Primary Care Physician’s Guide to HIV

By Julianne Griswold, DO, and Marisa Tungsiripat, MD
Dear Healthcare Provider,

Welcome to Cleveland Clinic’s Primary Care Physician’s Guide to HIV, an information-packed resource brought to you by Cleveland Clinic Disease Management in collaboration with BulletinHealthcare, the leading provider of medical news updates to healthcare professionals like yourself.

This guide covers a comprehensive range of topics from the pathophysiology of HIV to signs and symptoms, diagnosis, treatment, outcomes, and prevention. And it was researched and written by two leading experts in the field — Julianne Griswold, DO, and Marisa Tungsiripat, MD.

We hope you find Cleveland Clinic’s Primary Care Physician’s Guide to HIV and the updates helpful, informative, and of value in your efforts to diagnose, treat, and provide positive patient outcomes. We look forward to hearing your thoughts about this content. Please send me your comments at diseasemanagement@ccf.org.

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Definition and Causes
Human immunodeficiency virus (HIV) is a retrovirus that targets primarily CD4+ T helper cells. Depletion of CD4+ T cells causes progressive immunologic decline and when CD4+ T cell counts fall below 200 cells/mm³ opportunistic infections occur and an infected patient is described as having acquired immunodeficiency syndrome (AIDS).

Epidemiology
At the end of 2011, an estimated 1.2 million people ≥13 years of age in the United States were living with HIV. Of those living with HIV, approximately 14% were undiagnosed and persons aged 13 to 24 years accounted for over half of the undiagnosed cases. The Centers for Disease Control and Prevention (CDC) estimates that from 2007 to 2011 the number of persons infected with HIV increased by 7.2% with the highest prevalence of infection among individuals 45 to 54 years of age (954/100,000 population).¹

Males account for the majority (76.7%) of diagnosed and undiagnosed Americans living with HIV. In males diagnosed with HIV, most (70.3%) acquired infection via male-to-male sexual contact. This differs from males with undiagnosed infection, in whom the highest percentage of infection (19.1%) is attributed to heterosexual contact.¹

The global HIV/AIDS epidemic vastly exceeds what is seen in the US. At the end of 2012, approximately 35.3 million people worldwide were living with HIV. The epidemic continues to disproportionately affect sub-Saharan Africa, which accounted for approximately 70% of all new HIV infections in 2012.²

Pathophysiology and Natural History
Human immunodeficiency virus infection was first described in 1981 when an epidemic of Pneumocystis jiroveci (formerly identified as Pneumocystis carinii) pneumonia was noted in homosexual men.³ In 1984, HIV was identified as the causative agent of AIDS.

The human immunodeficiency viruses belong to the lentivirus subfamily of the RNA retroviruses. Like most retroviruses, the HIV genome consists of three structural genes:

- **gag** codes for viral capsid proteins;
- **env** codes for viral envelope proteins; and
- **pol** codes for proteins responsible for viral replication, including the RNA-dependent DNA polymerase known as reverse transcriptase.

In addition, several other regulatory genes are present, including **nef, rev, and tat**.
Most commonly, transmission of the virus occurs after a breach in the integument or mucous membranes. Human immunodeficiency virus infection occurs when the viral envelope subunit gp120 binds to the human CD4+ T cell receptor found primarily on lymphocytes and monocyte-derived macrophages. In addition, binding also requires the presence on the host cell of the chemokine receptor CCR5 or CXCR4. The viral envelope then fuses with the host cell, allowing release of the viral core into the host cell. Viral DNA is synthesized by reverse transcriptase and incorporated into the host genome by the protein integrase. Once the viral gene products are transcribed and assembled, the HIV protease mediates packaging of new virions for release into serum to propagate the infection.  

Over time, infected persons have a progressive loss of CD4+ lymphocytes. In the early stages of infection, this may not be associated with clinical illness. The rate of CD4+ cell loss is variable and depends on viral and host factors. On average, infected persons lose 40 to 80 CD4+ cells/mm3/year. However, there is a subset of patients who tend to progress rapidly and another subset of patients (approximately 5%) who have little or no progression of clinical disease or decline in CD4+ counts over 10 years even without use of antiretroviral therapy (known as long-term nonprogressors).

