

# ACUTE HIV INFECTION IN PREGNANCY

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## I. Introduction

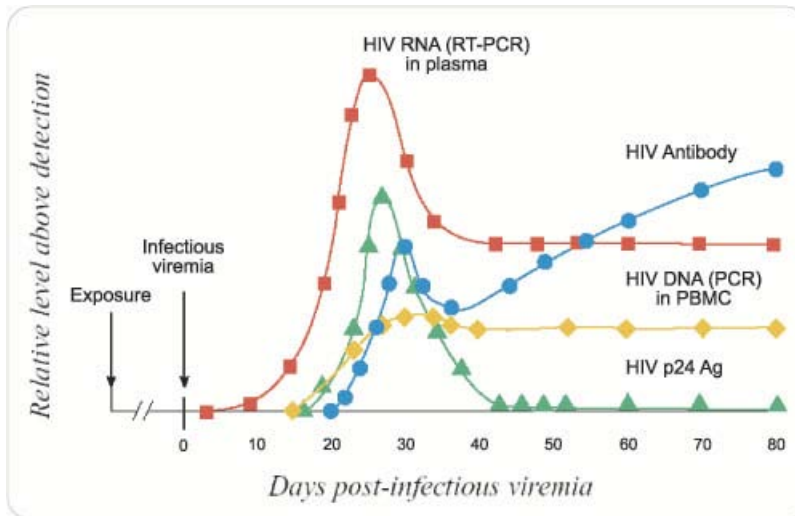
### RECOMMENDATION:

**Clinicians should counsel patients during pregnancy about the increased risk of transmitting HIV during acute HIV infection.**

The syndrome of acute HIV infection has increasingly been recognized as an important factor in HIV transmission.<sup>1</sup> Patients are at greatest risk of transmitting HIV during the period of high-level viremia prior to the viral setpoint.<sup>1,2</sup> Clinicians should counsel acutely infected patients about the increased risk of transmitting HIV during the 6-month period after infection.

The hallmarks of acute HIV infection are elevated plasma HIV RNA and p24 antigen levels with absent or undetectable HIV antibodies (see Figure 1).

**Figure 1. Virological and Serological Approaches to Diagnosing HIV Infection**



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Recent New York State (NYS) data support the role of acute HIV infection in the increased risk for mother-to-child HIV transmission (MTCT).<sup>3,4</sup> One cohort analysis showed that from 2002 to 2006, 9 infants with HIV infection were born to women who had a previously documented negative maternal HIV test during the pregnancy with subsequent documentation of HIV infection.<sup>3</sup> Although maternal acquisition of HIV infection during pregnancy was documented in

only 1.3% of perinatal HIV exposures, it was associated with 9 of the 65 cases in which transmission occurred. Based on medical record reviews and testing performed at the Pediatric HIV Testing Service at the Wadsworth Center, NYSDOH, the transmission rate for infants born to mothers who became infected during pregnancy was 22% (9 infected infants born to 41 mothers [ $p < .001$ ]). The transmission rate for infants born to mothers known to be positive prior to the pregnancy or who tested positive on their initial prenatal HIV test was 1.8% (56 infected infants born to 3,061 mothers).

**Key Point:**

In addition to previously identified factors, such as breastfeeding and lack of antiretroviral medications, NYS found that the factors of inadequate prenatal care, substance use during pregnancy, and low neonatal birth weight also increased the risk for MTCT.<sup>3</sup>

## **II. Presentation of Acute HIV Infection**

### **RECOMMENDATIONS:**

**When pregnant or breastfeeding women present with a febrile, “flu”- or “mono”-like illness, or rash that is not otherwise explained, clinicians should evaluate the potential for acute HIV infection by inquiring about the following (AII):**

- **Sexual exposures with a known HIV-infected partner or a partner of unknown HIV serostatus in the past 2 to 6 weeks**
- **Acquisition of any other sexually transmitted infection**
- **Needle-sharing practices with a known HIV-infected partner or a partner of unknown HIV serostatus in the past 2 to 6 weeks (see [Diagnosis and Management of Acute HIV Infection](#))**

**Clinicians should continue to be vigilant for signs and symptoms of acute HIV infection during the postpartum period for all breastfeeding women.**

See Section III. *Diagnosis of Acute HIV Infection*, for recommendations on testing to detect acute HIV infection.

