HIV/AIDS: Epidemic Update

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician, behavioral health professional, or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
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Faculty

Jane C. Norman, RN, MSN, CNE, PhD, received her undergraduate education at the University of Tennessee, Knoxville campus. There she completed a double major in Sociology and English. She completed an Associate of Science in Nursing at the University of Tennessee, Nashville campus and began her nursing career at Vanderbilt University Medical Center. Jane received her Masters in Medical-Surgical Nursing from Vanderbilt University. In 1978, she took her first faculty position and served as program director for an associate degree program. In 1982, she received her PhD in Higher Education Administration from Peabody College of Vanderbilt University. In 1988, Dr. Norman took a position at Tennessee State University. There she has achieved tenure and full professor status. She is a member of Sigma Theta Tau National Nursing Honors Society. In 2005, she began her current position as Director of the Masters of Science in Nursing Program.

John M. Leonard, MD, Professor of Medicine Emeritus, Vanderbilt University School of Medicine, completed his post-graduate clinical training at the Yale and Vanderbilt University Medical Centers before joining the Vanderbilt faculty in 1974. He is a clinician-educator and for many years served as director of residency training and student educational programs for the Vanderbilt University Department of Medicine. Over a career span of 40 years, Dr. Leonard conducted an active practice of general internal medicine and an inpatient consulting practice of infectious diseases.

Faculty Disclosure

Contributing faculty, Jane C. Norman, RN, MSN, CNE, PhD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, John M. Leonard, MD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for all nurses, physicians, and allied healthcare professionals involved in the care of patients with HIV/AIDS.

Accreditations & Approvals

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Successful completion of this CME activity, which includes participation in the activity with individual assessments of the participant and feedback to the participant, enables the participant to earn 5 MOC points in the American Board of Pediatrics' (ABP) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABP MOC credit.

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NetCE designates this continuing education activity for 5 ANCC contact hours.

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The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

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Disclosure Statement

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Course Objective

HIV infection is now endemic in the United States and throughout much of the world, and HIV/AIDS has become less about cure and more about management and control. As with most chronic diseases, treatment protocols and management strategies change over time. The purpose of this course is to provide a basic, practical review and update of knowledge concerning HIV/AIDS, addressing the key issues that impact clinical care and public health practice.

Learning Objectives

Upon completion of this course, you should be able to:

1. Discuss the background and significance of the HIV/AIDS epidemic.
2. Outline the viral pathogenesis and disease course of HIV.
3. Utilize knowledge of HIV transmission and risk behaviors to effectively counsel patients who have the infection and others who are at risk of exposure.
4. Describe the natural history, clinical characteristics, and stages of chronic HIV infection and disease progression.
5. Identify and devise the appropriate antiretroviral treatment regimen and follow-up for a given patient, in consultation with an infectious disease specialist.
6. Anticipate and assess the variations in the clinical presentation, treatment, and preventive aspects of HIV infection in women, children, and the elderly.
7. Discuss effective and emerging approaches to HIV/AIDS prevention.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Despite scientific advances in our understanding of pathogenesis and transmission and expanded options for prevention and treatment, human immunodeficiency virus (HIV) infection remains a complex, challenging clinical problem and health concern. In the United States, the prevalence of infection has increased substantially among young women and among the elderly in recent decades. The former has serious implications for maternal and child health; the latter presents new challenges for nurses and physicians who provide elder care.

The purpose of this course is to provide a basic, practical review and update of knowledge concerning HIV infection and acquired immune deficiency syndrome (AIDS), addressing the key issues that impact clinical and public health practice. Topics to be addressed include immunopathogenesis, modes of transmission, natural history and clinical staging, risk behavior assessment, prevention (including postexposure prophylaxis), diagnosis, management, and follow-up.

EPIDEMIOLOGY

GLOBAL IMPACT

The global healthcare community first became aware of the illness now known as HIV/AIDS in 1981. In subsequent decades, the HIV pandemic, and associated disease burden of AIDS, emerged as a major public health issue worldwide. The incidence of HIV infection continues to escalate in some developing countries of the world, compared with a notable stabilization in new cases and fatalities in most developed countries.

Two human immunodeficiency viruses, HIV-1 and HIV-2, have been identified and both cause AIDS. Researchers in the United States and England have traced the ancestry of the HIV-1 virus to two strains found in African red-capped mangabeys and greater spot-nosed monkeys. The strains most likely combined in chimpanzees that ate the monkeys, resulting in the chimpanzees developing simian

immunodeficiency virus (SIV). Chimpanzees then transmitted the virus to humans, likely around 1908 [1]. Genetic studies suggest that the lower monkeys first became infected with SIV 100,000 years ago [2].

HIV-2 is believed to be endemic in West Africa, though even areas with previously high rates (e.g., Senegal) are seeing HIV-2 being increasingly overtaken by HIV-1 [1]. Several well-documented cases of HIV-2 infection have been reported in Europeans and among West Africans residing abroad. A total of 242 cases meeting the Centers for Disease Control and Prevention's (CDC's) definition of HIV-2 infection were reported between 1988 and 2010 in the United States, the majority of which were associated with immigration from, travel to, or a sexual partner from West Africa [3]. Differences in the global spread are attributed to differences in transmissibility and duration of infectiousness [4].

According to the World Health Organization (WHO), an estimated 37.7 million individuals worldwide were living with HIV by the end of 2020, of whom more than two-thirds (25.4 million) were in the WHO African Region [5]. Northern Africa, the Middle East, and eastern Europe and central Asia (particularly the Russian Federation) have had the fastest growing epidemics—new HIV infections in these regions have approximately doubled in the past 20 years. In 2020, an estimated 680,000 people died from HIV-related causes and 1.5 million people acquired HIV infection [5]. It is important to note that despite increases in certain geographic areas and demographic groups, overall, the rate of new infections was declining prior to the COVID-19 pandemic. Service disruptions during COVID-19 have slowed the pace of public health response to HIV, raising concern that increasing HIV infections and excess HIV-related deaths may erode the progress made in sub-Saharan Africa [5].

Beginning in 2003, the U.S. government has worked to fight the disease in Africa, partially through the implementation of the President's Emergency Plan for AIDS Relief (PEPFAR) [6]. PEPFAR was reauthorized in 2008, with a total of $48 billion in funds over the following five years and expansion to address additional health issues, including malaria, tuberculosis, maternal health, and clean water [7]. This was extended to 2023 with the PEPFAR Extension Act of 2018 [8].

UNITED STATES STATISTICS

At year-end 2019, an estimated 1.2 million individuals 13 years of age or older were living with HIV/AIDS in the United States [9]. The CDC estimates that approximately 13% of these individuals were unaware of their infection [9]. When reviewing trends in HIV transmission, one should keep in mind that the widespread use of antiretroviral therapy has resulted in fewer deaths and longer survival.

As of 2019, the Centers for Disease Control and Prevention (CDC) report several statistics and trends in the HIV/AIDS epidemic [9]:

- By region, the prevalence rates are 50% higher in the Northeast and South (525 per 100,000) than in the West (365 per 100,000) and Midwest (253 per 100,000).
- By race/ethnicity, 40% are Black/African American, 28% White, 25% Hispanic, and less than 1% are American Indian/Alaska Native or Asian/Pacific Islander.
- By sex at birth, 78% of adults and adolescents living with HIV are male.

A BRIEF OVERVIEW OF HIV DISEASE

VIRAL PATHOGENESIS

HIV, known formerly as human T cell lymphotropic virus (HTLV-III), is a member of the retrovirus group and as such carries a ribonucleic acid (RNA) genome and a reverse transcriptase enzyme (RNA-directed DNA polymerase) that enables the virus to replicate within infected host cells. Susceptibility in humans is determined by the binding affinity of virion envelope proteins for a specific cell surface receptor molecule (CD4+) found on tissue dendritic cells, macrophages, and CD4+ T lymphocytes. The pathogenesis of infection, and the subsequent perpetuation of the disease state, involves a complex set of interactions by which HIV is able to take advantage of cellular pathways while avoiding or neutralizing various components of the immune system [11; 12].

The most common mode of HIV infection is sexual transmission across exposed mucosal epithelium. Dendritic cells and macrophages are found beneath the mucosal epithelium of the anogenital and cervicovaginal tracts, as well as within tonsillar and adenoidal tissue. Studies in primates demonstrate that after the virus penetrates the mucosal epithelium, infection is initiated within nearby dendritic cells and macrophages. Infected dendritic cells then fuse with CD4+ T lymphocytes and the infection extends to deeper tissue and, shortly thereafter, to regional lymph nodes [12]. Within days, this proliferation of infected CD4+ T lymphocytes, combined with the migration of infected macrophages, leads to the appearance of viral RNA in the blood stream. This is followed by widespread secondary amplification of infection within the lymphoid tissue of the gastrointestinal tract, spleen, and bone marrow.

Once the virus enters the cell, it may replicate, induce cell fusion and propagation of infection, or lead to cell death [12]. HIV targets the immune system, and the defining characteristic of HIV disease is progressive immunodeficiency caused by ongoing viral replication and cell-to-cell transmission within lymphoid tissue. With chronicity there is a progressive depletion of CD4 (helper-inducer) lymphocytes, the very T lymphocyte cohort whose function it is to direct other cells in the immune system, and to orchestrate the inactivation of virus antigen. The result is a depressed T lymphocyte functional capacity, characterized by depletion of helper T cells (T4), impaired killer T cell activity, and increased suppressor T cells (T8). Eventually, impaired immunity renders the individual vulnerable to opportunistic infection and certain malignancies. The common laboratory measure of immune function is the CD4 cell count. In persons with intact lymphocyte immune systems, the normal number of CD4 T cells ranges from 600 – 1,200 cells/mcL, depending on the stage and duration of infection.

