

# Emergency Medicine Reports

The Practical Journal for Emergency Physicians

Volume 33, Number 16 / July 16, 2012

www.emreports.com

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## Statement of Financial Disclosure

To reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Farel (CME question reviewer) owns stock in Johnson & Johnson. Dr. Stapczynski (editor) owns stock in Bristol Myers Squibb. Dr. Schneider (editor), Dr. Serrano (author), Dr. Westergaard (author), Dr. LoVecchio (peer reviewer), Ms. Mark (executive editor), and Ms. Hamlin (managing editor) report no financial relationships with companies related to the field of study covered by this CME activity.

## Diagnosis and Management of Acute HIV in the Emergency Department

*While human immunodeficiency virus (HIV) infection no longer carries the death sentence it once did, it still carries an enormous cost both in terms of financial burden for treatment as well as the social and medical issues associated with long-term disease. Attention has shifted, in part, from the treatment of the disease to prevention.*

*The role of the emergency physician has changed, too, from treating the immediate life-threatening complications of the disease to recognition of early disease. Many states and institutions have mandated that emergency departments and outpatient clinics make HIV testing available. This has created new problems for emergency providers, who now struggle with communicating test results to patients and providing linkages to chronic care facilities.*

*This paper discusses another important role for emergency providers in the recognition of early, acute HIV. Our role here is not only to get the person into treatment, but to prevent the spread of disease to others. There is good evidence that the vast majority of individuals will alter their behavior after being diagnosed with HIV. There is also evidence discussed below that most of the spread of HIV is now suspected to be in this early phase, before the HIV test becomes positive.*

— Sandra M. Schneider, MD, Editor

## Introduction

In the United States, an estimated 1.2 million people are living with HIV infection, and approximately 50,000 Americans are newly infected with HIV each year.<sup>1</sup> Most patients who contract HIV develop an acute, self-limited febrile illness, and many seek care for their symptoms in emergency departments (EDs) and primary clinics.<sup>2</sup> However, HIV infection is rarely identified in the acute phase, and most people with HIV infection receive the diagnosis much later in the course of their illness.<sup>3</sup> The lack of early diagnosis of HIV infection has tremendous public health implications, and acute HIV infection has been termed a public health emergency.<sup>4</sup> In addition, data suggest patient outcomes may be improved when HIV infection is identified and treated early in its course. Therefore, it is critical that the medical community improve its acumen in recognizing acute HIV infection. This is especially important for emergency physicians, who are uniquely situated to identify acute HIV among the many patients who will seek care in emergency departments for their symptoms.

Acute infection represents the peak of infectious potential, characterized by high levels of viremia and viral shedding, and patients are more infectious than even in end-stage AIDS.<sup>5</sup> (See Figure 1.) In addition, patients are typically unaware they are infected and may inadvertently transmit the virus to others via unprotected sex or needle sharing. Epidemiological and in vivo studies suggest as many as half of HIV cases are transmitted from patients with primary infection.<sup>6</sup> Thus, identifying early cases of HIV infection has the potential to reduce

## Executive Summary

- Acute HIV occurs during the acute viremic phase of the disease. Current HIV screening tests used in many departments measure the antibody response to the virus. In acute HIV, that response has not yet occurred, so screening tests may be negative.
- Patients with acute HIV present with typical viral symptoms, including rash, malaise, and myalgias. There may be headache, anorexia, nausea, and vomiting.
- During an acute HIV infection, viral loads may be extremely high and the patient is very infectious.
- Acute HIV infection should be considered in patients with viral-like syndromes who are at risk for HIV. At highest risk are men who have sex with men, and blacks.

the spread of HIV.

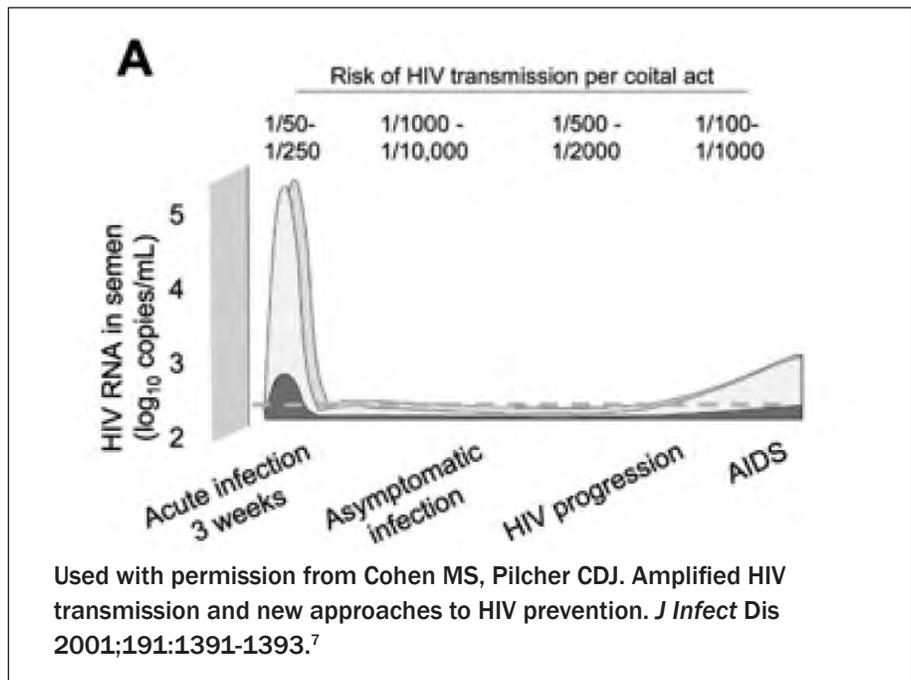
There are both patient- and provider-specific reasons why HIV infection is not diagnosed during the acute phase of illness. Many patients do not seek medical care due to the nonspecific and self-limited nature of their symptoms. For those patients who do seek care, however, there are several provider knowledge gaps that contribute to lack of diagnosis. Acute HIV is not on the radar of most emergency physicians, and providers may not inquire about HIV risk factors in patients presenting with a viral illness. Patients with acute HIV are commonly misdiagnosed with pharyngitis, influenza, infectious mononucleosis, or other nonspecific viral illnesses. In addition, many providers are not aware of the diagnostic tests needed to identify acute HIV infection during the so-called “window period,” when patients are viremic with high viral loads but HIV antibody tests are negative.

