

# Acute and Recent HIV Infection

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Module 1: [Screening and Diagnosis](#)  
Lesson 4: [Acute and Recent HIV Infection](#)

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<https://www.hiv.uw.edu/go/screening-diagnosis/acute-recent-early-hiv/core-concept/all>.

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## Background

Following the acquisition of HIV, more than 50% of individuals will develop a transient, symptomatic illness, with nonspecific features, referred to as acute HIV retroviral syndrome.[1,2,3] This illness, also known as primary HIV or acute retroviral syndrome, is frequently mistaken for an alternate viral infection, such as mononucleosis or influenza. Acute HIV represents the time period with an enhanced risk of transmitting HIV to others, primarily because of their very high HIV RNA levels and lack of awareness of HIV status.[4,5,6]. Early antiretroviral therapy arrests the explosive burst of viremia associated with acute HIV infection and thereby reduces symptoms and may improve long-term health outcomes. Furthermore, by reducing HIV RNA levels, which are often extremely elevated during acute infection, treatment decreases the likelihood of transmission to others.[2] Thus, recognition and diagnosis of acute HIV, followed by early initiation of antiretroviral therapy, is critical for both the health of the individual who has acquired HIV and for the prevention of transmission to others. The following will review the clinical manifestations, diagnosis, and management of persons with acute HIV.

## Definitions

- **Founder Virus:** Although HIV generally exists as a quasispecies or a mixture of mutant strains, usually only one strain (or a few strains) successfully establishes an initial infection; the infecting strain is known as the founder virus.[7,8] Available data indicate this founder virus has unique fitness properties that maximize its transmission capability (Figure 1).[8,9]
- **Eclipse Phase:** The short interval following HIV acquisition in which no diagnostic test is capable of detecting HIV.[10,11] This interval is typically 8 to 10 days in duration before the HIV RNA becomes detectable in blood (Figure 2).[10,12,13]
- **Seroconversion Window Period:** This term refers to the interval between HIV acquisition and the first detection of anti-HIV antibodies (Figure 3).[11]. The duration of the window period depends on the sensitivity of the antibody assay used; combined IgM/IgG HIV antibody tests detect HIV sooner than IgG-only HIV antibody tests.

- **Acute HIV Infection:** Defined as the phase of HIV disease that occurs soon after HIV acquisition and is characterized by detectable HIV RNA or HIV p24 antigen in the absence of anti-HIV antibodies ([Figure 4](#)).<sup>[2]</sup> An acute symptomatic illness, referred to as acute retroviral syndrome, may develop during the acute HIV infection phase.<sup>[14,15]</sup>
- **Recent HIV Infection:** Defined as the period after acute infection when anti-HIV antibodies become detectable, through the first 6 months after infection ([Figure 5](#)).<sup>[16]</sup>
- **Early HIV Infection:** Early infection is generally used to describe both acute and recent HIV time periods, which extend out to 6 months after HIV acquisition ([Figure 6](#)).<sup>[16]</sup>

## Immunopathogenesis

The immunopathogenesis of acute HIV infection is best understood within the context of HIV transmission via the genital mucosa and the events that follow transmission at that site.[3,17] Therefore, the following discussion will focus on immunopathogenesis related to the sexual transmission of HIV. Studies of intravaginal inoculation of simian immunodeficiency virus (SIV) in rhesus monkeys helped generate a model for early events of human sexual transmission of HIV, which involves transmission of HIV at the site columnar epithelial cells in the rectum and cervix (Figure 7).[2,3,17,18] In the vagina, ectocervix, and inner side of the penile foreskin, there are thicker barriers consisting of stratified squamous epithelium; in those regions, HIV can also initially infect Langerhans cells (tissue dendritic cells located just below the mucosa).[19]

### Establishment of HIV Infection

Almost always, the transmitted HIV is R5-tropic, which preferentially binds to these CCR5 coreceptors on CD4 cells, Langerhans cells, and dendritic cells. The dendritic cells that are infected with HIV can migrate to lymph nodes, where they interact with and potentially fuse with CD4 cells, causing the spread of HIV to deeper tissues.[18] Within a few days of inoculation, HIV is present within gut-associated lymphoid tissue and other tissues of the lymphoreticular system, causing irreversible depletion of helper T cells and establishment of viral latency (integration into the genome of resting T cells).[2,20,21] Investigators have shown that humans typically develop HIV viremia within 11 days of initial transmission.[10,22]

### Initial Immune Response

The uncontrolled initial burst of viremia in the acute phase typically causes very high plasma HIV RNA levels, often exceeding 200,000 copies/mL, and is associated with a surge of inflammatory cytokines.[2] Although antibody responses against HIV are generated, the initial neutralizing antibodies have weak neutralizing activity against primary HIV isolates and thus probably contribute very little to the initial control of HIV.[23] The initial burst of viremia is followed by a decrease in HIV RNA levels, predominantly as a result of a potent CD8 cytotoxic lymphocyte response targeted against HIV.[23,24] The HIV RNA levels reach a steady state—referred to as a set point—within 3 months after infection and, if untreated, remain at a similar level for years thereafter; the set point in men is typically higher than in women (Figure 8).[25,26,27]

### Early Immune Response as Predictor of Disease Progression

Investigators have shown that different individuals have qualitatively distinct immune responses to primary HIV infection.[28] Several research groups have shown that persons with strong initial CD8 T cell (cytotoxic T-lymphocyte) responses have lower HIV RNA levels after 6 to 12 months and subsequently experience a slower progression of their HIV disease (Figure 9).[28,29,30] More recently, the importance of the epitope-specific type of CD8 T cell response in controlling HIV has been elucidated.[31] In most persons who newly acquire HIV, high initial HIV RNA levels predict an accelerated course of HIV disease progression,[32] but this correlation is not universal.[28,33] Similarly, several reports have suggested that development of clinically apparent acute retroviral syndrome portends a faster progression to AIDS.[34]

## Clinical Manifestations

### Acute Retroviral Syndrome

Acute retroviral syndrome ranges from an asymptomatic infection, to a mild nonspecific viral illness resembling mononucleosis, to a severe systemic illness that requires hospitalization.[14,15] The onset of the clinical illness usually begins within 28 days of HIV acquisition and manifestations are typically nonspecific, protean, and self-limited; some individuals do not develop a symptomatic illness.[35,36] Some patients develop a diffuse morbilliform or maculopapular rash that most often involves the trunk; this rash may resemble the rash seen with secondary syphilis, measles, or pityriasis rosea (Figure 10). In addition to the skin rash, other common manifestations associated with acute HIV include fever, fatigue, myalgia, headache, pharyngitis, and cervical adenopathy (Table 1).[3,14,37,38,39] Less commonly, neurological complications may occur, such as aseptic meningitis, encephalitis, facial palsy, or Guillain-Barré syndrome.[40] Rarely, acute HIV causes such a substantial drop in CD4 cell count that patients may initially present with a major AIDS-defining opportunistic infection.

### Duration of Symptoms

In a study of 46 individuals with acute HIV who did not receive antiretroviral therapy during the acute illness, those who developed a symptomatic illness had a median duration of symptoms of 14 days.[15] Symptom duration can range from days to weeks, and the severity and duration of clinical manifestations often correlate with disease progression.[3,37]

### Differential Diagnosis

A high index of suspicion is necessary to correctly identify nonspecific symptoms as acute HIV and differentiate it from other common illnesses with similar symptoms. For example, acute Epstein-Barr virus infection (mononucleosis), secondary syphilis, acute cytomegalovirus, acute toxoplasmosis, acute hepatitis B, streptococcal pharyngitis, influenza, and measles can all present with symptoms comparable to those seen in patients with acute HIV. Routine laboratory studies taken from persons acutely infected with HIV may show leukopenia, thrombocytopenia, and increases in hepatic aminotransferase levels, all of which are also nonspecific and can be seen with a number of other illnesses and infections.

## Laboratory Diagnosis

Based on serial blood samples from 99 people who were closely followed after the acquisition of HIV, investigators described 6 stages of early HIV infection that were based on the timing and results of HIV diagnostic tests; the stages identified in this study are referred to as the Fiebig stages of early HIV infection ([Figure 11](#)).[\[10\]](#) This study, as well as others, have shown that individuals who present with symptomatic acute HIV infection typically have a very high HIV RNA level and a negative HIV antibody test; most will also have a positive p24 antigen test.[\[1,10,41\]](#) The laboratory diagnosis of acute HIV requires a nonreactive HIV antibody assay in combination with either a positive HIV RNA or a positive p24 antigen.[\[16\]](#) Since the vast majority of new HIV infections in the United States are HIV-1 infections, the following discussion will focus on the diagnosis of acute HIV-1 infection.

### HIV-1 RNA Tests

Approximately 8 to 10 days after initial HIV-1 acquisition, plasma HIV-1 RNA levels become detectable.[\[10,12,13\]](#) At around day 10, the HIV-1 RNA levels begin to rapidly ramp up, reaching very high levels in the subsequent 1–2 weeks and typically peaking at about 250,000 copies/mL.[\[10,41,42\]](#) Many HIV-1 RNA assays are now available that can accurately detect HIV-1 RNA, even at very low levels.[\[43,44,45\]](#) Many clinicians use a quantitative HIV-1 RNA assay (those typically used for monitoring response to treatment with chronic HIV-1 infection) for making a diagnosis of acute HIV-1, since these tests have similar lower limits of detection, are more readily accessible, and also provide a quantitative HIV-1 RNA level for positive samples.[\[46\]](#)

### HIV-1/2 Antigen-Antibody Tests

Using laboratory-based tests, detection of HIV-1 p24 antigen occurs approximately 1 week after HIV-1 RNA and approximately 1 week prior to detection of IgM/IgG-sensitive antibody test ([Figure 12](#)).[\[47,48,49\]](#) The use of a screening test that detects HIV-1 p24 antigen will increase the diagnostic yield of persons with acute HIV-1 infection compared with using antibody tests alone for screening.[\[11,50\]](#) The p24 antigen typically becomes reactive when the HIV RNA level exceeds 10,000–20,000 copies/mL.[\[10,16\]](#) Although the point-of-care HIV-1/2 Ag/Ab tests are more sensitive for detecting early HIV than IgM/IgG-sensitive antibody tests, they are not as sensitive as laboratory-based HIV-1/2 antigen-antibody assays.[\[51,52,53\]](#) Among the HIV-1/2 antigen-antibody immunoassays, only a few differentiate the HIV-1 p24 antigen from the anti-HIV antibodies.[\[54,55\]](#) Therefore, for most of the approved assays, a reactive result can indicate either the detection of p24 antigen, HIV antibody, or both. From a practical standpoint, a positive HIV-1/2 antigen-antibody immunoassay, followed by a nonreactive differentiation HIV-1/HIV-2 antibody assay, likely indicates reactivity of the p24 antigen component.

### HIV Antibody Tests

Laboratory-based IgM/IgG-sensitive HIV-1 antibody tests first become reactive at approximately 23 days after HIV acquisition, whereas laboratory-based IgG-sensitive HIV antibody tests and point-of-care HIV antibody tests typically become reactive about 4 to 5 weeks after infection.[\[10\]](#) The characteristic formation of anti-HIV antibodies may be altered in persons with acute HIV infection who receive antiretroviral therapy prior to seroconversion; in this scenario, individuals with recent HIV acquisition may have incomplete evolution of antibody responses, including rare cases of seroreversion.[\[56,57,58\]](#) A modified, less sensitive HIV antibody test, the so-called "detuned" assay, has been used in research settings to differentiate those with recent HIV infection (acquired HIV within the previous 4 to 5 months) from those with well-established chronic HIV infection.[\[59\]](#) Although this test can help to identify those with recent HIV infection who have already passed through the window period, it is primarily used for research and not in clinical practice.

## Detection of Acute HIV with Routine Screening for HIV

The HIV testing algorithm recommended by the Centers for Disease Control (CDC) and Association of Public Health Laboratories (APHL), which utilizes a laboratory-based HIV-1/2 antigen-antibody immunoassay as the initial screening test, will detect approximately 80 to 85% of persons with acute HIV infection.[\[11,60,61,62\]](#) With this algorithm, persons with acute HIV typically have a positive initial screening test with an HIV-1/2 antigen-antibody immunoassay, followed by a negative HIV-1/HIV-2 antibody differentiation immunoassay, and then a positive HIV-1 RNA test ([Figure 13](#)).[\[11\]](#) The ability of this routine screening algorithm to detect most persons with acute HIV is one of the primary reasons the CDC now advocates using this HIV testing approach for routine screening (as opposed to starting with an antibody-only test, which was the previously used strategy).[\[11,50\]](#) In the situation where the routine screening testing algorithm detects HIV, follow-up antibody testing in 3 to 6 months should be performed to document seroconversion.[\[16\]](#) Routine screening for HIV infection using an HIV-1 RNA test is not practical due to cost.

## **Testing for Suspected Very Early Acute HIV Infection**

For individuals in whom there is a strong clinical suspicion of acute HIV infection but initial testing with the HIV-1/2 antigen-antibody immunoassay is nonreactive, additional testing should be performed with an HIV-1 RNA assay. The rationale for this approach is that individuals with very early HIV infection can have a negative HIV-1 p24 antigen test, and the only assay that would detect HIV in that setting is an HIV-1 RNA assay. Individuals are presumptively diagnosed with acute HIV infection if they have a positive HIV RNA (especially at a high level) and nonreactive or indeterminate HIV antibody assay.[\[16\]](#)

## Rationale for Treatment of Early HIV Infection

The potential benefits of initiating antiretroviral therapy for patients with early (acute and recent) HIV infection include (1) accelerated resolution of symptomatic acute retroviral syndrome, (2) minimized immunologic damage, (3) diminished size of the latent HIV reservoir pool, and (4) prevention of HIV transmission to others.[63,64,65,66]

## Preservation of Immune Function and Delayed Disease Progression

Antiretroviral therapy initiated during early HIV infection can reduce HIV RNA levels and thereby stop CD4 decline, preserve immune function, and stop HIV disease progression.[64,65,67,68] One study analyzed differences between a group of individuals who started antiretroviral therapy within 2 weeks of seroconversion (acute treatment arm), a group who started between 2 weeks and 6 months of seroconversion (early treatment arm), and a group who declined to initiate therapy; individuals in the acute and early treatment arms took therapy for at least 3 months then stopped.[69] At 6 months after treatment interruption, groups who initiated treatment had lower HIV RNA levels and higher CD4 counts, with the greatest benefit seen in those who initiated within 2 weeks of seroconversion.[69] Multiple studies, including the Setpoint Study (ACTG A5217), Primo-SHM, and SPARTAC, have demonstrated a reduction in viral set point and slower disease progression after initiation of antiretroviral therapy during early HIV infection.[70,71,72] The SABES study in Peru randomized men who have sex with men (MSM) who developed acute or early HIV to receive either immediate or deferred (for 6 months) antiretroviral therapy initiation.[73] Importantly, prompt initiation of antiretroviral therapy had several significant health benefits, including fewer opportunistic infections, fewer respiratory tract infections, higher CD4 cell count rebound at 2 years, and improved inflammatory cytokine profiles.[73]

## Impact on Latent Reservoir

One report documented 14 individuals who initiated antiretroviral therapy during acute HIV—and continued therapy for a mean of 36.5 months—who maintained low HIV RNA levels following cessation of therapy.[74] The investigators reported spontaneous control of viremia after treatment interruption in 15% of the group treated during acute infection versus less than 1% in those not treated.[74] Other studies have shown that treatment during the first 6 months after HIV infection has a favorable impact on cellular reservoirs.[75] These data, taken together, suggest that treatment during acute infection can significantly reduce latent HIV reservoirs and may aid in future efforts to achieve a functional cure. In one study, use of a potent five-drug regimen did not have a greater impact on HIV reservoirs when compared with a standard triple-drug antiretroviral regimen.[76] In clinical practice, the diagnosis of acute HIV and immediate initiation of a standard antiretroviral therapy regimen is beneficial, and antiretroviral therapy should be continued long-term and not interrupted.