CLINICAL MANIFESTATIONS AND DISEASE COURSE

The clinical manifestations of HIV disease are determined by the stage of primary infection and the chronicity and degree of the resultant cellular immunodeficiency state. Acute, primary HIV infection may be asymptomatic, but most often it is manifest by a subacute viral syndrome of malaise and fatigue, fever, sore throat, rash, myalgia, headache, and lymphadenopathy—clinical features similar in many respects to that seen with Epstein-Barr virus mononucleosis, cytomegalovirus (CMV), and certain types of herpes simplex infections [12]. A variety of atypical symptoms and signs may be seen, including aseptic meningitis syndrome, genital ulcers, and ulcerations involving the gingiva, palate, or buccal mucosa. The acute illness usually resolves in less than 14 days but may follow a protracted course over many weeks [12].

Early in the chronic phase of HIV infection, when the CD4 lymphocyte population is only modestly depressed and declining slowly, patients are often asymptomatic or may exhibit generalized lymphadenopathy and recurrent oropharyngeal candidiasis (thrush). During this stage, a reservoir of HIV is established throughout the lymphoid tissue system, including the spleen. Gradually, wandering (infected) macrophages disseminate the virus to certain internal organs, notably the brain, kidney, and adrenal glands.

Chronic HIV disease follows a variable course but eventually leads to a variety of clinical manifestations, some of which are directly related to the impact of chronic infection on vital organs. Common syndromes include HIV encephalopathy and dementia, peripheral neuropathy, interstitial nephropathy, a variety of skin eruptions, and signs of adrenal insufficiency.

The late clinical manifestations of HIV disease are most frequently the result of acquired immunodeficiency syndrome (AIDS) that follows progressive depletion of CD4+ T lymphocytes to levels <200 cells/mcL. AIDS-defining illnesses include secondary, opportunistic infections and certain malignancies usually encountered only in clinical settings of severely impaired cellular immunity.

Opportunistic infections are very common in persons with undiagnosed or poorly treated chronic HIV infection and are of two types. The first type is infection newly acquired by exposure to microorganisms normally nonpathogenic, or of low pathogenicity, for persons with a healthy immune system. Examples are *Pneumocystis jiroveci*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, and atypical mycobacteria, all of which are commonly associated with inhalational exposures and transient colonization of the respiratory tract in healthy individuals. The second type is reactivation of latent infection acquired earlier in life, which typically remains dormant throughout life. Examples of this type are CMV, *Toxoplasma gondii*, *Mycobacterium tuberculosis*, and *Histoplasma capsulatum*. The advent of an opportunistic infection may serve as the herald sign of unrecognized, undiagnosed chronic HIV infection/AIDS.

Clinically, these infections tend to present in one of several distinct syndromes, with useful differential diagnosis considerations:

- Pneumonia: *Pneumocystis jiroveci* pneumonia (PJP), *Mycobacterium avium* complex (MAC), cryptococcosis, histoplasmosis
- Meningoencephalitis: Toxoplasmosis, cryptococcosis, tuberculosis
- Gastrointestinal disease (diarrhea): Common bacterial dysentery, cryptosporidium, fungal and atypical mycobacterial infection
- Fever of unknown origin (often with abdominal complaints, hepatosplenomegaly, and/or lymphadenopathy): CMV, MAC, tuberculosis, histoplasmosis

Late clinical manifestations related to HIV-induced malignancy include Kaposi sarcoma of the skin or respiratory tract and lymphoma presenting as lymphadenopathy, splenomegaly, or focal gastrointestinal disease.

Without satisfactory antiretroviral therapy, the usual patient with HIV/AIDS experiences a slow, inexorable wasting illness punctuated by periods of feverishness and diarrhea, becoming increasingly anorectic, malnourished, and lethargic. Late clinical signs include muscle wasting and weakness, anemia and thrombocytopenia, lymphadenopathy, pulmonary infiltrates, and neurologic abnormalities (such as dementia, peripheral neuropathy, and tremors). The median survival of patients with advanced HIV/AIDS (CD4 count <50 cells/mcL) is approximately 12 to 18 months. Patients succumb to complications of uncontrolled infection, malignancy, or critical organ failure (such as uremia or adrenal insufficiency).

HIV TESTING

There are several recommendations for HIV screening. The U.S. Preventive Services Task Force (USPSTF) and the Agency for Healthcare Research and Quality (AHRQ) recommend screening for HIV infection in all adolescents and adults 15 to 65 years of age, younger adolescents and older adults at increased risk, and all pregnant women [13; 14].

The initial testing for HIV generally consists of an FDA-approved, fourth-generation antigen/antibody combination immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen to identify both established and acute infections [15]. If this test is reactive, repeat testing is recommended to differentiate HIV-1 antibodies from HIV-2 antibodies. If this second test is non-reactive, testing with an FDA-approved HIV-1 nucleic acid test is indicated [15]. It is important to note that HIV-2 is not reliably identified by usual immunoblot antibody tests. Additional testing specific to HIV-2 should be considered if HIV-1 test results are atypical or inconsistent with clinical findings, especially for persons from West Africa [3].

Other available tests, including enzyme-linked immunosorbent assay, may be used if the preferred combination immunoassay is not available. The HIV-1 Western blot and HIV-1 immunofluorescence assay, previously recommended to make a laboratory diagnosis of HIV-1 infection, are no longer part of the recommended testing algorithm [15].

TRANSMISSION OF HIV

HIV is transmitted person-to-person across mucosal or cutaneous barriers by exposure to infected genital secretions or blood and blood products. The common modes of transmission are sexual intercourse, injection drug use, infusion of blood products, and perinatal transmission. The risk from whole blood, packed cell, and fresh frozen plasma is, at present, extremely low by virtue of more sensitive crossmatching and screening techniques.

RISK CATEGORIES

On the basis of newly reported cases, the transmission categories are [10]:

- Male-to-male sexual contact (MSM)
- Injecting drug users (IDUs)
- MSM who inject drugs
- Heterosexual contact
- Perinatal transmission
- Other (includes hemophilia, blood transfusion, and risk factor not reported or not identified)

The CDC has published guidelines for medical professionals to integrate HIV prevention into the regular medical care of those living with HIV. The three major components of the recommendation are: screening for HIV transmission risk behaviors and sexually transmitted infections (STIs); providing brief, behavioral risk-reduction interventions in the office setting and referring selected patients for additional prevention interventions and other related services; and facilitating notification and counseling for sex and needle-sharing partners of infected persons [16; 17].

MODES OF TRANSMISSION

Sexual Transmission of HIV

HIV has been isolated from blood, seminal fluid, spermatozoa, pre-ejaculate, vaginal secretions, urine, cerebrospinal fluid, saliva, tears, and breast milk of infected individuals. No cases of HIV infection have been traced to saliva or tears (though traces of the virus are present in these fluids) [18]. The virus is found in greater concentration in semen than in vaginal fluids, leading to a hypothesis that male-to-female transmission could occur more easily than female-to-male. Sexual behavior that involves exposure to blood is likely to increase transmission risks. Transmission could also occur through contact with infected bowel epithelial cells in anal intercourse, in addition to access to the bloodstream through breaks in the rectal mucosa.

Posing the highest risk of infection is unprotected anal receptive intercourse, followed by unprotected vaginal intercourse and unprotected insertive anal intercourse (particularly for uncircumcised men) [19; 20]. Risk is reduced through the use of latex condoms. For the wearer, latex condoms provide a mechanical barrier limiting penile exposure to infectious cervical, vaginal, vulvar, or rectal secretions or lesions. Likewise, the partner is protected from infectious pre-ejaculate, semen, and penile lesions. Oil-based lubricants may make latex condoms ineffective and should not be used; water-soluble lubricants are considered safe. Natural membrane condoms (made from lamb cecum) contain small pores and do not block HIV passage. It is estimated that latex condom use reduces the risk of HIV transmission by approximately 70% to 80% [21; 22; 23]. Although abstinence from sexual contact is the sole way to absolutely prevent transmission, sexual activity in a mutually monogamous relationship in which neither partner is HIV-infected and no other risk factors are present is considered safe [4]. However, men who identify publicly as heterosexual and generally have committed relationships with women, but who also engage in sexual activity with other men, may be a transmission bridge to heterosexual women [24]. To better understand the actual extent of this behavior and its impact on HIV transmission, more research is necessary.

Numerous studies have demonstrated that oral sex can result in the transmission of HIV and other STIs. While the risk of HIV transmission through oral sex is much smaller than the risk from anal or vaginal sex, there are several co-factors that can increase this risk, including oral ulcers, bleeding gums, genital sores, and the presence of other STIs. Prevention includes the use of latex condoms, a natural rubber latex sheet, plastic food wrap, a cut open condom, or a dental dam, all of which serve as a physical barrier to transmission [25].

Blood Donor Products

It has been estimated that a milliliter of HIV-infected human blood contains up to 10,000 copies of the virus. In comparison, a milliliter of blood infected with hepatitis B virus has 100 million to 1 billion infective organisms [26; 27]. Even so, HIV is transmitted via blood, primarily through sharing of contaminated needles among IDUs and, rarely, through blood transfusion. Transmission of HIV-1 has occurred after transfusion of the following components: whole blood, packed red blood cells (including washed and buffy coat poor), fresh frozen plasma, cryoprecipitate, platelets, and plasma-derived products, depending on the production process. With the implementation of a donor screening program of the nation's blood supply in 1985 and advances in the treatment of donated blood products, blood transfusion is now even safer; the current risk of transmission of HIV through this route is conservatively estimated to be between 1 in 1.5 million [28]. It is possible that before blood screening implementation, more than 12,000 people were infected [29]. A large percentage of persons with hemophilia acquired HIV in this manner. Donor screening, HIV testing, and heat treatment of the clotting factor have greatly reduced the risks.