Clinicians should maintain a high index of suspicion, recognize the clinical manifestations of acute infection, have a low threshold for testing, and understand the diagnostic tools required to identify acute HIV infection. Emergency departments may need to expand current HIV testing protocols to include testing for acute HIV.

### Stages of HIV Infection

Acute infection is defined as the period of time from acquisition of the virus to completion of the initial immune response (seroconversion).

**Figure 1:** Viral Load and Risk of HIV Transmission



The duration is variable but generally lasts between 2-3 months.<sup>8</sup>

Chronic HIV infection can last for years and is categorized based on degree of immunosuppression:

1. Early stage: CD4+ T cell count > 500/ $\mu$ L
2. Intermediate stage: CD4+ T cell count 200-500/ $\mu$ L
3. Advanced stage: CD4+ T cell count < 200/ $\mu$ L

AIDS, or acquired immune deficiency syndrome, is the advanced-stage of HIV infection, characterized by severe impairment of cellular immunity. It can be defined using either laboratory criteria (CD4+ T cell count < 200/ $\mu$ L) or via occurrence of an AIDS-defining illness, which may be one of

numerous opportunistic infections or malignancies.

### Epidemiology

HIV is a blood-borne, sexually transmissible RNA retrovirus in the *Retroviridae* family, Lentivirus genus. Two distinct species, HIV-1 and HIV-2, have been identified. HIV-2 is rare in developed countries, and the majority of research and drug development has focused on HIV-1.

The virus can be transmitted sexually from exposure of mucosal surfaces to infected genital secretions (the most common method of transmission worldwide), parenterally by sharing of contaminated needles from IV drug use, or vertically

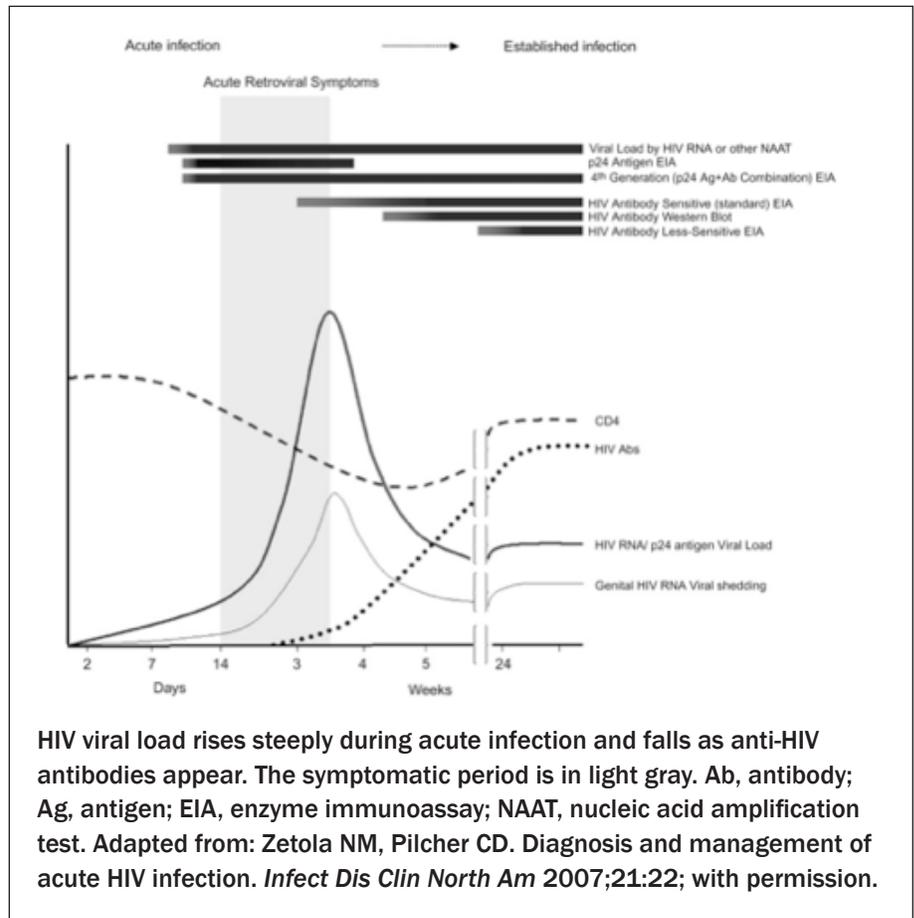
from mother to child, which can occur during birth or breastfeeding. Historically, HIV has been transmitted via blood transfusion, but meticulous screening of the blood supply makes this an exceedingly rare event today.<sup>9</sup>

The CDC reports that as of 2008, nearly 1.2 million Americans are infected with HIV, and among these, an estimated 20% are not aware of their diagnosis.<sup>10</sup> The rate of new infections has remained stable over the past decade, with approximately 50,000 Americans newly diagnosed with HIV each year.<sup>11</sup> In the United States, male-to-male sexual contact is the most common method of transmission, accounting for 61% of all new cases of HIV in 2009, followed by heterosexual contact in 27% and injection drug use in 9% of all new cases, respectively.<sup>12</sup> Routine pregnancy screening and antiviral treatment of HIV-positive mothers has resulted in a sharp decline in vertical transmission since the advent of the AIDS epidemic, and perinatally acquired infection remains quite rare in this country.<sup>13</sup> This epidemiologic pattern is distinct from that of Sub-Saharan Africa, where the burden of HIV is heaviest worldwide; in those countries, most infections are acquired heterosexually, and mother-to-child transmission remains a significant problem.<sup>14</sup>

