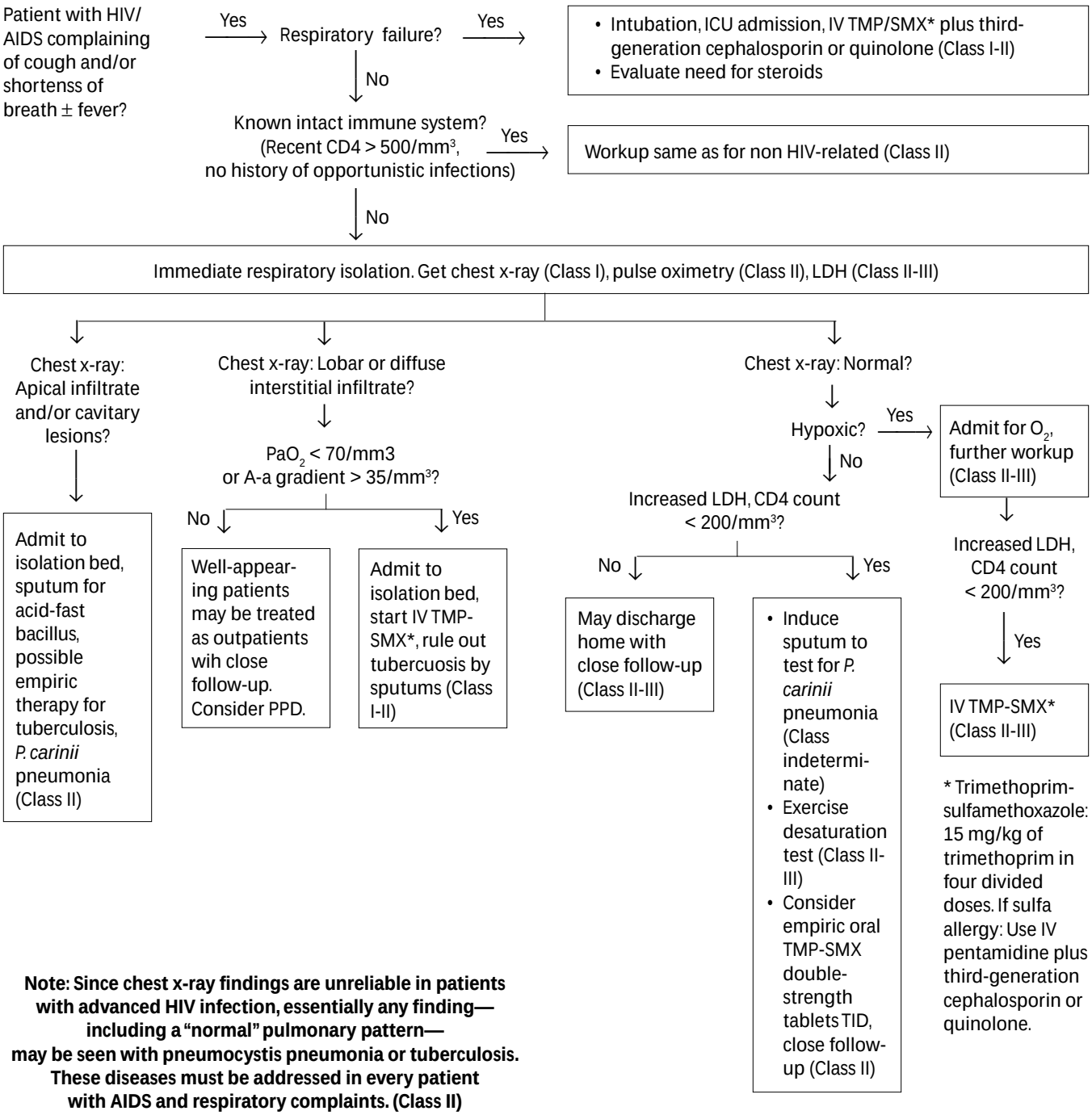
↓ No

Consider outpatient management if no contraindications (see above) and follow-up ensured (Class III)

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: Evaluation Of Respiratory Complaints In HIV/AIDS Patients

