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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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).[2] An acute symptomatic illness, referred to as acute retroviral syndrome, may develop during the acute HIV infection phase.[14,15]

- **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).[16]

- **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).[16]

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 reactivitity 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.

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[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

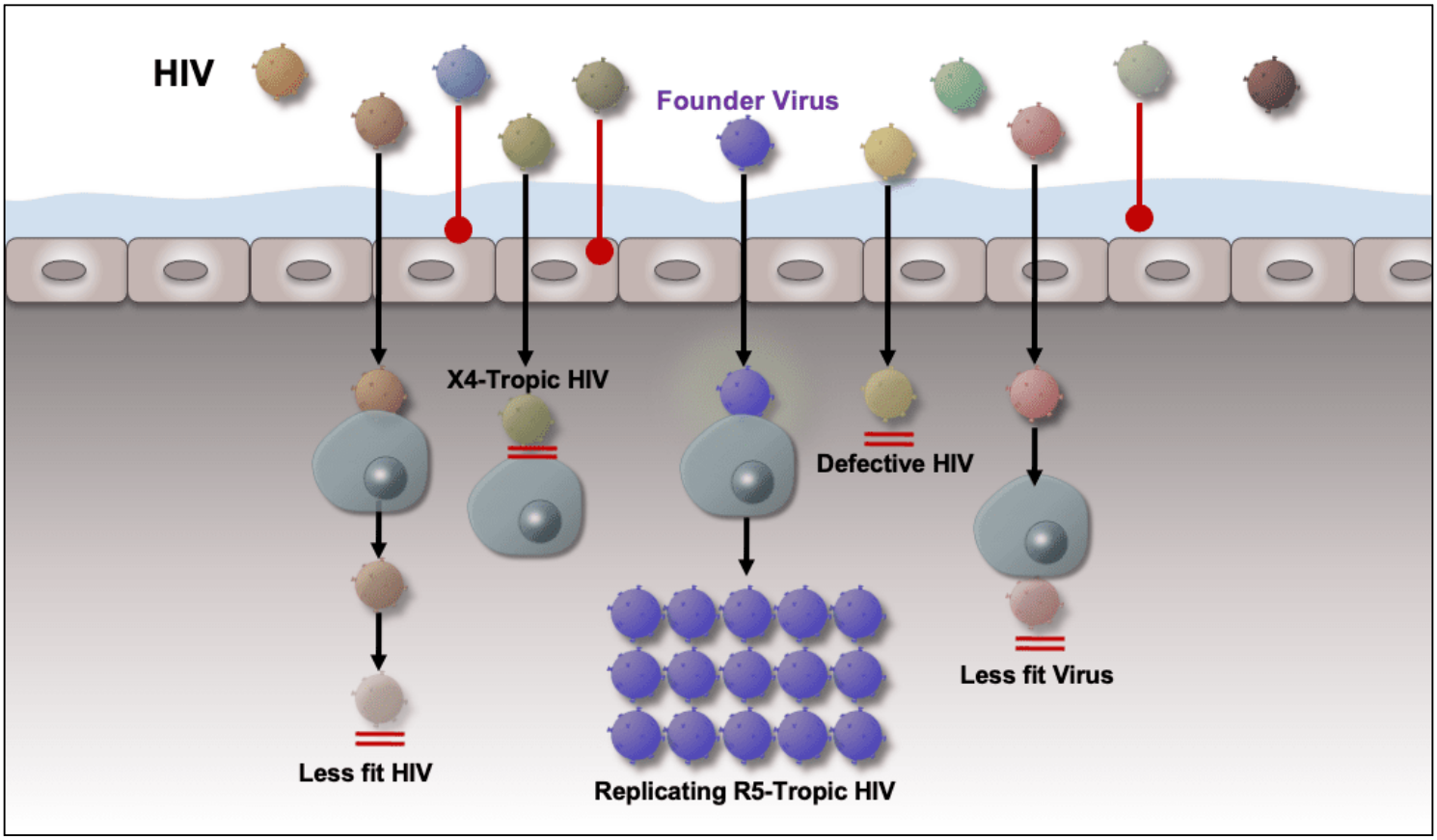

Figure 2 HIV Eclipse Phase

Illustration: David H. Spach, MD

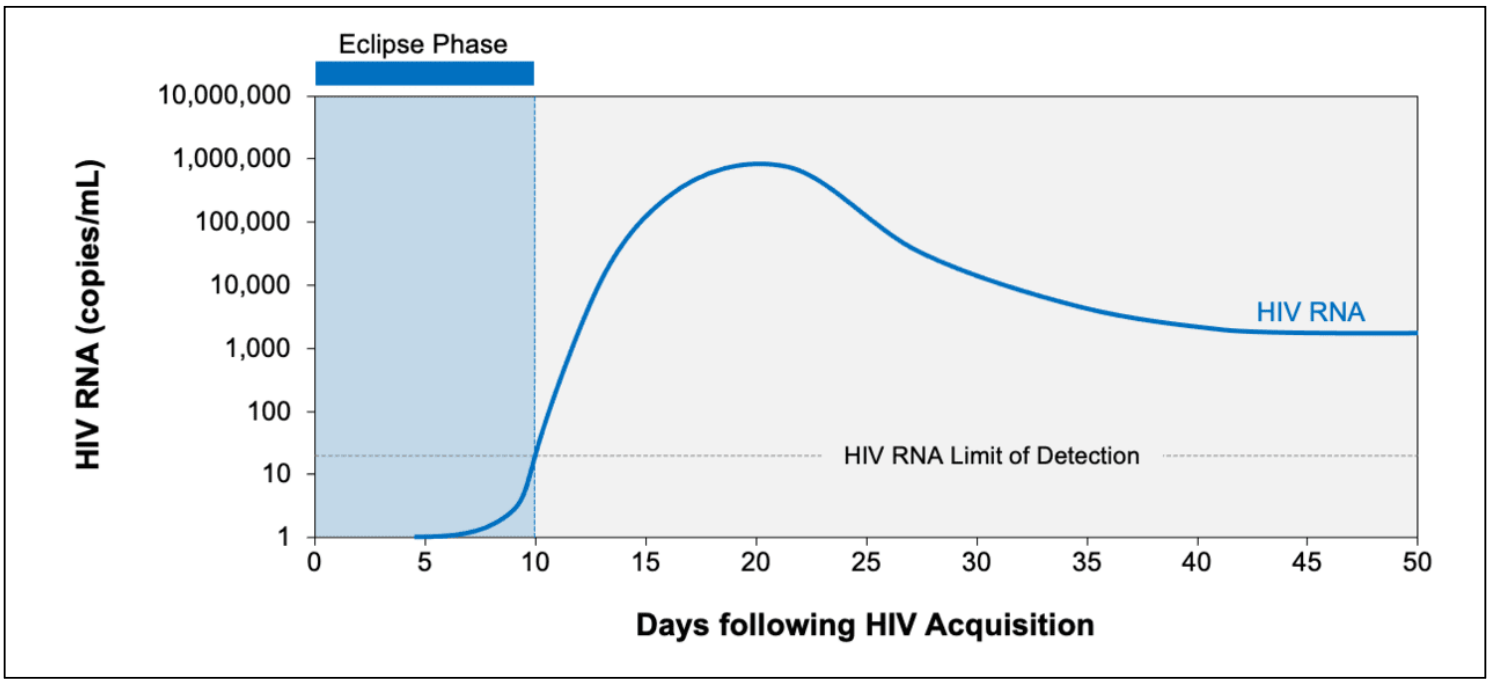

Figure 3 HIV Seroconversion Window Period

Illustration: David H. Spach, MD

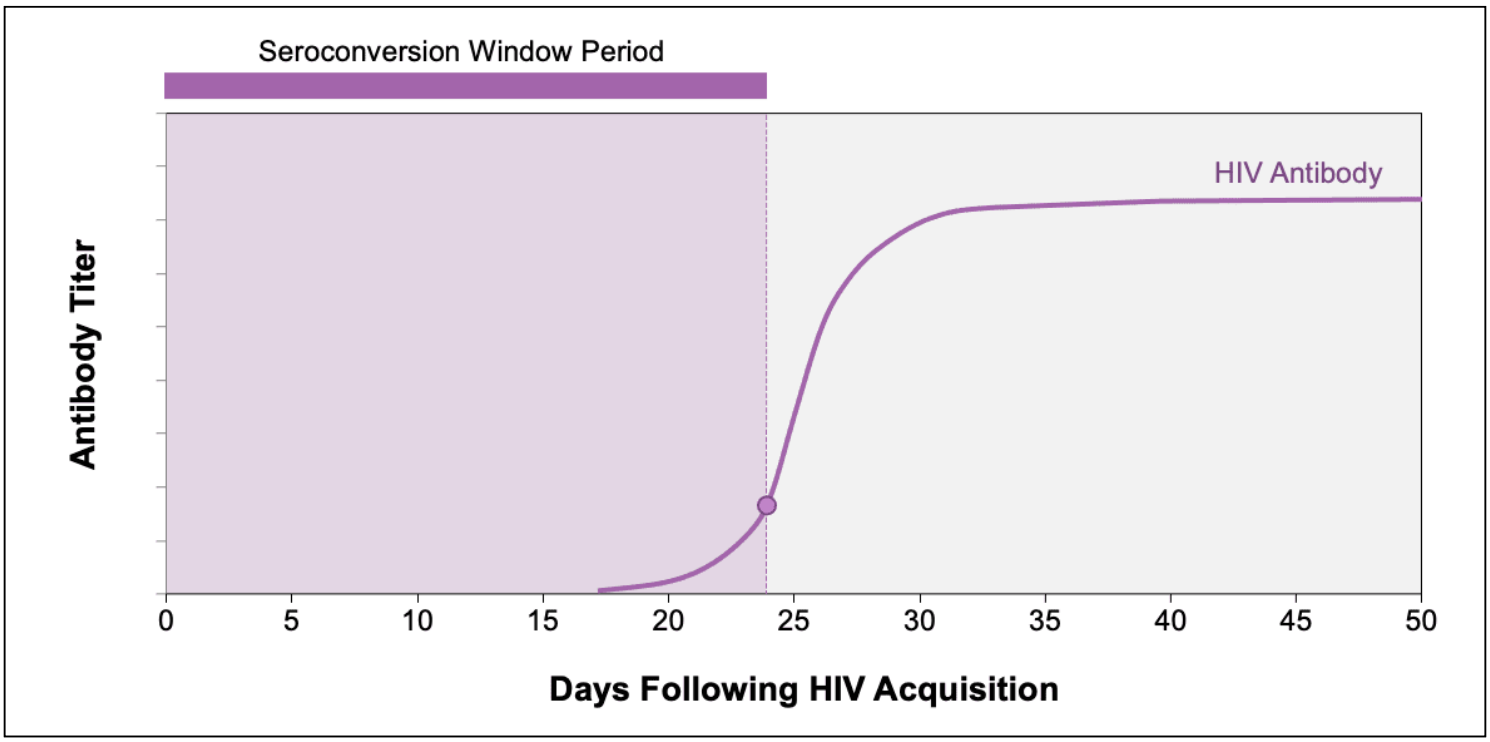

Figure 4 Acute HIV Infection

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

Illustration: David H. Spach, MD

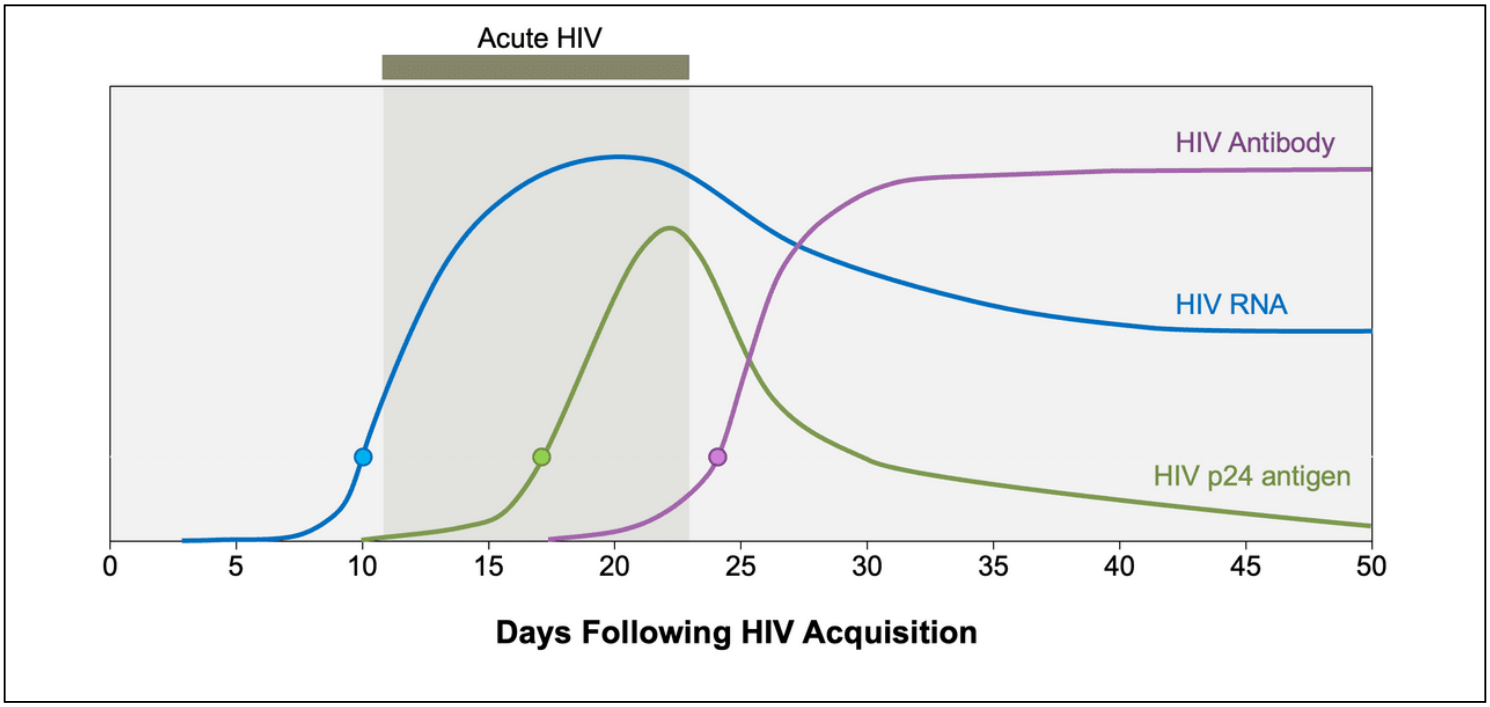

Figure 5 Recent HIV Infection