## Populations at Risk for HIV

Certain populations are disproportionately affected by HIV. In the United States, men who have sex with men (MSM) account for the majority of HIV cases, yet comprise only 2% of the population.<sup>15</sup> Black Americans also bear a disproportionate burden of HIV. Blacks represent 14% of the U.S. population, but infections in blacks accounted for 44% of new HIV infections in 2009, according to the CDC.<sup>16</sup> The rate of new HIV infections in black men is six and a half times higher than that of white men, and two and half times higher than black women or Latino men.<sup>17</sup> The CDC estimates that 1 in 16 black men and 1 in 32 black

**Figure 2:** Dynamics of CD4+ Cell Count, Viral Load, and Diagnostic Testing During Primary HIV Infection



women will be diagnosed with HIV at some point in their lifetimes.<sup>18</sup>

Young, black MSM are currently the sub-population with the highest HIV incidence in the United States, and are the main target of HIV prevention campaigns in numerous U.S. cities. Treatment optimism is one of the proposed explanations for growth of the epidemic among young MSM.<sup>19</sup> Adolescents and many young adults did not live through the pre-HAART era when HIV was a fatal diagnosis, and therefore may doubt the seriousness of the disease or have undue confidence in available treatments and continue to engage in risky behavior.

## Pathophysiology

When HIV infection occurs via mucosal contact, as in sexual transmission, intact mucosal surfaces serve as a barrier to infection. Preexisting sexually transmitted infections lead to inflammation and breaks in the

mucosa and serve to enhance transmission of HIV.<sup>20</sup> Infection begins when the viral envelope glycoprotein (gp) 120 binds to the CD4+ receptor on T cells, macrophages, and dendritic cells, resulting in a conformational change in gp120 and binding to a co-receptor on the cellular membrane, CCR5 or CXCR4, facilitating viral entry into cells.<sup>21</sup> The virus then replicates within cells and spreads locally to other CD4+ target cells. By 72 hours, infection is established at the site of inoculation and draining lymphatic system.<sup>22</sup> After approximately seven days, the virus has spread systemically and the virus can be detected in the bloodstream via nucleic acid amplification tests.<sup>23</sup> The subsequent 8-30 days are characterized by massive viral replication, with doubling of viral load every eight hours and severe loss of CD4+ cells.<sup>24</sup> Rising viral load results in broad immune system activation and correlates with onset of clinical

**Table 1:** Prevalence of Signs and Symptoms in Patients with Acute HIV Compiled from Case Series and Case-Control Studies

Sign or Symptom	Approximate Prevalence (%)	Reported Odds Ratio from Literature
Fever	> 70	2.8-10.6
Lymphadenopathy	35-70	1.9-3.3
Sore throat	40-70	1.7-3.3
Rash	20-70	2.1-4.0
Joint pain	30-60	1.6-6.4
Diarrhea	25-50	3.1
Anorexia or weight loss	15-70	2.5-9.9
Night sweats	50	2.2-11.2
Myalgia	40-70	2.1-6.8
Malaise or fatigue	> 70	1.6-8.0
Headache	30-40	2.0-3.0
Vomiting	10-30	4.8
Too sick to work	60	4.0
Hospitalized	10-20	7.4
Oral or genital ulcer disease	10-20	2.1-2.6

Adapted from Zetola NM, Pilcher CD. Diagnosis and management of acute HIV infection. *Infect Dis Clin North Am* 2007;21:24; with permission.

symptoms of acute HIV.<sup>25</sup> (See Figure 2.)

By 3-7 weeks post-infection, HIV-specific antibodies can be detected in the patient's blood, an event known as seroconversion.<sup>26</sup> By four weeks post-infection, the viral load declines steeply, both due to the body's HIV-specific immune response, but probably also because the decimation of the CD4+ cell population means there are fewer hosts for viral replication.<sup>27</sup>

By causing depletion of helper T lymphocytes (CD4+ cells), HIV infection results in a state of cellular immune deficiency. This ultimately leads to immune system collapse and development of opportunistic infections and neoplasms, which characterize advanced AIDS.

### Clinical Presentation

The clinical presentation of acute HIV infection, also known as acute retroviral syndrome, was first described in 1985 as a mononucleosis-like illness that occurred

before antibodies to HIV appeared in the serum.<sup>28</sup> The percentage of patients newly infected with HIV who develop symptoms is difficult to measure. Many patients with acute HIV do not seek medical care, owing to the nonspecific and self-resolving nature of their symptoms. In addition, among those who do seek care, acute HIV is rarely diagnosed, both due to failure of practitioners to consider acute HIV in the differential of febrile illness and also because of limitations of standard testing during the acute period of infection. Nonetheless, experts estimate that 60-90% of patients acutely infected with HIV develop symptoms consistent with acute retroviral syndrome.<sup>29</sup> More severe symptoms during primary infection correlate with higher viral loads and predict faster progression to clinical AIDS.<sup>30</sup>

The classic presentation of acute HIV infection is the abrupt onset of symptoms following a 10-14 day incubation period.<sup>31</sup> Symptoms are nonspecific and include fever

(present in 80-90%),<sup>32</sup> malaise, myalgias, arthralgias, night sweats, anorexia, nausea, vomiting, headache, sore throat, and rash.<sup>33</sup>

Headache may be described as retrobulbar pain exacerbated by eye movements.<sup>34</sup> Oral, esophageal, and genital ulcers may be seen, but are less common.<sup>35</sup> (See Table 1.) No combination of symptoms has been shown to reliably include or exclude acute HIV.