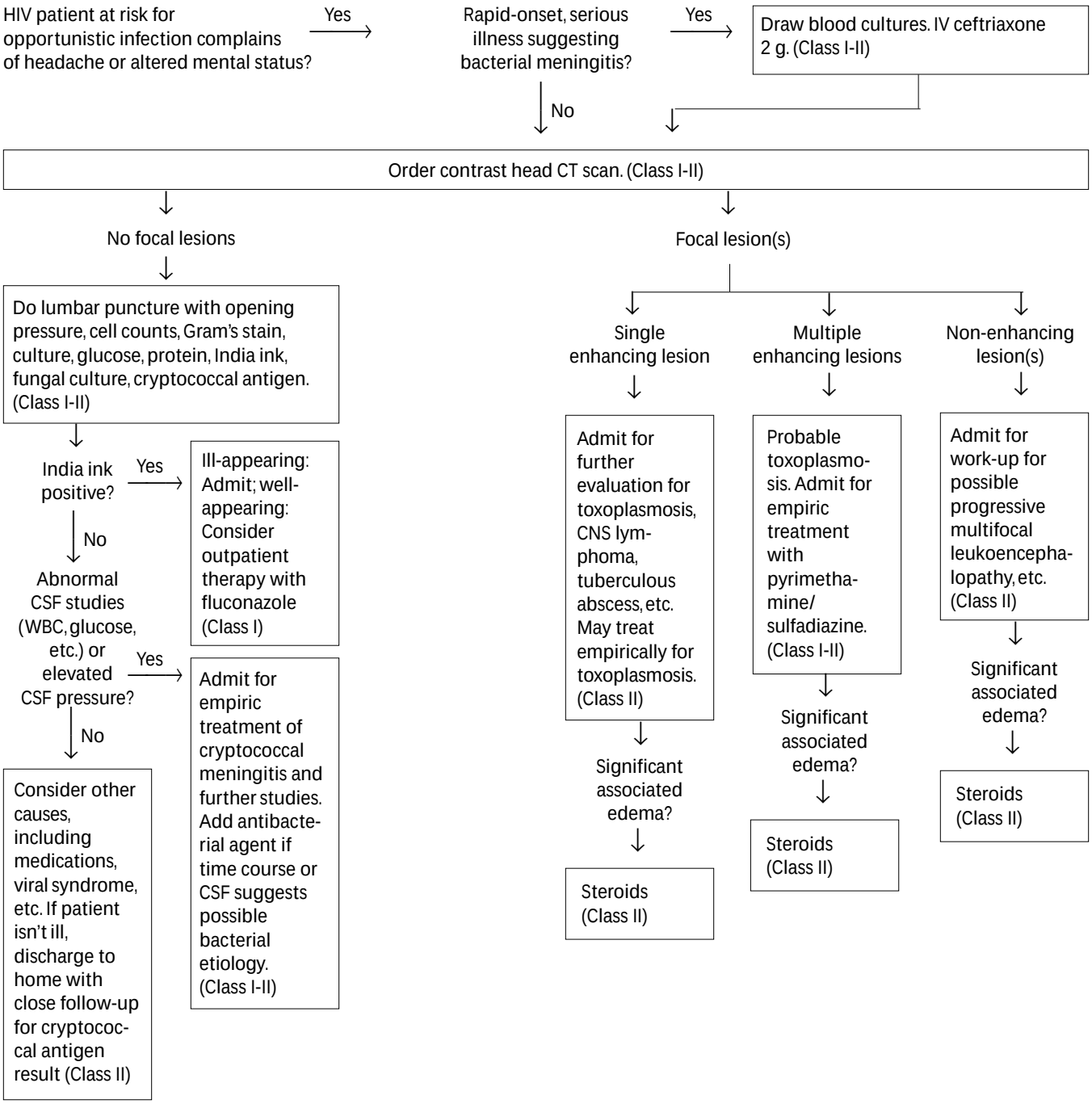


Note: Since chest x-ray findings are unreliable in patients with advanced HIV infection, essentially any finding—including a "normal" pulmonary pattern—may be seen with pneumocystis pneumonia or tuberculosis. These diseases must be addressed in every patient with AIDS and respiratory complaints. (Class II)

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: Evaluation Of CNS Complaints In HIV/AIDS Patients



The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Continued from page 11

infection; and MAC. In late-stage AIDS patients, CMV and MAC frequently cause chronic diarrhea that is resistant to treatment. CMV colitis develops in approximately 8%-16% of patients with advanced AIDS, resulting in chronic diarrhea.[127]

"From this moment on, our response to AIDS must be no less comprehensive, no less relentless and no less swift than the pandemic itself. I was a soldier and I know of no enemy in war more insidious or vicious than AIDS, an enemy that poses a clear and present danger to the world."
—U.S. Secretary of State Colin Powell