## Reduced Risk for HIV Transmission

Individuals with recent acquisition of HIV have a significant increase in risk of transmitting HIV to others due to several factors: (1) they have initial uncontrolled viremia with associated high HIV RNA levels in the genital tract, (2) their initial HIV quasispecies is less varied and probably better adapted for transmission than later in the course of HIV infection, and (3) they are often unaware of their HIV status.[2,3] Studies have estimated that approximately 4–9% of the new HIV infections in the United States involved transmission from a person with acute HIV.[77,78] Research has shown that among untreated men with HIV, semen and blood HIV RNA levels are markedly higher during acute than chronic HIV infection, thus providing a biologic basis for the reported increases in HIV transmission during early HIV infection.[5] Models have been generated that calculate the probabilities of male-to-female HIV transmission per coital act, and they project a marked increase in risk of HIV transmission during acute HIV infection (Figure 14).[6] In addition, other investigators have shown that for every 10-fold increase in viral load, the risk of transmission increases by a factor of 2.5, so a prompt reduction in the very high HIV RNA levels with acute or early HIV infection could significantly

reduce HIV transmission during this period.[\[2,79\]](#)

## Antiretroviral Treatment for Early HIV

The Adult and Adolescent ARV Guidelines strongly recommend that all persons with early (acute and recent) HIV infection should receive antiretroviral treatment, ideally as soon as possible after HIV diagnosis.[\[16,80\]](#) Rapid initiation of antiretroviral therapy in this situation improves long-term outcomes for the individual who has acquired HIV and, as described above, significantly reduces the likelihood of transmission of HIV to others.[\[16\]](#) The approach to baseline evaluation, treatment, and monitoring in the setting of acute HIV is the same as with chronic HIV.[\[16,80\]](#) Prior to initiating antiretroviral therapy, a blood sample should be obtained for genotypic drug resistance testing; antiretroviral therapy should not be delayed while awaiting these results.[\[16,80\]](#) When the result of the genotypic drug resistance test returns, which often takes 2 to 4 weeks, the antiretroviral regimen can be modified, if needed.[\[16\]](#)

### Antiretroviral Therapy Regimens for Acute (Early) HIV

The recommendations for antiretroviral therapy for early (acute and recent) HIV are the same as initial therapy for persons with chronic HIV, with the exception that the 2-drug regimen dolutegravir-lamivudine is not an option when treating early HIV.[\[16,80\]](#) With treatment of early or chronic HIV, the choice of the initial antiretroviral regimen depends on whether the individual has a history of taking long-acting cabotegravir for HIV preexposure prophylaxis (PrEP).[\[16,80\]](#) The recommended antiretroviral regimens include the anchor drugs bictegravir, dolutegravir, or boosted darunavir because of their high potency, relatively high barrier to resistance, and low rates of resistance to these drugs among transmitted HIV strains.[\[16\]](#) Once a person initiates antiretroviral therapy for early HIV, they should continue antiretroviral therapy indefinitely, the same as if initiated during chronic infection.[\[16,80\]](#) The following table summarizes the recommended antiretroviral regimens for the treatment of early (acute and recent) HIV infection ([Table 2](#)).[\[16\]](#)

## Summary Points

- Early HIV infection is defined as the first 6 months after HIV infection; this period includes acute and recent HIV infection.
- Symptoms of acute HIV infection are nonspecific and mimic many other viral or bacterial infections. The diagnosis of acute HIV-1 is typically confirmed by a nonreactive HIV-1 antibody test in conjunction with a positive HIV-1 RNA assay (or p24 antigen assay).
- Acute HIV is generally associated with high HIV RNA levels (average of about 250,000 copies/mL) and an enhanced risk of transmitting HIV.
- The HIV testing algorithm recommended by the CDC and APHL uses an HIV-1/2 antigen-antibody immunoassay as the initial HIV screening test; the characteristic algorithm pattern with acute HIV-1 infection is a reactive HIV-1/2 antigen-antibody immunoassay, a negative HIV-1/HIV-2 antibody differentiation assay, and a positive HIV-1 RNA test.
- Immediate initiation of antiretroviral treatment is recommended for all people diagnosed with early HIV infection. The rationale for initiating antiretroviral therapy during early infection is to stop disease progression, reduce the viral reservoir burden, and prevent transmission of HIV to others.
- Genotypic HIV drug resistance testing is recommended in all persons prior to initiating antiretroviral therapy. Persons with acute HIV who were recently or currently taking long-acting cabotegravir should have an integrase genotypic drug resistance test ordered (in addition to the standard HIV drug resistance test).
- Antiretroviral therapy should be initiated prior to obtaining the genotypic HIV drug resistance test results; regimens can be modified, if needed, after the test results become available.
- The antiretroviral regimen for persons with acute HIV should include an anchor drug that has excellent potency and a strong genetic barrier to resistance. The choice of the initial regimen depends on whether the newly diagnosed individual has a history of receiving long-acting cabotegravir.

## Citations

1. Cohen MS, Gay CL, Busch MP, Hecht FM. The detection of acute HIV infection. *J Infect Dis.* 2010;202 Suppl 2:S270-7.  
[\[PubMed Abstract\]](#) -
2. Cohen MS, Shaw GM, McMichael AJ, Haynes BF. Acute HIV-1 infection. *N Engl J Med.* 2011;364:1943-54.  
[\[PubMed Abstract\]](#) -
3. Kahn JO, Walker BD. Acute human immunodeficiency virus type 1 infection. *N Engl J Med.* 1998;339:33-9.  
[\[PubMed Abstract\]](#) -
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;191:1403-9.  
[\[PubMed Abstract\]](#) -
5. Pilcher CD, Joaki G, Hoffman IF, et al. Amplified transmission of HIV-1: comparison of HIV-1 concentrations in semen and blood during acute and chronic infection. *AIDS.* 2007;21:1723-30.  
[\[PubMed Abstract\]](#) -
6. Pilcher CD, Tien HC, Eron JJ Jr, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis.* 2004;189:1785-92.  
[\[PubMed Abstract\]](#) -
7. Fennessey CM, Keele BF. Using nonhuman primates to model HIV transmission. *Curr Opin HIV AIDS.* 2013;8:280-7.  
[\[PubMed Abstract\]](#) -
8. Keele BF, Giorgi EE, Salazar-Gonzalez JF, et al. Identification and characterization of transmitted and early founder virus envelopes in primary HIV-1 infection. *Proc Natl Acad Sci U S A.* 2008;105:7552-7.  
[\[PubMed Abstract\]](#) -
9. Carlson JM, Schaefer M, Monaco DC, et al. HIV transmission. Selection bias at the heterosexual HIV-1 transmission bottleneck. *Science.* 2014;345:1254031.  
[\[PubMed Abstract\]](#) -
10. Fiebig EW, Wright DJ, Rawal BD, et al. Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. *AIDS.* 2003;17:1871-9.  
[\[PubMed Abstract\]](#) -
11. Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory testing for the diagnosis of HIV infection: updated recommendations. June 27, 2014.  
[\[CDC\]](#) -
12. Konrad BP, Taylor D, Conway JM, Ogilvie GS, Coombs D. On the duration of the period between exposure to HIV and detectable infection. *Epidemics.* 2017;20:73-83.  
[\[PubMed Abstract\]](#) -
13. Rolland M, Tovanabutra S, Dearlove B, et al. Molecular dating and viral load growth rates suggested that the eclipse phase lasted about a week in HIV-1 infected adults in East Africa and Thailand. *PLoS Pathog.* 2020;16:e1008179.

[\[PubMed Abstract\]](#) -

14. Daar ES, Pilcher CD, Hecht FM. Clinical presentation and diagnosis of primary HIV-1 infection. *Curr Opin HIV AIDS*. 2008;3:10-5.  
[\[PubMed Abstract\]](#) -
15. Schacker T, Collier AC, Hughes J, Shea T, Corey L. Clinical and epidemiologic features of primary HIV infection. *Ann Intern Med*. 1996;125:257-64.  
[\[PubMed Abstract\]](#) -
16. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Considerations for Antiretroviral Therapy Use in Special Populations. Early (Acute and Recent) HIV Infection. September 12, 2024.  
[\[HIV.gov\]](#) -
17. Haase AT. Early events in sexual transmission of HIV and SIV and opportunities for interventions. *Annu Rev Med*. 2011;62:127-39.  
[\[PubMed Abstract\]](#) -
18. Spira AI, Marx PA, Patterson BK, Mahoney J, Koup RA, Wolinsky SM, Ho DD. Cellular targets of infection and route of viral dissemination after an intravaginal inoculation of simian immunodeficiency virus into rhesus macaques. *J Exp Med*. 1996;183:215-25.  
[\[PubMed Abstract\]](#) -
19. Sugaya M, Lore K, Koup RA, Douek DC, Blauvelt A. HIV-infected Langerhans cells preferentially transmit virus to proliferating autologous CD4(+) memory T cells located within Langerhans cell-T cell clusters. *J Immunol*. 2004;172:2219-24.  
[\[PubMed Abstract\]](#) -
20. Guadalupe M, Reay E, Sankaran S, et al. Severe CD4+ T-cell depletion in gut lymphoid tissue during primary human immunodeficiency virus type 1 infection and substantial delay in restoration following highly active antiretroviral therapy. *J Virol*. 2003;77:11708-17.  
[\[PubMed Abstract\]](#) -
21. Mehandru S, Poles MA, Tenner-Racz K, et al. Primary HIV-1 infection is associated with preferential depletion of CD4+ T lymphocytes from effector sites in the gastrointestinal tract. *J Exp Med*. 2004;200:761-70.  
[\[PubMed Abstract\]](#) -
22. Niu MT, Stein DS, Schnittman SM. Primary human immunodeficiency virus type 1 infection: review of pathogenesis and early treatment intervention in humans and animal retrovirus infections. *J Infect Dis*. 1993;168:1490-501.  
[\[PubMed Abstract\]](#) -
23. Letvin NL, Walker BD. Immunopathogenesis and immunotherapy in AIDS virus infections. *Nat Med*. 2003;9:861-6.  
[\[PubMed Abstract\]](#) -
24. Koup RA, Safrit JT, Cao Y, et al. Temporal association of cellular immune responses with the initial control of viremia in primary human immunodeficiency virus type 1 syndrome. *J Virol*. 1994;68:4650-5.  
[\[PubMed Abstract\]](#) -

25. Sterling TR, Vlahov D, Astemborski J, Hoover DR, Margolick JB, Quinn TC. Initial plasma HIV-1 RNA levels and progression to AIDS in women and men. *N Engl J Med*. 2001;344:720-5.  
[\[PubMed Abstract\]](#) -
26. Lyles RH, Munoz A, Yamashita TE, et al. Natural history of human immunodeficiency virus type 1 viremia after seroconversion and proximal to AIDS in a large cohort of homosexual men. Multicenter AIDS Cohort Study. *J Infect Dis*. 2000;181:872-80.  
[\[PubMed Abstract\]](#) -
27. Robb ML, Eller LA, Kibuuka H, et al. Prospective Study of Acute HIV-1 Infection in Adults in East Africa and Thailand. *N Engl J Med*. 2016;374:2120-30.  
[\[PubMed Abstract\]](#) -
28. Pantaleo G, Demarest JF, Schacker T, et al. The qualitative nature of the primary immune response to HIV infection is a prognosticator of disease progression independent of the initial level of plasma viremia. *Proc Natl Acad Sci U S A*. 1997;94:254-8.  
[\[PubMed Abstract\]](#) -
29. Patke DS, Langan SJ, Carruth LM, et al. Association of Gag-specific T lymphocyte responses during the early phase of human immunodeficiency virus type 1 infection and lower virus load set point. *J Infect Dis*. 2002;186:1177-80.  
[\[PubMed Abstract\]](#) -
30. Walker BD, Goulder PJ. AIDS. Escape from the immune system. *Nature*. 2000;407:313-4.  
[\[PubMed Abstract\]](#) -
31. Streeck H, Lu R, Beckwith N, et al. Emergence of Individual HIV-Specific CD8 T Cell Responses during Primary HIV-1 Infection Can Determine Long-Term Disease Outcome. *J Virol*. 2014;88:12793-801.  
[\[PubMed Abstract\]](#) -
32. Henrard DR, Phillips JF, Muenz LR, Blattner WA, Wiesner D, Eyster ME, Goedert JJ. Natural history of HIV-1 cell-free viremia. *JAMA*. 1995;274:554-8.  
[\[PubMed Abstract\]](#) -
33. Schacker TW, Hughes JP, Shea T, Coombs RW, Corey L. Biological and virologic characteristics of primary HIV infection. *Ann Intern Med*. 1998;128:613-20.  
[\[PubMed Abstract\]](#) -
34. Dorrucchi M, Rezza G, Vlahov D, et al. Clinical characteristics and prognostic value of acute retroviral syndrome among injecting drug users. Italian Seroconversion Study. *AIDS*. 1995;9:597-604.  
[\[PubMed Abstract\]](#) -
35. Gabert R, Lama JR, Valdez R, et al. Acute retroviral syndrome is associated with lower CD4 nadir and delayed viral suppression, which are blunted by immediate ART initiation. *AIDS*. 2023 Feb 9. Online ahead of print.  
[\[PubMed Abstract\]](#) -
36. Pincus JM, Crosby SS, Losina E, King ER, LaBelle C, Freedberg KA. Acute human immunodeficiency virus infection in patients presenting to an urban urgent care center. *Clin Infect Dis*. 2003;37:1699-704.  
[\[PubMed Abstract\]](#) -
37. Vanhems P, Hughes J, Collier AC, et al. Comparison of clinical features, CD4 and CD8 responses among patients with acute HIV-1 infection from Geneva, Seattle and Sydney. *AIDS*. 2000;14:375-81.