**Risk of Transmission**

The risk of HIV transmission depends on the exposure and degree of viremia of the source. Transmission occurs through contact with infected body fluids such as blood, semen, and vaginal fluid. The most common modes of transmission are sexual contact (male-to-male or heterosexual sex), parenteral exposure to blood and blood products, and vertical transmission during pregnancy. Factors that are thought to increase the risk of transmission include high viral load, concomitant sexually transmitted infections (STIs), and acute- and late-stage infection. Factors that decrease the risk of transmission include condom use, antiretroviral treatment, male circumcision, and preexposure prophylaxis.

Risk of HIV transmission is highest from an infected blood transfusion and occurs at a rate of approximately 92.5% although this is now exceedingly rare given advancements in screening technologies and techniques. In terms of other parenteral exposures, needle-sharing during injection drug use confers an approximate 0.63% risk while exposure from a percutaneous (incidental needle stick) carries a 0.23% risk. Risk from receptive anal intercourse carries a 1.38% risk while insertive anal intercourse has a 0.11% risk. In terms of penile-vaginal intercourse, receptive intercourse confers a 0.08% risk and insertive intercourse carries a 0.04% risk. These rates of transmission are influenced by the factors listed previously that are thought to increase and decrease transmission risk. The risk of vertical transmission from mother to fetus without any preventive therapy is approximately 23%.
Acute HIV Infection

In an estimated 40% to 90% of individuals, HIV seroconversion is associated with a clinical syndrome known as acute (or primary) HIV infection or acute retroviral syndrome. Many patients with acute HIV infection are symptomatic and seek medical care but are not diagnosed. In one prospective study, 95% of individuals with symptoms at the time of seroconversion sought medical care, but only one-fourth were diagnosed at the first visit. Despite this, acute HIV infection is rarely diagnosed partly because the signs and symptoms are nonspecific. The onset of illness associated with acute HIV infection occurs after viral transmission and symptoms are believed to correlate with peak viremia, which is often in excess of 1 million viral copies/mL. Common symptoms include fever, rash, lymphadenopathy, nonexudative pharyngitis and myalgias/arthralgias (Table 1).

Table 1: Acute HIV infection: frequency of associated signs and symptoms

<table>
<thead>
<tr>
<th>Sign or Symptom</th>
<th>Frequency, %</th>
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<tbody>
<tr>
<td>Fever</td>
<td>75</td>
</tr>
<tr>
<td>Fatigue</td>
<td>68</td>
</tr>
<tr>
<td>Myalgia</td>
<td>49</td>
</tr>
<tr>
<td>Rash</td>
<td>48</td>
</tr>
<tr>
<td>Headache</td>
<td>45</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>40</td>
</tr>
<tr>
<td>Cervical adenopathy</td>
<td>39</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>30</td>
</tr>
<tr>
<td>Night Sweats</td>
<td>28</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>27</td>
</tr>
</tbody>
</table>

Data from Daar et al.

Exam findings in acute or primary HIV infection are often nonspecific. Most often, the rash is reminiscent of a viral exanthem with erythematous maculopapular lesions on the face and trunk, although many types of lesions have been described. Headache with or without cerebrospinal fluid pleocytosis, myalgia, and gastrointestinal symptoms are also common. Although not present in all patients, oral or genital ulcers can be an important diagnostic clue. Laboratory abnormalities, specifically leukopenia, thrombocytopenia, and elevated transaminase levels, are not uncommon. Opportunistic infections such as mucocutaneous candidiasis and P jiroveci pneumonia may manifest during acute HIV infection as a result of transient but dramatic CD4+ cell count depletion caused by a high viremia level.
The symptoms of acute HIV infection are self-limited and most likely correlate with viremia. After reaching high levels, the viral load declines to a steady state or set point, and the CD4+ count recovers. HIV-1 specific cytotoxic T lymphocytes are present in high titer and appear to play an important role in controlling viral replication. The magnitude of the viral set point and the severity of initial symptoms predict disease progression. Whether early antiretroviral treatment changes an individual’s disease course remains unclear. However, antiretroviral therapy is now recommended in all HIV-infected individuals, including those with early or acute HIV infection. Recognition of this syndrome has implications for HIV transmission and public health.