History And Physical Exam

Obtaining a drug history is important in patients presenting with abdominal pain. Pancreatitis occurs in up to 10% of patients taking ddI, and it is also associated with ddC, 3TC, TMP-SMX, pentamidine, and others. Indinavir can cause kidney stones in about 10%. Also ask about recent antibiotic use. Because AIDS patients are frequently on prolonged courses of antibiotics, diarrhea due to *C. difficile* is common and can present as a fulminant illness.[128]

In addition to the routine questions regarding the history of present illness, consider the sexuality of those who present with acute diarrhea. Persons practicing receptive anal intercourse are at increased

Ten Excuses That Don't Work In Court

1. "I didn't know the patient had HIV."
Many patients who present with AIDS-related complications have not previously been diagnosed with HIV. HIV should always be considered in patients with possible infection, especially pneumonia and CNS infections. When you see an adult with oral thrush, think HIV.

2. "The chest x-ray was negative."
PCP and TB can have subtle presentations, and the chest x-ray is sometimes negative early in the course of illness. Oxygen desaturation with exercise or increased A-a gradient may be clues to early PCP.

3. "The infiltrate on the chest x-ray looked lobar, so I didn't treat for PCP."
Chest x-ray cannot reliably determine the etiology of pneumonia. Do not exclude PCP, bacterial pneumonia, or TB based on radiographic appearance. In patients with immunosuppression due to HIV, TB usually does not have the classic appearance of apical infiltrate or cavitation. It is commonly misdiagnosed as bacterial pneumonia or PCP. Ideally, all admitted HIV patients with pneumonia should be isolated until TB is ruled out.

4. "I sent him home because I know PCP can be treated on an outpatient basis."
True, but this gentleman had a pulse ox of 87% and was homeless. Because patients with PCP can sometimes deteriorate despite therapy, outpatient therapy is recommended only in suitable candidates with ensured follow-up.

5. "The patient didn't have any meningeal signs."
Most patients with cryptococcal meningitis do *not* have meningeal signs. Fever and/or headache are the most common presenting symptoms.

6. "The CSF profile was unremarkable."
CSF glucose, protein, and cell counts are often normal with cryptococcal meningitis. An India-ink stain will identify about 75% of cases. Cryptococcal antigen is the most sensitive test, but results may not be available until the next day.

7. "The patient had no focal deficits, so I didn't do a CT scan."
Patients with CNS lesions due to toxoplasmosis or other etiologies often do not exhibit focal findings on neurologic exam. A CT scan should be performed prior to LP in patients with immunosuppression due to HIV.

8. "I didn't see any findings on ophthalmoscopic exam."
CMV retinitis often involves the peripheral retina in early stages. Treatment will prevent further visual loss but is not very effective in reversing retinal damage. It is important to promptly refer HIV patients with visual complaints for full evaluation by an ophthalmologist.

9. "I thought the fever was just due to a simple viral syndrome."
A new fever or change in fever pattern in an AIDS patient warrants investigation. Common causes of fever without an apparent source include occult pneumonia (including PCP), CNS infection, TB, disseminated MAC, lymphoma, and drug reactions.

10. "I didn't know what medications he was taking."
Patients with HIV are often taking complicated medical regimens. Many of the drugs have severe toxicities that must be considered when patients present with emergent complaints. Available sources of data may include old records, a call to the patient's home to collect pill bottles, pharmacy records, and the primary care provider. ▲

risk of proctocolitis due to sexually transmitted organisms such as gonorrhea, chlamydia, herpes, or syphilis.

Laboratory Studies

The utility of laboratory studies in the evaluation of abdominal pain in the HIV patient varies between patients and tests. While some consider a CBC obligatory, remember that HIV patients with surgical disease may have a normal or low WBC count.[122] (Of course, this is also true for the non-HIV individual as well!) In one small study, six of the nine HIV-positive patients with appendicitis did *not* have an elevation in the WBC count.[129]

A serum lipase and/or amylase may be especially useful in the patient on antiretroviral therapy to look for drug-induced pancreatitis. Because ddI causes pancreatitis in up to 10% of patients, order a serum amylase and lipase when a patient on ddI presents with vomiting and epigastric pain. The value of routine liver function tests remains unknown but may be indicated in those with jaundice or right upper quadrant pain. A markedly elevated alkaline phosphatase is characteristic of AIDS cholangiopathy. (For a complete discussion of diagnostic tests in abdominal pain, see the premier issue of *Emergency Medicine Practice*, "Assessing Abdominal Pain In Adults: A Rational, Cost-Effective, And Evidence-Based Strategy.")