[\[PubMed Abstract\]](#) -

38. Hecht FM, Busch MP, Rawal B, et al. Use of laboratory tests and clinical symptoms for identification of primary HIV infection. *AIDS*. 2002;16:1119-29.  
[\[PubMed Abstract\]](#) -
39. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update. A Clinical Practice Guideline. March 2018:1-59.  
[\[CDC\]](#) -
40. Newton PJ, Newsholme W, Brink NS, Manji H, Williams IG, Miller RF. Acute meningoencephalitis and meningitis due to primary HIV infection. *BMJ*. 2002;325:1225-7.  
[\[PubMed Abstract\]](#) -
41. Daar ES, Little S, Pitt J, et al. Diagnosis of primary HIV-1 infection. Los Angeles County Primary HIV Infection Recruitment Network. *Ann Intern Med*. 2001;134:25-9.  
[\[PubMed Abstract\]](#) -
42. Rich JD, Merriman NA, Mylonakis E, et al. Misdiagnosis of HIV infection by HIV-1 plasma viral load testing: a case series. *Ann Intern Med*. 1999;130:37-9.  
[\[PubMed Abstract\]](#) -
43. Giachetti C, Linnen JM, Kolk DP, et al. Highly sensitive multiplex assay for detection of human immunodeficiency virus type 1 and hepatitis C virus RNA. *J Clin Microbiol*. 2002;40:2408-19.  
[\[PubMed Abstract\]](#) -
44. Pierce VM, Neide B, Hodinka RL. Evaluation of the Gen-Probe Aptima HIV-1 RNA qualitative assay as an alternative to Western blot analysis for confirmation of HIV infection. *J Clin Microbiol*. 2011;49:1642-5.  
[\[PubMed Abstract\]](#) -
45. U.S. Food and Drug Administration. APTIMA HIV-1 RNA Qualitative Assay  
[\[U.S. FDA\]](#) -
46. Kuruc JD, Cope AB, Sampson LA, et al. Ten Years of Screening and Testing for Acute HIV Infection in North Carolina. *J Acquir Immune Defic Syndr*. 2016;71:111-9.  
[\[PubMed Abstract\]](#) -
47. Bentsen C, McLaughlin L, Mitchell E, et al. Performance evaluation of the Bio-Rad Laboratories GS HIV Combo Ag/Ab EIA, a 4th generation HIV assay for the simultaneous detection of HIV p24 antigen and antibodies to HIV-1 (groups M and O) and HIV-2 in human serum or plasma. *J Clin Virol*. 2011;52 Suppl 1:S57-61.  
[\[PubMed Abstract\]](#) -
48. Chavez P, Wesolowski L, Patel P, Delaney K, Owen SM. Evaluation of the performance of the Abbott ARCHITECT HIV Ag/Ab Combo Assay. *J Clin Virol*. 2011;52 Suppl 1:S51-5.  
[\[PubMed Abstract\]](#) -
49. Eshleman SH, Khaki L, Laeyendecker O, et al. Detection of individuals with acute HIV-1 infection using the ARCHITECT HIV Ag/Ab Combo assay. *J Acquir Immune Defic Syndr*. 2009;52:121-4.  
[\[PubMed Abstract\]](#) -
50. Centers for Disease Control and Prevention and Association of Public Health Laboratories. 2018 Quick reference guide: Recommended laboratory HIV testing algorithm for serum or plasma specimens.

Published January 27, 2018.

[[CDC](#)] -

51. Duong YT, Mavengere Y, Patel H, et al. Poor performance of the determine HIV-1/2 Ag/Ab combo fourth-generation rapid test for detection of acute infections in a National Household Survey in Swaziland. *J Clin Microbiol.* 2014;52:3743-8.  
[[PubMed Abstract](#)] -
52. Rosenberg NE, Kamanga G, Phiri S, et al. Detection of acute HIV infection: a field evaluation of the determine® HIV-1/2 Ag/Ab combo test. *J Infect Dis.* 2012;205:528-34.  
[[PubMed Abstract](#)] -
53. Masciotra S, Luo W, Youngpairoj AS, et al. Performance of the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test with specimens from HIV-1 seroconverters from the US and HIV-2 infected individuals from Ivory Coast. *J Clin Virol.* 2013;58 Suppl 1:e54-8.  
[[PubMed Abstract](#)] -
54. U.S. Food and Drug Administration. BioPlex 2200 HIV Ag-Ab Assay.  
[[U.S. FDA](#)] -
55. U.S. Food and Drug Administration. Alere Determine HIV-1/2 Ag/Ab Combo.  
[[U.S. FDA](#)] -
56. Hare CB, Pappalardo BL, Busch MP, et al. Seroreversion in subjects receiving antiretroviral therapy during acute/early HIV infection. *Clin Infect Dis.* 2006;42:700-8.  
[[PubMed Abstract](#)] -
57. Kassutto S, Johnston MN, Rosenberg ES. Incomplete HIV type 1 antibody evolution and seroreversion in acutely infected individuals treated with early antiretroviral therapy. *Clin Infect Dis.* 2005;40:868-73.  
[[PubMed Abstract](#)] -
58. Killian MS, Norris PJ, Rawal BD, Lebedeva M, Hecht FM, Levy JA, Busch MP. The effects of early antiretroviral therapy and its discontinuation on the HIV-specific antibody response. *AIDS Res Hum Retroviruses.* 2006;22:640-7.  
[[PubMed Abstract](#)] -
59. Rawal BD, Degula A, Lebedeva L, et al. Development of a new less-sensitive enzyme immunoassay for detection of early HIV-1 infection. *J Acquir Immune Defic Syndr.* 2003;33:349-55.  
[[PubMed Abstract](#)] -
60. Patel P, Mackellar D, Simmons P, et al. Detecting acute human immunodeficiency virus infection using 3 different screening immunoassays and nucleic acid amplification testing for human immunodeficiency virus RNA, 2006-2008. *Arch Intern Med.* 2010;170:66-74.  
[[PubMed Abstract](#)] -
61. Pandori MW, Hackett J Jr, Louie B, Vallari A, Dowling T, Liska S, Klausner JD. Assessment of the ability of a fourth-generation immunoassay for human immunodeficiency virus (HIV) antibody and p24 antigen to detect both acute and recent HIV infections in a high-risk setting. *J Clin Microbiol.* 2009;47:2639-42.  
[[PubMed Abstract](#)] -
62. Peters PJ, Westheimer E, Cohen S, et al. Screening Yield of HIV Antigen/Antibody Combination and Pooled HIV RNA Testing for Acute HIV Infection in a High-Prevalence Population. *JAMA.*

2016;315:682-90.

[\[PubMed Abstract\]](#) -

63. De Clercq J, Rutsaert S, De Scheerder MA, Verhofstede C, Callens S, Vandekerckhove L. Benefits of antiretroviral therapy initiation during acute HIV infection. *Acta Clin Belg.* 2020;1-9.  
[\[PubMed Abstract\]](#) -
64. Smith MK, Rutstein SE, Powers KA, et al. The detection and management of early HIV infection: a clinical and public health emergency. *J Acquir Immune Defic Syndr.* 2013;63 Suppl 2:S187-99.  
[\[PubMed Abstract\]](#) -
65. Okulicz JF, Le TD, Agan BK, et al. Influence of the timing of antiretroviral therapy on the potential for normalization of immune status in human immunodeficiency virus 1-infected individuals. *JAMA Intern Med.* 2015;175:88-99.  
[\[PubMed Abstract\]](#) -
66. Hamlyn E, Ewings FM, Porter K, et al. Plasma HIV viral rebound following protocol-indicated cessation of ART commenced in primary and chronic HIV infection. *PLoS One.* 2012;7:e43754.  
[\[PubMed Abstract\]](#) -
67. Rosenberg ES, Altfeld M, Poon SH, et al. Immune control of HIV-1 after early treatment of acute infection. *Nature.* 2000;407:523-6.  
[\[PubMed Abstract\]](#) -
68. Malhotra U, Berrey MM, Huang Y, et al. Effect of combination antiretroviral therapy on T-cell immunity in acute human immunodeficiency virus type 1 infection. *J Infect Dis.* 2000;181:121-31.  
[\[PubMed Abstract\]](#) -
69. 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;194:725-33.  
[\[PubMed Abstract\]](#) -
70. Grijzen M, Koster G, van Vonderen M, et al. Temporary antiretroviral treatment during primary HIV-1 infection has a positive impact on health-related quality of life: data from the Primo-SHM cohort study. *HIV Med.* 2012;13:630-5.  
[\[PubMed Abstract\]](#) -
71. SPARTAC Trial Investigators, Fidler S, Porter K, et al. Short-course antiretroviral therapy in primary HIV infection. *N Engl J Med.* 2013;368:207-17.  
[\[PubMed Abstract\]](#) -
72. Hogan CM, Degruittola V, Sun X, et al. The setpoint study (ACTG A5217): effect of immediate versus deferred antiretroviral therapy on virologic set point in recently HIV-1-infected individuals. *J Infect Dis.* 2012;205:87-96.  
[\[PubMed Abstract\]](#) -
73. Lama JR, Ignacio RAB, Alfaro R, et al. Clinical and Immunologic Outcomes After Immediate or Deferred Antiretroviral Therapy Initiation During Primary Human Immunodeficiency Virus Infection: The Sabes Randomized Clinical Study. *Clin Infect Dis.* 2021;72:1042-1050.  
[\[PubMed Abstract\]](#) -
74. Sáez-Cirión A, Bacchus C, Hocqueloux L, et al. Post-treatment HIV-1 controllers with a long-term virological remission after the interruption of early initiated antiretroviral therapy ANRS VISCONTI Study. *PLoS Pathog.* 2013;9:e1003211.

[\[PubMed Abstract\]](#) -

75. Strain MC, Little SJ, Daar ES, et al. Effect of treatment, during primary infection, on establishment and clearance of cellular reservoirs of HIV-1. *J Infect Dis.* 2005;191:1410-8.  
[\[PubMed Abstract\]](#) -
76. Chéret A, Nembot G, Mélard A, et al. Intensive five-drug antiretroviral therapy regimen versus standard triple-drug therapy during primary HIV-1 infection (OPTIPRIM-ANRS 147): a randomised, open-label, phase 3 trial. *Lancet Infect Dis.* 2015;15:387-96.  
[\[PubMed Abstract\]](#) -
77. Li Z, Purcell DW, Sansom SL, Hayes D, Hall HI. Vital Signs: HIV transmission along the continuum of care - United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2019;68:267-72.  
[\[PubMed Abstract\]](#) -
78. Pinkerton SD. How many sexually-acquired HIV infections in the USA are due to acute-phase HIV transmission? *AIDS.* 2007;21:1625-9.  
[\[PubMed Abstract\]](#) -
79. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med.* 2000;342:921-9.  
[\[PubMed Abstract\]](#) -
80. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. What to Start. Initial Combination Antiretroviral Regimens for People With HIV. September 12, 2024.  
[\[HIV.gov\]](#) -

## References

- Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. *N Engl J Med.* 2016;375:830-9.  
[\[PubMed Abstract\]](#) -
- Girometti N, McCormack S, Tittle V, McOwan A, Whitlock G. Rising rates of recent preexposure prophylaxis exposure among men having sex with men newly diagnosed with HIV: antiviral resistance patterns and treatment outcomes. *AIDS.* 2022;36:561-6.  
[\[PubMed Abstract\]](#) -
- Grijzen ML, Steingrover R, Wit FW, et al. No treatment versus 24 or 60 weeks of antiretroviral treatment during primary HIV infection: the randomized Primo-SHM trial. *PLoS Med.* 2012;9:e1001196.  
[\[PubMed Abstract\]](#) -
- Hamlyn E, Jones V, Porter K, Fidler S. Antiretroviral treatment of primary HIV infection to reduce onward transmission. *Curr Opin HIV AIDS.* 2010;5:283-90.  
[\[PubMed Abstract\]](#) -
- Hoen B, Dumon B, Harzic M, et al. Highly active antiretroviral treatment initiated early in the course of symptomatic primary HIV-1 infection: results of the ANRS 053 trial. *J Infect Dis.* 1999;180:1342-6.  
[\[PubMed Abstract\]](#) -
- Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. *J Infect Dis.* 2008;198:687-93.