**Chronic HIV Infection**

A number of historical details, findings on physical examination, and laboratory abnormalities should prompt testing to identify persons with established HIV infection. As expected, these findings are more prominent in patients with more advanced disease. Often, the initial diagnosis of HIV infection is made when the patient develops an AIDS indicator condition (Table 2). However, the astute clinician can often detect signs and symptoms of HIV infection earlier in the course of disease, allowing access to appropriate therapy and prophylaxis before significant illness develops.

**Table 2: AIDS-indicator conditions**

- Candidiasis of the esophagus, bronchi, trachea, or lungs
- Cervical cancer, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1-month duration)
- Cytomegalovirus disease of any organ other than the liver, spleen, nodes
- Encephalopathy, HIV-related
- Herpes simplex with mucocutaneous ulcer >1-month duration, or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1-month duration)
- Kaposi sarcoma
- Lymphoma, Burkitt’s, immunoblastic, or primary CNS involvement
- Mycobacterium avium complex or M. kansasii, extrapulmonary
- M. tuberculosis, any site
- Pneumocystis jiroveci pneumonia
- Pneumonia, recurrent bacterial (2 or more episodes in 1 year)
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis, CNS
- Wasting syndrome caused by HIV

CNS = central nervous system; HIV = human immunodeficiency virus (HIV).

*Data from Centers for Disease Control.*
A history of certain illnesses can also be suggestive of HIV infection. Infections such as active tuberculosis, recurrent community-acquired pneumonia, esophageal candidiasis, undifferentiated interstitial lung disease, and either multidematomal herpes zoster or zoster in younger adults should lead to HIV testing. Neoplastic diseases such as B-cell lymphoma, severe anal or cervical dysplasia, or invasive carcinoma and Kaposi sarcoma are indications for HIV testing, as is idiopathic dilated cardiomyopathy. The evaluation of fever of unknown origin or unexplained weight loss should always include an HIV test, even in older patients without identified risk factors.

Various findings on physical examination may suggest coexisting HIV infection. Examination of the skin can be particularly revealing. Seborrheic dermatitis or molluscum contagiosum are common in early disease as is psoriasis. Oral candidiasis can be seen typically with CD4+ counts below 200 cells/mm³.15 Generalized lymphadenopathy is common. Recurrent or severe lesions of herpes simplex virus may be indicative of underlying HIV infection. Neurologic findings such as unexplained peripheral neuropathy or dementia are also suggestive.

On laboratory evaluation, idiopathic thrombocytopenia, unexplained anemia, neutropenia, and/or leukopenia are frequent, early clues to underlying HIV infection. An elevated total protein level or globulin fraction is also suggestive.

Diagnosis

Numerous tests have been developed to aid the diagnosis of HIV; however, only a few tests have application for routine use. It is important for the primary care physician to be familiar with available diagnostic tests and with guidelines regarding patient populations that are appropriate for HIV screening.

Screening Guidelines

Both the United States Preventative Services Task Force (USPSTF) and CDC recommend routine screening for HIV.16,17 The USPSTF recommends that all individuals aged 15 to 65 years and pregnant women be tested for HIV at least once regardless of perceived risk factors. Younger adolescents and older adults who are at increased risk of infection also should be screened.

