Acute and Recent HIV Infection

This is a PDF version of the following document:
Section 1: Screening and Diagnosis
Topic 4: Acute and Recent HIV Infection

You can always find the most up to date version of this document at https://www.hiv.uw.edu/go/screening-diagnosis/acute-recent-early-hiv/core-concept/all.

Background and Definitions

Background

Following acquisition of HIV, more than 50% of individuals will develop a transient, symptomatic illness, with nonspecific features, that often goes undiagnosed.[1,2,3] This illness, also known as acute retroviral syndrome, is frequently mistaken for an alternate viral infection, such as mononucleosis or influenza. Early antiretroviral therapy arrests the explosive burst of viremia associated with acute infection and thus may improve long-term health outcomes for acutely infected individuals and decrease the likelihood of viral transmission.[2] Most individuals in the acute phase of HIV infection are highly infectious to others, primarily because of high HIV RNA levels, and often lack of awareness of their HIV status.[4,5,6]. Thus, accurate and timely detection of primary HIV infection is critical to both the future health of the infected individual and for preventing forward transmission of HIV. The following will review the manifestations and diagnosis of acute retroviral syndrome, as well as explore considerations for treatment in such instances.

Definitions

• Acute HIV: Defined as the phase of HIV disease that occurs immediately after HIV acquisition and is characterized by detectable HIV RNA or HIV p24 antigen in the absence of anti-HIV antibodies (Figure 1).[2] The term acute HIV was previously used interchangeably with the term primary HIV, but acute HIV is now the preferred term.
• Acute Retroviral Syndrome: An acute symptomatic illness that develops in many individuals during the acute HIV infection phase.[7,8]
• Early HIV Infection: Refers to the initial 6-month time period following HIV acquisition; this term encompasses three time periods—the time from infection until acute HIV, acute HIV infection, and recent recent HIV infection (Figure 2).[9]
• Eclipse Phase: The short interval, typically 10-12 days in duration, following HIV acquisition in which a person is infected with HIV, but HIV RNA has not reached detectable levels (Figure 3).[10] The eclipse phase is often also defined as the initial interval after HIV infection when no laboratory markers are consistently detectable.[11]
• Fiebig Stages of Early HIV Infection: The classification system used to describe various stages of early HIV infection and based on the timing and results of diagnostic tests (Figure 4).[10]
• Founder Virus: The initial virus (or small cluster of viruses) that succeeds in catalyzing HIV mucosal infection (Figure 5).[12]
• Seroconversion Window Period: The 3- to 4-week period after HIV acquisition before anti-HIV antibodies are detected; the time period between initial infection and presence of anti-HIV antibodies is referred to as the serologic window period (Figure 6).[11] During the latter part of the serologic window period, direct viral tests, such as HIV p24 antigen or HIV RNA or HIV p24 antigen assays can detect HIV. The duration of the window period depends on the
sensitivity of the antibody assay used.

- **Set point**: The relatively stable HIV RNA level reached about 1-2 months after the peak HIV RNA levels associated with acute HIV infection. Without antiretroviral therapy, the HIV RNA levels tend to chronically remain near the set point established early in HIV infection (Figure 7).[13,14]
Immunopathogenesis

Initial Infection

The immunopathogenesis of acute HIV infection is best understood with regard to transmission via the genital mucosa.[1, 15] 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 (Figure 8).[1, 2, 15, 16] In the proposed model, HIV first infects Langerhans cells (tissue dendritic cells located just below the mucosa).[17] On the surface of the Langerhans cell, HIV initially binds to the CD4 molecule, followed by binding to the CCR5 cellular coreceptor; the Langerhans cells express CCR5 coreceptors, but usually not CXCR4 coreceptors. Most often, the transmitted HIV is macrophage-tropic HIV (also known as R5 HIV), which preferentially binds to the CCR5 coreceptor. The infected dendritic cells can migrate to lymph nodes, where they interact with and potentially fuse with CD4 cells, causing spread of HIV to deeper tissues.[16] 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, 18, 19] Although HIV generally exists as a quasispecies or a mixture of mutant strains, usually only one strain (or a small number of strains) successfully establishes initial infection; the infecting strain is known as the founder virus.[12, 20] Data indicate that selection bias leads to transmission of virus species with greater relative fitness.[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 greater than 100,000 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, or so called "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.[25, 26, 27] In addition, higher set points are usually associated with more rapid progression of HIV disease, if untreated.