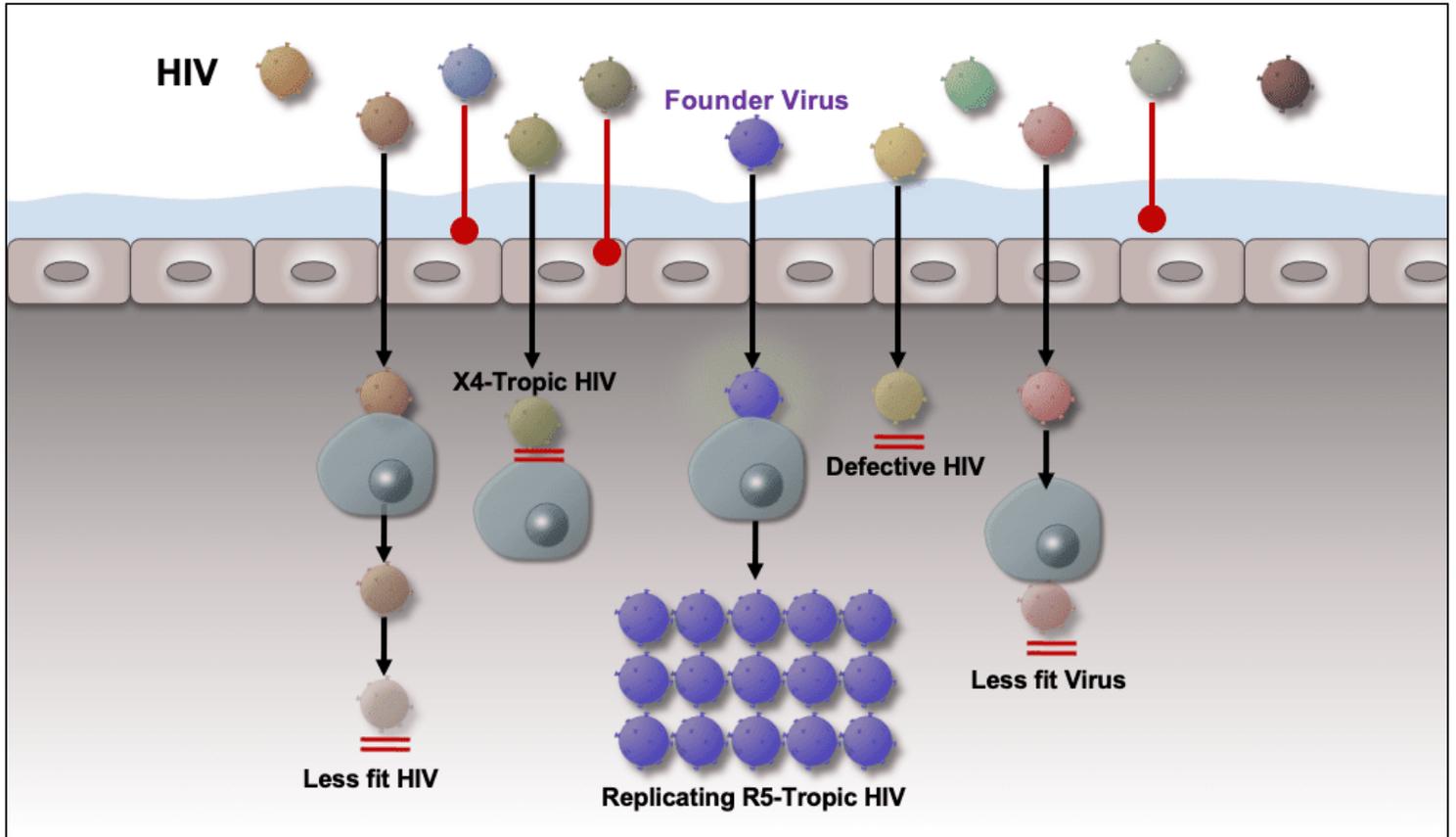
[\[PubMed Abstract\]](#) -

- Karris MY, Anderson CM, Morris SR, Smith DM, Little SJ. Cost savings associated with testing of antibodies, antigens, and nucleic acids for diagnosis of acute HIV infection. *J Clin Microbiol.* 2012;50:1874-8.  
[\[PubMed Abstract\]](#) -
- Landovitz RJ, Li S, Eron JJ Jr, et al. Tail-phase safety, tolerability, and pharmacokinetics of long-acting injectable cabotegravir in HIV-uninfected adults: a secondary analysis of the HPTN 077 trial. *Lancet HIV.* 2020;7:e472-e481.  
[\[PubMed Abstract\]](#) -
- Lavreys L, Baeten JM, Chohan V, et al. Higher set point plasma viral load and more-severe acute HIV type 1 (HIV-1) illness predict mortality among high-risk HIV-1-infected African women. *Clin Infect Dis.* 2006;42:1333-9.  
[\[PubMed Abstract\]](#) -
- Lillo FB, Ciuffreda D, Veglia F, et al. Viral load and burden modification following early antiretroviral therapy of primary HIV-1 infection. *AIDS.* 1999;13:791-6.  
[\[PubMed Abstract\]](#) -
- Madec Y, Boufassa F, Porter K, et al. Natural history of HIV-control since seroconversion. *AIDS.* 2013;27:2451-60.  
[\[PubMed Abstract\]](#) -
- Manak MM, Jagodzinski LL, Shutt A, et al. Decreased Seroreactivity in Individuals Initiating Antiretroviral Therapy during Acute HIV Infection. *J Clin Microbiol.* 2019;57:pii: e00757-19.  
[\[PubMed Abstract\]](#) -
- Schuetz A, Deleage C, Sereti I, et al. Initiation of ART during early acute HIV infection preserves mucosal Th17 function and reverses HIV-related immune activation. *PLoS Pathog.* 2014;10:e1004543.  
[\[PubMed Abstract\]](#) -
- Strongin Z, Sharaf R, VanBelzen DJ, et al. Effect of Short-Term Antiretroviral Therapy Interruption on Levels of Integrated HIV DNA. *J Virol.* 2018;92:pii:e00285-18.  
[\[PubMed Abstract\]](#) -

# Figures

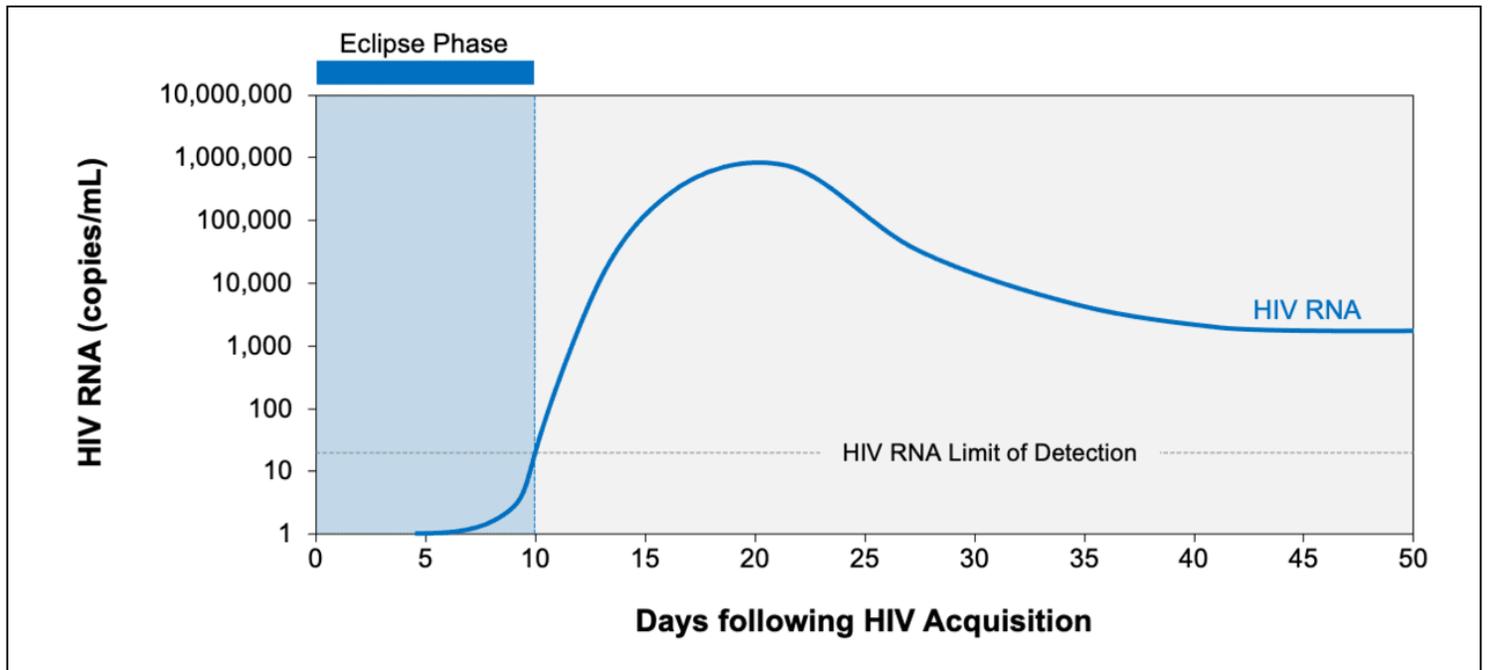
## Figure 1 Founder Virus

Source: Keele BF, Giorgi EE, Salazar-Gonzalez JF, et al. Identification and characterization of transmitted and early founder virus envelopes in primary HIV-1 infection. Proc Natl Acad Sci U S A. 2008;105:7552-7.  
Illustration: David H. Spach, MD



