

DIAGNOSIS AND MANAGEMENT OF ACUTE HIV INFECTION

Editor's Note:

In the medical literature, as in this chapter, the terms *acute HIV infection* and *primary HIV infection* are interchangeable. For consistency, the term *acute HIV infection* is used in these guidelines.

IMPORTANT NOTE (OCTOBER 2012)

- Clinicians should obtain a plasma HIV RNA assay to exclude HIV infection when there is a discrepancy between an HIV screening test and an HIV confirmatory test, such as the Western blot. See the New York City Department of Health and Mental Hygiene [2012 Health Advisory #29](#).

I. INTRODUCTION

Studies suggest that as many as 50% of HIV transmissions occur during the acute and early stage of the illness.¹⁻⁵ A number of factors contribute to the increased risk for transmission during acute infection:

- Markedly increased viral load levels during acute infection (often much greater than 10 million viral copies/mm³)
- Likelihood that risky behaviors are ongoing during this period because the individual is unaware of his/her HIV status
- The nonspecific “flu-” or “mono-like” symptoms of acute HIV infection that are frequently unrecognized as an indication of HIV infection

Detection of acute HIV infection provides an opportunity to follow patients prospectively soon after infection and thereby reduce disease progression and incidence of OIs. Because patients with a recent diagnosis of HIV are more likely to reduce risk behaviors if they are linked to primary HIV care than if they are not receiving care,⁶ early detection may also be a critical component of preventing further transmission.

II. PRESENTATION AND DIAGNOSIS OF ACUTE HIV INFECTION

RECOMMENDATIONS:

Clinicians should evaluate the following populations for acute HIV infection, particularly when they present with a febrile, “flu”-, or “mono”-like illness that is not otherwise explained:

- Those who present for HIV testing (AIII)
- Those who report a recent sexual or parenteral exposure with a known HIV-infected partner or a partner of unknown HIV serostatus in the past 2 to 6 weeks (AII)
- Men who report having unsafe sexual practices with other men (AII)
- Those who report needle-sharing (AII)
- Those who present with a newly diagnosed sexually transmitted infection (AII)
- Those who present with aseptic meningitis (AII)
- Pregnant or breastfeeding patients (AIII)

When acute HIV infection is suspected:

- An HIV serologic screening test should be used in conjunction with a plasma HIV RNA assay (AII); the plasma RNA test should be performed even if the serologic screening test is negative (AIII); a fourth-generation HIV antigen/antibody combination test is the preferred serologic screening test if available
- Detection of HIV RNA or antigen in the absence of HIV antibody should be considered a preliminary positive result; HIV RNA testing from a new specimen should be repeated immediately to confirm the presence of HIV RNA
- Both serologic and RNA testing should be repeated to exclude a false-positive result when low-level quantitative results (<5,000 copies/mL) from an HIV RNA assay are reported in the absence of serologic evidence of HIV infection (AII)

HIV serologic testing should be repeated 2 to 3 weeks after diagnosis by HIV RNA testing to confirm infection. (AII) However, clinicians should *not* wait for HIV serologic confirmatory test results to initiate ART when pregnant women are diagnosed with acute HIV infection by HIV RNA testing. Initiation of ART is strongly recommended for pregnant women (see [Acute HIV Infection in Pregnancy](#)). (AII)

Clinicians must report confirmed cases of HIV according to [New York State Law](#) (for more information about required reporting, see www.health.ny.gov/diseases/aids/regulations/partner_services/index.htm).

Key Point:

The diagnosis of acute HIV infection requires a high degree of clinical awareness. The nonspecific signs and symptoms of acute HIV infection are often not recognized. Diagnostic HIV RNA testing should be considered for patients who present with compatible symptoms (see Appendix A), particularly in the context of a sexually transmitted infection or a recent sexual or parenteral exposure with a known HIV-infected partner or a partner of unknown HIV serostatus.