Early Immune Response as Predictor of Disease Progression

Investigators have shown that individuals have qualitatively different 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).[14, 28, 29] More recently, the importance of the epitope-specific type of CD8 T cell response in controlling HIV has been elucidated.[30] In most persons newly infected with HIV, higher initial HIV RNA levels predict an accelerated course of HIV disease progression.[31] but this correlation is not universal.[28, 32] Similarly, several reports have suggested that development of clinically apparent acute retroviral syndrome portends a faster progression to AIDS.[33] One study found that among 218 African women with HIV-1 infection, a greater set point viral load or greater severity of acute HIV illness predicted faster progression to death (with each additional symptom of acute HIV contributing to a higher mortality).[34]
Clinical Manifestations

Acute Retroviral Syndrome

The transient surge of viremia and associated drop in CD4 cell count that accompanies primary HIV infection cause most of the manifestations of acute disease. Acute retroviral syndrome ranges from an asymptomatic infection, to a mild nonspecific viral illness resembling mononucleosis, to a severe illness that requires hospitalization.[7, 8] The signs and symptoms are nonspecific, protean, and self-limited. Therefore, a high index of suspicion and inquiry of risk factors are generally necessary to identify primary infection.[35] Symptoms of primary HIV typically begin within 28 days of infection, with the most common manifestations consisting of fever, fatigue, myalgia, skin rash, headache, pharyngitis, and cervical adenopathy (Table 1).[1, 7, 36, 37, 38] The skin rash is typically morbilliform or maculopapular and most often involves the trunk (Figure 10). Less commonly, neurological complications may occur, such as aseptic meningitis, facial palsy, or Guillain-Barré syndrome.[39] Rarely, acute infection causes such a substantial drop in CD4 T-cell count that patients may initially present with oral candidiasis or even major AIDS-defining opportunistic infections.

Duration of Symptoms

In a study of 46 individuals with primary infection in which 89% developed a symptomatic illness, the median duration of symptoms was 14 days.[8] The duration of symptoms can range from days to weeks and the severity and duration of symptoms may correlate with disease progression.[1, 36]

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 (EBV) infection (mononucleosis), secondary syphilis, acute cytomegalovirus (CMV), acute toxoplasmosis, acute hepatitis B, streptococcal pharyngitis, influenza, and enterovirus infection 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

Patients who present with symptoms of acute HIV infection typically have a very high HIV RNA level and a negative HIV antibody test.[3] In addition, most patients diagnosed with acute HIV infection will also have a positive p24 antigen test. Accordingly, the laboratory diagnosis of acute HIV requires a negative (or indeterminate) HIV antibody assay in conjunction with either a high HIV RNA level or a positive p24 antigen test.[9]

HIV RNA Tests

Approximately 10 days after initial HIV acquisition, plasma HIV RNA levels become detectable.[10] The HIV RNA levels rapidly ramp up to very high levels, typically peaking above 200,000 copies/mL.[10] Currently, only the Aptima HIV-1 qualitative assay, a nucleic acid amplification test, is FDA-approved for the diagnosis of HIV-1 (including acute HIV); this test provides a qualitative detection of HIV RNA, not a quantitative measurement. This assay has a reported lower limit of detection of 33 copies/mL. Some clinicians have used a quantitative HIV RNA assay (those typically used for monitoring response to treatment with chronic HIV) for making a diagnosis of acute HIV, since the quantitative can provide an actual HIV RNA level. Since quantitative HIV RNA assays are not FDA-approved for the diagnosis of HIV, laboratories cannot reflex to perform this test on persons with a positive screening fourth-generation antigen-antibody combination test. If a quantitative HIV RNA assay is used to diagnose acute HIV, most true positive HIV RNA results are greater than 100,000 copies/mL.[40,41] The use of HIV RNA testing as a routine screening test for HIV has not been utilized due to cost and the failure to detect HIV in some persons with chronic HIV who have inherently undetectable HIV RNA levels. The use of HIV RNA testing on pooled samples, in conjunction with antibody testing, has been utilized as a more cost-effective approach to screening for both chronic and acute HIV.[42]