Physical examination findings are variable and may include generalized lymphadenopathy, most pronounced in axillary, cervical, and occipital nodes,<sup>36</sup> mild hepatosplenomegaly, nonexudative pharyngitis, and mucocutaneous ulcers.<sup>37</sup> The rash is typically a fine maculopapular rash involving the thorax, face, and limbs, including the palms and soles, which appears 2-3 days after fever onset and persists 5-8 days.<sup>38</sup> Mucocutaneous ulcers are shallow, sharply demarcated lesions on the mouth, esophagus, anus, and genitalia.<sup>39</sup> Mucocutaneous candidiasis including oral thrush or vaginitis may be present. Meningeal signs and other neurologic findings such as cranial nerve palsies (especially cranial nerve VII), radiculopathy, and encephalopathy have been reported.<sup>40</sup> Severe opportunistic infections such as pneumocystis pneumonia may rarely occur during acute infection.<sup>41</sup>

While the majority of these signs and symptoms are nonspecific and can be seen with any viral illness, generalized lymphadenopathy, rash, mucosal ulceration, and candidiasis are relatively uncommon in adults with febrile illnesses and should raise the clinician's suspicion for acute HIV.<sup>42</sup> Symptoms of acute HIV generally resolve after 10-14 days, although malaise and generalized lymphadenopathy can persist for months.<sup>43</sup>

Laboratory findings in acute HIV infection are nonspecific and are similar to those seen in many other acute viral infections: mild anemia, leukopenia, thrombocytopenia, and transaminitis.<sup>44</sup> Testing for mononucleosis is sometimes performed in evaluating an adult with a febrile

illness. However, the heterophile antibody test may be positive during acute HIV infection, and it is unknown whether this represents a false-positive test or concurrent infection with HIV and Epstein-Barr virus.<sup>45</sup> Therefore, a positive monospot test should not be used to establish an alternative diagnosis when acute HIV is suspected.

### Testing for Acute HIV in the ED: A Public Health Imperative

The prevalence of acute HIV in patients presenting to the ED with symptoms is probably higher than most emergency physicians appreciate.<sup>46</sup> Rosenberg et al found that 1.2% of patients tested for infectious mononucleosis had serologic results consistent with acute HIV infection.<sup>47</sup> Pincus et al tested 499 patients presenting to a Boston urgent care center with “any viral symptoms” plus a risk factor for HIV and found that 1.0% tested positive for acute HIV infection.<sup>48</sup> In a high-risk population, such as in MSM, or in geographic areas with a high prevalence of HIV infection, the prevalence of acute HIV is probably higher.

Correctly making the diagnosis when acute HIV is suspected is critical from both public health and individual patient reasons. Epidemiologic studies suggest that between 17% and 50% of all cases of HIV were contracted from someone with an acute HIV infection,<sup>49</sup> underscoring the importance that acute infection plays in sustaining the HIV epidemic. One study of HIV-discordant couples reported that the rate of HIV transmission was 10 times higher when the infected partner had acute infection compared to chronic infection.<sup>50</sup> Mathematical modeling studies echo these figures, estimating an eight- to ten-fold increase in HIV transmission from an acutely infected person.<sup>51</sup> When the diagnosis of HIV is made, patients can be counseled on abstinence, safe sex, and safe needle practices, and data suggest patients do modify their behavior

**Table 2:** Results of Diagnostic Tests During Acute and Chronic HIV Infection

Type of Test	No HIV Infection	Acute HIV Infection	Chronic HIV Infection
Enzyme immunoassay (EIA) antibody tests (e.g., OraQuick Advance®)	Negative	Usually negative	Positive
Nucleic acid antibody tests (NAAT) (e.g., Roche Amplicor® HIV-1 DNA PCR)	Negative	Positive	Positive
p24 Antigen test	Negative	Positive	Positive or negative

Adapted from Self WH. Acute HIV infection: Diagnosis and management in the emergency department. *Emerg Med Clin North Am* 2010;28:386, with permission.

when they are aware of their diagnosis.<sup>52</sup> In addition, exposed contacts can be identified and tested.

From an individual standpoint, there is growing evidence that outcomes are improved when treatment is initiated early in the course of infection. Because HIV infection has a long chronic asymptomatic stage, diagnosis is often delayed until very late in its course when opportunistic infections appear. Therefore, patients miss the survival benefit of initiating antiretroviral treatment prior to onset of AIDS.<sup>53</sup> In addition, emerging data suggest that treatment initiated during acute infection may speed immune system reconstitution and impact the natural course of the disease.<sup>54</sup> Therefore, early recognition of HIV infection has the potential to prolong survival and improve patient outcomes.

### Approach to the Patient

The diagnosis should be considered in patients with fever and viral syndromes who have exposure to an HIV-positive partner, unprotected sex, multiple sexual partners, history of sexually transmitted infection, anal receptive intercourse, active genital ulcer in self or partner, injection drug use, and needle sharing. Patients who have symptoms of a viral illness plus one or more HIV risk factors should be considered for testing for acute HIV. When acute