Needle Sharing

Transmission of HIV among IDUs occurs primarily through contamination of injection paraphernalia with infected blood. The risk of sustaining HIV infection from a needle stick with infected blood is approximately 1 in 300 [30]. Behavior such as needle sharing, "booting" the injection with blood, and performing frequent injections increases the risk. Crack cocaine use (by injection or smoking) is associated with a higher prevalence of HIV infection. This may in part be attributed to the exchange of cocaine for sex. Sharing of equipment is common due to legal and financial restrictions and cultural norms, and some studies have linked higher levels of psychologic distress (e.g., anxiety and depressive symptoms) with an increased risk for needle sharing [31]. Secondary transmission occurs to children and sexual partners. Preventative strategies include medication-assisted drug treatment, onsite medical care in a drug treatment program, recruitment of "street" outreach workers for intensive drug and sex risk-reduction educational campaigns, teaching addicts to sterilize their equipment between use, the free provision or exchange of sterile injection equipment (as allowed by law), distribution of condoms and bleach to clean drug use equipment, or a combination of these interventions.

Perinatal Transmission

In the absence of prophylactic treatment, approximately 25% to 30% of children born to HIV-infected mothers will contract HIV infection; this increases to 50% with prolonged breastfeeding [32]. HIV is transmitted to infants by transplacental spread from mother to fetus in utero, during parturition, or through breastfeeding after birth. Because infants have underdeveloped natural resistance systems, they are highly susceptible to many infections, including HIV. Transmission usually occurs during labor and delivery and the early breastfeeding stage [33].

Worldwide, perinatal transmission accounts for most HIV infections among children. In the United States, perinatal transmission has been markedly decreased, by more than 90%, since the mid-1990s [34]. Studies have shown the beneficial effect of treating pregnant women and newborns with zidovudine (ZDV) to prevent transmission to the child, resulting in dramatic declines in the incidence of perinatally acquired HIV [35]. Standard screening of all pregnant women is necessary to reduce transmission of HIV to infants.

Organ Transplantation

Because these procedures are less common than other transmission-related activities, there have been very few case reports of HIV acquisition by this route. HIV has been transmitted via transplanted kidneys, liver, heart, pancreas, bone, and, possibly, skin grafts and through artificial insemination. HIV testing is used in these circumstances to rule out infection. Most cases of transmission through transplants of organs, bone, or tissue occurred before HIV screening was available. However, in 2007, four organ transplant recipients contracted HIV and hepatitis C from a single organ donor, and in 2009, HIV was transmitted by a living kidney donor [36; 37]. These were the first cases of HIV infection resulting from transplantation since 1985. Though the donors were tested for HIV and hepatitis, the tests resulted in false negatives. As with blood transfusions, donors testing antibody seronegative may pass HIV infection on to recipients. The use of nucleic acid testing and reconsideration of the use of high-risk donors have both been recommended to ensure the safety of donor recipients [36].

Occupational Exposures

Transmission due to occupational exposure of healthcare workers has occurred in needlestick accidents and blood splashes to the mucous membranes. Needlestick is the most common route. Thousands of healthcare personnel who were so exposed have been studied, and only 58 cases of well-documented infection have been reported in the United States (24 of which were nurses) [38]. The risk of infection through this route is low, and every effort should be made to decrease the exposure rate. Educational efforts, implementation of engineering controls in needled and sharp-edged medical devices, the use of hard plastic needle disposal units where these devices are most frequently used, and the development of procedural details to avoid blood and body fluid contact have greatly reduced the exposure rate. Healthcare personnel should apply Universal Precautions, as discussed in the Occupational Safety and Health Administration (OSHA) Bloodborne Pathogens standard regulations, to all activities to avoid contact with human fluids.

Postexposure Prophylaxis

The U.S. Public Health Service (PHS) provides updated guidance for managing healthcare personnel who have occupational exposure to blood and/or other bodily fluids from a person suspected or known to have HIV infection [39]. Because most occupational HIV exposures do not result in transmission of HIV, potential toxicity should be carefully considered when prescribing postexposure prophylaxis (PEP). The 2013 updated guidelines for occupational PEP focused on tolerability, side effects, toxicity, safety in pregnancy and lactation, pill burden, and frequency of dosing to maximize adherence to a PEP regimen. Although the principles of exposure management remain unchanged, recommended PEP regimens and the duration of follow-up HIV testing for exposed personnel were updated in 2018 [39]. When possible, these recommendations should be implemented in consultation with persons having expertise in antiretroviral therapy and HIV transmission, due to the complexity of selecting appropriate treatment.

The 2018 updated PHS guidelines recommend initiating PEP medication as soon as possible after occupational exposure to HIV and to continue the regimen for four weeks. PEP regimens should contain three (or more) antiretroviral drugs for all occupational exposures to HIV [39]. Examples of recommended PEP regimens include those consisting of a dual nucleoside reverse transcriptase inhibitor (NRTI) backbone plus an integrase strand transfer inhibitor (INSTI), protease inhibitor (PI) (boosted with ritonavir), or non-nucleoside reverse transcriptase inhibitor (NNRTI). The PHS preferred regimen for management of most healthcare professionals' exposures to HIV is emtricitabine and tenofovir dispensed together as Truvada, a fixed-dose combination tablet, 1 mg once daily, plus raltegravir, 400 mg twice daily [39]. This preparation is available as a starter packet that should be stocked at every healthcare facility where exposure to HIV is possible. As discussed, the regimen has been selected for its tolerability and safety profile. There are several alternative regimens that may be selected due to individual patient concerns. For example, tenofovir is associated with renal toxicity, and an alternative NRTI/NNRTI pair, such as zidovudine plus lamivudine (available as Combivir), would be selected for patients with renal disease [39].

Healthcare professionals with occupational exposure to HIV should receive close follow-up to assure counseling, baseline and follow-up HIV testing, and medical evaluation regardless of whether they receive PEP. The 2018 PHS guideline highlights the importance of follow-up within 72 hours of an HIV exposure to allow the initial shock to fade and to provide greater opportunity for full understanding of the risks and benefits of PEP; confirmation testing

to ensure the necessity of PEP; increase adherence to PEP; monitoring for adverse reactions and side effects; and treating comorbidities and altering the regimen [39]. This window provides an opportunity to discuss the importance of preventing secondary transmission of HIV in the 6 to 12 weeks following initial infection. If a newer fourth-generation HIV p24 antigen-HIV antibody test is utilized for follow-up, then HIV-antibody testing may be concluded at four months after exposure. If a newer testing platform is not available, follow-up HIV testing should be performed for a six-month postexposure period (e.g., at 6 weeks, 12 weeks, and 6 months) [39]. It is unclear whether an extended follow-up period (e.g., 12 months) is indicated for individuals not coinfected with hepatitis C and HIV. If PEP is used, drug-toxicity monitoring should be performed at baseline and again two weeks after starting PEP. Clinical judgment, based on medical conditions that may exist in pre-exposure and/or as a result of the regimen, should determine the scope of testing. If the source patient is found to be HIV negative, PEP should be discontinued immediately [39].

Nonoccupational Postexposure Prophylaxis (nPEP)

In 2016, the CDC published updated guidelines for the recommendation of PEP for nonoccupational exposures. This section is taken from Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016.

Healthcare providers should evaluate persons rapidly for nPEP when care is sought within 72 hours after a potential nonoccupational exposure that presents a substantial risk for HIV acquisition. All persons considered for nPEP should have determination of their HIV infection status by HIV testing, preferably by using rapid combined Ag/Ab, or antibody blood tests. If rapid HIV blood test results are unavailable, and nPEP is otherwise indicated, it should be initiated without delay and can be discontinued if the patient is later determined to have HIV infection already or the source is determined not to have HIV infection. nPEP is recommended when the source of the body fluids is known to be HIV-positive and the reported exposure presents a substantial risk for transmission. nPEP is not recommended when the reported exposure presents no substantial risk of HIV transmission or when care is sought more than 72 hours after potential exposure. A case-by-case determination about the nPEP is recommended when the HIV infection status of the source of the body fluids is unknown and the reported exposure presents a substantial risk for transmission if the source did have HIV infection.

Healthcare providers should evaluate persons rapidly for nPEP when care is sought within 72 hours after a potential nonoccupational exposure that presents a substantial risk for HIV acquisition. All persons considered for nPEP should have determination of their HIV infection status by HIV testing, preferably by using rapid combined Ag/Ab, or antibody blood tests. If rapid HIV blood test results are unavailable, and nPEP is otherwise indicated, it should be initiated without delay and can be discontinued if the patient is later determined to have HIV infection already or the source is determined not to have HIV infection. nPEP is recommended when the source of the body fluids is known to be HIV-positive and the reported exposure presents a substantial risk for transmission. nPEP is not recommended when the reported exposure presents no substantial risk of HIV transmission or when care is sought more than 72 hours after potential exposure. A case-by-case determination about the nPEP is recommended when the HIV infection status of the source of the body fluids is unknown and the reported exposure presents a substantial risk for transmission if the source did have HIV infection.

All persons offered nPEP should be prescribed a 28-day course of a three-drug antiretroviral regimen. The preferred regimen for otherwise healthy adults and adolescents is tenofovir disoproxil fumarate (300 mg) with emtricitabine (200 mg) once daily plus raltegravir 400 mg twice daily or dolutegravir 50 mg daily.

