

DIAGNOSIS AND MANAGEMENT OF ACUTE HIV INFECTION

What's New - January 2010 Update

- The Medical Care Criteria Committee recognized the need to raise clinical awareness for assessment and identification of acute HIV infection; consequently, these guidelines have been revised to emphasize the importance of testing for acute HIV infection, especially in the setting of a febrile, “flu”-, or “mono”-like illness that is not otherwise explained (see Section II. *Presentation and Diagnosis of Acute HIV Infection*).

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.

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, a plasma HIV RNA assay should be used in conjunction with an HIV-1 antibody test to diagnose acute HIV infection. (AII) 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. (AII)

Confirmatory HIV antibody testing should be performed 3 to 6 weeks after diagnosis by HIV RNA testing. (AII)

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 Point:

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.

III. MANAGEMENT OF ACUTE HIV INFECTION

RECOMMENDATIONS:

Clinicians should offer assistance with partner notification, or refer patients to other sources for partner notification assistance (CNAP, PNAP).

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** (see Appendix B) (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 (see Appendix B for a list of ongoing trials).

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](#)).

REFERENCES

1. Brenner BG, Roger M, Routy JP, et al. High rates of forward transmission events after acute/early HIV-1 infection. *J Infect Dis* 2007;195:951-959. [[PubMed](#)]
2. Yerly S, Vora S, Rizzardì P, et al; Swiss HIV Cohort Study. Acute HIV infection: Impact on the spread of HIV and transmission of drug resistance. *AIDS* 2001;15:2287-2292. [[PubMed](#)]
3. Cohen MS, Pilcher CD. Amplified HIV transmission and new approaches to HIV prevention. *J Infect Dis* 2005;191:1391-1393. [[PubMed](#)]
4. Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection in Rakai, Uganda. *J Infect Dis* 2005;191:1403-1409. [[PubMed](#)]
5. Remien RH, Higgins JA, Correale J, et al. Lack of understanding of acute HIV infection among newly-infected persons: Implications for prevention and public health: The NIMH Multisite Acute HIV Infection Study: II. *AIDS Behav* 2009;13:1046-1053. [[PubMed](#)]
6. Metsch LR, Pereyra M, Messinger S, et al. HIV transmission risk behaviors among HIV-infected persons who are successfully linked to care. *Clin Infect Dis* 2008;47:577-584. [[PubMed](#)]
7. Apoola A, Ahmad S, Radcliffe K. Primary HIV infection. *Int J STD AIDS* 2002;13:71-78. [[PubMed](#)]
8. Pilcher CD, Price MA, Hoffman IF, et al. Frequent detection of acute primary HIV infection in men in Malawi. *AIDS* 2004;18:517-524. [[PubMed](#)]
9. Pilcher CD, Tien HC, Eron JJ, et al. Brief but efficient: Acute HIV infection and the sexual transmission of HIV. *J Infect Dis* 2004;189:1785-1792. [[PubMed](#)]
10. Streeck H, Jessen H, Alter G, et al. Immunological and virological impact of highly active antiretroviral therapy initiated during acute HIV-1 infection. *J Infect Dis* 2006;194:734-739. [[PubMed](#)]
11. Pires A, Hardy G, Gazzard B, et al. Initiation of antiretroviral therapy during recent HIV-1 infection results in lower residual viral reservoirs. *J Acquir Immune Defic Syndr* 2004;36:783-790. [[PubMed](#)]
12. Koegl C, Wolf E, Hanhoff N, et al. Treatment during primary HIV infection does not lower viral set point but improves CD4 lymphocytes in an observational cohort. *Eur J Med Res* 2009;14:277-283. [[PubMed](#)]

FURTHER READING

- Hecht FM, Wang L, Collier A, et al. A multicenter observational study of the potential benefits of initiating combination antiretroviral therapy during acute HIV infection. *J Infect Dis* 2006;194:725-733. [[PubMed](#)]
- 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](#)]
- Streeck H, Jessen H, Kuecherer C, et al. Epidemiologically linked transmission of HIV-1 illustrates the impact of host genetics on virological outcome. *AIDS* 2009;23:259-262. [[PubMed](#)]

APPENDIX A

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.

APPENDIX B

November 2009

CURRENT RESEARCH ON ACUTE HIV INFECTION BY NEW YORK HIV RESEARCH CENTERS CONSORTIUM*

Center	Type(s) of Research	Contact Information
Aaron Diamond AIDS Research Center (ADARC)	<ul style="list-style-type: none">• Basic Laboratory Science• Clinical/Biomedical Science	Martin Markowitz, MD Clinical Director and Principal Investigator on Acute Infection and Early Disease Research Program Grant mmarkowitz@adarc.org
Center for AIDS Research (CFAR) New York University School of Medicine	<ul style="list-style-type: none">• Basic Laboratory Science• Clinical/Biomedical Science• Behavioral/Prevention Science	First Call NYU firstcallnyu@nyumc.org 1-212-263-3544

* As of November 2009.