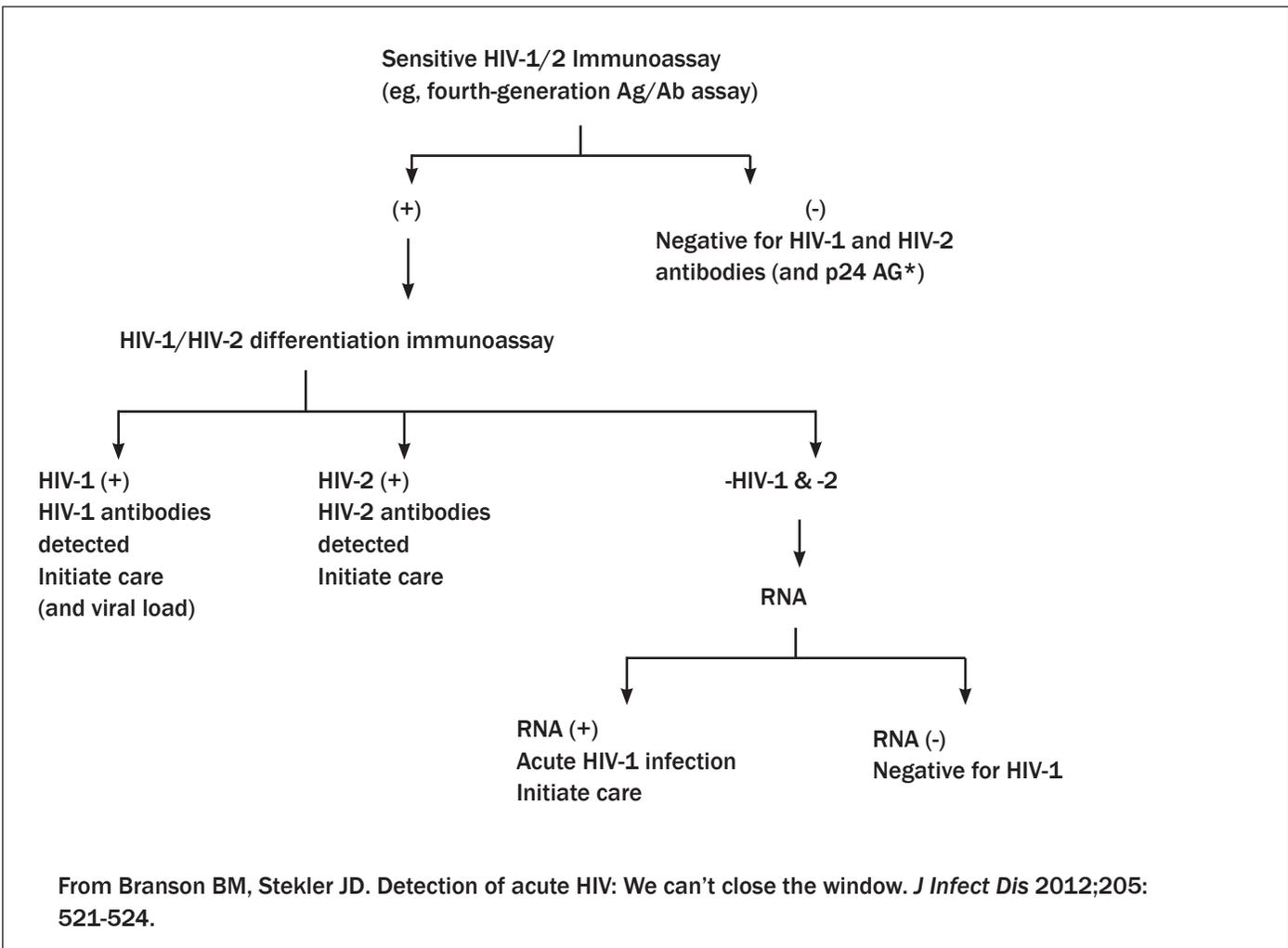
HIV is considered, examination of the oropharynx, genitals, and lymph nodes may be helpful. Patients who do not have classic HIV risk factors but exhibit a constellation of signs and symptoms concerning for acute HIV, such as generalized lymphadenopathy, diffuse rash, and mucosal ulceration, may be considered for testing.

### Diagnostic Testing

There are two major categories of tests used in the diagnosis of HIV. Antibody-based tests, including enzyme-linked immunosorbent assays (EIAs) and Western blot, are indirect tests that detect the presence of anti-HIV antibodies produced by the body. Their main limitation is their false-negative rate during the window period of acute infection, when patients are viremic but do not yet have detectable antibodies. Nucleic acid amplification tests (NAATs), such as polymerase chain reaction (PCR), directly measure viral RNA in the patient’s blood and are highly sensitive in acute HIV. Their drawbacks include high cost, prolonged turnaround time, and a moderate false-positive rate, which is problematic in a low prevalence population.<sup>55</sup> In addition, they only detect HIV-1, not the much rarer HIV-2.

The sensitivity of antibody tests for acute infection depends on the

**Figure 3:** Proposed Testing Algorithm for Diagnosis of HIV-1 and HIV-2 Infection



generation of test used. First- and second-generation EIA tests typically turn positive two to three months post-infection.<sup>56</sup> Third-generation tests, which detect earlier-appearing IgM antibodies in addition to IgG, narrow the window period and can identify infection as early as four weeks post-infection or two weeks after onset of symptoms.<sup>57</sup> The newest fourth-generation tests screen for both anti-HIV antibodies and p24 antigen and can detect infection within 2-3 weeks of infection or 7-10 after onset of symptoms. Clinicians should be aware that at this time, most of the rapid or point-of-care HIV tests utilized in EDs are second-generation EIA antibody tests, which means they have high sensitivity in patients who have already seroconverted, but are not reliable in identifying

acute infection.<sup>58</sup> (See Table 2.) Of note, newer EIA tests have comparable sensitivity and are much less resource-intensive than traditional Western blot, leading some centers to phase out Western blot testing as part of revised test algorithms.

When acute HIV infection is suspected, it is reasonable to perform a rapid (EIA) test, with the understanding that a negative result cannot rule out infection. There are currently five rapid HIV tests licensed for use in the United States (OraQuick Advance<sup>®</sup>, Uni-Gold Recombigen<sup>®</sup> Reveal G-3<sup>®</sup>, MultiSpot HIV-1/HIV-2<sup>®</sup>, Clearview HIV 1/2 Stat-pak<sup>®</sup>, and Clearview Complete 1/2<sup>®</sup>). If the rapid test is negative and acute HIV is suspected, nucleic acid amplification testing can be performed.