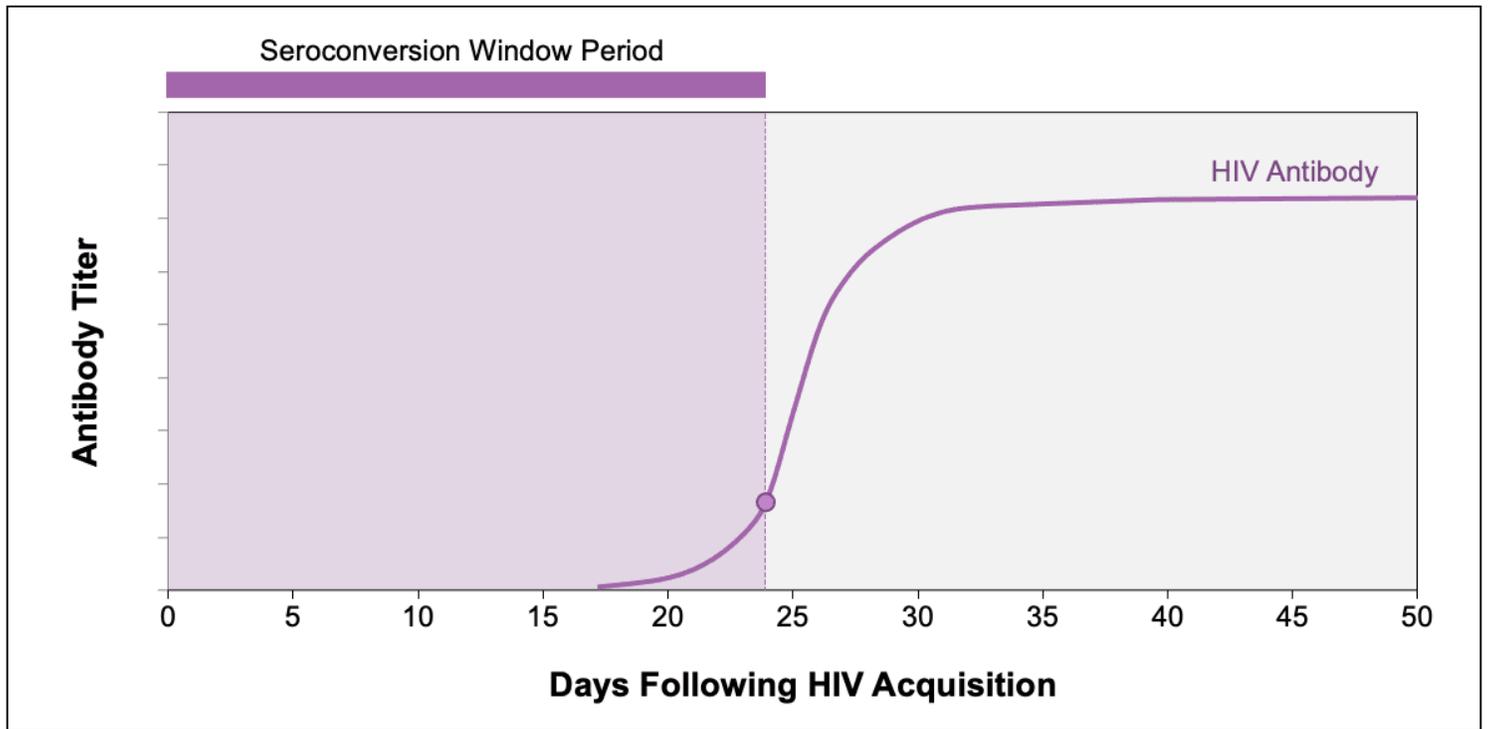
### Figure 2 HIV Eclipse Phase

Illustration: David H. Spach, MD



### Figure 3 HIV Seroconversion Window Period

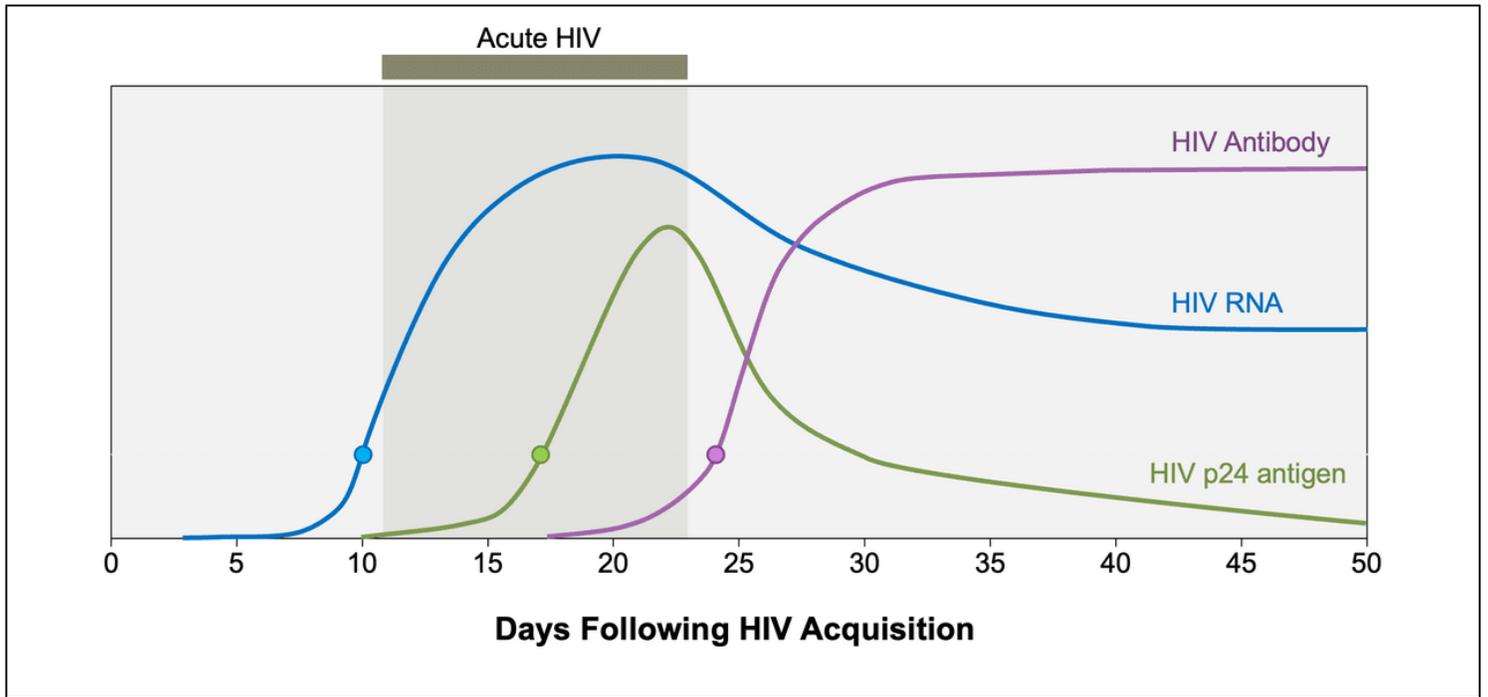
Illustration: David H. Spach, MD



### Figure 4 Acute HIV Infection

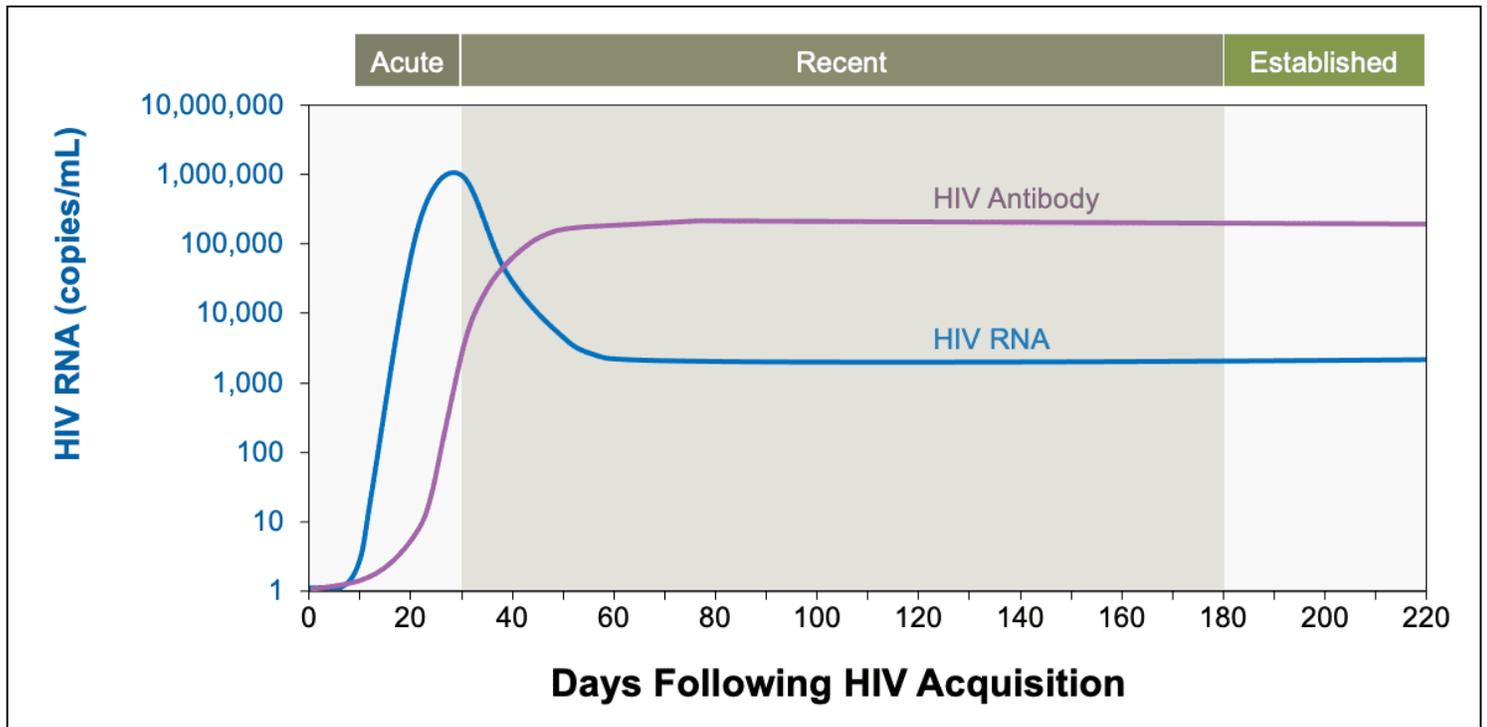
The colored circles indicate the typical time for first detection of a positive test after acquisition of HIV.

Illustration: David H. Spach, MD



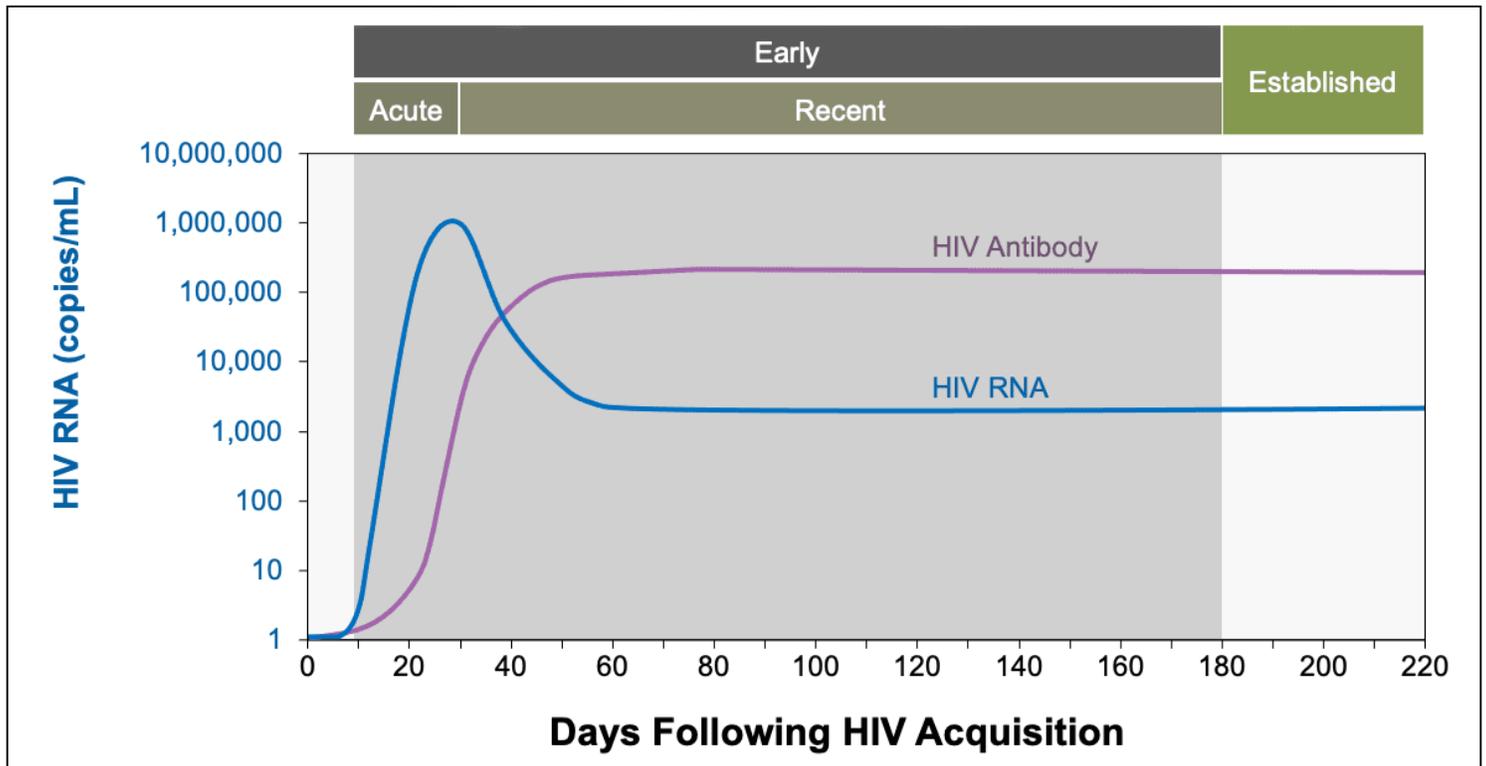
### Figure 5 Recent HIV Infection

Illustration: David H. Spach, MD



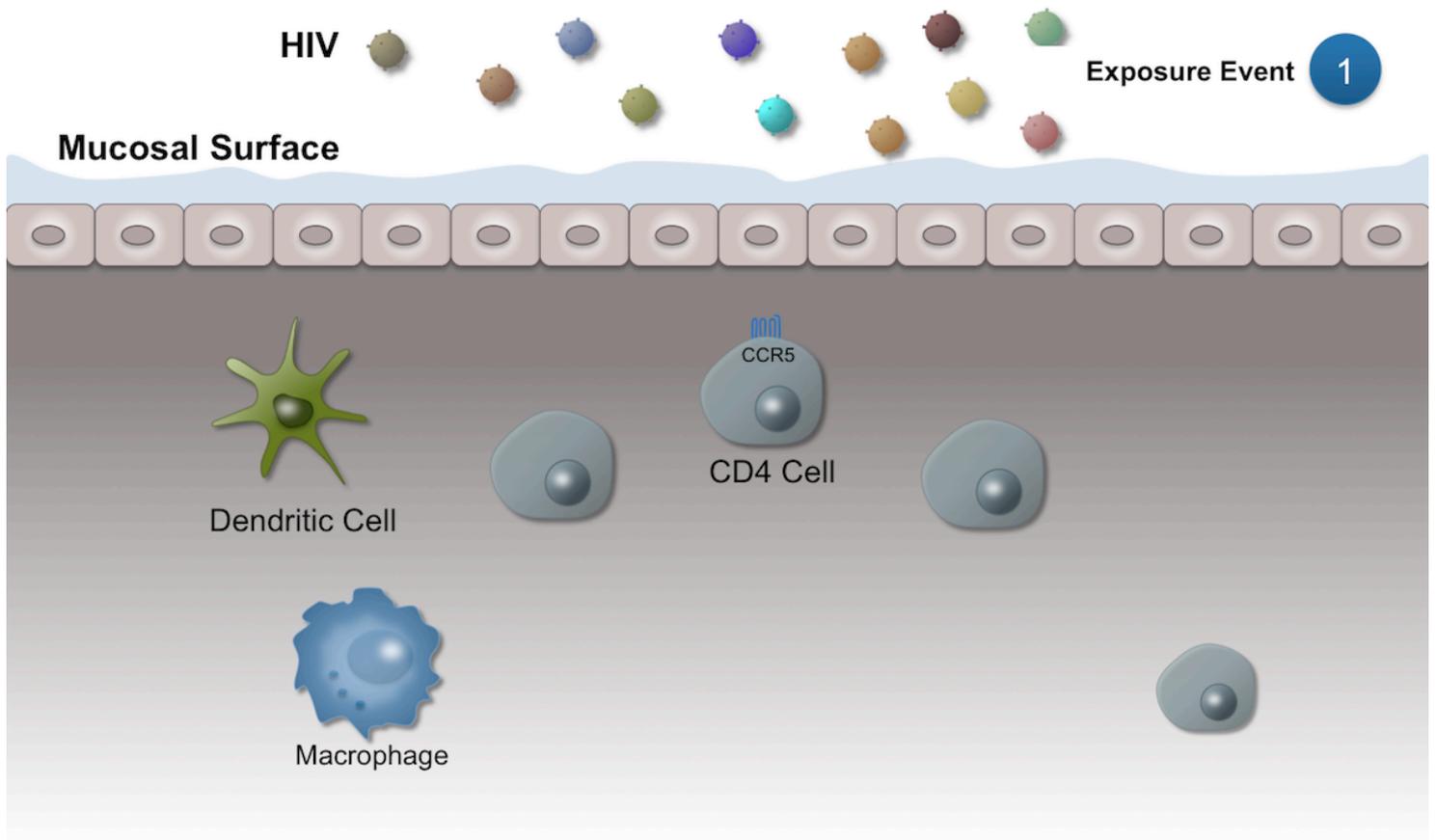
**Figure 6 Early HIV Infection**

Illustration: David H. Spach, MD



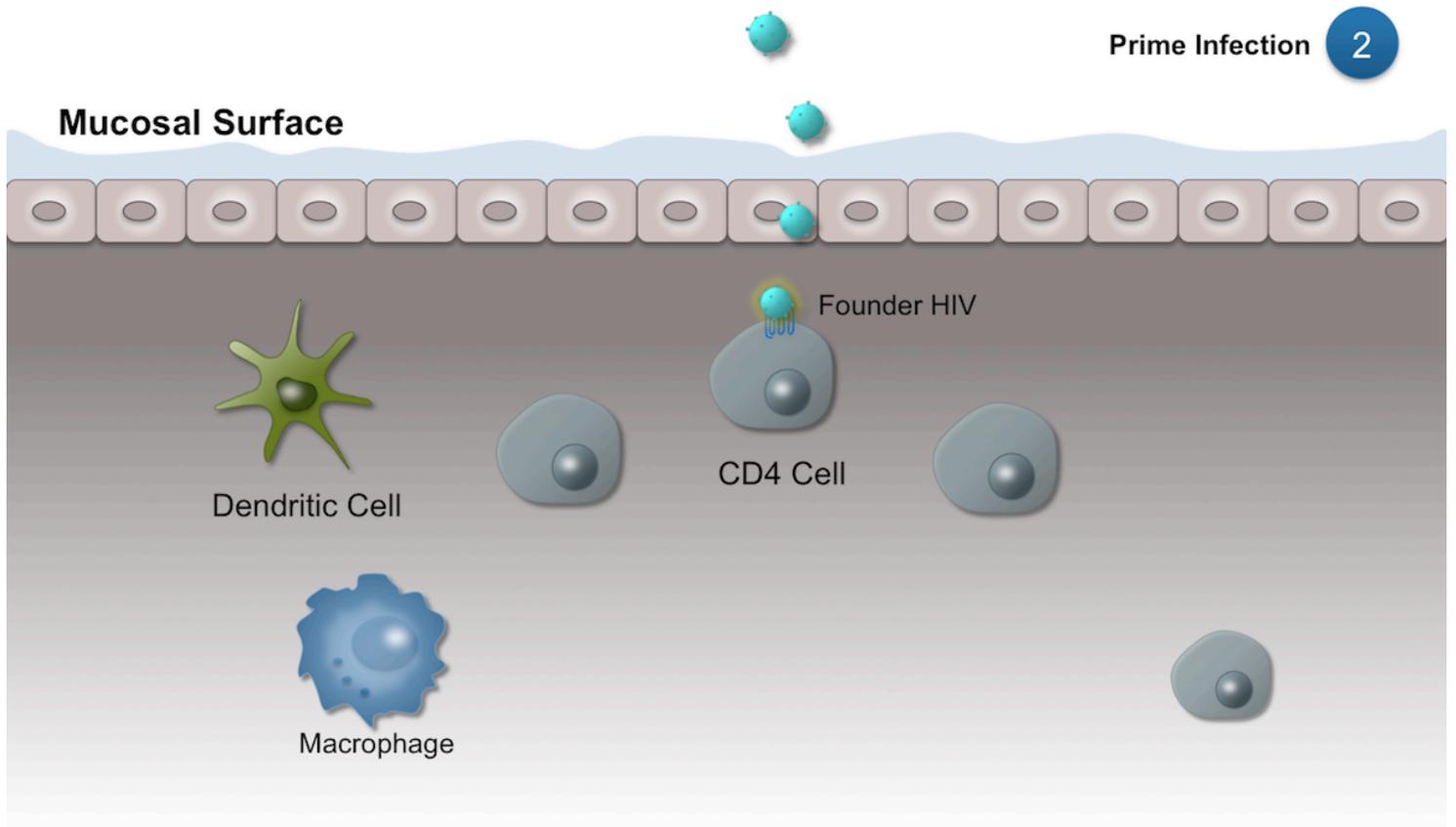
**Figure 7 (Image Series) - Model for Sexual Transmission of HIV (Image Series) - Figure 7 (Image Series) - Model for Sexual Transmission of HIV  
Image 7A: Exposure Event**