Patients acutely infected with HIV will often experience at least some symptoms of the acute retroviral syndrome. Signs and symptoms such as fever and fatigue are common in acute HIV infection but are frequently mistaken for a flu-like syndrome and are often underreported by patients and unrecognized by clinicians. Rash, mucocutaneous ulcers, oropharyngeal candidiasis, and meningismus are more specific and should raise the index of suspicion. Plasma HIV RNA levels during seroconversion do not appear significantly different in patients who have acute symptoms versus those who are asymptomatic.<sup>5</sup> See Appendix A for a more extensive list of signs and symptoms of acute HIV infection.

Recognition of the signs and symptoms of acute HIV infection in pregnant women is critical because acute infection increases the risk for MTCT due to the markedly elevated plasma viral load associated with acute infection. Elevated viral load increases the risk for MTCT by exposing the infant to high levels of HIV<sup>6-8</sup> and altering the natural placental defenses against HIV transmission.<sup>9</sup> Risk for MTCT would thus likely be increased when acute HIV infection occurs during pregnancy.

The postpartum period remains a time of risk for MTCT for breastfed infants, especially in the setting of postnatal acute HIV infection. Rates of HIV transmission among infants who were breastfed by women who experienced seroconversion postpartum<sup>10</sup> have been reported to be 35% compared to a rate of 9% to 16% in infants breastfed by chronically infected women.<sup>11,12</sup> Therefore, clinicians should continue to be vigilant for signs and symptoms of acute infection in women who are breastfeeding.

### **III. Diagnosis of Acute HIV Infection**

#### **RECOMMENDATIONS:**

**When acute HIV infection is suspected, clinicians should immediately screen for acute infection by obtaining the following (AIII):**

- **An HIV serologic screening test in conjunction with a plasma HIV RNA assay. The plasma RNA test should be performed even if the serologic screening test is negative. If available, a fourth-generation HIV antigen/antibody combination test is the preferred serologic screening test.**

**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.**

**To exclude a false-positive result, clinicians should repeat both serologic and RNA testing 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. (AII)**

Standard antibody tests will not detect HIV during the “window period.” The window period is the time from initial infection, when virus is present and HIV RNA levels in the plasma are high, often exceeding 100 million copies/mL, and HIV antibodies are generally not detectable using currently available antibody tests. Viremia occurs approximately 2 weeks prior to the detection of a specific immune response and HIV RNA tests can detect acute HIV infection approximately

2 weeks sooner than antibody tests (see Figure 1). If available, fourth-generation combination HIV antigen/antibody screening tests are preferable for screening for acute HIV infection because they can detect the p24 antigen about 5 to 7 days sooner than antibody-only tests.

When suspicion for acute infection is high (e.g., in a patient who reports recent risk behavior in association with symptoms and signs of the acute retroviral syndrome) and a serologic screening test is negative, a qualitative HIV-1 RNA test that has been approved by the FDA for aiding in the diagnosis of acute HIV infection should be performed.<sup>13,14</sup> High levels of HIV RNA as determined by a quantitative HIV RNA test (viral load) in combination with a negative HIV antibody test is evidence to support the diagnosis of acute HIV infection. A low-level quantitative result (<5000 copies/mL) from an HIV RNA assay in the absence of any serologic evidence of HIV infection should be interpreted cautiously. Although HIV RNA levels tend to be very high in acute infection, a low value may represent any point on the upward or downward slope of the viremia associated with acute infection. Both serologic and RNA testing should be repeated, preferably on a newly collected specimen, to exclude a false-positive result. A fourth-generation combination HIV antigen/antibody screening test is the preferred serologic screening test for acute infection, and should be used, if available, in conjunction with an HIV RNA assay to diagnose acute HIV infection.

HIV serologic testing should be repeated 2 to 3 weeks after diagnosis by HIV RNA testing to confirm infection.