Unfortunately, NAATs take several

hours to run, which means that results are not available during the usual time frame of an ED visit. Therefore, EDs should consider developing an institution-specific HIV testing policy whereby patients are either tested on site and notified of results after discharge, or else referred where expeditious outpatient viral testing can be performed. It should be noted that NAATs do have a measurable false-positive rate, but are usually marked by a low viral load that would not be consistent with acute infection.<sup>59</sup> Patients who have a positive test should be referred for further confirmatory testing and initiation of care with an HIV specialist. In addition, clinicians should be aware that there is still a window period for NAATs, which may be negative if checked very early after transmission. Therefore, if the

suspicion for acute HIV is high, repeat testing several days later can be performed.

Historically, emergency physicians have been reluctant to perform tests requiring complicated follow-up, such as HIV testing, instead seeing this as the domain of primary care clinics that are better equipped to follow patients and arrange further care. A 2002 survey of 154 emergency department providers found that only 10% routinely recommended that patients diagnosed with sexually transmitted infection be tested for HIV, and concern about follow-up was the most commonly cited reason.<sup>60</sup> However, many of the patients at risk for HIV do not have insurance or primary care physicians, and use the ED primarily for their health care needs. Therefore, not performing testing under the faulty assumption that it can be managed by a primary care physician misses a critical public health opportunity to identify cases of acute HIV early and intervene in the disease epidemic. This is an ideal scenario for EDs to partner with state public health departments, which are highly invested in monitoring HIV and well-suited to facilitate testing, referral, and patient tracking.

Much debate has centered around the cost-effectiveness of screening patients with viral symptoms for acute HIV, given the fact that the majority of patients tested will not turn out to have acute HIV as the cause of their symptoms. A cost-effectiveness analysis by Coco et al determined that screening patients with fever and viral symptoms and one HIV risk factor with a fourth-generation EIA antibody test had a high probability of being cost effective, in part because identifying cases of acute HIV in an individual could prevent subsequent infections in the patient's network of contacts.<sup>61</sup>

### **What's on the Horizon: The Future of HIV Testing**

An issue related to acute HIV testing in symptomatic patients is screening of asymptomatic patients for HIV infection. In 2006 the CDC

published revised guidelines for HIV testing, which advocate routine testing of patients in all health care settings, including primary care and emergency care, unless they specifically decline the test (opt-out screening).<sup>62</sup> In an effort to remove barriers, they no longer required separate written consent for HIV testing; rather, the general consent obtained for medical treatment is deemed sufficient to encompass HIV testing. In addition, the requirement that HIV counseling be provided at the time of testing is also waived.

Despite the intention of simplicity, many believe these guidelines are impractical for busy EDs and, in fact, few EDs have been able to implement them. A survey of 131 academic medical centers and 450 community EDs regarding their HIV testing policies one year after the guidelines were published found that only 16% of academic medical center EDs and 6% of community EDs performed routine testing for HIV as recommended by the CDC.<sup>63</sup>

The traditional HIV screening algorithm, dating from 1989, starts with an EIA antibody test, which, if positive for the presence of anti-HIV antibodies, is followed by a confirmatory Western blot test to detect viral antigen. As previously discussed, antibody tests may miss cases of acute HIV in patients who have high viral titers but undetectable antibodies. Given the significant contribution that acute HIV plays in sustaining the HIV epidemic, much interest has been focused on developing screening tests that can detect acute HIV infection.

At the time of this writing, the CDC is updating its HIV testing algorithm, with new guidelines set to be published in late 2012.<sup>64</sup> The proposed guidelines endorse using a fourth-generation EIA that detects p24 antigen and anti-HIV-1/HIV-2 antibodies and has enhanced sensitivity for acute infection, followed by a confirmatory HIV-1/HIV-2 test if positive, and viral RNA assay if negative.<sup>65</sup> (See Figure 3.) This testing strategy shortens the window period significantly compared to the prior

algorithm, detecting infection by 7-10 days after onset of symptoms.

Other tests currently in development include a rapid NAAT test, which would allow point-of-care ED screening for acute HIV infection,<sup>66</sup> and an over-the-counter rapid HIV fourth-generation antibody test.

### **Management of Acute HIV**

Priorities in the management of acute HIV include referral to an HIV specialist, consideration of initiating highly active antiretroviral therapy (HAART), providing counseling on abstinence, safe sex, and avoidance of needle sharing to prevent further transmission, identification and testing of contacts, and psychosocial support. Concomitant conditions such as sexually transmitted infections or, rarely, opportunistic infections such as thrush, should also be treated.

Follow-up in an HIV clinic is important for all patients diagnosed with acute HIV. HIV specialists will provide disease monitoring including quantitative viral load measurements, initiation and modification of antiretroviral regimens, initiation of prophylactic antibiotics when CD4+ levels fall, and counseling and support.

The decision to start HAART should be made in consultation with an infectious disease specialist. Preliminary studies suggest that there may be a benefit to starting antiretroviral treatment as early as possible during acute HIV infection. These benefits include slowing depletion of the CD4+ cell population, limiting viral mutations and thereby decreasing the likelihood of antiviral resistance, improving symptoms of acute retroviral syndrome, and speeding immune system reconstitution.<sup>67</sup> While initiation of HAART during acute infection has been shown to improve laboratory markers of disease progression, there are no randomized controlled trials demonstrating improved long-term survival with antiretroviral treatment in primary infection compared to treatment started later during the

course of infection.<sup>68</sup> The early initiation of treatment does expose the patient to a longer lifetime course of medications with their inherent side effects. Nonetheless, given the clear survival benefit from HAART therapy in chronic HIV infection,<sup>69</sup> with improved survival corresponding to earlier initiation of treatment, many experts favor starting antiretroviral therapy in acute infection.