Illustration: David H. Spach, MD



**Figure 7 (Image Series) - Model for Sexual Transmission of HIV**  
**Image 7B: Prime Infection with Founder Virus**

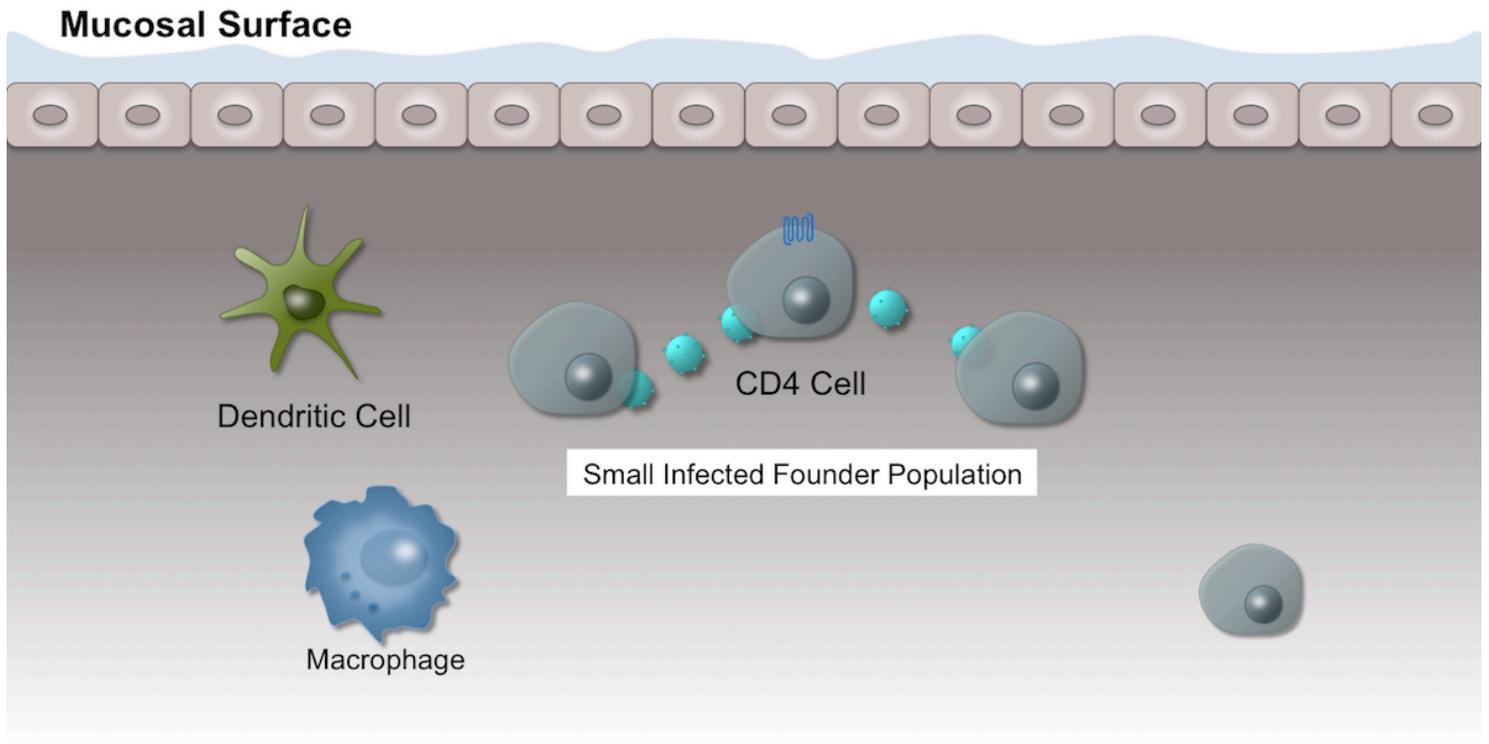
Illustration: David H. Spach, MD



**Figure 7 (Image Series) - Model for Sexual Transmission of HIV**  
**Image 7C: Initial Propagation with Small HIV Founder Population**

Illustration: David H. Spach, MD

Initial Propagation **3**

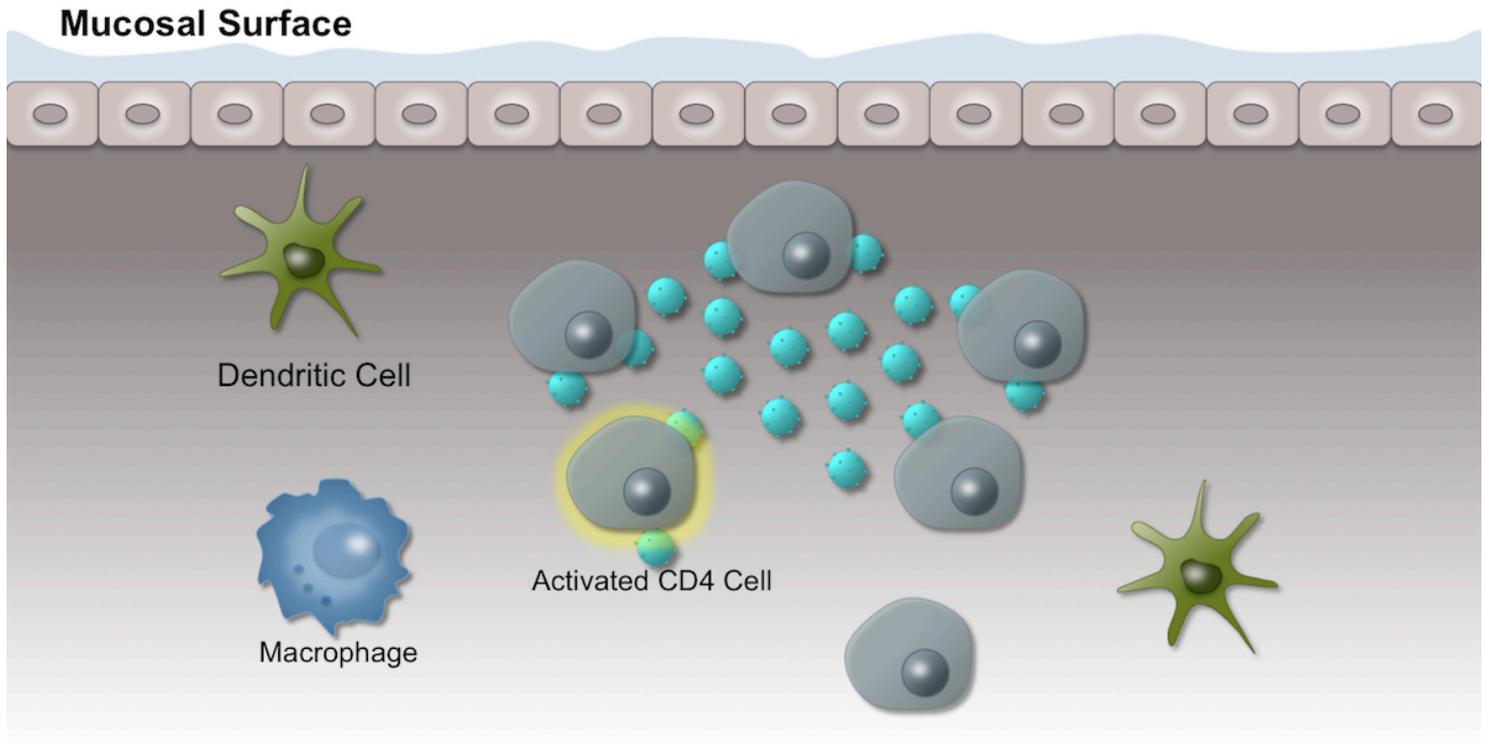


**Figure 7 (Image Series) - Model for Sexual Transmission of HIV**  
**Image 7D: Local Expansion**

Illustration: David H. Spach, MD

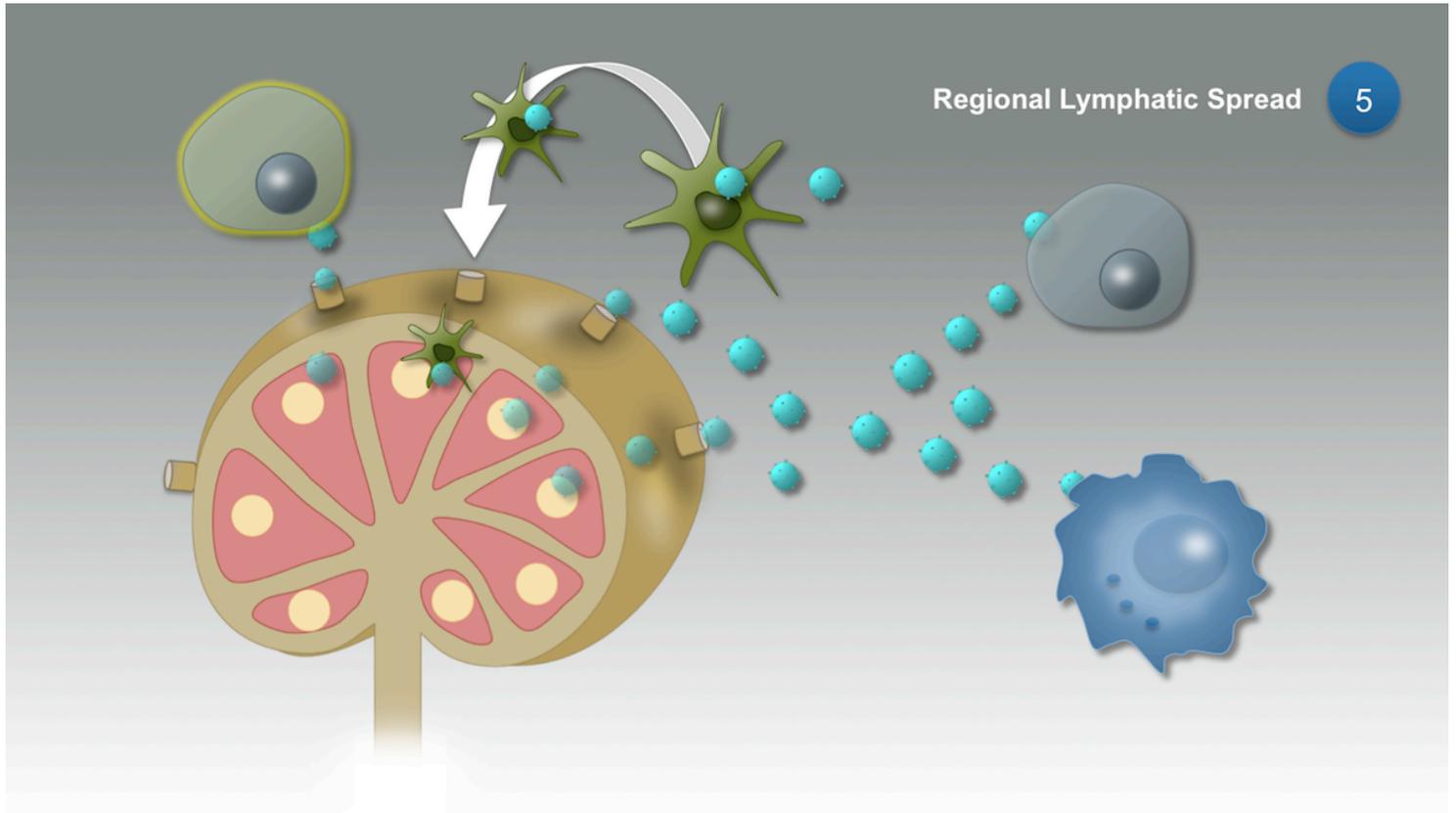
Local Expansion

4



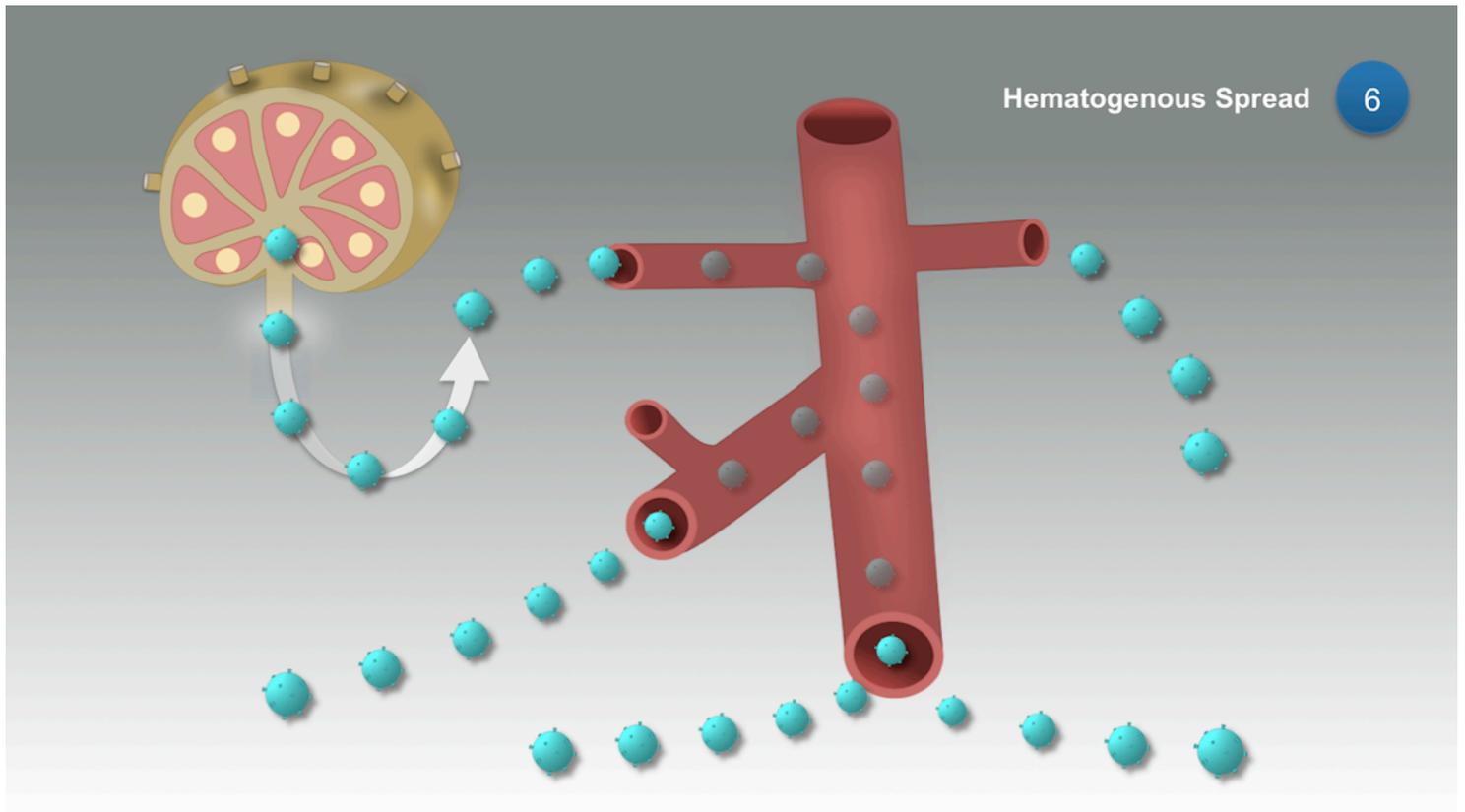
**Figure 7 (Image Series) - Model for Sexual Transmission of HIV**  
**Image 7E: Regional Lymphatic Spread**