All persons evaluated for possible nPEP should be provided any indicated prevention, treatment, or supportive care for other exposure-associated health risks and conditions (e.g., bacterial sexually transmitted infections, traumatic injuries, hepatitis B virus and hepatitis C virus infection, or pregnancy). All persons who report behaviors or situations that place them at risk for frequently recurring HIV exposures (e.g., injection drug use, sex without condoms) or who report receipt of a course of nPEP in the past year should be provided risk-reduction counseling and intervention services, including consideration of pre-exposure prophylaxis.

NATURAL HISTORY AND CLASSIFICATION OF HIV INFECTION

LATENCY PERIOD

Clinical latency, sometimes referred to as the window period, is the time elapsed between acquisition of the virus and the body's immune response sufficient to generate detectable antibody. This latent period is longer for HIV than for most other viral pathogens and is variable among newly infected individuals.

ACUTE HIV INFECTION

As discussed, HIV infection is a protracted illness that passes through several stages and, if untreated, carries an 80% mortality rate at 10 years. Within 15 to 30 days after acquisition of HIV infection, the majority of patients (50% to 90% in reported series) develop an acute retroviral syndrome similar to infectious mononucleosis [12]. Symptoms include fever, sore throat, malaise, rash, diarrhea, lymphadenopathy, mucocutaneous ulcerations and weight loss averaging 10 pounds. A variety of neurologic syndromes including encephalitis may occur. The illness is self-limited, with an average duration of two to three weeks. Laboratory abnormalities include lymphopenia, atypical lymphocytosis, thrombocytopenia, and a decreased CD4 cell count. During this early phase of clinical illness, HIV antibody tests are often negative and the diagnosis rests on the demonstration of HIV P24 antigen or, preferably, quantitative plasma HIV RNA. Concentrations of HIV RNA in the blood (viral load) are high during the acute syndrome.

Following the host immune response, coincident with seroconversion and the rise in CD8 cytotoxic T cells, the viral load decreases steadily, reaching a relatively stable level at about six months. At this juncture, the degree of viral load correlates with the subsequent pace of disease progression. Patients having the highest viral loads, exhibit the most rapid progression to AIDS. As a result of the ongoing, protracted infection of target lymphocytes, the CD4 count gradually declines over time in the absence of treatment, at the average annual rate of about 50 cells/mcL.

ASYMPTOMATIC HIV INFECTION

Approximately 10% to 20% of persons with newly acquired HIV are asymptomatic during the initial two months following acute infection. While initial routine laboratory studies are relatively normal, serologic and virologic studies are positive and these patients show the same host-virus dynamics, including gradual decline in CD4 count, as that seen in symptomatic patients.

The serologic diagnosis of HIV infection in an asymptomatic patient does not, in and of itself, establish how recently the patient became infected. The stage of infection may be estimated on the basis of careful history and physical examination, and a standard laboratory evaluation that includes complete blood counts, lymphocyte subsets or CD4 count, and viral load. The duration of this asymptomatic stage is variable depending on prevailing CD4 count and viral load and is amenable to treatment with combination antiretroviral therapy (cART).

PERSISTENT GENERALIZED LYMPHADENOPATHY

In the months following acute infection, whether symptomatic or not, many patients have persistent, painless generalized lymphadenopathy (PGL) without other disease manifestations. PGL is defined as palpable lymph node enlargement of 1 cm or greater at two or more extrainguinal sites that persists for more than three months in the absence of a concurrent illness or explanation other than HIV infection. In some cases, lymphadenopathy regresses as HIV disease advances, probably because the architecture of the lymph node is gradually destroyed [4].

CHRONIC HIV AND DISEASE PROGRESSION

Chronic, asymptomatic HIV infection with ongoing low-level viral activity may last for many years before eventual progression to AIDS. Symptomatic illness can be expected to supervene as the CD4 count declines to a level less than 200 cells/mcL, as this correlates with severe immunodeficiency. The CDC defines late-stage HIV infection as AIDS on the basis of two criteria: CD4 count less than 200 cells/mcL or a characteristic AIDS-defining illness such as PJP, central nervous system (CNS) toxoplasmosis, or other opportunistic infections or tumors (Kaposi sarcoma). A variety of clinical syndromes may supervene at this juncture including dementia, peripheral neuropathy, wasting syndrome, and chronic diarrhea. In the United States, the most common AIDS-defining opportunistic diseases are: PJP, Kaposi sarcoma, candidiasis, cryptococcosis, cryptosporidiosis, CMV, atypical mycobacteriosis, systemic herpes, toxoplasmosis, and tuberculosis [41].

In the absence of effective therapy, the average survival is approximately 3.5 years after the patient's CD4 count has reached 200 cells/mcL and 1.5 years for the patient who has developed an AIDS-defining diagnosis. The natural history and the prognosis for the patient with chronic HIV infection have been dramatically altered by antiretroviral therapy, especially by the use of cART that followed the introduction of protease inhibitors (PIs) and NNRTIs in 1996.

MANAGEMENT OF HIV INFECTION

Primary care providers in consultation with specialists are playing an increasing role in the care of HIV-infected individuals. It is not possible for all care to be delivered by infectious disease and oncology specialists. Moreover, with early cART and prophylaxis for opportunistic infections, HIV disease shares features of other multisystem, chronic diseases characterized by acute exacerbations and end-stage manifestations. A study of serodifferent heterosexual and MSM couples in which the HIV-positive partner was on cART found no documented cases of within-couple transmission of HIV, despite engaging in condomless sex, after an average of 1.3 years [78].

Primary care providers should conduct risk factor assessment of their patients and, when appropriate, screen for HIV infection with pretest and post-test counseling. For persons who test positive, information on available medical and mental health services should be provided as well as guidance for contacting sexual or needle-sharing partners. Patients with HIV infection should be seen at regular intervals by a primary care provider to perform periodic physical examinations, monitor prognostic markers (e.g., CD4 count, viral load), initiate and monitor antiviral and prophylactic therapy, and provide supportive counseling. Specialists should be consulted for patients intolerant of standard drugs, those in need of systemic chemotherapy, and those with complicated opportunistic infections. In some cases, a single specialist consultation with follow-up to the primary care physician will provide the needed expertise while ensuring continuity of care.

Standard laboratory tests for patients with HIV infection may include:

- HIV serology
- Quantitative HIV RNA
- CD4 count
- Complete blood count (CBC)
- Chest x-ray

- Hepatitis serology and liver chemistry panel
- Syphilis serology
- Purified protein derivative (PPD) skin test to diagnose tuberculosis

ANTIRETROVIRAL THERAPY

HIV disease is treated with therapeutic regimens consisting of a combination of three or more antiretroviral drugs. Current cART does not cure HIV infection but does suppress viral replication and allow immune system recovery sufficient to restore a sense of well-being and regain the capacity to avoid opportunistic infections. Since 2016, the WHO has recommended that all people living with HIV be provided lifelong ART, including children, adolescents, adults, and pregnant and breastfeeding women, regardless of clinical status or CD4 cell count [5]. By June 2021, 187 countries had adopted this recommendation, covering 99% of all people living with HIV globally.

cART consists of two or more drugs selected from eight major classes of agents: NRTIs, NNRTIs, PIs, fusion inhibitors (FIs), INSTIs, chemokine (C-C motif) receptor 5 (CCR5) antagonists, gp120 attachment inhibitors, and capsid inhibitors. Initiated in 1995 in the United States, antiretroviral therapy regimens have been effective in dramatically decreasing HIV-related morbidity and mortality and should be considered for all HIV-infected persons who qualify for such therapy. In addition to combination therapy, the sequencing of drugs and the preservation of future treatment options are also important. Two types of combination regimens are recommended as initial therapy: INSTI-based regimens or a PI-based regimen. The goal of these regimens is to effectively reduce HIV-associated morbidity, prolong the duration and quality of survival, restore and preserve immunologic function, and prevent HIV transmission while also avoiding drug resistance [42]. A significant proportion of patients starting cART are infected with drug-resistant strains of HIV, which may lead to suboptimal virologic responses. Therefore, pretreatment genotypic resistance testing should be used to guide selection of the most optimal initial regimen [42].

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

NRTIs, used singularly or in combination, can increase CD4 count, decrease viral load, and prolong survival. Sequential monotherapy is followed eventually by clinical failure based on the emergence of drug resistance in HIV. Combinations of two NRTIs result in better viral suppression, more sustained CD4 counts and decreased emergence of resistance. Available NRTI agents include: abacavir (Ziagen, ABC); zidovudine (Retrovir, ZDV, AZT); lamivudine (Epivir, 3TC); and emtricitabine (Emtriva, FTC) [43]. Tenofovir (Viread, TDF) is often categorized as an NRTI but is actually a nucleotide reverse transcriptase inhibitor.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

NNRTIs have a high affinity for the active site of HIV-RT. When used as a single agent, this class is associated with rapid emergence of resistance in as little as six weeks. Thus, these drugs should not be used as single agents but are best employed in combination regimens for patients who have not received prior antiretroviral therapy. Available agents include: efavirenz (Sustiva, EFV); doravirine (Pifeltro, DOR); nevirapine (Viramune, NVP; viramune XR); etravirine (Intelence); and rilpivirine (Edurant) [43].

Protease Inhibitors (PIs)

Development of mature infectious virus depends upon enzymatic cleavage of HIV transcribed polyprotein by HIV protease. In binding to the active site of the HIV protease, PIs interrupt the formation of mature infectious particles and reduce viral replication by as much as 99%. Resistance to PIs develops rapidly when these agents are used alone. However, in combination with nucleoside analogs the effect can last for years, often resulting in a reduction of viral load to undetectable levels. Available agents include: ritonavir (Norvir, RTV); saquinavir (Invirase, Fortovase, SQV); atazanavir (Reyataz, ATZ); tipranavir (Aptivus, TPV); darunavir (Prezista; DRV); and fosamprenavir (Lexiva, FPV) [43].