Illustration: David H. Spach, MD

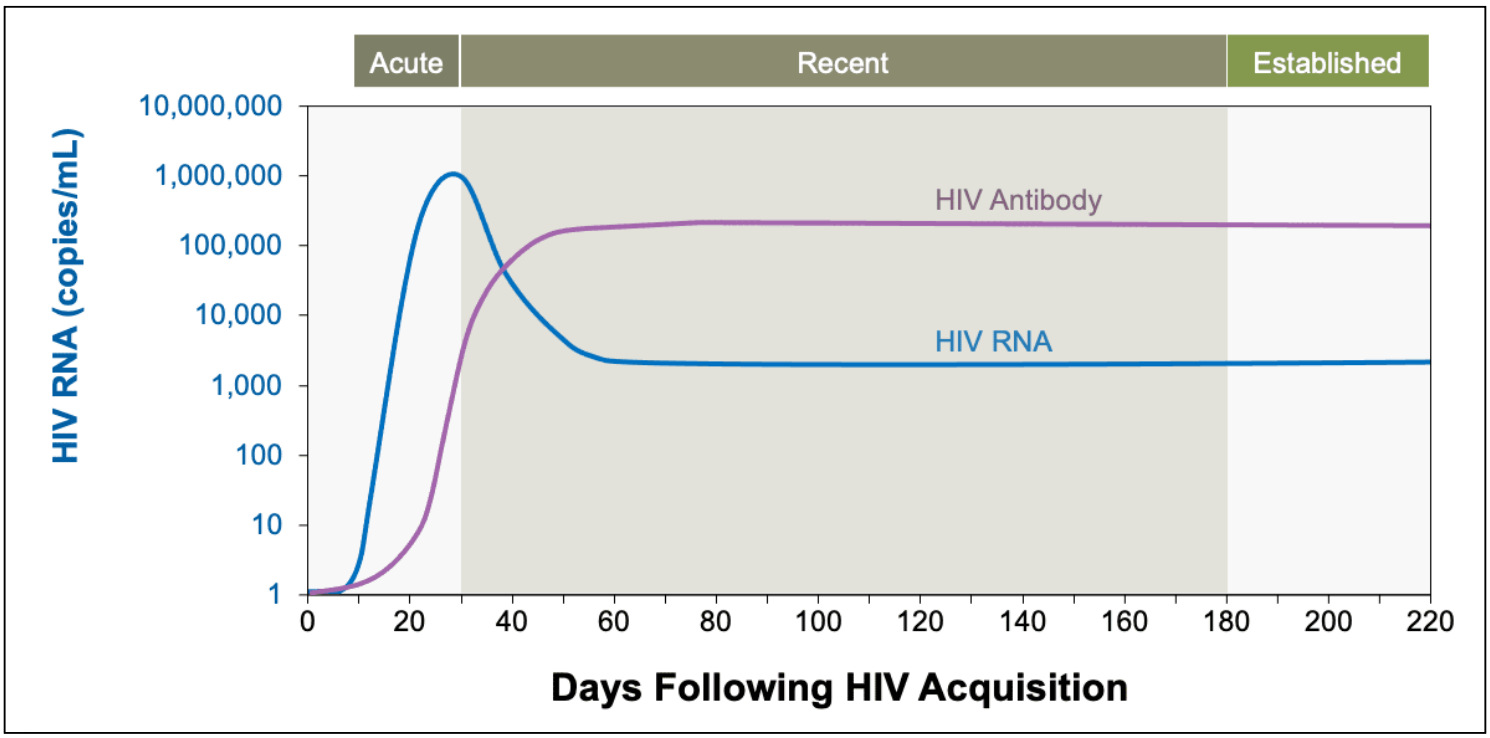

Figure 6 Early HIV Infection

Illustration: David H. Spach, MD

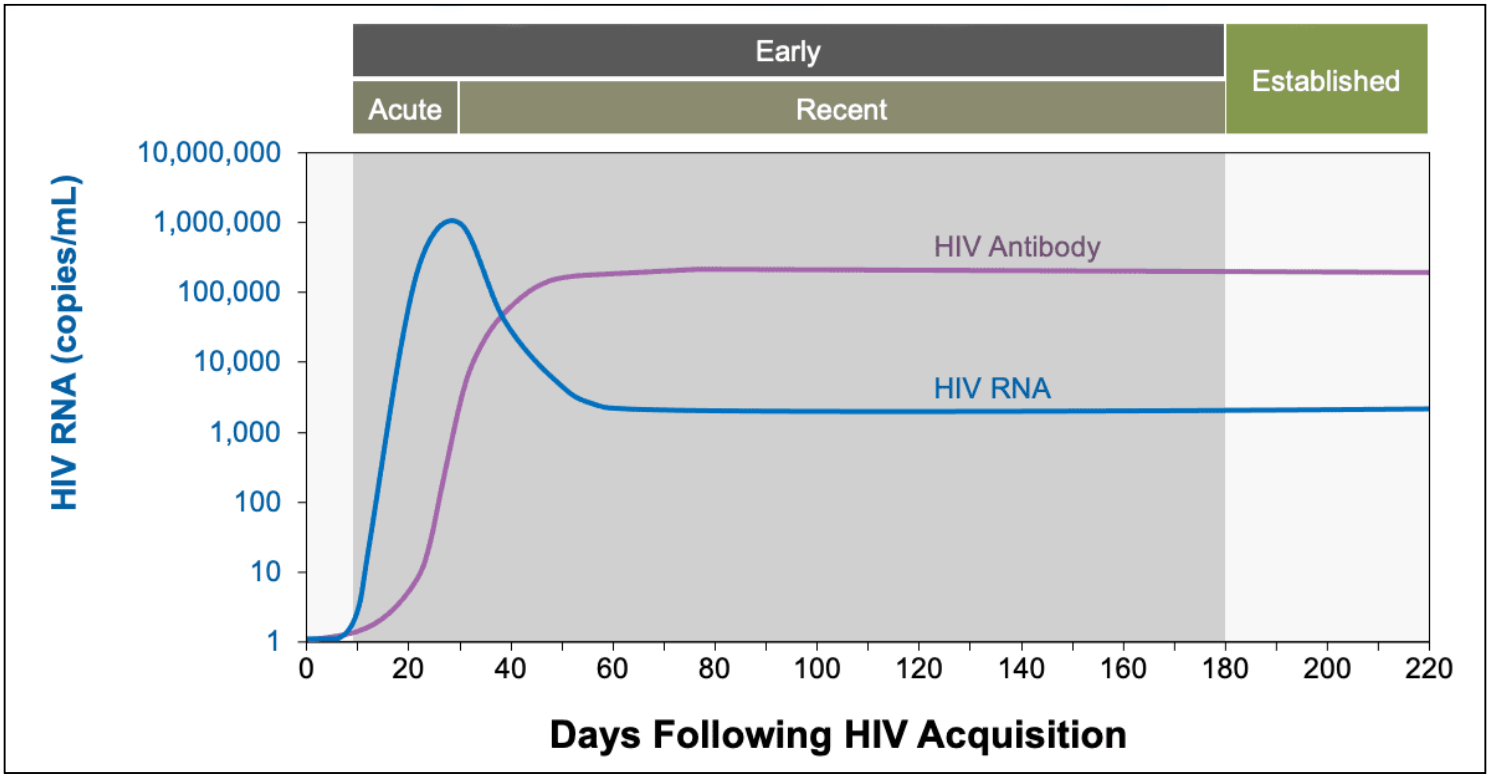

Figure 7 (Image Series) - Model for Sexual Transmission of HIV (Image Series) - Figure 7 (Image Series) - Model for Sexual Transmission of HIV
Image 7A: Exposure Event

Illustration: David H. Spach, MD

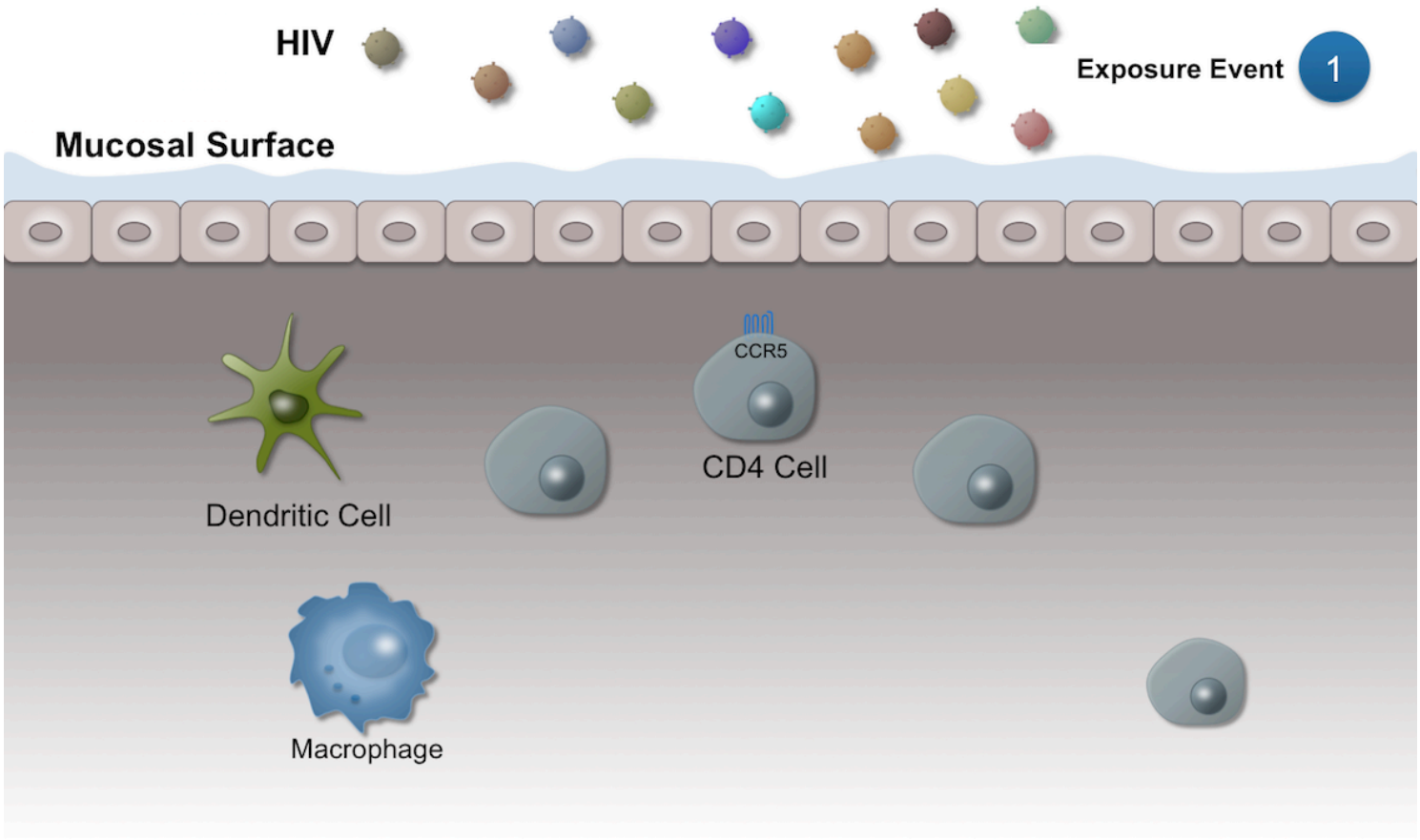

Figure 7 (Image Series) - Model for Sexual Transmission of HIV
Image 7B: Prime Infection with Founder Virus

