ARxCH
Annual Review of Changes in Healthcare

# Review of Human Immunodeficiency Virus and Updated Guidelines

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**Learning Objectives**
- Identify preventative strategies for HIV
- Identify short-term and long-term effects of antiretroviral therapy
- Describe new updates to the guidelines for HIV

**Abstract**

HIV is a challenging diagnosis for patients with many lifelong implications. It was once a disease state that was associated with a relatively short life expectancy. However, as new drugs have been developed the outcomes have improved drastically. As a healthcare team, it is a duty to keep up with new treatments and therapies that will improve the lives of patients. The HIV/AIDS guidelines are updated regularly, and the most current updated portions are highlighted for easy differentiation. This review will cover some of the updates that occurred in July 2016 and provide a background on the disease state.

## Background

Human immunodeficiency virus (HIV) is a viral infectious disease that can be transmitted through multiple body fluids, such as blood, semen, vaginal fluids, and breast milk. HIV can also be transmitted by objects in contact with blood, such as needles. HIV is a retrovirus that attacks the T helper cells and macrophages of the immune system, which help guard against infections and malignancies.[1] Not managed, HIV can cause significant damage to the immune system and transition into acquired immunodeficiency syndrome (AIDS).

The Centers for Disease Control and Prevention (CDC) recommends that persons 13 to 64 years of age get tested for HIV to know his or her status. About 1.2 million individuals in the United States are living with HIV, and it is estimated that one in eight (12.5%) are unaware that they are infected.[2] Men who have sex with men (MSM), African American men, and IV drug abusers are the greatest affected groups in the United States.[2]

Since HIV is not curable, prevention is critical. An important strategy for prevention is awareness of a person's HIV status because knowledge is key. If an individual is HIV positive and desires to remain sexually active, there are options that will provide protection against spreading HIV to his or her partner(s). The individuals involved should use protection, such as a condom or other barrier device. There is also a medication called Truvada® that can be taken for pre-exposure prophylaxis (PrEP) for long-term partners or IV drug abusers, but it should be taken consistently every day.[3] Truvada® is a combination of tenofovir and emtricitabine and can be prescribed to a patient who is at a substantial risk of contracting HIV.[3] When taken properly, the HIV-negative individual has a 92% reduction in risk of being infected.[3] Patients taking Truvada® for PrEP should follow-up with their healthcare provider every three months.[3]

Post-exposure prophylaxis (PEP) is also available for patients. If a patient is involved in a high-risk event, antiretroviral drugs can be administered within 72 hours and can be effective at preventing infection.[4] The therapy is continued for 28 days and must be taken as directed to be effective in preventing HIV.[4]

### *Transmission*

Illicit drug use is a challenge in the treatment of HIV infection. In the United States, the use of injection drugs accounts for the second most common mode of transmission.[5] Regardless if the illicit drug involves a needle, the risk for transmission is elevated. Common reasons for drug use include depression or anxiety, self-treatment of withdrawals, or recreational use.[5] Drug use poses a significant risk of transmission of the HIV virus and co-infection of other viruses because there is a potential of sharing contaminated needles. Additionally, there is an increased incidence for high-risk sexual behavior in this population, especially MSM.[5] It is important to be able to recognize the signs of drug abuse and direct the patient on how to receive help for the underlying problem. If the patient is unwilling to seek help for their addiction, providing information on HIV and

counseling the patient on prevention strategies should be considered.

*Use of Antiretrovirals*

When an individual with HIV is adherent to their medication regimen, antiretroviral therapy is highly effective at preventing HIV transmission and slowing the progression of the infection.[5,6] Before initiation of antiretroviral therapy, the plasma viral load should be measured.[6] After initiation of antiretroviral medication, the plasma viral load should be measured in two to four weeks, and then again four to eight weeks later until the viral load measurement falls below the assay's limit of detection.[6] It takes eight to twenty-four weeks for full viral suppression to be achieved.[6] At that point, the viral load needs to be measured every three to four months to monitor the viral suppression status.[6] Another important lab measurement is the CD4 cell count, which should be measured prior to medication therapy initiation and then three to six months or annually thereafter.[6] The measurement will assess the need for prophylactic treatment of opportunistic infections, which may occur in patients with a more advanced HIV infection who have a severely suppressed immune system (CD4 cell count less than 200). There are several combinations of antiretroviral medications; patients will normally need to use three active drugs from at least two different classes.[6] If the drug regimen is changed, the combination needs to involve at least two active drugs or viral suppression could fail due to viral rebound.[6]