Counseling on risk reduction is a critical component of the management of acute HIV. Patients should be counseled on the extreme infectious potential of acute HIV and strategies to prevent transmission, including practicing sexual abstinence, using condoms, avoiding needle sharing, and refraining from donating blood. Brief risk-reduction counseling has been shown to be highly effective in reducing risky behaviors that could contribute to spread of HIV, particularly in individuals newly diagnosed with HIV.<sup>70</sup>

HIV is a nationally reportable disease, and all new cases of HIV should be reported to the public health department. By partnering with local and state public health officials, the index patient's recent sexual or needle-sharing contacts can be identified and screened for HIV. This strategy has been shown to be effective in identifying a network of people who are at high risk for HIV, and can result in identification of other infected individuals.<sup>71</sup>

## Summary and Recommendations

Most patients acutely infected with HIV will develop a symptomatic episode of a viral illness, and many will seek medical care in emergency departments for their symptoms. Clinicians need to maintain a high index of suspicion that patients presenting with a febrile illness may in fact have acute HIV. Patients who have a risk factor for HIV or who have physical findings suggestive of acute HIV should be screened using viral RNA testing, which is most sensitive for acute infection. Special attention should be paid to the MSM and black male populations, who are

at especially high risk for HIV infection in this country.

Diagnosing acute HIV represents a critical public health opportunity to intervene in the disease epidemic. By identifying patients when they are at the peak of infectivity, and counseling them on risk-reduction behaviors to prevent transmission to others, additional cases of HIV infection can be prevented. Patients identified with acute HIV infection can be referred to infectious disease clinics and begin treatment for HIV early in the course of illness, an intervention that may lead to improved disease outcomes. EDs need to expand current HIV testing protocols to include testing for acute HIV.

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## Physician CME Questions

- During the natural history of HIV infection, the stage of infection when patients are most infectious and most likely to transmit the virus to other is:
  - in advanced AIDS
  - in the chronic asymptomatic phase of infection
  - during acute infection
  - any time the CD4+ count drops below 500
  - none of the above
- The population group most severely affected by HIV in the United States is:
  - men who have sex with men
  - injection drug users
  - heterosexual women
  - Hispanic ethnicity
  - individuals younger than the age of 20 years
- The most common means of transmission of HIV (both in the United States and worldwide) is:
  - injection drug use
  - vertical transmission from mother to child
  - via contaminated blood in blood transfusions
  - sexual transmission
- Symptoms of acute HIV infection, or antiretroviral syndrome, are believed to occur in what percent of individuals infected with HIV?
  - 1%
  - 10%
  - 50%
  - > 60-90%
- The most common symptoms of acute HIV include:
  - no symptoms; most individuals are asymptomatic
  - fever, malaise, myalgias, anorexia, sore throat, and rash
  - vomiting, diarrhea, and abdominal pain
  - fever, productive cough, and shortness of breath
  - neurologic symptoms like vertigo, cranial nerve palsies, and paresthesias
- Physical exam findings in the ED that should trigger concern for acute HIV infection in an at-risk individual include all of the following *except*:
  - generalized lymphadenopathy
  - thrush
  - nystagmus
  - oral and genital ulcers
  - maculopapular rash
- The "window period" of acute HIV infection refers to:
  - the first six months of infection
  - the period of time between acquisition of the virus and development of clinical AIDS
  - the period of time during which patients are viremic with high viral loads but antibody tests are negative
  - the time between initiation of antiretroviral treatment and fall of viral load
- When acute HIV is suspected, the following diagnostic strategy should be utilized:
  - An antibody test should be performed, and if the test is negative, it excludes acute HIV infection.
  - An antibody test can be performed first, but if negative, infection is not excluded. Instead, direct viral testing with nucleic acid amplification tests should be performed.
  - A Western blot should be performed, which is most sensitive for acute infection.
  - A viral culture from the patient's sputum should be performed.
  - A chest X-ray and blood cultures should be ordered.
- When a patient is identified as having acute HIV, he or she should be:
  - referred to an infectious disease specialist for ongoing care
  - counseled on risk-reduction behaviors, including abstinence, condom use, and avoidance of needle-sharing and blood donation
  - provided psychosocial support
  - referred to the public health department so that high-risk contacts can be identified and screened for HIV
  - all of the above
- Acute HIV has been termed a public health emergency because:
  - Acute HIV is the most infectious stage of HIV when patients have high viral loads and high levels of viral shedding.
  - Patients are often unaware they are infected and may unwittingly transmit the virus to others by continuing in the same risky behaviors from which they acquired it in the first place.
  - A significant percentage of all cases of HIV are acquired from someone with acute infection and, as such, acute HIV contributes substantially to sustaining the HIV epidemic.
  - All of the above

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*Upon completion of this educational activity, participants should be able to:*

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- apply state-of-the-art diagnostic and therapeutic techniques to patients with the particular medical problems discussed in the publication;
- discuss the differential diagnosis of the particular medical problems discussed in the publication;
- explain both the likely and rare complications that may be associated with the particular medical problems discussed in the publication.