Illustration: David H. Spach, MD

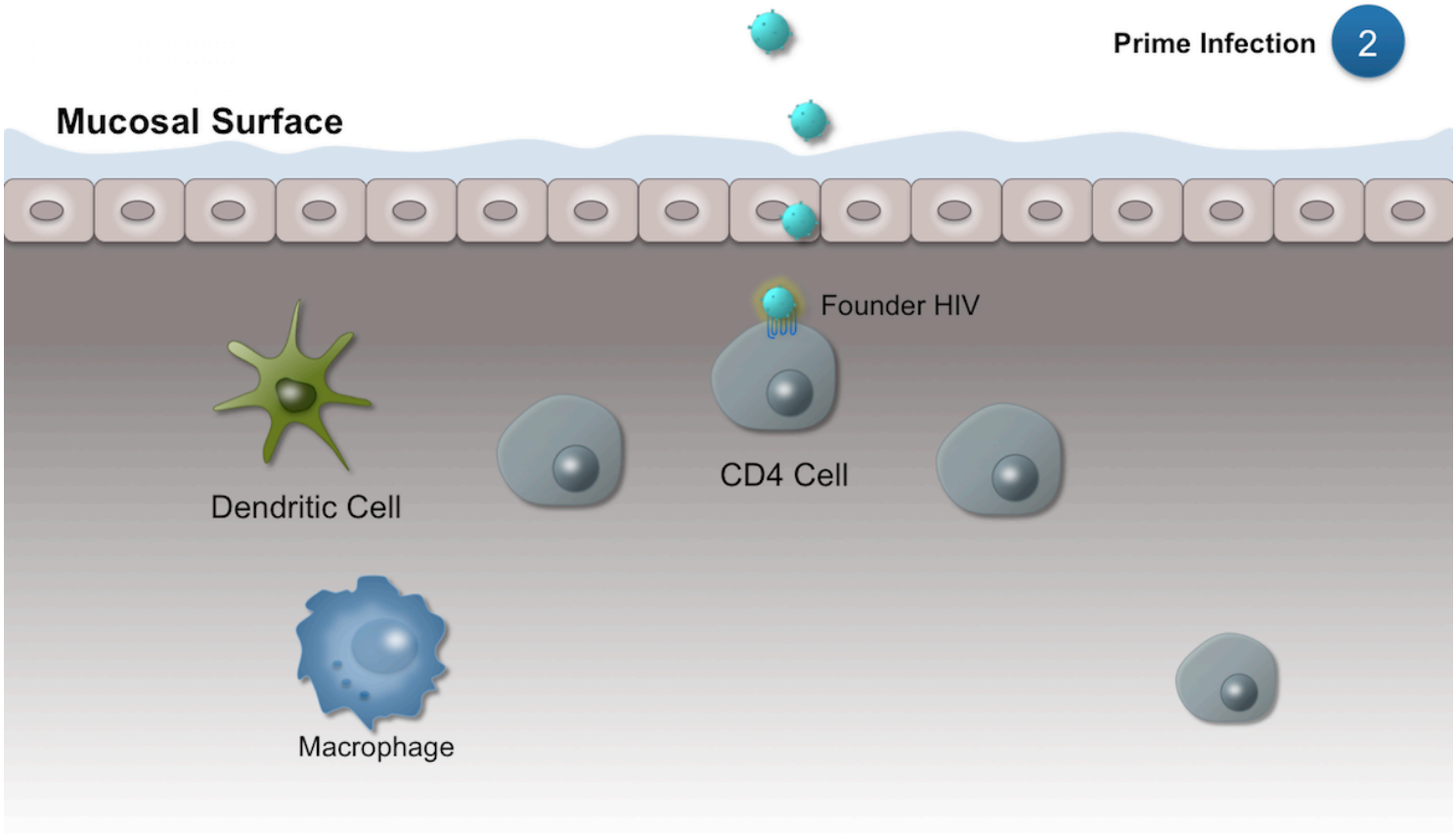

Figure 7 (Image Series) - Model for Sexual Transmission of HIV
Image 7C: Initial Propagation with Small HIV Founder Population

Illustration: David H. Spach, MD

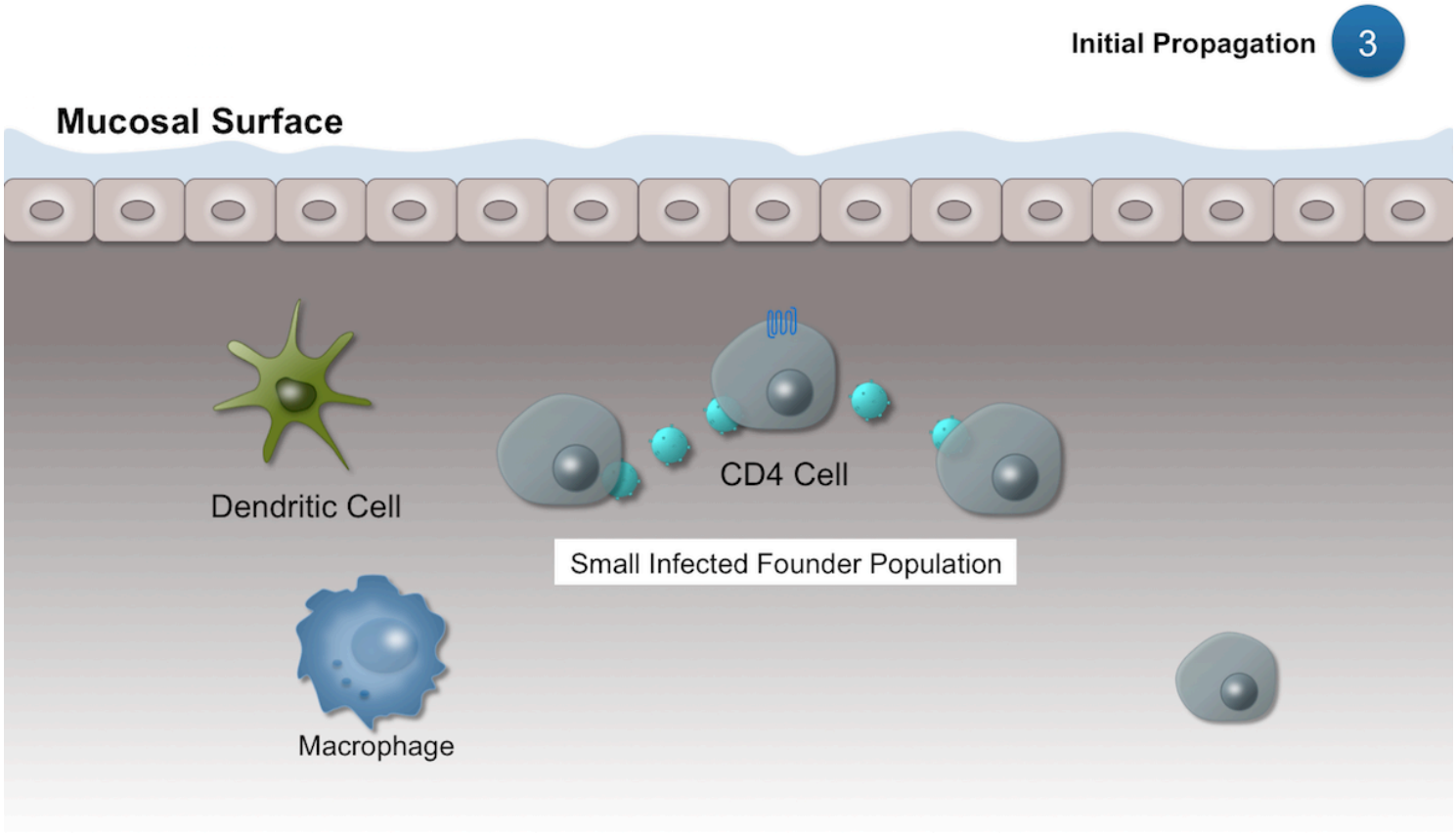

Figure 7 (Image Series) - Model for Sexual Transmission of HIV
Image 7D: Local Expansion

Illustration: David H. Spach, MD

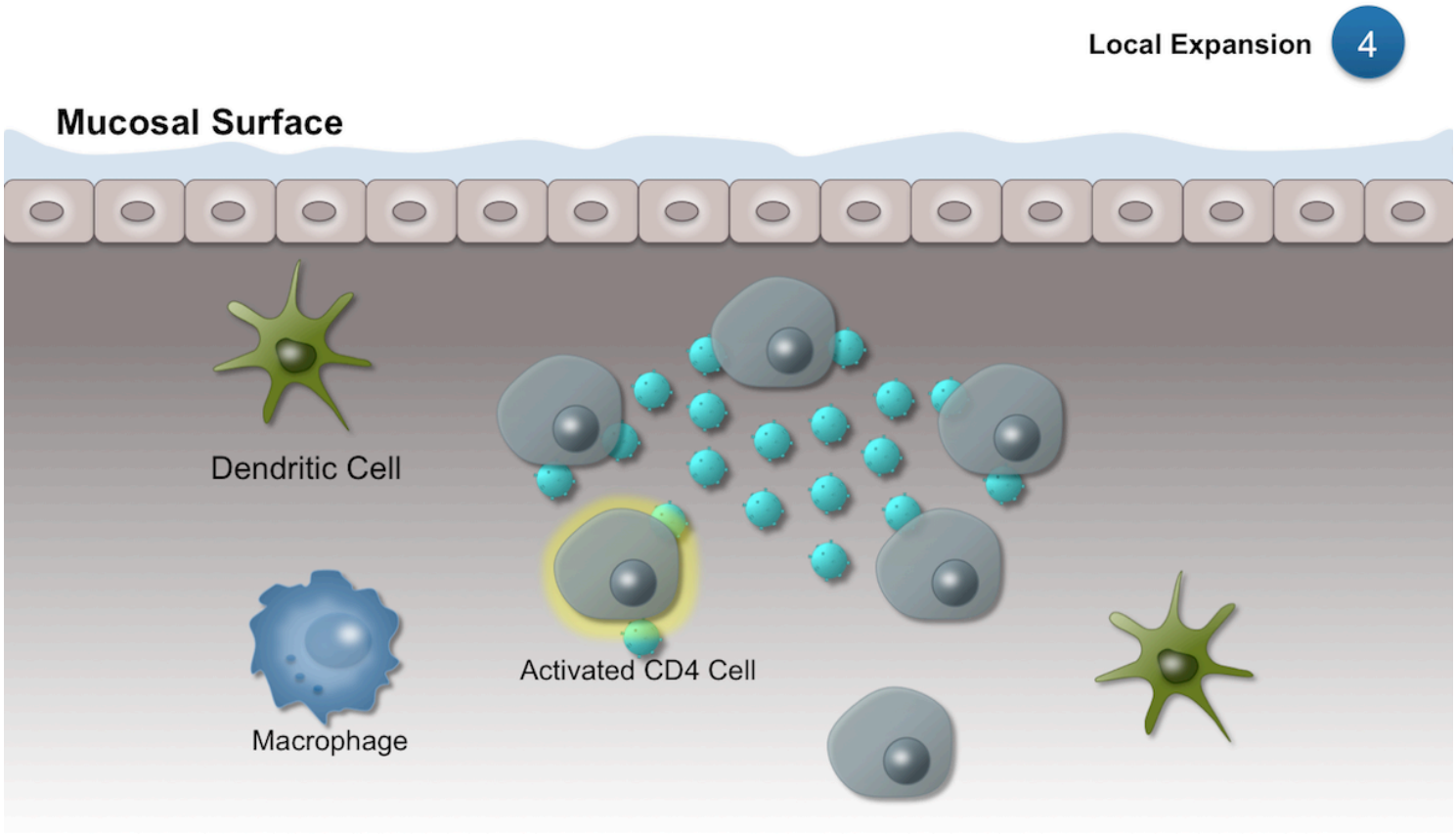

Figure 7 (Image Series) - Model for Sexual Transmission of HIV
Image 7E: Regional Lymphatic Spread