Patients who have a high risk for contracting HIV should be screened at more frequent intervals; the CDC recommends at least yearly screening for high-risk patients. Individuals considered to be at an increased risk of infection include men who have sex with men, those engaging in active injection drug use, as well as those who have other sexually transmitted infections or who request testing for STIs. Other behavioral risk factors for HIV infection include having unprotected anal or vaginal intercourse, having HIV-infected sexual partners, or having sexual partners who are bisexual or have a history of intravenous drug use. Receiving money or drugs in exchange for sex is also a high-risk behavior.16
To decrease barriers to HIV testing, the CDC recommends not mandating written consent for HIV testing or counseling. Testing laws vary by state, but most are consistent with these CDC recommendations.\textsuperscript{18}

**Diagnostic Tests**

To diagnose HIV infection, the CDC recommends beginning with a combination immunoassay that detects HIV-1 and HIV-2 antibodies as well as the HIV-1 p24 antigen in the serum or plasma. If this test is reactive, then a confirmatory test is needed to differentiate HIV-1 from HIV-2 antibodies. If the HIV-1/HIV-2 antibody differentiation assay is intermediate or negative, further testing with a HIV-1 nucleic acid test (NAT) is needed. A reactive NAT confirms the diagnosis of HIV-1 infection.

The current diagnostic test is notably different from the previously used HIV enzyme-linked immunosorbent assay (ELISA) and the confirmatory Western blot test. The new laboratory testing algorithm\textsuperscript{19} (Figure 1) has advantages over the previous recommended test including improved accuracy of diagnosis of acute HIV-1 infection, more accurate diagnosis of HIV-2 infection, fewer indeterminate test results, and faster turnaround time.

**Figure 1: Recommended diagnostic laboratory HIV testing algorithm for serum or plasma specimens**

\textsuperscript{19}Reprinted from Centers for Disease Control.
Current CDC recommendations do not include the rapid HIV-1/HIV-2 antigen/antibody combination test that was approved by the Food and Drug Administration (FDA) in August 2013 because of insufficient evidence. The recommendations also do not include non-FDA approved HIV-2 nucleic acid tests. That being said, a positive result on the rapid combination test requires further investigation with the above stated algorithm.19

Evaluation of Patients with HIV

Once a diagnosis of HIV infection has been made, several baseline laboratory studies should be obtained to establish an appropriate treatment plan for the patient. HIV infection should be staged with a CD4+ count and HIV RNA viral load measurement. Genotypic resistance testing is recommended irrespective of whether antiretroviral therapy initiation is deferred. If antiretroviral therapy is deferred, reassessing genotype can be considered. In patients with viral loads below 500 to 1,000 copies per mL, the viral amplification performed for resistance testing may not be successful.20 Additional studies include complete blood count, complete metabolic panel (including transaminase levels), urinalysis, and hepatitis A, B, and C serologies. Fasting lipids and glucose should be checked as well as testing for genotypic resistance.

Patients should also be tested for concomitant Mycobacterium tuberculosis infection via either tuberculin skin test of interferon gamma release assay. A baseline chest x-ray, serologic testing for Toxoplasma gondii, and screening for syphilis are also indicated. Depending on exposure history, gonorrhea and chlamydia screening should be ordered.

HLA B*5701 screening should be ordered if abacavir is part of the treatment regimen. If therapy with a CCR5 antagonist is planned, it is important to order a coreceptor tropism assay.

Women with HIV should have a Pap smear on initial diagnosis. A Pap smear should be repeated every 6 months until results are normal, at which point the screening interval is lengthened to every 12 months. Women with HIV should also be screened for trichomoniasis.21

A complete list of necessary additional testing is provided in Table 3.
Table 3: Initial laboratory evaluation of patients with HIV

- Complete blood count, including differential and platelets
- Determination of levels of electrolytes, blood urea nitrogen, creatinine, transaminases, alkaline phosphate, glucose-6-phosphate dehydrogenase
- Rapid plasma regain or VDRL testing
- *Toxoplasma gondii* IgG determination
- Hepatitis A, B and C serologies
- CD4+ count
- Quantitative HIV RNA level
- HIV genotype
- PPD test or interferon gamma release assay
- Baseline chest x-ray
- Consider coreceptor tropism assay or HLA B*5701
- Women should undergo Pap smear and trichomoniasis testing

HIV = human immunodeficiency virus; IgG = immunoglobulin G; PPD = purified protein derivative; RNA = ribonucleic acid; VDRL = venereal disease research laboratory.