All medical personnel play a crucial role in HIV awareness, prevention, and education. Creating an open and honest relationship with patients about the HIV infection, lifelong medication outcomes, responsibilities, illicit drug use, and preventative care for sexual partners will decrease the risk of transmission.[5]

*Complications with the Use of Antiretrovirals*

It is important to assess a patient's awareness and readiness to begin therapy.[5] Initiating antiretroviral therapy in a patient that may not be adherent to the regimen may create resistant strains of the virus. Patients can experience a wide array of side-effects from antiretroviral medications. Some of the immediate effects include CNS-effects, such as abnormal dreams, dizziness, headache, and depression, skin rash, and gastrointestinal side-effects.[5,6] For some patients, the side-effects have a negative impact on adherence. Therefore, this is an important counseling point. Creating an open dialogue about medication complications and adherence at every visit may improve outcomes.[5] Long-term adverse effects of antiretroviral medication use can be cardiovascular disease, diabetes mellitus/insulin resistance, bone density effects, dyslipidemia, severe hepatotoxicity, lactic acidosis, lipodystrophy, myopathy, psychiatric effects, renal effects and CKD, and severe hypersensitivity reactions, including Stevens-Johnson syndrome.[6]

Other long term effects of antiretroviral therapy can be seen in renal and liver function. An institution-based retrospective study (n=275) was conducted in Ethiopia from 2010 to 2015 to look at long-term antiretroviral effects on the kidney and liver.[7] The included participants needed to have been taking antiretroviral

drugs for at least three years, registered for primary care at the University of Gondar Hospital ART clinic, and screened for renal and liver dysfunction prior to initiation of therapy.[7] This study found that the overall prevalence of CKD increased after treatment with antiretrovirals, and a majority of the CKD cases after treatment were in stage 3 of CKD.[7] Other studies have shown a higher prevalence of patients with stage 2 CKD after treatment with an antiretroviral.[7] In addition to the increased prevalence in CKD, the study by Biadgo, et al. showed that forty-six of the participants had a presence of hepatotoxicity after treatment with an antiretroviral.[7]

Knowledge Check: Possible immediate adverse effects of antiretroviral medications include:

a) Headache
b) GI side-effects
c) Skin rash
d) Dizziness
e) Abnormal dreams
f) Three of the above
g) All of the above

Answer: G

**HIV Guideline Update**

HIV therapy guidelines are updated regularly. The Panel members involved in the HIV guideline committee have monthly teleconferences in which they discuss modifications and updates to the most recent guidelines.[6] There is at least one representative on the Panel from the U.S. Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC), U.S. Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), and National Institutes of Health (NIH), which consists of about forty-five elected members with expertise in HIV care and research.[6]

In July of 2016, the guidelines were updated. The key updates to the guidelines were for HIV-infected women, tuberculosis (TB)/HIV coinfection, combination regimens for antiretroviral-naive patients, regimen switching, Hepatitis B Virus (HBV)/HIV coinfection, and Hepatitis C Virus (HCV)/HIV coinfection.[6]

For all HIV-infected women, the Panel emphasized recommending antiretroviral therapy (ART).[6] This strong recommendation is evidenced by one or more randomized trials with clinical outcomes. Expert opinion strongly recommends that if a woman is not planning on getting pregnant that she should take an oral contraceptive.[6] If the antiretroviral (ARV) drug regimen has a significant interaction with hormonal contraceptives, then it is appropriate to use alternative or additional contraceptives.[6] Switching to a different ARV drug is an option, however, it is only moderately backed by expert opinion.[6] If an HIV-infected woman does become pregnant and was not on an ARV combination, it is necessary to discuss the risks and benefits of ARV use during and after pregnancy. The updated guidelines increase the amount of counseling that should be done with HIV-infected women.[6] Expert opinion strongly suggests initiating