Many patients presenting with recurrent or chronic diarrhea have already had multiple outpatient stool studies in an attempt to identify a pathogen. It is not necessary to repeat studies on a patient with chronic diarrhea, but newly developed diarrhea or a significant change in the pattern of diarrhea merits evaluation. Stool cultures may identify potentially treatable bacterial pathogens. Giardiasis is identified by stool ova and parasite exams, while a modified acid-fast stain can detect *Cryptosporidium* and *Isospora*.

Radiologic Studies

Laparotomy is unnecessary in most AIDS patients with abdominal pain.[130] In one small study of HIV-infected patients with appendicitis, only one-third of AIDS patients with right lower quadrant pain had appendicitis, while more than 90% of HIV-positive patients without AIDS had the disease.[131] Rational use of the abdominal CT scan can help avoid unwarranted surgery in the AIDS patient.[132] A non-contrast helical CT is useful in the patient with flank pain and fever, especially in those on medications that predispose to renal stones (like indinavir). Ultrasound may also be useful in those with right upper quadrant pain. In AIDS cholangiopathy, ultrasound reveals dilatation of intra- and extrahepatic bile ducts with wall thickening.[133] Papillary stenosis is narrowing of the papilla duodeni, where the common bile duct enters the duodenum. It occurs in about half of patients with AIDS cholangiopathy, and stones are typically absent.

Pelvic ultrasound is recommended in women with AIDS and pelvic inflammatory disease, as these have a very high incidence of tubo-ovarian abscess.[134] Tubo-ovarian abscesses may occur in up to one-third of HIV-positive women with salpingitis.[135]

Endoscopy

Because *C. albicans* is such a common etiology of esophagitis, empiric therapy is preferred to testing as an initial strategy (based on class IIA evidence).[136] Follow-up must be arranged, so that patients who worsen or fail to improve within 7-10 days can undergo further testing (including esophagoscopy) to rule out CMV, herpes esophagitis, or resistant fungi.

In patients with cholangitis, endoscopic retrograde cholangiopancreatography is usually done to visualize the biliary tree. The gastroenterologist can collect

Key Points For HIV-Related Emergencies

- Consider the possibility of occult HIV infection and possible opportunistic infection in any patient presenting to the ED with symptoms of infection.
- Assess the risk of opportunistic infection using past medical history, CD4 counts, absolute lymphocyte count, and physical signs such as thrush, Kaposi's sarcoma, and weight loss.
- Watch for subtle presentations of *Pneumocystis carinii* pneumonia.
- Consider TB in all HIV patients with respiratory infection, and isolate patients who are admitted for pneumonia. Liberally apply PPDs to those treated as outpatients.
- Treat for possible bacterial infection in patients who appear to have PCP.
- Obtain CNS imaging prior to LP in HIV patients presenting with headache or altered mental status. Check the opening pressure when performing the LP.
- Watch for subtle presentations of cryptococcal meningitis. Meningeal signs are absent in most, and CSF may appear normal on routine studies.
- Refer AIDS patients with visual complaints for ophthalmology evaluation promptly, even if the retina appears normal on funduscopy.
- For AIDS patients with unexplained fever, consider the most likely sources first—lungs and CNS.
- Watch for drug toxicities.

specimens for culture and staining as well as perform therapeutic papillotomy if stenosis is found.

Colonoscopy is occasionally employed in cases of refractory diarrhea. CMV colitis is suggested by erythematous, friable mucosa, and the diagnosis is verified by biopsy.

Treatment

Oral and esophageal candidal infections can be treated with fluconazole 200 mg on day 1 and then 100 mg daily.[137] Patients with oral infection alone require two weeks of therapy, while those with esophagitis require three weeks of therapy (or therapy that lasts two weeks longer than symptoms).[138] Some patients with severe or resistant esophageal candidiasis may require hospital admission for amphotericin B therapy.[139] Herpes esophagitis is treated with acyclovir.