Data from US Department of Health and Human Services.20

Treatment

Appropriate treatment of patients with HIV requires consideration of antiretroviral therapy and consideration of the medical, social, medication history (including alternative and herbal supplements) along with a thorough physical examination. Assessment of the patient’s knowledge of HIV, understanding of the course of disease, emotional well-being, and presence or absence of support systems is as important as a discussion of safer sex practices and contraception. Notification of sex partners is vital; the laws regarding partner notification vary from state to state. Identification of a durable power of attorney and discussion of advanced directives are valuable early in the course of the disease.

Prevention

Preventive care is essential to treating patients with HIV. Some infections can be minimized by avoiding uncooked and undercooked foods such as seafood, eggs, and meats; abstaining from drinking lake and river water; avoiding contact with cat litter boxes and animals with diarrhea; and careful hand washing. Other preventive measures are appropriate vaccinations, medications for the prevention of opportunistic infections, and preexposure prophylaxis for individuals without HIV.
Vaccinations
The patient’s vaccination history should be carefully reviewed. All patients should receive the pneumococcal vaccine with an initial dose of PCV13 (Prevnar 13) with a subsequent dose of PPV23 (Pneumovax) at least 8 weeks after the initial PCV13.21 A second dose of PPV23 is recommended 5 years after the initial dose. Yearly influenza vaccination is recommended as is hepatitis B vaccination if the patient is seronegative. Hepatitis A vaccination is recommended for all susceptible men who have sex with men in addition to other susceptible individuals, and it should be considered in all patients with HIV infection. Tetanus boosters are indicated every 10 years.21

Other vaccinations such as the oral polio vaccine are contraindicated, but the inactivated polio vaccine should be given if indicated (patients traveling to endemic areas). Varicella vaccination is considered in select settings, particularly in patients with CD4 counts ≥200 cells/mm³ who are not immune to varicella. The safety of vaccination against herpes zoster is unknown but vaccination can be considered in patients >60 years old with CD4 counts ≥200 cells/mm³.21

Prophylaxis
Patients with advanced HIV disease require prophylaxis to prevent opportunistic infections. If the CD4⁺ count is <200 cells/mm³ (or CD4⁺ percentage <14%), prophylaxis against P. jiroveci pneumonia should be initiated. The first-line agent is trimethoprim-sulfamethoxazole (TMP-SMX), commonly 1 double-strength tablet daily. Dapsone, 100 mg/day, is recommended for patients who are TMP-SMX intolerant and not G6PD-deficient. If the CD4⁺ count is <100 cells/mm³, patients with positive T. gondii IgG serologies require prophylaxis to prevent reactivation. Daily double-strength TMP-SMX is again the drug of choice. Patients receiving dapsone require the addition of weekly pyrimethamine. Although Mycobacterium avium complex prophylaxis is recommended at CD4⁺ counts <50 cells/mm³, initiation is never emergent. Active Mycobacterium avium complex disease should be ruled out before starting prophylaxis if the patient has any suggestive symptoms. The most common regimen is azithromycin, 1200 mg/week.

More detailed information can be obtained from the CDC and Infectious Disease Society of America guidelines for the prevention of opportunistic infections.22

HAART
Highly active antiretroviral therapy (HAART) is the mainstay of HIV treatment; however, selection of HAART has become increasingly complex and recommendations are constantly changing as new classes and agents become available. Antiretroviral resistance limits future HAART options. Thus, it is recommended that the selection of HAART be left to a clinician who has experience and specializes in managing HIV infection.
The Department of Health and Human Services (DHHS) updated their HAART treatment guidelines in April 2015. They now recommend highly active antiretroviral therapy for all HIV-infected patients to reduce disease progression and to prevent transmission to noninfected individuals. Highly active antiretroviral therapy is indicated at all CD4 cell counts.20

There are currently more than 25 drugs in six classes that are FDA approved to treat HIV infection.20 Classes of medications include nucleoside/nucleotide reverse transcriptase inhibitors, nonnucleoside reverse transcriptase inhibitors, protease inhibitors, a fusion inhibitor, a CCR5 antagonist, and integrase strand transfer inhibitors. There are also two drugs classified as pharmacokinetic enhancers that are used to improve the pharmacokinetics of the protease inhibitors and one of the integrase strand transfer inhibitors (elvitegravir).