Fusion Inhibitors (FIs)

Enfuvirtide, a fusion inhibitor, works by blocking the ability of HIV to infect healthy CD4 cells [43]. When used in combination with other anti-HIV medications, enfuvirtide can reduce the amount of HIV in the blood and increase the number of CD4 cells, slowing the progression of HIV in patients who have developed resistance to currently available medications.

CCR5 Antagonists

Maraviroc is a CCR5 antagonist; it blocks replication of the virus by preventing it from entering noninfected CD4 cells via the predominant route of entry, the CCR5 co-receptor [44]. This medication is intended for use in combination with other antiretroviral agents in treatment-experienced patients with evidence of viral replication and HIV-1 strains resistant to multiple agents [44]. Because both fusion inhibitors and CCR5 antagonists block HIV from entering CD4 cells, they are sometimes grouped together under the category of entry inhibitors.

Integrase Strand Transfer Inhibitors (INSTIs)

In 2007, the FDA approved raltegravir, the first agent in a class known as integrase strand transfer inhibitors, or INSTIs [46]. Two additional integrase inhibitors, dolutegravir and elvitegravir, were approved by the FDA in 2013 and 2014 [43]. These agents act by preventing the viral DNA from inserting into the host DNA, effectively limiting infection of additional cells and decreasing viral load [46]. INSTIs are approved for use in combination with other antiretrovirals in treatment-experienced and treatment-naïve patients with evidence of HIV replication.

gp120 Attachment Inhibitors

In 2020, the FDA approved the first gp120 attachment inhibitor, fostemsavir, for the treatment of HIV in patients whose infection cannot be successfully treated with other therapies because of resistance, intolerance, or safety considerations [80].

Capsid Inhibitors

In 2022, the FDA approved lenacapavir, the first capsid inhibitor, for the treatment of HIV-1 infection in adults for whom other available treatments have failed or are inappropriate due to resistance, intolerance, or safety considerations [83]. These agents directly target virus' protein shell (the capsid), interfering with multiple essential steps of the viral lifecycle. Lenacapavir is initiated either with 2 or 15 days of oral therapy, followed by subcutaneous injections (927 mg) every six months thereafter.

Pharmacokinetic Enhancers

In an effort to improve the efficacy of other antiretroviral medications in a cART regimen, a pharmacokinetic enhancer may also be included. The agents most commonly used for this purpose are ritonavir (a PI) and cobicistat. Both of these agents inhibit cytochrome P450 (CYP) 3A enzymes, prolonging the effects of other medications [47]. However, they are not interchangeable; cobicistat is a more potent inhibitor of CYP [47]. The use of pharmacokinetic enhancers increases systemic exposure of effective antiretroviral medications, allowing for less frequent dosing and a lower pill burden.

Post-Attachment Inhibitors

Post-attachment inhibitors block CD4 receptors on the surface of certain immune cells that HIV needs to enter the cells [43]. In 2018, the FDA approved ibalizumab (Trogarzo, IBA), the first of its class.

Multi-Class Combination Products

Patient compliance may be improved with therapies that combine more than one drug into a single pill, making it easier for patients to comply with their medication regimen. As of 2022, there were 23 combination medications available [43]:

- Atripla: Efavirenz, emtricitabine, and tenofovir
- Biktarvy: Bictegravir, emtricitabine, and tenofovir alafenamide
- Cabenuva: Cabotegravir and rilpivirine
- Cimduo: Lamivudine and tenofovir disoproxil fumarate

- Combivir: Lamivudine and zidovudine
- Complera: Emtricitabine, rilpivirine, and tenofovir
- Delstrigo: Doravirine, lamivudine, and tenofovir disoproxil fumarate
- Descovy: Emtricitabine and tenofovir
- Dovato: Dolutegravir and lamivudine
- Epzicom: Abacavir and lamivudine
- Evotaz: Atazanavir and cobicistat
- Genvoya: Elvitegravir, cobicistat, emtricitabine, and tenofovir
- Juluca: Dolutegravir and rilpivirine
- Kaletra: Lopinavir and ritonavir
- Odefsey: Emtricitabine, rilpivirine, and tenofovir
- Prezcobix: Darunavir and cobicistat
- Stribild: Elvitegravir, cobicistat, emtricitabine, and tenofovir
- Symfi: Efavirenz, lamivudine, and tenofovir disoproxil fumarate
- Symfi Lo: Efavirenz, lamivudine, and tenofovir disoproxil fumarate
- Symtuza: Darunavir, cobicistat, emtricitabine, and tenofovir alafenamide
- Triumeq: Abacavir, dolutegravir, and lamivudine
- Trizivir: Abacavir, lamivudine, and zidovudine
- Truvada: Emtricitabine and tenofovir

In 2021, the FDA approved the first monthly injectable cART–Cabenuva (cabotegravir/rilpivirine) [81]. This monthly injectable is an optional regimen to replace a current ART regimen in patients who are virologically suppressed on a stable regimen with no history of treatment failure and with no known HIV resistance to either cabotegravir or rilpivirine. This regimen is intended to improve compliance and quality of life for patients who have achieved control of HIV on daily oral therapy. Prior to initiating injectable therapy, oral therapy with cabotegravir/rilpivirine is started to ensure the agents are well-tolerated.

Initiation of Therapy

The decision to initiate antiretroviral therapy is one that requires careful discussion with the patient, usually in consultation with an infectious disease specialist or other physician well versed in the use of cART. Physicians and patients alike should be aware of the advantages, potential toxicities, and complexity of monitoring therapy. Clinicians should consult PHS, the National Institutes of Health (NIH), and Infectious Diseases Society of America (IDSA) published guidelines for the use of antiretroviral agents in adults and adolescents living with HIV [42]. A typical initial regimen consists of three HIV medications from two drug classes. At the present time, the most active triple-drug regimen in a previously untreated patient can be expected to reduce the viral load below detectable levels, increase CD4 counts by an average of 100–150 cells/mcL, reduce the risk of HIV-associated complications, and prolong survival. However, the ability to achieve this advantage depends on the patient's willingness to accept a complex medical regimen that requires "many pills," rigorous compliance, frequent follow-up, and moderate risk for drug toxicity. In reaching a decision it is helpful to bear in mind that prognosis is determined by viral load and the CD4 count. Patients having a viral load in excess of 60,000 copies per milliliter have a relatively rapid course and average survival of a little more than four years. In contrast, those with less than 6,000 copies per milliliter have an average survival of more than 10 years. The CD4 count is also a prognostic factor, as counts less than 350 cells/mcL indicate severe damage to immune function and corresponding risk for opportunistic infection.

Antiretroviral therapy should be initiated immediately for all patients infected with HIV in order to reduce the risk of disease progression and limit transmission [42]. There is growing evidence that early initiation of cART is effective in preventing clinical events (e.g., non-AIDS malignancies, infection, AIDS-defining illness) regardless of pre-treatment CD4 count [48; 49]. Advances in the development of antiretroviral medications and combination tablets makes adherence to therapy more effective, more convenient, and better tolerated than regimens used in the past. Deferral of therapy may be considered in patients with high CD4 counts (e.g., more than 500 cells/mcL) if adherence will be very difficult or impossible, comorbidities complicate or prohibit antiviral therapy, or a patient is considered a long-term non-progressor [42].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Panel on Antiretroviral Guidelines for Adults and Adolescents, antiretroviral therapy is recommended for all individuals with HIV, including those with early HIV infection and should be initiated as soon as possible after diagnosis.

(https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Last accessed March 11, 2022.)

Strength of Recommendation: AII (Strong recommendation based on well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes)

For treatment-naïve patients, initial recommended therapy generally consists of two NRTIs in combination with a third active antiretroviral drug from one of three drug classes: an INSTI, an NNRTI, or a PI with a pharmacokinetic enhancer (cobicistat or ritonavir) [42]. These regimens result in maximum reduction of viral load for the longest period of time. When used as initial therapy, these regimens will achieve the goal of no detectable virus in the majority of patients after four to six months [42].

PREVENTION OF OPPORTUNISTIC INFECTIONS

Absent timely diagnosis and treatment of HIV, opportunistic infections are often the first clinical indication a patient has AIDS. Pneumocystis pneumonia, toxoplasma encephalitis, cytomegalovirus retinitis, cryptococcal meningitis, and disseminated atypical mycobacterial infection are often hallmarks of AIDS. Before effective cART, these complications occurred on average 7 to 10 years after HIV infection, and patients usually survived only 1 to 2 years after the initial manifestation of AIDS [50].

Depending on the CD4 count and other risk factors, asymptomatic patients with HIV may benefit from prescribed prophylaxis against opportunistic infections. Achieving and maintaining durable viral suppression with cART is important in prevention of infection; however, the CDC estimates only about half of diagnosed patients linked to care have durable viral suppression [50]. Poor adherence and unfavorable pharmacokinetics are among causes for suboptimal response to treatment. Recommendations for antimicrobial prophylaxis of opportunistic infections are summarized in ***Table 1*** according to guidelines provided by the CDC, the NIH, and IDSA [50]. Prophylactic therapy for these conditions is strongly recommended because these infections are relatively common in patients with HIV, preventive therapy is simple and cost-effective, and efficacy has been established in clinical studies. In addition, all patients should be vaccinated with pneumococcal vaccine. Hepatitis B vaccination should be considered in patients whose serologic testing indicates susceptibility.

The CDC, the National Institutes of Health, and the IDSA have developed guidelines for the prevention of opportunistic infections among HIV-infected individuals [50]. The guidelines are specific to each opportunistic infection and can be viewed at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection.

PROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE AMONG ADULTS AND ADOLESCENTS INFECTED WITH HIV			
Pathogen	**Indication**	**Preventive Regimen**	
		Preferred[a]	**Alternative**
Pneumocystis jiroveci pneumonia (PJP)	CD4 count <200 cells/mcL (AI); or oropharyngeal candidiasis (AII), or CD4 <14% (BII); or history of AIDS-defining illness (BII), or CD4 count >200 but <250 cells/mcL if monitoring CD4 cell count every three months is not possible (BII)	Trimethoprim-sulfamethoxazole (TMP-SMZ) 1 double-strength (DS) daily (AI), or TMP-SMX 1 single-strength (SS) daily (AI)	TMP-SMX 1 DS three times weekly (TIW) (BI); or dapsone 100 mg daily or 50 mg twice daily (BI); or dapsone 50 mg daily + pyrimethamine 50 mg + leucovorin 25 mg weekly (BI); or dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg weekly (BI); or aerosolized pentamidine 300 mg via Respirgard II nebulizer every month (BI); or atovaquone 1,500 mg daily (BI); or atovaquone 1,500 mg + pyrimethamine 25 mg + leucovorin 10 mg daily (CIII)
Toxoplasma gondii encephalitis	*Toxoplasma* immunoglobulin G (IgG)-positive patients with CD4 count <100 cells/mcL (AII). Seronegative patients receiving PJP prophylaxis not active against toxoplasmosis should have *Toxoplasma* serology retested if CD4 count decline to <100 cells/mcL (CIII). Prophylaxis should be initiated if seroconversion occurred (AII).	TMP-SMX 1 DS daily (AII)	TMP-SMX 1 DS TIW (BIII); or TMP-SMX 1 SS daily (BIII); or dapsone 50 mg daily + pyrimethamine 50 mg + leucovorin 25 mg weekly (BI); or dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg weekly (BI); or atovaquone 1,500 mg daily (CIII); or atovaquone 1,500 mg + pyrimethamine 25 mg + leucovorin 10 mg daily (CIII)
Latent *Mycobacterium tuberculosis* infection (LTBI)	A positive screening test for LTBI, with no evidence of active TB and no prior treatment for active TB or LTBI (AI); or close contact with a person with infectious TB, regardless of screening test results (AII)	Isoniazid (INH) 300 mg + pyridoxine 25 mg daily for nine months (AII); or INH 900 mg biweekly (by direct-observation therapy) + pyridoxine 25 mg daily for nine months (BII).	Rifampin 600 mg daily for four months (BIII); or rifabutin (dose adjusted based on concomitant ART) for four months (BIII). For drug-resistant TB, consult an expert or public health authorities (AII).
Disseminated *Mycobacterium avium* complex (MAC) disease	CD4 count <50 cells/mcL after ruling out active disseminated MAC disease based on clinical assessment (AI)	Azithromycin 1,200 mg once weekly (AI); or clarithromycin 500 mg twice daily (AI); or azithromycin 600 mg twice weekly (BIII)	Rifabutin 300 mg daily (dose adjusted based on concomitant ART) (BI); rule out active TB before starting
Streptococcus pneumoniae infection	Individuals who have not received any pneumococcal vaccine, regardless of CD4 count	13-valent pneumococcal conjugate vaccine (PCV13) 0.5 mL IM (AI), followed in eight weeks by PPV23 if CD4 count ≥ 200 cells/mcL	23-valent pneumococcal polysaccharide vaccine (PPV23) 0.5 mL IM (BII). For individuals who have previously received PPV23, one dose of PCV13 should be given at least one year after the last receipt of PPV23 (AII).
	Re-vaccination is recommended for patients 19 to 64 years of age and ≥5 years since the first PPV23 dose; or ≥65 years of age and ≥5 years since the previous PPV23 dose.	PPV23 0.5 mL IM or SQ (BIII)	—

Table 1 continues on next page.

PROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE AMONG ADULTS AND ADOLESCENTS INFECTED WITH HIV *(Continued)*			
Pathogen	**Indication**	**Preventive Regimen**	
		Preferred[a]	**Alternative**
Influenza A and B virus infection	All HIV-infected patients (AIII)	Inactivated influenza vaccine annually (AIII)	Note: Live-attenuated influenza vaccine is contraindicated in HIV-infected patients (AIII).
Syphilis	Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis within 90 days preceding the diagnosis, even if serologic test results are negative (AIII), or who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis >90 days before the diagnosis should be treated presumptively for early syphilis if serologic test results are not immediately available and the opportunity for follow-up is uncertain (AIII).	Benzathine penicillin G 2.4 million units IM for 1 dose (AII)	For penicillin-allergic patients: doxycycline 100 mg twice daily for 14 days (BII); or ceftriaxone 1 g IM or IV daily for 8–10 days (BII); or azithromycin 2 g for 1 dose (BII) (not recommended for MSM or pregnant women [AII])
Histoplasma capsulatum infection	CD4 count <150 cells/mcL and at high risk because of occupational exposure or living in a community with a hyperendemic rate of histoplasmosis (>10 cases/100 patient-years) (BI)	Itraconazole 200 mg daily (BI)	—
Coccidioidomycosis	A new positive IgM or IgG serologic test in patients who live in a disease-endemic area and with CD4 count <250 cells/mcL (BIII)	Fluconazole 400 mg daily (BII) or itraconazole 200 mg twice daily (BII)	Voriconazole 200 mg twice daily after a loading dose of 400 mg twice on first day; or posaconazole (delayed-release tablet) 300 mg daily; or posaconazole (oral suspension) 400 mg twice daily
Varicella-zoster virus (VZV) infection (pre-exposure)	Patients with CD4 counts ≥200 cells/mcL who have not been vaccinated, have no history of varicella or herpes zoster, or who are seronegative for VZV (CIII); vaccination not recommended for patients with CD4 counts <200 cells/mcL (AIII)	Primary varicella vaccination (Varivax), 2 doses (0.5 mL SQ each) administered three months apart (CIII).	VZV-susceptible household contacts of susceptible HIV-infected persons should be vaccinated to prevent potential transmission of VZV to their HIV-infected contacts (BIII).
Varicella-zoster virus (VZV) infection (post-exposure)	Close contact with a person with chickenpox or herpes zoster and is susceptible (i.e., no history of vaccination or of either condition or known to be VZV seronegative) (AIII)	Varicella-zoster immune globulin (VariZIG) 125 IU IM per 10 kg (maximum: 625 IU), administered as soon as possible and within 10 days after exposure (AIII)	Acyclovir 800 mg five times per day for 5–7 days (BIII); or valacyclovir 1 g three times per day for 5–7 days (BIII)

Table 1 continues on next page.

PROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE AMONG ADULTS AND ADOLESCENTS INFECTED WITH HIV *(Continued)*			
Pathogen	**Indication**	**Preventive Regimen**	
		Preferred[a]	**Alternative**
Human papillomavirus (HPV) infection	Age 11 to 26 years (BIII)	HPV 9-valent vaccine 0.5 mL IM at months 0,1–2, and 6 for men and women (BIII); patients that have completed the recombinant bivalent or quadrivalent vaccine series should receive the 9-valent vaccine as it protects against additional strains (CIII)	—
Hepatitis B virus (HBV) infection	Patients without chronic HBV or without immunity to HBV (i.e., anti-HBs <10 IU/mL) (AII); or patients with isolated anti-HBc and negative HBV DNA (BII). Early vaccination is recommended before CD4 count falls below 350 cells/mcL (AII). However, in patients with low CD4 cell counts, vaccination should not be deferred until CD4 count reaches >350 cells/mcL, because some patients with CD4 counts <200 cells/mcL do respond to vaccination (AII).	HBV vaccine IM (Engerix-B 20 mcg/mL or Recombivax HB 10 mcg/mL) at 0, 1, and 6 months (AII); HBV vaccine IM (Engerix-B 40 mcg/mL or Recombivax HB 20 mcg/mL), 0, 1, 2 and 6 months (BI); or combined HAV and HBV vaccine (Twinrix) 1 mL IM as a 3-dose (0, 1, and 6 months) or 4-dose (days 0, 7, 21 to 30, and 12 months) series (AII)	Some experts recommend vaccinating with 40-mcg doses of either recombinant HBV vaccine (CIII); some experts recommend a 4-dose schedule (BI). Data for a two-dose hepatitis B vaccine conjugated to a TLR9 agonist (Heplisav-B) are lacking in patients with HIV, but it is an option with a CIII recommendation. (In four randomized controlled trials, Heplisav-B was superior to 3 doses of recombinant vaccine in HIV-negative persons.)
	Vaccine non-responders: anti-HBs <10 IU/mL 1 month after vaccination series	Re-vaccinate with a second vaccine series (BIII)	HBV vaccine IM (Engerix-B 40 mcg/mL or Recombivax HB 20 mcg/mL), 0, 1, 2 and 6 months (BI)
Malaria	Travel to disease-endemic area	Recommendations are the same for HIV-infected and HIV-uninfected patients.	—
Penicillium marneffei	Patients with CD4 cell counts <100 cells/mcL who live or stay for a long period in rural areas in northern Thailand, Vietnam, or Southern China (BI)	Itraconazole 200 mg once daily (BI)	Fluconazole 400 mg once weekly (BII)
[a]All medications are taken orally unless otherwise indicated.			
Source: [50]			*Table 1*

TUBERCULOSIS AND HIV

Tuberculosis is the leading cause of morbidity and mortality among people living with HIV worldwide, with 1 million reported cases and 374,000 deaths in 2017 [52]. People coinfected with HIV and latent tuberculosis have a 20 to 30 times greater risk of developing active tuberculosis compared with people not infected with HIV [51]. While cART significantly decreases the risk of conversion from latent to active disease, patients with HIV remain at higher risk of tuberculosis disease than the general population [50]. Among individuals in the United States with tuberculosis, an estimated 8.6% are coinfected with HIV [51].