ART as soon as possible to prevent mother-to-child transmission (MTCT) of HIV.[6]

The Panel recommended an update on the treatment of latent tuberculosis infection (LTBI) because the treatment of LTBI reduces the risk of active TB in HIV-infected patients.[6] Guidelines suggest that any ART regimen can be used if the patient is taking isoniazid alone for LTBI treatment.[6] If the patient is receiving once-weekly isoniazid plus rifapentine for LTBI, then expert opinion strongly suggests an efavirenz (EFV) or raltegravir (RAL)-based ART regimen.[6] The once weekly isoniazid (INH) and rifapentine regimen is given for twelve weeks.[6] The CDC also recommends either isoniazid daily or twice weekly for nine months or rifampin daily for four months.[6] In all patients with active TB who are not on therapy, an antiretroviral should be initiated.[6] The addition to the guidelines pertains to patients with CD4 counts of at least 50 cells/mm.[3,6] The TEMPRANO randomized study consisted of 2,056 HIV-infected patients who did not meet the WHO criteria for ART initiation.[6] There were four study arms. One arm deferred ART initiation. The second arm deferred ART plus INH preventative therapy (IPT). The third arm initiated early ART, and the fourth arm initiated early ART plus IPT. For patients with CD4 counts greater than 500 cells/$mm^3$, the early initiation of ART immediately had positive effects by reducing the risk of death and HIV-related illness by 44 percent.[6] Six months of IPT reduced the risk of HIV morbidity by 35 percent.[6] Expert opinion strongly suggests initiating ART within eight weeks of initiating TB treatment.[6] The PREVENT TB study showed that there was no significant difference in safety and effectiveness of preventing active TB between rifapentine plus INH for twelve weeks compared to nine months of INH alone in patients who were not on ART.[6] An important drug interaction to consider is with rifamycins, which are important in TB treatment.[6] The drugs in the class pose a variety of interactions.[6] Tenofovir alafenamide (TAF) is a P-gp substrate and is impacted by concomitant administration of rifamycin.[6] Due to this drug-drug interaction, administration of both TAF and rifamycin is not recommended.[6]

Based on observational studies, the Panel recommends to use a combination of tenofovir disoproxil fumarate (TDF) with emtricitabine (FTC) or lamivudine (3TC) or use tenofovir alafenamide and emtricitabine (TAF/FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of the ARV drug regimen for patients coinfected with HIV and HBV (hepatitis B virus).[6] The update includes recommendations on the potential use and restrictions of TAF/FTC-containing regimens.[6] TAF/FTC-containing regimens are not recommended to be used in patients with a creatinine clearance less than 30 ml/min.[6] Switching to elvitegravir/ cobicistat/tenofovir/alafenamide/emtricitabine (EVG/c/TAF/FTC) can reduce renal and bone toxicity while effectively suppressing HBV.[6] Adefovir is associated with a high incidence of renal disease, and telbivudine is associated with myopathy, HBV treatment failure, and neuropathy. Therefore, the Panel is currently not recommending adefovir and telbivudine for HBV/HIV-coinfected patients.[6]

## Conclusion

Overall, there were many important updates to the guidelines for HIV in July 2016. Women of reproductive age that are infected with HIV and are not planning on becoming pregnant, should consider taking an oral contraceptive and ART.[6] Women who are pregnant should weigh the risks and benefits of using ART to reduce the risk of MTCT.[6] The updated guidelines increase the amount of counseling that should be done with HIV-infected women. HIV/TB co-infected patients have better outcomes taking ART and TB treatment compared to TB treatment without ART.[6] The Panel recommends a combination of TDF with FTC or 3TC or use TAF/FTC as the NRTI backbone of the ARV drug regimen for HIV patients coinfected with HBV.[6] HIV therapy is going to continue to evolve to try to improve the quality of life for over a million patients in the United States.

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