Illustration: David H. Spach, MD

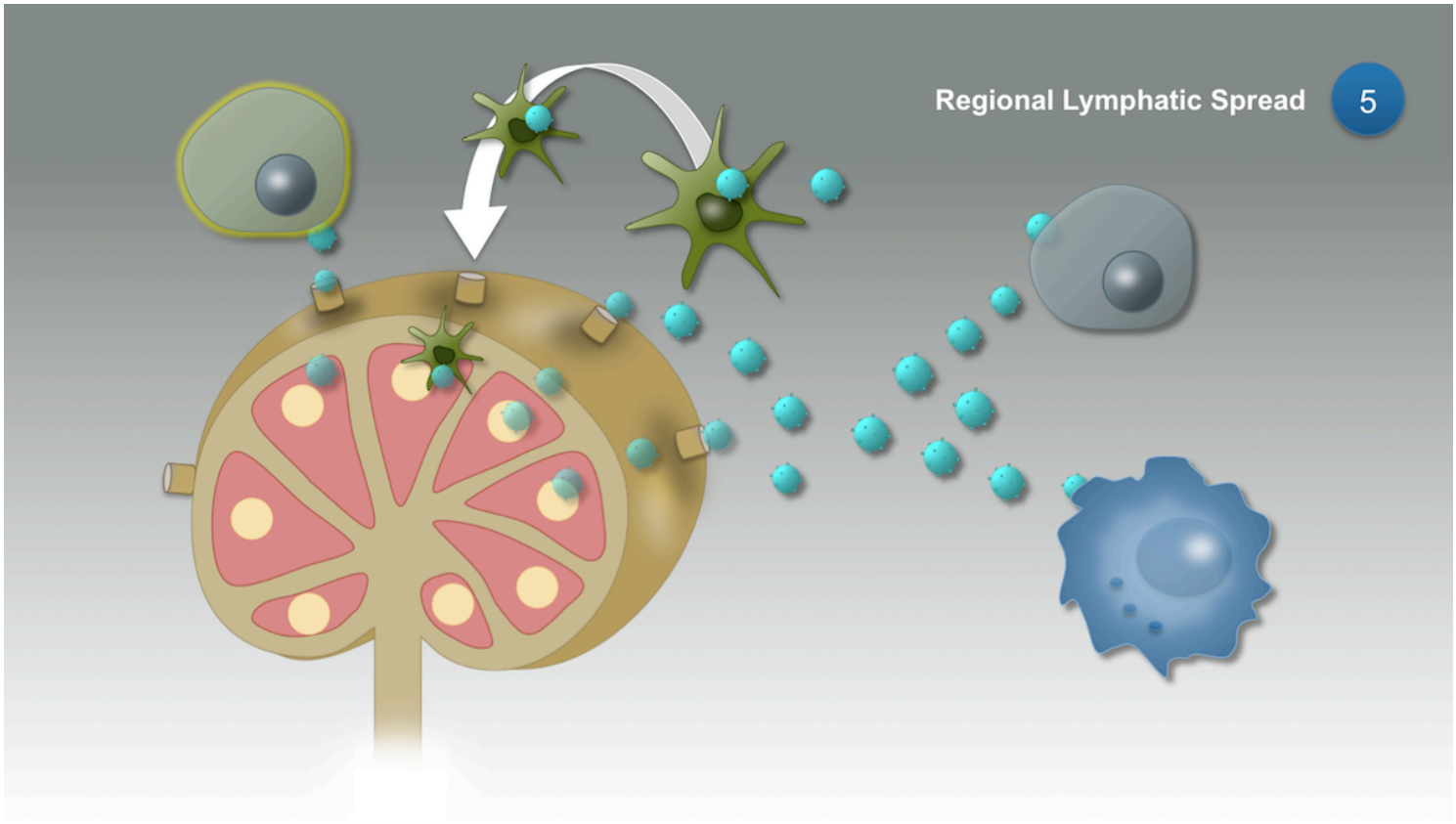

Figure 7 (Image Series) - Model for Sexual Transmission of HIV
Image 7F: Hematogenous Spread