RECOMMENDATIONS RATING SCHEME	
Category	**Definition**
Strength of Recommendation	
A	Strong
B	Moderate
C	Optional
Level of Evidence	
I	One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II	One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
III	Expert opinion

In addition to the recommended prophylaxis to prevent a first episode of opportunistic tuberculosis, NIH/IDSA guidelines for the treatment of HIV-related active tuberculosis have been published [52]. In general, treatment of suspected tuberculosis for individuals with HIV is the same as treatment for individuals without HIV and should include an initial four-drug combination of isoniazid, rifampin, ethambutol, and pyrazinamide until susceptibility to isoniazid and rifampin has been confirmed [52]. If rapid drug sensitivity testing indicates resistance to rifampin, a multidrug-resistant tuberculosis regimen (including levofloxacin or moxifloxacin and either an aminoglycoside or capreomycin) should be used initially until conventional sensitivity results are available [52]. Guideline recommendations call for directly observed therapy for all patients with HIV-related tuberculosis; prolonged treatment (up to nine months) for patients with a delayed clinical or bacteriologic response to therapy or perhaps with cavitary disease on chest radiograph; and rifabutin-based regimens given at least three times a week for patients with tuberculosis and advanced HIV disease [52]. Special considerations apply to children and pregnant women with HIV-related tuberculosis.

Optimal management of HIV-related tuberculosis is complex, involving decisions around duration of therapy, timing of cART, and support services to assure adherence to observed therapy and regular follow-up care. Healthcare professionals should consult the guidelines to ensure use of the most effective management strategies for patients with tuberculosis and HIV, while concurrently promoting optimal cART for these patients.

COVID-19 AND HIV

The Office of AIDS Research Advisory Council provides interim guidance regarding COVID-19 risk and management for people with HIV [45]. The preponderance of evidence from clinical studies indicates that people with HIV are at risk for severe outcomes with COVID-19 compared with those without HIV and should be included in the category of high-risk medical conditions when developing vaccine priority. SARS-CoV-2 vaccination is recommended for persons with HIV regardless of CD4 or viral load, because the potential benefits outweigh potential risks [45]. Patients with HIV who have COVID-19 should be clinically managed in the same way as those in the general population with COVID-19, including when making medical triage determinations.

HIV INFECTION IN SPECIAL POPULATIONS

WOMEN LIVING WITH HIV INFECTION

Women now make up nearly half of all AIDS cases worldwide and approximately 25% in the United States [53]. The rate of HIV infection in women had been rising rapidly, but the proportion of new HIV diagnoses among women in 2010 (20%) represented a 21% decrease since 2008 [53; 56]. From 2016 to 2019, the annual incidence of HIV infection in women remained stable in the United States at 4,5 per 100,000; by comparison, the rate among men was five times higher (21.0) [9]. In the last 30 years, the proportion of AIDS cases in women has tripled, from 8% in 1985 to 24% in 2016 [53; 56]. In 1993, when the CDC expanded the case definition of AIDS, there was a 151% increase in the number of AIDS cases in women and a 105% increase in cases in men. More women were found to meet the AIDS case definition when the CD4+ T-lymphocyte count of <200 cells/mcL was added to the criteria. This may be evidence that the previous case definitions based on the clinical characteristics of men did not accurately reflect the clinical manifestations of HIV in women [54].

AIDS is no longer a leading cause of death in women overall in the United States, but it remains the fifth leading cause of death in African American women 35 to 44 years of age [55]. Women of color have been disproportionately affected by HIV/AIDS, with Black women accounting for 64% of new HIV diagnoses among women in the United States while representing only 13% of the female population [53]. Women of color also tend to contract HIV at a younger age than their White counterparts.

The risk for acquisition of HIV and the factors that may affect seroconversion in heterosexual women are areas of research. It is clear that, in the absence of protective measures, women are much more likely to become infected with HIV through heterosexual sex (i.e., vaginal or anal receptive sex) than men. Although latex condoms are effective at preventing transmission of HIV when used correctly and consistently, some women may be afraid of the repercussions of insisting on condom use with their partners [56].

Clinical Manifestations

Many symptoms and signs of acute HIV infection and non-specific manifestations, such as fevers, weight loss, and fatigue, are the same for women and men. Because past research has either excluded women altogether or included only small cohorts of women, it has been difficult to determine gender differences in the clinical course of HIV disease. More recent research indicates that women with HIV initially present with lower viral loads but may be more likely than men to progress to AIDS, regardless of the viral load [57]. cART appears to be more effective in preventing opportunistic infections and disease progression among women with HIV than among men, but it is also more likely to result in toxicities among women and men [58; 59].

Gender-specific manifestations of HIV disease include irregular menstruation, recurrent vulvovaginal candidiasis, human papillomavirus (HPV)-related cervical dysplasia (abnormal, precancerous cell growth), and cervical cancer [59]. HIV-infected women have a higher prevalence of HPV infection, a higher risk of progression from infection to disease, and an increased risk of invasive cervical cancer and other HPV-related cancers than non-infected women [59]. Research indicates that cART does not significantly decrease the incidence of HPV-related

cancers. As such, the American College of Obstetricians and Gynecologists recommends that women with HIV should have cervical cytology screening twice in the first year after diagnosis and annually thereafter [60].

Hormonal contraception also has an effect on the manifestations of HIV, the risk of acquisition/transmission, and treatment efficacy. An older study found that combined oral contraceptive use was associated with lower absolute CD4 cell count [61]. Research focusing on HIV in women using hormonal contraceptive has indicated a slightly increased risk of acquisition and transmission, particularly with injectable methods of birth control [62; 63]. There has been some evidence of an increased risk of HIV transmission to an uninfected male partner if the woman is using hormonal contraceptives [59]. Hormonal birth control may interact with cART to create additional drug toxicities and treatment failures, and cART may reduce the effectiveness of some hormonal contraceptives [59].

Prognosis and Treatment Considerations

Studies have shown that women with AIDS have a poorer prognosis than men (mainly attributed to socioeconomic factors), though the majority of research was completed in the pre-cART era. Researchers have speculated that poorer access to or use of healthcare resources (later diagnosis), domestic violence, homelessness, and lack of community support may contribute to the seemingly higher mortality rate for HIV-infected women [64].

There are some unique clinical and therapeutic issues to consider when caring for women with HIV, and care providers should consult published guidance provided by the NIH/PHS [35]. For example, some drugs have significant pharmacokinetic interactions with hormonal contraceptives and hormone replacement therapy. Postmenopausal risks of osteopenia, osteoporosis, and fractures are exacerbated by HIV and some antiretroviral drugs. Women are more susceptible than men to cART-associated weight gain, a difference reported across all classes of cART but particularly notable for INSTI-based regimens [35].

Considerations for Antiretroviral Therapy in the HIV-Infected Pregnant Individuals

HIV counseling and the offer of HIV testing to pregnant persons have been universally recommended in the United States and are now mandatory in some states. A pregnancy test should be performed for those with childbearing potential before initiating cART. Care of the HIV-infected pregnant individuals should involve collaboration between the HIV specialist caring for the patient when they are not pregnant, an obstetrician, and the patient. Treatment recommendations for HIV-infected pregnant patients are based on the belief that therapies of known benefit should not be withheld during pregnancy unless there are known adverse effects on the mother, fetus, or infant that outweigh the potential benefit. When selecting cART for a pregnant individual, clinicians should consider available safety and efficacy data on the use of each agent during pregnancy. The risks and benefits of ART during pregnancy should be discussed with all individuals of child-bearing potential, and clinicians should consult the most recent perinatal guidelines when designing a regimen [35].

Initiation of cART is recommended for pregnant patients with HIV in all stages of pregnancy. Regardless of the stage of pregnancy or childbirth, if a patient is found to be HIV-positive, there are treatment options that should be explored [35].

Patients should be registered with the Antiretroviral Pregnancy Registry, which collects observational, nonexperimental data. The registry is sponsored by GlaxoSmithKline, in affiliation with the CDC and Kendle International, Inc. Those who have been treated with cART at any time during their pregnancies are eligible for registry enrollment. The telephone number for registration is (800) 258-4263, and the website is http://www.apregistry.com.

INFANTS AND CHILDREN WITH HIV

In the United States today, the predominant route of infection with HIV in children is perinatal (from an infected pregnant woman to her fetus or infant) [65]. Thus, the epidemic in children is closely linked to the epidemic in women.

Clinical Symptoms in Children with HIV Infection

Children with HIV/AIDS may have more than one infection at the same time or in succession (multiple opportunistic infections). Conditions associated with HIV infection in children are [66]:

- Serious bacterial infections, multiple or recurrent (only among children younger than six years of age)
- Candidiasis (esophageal or pulmonary)
- Invasive cervical cancer (only among adolescents and children six years of age or older)
- Disseminated coccidioidomycosis
- Extrapulmonary cryptococcosis
- Cryptosporidiosis or isosporiasis with diarrhea persisting longer than one month
- CMV disease
- Encephalopathy
- Herpes simplex virus infection causing bronchitis, pneumonitis, or esophagitis or causing a mucocutaneous ulcer that persists for longer than one month
- Disseminated or extrapulmonary histoplasmosis
- Kaposi sarcoma
- Lymphoma
- Disseminated or extrapulmonary *Mycobacterium tuberculosis*
- Disseminated *Mycobacterium avium* or *kansasii*
- PJP
- Progressive multifocal leukoencephalopathy
- Recurrent *Salmonella* septicemia (nontyphoid)
- Toxoplasmosis of the brain
- Wasting syndrome

Antiretroviral Treatment in Children

As with adults, cART is believed to play a major role in slowing progression of HIV in children and adolescents. Children receiving cART should be monitored for side effects, adherence, efficacy and toxicity. Recommendations for initial antiretroviral therapy of HIV infection in children have been updated based on FDA approvals and new data; clinicians should consult Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection when making management decisions for pediatric HIV care [67]. Following initiation of cART, all pediatric patients should be evaluated within one to two weeks to monitor compliance, side effects, and response to treatment. Subsequent visits should be scheduled every three to four months [67]. Strategies to improve adherence should focus on selecting an appropriate regimen, educating the family/caregiver, and consistent follow-up.

