HIV/AIDS: An 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.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

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

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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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ACCME for the purpose of granting ABIM MOC credit. Completion of this course constitutes permission to share the completion data with ACCME.

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This activity has been designated for 5 Lifelong Learning (Part II) credits for the American Board of Pathology Continuing Certification Program.

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

This activity was planned by and for the healthcare team, and learners will receive 5 Interprofessional Continuing Education (IPCE) credits for learning and change.

NetCE designates this continuing education activity for 6 hours for Alabama nurses.

NetCE designates this continuing education activity for 1 pharmacotherapeutic/pharmacology contact hour.

AACN Synergy CERP Category A.

Social workers completing this intermediate-to-advanced course receive 5 Non-Clinical continuing education credits.

NetCE designates this continuing education activity for 2 NBCC clock hours.

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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. Genetic studies suggest that the lower monkeys first became infected with SIV 100,000 years ago [1]. HIV-1 is the most common type of HIV, accounting for more than 99.5% of all cases globally [3].

HIV-2 accounts for less than 1% of all cases of HIV and 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, the majority of which were associated with immigration from, travel to, or a sexual partner from an endemic country. Differences in the global spread are attributed to differences in transmissibility and duration of infectiousness [2].

According to the World Health Organization (WHO), an estimated 39.9 million individuals worldwide were living with HIV at the end of 2023, 65% of whom are in the WHO African Region [5]. One study using HIV prevalence data from 68 countries noted that, in 2022, among the 37 million individuals infected with HIV, 53% were located in Southern/East Africa in one of 14 high-prevalence countries (defined as an HIV-prevalence rate of >3.5%); the remaining 47% of HIV-infections were spread across the globe. This study highlights that in 2022, although the overall rate of new infections were lower, for the first time there were more new HIV infections (770,000 vs. 468,000), more HIV-related deaths (383,000 vs. 225,000), higher rates of mother-to-child transmission (16% vs. 9%), and lower antiretroviral therapy (ART) coverage (67% vs. 83%) in low-prevalence countries versus high-prevalence countries. The annual epidemic growth rate in 2022 was 2.41% for high-prevalence countries, compared with 4.41% for low-prevalence countries; the highest epidemic growth rates (>5.2%) were found in Central and South America, Central Africa, and Central and East Asia [4; 7]. Allocation of funding for treatment and prevention is noted as a potential cause for the shift in epidemic growth rates, as the majority of global efforts are concentrated in Southern and East Africa.

Beginning in 2003, the U.S. government has worked to fight HIV/AIDS on a global level, partially through the implementation of the President's Emergency Plan for AIDS Relief (PEPFAR) [6]. PEPFAR operates in more than 50 countries, including Africa, Asia, and the Western Hemisphere, and provided HIV treatment for more than 20.6 million people in 2024 alone, including 566,000 children. PEPFAR continuously operated with bipartisan support in Congress from 2003 through 2025; however, a freeze to U.S. foreign aid in January 2025 left many programs without resources to continue HIV prevention services and treatments. Additionally, systems for the management of clinical data, survey data, and other critical strategic information for planning and program management were interrupted by the funding freeze. Although granted a limited waiver to implement urgent life-saving HIV treatment services, the future of PEPFAR funding and recipients who immediately rely on the services provided are uncertain as of March 2025 [44; 45].

UNITED STATES STATISTICS

At year-end 2022, an estimated 1.238 million individuals 13 years of age or older were living with HIV/AIDS in the United States. The CDC estimates that approximately 11% of these individuals were unaware of their infection [9]. In 2022, the Centers for Disease Control and Prevention (CDC) report several statistics and trends in the prevalence of HIV/AIDS in the United States [9]:

- By region, the prevalence rates are nearly 40% higher in the Northeast and South (513.2 and 533.9 per 100,000, respectively) than in the West (379.7 per 100,000) and Midwest (263.6 per 100,000).
- By race/ethnicity, 40% are Black/African American, 28% White, 26% Hispanic, 5% are multiracial, less than 2% are Asian/Pacific Islander, and less than 0.5% are American Indian/Alaska Native.

- By age, the highest rate is seen in those 55 to 64 years of age (25%), followed by 45 to 54 years (21%), 35 to 44 years (20%), 25 to 34 years (18%), ≥65 years (13%), and 13 to 24 years (3%).
- By sex at birth, 78% of adults and adolescents living with HIV are male.
- By transmission category, 60% of HIV infections are related to male-to-male sexual contact, followed by heterosexual contact (25%), injection drug use (10%), and combined male-to male sexual contact and injection drug use (5%). Among HIV transmission by heterosexual contact, nearly 70% of all individuals infected are female.