Illustration: David H. Spach, MD

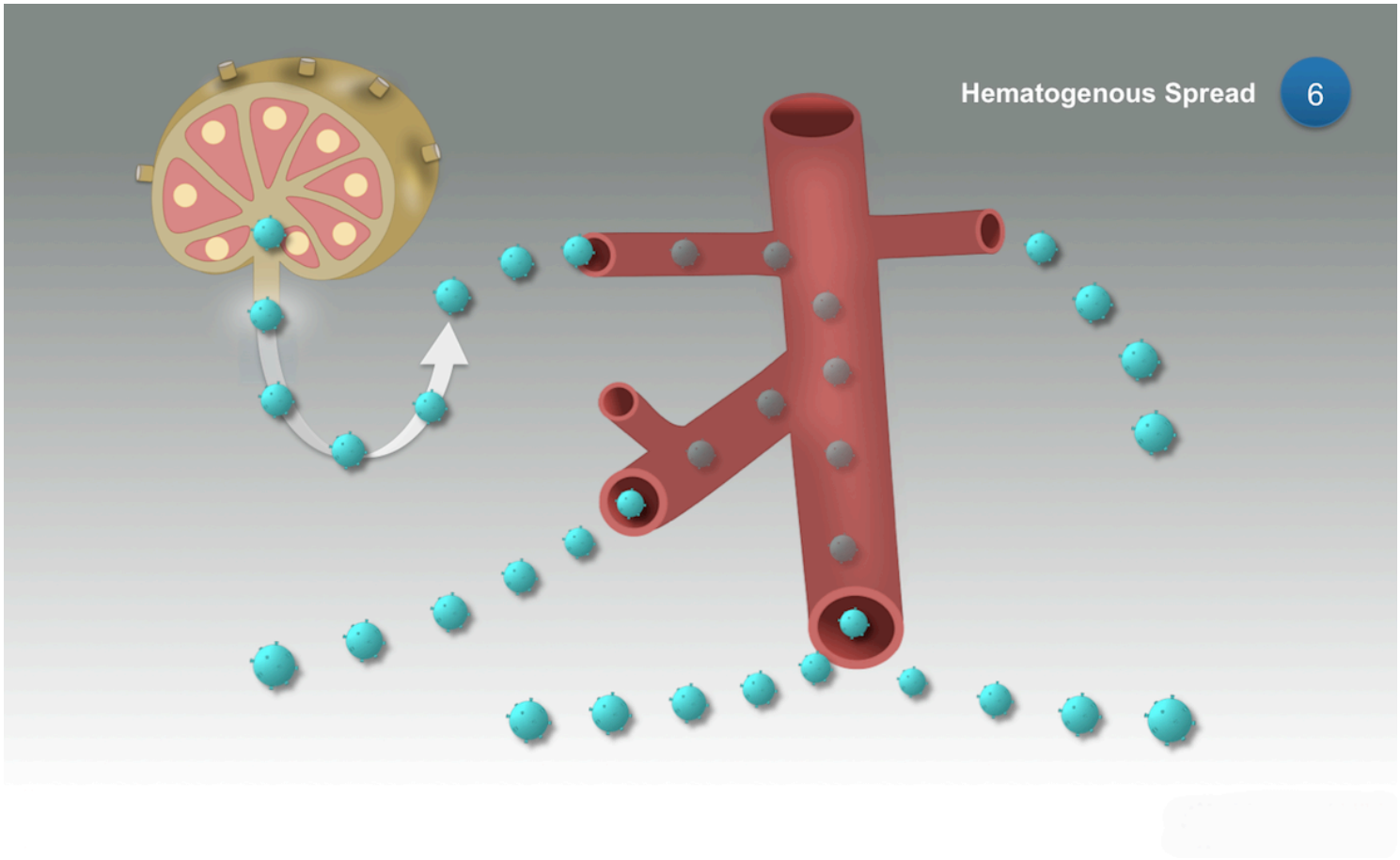

Figure 8 Set Point Following Acquisition of HIV

Illustration: David H. Spach, MD

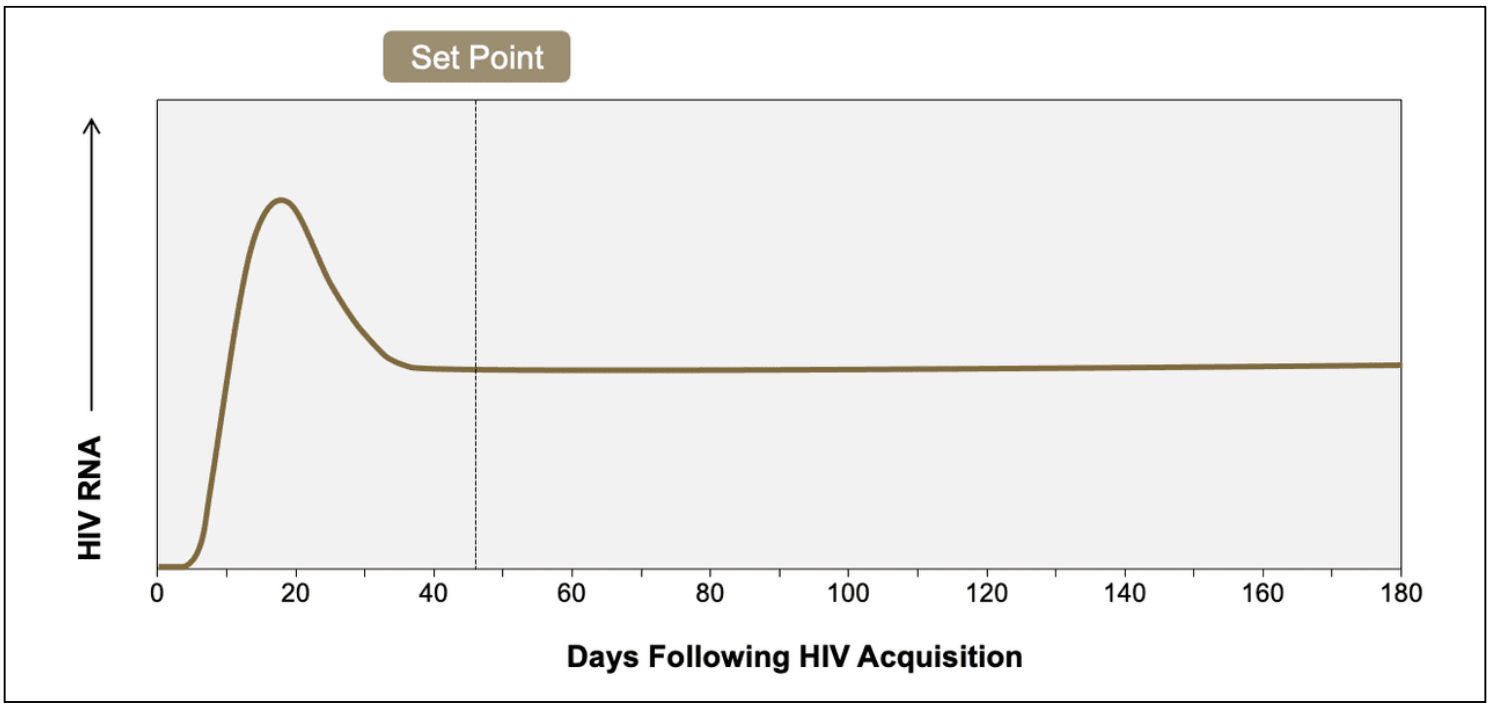

Figure 9 Cytotoxic T-Lymphocyte Response Following Acute HIV Infection

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

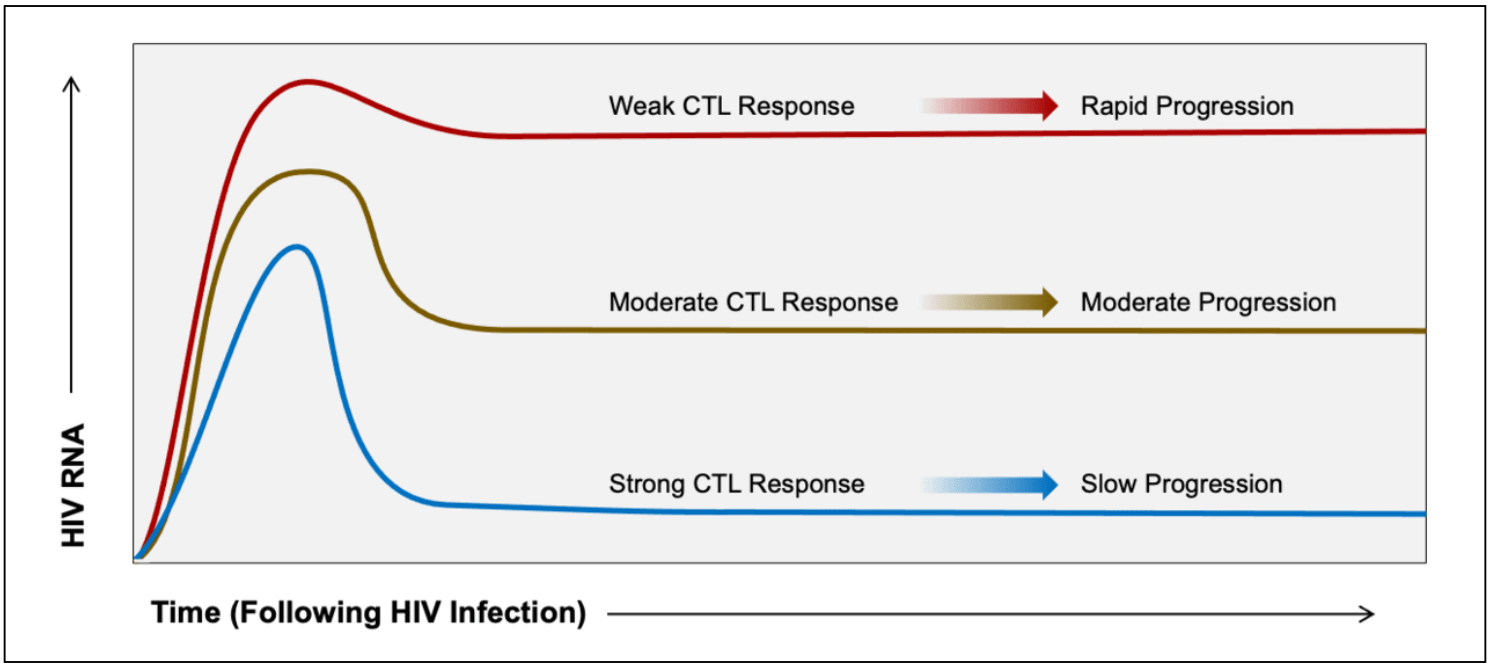

Figure 10 Acute HIV: Skin Rash

Source: photograph by David H. Spach, MD

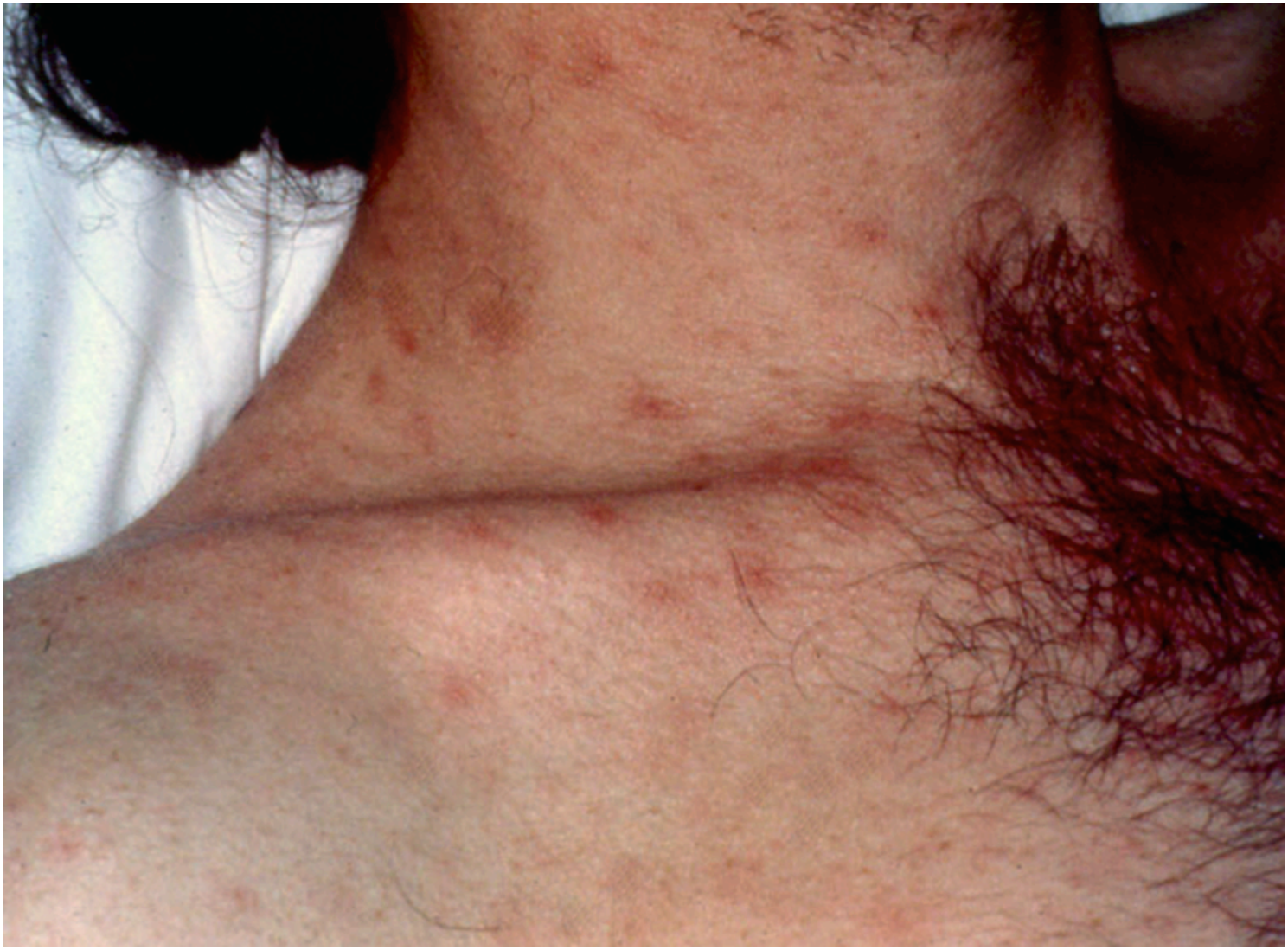