OLDER PEOPLE WITH HIV

Approximately 17% of newly diagnosed cases of HIV in 2018 occurred in individuals 50 years of age or older; 51% of all persons living with HIV/AIDS are 50 years of age or older [68]. Until recently, there had been little attention given to this group. HIV/AIDS has traditionally been thought to be the disease of the young; therefore, in the past, prevention and education campaigns had not been targeted toward older adults. However, evidence points to the increasing number of infected older people and a need for change in prevention and education campaigns. Some older persons may have less knowledge about HIV and risk reduction strategies. Due to divorce or being widowed and the availability of medications to treat erectile dysfunction, increasing numbers of older people are becoming sexually active with multiple partners [68]. For postmenopausal women, contraception is no longer a concern, and they are less likely to use a condom. Furthermore, vaginal drying and thinning associated with aging can result in small tears or cuts during sexual activity, which also raises the risk for infection with HIV/AIDS [68]. Studies indicate that at-risk individuals in this age group are significantly less likely than younger at-risk adults to use condoms during sex [69]. In addition, healthcare professionals are less likely to discuss sexual activity or take a sexual history if the patient is older than 50 years of age [69]. The combination of these factors increases the risk for unprotected sex with new or multiple partners in this age group, thereby increasing their risk for AIDS. This increase should be considered when evaluating older patients.

Early possible signs of immunosuppression that are frequently overlooked or mistakenly attributed to aging include thrush and skin problems, especially seborrheic dermatitis and herpes zoster. When HIV is not recognized or treated, the most typical opportunistic infections are PJP and recurrent bacterial pneumonia, CMV, and *Mycobacterium tuberculosis* or *Mycobacterium avium* complex. PJP can present as bacterial pneumonia, bronchitis, or congestive heart failure. Early HIV symptoms in the elderly, such as fatigue and weight loss, may appear to be a normal part of aging, and AIDS-related dementia is often mistaken for Alzheimer disease.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Panel on Antiretroviral Guidelines for Adults and Adolescents asserts that older persons with HIV are probably at an even greater risk of polypharmacy-related adverse consequences than younger or similarly aged people without HIV, and it is very important to remain vigilant to potential drug-drug interactions given the high prevalence of polypharmacy in this population.

(https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Last accessed March 11, 2022.)

Strength of Recommendation: Expert Opinion/ Consensus Statement

AIDS PREVENTION

PRE-EXPOSURE PROPHYLAXIS

In 2012, the FDA approved the first medication for the prevention of sexually transmitted HIV infection, the combination drug Truvada (emtricitabine/ tenofovir DF) [70]. In 2019, another combination drug—Descovy (emtricitabine/tenofovir alafenamide)—was approved to prevent HIV infection [79].

In 2021, the FDA approved the first injectible agent for the prevention of HIV infection; cabotegravir is given first as two initiation injections administered one month apart, and then every two months thereafter [82]. In conjunction with safer sex practices, these agents have been found to be partially effective as pre-exposure prophylaxis in high-risk patients. The Chemoprophylaxis for HIV Prevention in Men study, also known as iPrEx, studied the effect of once-daily Truvada in 2,499 HIV-seronegative men or transgender women who have sex with men compared to placebo [71]. Researchers found that persons receiving Truvada experienced a 44% reduction in the incidence of HIV after a median of 1.2 years compared to placebo. Pre-exposure prophylaxis was most effective among participants at particularly high risk for HIV (i.e., self-reports of unprotected receptive anal intercourse). Research has indicated that Descovy and cabotegravir are similarly effective [79].

In 2021, the CDC and the U.S. Department of Health and Human Services updated their clinical practice guidelines for pre-exposure prophylaxis for the prevention of HIV infection [72]. This guideline outlines indications for prophylaxis as one prevention option for HIV transmission. The most important first step in determining if an individual is a candidate for pre-exposure prophylaxis is a thorough history, including sexual and injection drug activities. All candidates will be adults without an acute or established HIV diagnosis. Pre-exposure prophylaxis is indicated for high-risk MSM, meaning those who have had any male sex partners in the past six months, are not in a monogamous partnership with a recently tested, HIV-negative man, and have one of the following [72]:

- Anal sex without condoms (receptive or insertive) in the past six months
- Any STI diagnosed or reported in the past six months
- An ongoing sexual relationship with an HIV-positive man

Prophylaxis is also recommended for high-risk heterosexual adults who have had sex with an opposite sex partner(s) in the past six months, are not in a monogamous partnership with a recently tested, HIV-negative partner, and one of the following [72]:

- Is a man who has sex with both women and men (behaviorally bisexual)
- Infrequently uses condoms during sex with one or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (IDU or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner

IDUs are also considered candidates for pre-exposure prophylaxis if they meet certain criteria. The guideline states that persons who have injected drugs not prescribed by a clinician in the past six months may be candidates for prophylaxis if they also are positive for one of the following factors [72]:

- Any sharing of injection or drug preparation equipment in the past six months
- Increased risk of sexual acquisition (based on the previously outlined criteria)

Injection cabotegravir given bimonthly and fixed-dose combination tenofovir and emtricitabine (Truvada or Descovy) taken daily are approved for pre-exposure prophylaxis, and they are considered the recommended first-line option [70; 72; 79; 82]. However, because tenofovir alone has been proven effective in trials with IDU and heterosexually active men and women, it is the alternative option for these populations [72]. No other antiretroviral regimens should be used for pre-exposure prophylaxis.

All patients prescribed pre-exposure prophylaxis must have a negative HIV test prior to initiating treatment and every three months thereafter. In addition, patients should be advised regarding possible side effects and the continued necessity for safe sex practices. Eligible patients should also be screened for hepatitis B and have a confirmed creatinine clearance of 60 mL per minute or greater [72].

AIDS VACCINE

Both preventive and therapeutic vaccines are being studied for use in the fight against HIV. Preventive vaccines are developed to protect individuals from contracting HIV, while the goal of therapeutic vaccines is to boost immune response to and better control existing HIV infection. Of course, the ultimate goal in vaccine research is a vaccine that will prevent infection; however, despite many trials, no vaccine effective in preventing HIV has been discovered.

Most progress on HIV vaccine development may be monitored through the International AIDS Vaccine Initiative (IAVI). The IAVI has three main objectives: accelerating the development of AIDS vaccines, establishing partnerships to expand the diversity and number of AIDS vaccine candidates, and building support for AIDS vaccine research and development [73].

TOPICAL MICROBICIDES

Because HIV is spread predominantly through sexual transmission, the development of chemical and physical barriers that can be used intravaginally or intrarectally to inactivate HIV and other STI pathogens is critically important for controlling HIV infection.

Researchers are developing and testing new creams or gels (topical microbicides) that could be applied before intercourse to protect individuals against HIV and other sexually transmitted organisms [74]. One of the most promising is 1% vaginal gel formulation of tenofovir, which showed a 54% decrease in the incidence of HIV infection in high adherers in one clinical trial [75]. Another option is a flexible silicone matrix polymer ring containing dapirivine, an NNRTI, which is slowly released over the course of one month [74]. However, there are concerns regarding compliance with recommendations to ensure protection.

New topical microbicide candidates would ideally be non-irritating and inexpensive. In addition, they should be available in both spermicidal and non-spermicidal formulations so women do not have to put themselves at risk for acquiring HIV and other STIs in order to conceive a child.

EDUCATION TO PREVENT HIV INFECTION

Many adolescents engage in behaviors that put them at risk for HIV infection. According to the CDC, 39.5% of high school students [76]. Approximately 45.7% of currently sexually active high school students had not used a condom at last sexual intercourse; 1.6% had ever injected an illegal drug [76]. Although 85.3% of adolescents report having received education on HIV prevention in school, the content of these discussions may not provide adequate information on the subject. Furthermore, the American Academy of Pediatrics determined that school-based education and intervention programs do not provide the necessary opportunities of confidential discussions or targeted counseling [77]. Healthcare professionals have a unique opportunity to intervene in this population to provide accurate and complete information on HIV transmission and risk reduction.

CONSIDERATIONS FOR NON-ENGLISH-PROFICIENT PATIENTS

For patients who are not proficient in English, it is important that education regarding the risks, prevention, and treatment of HIV be provided in language that they understand. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required. Interpreters can be a valuable resource to help bridge the communication and cultural gap between patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers who ultimately enhance the clinical encounter. In any case in which information regarding treatment options and medication/treatment measures are being provided, the use of an interpreter should be considered. Print materials are also available in many languages, and these should be offered whenever necessary.

SUMMARY

Although prevention and new medical interventions may reduce the pace of the epidemic, HIV will be a significant disease for many years both in the United States and the world. Education provides the opportunity to ensure that healthcare professionals have the information necessary to provide the best possible care for persons with HIV. Those who specialize in HIV care should identify ways to renew themselves through education, individual support, staff support, and variation of workload so that they can continue to contribute their valuable expertise to patients with HIV. With no easy cure in sight, healthcare professionals have the opportunity to work with patients to help them achieve and maintain their optimal level of health during the continuum of HIV disease.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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