While the care of specific intra-abdominal conditions is beyond the scope of this article, the emergency physician must recognize certain life threats. Pancreatitis in the AIDS patient is especially dangerous. In one recent review, nearly one-third of AIDS patients hospitalized with pancreatitis died.[140] Standard scoring systems (such as Ranson's and Imrie's criteria and the APACHE II system) failed to predict severity of the disease. Even "routine" conditions become more ominous in the compromised host and call for heightened vigilance. AIDS patients with appendicitis have a perforation rate of up to 40%.[141]

If bacterial infection is strongly suspected because of acute severe diarrhea with fever, empiric treatment with an antibiotic such as ciprofloxacin (500 mg PO BID x 3-5 days) would be appropriate. Quinolones have activity against the most common bacterial pathogens, such as *Salmonella*, *Shigella*, and *Campylobacter*. Treatment for parasitic infection is often ineffective; no uniformly effective anti-cryptosporidial therapy is available, although some patients respond to paromomycin plus azithromycin.[142] TMP-SMX is usually effective for treating isosporiasis, though continued suppressive therapy may be required due to the high incidence of recurrence.[143] Symptomatic treatment with diphenoxylate or loperamide may be the most reasonable way to manage AIDS-related diarrhea, especially in late-stage patients with chronic diarrhea. Efficacy of ganciclovir and foscarnet for CMV colitis or esophagitis is not well-established. Most patients will improve, but relapse is common.[144]

Antimicrobial Therapy Used In The Management Of HIV Infections

The antimicrobial therapy for HIV infections falls into two categories: prophylaxis and treatment of opportunistic infections, and direct suppression of HIV replication. An emergency physician should be able to recognize the common medications used and their customary toxicities. (See **Table 3**.)

Pneumocystis pneumonia prophylaxis is now the standard of care for a patient with a CD4 count below

Table 3. Common Adverse Reactions To Drugs Used In HIV-Infected Patients.

3TC: Anemia, headache, nausea, diarrhea

AZT: Anemia, leukopenia, nausea, fatigue, nail pigmentation, myositis

d4T: Peripheral neuropathy, anemia, leukopenia

ddC: Peripheral neuropathy, rash, pancreatitis,* oral ulcers, hepatitis, neutropenia

ddI: Pancreatitis,* peripheral neuropathy, hypocalcemia, hypokalemia, diarrhea, hepatitis, arrhythmias

Abacavir: Hypersensitivity reaction (fever, rash), headache, gastrointestinal upset

Amprenavir: Rash, nausea, diarrhea, paresthesias, depression, hyperglycemia

Atovaquone: Headache, diarrhea, nausea, rash, fever

Cidofovir: Renal toxicity common, gastrointestinal upset, neutropenia

Dapsone: Hemolytic anemia,* rash, methemoglobinemia, headache, nephrotic syndrome

Delavirdine: Rash common, headache, gastrointestinal upset, abnormal liver function tests

Efavirenz: Dizziness, insomnia, rash, hepatitis

Fluconazole: Drug interactions common (e.g., warfarin, phenytoin), nausea, abnormal liver function tests

Foscarnet: Renal insufficiency, electrolyte abnormalities, headache, tremors

Ganciclovir: Bone marrow suppression, increased liver function tests

Indinavir: Nausea, kidney stones,* abnormal liver function tests

Lopinavir/Ritonavir: Nausea, diarrhea, abnormal liver function tests, drug interactions common

Nelfinavir: Diarrhea, abnormal liver function tests

Nevirapine: Rash common and may be severe, gastrointestinal upset, abnormal liver function tests

Pentamidine: Hypotension,* hypoglycemia,* hyperglycemia, hyperkalemia, arrhythmias, renal insufficiency

Pyrimethamine: Anemia, leukopenia, thrombocytopenia (requires folinic acid), nausea, seizures

Rifabutin: Fever, nausea, rash, abdominal pain, uveitis

Ritonavir: Nausea, diarrhea, abnormal liver function tests, drug interactions common

Saquinavir: Diarrhea, nausea, abdominal pain

TMP/SMX: Rash, fever, neutropenia, anemia, nausea, hepatitis, photosensitivity

Trimetrexate: Anemia, leukopenia, thrombocytopenia (requires folinic acid), nausea, renal insufficiency, hepatitis

* Indicates most significant causes

200/mm^3. It is also used in certain high-risk patients, such as those newly diagnosed with an AIDS-defining illness.[145,146] TMP-SMX is most commonly prescribed, but some patients, due to allergy, may take alternative therapies such as dapsone, aerosolized pentamidine, clindamycin plus primaquine, or atovaquone. These alternative therapies are generally less effective than TMP-SMX.[147] Azithromycin (1200 mg weekly) or rifabutin (300 mg daily) are prescribed as prophylaxis against MAC for patients with a CD4 count less than 50/mm^3.[146] Recognize that no prophylaxis regimen is 100% effective, and infection can occur despite faithful adherence.