Illustration: David H. Spach, MD



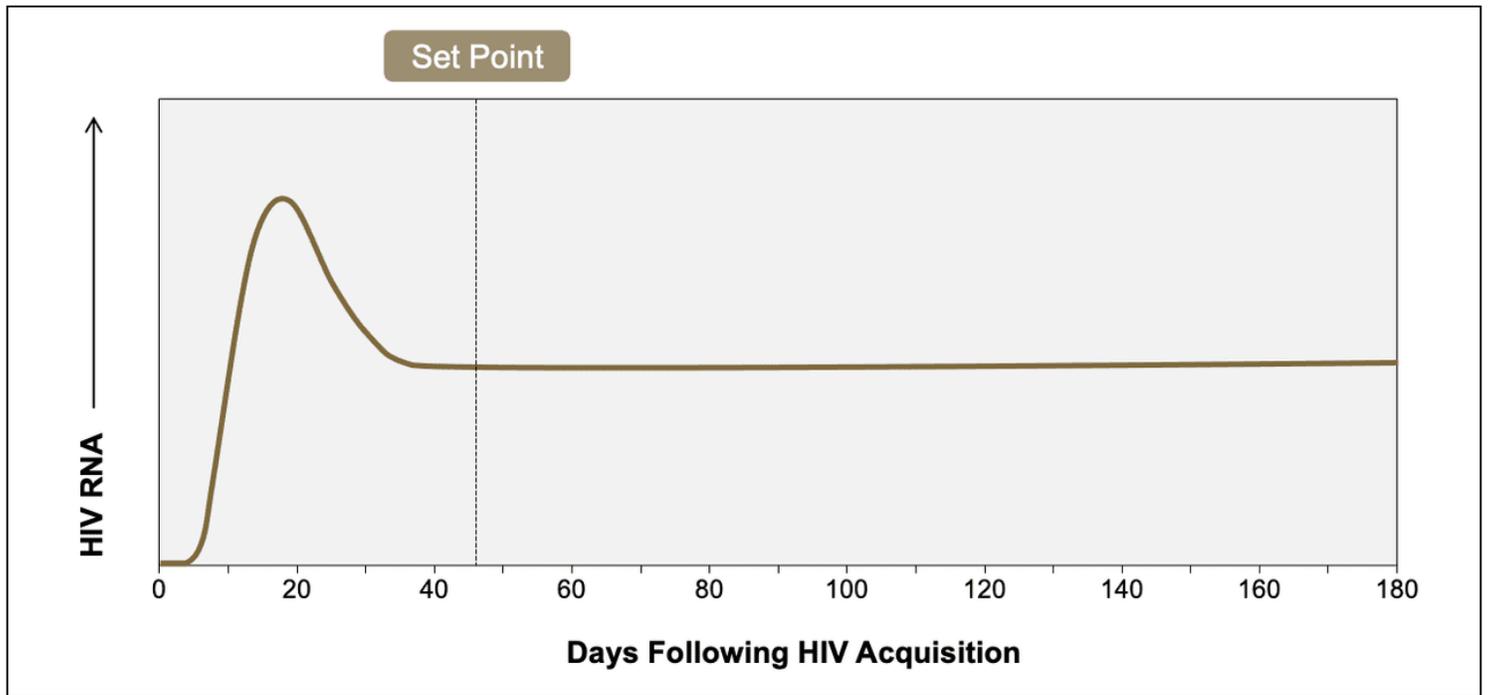
**Figure 7 (Image Series) - Model for Sexual Transmission of HIV**  
**Image 7F: Hematogenous Spread**

Illustration: David H. Spach, MD



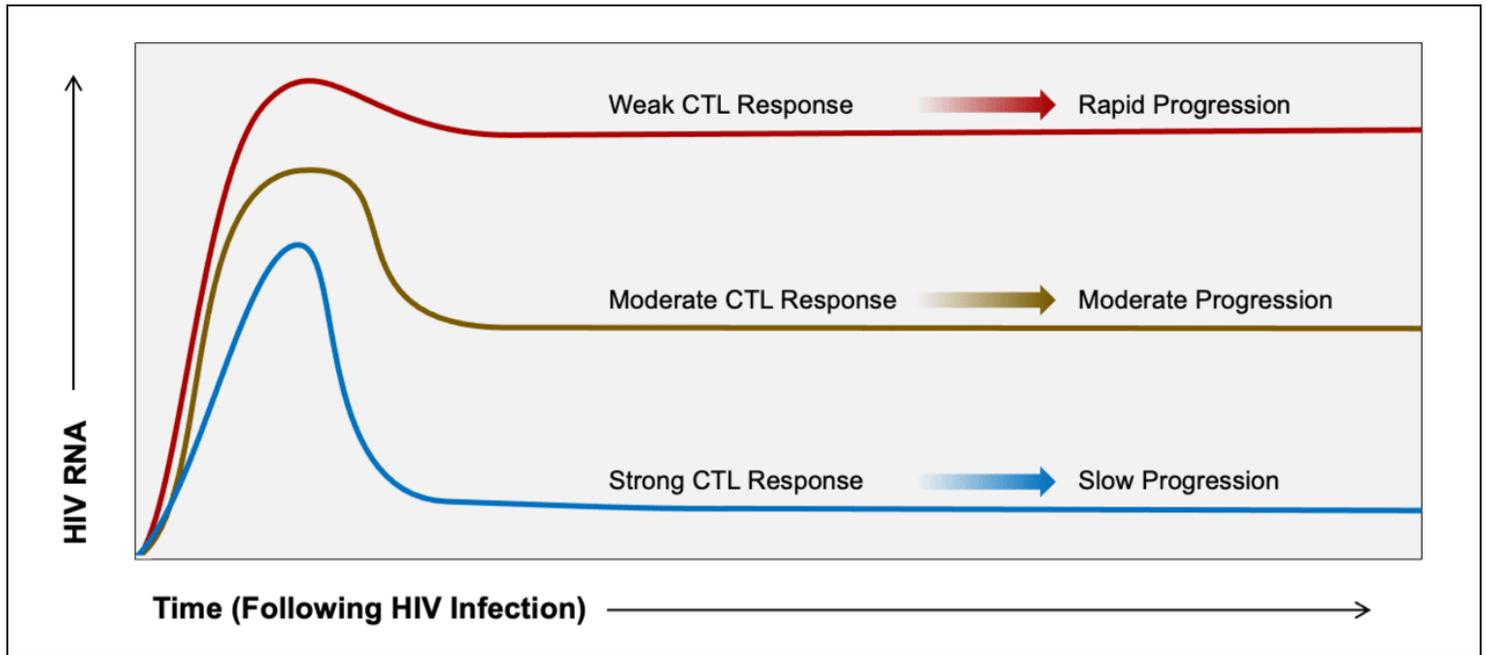
### Figure 8 Set Point Following Acquisition of HIV

Illustration: David H. Spach, MD



### Figure 9 Cytotoxic T-Lymphocyte Response Following Acute HIV Infection

Source: Walker BD, Goulder PJ. AIDS. Escape from the immune system. Nature. 2000;407:313-4. Illustration: David H. Spach, MD



**Figure 10 Acute HIV: Skin Rash**

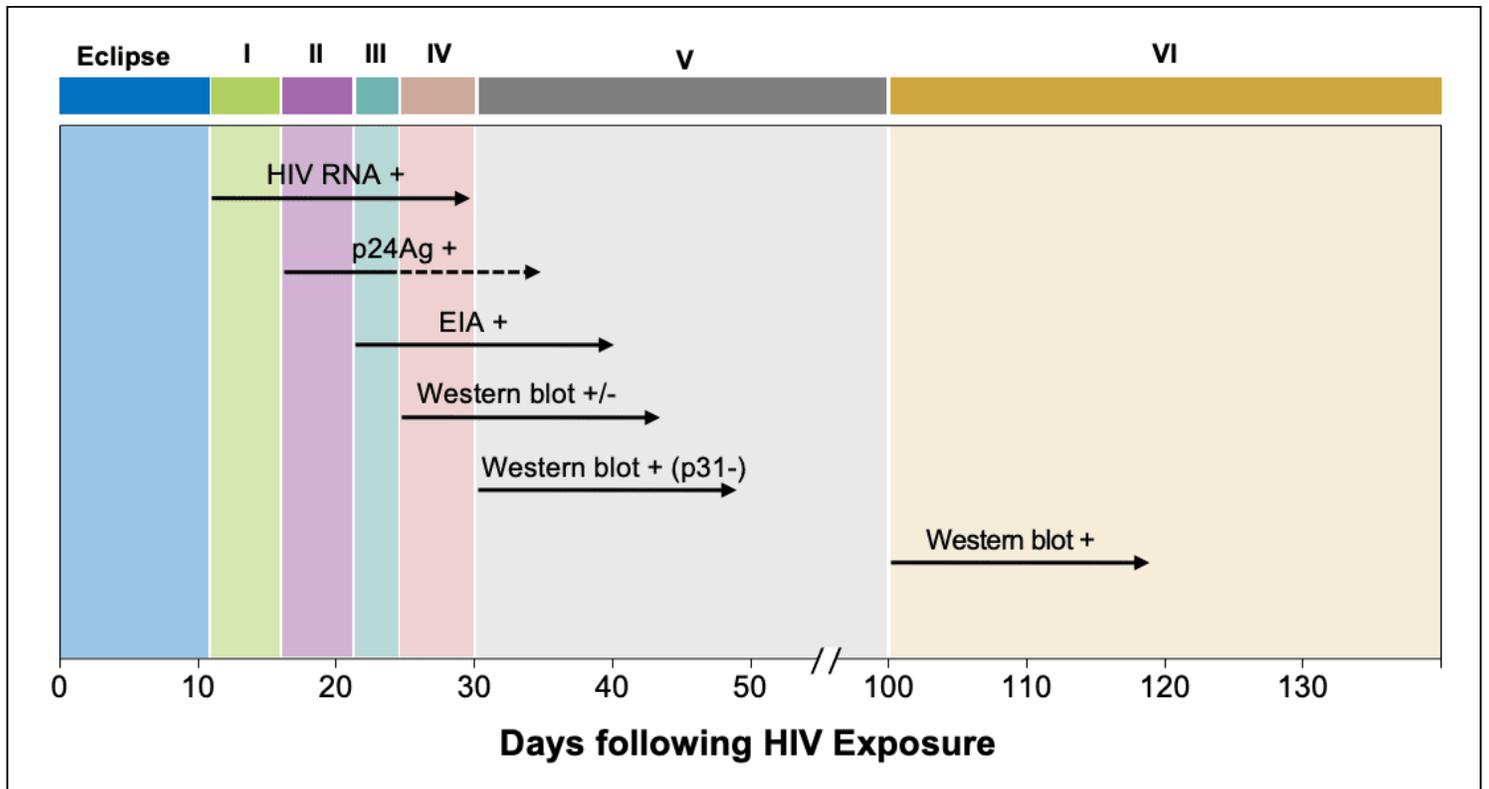
Source: photograph by David H. Spach, MD