Figure 11 Fiebig Laboratory Staging of Early HIV Infection

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.

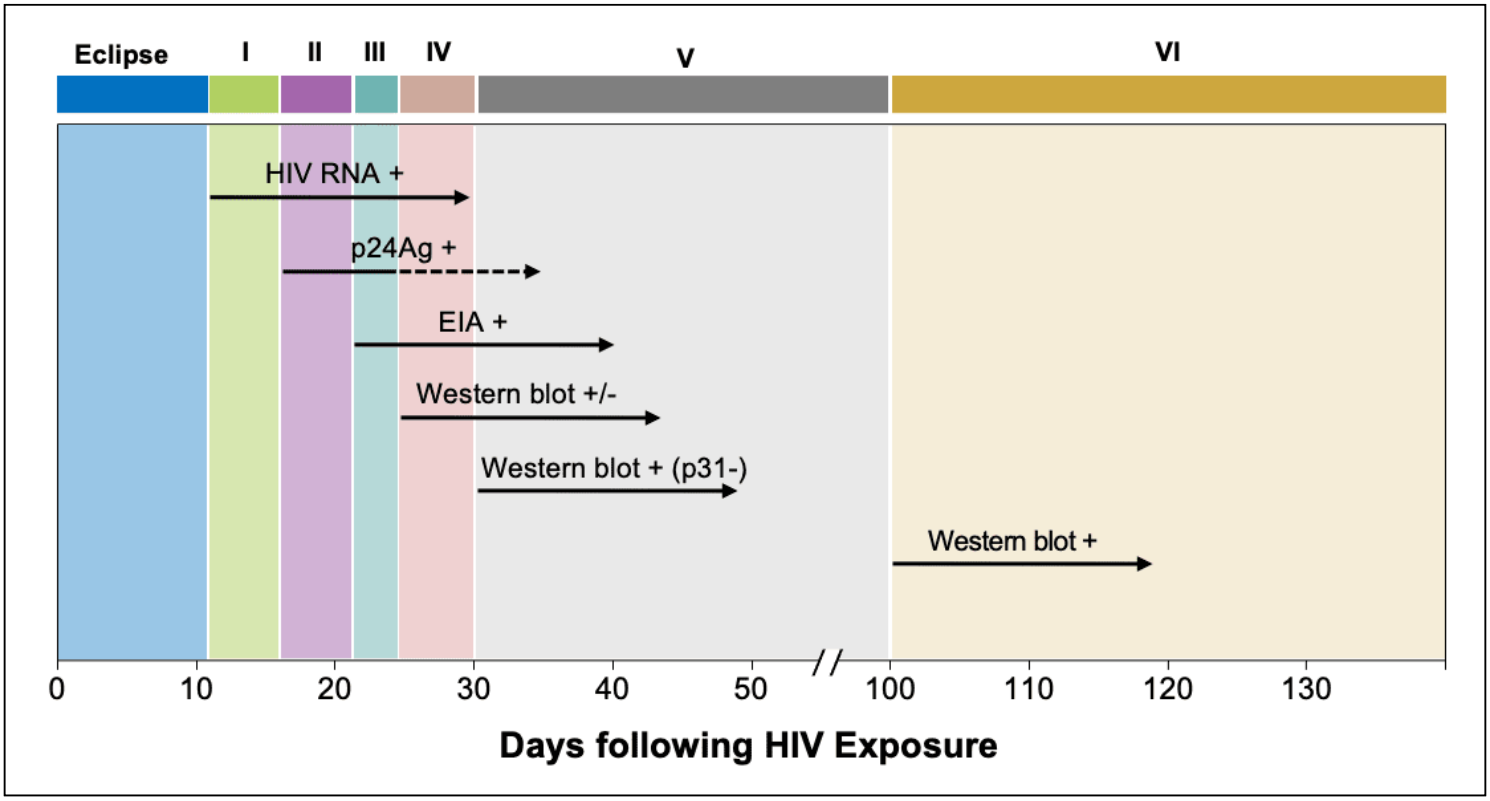

Figure 12 Timing of Positivity for HIV Diagnostic Tests Following Initial HIV Infection

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.

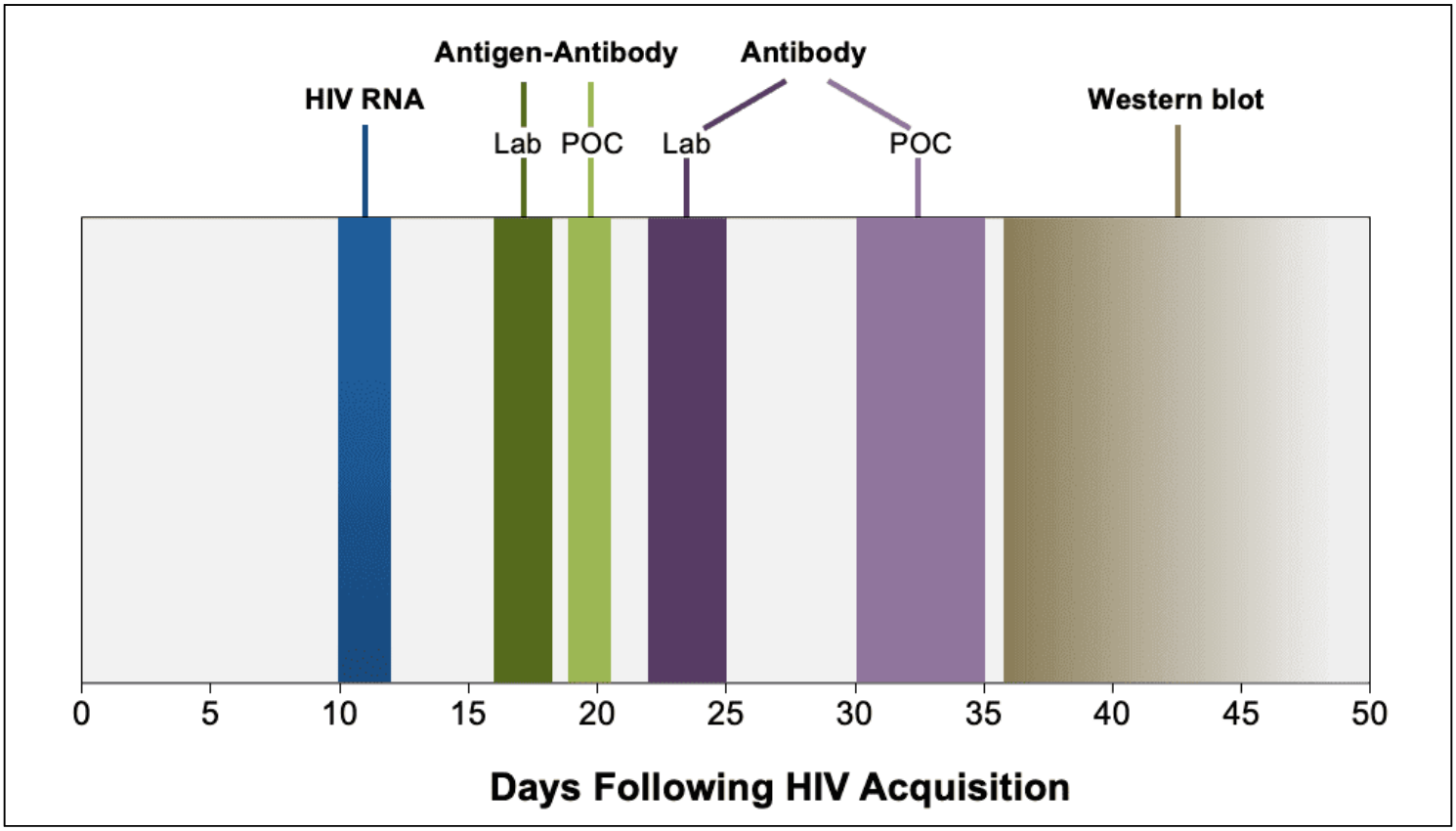

Figure 13 HIV Laboratory Testing Algorithm As Recommended by the CDC and APHL

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.