Although emergency physicians are not expected to manage antiretroviral therapy in AIDS patients, we should be familiar with the basic principles of antiretroviral therapy and the drugs used.[148] Initiating antiretroviral therapy for new HIV infections is best left to the specialist. Changes to a patient's regimen by an emergency physician should only extend to stopping medications in the event of an adverse reaction.

Antiretroviral therapy is typically given in combination. Most commonly, two nucleoside analogs are combined with a protease inhibitor. (See **Table 4**.) A non-nucleoside reverse transcriptase inhibitor is sometimes used in place of a protease inhibitor. The viral load is measured periodically to determine response. If the viral load increases or fails to decline, the drug regimen is changed. Unfortunately, many patients find it difficult to comply with complicated and often toxic antiretroviral regimens. For example, in one large cohort over one year, 29% of patients with HIV had their regimens modified due to toxicity, and 26% stopped the medications altogether.[149]

At any given time, an AIDS patient is likely to be taking many powerful medications; 8-10 drugs taken concurrently is not uncommon. Almost every drug used for HIV infection can cause headache, malaise, nausea, abdominal discomfort, and diarrhea, and many have severe toxicity that may result in an ED visit. (See Table 3.) Drug interactions are common.[150]

"AIDS obliges people to think of sex as having, possibly, the direst consequences: suicide. Or murder."
—Susan Sontag (b. 1933), U.S. essayist.
AIDS and Its Metaphors, *chapter 7 (1989).*

Table 4. Antiretroviral Drugs.

Generic name	Brand name
Nucleoside analogs	
Zidovudine (AZT, ZDV)	Retrovir
Didanosine (ddI)	Videx
Zalcitabine (ddC)	HIVID
Stavudine (D4T)	Zerit
Lamivudine (3TC)	Epivir
Abacavir (ABC)	Ziagen
Non-nucleoside reverse transcriptase inhibitors	
Nevirapine	Viramune
Delavirdine	Rescriptor
Efavirenz	Sustiva
Protease inhibitors	
Saquinavir	Fortovase
Ritonavir	Norvir
Indinavir	Crixivan
Nelfinavir	Viracept
Amprenavir	Agenerase
Lopinavir/Ritonavir	Kaletra
Nucleotide reverse transcriptase inhibitor	
Tenofovir	Viread

Postexposure Prophylaxis For HIV

Depending on the circumstances, sticking oneself with a needle can be a profoundly disturbing event. Based on a number of assumptions, the cumulative risk of HIV infection over a 30-year ED career may be as high as 1.4%.[151]

In prospective studies, the average risk of HIV transmission after a *single* percutaneous exposure to HIV-infected blood is approximately 0.3% (95% confidence interval [CI], 0.2%–0.5%)[152] and after a mucous membrane exposure, approximately 0.09% (95% CI, 0.006%–0.5%).[153] The risk of transmission appears to depend on the amount of infected fluid to which the person is exposed and the amount of HIV in that fluid.[154]

Case-control studies demonstrate that postexposure prophylaxis with antiretroviral drugs may reduce the likelihood of seroconversion.[154,155] (See **Table 5** on page 20.) Because of the toxicity associated with these medications, provide adequate information to the patient so he or she can make an informed choice regarding postexposure prophylaxis.

Occasionally, patients may request HIV prophylaxis after sexual assault or after unprotected consensual sex. The risk for a specific sexual encounter cannot accurately be determined, but data exist to allow an estimate of the range of risk for various types of exposures.[156,157] The risk appears to be highest with unprotected receptive anal intercourse (0.008 to 0.032 per episode)—higher than the risk from occupational needlesticks. The risk from vaginal intercourse is higher for male-to-female transmission (0.0005 to 0.0015) than from female-to-male (0.0003 to 0.0009). Although the risk from oral-genital contact has not been reported, it appears to be low.