**Figure 11 Fiebig Laboratory Staging of Early HIV Infection**

Abbreviations: Ag = antigen; EIA = enzyme immunoassay

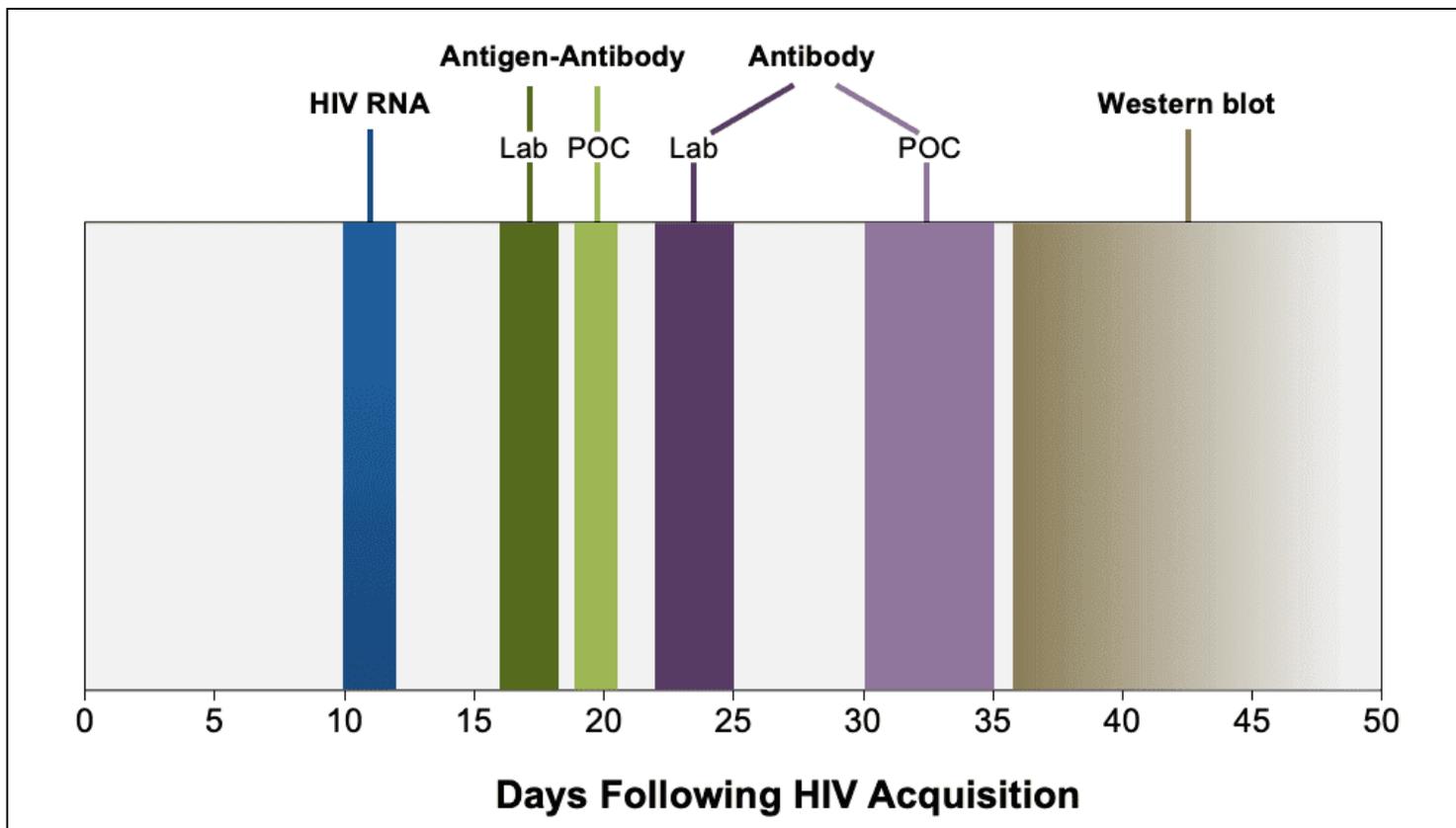
Source: Fiebig EW, Wright DJ, Rawal BD, et al. Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. AIDS. 2003;17:1871-9.



**Figure 12 Timing of Positivity for HIV Diagnostic Tests Following Initial HIV Infection**

Abbreviation: POC = point-of-care

Source: Illustration by David H. Spach, MD and modified from Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. Published June 27, 2014.

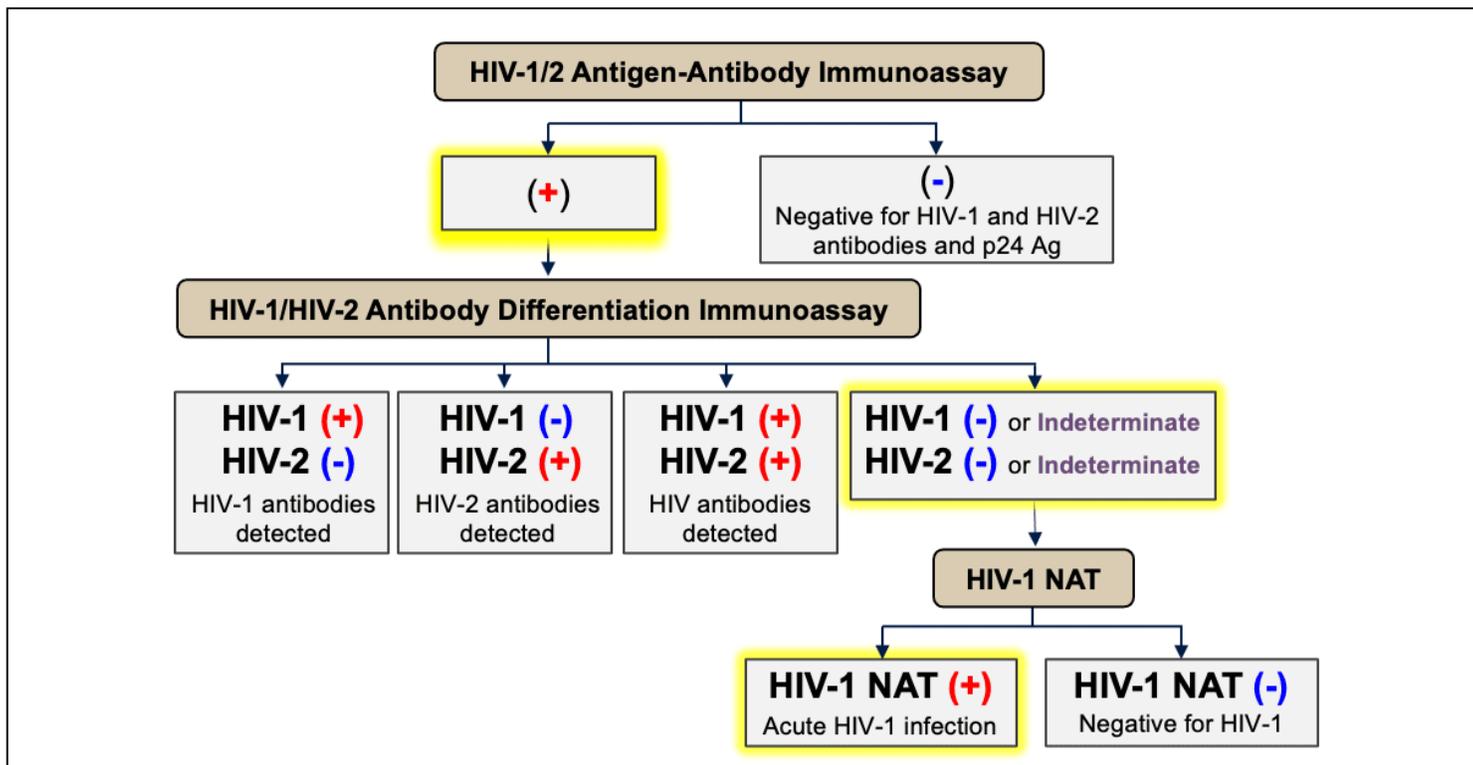


**Figure 13 HIV Laboratory Testing Algorithm As Recommended by the CDC and APHL**

The rectangles highlighted with a yellow border indicate the expected positive tests in a person with acute HIV.

Abbreviations: Ag = antigen; NAT = nucleic acid test

Source: Centers for Disease Control and Prevention and Association of Public Health Laboratories. 2018 Quick reference guide: Recommended laboratory HIV testing algorithm for serum or plasma specimens. Published January 27, 2018.



**Figure 14 Risk of Sexual Transmission of HIV During Early Infection**

Source: Pilcher CD, Tien HC, Eron JJ Jr, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis.* 2004;189:1785-92.

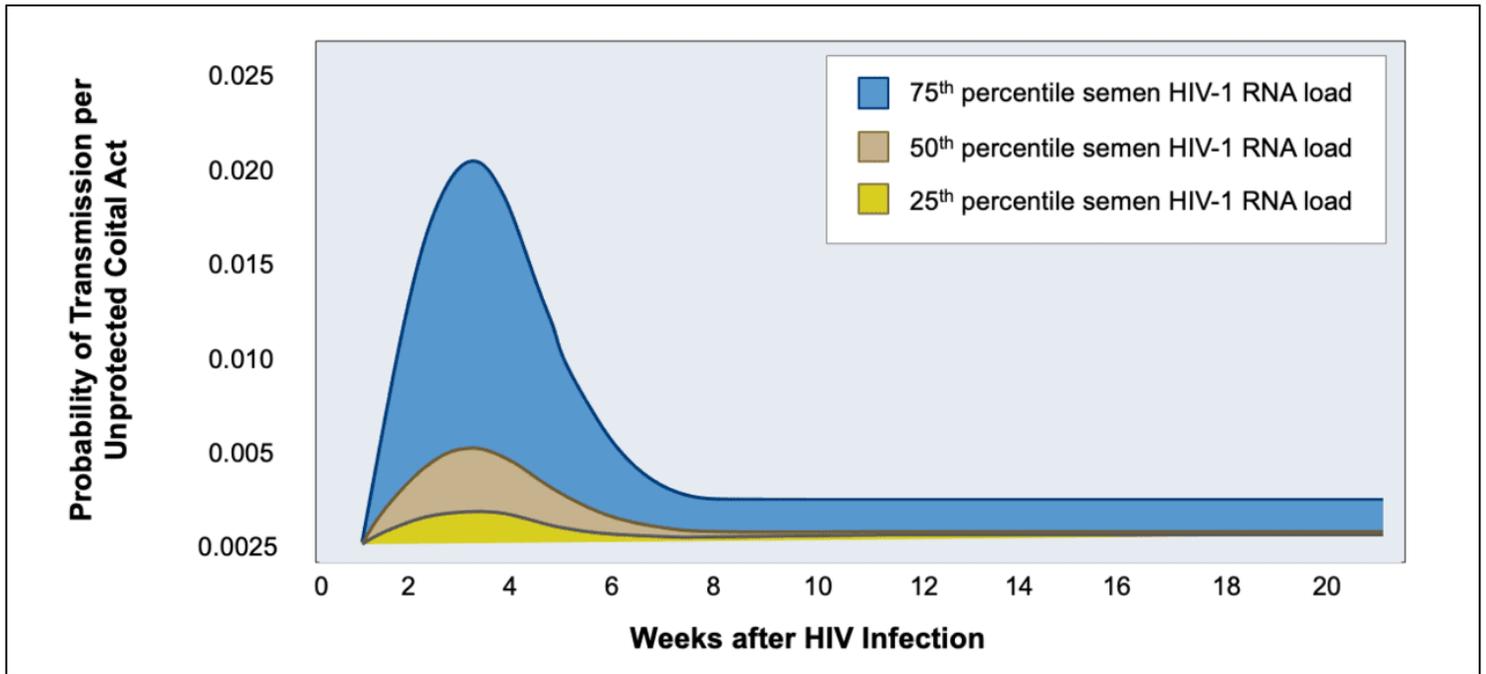


Table 1. Clinical Signs and Symptoms of Acute HIV Infection

Features (%)	Overall (n = 375)	Sex		Route of Transmission	
		Male (n = 355)	Female (n = 23)	Sexual (n = 324)	IDU (n = 34)
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

IDU = Injection drug use

Source:

- US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update. A Clinical Practice Guideline. March 2018:1-59. [[CDC](#)]

Table 2. Panel's Recommendations for Early (Acute and Recent) HIV Infection

<p>Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV</p> <p><b>Antiretroviral Therapy for Early<sup>a</sup> (Acute and Recent) HIV Infection</b></p> <ul style="list-style-type: none"> <li>• Antiretroviral therapy is recommended for all people with HIV, including those with early<sup>a</sup> HIV infection (AI). Antiretroviral therapy should be initiated as soon as possible after HIV diagnosis (AII).</li> <li>• The goals of antiretroviral therapy are to suppress plasma HIV RNA to undetectable levels (AI), prevent transmission of HIV (AI), and preserve immune function (AIII). Monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and antiretroviral drug-related adverse effects should be done as recommended for people with chronic HIV infection (AII).</li> <li>• A blood sample for genotypic resistance testing should be sent to the laboratory before initiating ART (AIII). <ul style="list-style-type: none"> <li>◦ Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes (AIII) for all people with early HIV.</li> <li>◦ Genotype testing for integrase strand transfer inhibitor (INSTI) resistance should be performed for those who acquire HIV during or after the use of long-acting cabotegravir (CAB-LA) as preexposure prophylaxis (PrEP), if transmitted integrase strand transfer inhibitor (INSTI) resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for HIV post-exposure prophylaxis (PEP) (AIII).</li> </ul> </li> <li>• Antiretroviral therapy can be initiated before drug-resistance testing results are available.</li> <li>• For those without a history of using long-acting injectable cabotegravir as HIV PrEP, one of the following antiretroviral regimens is recommended<sup>b</sup> (AIII): <ul style="list-style-type: none"> <li>◦ Bictegravir-tenofovir alafenamide-emtricitabine</li> <li>◦ Dolutegravir with (tenofovir alafenamide or tenofovir DF)<sup>c</sup> plus (emtricitabine or lamivudine)</li> </ul> </li> <li>• For those with a history of long-acting cabotegravir (CAB-LA) use as HIV PrEP, genotype testing done before the start of antiretroviral should include screening for integrase strand transfer inhibitor (INSTI)-resistance mutations: <ul style="list-style-type: none"> <li>◦ A regimen of cobicistat<sup>d</sup> or ritonavir boosted darunavir with (tenofovir alafenamide or tenofovir DF)<sup>c</sup> plus (emtricitabine or lamivudine) is recommended while awaiting the results of the genotype testing (AIII).</li> <li>◦ Use of empiric INSTI-containing regimen is not recommended unless genotype testing shows no evidence of INSTI resistance (AIII). This is because INSTI resistance may be present in those who acquire HIV during and possibly after the use of CAB-LA as HIV PrEP.</li> </ul> </li> <li>• In people with HIV RNA levels <math>\geq 200</math> copies/mL and who are taking HIV PrEP, immediate initiation of an effective HIV treatment regimen is recommended while awaiting confirmation of HIV diagnosis (AIII).</li> <li>• Pregnancy testing should be performed in women of childbearing potential before initiation of antiretroviral therapy (AIII).</li> <li>• When the results of drug-resistance tests are available, the treatment regimen can be modified if needed (AII).</li> <li>• Providers should inform individuals starting antiretroviral therapy of the importance of adherence to achieve and maintain viral suppression (AIII).</li> </ul> <p><b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Optional  <b>Rating of Evidence:</b> I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion</p> <p><b>Abbreviations:</b> PrEP = preexposure prophylaxis</p> <p><sup>a</sup>Early infection represents either acute or recent infection (<math>\leq 6</math> months) infection  <sup>b</sup>Because of the low rates of transmitted INSTI resistance in the United States at present, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based</p>
--

regimen can be started while awaiting the results of the INSTI genotype.

<sup>c</sup>Tenofovir alafenamide and tenofovir DF are two forms of tenofovir that are approved in the United States. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, while tenofovir DF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

<sup>d</sup>Cobicistat should be avoided in pregnancy because lower concentrations of cobicistat and darunavir have been reported during the second and third trimesters.

Source:

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Considerations for Antiretroviral Therapy Use in Special Populations. Early (Acute and Recent) HIV Infection. September 12, 2024. [[HIV.gov](https://www.hiv.gov)]