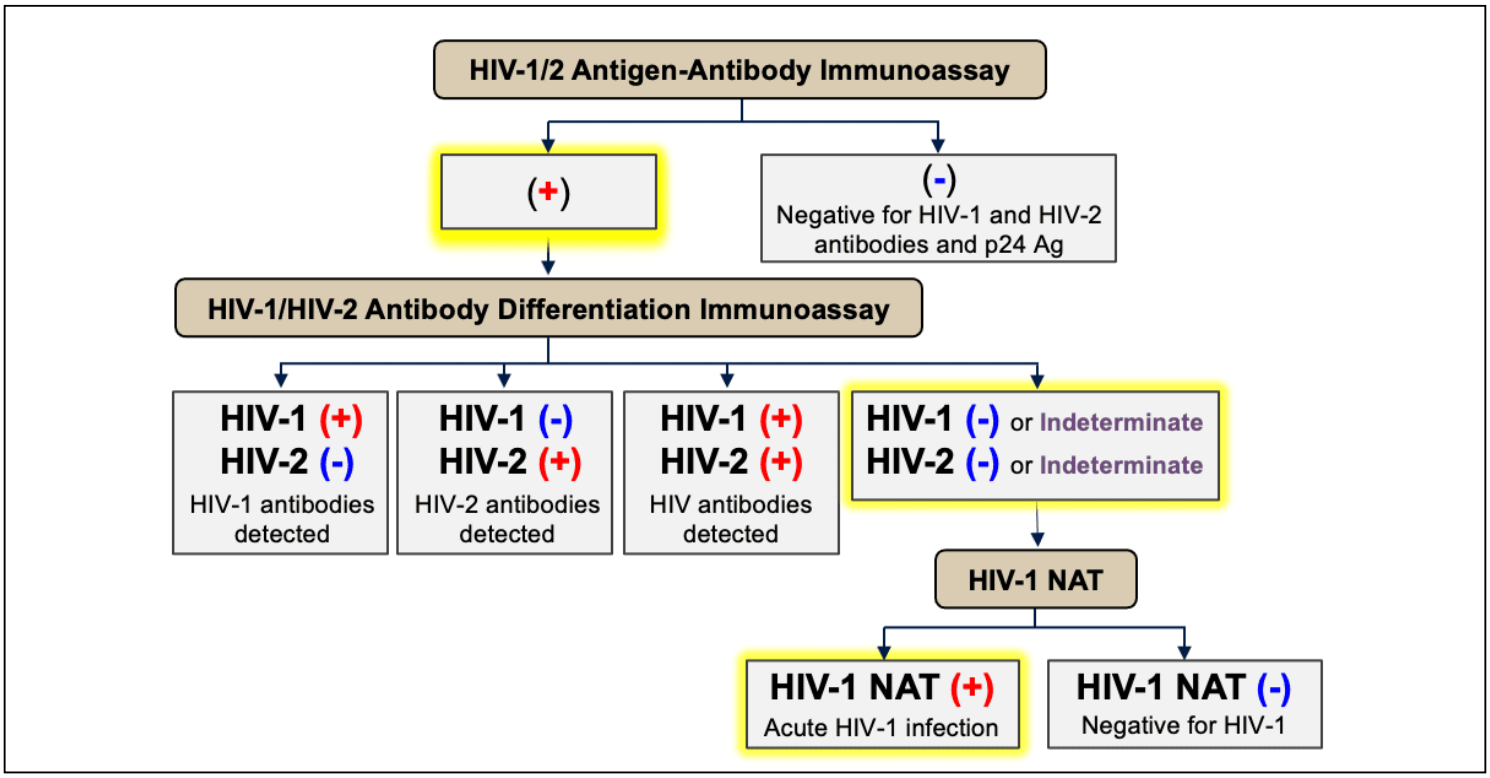

Figure 14 Risk of Sexual Transmission of HIV During Early Infection

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.

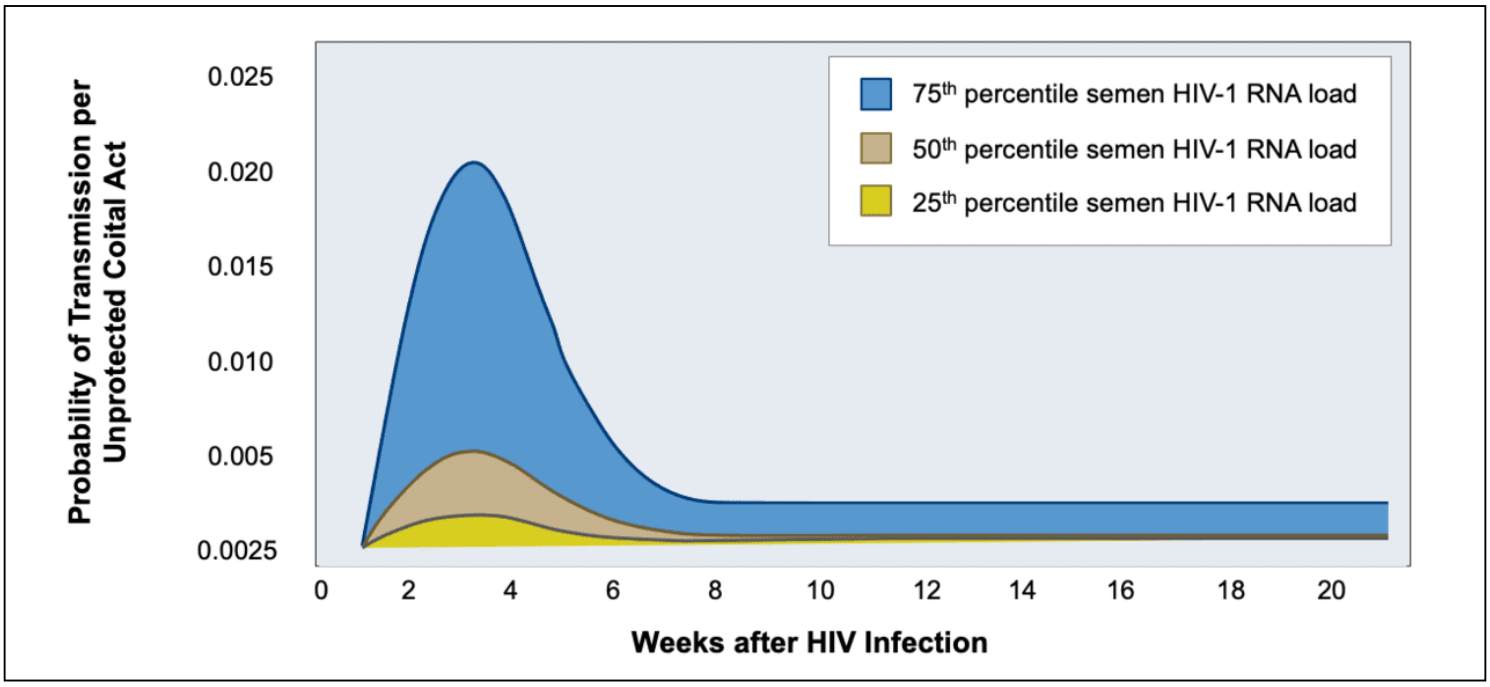

Table 1. Clinical Signs and Symptoms of Acute HIV Infection

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

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Antiretroviral Therapy for Early[a] (Acute and Recent) HIV Infection

- Antiretroviral therapy is recommended for all people with HIV, including those with early[a] HIV infection (AI)**.** Antiretroviral therapy should be initiated as soon as possible after HIV diagnosis (AII).
- 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).
- A blood sample for genotypic resistance testing should be sent to the laboratory before initiating ART (AIII).
    - Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes (AIII) for all people with early HIV.
    - 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 stand transfer inhibitor (INSTI) resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for HIV post-exposure prophylaxis (PEP) (AIII).
- Antiretroviral therapy can be initiated before drug-resistance testing results are available.
- For those without a history of using long-acting injectable cabotegravir as HIV PrEP, one of the following antiretroviral regimens is recommended[b] (AIII):
    - Bictegravir-tenofovir alafenamide-emtricitabine
    - Dolutegravir with (tenofovir alafenamide or tenofovir DF)[c] plus (emtricitabine or lamivudine)
- 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:
    - A regimen of cobicistat[d] or ritonavir boosted darunavir with (tenofovir alafenamide or tenofovir DF)[c] plus (emtricitabine or lamivudine) is recommended while awaiting the results of the genotype testing (AIII).
    - 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 and possibly after the use of CAB-LA as HIV PrEP.
- In people with HIV RNA levels ≥200 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).
- Pregnancy testing should be performed in women of childbearing potential before initiation of antiretroviral therapy (AIII).
- When the results of drug-resistance tests are available, the treatment regimen can be modified if needed (AII).
- Providers should inform individuals starting antiretroviral therapy of the importance of adherence to achieve and maintain viral suppression (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: 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

Abbreviations: PrEP = preexposure prophylaxis
[a]Early infection represents either acute or recent infection (≤6 months) infection
[b]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

regimen can be started while awaiting the results of the INSTI genotype.
[c]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.
[d]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]