Although there is no direct evidence that postexposure treatment will prevent HIV infection after sexual exposure, it is reasonable to believe that the risk can be reduced, given the data regarding occupational and perinatal exposures.[158] The decision to provide HIV prophylaxis after sexual contact involves an assessment of the risk of transmission, the potential benefit of prophylaxis, and the cost and

toxicity of antiretroviral drugs. For most sexual exposures, the patient should be informed of the risks and benefits of postexposure prophylaxis, but advised that the risk of infection is low and is likely outweighed by the cost and toxicity of postexposure prophylaxis. If postexposure prophylaxis is given, a two-drug regimen for four weeks would be appropriate for most, with three-drug regimens reserved for only the highest-risk exposures (e.g., receptive anal intercourse with a known HIV-infected individual).

Summary

Although the management of HIV-infected patients may seem complicated and intimidating, familiarity with the most common opportunistic infections will facilitate care of these patients. Because many HIV-infected people are unaware of their serologic status, it is important to consider the possibility of HIV in any patient presenting with complaints suggestive of opportunistic or unusual infection. Assess the patient's risk of opportunistic infection, and look for common sources of infection such as lungs and CNS. Don't hesitate to use your consultants, as HIV management is a rapidly changing field. ▲

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in the paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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Table 5. Recommended HIV Postexposure Prophylaxis For Percutaneous Injuries.

	Infection status of source				
Exposure type	**HIV-positive Class 1***	**HIV-positive Class 2***	**Source of unknown HIV status†**	**Unknown source§**	**HIV-negative**
Less severe¶	Recommend basic 2-drug PEP	Recommend expanded 3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††	Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings where exposure to HIV-infected persons is likely	No PEP warranted
More severe§§	Recommend expanded 3-drug PEP	Recommend expanded 3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††	Generally, no PEP warranted; however, consider basic 2-drug in settings where exposure to HIV-infected persons is likely	No PEP warranted

* HIV-positive, class 1—asymptomatic HIV infection or known low viral load (e.g., ≤ 1500 RNA copies/mL). HIV-positive, Class 2—symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of postexposure prophylaxis (PEP) should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.
† Source of unknown HIV status (e.g., deceased source person with no samples available for HIV testing).
§ Unknown source (e.g., a needle from a sharps disposal container).
¶ Less severe (e.g., solid needle and superficial injury).
** The designation "consider PEP" indicates that PEP is optional and should be based on an individualized decision between the exposed person and the treating clinician.
†† If PEP is offered and taken and the source is later determined to be HIV-negative, PEP should be discontinued.
§§ More severe (e.g., large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient's artery or vein).

Source: No authors listed. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. *MMWR Morb Mortal Wkly Rep* 2001 Jun 29:50(RR11);1-42. Table 4. (Go to http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.htm for the full text recommendations.)

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Physician CME Questions

1. A total lymphocyte count of less than 1000 cells/mm^3:
a. is unlikely to be associated with a CD4 count of less than 200 cells/mm^3.
b. is likely to be associated with a CD4 count of less than 200 cells/mm^3.
c. is diagnostic of AIDS.
d. is not at all predictive of CD4.

2. Pneumocystis pneumonia prophylaxis with TMP-SMX is now standard for:
a. any patient with HIV infection.
b. a patient with HIV and a history of tuberculosis.
c. a patient with HIV and a CD4 count below 500 cells/mm^3.
d. a patient with HIV and a CD4 count below 200 cells/mm^3.

3. The diagnosis of PCP may be aided by:
a. an exercise-induced decrease in oxygen saturation.
b. a Gram's stain of an expectorated sputum sample.
c. finding an LDH level in the normal range.
d. a routine blood culture.

4. Patients with AIDS and TB:
a. never have a normal chest radiograph.
b. have high rates of PPD positivity, but progress to active TB at a rate similar to the general population.
c. need to be immediately started on four-drug anti-TB therapy in the ED.
d. commonly present with hilar adenopathy or a lobar infiltrate on a chest radiograph.

5. All of the following are common etiologies of fever in AIDS patients *except:*
a. herpes simplex.
b. *P. carinii* and other pneumonias.
c. sinusitis.
d. cryptococcal meningitis.
e. bacteremia/sepsis.

6. Which of the following factors is associated with an increased risk of HIV infection?
a. Injection drug use
b. Prostitution
c. Heterosexual exposure to a partner at risk
d. Children born of mothers in a risk group
e. All of the above

7. Patients with AIDS who develop cerebral toxoplasmosis:

a. will have a single lesion on CT scan in over 70% of cases.
b. are unlikely to have positive toxoplasma antibody titers.
c. often lack signs and symptoms of mass lesions, despite finding mass lesions on CT scan.
d. should not receive steroids for surrounding cerebral edema, as this may impair the patient's immune response to the infection.