Fourth-Generation p24 Antigen-HIV Antibody Tests

Since HIV p24 antigen is detected approximately 1 week prior to HIV antibody, the fourth-generation HIV antigen-antibody tests have become an attractive initial screening test that has improved diagnosis of persons with acute HIV infection.[11] The United States FDA has approved four laboratory based fourth-generation antigen-antibody tests: (1) Abbott Architect HIV Ag/Ab Combo Assay, (2) Bio-Rad GS HIV Combo Ag/Ab EIA, (3) Bio-Rad 2200 HIV Ag-Ab, and (4) Advia Centaur HIV Ag/Ab Combo Assay; these assays detect HIV approximately one week after HIV RNA can be detected and at least 1 week prior to third-generation antibody tests (Figure 11).[43,44,45] Although the rapid fourth-generation test, Alere Determine HIV-1/2 Ag/Ab Combo test is more sensitive for detecting early HIV infection than all other rapid HIV antibody tests, it is not as sensitive as the laboratory-based fourth-generation assay (detects p24 antigen about 5 days after laboratory tests).[46,47,48] Among the fourth-generation antigen-antibody assays, only the Bio-Rad 2200 HIV Ag-Ab and the Alere Determine differentiate the p24 antigen from the HIV antibody results.

Serologic Tests

Serologic tests first turn positive at approximately 3 to 6 weeks after acquisition of HIV, with third-generation enzyme immunoassays (EIAs) typically turning positive at about 3 to 4 weeks. Most patients have a window period (positive HIV RNA and negative HIV antibody) of approximately 3 to 4 weeks.[10] Western blot testing initially shows an indeterminate pattern (presence of HIV specific bands that fail to meet criteria established by US FDA for positive HIV as reactivity to two of the following three bands: p24, gp41, and gp120/160). In addition, the presence of a positive Western blot without reactivity to p31 (pol) suggests antibody seroconversion within the preceding 2 to 3 months.[10] The characteristic formation of antibodies may be altered in patients with acute HIV infection who receive antiretroviral therapy (and have durable virologic suppression); in this scenario, patients may have incomplete evolution of antibody responses and rarely will show a
complete or partial seroreversion. A modified, less sensitive HIV EIA 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; this test can help to identify those with recent HIV infection who have already passed through the window period.

**Recommended Diagnostic Testing**

**Detection of Acute HIV with Routine Screening for HIV**

From a practical standpoint, routine screening for HIV infection using a conventional HIV antibody test and a confirmatory Western blot will fail to detect most individuals with acute HIV infection. Adding HIV RNA testing to routine screening for all patients is not practical due to cost consideration. In contrast, the 2014 CDC recommended HIV testing algorithm, which utilizes a fourth-generation p24 antigen-antibody combination assay as the initial screening test, detects approximately 85% of those with acute HIV infection. With this algorithm, persons with acute HIV would typically have a positive initial screening test with the fourth-generation p24 antigen-antibody combination assay, followed by a negative HIV-1/HIV-2 differentiation immunoassay, and then a positive HIV RNA ([Figure 12]). 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.