Current recommended therapy for a treatment-naïve individual consists of a backbone of two nucleoside reverse transcriptase inhibitors in combination with a third drug from one of the following classes: an integrase strand transfer inhibitor, a nonnucleoside reverse transcriptase inhibitor, or a protease inhibitor with a pharmacokinetic enhancer (cobicistat or ritonavir)20 as outlined in Table 4.

**Table 4: Recommended regimens for initial therapy in treatment-naïve patients**

<table>
<thead>
<tr>
<th><strong>Integrase strand transfer inhibitor-based regimens</strong></th>
<th></th>
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<tbody>
<tr>
<td>• Dolutegravir/abacavir/lamivudinea — only for patients who are HLA-B*5701 negative</td>
<td></td>
</tr>
<tr>
<td>• Dolutegravir plus tenofovir/emtricitabine</td>
<td></td>
</tr>
<tr>
<td>• Elvitegravir/cobicistat/tenofovir/emtricitabinea — only for patients with pre-antiretroviral therapy CrCl &gt;70 mL/min</td>
<td></td>
</tr>
<tr>
<td>• Raltegravir plus tenofovir/emtricitabine</td>
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</tbody>
</table>

**Protease inhibitor-based regimen**

- Darunavir/ritonavir plus tenofovir/emtricitabinea

CrCl = creatinine clearance.
aLamivudine may be substituted for emtricitabine or vice versa.

Data from US Department of Health and Human Services.20

Several alternative regimens are also available and are outlined in the DHHS guidelines. In some instances, these regimens may be preferred when taking into consideration additional factors including patient characteristics (pretreatment HIV RNA level, CD4 count, drug resistance testing results, HLA-B*5701 status), medical comorbidities, and regimen-specific constraints including adverse drug effects, interactions with other medications, convenience, and cost.20
Once HAART is initiated, the goals of HAART are to reduce HIV-associated morbidity and prolong survival, restore immune function, suppress HIV viral load, and prevent HIV transmission. The suppression of HIV-1 RNA to below the limits of assay detections usually occurs within the first 12 to 24 weeks of therapy.\textsuperscript{20}

The most critical and modifiable factor affecting success is patient adherence. Only 45\% of patients taking 90\% to 94.9\% of the prescribed doses of antiretroviral medications will achieve viral suppression (<400 copies/mL) compared with 78\% of patients taking ≥95\% of doses.\textsuperscript{23} Incomplete viral suppression leads to the development of drug resistance. Adherence to the antiviral regimen should be addressed at every visit in a detailed fashion, and the importance of careful adherence should be stressed. Once-daily dosing of many treatment regimens is now possible and changes in pill formulations have allowed more potent regimens to be prescribed with fewer total pills. Both pill burden and dosing frequency have been shown to correlate with adherence.

While the new HAART regimens are largely well tolerated by patients, there can be significant side effects that can be either class specific or individual to the medication itself. Side effects include hepatotoxicity, hyperglycemia, hyperlipidemia, lipodystrophy, lactic acidosis, skin rash, and effects on bones including osteonecrosis, osteoporosis, and osteopenia.\textsuperscript{24} There are also significant drug-drug interactions that can occur between antiretroviral agents and commonly prescribed medications that can lead to drug toxicities or reduction in levels of the drug or the antiretroviral agent rendering them ineffective. For a complete list of adverse effects, toxicities, and medication interactions, refer to the DHHS Antiretroviral Guidelines.\textsuperscript{20}

Outcomes

The advent of HAART has dramatically decreased morbidity and mortality for patients with HIV such that HIV is now considered to be a chronic disease with life expectancies approaching that of noninfected persons with similar comorbidities.\textsuperscript{25} In the US, deaths caused by AIDS declined sharply in 1996 and 1997 when protease inhibitors were first introduced. Among a cohort of adults with advanced HIV infection, death rates decreased from 29.4 per 100 person-years in 1995 to 8.8 per 100 person-years by the second quarter of 1997. Morbidity has declined as well, as measured by the incidence of opportunistic infection.\textsuperscript{26} Current efforts are focused on improving ease of use and decreasing toxicity of HAART in hopes of enhancing the quality of life of those infected with HIV.
Prevention of HIV Infection