In 2022, an estimated 31,800 individuals 13 years of age or older were newly diagnosed with HIV/AIDS in the United States. United States incidence trends mirror those of the prevalence trends of HIV, with the exception of regional demographics [8].

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. Acute primary HIV 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 [5].

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

- Pneumonia: *Pneumocystis pneumonia* (PCP), *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).

Advanced HIV disease is defined by the WHO as a CD4 count <200 cells/mcL in adults and adolescents, or HIV infection regardless of count in any child younger than 5 years of age. The median survival of adult and adolescent patients with advanced HIV is approximately 12 to 18 months. Patients succumb to complications of uncontrolled infection, malignancy, or critical organ failure (such as uremia or adrenal insufficiency) [5].

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, while the CDC recommends being tested for HIV as part of routine healthcare at least once for anyone 13 to 64 years of age [13; 14]. In addition, the OraQiuck HIV self-test was approved by the FDA in 2012 for individuals 17 years of age and older, and in 2024, the age was expanded to include individuals 14 years of age and older [46].

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 [2].

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 [8; 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 [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). 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 [9; 10].

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) [9]. 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 consistent use of latex condoms reduces the risk of HIV transmission by approximately 80% [16].

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. A study of serodifferent heterosexual and MSM couples in which the HIV-positive partner was on ART found no documented cases of within-couple transmission of HIV, despite engaging in condomless sex, after an average of 1.3 years [68]. 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 [10; 18]. 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 [10; 18].

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 [19]. 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 less than 1 per 1 million [20]. It is possible that before blood screening implementation, more than 12,000 people were infected [21]. 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 [22]. 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 15% to 45% 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 95%, since the mid-1990s; in 2019, there were 3,540 hospital-based live births among persons with an HIV diagnosis, of which 32 infants were diagnosed with perinatally acquired HIV [33]. Studies have shown that treating pregnant and breastfeeding women with antiretroviral therapy (ART) to achieve viral suppression results in a <1% infection rate of HIV transmitted mother-to-infant [32; 34]. The American Academy of Pediatrics recommends that for people with HIV in the United States, avoidance of breastfeeding is the only infant feeding option with 0% risk of HIV transmission; however, if an individual with HIV expresses an interest to breastfeed, a family-centered, nonjudgmental, harm-reduction approach to support the individual, including ensuring ART with sustained viral suppression less than 50 copies/mL, should be employed. Patients with HIV who are considering breastfeeding and are not on ART, or are on ART without viral suppression, should be advised not to breastfeed [41]. 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].

Cosmetic Procedures

In 2018, the CDC began investigating a spa in New Mexico, after a woman was diagnosed positive for HIV in connection to a micro-needling facial treatment. The woman received a "platelet-rich plasma" (PRP) with microneedling procedure (i.e., vampire facial) that involves drawing blood from the client, separating the blood into its components of plasma and cells, and using single-use disposable or multiuse sterile equipment (microneedles) to inject PRP in specific areas of the face, with the goal of skin rejuvenation and reduced appearance of scars [31]. Within months of the treatment, the woman received a positive HIV diagnosis, marking the first case of transmission by a nonsterile cosmetic injection procedure. As of 2023, five people were found to have been diagnosed positive with HIV in relation to the PRP facial at the spa; four women who directly received the procedure at least once, and one male who was a sexual partner of one of the directly infected women. In the investigation, the CDC found several violations and examples of unsafe infection control practices in the spa, highlighting the need for adherence to established infection control practices and public education for consumers of these services to be aware of the risks [27; 31].

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), and only one case has been reported since 2008 [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 [27].

Postexposure Prophylaxis

The U.S. Public Health Service (PHS) provides 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 continuation of 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 raltegravir 400 mg twice daily plus Truvada (combination emtricitabine 200 mg and tenofovir 300 mg) once 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 [40].

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 [11].

ACUTE HIV INFECTION

HIV infection is a protracted illness that passes through several stages and, if untreated, is ultimately fatal, with a median survival time from seroconversion of 8 to 10 years [28; 29]. 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 [11].

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 load, 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 an average annual rate of about 50 cells/mcL [11].

ASYMPTOMATIC HIV INFECTION

Approximately 10% to 20% of individuals with newly acquired HIV are asymptomatic during the initial two months following acute infection [11; 12]. 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 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 antiretroviral therapy (ART) [11].