A. Presentation

Patients acutely infected with HIV will often experience at least some symptoms of the acute retroviral syndrome. Fever and flu- or mono-like symptoms are common in acute HIV infection but are nonspecific. Rash, mucocutaneous ulcers, oropharyngeal candidiasis, and meningismus are more specific and should raise the index of suspicion. See Appendix A for a more extensive list of signs and symptoms. The mean time from exposure to onset of illness is generally 2 to 4 weeks, with a range of 5 to 29 days; however, some cases have presented with symptoms up to 3 months after exposure.⁷

B. Diagnosis

Acute HIV infection is often not recognized in the primary care setting because of the similarity of the symptom profile with that of the flu or other common illnesses. Furthermore, patients often do not recognize that they may have recently been exposed to HIV. Therefore, the clinician should have a high index of suspicion for acute HIV infection in a patient who may have recently engaged in behavior involving sexual or needle exposure and who is presenting with febrile, flu-, or mono-like illness.

When clinicians suspect acute infection (e.g., in a patient with a report of recent risk behavior in association with symptoms and signs of the acute retroviral syndrome), a test for HIV RNA should be performed. High levels of HIV RNA detected in plasma through use of sensitive amplification assays (PCR, bDNA, or NASBA), in combination with a negative or indeterminate HIV antibody test, support the diagnosis of acute HIV infection. Low-level positive PCR results (<5000 copies/mL) are often not diagnostic of acute HIV infection and should be repeated to exclude a false-positive result. HIV RNA levels tend to be very high in acute infection; however, a low value may represent any point on the upward or downward slope of the viremia associated with acute infection. Plasma HIV RNA levels during seroconversion do not appear significantly different in patients who have acute symptoms versus those who are asymptomatic.⁸ Viremia occurs approximately 2 weeks prior to the detection of a specific immune response. Patients diagnosed with acute HIV infection by HIV RNA testing still require antibody testing with confirmatory Western blot 3 to 6 weeks later.

Key Points:

- Patients undergoing HIV testing who are not suspected to be in the acute stages of infection should receive HIV antibody testing according to standard protocol (see [Diagnostic, Monitoring, and Resistance Laboratory Tests for HIV](#)). Antibody test results that are initially negative should be followed up with HIV antibody testing at 3 months to identify HIV infection in individuals who may not yet have seroconverted at the time of initial presentation.
- Diagnostic HIV laboratory tests and interpretation algorithms evolve; individual laboratories have internal protocols for reporting tests with preliminary results. *Indeterminate*, *inconclusive*, *non-diagnostic*, and *pending validation* are among the terms used when preliminary results cannot be classified definitively. The clinician should contact the appropriate laboratory authority to determine the significance of the non-definitive results and the supplemental testing that would be indicated. This is of particular importance in tests from patients with suspected acute HIV infection. Clinicians should become familiar with the internal test-reporting policies of their institutions.

III. MANAGEMENT OF ACUTE HIV INFECTION

RECOMMENDATIONS:

Clinicians should offer assistance with partner notification, or refer patients to other sources for partner notification assistance ([Partner Services](#) or [CNAP](#)).

Clinicians should counsel patients about the increased risk of transmitting HIV during acute HIV infection. (AII)

Clinicians should obtain baseline genotypic testing in the setting of acute infection, regardless of whether ARV therapy is being initiated. (AIII)

As part of the management of acute HIV infection, clinicians should:

- **Consult with a provider who has extensive experience in HIV treatment to determine whether to initiate treatment and to discuss possible ARV regimens (see [Clinical Education Initiative](#) sites available for phone consultation) (AIII)**
- **Refer for research opportunities as appropriate (AIII)**
- **Counsel patients regarding potential advantages and limitations of ARV therapy during acute infection (AIII)**

If the clinician and patient have made a decision to initiate ARV therapy to treat acute HIV infection, then:

- **Treatment should be implemented with the goal of suppressing plasma HIV RNA to below detectable levels (AII)**
- **Therapy should not be withheld while awaiting the results of recommended resistance testing; adjustments may be made to the regimen once resistance results are available (AII)**

Patients are at greatest risk for transmitting HIV during the period of viremia prior to the viral setpoint.^{1,9} Clinicians should counsel acutely infected patients about this increased risk of transmitting HIV during the 6-month period after infection.

Although evidence suggests that early ARV treatment has a beneficial effect on clinical outcome,¹⁰⁻¹² the long-term clinical effect of initiating potent treatment regimens early in HIV infection is currently unclear. The clinician and the patient should be aware that therapy for acute HIV infection is primarily based on theoretical considerations, and the potential benefits should be weighed against the potential risks (see Table 1). Data from ongoing clinical trials may help clarify the long-term benefits of treatment of acute infection.