Because a large portion of patients infected with HIV are unaware of their infection, it is important for primary care doctors to screen patients. The UPSTF and CDC recommend screening for HIV in adolescents and adults aged 15 to 65 years and in pregnant women at least once regardless of perceived risk factors. Patients should be tested unless they decline (opt-out testing). Younger adolescents and older adults who are at an increased risk of infection should also be tested for HIV. Primary care doctors should also incorporate into practice available therapies for prevention primarily through education of safe sex practices, information regarding needle sharing, and, most notably, preexposure prophylaxis.

It is important for primary care physicians to conduct a thorough, nonjudgmental assessment of their patients to determine risk factors for HIV infection. Patients at increased risk for HIV infection include those with a history of intravenous drug abuse, sexually transmitted diseases, and receipt of blood products between 1977 and 1985. Men who have had sex with men, sex workers, and heterosexual persons with more than one partner since their last HIV test are also considered to be at high risk, as are the sexual partners of high-risk or HIV-infected persons. Mental illness and incarceration may serve as markers for high-risk behavior, as does a history of hepatitis B or C infection. Persons who consider themselves at risk should be tested even if their risk behaviors are not disclosed.

Preexposure Prophylaxis

Preexposure prophylaxis is defined as the use of antiretroviral medication to reduce the risk of HIV transmission in sexually active adults who are HIV-negative and at an increased risk of acquiring HIV. Currently, the only FDA-approved therapy for preexposure prophylaxis is the daily oral use of combination of tenofovir 300 mg and emtricitabine 200 mg (Truvada). Preexposure prophylaxis is currently recommended in several patient populations including women who have sex with HIV-positive men, men who have sex with men who are at a high risk of contracting HIV, heterosexual sexually active men and women at an increased risk of HIV, and in adult intravenous drug users at high risk of acquiring HIV. High-risk behaviors include high number of sexual partners, HIV-positive partner, inconsistent condom use, commercial sex work, recent STI, and those living in a high-prevalence area or network. Those who abuse intravenous drugs are considered at high risk if they share injection materials or have undergone recent treatment for addiction. Preexposure prophylaxis is not currently approved for the adolescent population because of insufficient evidence regarding safety and efficacy. Preexposure prophylaxis can be offered once an HIV test is documented negative and a review of the patient’s medication list, renal function, and hepatitis B status shows no contraindications. In addition, a clinical exam would be assessed for signs of acute HIV infection.
Guidelines recommend screening patients on preexposure prophylaxis for HIV infection every 3 months to prevent inadequate treatment in the event of HIV acquisition particularly because this may result in increased resistance to either or both medications.\textsuperscript{27} It is also recommended that the patient is counseled every 3 months regarding medication adherence, pregnancy intent, and risk reduction in order for preexposure prophylaxis to be used in combination with other means of HIV prevention.

Summary

- Acute HIV infection is associated with fever, rash, lymphadenopathy, and nonexudative pharyngitis. Between 40\% to 90\% of patients with HIV seroconversion are symptomatic but few are diagnosed with HIV at their initial presentation.

- In 2011, an estimated 1.2 million Americans aged $\geq$13 years were living with HIV and approximately 14\% of them were undiagnosed.

- United States Preventative Services Task Force recommends HIV screening in adolescents and adults aged 15 to 65 years and in pregnant women. Younger adolescents and older adults who are at an increased risk of infection should also be screened. Consent for testing should be obtained using opt-out approaches.

- There is no CD4$^+$ T cell count at which antiretroviral therapy is contraindicated.

- Recommended initial antiretroviral regimens include at least three different medications to suppress the virus.

- Preexposure prophylaxis has been shown to reduce HIV transmission in HIV-negative individuals who are at risk of infection through sexual transmission.
Suggested Reading & References

Suggested Reading


References


**Disclosures:** Julianne Griswold, DO; nothing to disclose. Marisa Tungsiripat, MD; nothing to disclose.