**Key Points:**

- **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.**
- If acute HIV infection is suspected, immediate consultation with a provider who has expertise in the diagnosis and evaluation of acute HIV infection can result in earlier diagnosis and treatment to reduce the risk of MTCT. Clinicians who need support from a provider with experience in acute HIV infection may call the CEI Line at 1-866-637-2342.
- Testing for acute HIV infection during pregnancy may be accessed by contacting:
  - **In New York City:** New York City Department of Health & Mental Hygiene, HIV Surveillance and Epidemiology Program, Provider Line **(212) 442-3388**
  - **Outside New York City:** New York State Department of Health, Wadsworth Center, Bloodborne Viruses Laboratory **(518) 474-2163**
- To aid in the diagnosis of acute HIV infection, providers should specifically indicate when contacting testing sites that acute HIV infection is suspected in the pregnant woman

For more information about acute HIV infection, see [Diagnosis and Management of Acute HIV Infection](#).

## IV. Management of Pregnant Women With Acute HIV Infection

### RECOMMENDATIONS:

**Pregnant women with acute HIV infection should receive health care from a multidisciplinary team including providers who have experience with HIV management and obstetrical care providers. A pediatric care provider with HIV expertise also should be part of the care team. (AIII)**

**Clinicians should obtain baseline genotypic testing in the setting of acute infection, even if the woman declines treatment. Initiation of prophylaxis should not be delayed while awaiting results of resistance testing. When results are available, treatment choice can be changed based on the results of genotypic testing and implemented with the goal of suppressing plasma HIV RNA levels to below detectable levels. (AII)**

HIV treatment and care have become increasingly complex. Most obstetrical care providers lack the experience of managing patients receiving ART and should consult with providers who have experience with HIV management to select regimens and interpret drug resistance test results. Decisions about how and when to start medication, change medication, and how to recognize and monitor medication side effects and HIV symptoms requires specific knowledge and attention to the current literature. The impact of treatment on fetal development and the ability to distinguish normal pregnancy symptoms from HIV medication side effects can be improved if obstetrical and HIV care providers collaborate to design a treatment and follow-up plan.

When pregnant women are diagnosed with acute HIV infection by HIV RNA testing, clinicians should not wait for HIV antibody confirmatory test results before initiating ART. Early initiation of ART may reduce MTCT; further treatment may be changed or discontinued based on the results of the confirmatory test.

Treatment with ART is designed to rapidly decrease HIV plasma viral load. Decreasing plasma viral load to undetectable levels decreases the risk of HIV transmission.<sup>13,14</sup> The selection of an ART regimen should be consistent with resistance test results and with current guidelines for treatment during pregnancy (see [Antiretroviral Therapy](#), Section V. 3: [HIV Resistance Assays](#)).

Follow-up testing for viral load suppression, CD4 count, and physiologic response including side effects to HIV medication should be conducted in accordance with standard recommendations for HIV therapy (see [Antiretroviral Therapy](#), Section VI: [Monitoring of Patients Receiving ART](#) guidelines).

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## APPENDIX A

### Acute Retroviral Syndrome: Signs and Symptoms (Expected Frequency)\*

<b>TABLE 1</b> <b>ACUTE RETROVIRAL SYNDROME: SIGNS AND SYMPTOMS (EXPECTED FREQUENCY)*</b>
<ul style="list-style-type: none"><li>• Fever (80%)</li><li>• Tired or fatigued (78%)</li><li>• Malaise (68%)</li><li>• Arthralgias (joint pain) (54%)</li><li>• Headache (54%)</li><li>• Loss of appetite (54%)</li><li>• Rash (51%)</li><li>• Night sweats (51%)</li><li>• Myalgias (pain in muscles) (49%)</li><li>• Nausea (49%)</li><li>• Diarrhea (46%)</li><li>• Fever and rash (46%)</li><li>• Pharyngitis (sore throat) (44%)</li><li>• Oral ulcers (mouth sores) (37%)</li><li>• Stiff neck (34%)</li><li>• Weight loss (&gt;5lb; 2.5 kg) (32%)</li><li>• Confusion (25%)</li><li>• Photophobia (24%)</li><li>• Vomiting (12%)</li><li>• Infected gums (10%)</li><li>• Sores on anus (5%)</li><li>• Sores on genitals (2%)</li></ul>
Data are from Hecht FM, Busch MP, Rawal B, et al. Use of laboratory tests and clinical symptoms for identification of primary HIV infection. <i>AIDS</i> 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.