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 [11; 12].

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 PCP, central nervous system (CNS) toxoplasmosis, or other opportunistic infections or tumors (Kaposi sarcoma). As noted, the WHO defines advanced HIV disease as a CD4 count <200 cells/mcL in adults and adolescents, or HIV infection regardless of count in any child younger than 5 years of age [5].

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: PCP, Kaposi sarcoma, candidiasis, cryptococcosis, cryptosporidiosis, CMV, atypical mycobacteriosis, systemic herpes, toxoplasmosis, and tuberculosis [50].

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, with studies finding that the average life expectancy of an individual with a CD4 count of greater than 500 cells/mcL on sustained long-term ART is nearly the same as the general population [28; 29].

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 ART and prophylaxis for opportunistic infections, HIV disease shares features of other multisystem, chronic diseases characterized by acute exacerbations and end-stage manifestations.

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 ART 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]. In 2024, the U.S. Department of Health and Human Services (HHS) released updated guidelines for ART, a collaborative effort of a Panel comprised of more than 50 members with expertise in HIV care and research, and represented by members from the U.S. Food and Drug Administration (FDA), Health Resource and Services Administration (HRSA), and National Institutes of Health (NIH), among others [43].

ART (also known as cART or HAART) consists of a combination of three or more drugs selected from nine major classes of agents, including [42]:

- Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Protease inhibitors (PIs)
- Fusion inhibitors (FIs)
- Integrase strand transfer inhibitors (INSTIs)
- Chemokine (C-C motif) receptor 5 (CCR5) antagonists
- gp120 attachment inhibitors
- Capsid inhibitors
- Post-attachment 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. In addition to combination therapy, the sequencing of drugs and the preservation of future treatment options are also important. A significant proportion of patients starting ART 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. The 2024 guidelines recommend initial ART regimens based on an oral second-generation INSTI plus two NRTIs. If INSTI resistance is possible and/or if genotype results are not yet available, a boosted PI in combination with two NRTIs is recommended [42]. 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.

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 [43].

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, ETR); and rilpivirine (Edurant, RPV, Endurant PED) [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: atazanavir (Reyataz, ATZ); tipranavir (Aptivus, TPV); darunavir (Prezista; DRV); fosamprenavir (Lexiva, FPV); and ritonavir (Norvir, RTV) [43]. Although ritonavir is a PI, it is generally used as a pharmacokinetic enhancer [42; 43].

Fusion Inhibitors (FIs)

Enfuvirtide (Fuzeon, T-20), 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 (Selzentry, MVC) 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. 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 [43]. 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)

Integrase strand transfer inhibitors act by preventing the viral DNA from inserting into the host DNA, effectively limiting infection of additional cells and decreasing viral load. INSTIs are approved for use in combination with other antiretrovirals in treatment-experienced and treatment-naïve patients with evidence of HIV replication. Available agents include raltegravir (Isentress, RAL, Isentress HD), dolutegravir (Tivicay, DTG, Tivicay PD), and cabotegravir (Vocabria, CAB) [43].

gp120 Attachment Inhibitors

In 2020, the FDA approved the first gp120 attachment inhibitor, fostemsavir (Rukobia, FTR), for the treatment of HIV in patients whose infection cannot be successfully treated with other therapies because of resistance, intolerance, or safety considerations. Fostemsavir acts by binding to the gp120 protein on the outer surface of the HIV virus, preventing it from entering CD4 cells [58].

Capsid Inhibitors

In 2022, the FDA approved lenacapavir (Sunlenca, GS-6207, GS-HIV, GS-CA2, GS-CA1), 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. These agents directly target virus' protein shell (the capsid), interfering with multiple essential steps of the viral lifecycle [43].

Post-Attachment Inhibitors

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

Pharmacokinetic Enhancers

In an effort to improve the efficacy of other antiretroviral medications in an ART regimen, a pharmacokinetic enhancer may also be included. The agents most commonly used for this purpose are cobicistat and ritonavir (a PI). Both of these agents inhibit cytochrome P450 (CYP) 3A enzymes, prolonging the effects of other medications [43; 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.

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. Available oral combination medications include [43]:

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

In addition to oral medications, in 2021 the FDA approved the first monthly injectable ART—Cabenuva (cabotegravir/rilpivirine). 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 [43; 59].