**Testing for Suspected Acute HIV Infection**

For patients in whom there is a strong clinical suspicion of acute HIV infection, we recommend testing with a quantitative HIV RNA and HIV antibody. Persons are presumptively diagnosed with acute HIV infection if they have a positive HIV RNA (especially at a high level and negative or indeterminate HIV antibody assay; in this scenario, they should have follow-up antibody testing in 3 to 6 months to document seroconversion.[9]

**Testing for Recent HIV Infection**

In patients with a positive HIV antibody test and suspected recent infection, it is important to try and determine the last negative HIV antibody test. In this setting, a negative antibody test in the prior 6 months would support a diagnosis of recent HIV infection. From a research standpoint, the detuned HIV antibody assay could confirm recent infection, but this test is not widely available in clinical settings.
Treatment Considerations

Rationale for Treatment of Acute and Recent (Early) HIV Infection

The potential benefits of initiating antiretroviral therapy for patients with acute and recent (early) HIV infection include the following: (1) lessening of symptoms of acute retroviral syndrome, (2) minimizing immunologic damage, (3) diminished size of the latent HIV reservoir, and (4) prevention of HIV transmission to others.[55, 56]

Preservation of Immune Function and Delayed Disease Progression

Early antiretroviral therapy can help preserve immune function and slow HIV disease progression by slowing CD4 decline and reducing HIV RNA levels.[55, 56, 57, 58] 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.[59] 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.[59] Multiple studies, including the Setpoint Study (ACTG A5217),[13] Primo SHM,[60], and SPARTAC,[61] have demonstrated a reduction in viral set point and slower disease progression after initiation of antiretroviral therapy during early HIV infection.

Impact on Latent Reservoir

One report documented 14 individuals who initiated antiretroviral therapy during primary infection (with continuation of therapy for a mean 36.5 months) and were able to control viremia on their own following cessation of therapy (so-called “post-treatment controllers”); the investigators reported a likelihood of spontaneous control of viremia after treatment interruption among 15% in the group who were treated during acute infection, as opposed to less than 1% of those not treated.[62] These data suggest that treatment during acute infection can significantly reduce latent HIV reservoirs and may aid in future efforts to achieve 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.[63]

Reduced Risk for HIV Transmission

In the acute phase, newly infected persons have a significant increase in risk of transmitting HIV to others due to several factors: (1) they have initial uncontrolled viremia with associated high levels of HIV 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.[1, 2] As might be expected, individuals with primary infection contribute disproportionately to the number of new HIV transmissions. The Duke-UNC-Emory Acute HIV Consortium examined viral dynamics at different phases of HIV disease and found markedly higher semen and blood HIV RNA levels in men during acute HIV infection than with chronic HIV, thus providing a biologic basis for the reported increases in HIV transmission during early HIV infection.[5] This same group also generated models for calculating probabilities of male-to-female HIV transmission per coital act that projected a markedly higher risk of HIV transmission during acute HIV infection than in the subsequent months after acute infection (Figure 13).[6] In addition, other groups of 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 play a key in preventing HIV transmission.[2, 64] Accordingly, large-scale efforts to identify persons with acute or early HIV infection and promptly initiate antiretroviral therapy could play an important role in overall HIV prevention efforts.[2, 55, 65]
**Recommended Treatment of Acute or Early HIV**

**Recommendations for Treatment of Acute or Early HIV**

The Adult and Adolescent ARV Guidelines specific recommendations for persons diagnosed with acute or early HIV infection [Table] Panel's Recommendations for Acute and Recent (Early) HIV Infection.[9]

**Duration of Therapy**

Several studies have examined the strategy of starting antiretroviral therapy for acute HIV infection and then discontinuing therapy after approximately 6 months.[13, 60, 61, 66] Although this strategy has shown beneficial impact on immune status when compared with no treatment during acute HIV, other studies have shown that treatment interruption in patients with chronic HIV infection results in increased in laboratory markers of inflammation, immune activation, and coagulation, as well as an increase in risk of clinical AIDS and non-AIDS-related events.[67, 68] In addition, persons with HIV infection at any stage of disease will reduce their risk of transmitting HIV to others if they are consistently taking recommended antiretroviral therapy. For these reasons, experts recommend continuing antiretroviral therapy indefinitely if started in the acute or early phase.