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Periodicals Postage Paid at Atlanta, GA 30304 and at  
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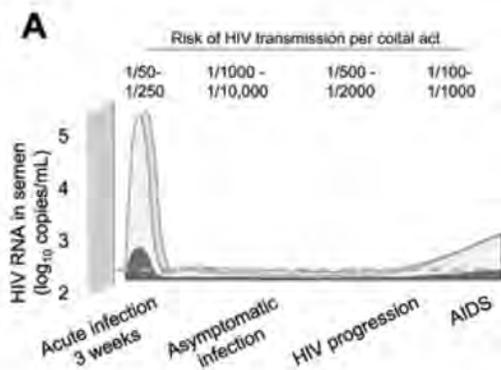
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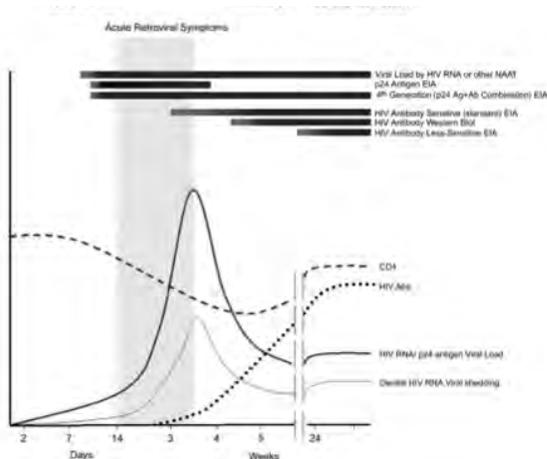
## Acute HIV in the ED

### Viral Load and Risk of HIV Transmission



Used with permission from Cohen MS, Pilcher, CDJ. Amplified HIV transmission and new approaches to HIV prevention. *J Infect Dis* 2001;191:1391-1393.<sup>7</sup>

### Dynamics of CD4+ Cell Count, Viral Load, and Diagnostic Testing During Primary HIV Infection



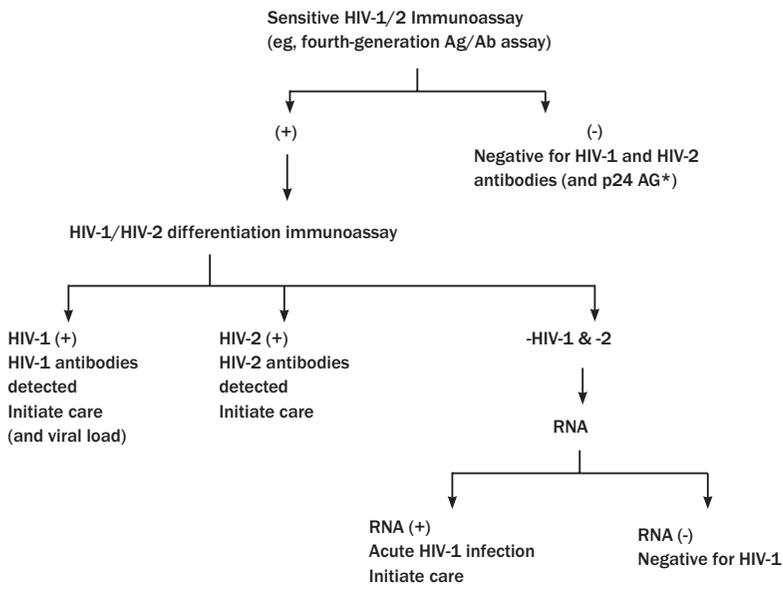
HIV viral load rises steeply during acute infection and falls as anti-HIV antibodies appear. The symptomatic period is in light gray. Ab, antibody; Ag, antigen; EIA, enzyme immunoassay; NAAT, nucleic acid amplification test. Adapted from: Zetola NM, Pilcher CD. Diagnosis and management of acute HIV infection. *Infect Dis Clin North Am* 2007;21:22; with permission.

### Prevalence of Signs and Symptoms in Patients with Acute HIV Compiled from Case Series and Case-Control Studies

Sign or Symptom	Approximate Prevalence (%)	Reported Odds Ratio from Literature
Fever	> 70	2.8-10.6
Lymphadenopathy	35-70	1.9-3.3
Sore throat	40-70	1.7-3.3
Rash	20-70	2.1-4.0
Joint pain	30-60	1.6-6.4
Diarrhea	25-50	3.1
Anorexia or weight loss	15-70	2.5-9.9
Night sweats	50	2.2-11.2
Myalgia	40-70	2.1-6.8
Malaise or fatigue	> 70	1.6-8.0
Headache	30-40	2.0-3.0
Vomiting	10-30	4.8
Too sick to work	60	4.0
Hospitalized	10-20	7.4
Oral or genital ulcer disease	10-20	2.1-2.6

Adapted from Zetola NM, Pilcher CD. Diagnosis and management of acute HIV infection. *Infect Dis Clin North Am* 2007;21:24; with permission.

## Proposed Testing Algorithm for Diagnosis of HIV-1 and HIV-2 Infection



From Branson BM, Stekler JD. Detection of acute HIV: We can't close the window. *J Infect Dis* 2012;205: 521-524.

## Results of Diagnostic Tests During Acute and Chronic HIV Infection

Type of Test	No HIV Infection	Acute HIV Infection	Chronic HIV Infection
Enzyme immunoassay (EIA) antibody tests (e.g., OraQuick Advance®)	Negative	Usually negative	Positive
Nucleic acid antibody tests (NAAT) (e.g., Roche Amplicor® HIV-1 DNA PCR)	Negative	Positive	Positive
p24 Antigen test	Negative	Positive	Positive or negative

Adapted from Self WH. Acute HIV infection: Diagnosis and management in the emergency department. *Emerg Med Clin North Am* 2010;28:386, with permission.

Supplement to *Emergency Medicine Reports*, July 16, 2012: "Acute HIV in the Emergency Department." Authors: **Karen D. Serrano, MD**, Clinical Instructor, Emergency Medicine Residency Program, University of Wisconsin School of Medicine and Public Health; and **Ryan P. Westergaard, MD, MPH**, Assistant Professor of Medicine, Division of Infectious Diseases, University of Wisconsin School of Medicine and Public Health.

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