TABLE 1
THEORETICAL RATIONALE FOR AND DISADVANTAGES OF
INITIATING ARV THERAPY DURING ACUTE INFECTION

Rationale for ARV therapy	<ul style="list-style-type: none"> • To reduce the risk of viral transmission • To preserve HIV-specific immune function, including promoting the survival of CD4 cells that are involved in the initial response to HIV infection • To suppress the initial burst of viral replication and decrease the magnitude of viral dissemination • To potentially lower the initial viral setpoint, which may ultimately affect the rate of disease progression • To potentially reduce the emergence of viral mutations as a result of the suppression of viral replication
Disadvantages of ARV therapy	<ul style="list-style-type: none"> • Adverse effects on quality of life as a result of drug toxicities and complex treatment regimens • Potential for the development of drug resistance if therapy fails due to nonadherence or to insufficient suppression of viral replication, which may limit future treatment options • Earlier commitment to lifetime ARV therapy • Less time to educate the patient about ARV therapy • Insufficient data regarding effectiveness of early treatment

If the clinician and patient have made the decision to use ARV therapy for acute HIV infection, treatment should be implemented with the goal of suppressing plasma HIV RNA levels to below detectable levels. The patient should be counseled regarding potential limitations, and individual decisions should be made only after weighing the risks of therapy against the theoretical benefit of treatment.

Key Point:

Because there are insufficient data to make firm conclusions regarding specific drug recommendations for treating acute HIV infection, a provider with extensive experience in HIV treatment should be consulted when choosing an ARV regimen for a patient with acute HIV infection. The New York State Department of Health AIDS Institute’s [Clinical Education Initiative line](#) is available for consultation.

Resistance testing should be obtained to optimize the initial ARV regimen. The increasing incidence of transmission of ARV resistance argues for resistance testing at baseline in all HIV-infected patients, including those who are acutely infected. If information about the source person is available, history of ARV drug resistance should be obtained to assist in selection of a regimen.

Key Point:

The use of a genotypic assay may be preferred in the setting of acute infection because of its more rapid turnaround time. However, if the decision to initiate treatment has been made, therapy should *not* be withheld while awaiting the results of resistance testing. Adjustments may be made to the regimen once resistance results are available (see [Antiretroviral Therapy: VI. 3. Resistance Assays](#)).

If therapy is initiated during acute HIV infection, many clinicians would continue to treat the patient with ARV therapy indefinitely because viremia has been documented to reappear or increase after discontinuation of such therapy; however, this view may change as new evidence becomes available. When discussing whether or not therapy should be continued, clinicians should provide the patient with information regarding current clinical data.

Regardless of whether or not ARV therapy for acute HIV infection is initiated, follow-up for standard HIV testing and HIV primary care should be arranged (see [*Primary Care Approach to the HIV-Infected Patient*](#)).

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FURTHER READING

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- Patel P, Klausner JD, Bacon OM, et al. Detection of acute HIV infections in high-risk patients in California. *J Acquir Immune Defic Syndr* 2006;42:75-79. [[PubMed](#)]
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APPENDIX A. ACUTE RETROVIRAL SYNDROME

ACUTE RETROVIRAL SYNDROME: ASSOCIATED SIGNS AND SYMPTOMS (EXPECTED FREQUENCY AMONG PATIENTS WHO ARE SYMPTOMATIC)

- Fever (80%)
- Tired or fatigued (78%)
- Malaise (68%)
- Arthralgias (joint pain) (54%)
- Headache (54%)
- Loss of appetite (54%)
- Rash (51%)
- Night sweats (51%)
- Myalgias (pain in muscles) (49%)
- Nausea (49%)
- Diarrhea (46%)
- Fever and rash (46%)
- Pharyngitis (sore throat) (44%)
- Oral ulcers (mouth sores) (37%)
- Stiff neck (34%)
- Weight loss (>5 lb; 2.5 kg) (32%)
- Confusion (25%)
- Photophobia (24%)
- Vomiting (12%)
- Infected gums (10%)
- Sores on anus (5%)
- Sores on genitals (2%)

Data are from Hecht FM, Busch MP, Rawal B, et al. Use of laboratory tests and clinical symptoms for identification of primary HIV infection. *AIDS* 2002;16:1119-1129.

* The most specific symptoms in this study were oral ulcers and weight loss. Best predictors were fever and rash. Index of suspicion should be high when these symptoms are present.