**Treating Acute or Early HIV in Persons who Acquired HIV while Taking Preexposure Prophylaxis**

With increasing use of tenofovir DF-emtricitabine for preexposure prophylaxis, some individuals will have a diagnosis of acute or early HIV infection in the setting of taking preexposure prophylaxis. In this situation, the individual with new HIV infection may acquire emtricitabine-resistant HIV (and possibly tenofovir-resistant HIV) and thus resistance testing should be promptly obtained. While awaiting resistance testing results, most experts would recommend treatment with a regimen that includes an anchor drug with a high genetic barrier to resistance, preferably darunavir boosted with ritonavir or dolutegravir; in this situation the anchor drug should be given with dual nucleoside reverse transcriptase inhibitors.[9]
Summary Points

- Symptoms of acute HIV are nonspecific and mimic many other viral or bacterial infections. Thus, the diagnosis of acute HIV infection requires a high index of suspicion and careful history taking to identify recent (within 2 to 6 weeks) high-risk exposure to HIV.
- Acute HIV infection is defined as detectable HIV RNA or HIV p24 antigen combined with either a negative HIV antibody test or an indeterminate Western blot assay.
- The diagnosis of acute HIV is confirmed by negative or indeterminate antibody results with a positive p24 antigen or HIV RNA. Acute HIV is generally associated with high HIV RNA levels. Using the current CDC recommended HIV testing algorithm, which includes p24 testing in the initial test, will detect most, but not all persons with acute HIV.
- The detection of acute HIV is critical for timely initiation of antiretroviral therapy.
- The Adult and Adolescent ARV Guidelines recommend initiating antiretroviral treatment in all person with early HIV infection. The rationale for initiating antiretroviral therapy during acute infection is to reduce the level of the set point, slow progression of disease, reduce the viral reservoir, alleviate symptoms, and prevent transmission of HIV to other.
- In most situations, since therapy of acute HIV is initiated prior to results of the HIV drug resistant genotype becoming available, the antiretroviral regimen should include an anchor drug that has a strong genetic barrier to resistance. Specific recommended regimens for early HIV infection in the setting of pending drug-resistance testing data are (1) boosted darunavir plus either tenofovir DF-emtricitabine or tenofovir alafenamide or (2) dolutegravir plus either tenofovir DF-emtricitabine or tenofovir alafenamide.
Citations


49. Hare CB, Pappalardo BL, Busch MP, et al. Seroreversion in subjects receiving antiretroviral
[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

60. 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
[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

References

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]


Figures

Figure 1 Acute HIV Infection

Acute HIV infection is defined as the phase of HIV disease that occurs immediately after HIV acquisition and is characterized by detectable HIV RNA or HIV p24 antigen in the absence of detectable anti-HIV antibodies.
Figure 2 Early HIV Infection

Early HIV infection is the 6-month time period following initial HIV infection.

**Figure 3 HIV Eclipse Phase**

The HIV eclipse phase is defined as the time from acquisition to the time HIV RNA is detectable in plasma. The eclipse phase is typically about 10 days.

Figure 4 Fiebig Laboratory Staging of Early HIV Infection

Figure 5 Founder Virus

Despite presence of a diverse quasispecies of HIV present in semen, cervicovaginal secretions, or blood, a single virion (or a few virions) is usually responsible for catalyzing the initial HIV infection that results in a productive infection.

Figure 6 HIV Seroconversion Window Period

The HIV seroconversion window is the time from acquisition of HIV to time anti-HIV antibodies are detectable.