8. A 30-year-old Caucasian male with a history of HIV infection for five years and a recent CD4 count of 78 cells/mm^3 presents to your ED complaining of a mild-to-moderate headache, nausea, and fever. He has a previous history of cryptococcal meningitis two years ago but is not taking any medications now. His neurological exam is normal; he has no meningismus, but he does have a temperature of 39°C.

a. Cryptococcal meningitis is very unlikely if the patient has completed a six-month course of fluconazole after his previous infection.
b. An LP is indicated, but it can wait until after a CT scan rules out mass lesions (such as caused by toxoplasmosis and lymphoma).
c. Cryptococcal meningitis is unlikely because he has no meningismus or neurological exam abnormalities.
d. CSF analysis will usually reveal greater than 20 white blood cells/mm3 if the patient has cryptococcal meningitis.
e. It is not useful to send the CSF for India ink stain or cryptococcal antigen test, as these tests take too long for an ED diagnosis.

9. All of the following are true *except*:

a. The finding of oral candidiasis or hairy leukoplakia in a patient with a fever suggests an HIV-related illness.
b. Thrush is a sure sign of HIV infection.
c. Patients with oral lesions tend to have low CD4 counts and fast disease progression.
d. Other causes for oral candidiasis include out-of-control diabetes, recent antibiotic or inhaled steroid use, or chemotherapy.

10. Patients with AIDS and presumed toxoplasmosis:

a. require an immediate diagnosis, because the disease progresses very quickly.
b. should be admitted and treated with pyrimethamine and sulfadiazine, or pyrimethamine and clindamycin for those with sulfa allergies
c. should not receive steroids if significant surrounding edema is found.
d. is easily curable with appropriate therapy.

11. Patients with AIDS and chronic diarrhea:

a. rarely develop debilitating illness, as the diarrhea is usually mild.
b. should never be treated with diphenoxylate or loperamide, because decreasing gut motility in intestinal infections is life-threatening.
c. due to *Cryptosporidium* can often be cured with a prolonged course of TMP-SMX.
d. should have stool studies performed if they develop a significant change in the pattern of their diarrhea.

12. A patient with AIDS presents with complaints consistent with esophagitis and dysphagia. Which of the following statements is true?

a. The most common organism causing this condition is the herpes simplex virus.
b. Any antimicrobial therapy, such as oral fluconazole, should be preceded by esophagoscopy and biopsy.
c. Oral topical solutions for thrush, such as nystatin or clotrimazole troches, will reliably treat esophageal candidiasis.
d. Particularly resistant or severe esophageal candidiasis may require inpatient treatment with amphotericin B.

13. All of the following statements regarding drugs for HIV therapy are true *except*:

a. A patient experiencing a rash with abacavir (Ziagen) may be safely continued on his or her medication but may require antihistamine therapy for comfort.
b. Efavirenz is associated with a variety of CNS symptoms, including abnormal dreams and altered mental status.
c. Zidovudine (AZT) is associated with anemia and agranulocytopenia.
d. Patients taking Indinavir who develop sudden-onset flank pain and fever need a CT scan of their urinary tract.

14. Tuberculosis in AIDS patients:

a. often presents atypically.
b. is very rare.
c. doesn't require isolation.
d. generally produces the same chest x-ray findings as it does in the general population.

15. Which of the following can cause diarrhea in AIDS patients?

a. Bacterial pathogens such as *Salmonella, Shigella,* and *Campylobacter*
b. Parasitic, mycobacterial, or viral infection, including *Giardia lamblia, Cryptosporidium parvum,* and *Isospora belli*
c. Cytomegalovirus
d. Antimicrobials the patient is taking
e. All of the above

16. **When treating PCP:**
    a. steroids are not useful as adjunctive therapy for severe PCP.
    b. although dapsone can cause hemolytic anemia in patients who are G6PD deficient, it is the drug of choice for treating inpatient PCP.
    c. Patients with a mild rash while on TMP-SMX for severe PCP may often be safely treated through the rash, although they may require antihistamines for comfort.
    d. TMP-SMX causes a rash in up to 50% of patients, but hematological abnormalities are very rare.

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives an alpha-numerical score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case-control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

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