Figure 7 Set Point Following HIV Infection

Set Point
Figure 8 (Image Series) - Model for Sexual Transmission of HIV (Image Series) - Figure 8 (Image Series) - Model for Sexual Transmission of HIV
Image 8A: Exposure Event

HIV

Exposure Event

Mucosal Surface

Dendritic Cell

CD4 Cell

Macrophage

CCR5
Figure 8 (Image Series) - Model for Sexual Transmission of HIV
Image 8B: Prime Infection with Founder Virus
Figure 8 (Image Series) - Model for Sexual Transmission of HIV
Image 8C: Initial Propagation with Small HIV Founder Population

Mucosal Surface

- Dendritic Cell
- CD4 Cell
- Small Infected Founder Population
- Macrophage

Initial Propagation 3
Figure 8 (Image Series) - Model for Sexual Transmission of HIV
Image 8D: Local Expansion

Mucosal Surface

Dendritic Cell

Macrophage

Activated CD4 Cell
Figure 8 (Image Series) - Model for Sexual Transmission of HIV
Image 8E: Regional Lymphatic Spread
Figure 8 (Image Series) - Model for Sexual Transmission of HIV
Image 8F: Hematogenous Spread
Figure 9 Cytotoxic T-Lymphocyte Response Following Acute HIV Infection

Figure 10 Acute HIV: Skin Rash

Source: photograph by David H. Spach, MD
Figure 11 Timing of Positivity for HIV Diagnostic Tests Following Initial HIV Infection

Abbreviation: POC = point of care

**Figure 12 2014 CDC AHPL Recommended Laboratory Testing for the Diagnosis of HIV Infection**

This graphic shows the HIV testing algorithm as recommended in 2014 by the Centers for Disease Control and Prevention and Association of Public Health Laboratories. The rectangles highlighted with yellow border indicate the expected positive tests in a person with acute HIV infection.

Figure 13 Risk of Sexual Transmission of HIV During Early Infection

Table 1.

**Clinical Signs and Symptoms of Acute (Primary) HIV Infection**

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

IDU = Injection drug use

Source:

Panel's Recommendations for Acute and Recent (Early*) HIV Infection

- Antiretroviral therapy is recommended for all individuals with HIV-1 infection (AI) including those with early* HIV-1 infection.

- Once initiated, the goal of antiretroviral therapy is to suppress plasma HIV-1 RNA to undetectable levels (AIII). Testing for plasma HIV-1 RNA levels, CD4 T lymphocyte counts, and toxicity monitoring should be performed as recommended for patients with chronic HIV-1 infection (AII).

- Genotypic drug resistance testing should be performed before initiation of antiretroviral therapy to guide the selection of the regimen (AII).

- Antiretroviral therapy can be initiated before drug resistance test results are available. Either boosted darunavir or dolutegravir with emtricitabine plus either tenofovir DF or tenofovir alafenamide are recommended regimens in this setting (AIII). The rationales and precautions for these regimens are discussed below.

- A darunavir-based regimen is a good option for people with early HIV-1 infection, because resistance to pharmacokinetically enhanced protease inhibitors emerges slowly and clinically significant transmitted resistance to protease inhibitors is uncommon.

- A dolutegravir-based regimen is also a reasonable option; however, data regarding transmission of integrase strand transfer inhibitor-resistant HIV and the efficacy of dolutegravir regimens in early HIV infection are more limited (AIII).

- Preliminary data from Botswana suggested that infants born to women who were receiving dolutegravir at the time of conception have an increased risk of neural tube defects. Until more information are available, dolutegravir should not be prescribed for individuals:
  - Who are pregnant and within 12 weeks post-conception;
  - Who are of childbearing potential, who are sexually active, and who are not using effective contraception; or
  - Who are contemplating pregnancy.

- When results of drug resistance testing are available, the treatment regimen can be modified if warranted (AII). In patients without transmitted drug-resistant virus, therapy should be initiated with one of the combination regimens that is recommended for patients with chronic HIV-1 infection (AIII).

- Patients starting antiretroviral therapy should be willing and able to commit to treatment and should understand the importance of adherence (AIII). Patients may choose to postpone antiretroviral therapy, and providers, on a case-by-case basis, may recommend that patients defer therapy because of clinical or psychosocial factors.

* Early infection represents either acute or recent infection
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

Source:

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Considerations for antiretroviral use in special patient populations: acute and recent (early) HIV infection. October 28, 2018. [AIDSinfo]