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 ART. Physicians and patients alike should be aware of the advantages, potential toxicities, and complexity of monitoring therapy. Clinicians should consult the appropriate HHS guideline for antiretroviral agents; separate guidelines have been developed for adults and adolescents, pediatrics, and pregnant women with HIV infection [23; 24; 42]. For adults and adolescents, 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 multiple medications, 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 100,000 copies/mL are considered to have a high HIV viral load and a relatively rapid course of disease, significantly lowering the average survival rate to little more than a few years. In contrast, those with a viral load <20 copies/mL have reached viral suppression and have a life expectancy similar to that of the general population. The CD4 count is also a prognostic factor, as counts less than 350 cells/mcL indicate damage to immune function and corresponding risk for opportunistic infection [19].

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 ART is effective in preventing clinical events (e.g., non-AIDS malignancies, infection, AIDS-defining illness) regardless of pre-treatment CD4 count [42; 48; 49]. Advances in the development of antiretroviral medications, combination tablets, and injectable ART makes adherence to therapy more effective, more convenient, and better tolerated than regimens used in the past. Deferral of therapy should only 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 nonprogressor [42].

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/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Last accessed March 21, 2025.)

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

As noted, for treatment-naïve patients, initial recommended ART generally consists of an oral second-generation INSTI plus two NRTIs. If INSTI resistance is possible and/or if genotype results are not yet available, a boosted PI in combination with two NRTIs is recommended [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].

CHEMOPROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE AMONG ADULTS AND ADOLESCENTS INFECTED WITH HIV

Opportunistic Infection	Indication	Preventive Regimen	
		Preferred[a]	Alternative
Pneumocystis pneumonia (PCP)	CD4 count 100–200 cells/mcL, if plasma HIV RNA level is above detection limits (AI) CD4 count <100 cells/mcL, regardless of plasma HIV RNA (AII) Note: Patients who are receiving pyrimethamine/ sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).	Trimethoprim-sulfamethoxazole (TMP-SMX) 1 double-strength (DS) daily (AI), or TMP-SMX 1 single-strength (SS) daily (AI) Note: TMP-SMX also confers protection against toxoplasmosis and some protection against many respiratory bacterial infections	Regimens for individuals who are seropositive or seronegative for *Toxoplasma gondii*: TMP-SMX 1 DS three times weekly (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 Atovaquone 1,500 mg daily (BI) Regimens that should only be used in individuals seronegative for *Toxoplasma gondii*: Dapsone 100 mg daily or 50 mg twice daily (BI), or Aerosolized pentamidine 300 mg via nebulizer every month (BI), or Intravenous pentamidine 300 mg every 28 days (CIII)
Toxoplasma gondii encephalitis	*Toxoplasma* immunoglobulin G (IgG)-positive patients with CD4 count <100 cells/mcL (AII) Note: All regimens recommended for primary prophylaxis against toxoplasmosis also are effective as PCP prophylaxis.	TMP-SMX 1 DS daily (AII)	TMP-SMX 1 DS three time weekly (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 (CI), 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 (with no evidence of active TB), regardless of screening test results and CD4 count (AII)	3HP (three months of once-weekly isoniazid + rifapentine): Rifapentine (weight-based dosing) + isoniazid (INH) 15 mg/kg (900 mg maximum) + pyridoxine 50 mg weekly for 12 weeks (AI) Weekly weight-based rifapentine dose: 25.1–32 kg: 600 mg 32.1–49.9 kg: 750 mg >50 kg: 900 mg Note: 3HP is recommended only for virally suppressed persons receiving efavirenz, raltegravir, or once daily dolutegravir-based ARV regimen (AII) OR 3HR (three months of daily isoniazid + rifampin): INH 300 mg + rifampin 600 mg + pyridoxine 25–50 mg daily for 3 months (AI)	INH 300 mg + pyridoxine 25–50 mg daily for 6–9 months (AII), or 4R (four months of daily rifampin): Rifampin 600 mg daily for 4 months (BI), or 1HP (one month daily): Rifapentine (weight-based dosing) + INH 300 mg + pyridoxine 25–50 mg) once daily for 4 weeks (BI) Daily weight-based rifapentine dose: <35 kg: 300 mg 35–45 kg; 450 mg >45 kg: 600 mg Note: 1HP is recommended only for patients receiving an efavirenz-based ARV regimen (AI) For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts and public health authorities (AIII)

Table 1 continues on next page.

CHEMOPROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE AMONG ADULTS AND ADOLESCENTS INFECTED WITH HIV *(Continued)*			
Opportunistic Infection	**Indication**	**Preventive Regimen**	
		Preferred[a]	**Alternative**
Disseminated *Mycobacterium avium* complex (MAC) disease	CD4 count <50 cells/mcL and not receiving ART or remains viremic on ART or has no options for a fully suppressive ART regimen (AI) Not recommended for those who immediately initiate ART after HIV diagnosis (AII) Disseminated MAC disease should be ruled out before starting primary prophylaxis	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 to avoid monotherapy
Syphilis	Individuals exposed sexually within 90 days of the diagnosis of primary, secondary, or early latent syphilis of a sex partner, even if serologic test results are negative (AII), or Individuals exposed >90 days before syphilis diagnosis in a sex partner 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 10–14 days (BII)
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 *Coccidioides* IgM or IgG test in patients who previously tested negative; do not have signs, symptoms, or laboratory abnormalities compatible with active disease; and have CD4 count <250 cells/mcL	Fluconazole 400 mg daily (AIII)	—
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)
Malaria	Travel to disease-endemic area	Recommendations are the same for HIV-infected and HIV-uninfected patients and are based on the region of travel, malaria risk, and drug susceptibility in the region.	—

Table 1 continues on next page.

CHEMOPROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE AMONG ADULTS AND ADOLESCENTS INFECTED WITH HIV *(Continued)*			
Opportunistic Infection	**Indication**	**Preventive Regimen**	
		Preferred[a]	**Alternative**
Talaromycosis (Penicillosis)	Persons with HIV and CD4 cell counts <100 cells/mL, who are unable to have ART, or have treatment failure without access to effective ART options, and— Who reside in the highly endemic regions in northern Thailand, northern or southern Vietnam, or southern China (particularly in highland regions during rainy and humid months) (BI), or Who are from countries outside of the endemic region, and must travel to the region (BIII)	For persons who reside in endemic areas, itraconazole 200 mg once daily (BI) For those traveling to the highly endemic regions, begin itraconazole 200 mg once daily 3 days before travel, and continue for 1 week after leaving the endemic area (BIII)	For persons who reside in endemic areas, fluconazole 400 mg once weekly (BII) For those traveling to the highly endemic regions, take the first dose of fluconazole 400 mg 3 days before travel, continue 400 mg once weekly, and take the final dose after leaving the endemic area (BIII)
[a]All medications are taken orally unless otherwise indicated.			
Source: [50]			*Table 1*

RECOMMENDATIONS RATING SYSTEM	
Category	**Definition**
Strength of Recommendation	
A	Strong
B	Moderate
C	Weak
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

PREVENTION OF OPPORTUNISTIC INFECTIONS

In absence of timely diagnosis and treatment of HIV, opportunistic infections are often the first clinical indication of AIDS. *Pneumocystis* pneumonia, Kaposi sarcoma, toxoplasma encephalitis, cytomegalovirus, cryptococcal meningitis, and disseminated atypical mycobacterial infection are often hallmarks of AIDS. Before effective ART, 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 ART is important in prevention of infection; however, the CDC estimates that in 2022, only 65% of patients linked to care had durable viral suppression. Poor adherence, unfavorable pharmacokinetics, and/or unexplained biologic factors are among causes for suboptimal response to treatment [17; 50]. The NIH, HIV Medicine Association, and Infectious Diseases Society of America (NIH/

HIVMA/IDSA) released updated guidelines for opportunistic infections in patients with HIV in 2024. Recommendations for chemoprophylaxis to prevent opportunistic infections are summarized in ***Table 1*** [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 to chemoprophylaxis, it is recommended that patients with HIV receive immunizations similarly to the general population, with some exceptions. The following live virus vaccines are contraindicated in individuals with a CD4 count of <200 cells/mcL [50]:

- Measles
- Mumps
- Rubella
- Varicella
- Live attenuated typhoid Ty21a
- Yellow fever
- Live attenuated influenza vaccine (LAIV), not recommended regardless of CD4 counts

Vaccines that have specific recommendations for individuals with HIV, include [50]:

- COVID-19
- Hepatitis A (HAV)
- Hepatitis B (HBV)
- Meningococcus serogroup A, C, W, Y (MenACWY)
- Pneumococcal vaccines
- Human papillomavirus

Full recommendations for vaccines and the prevention of opportunistic infections among HIV-infected adults and adolescents specific opportunistic infection and can be viewed at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections [50].

Tuberculosis and HIV

Tuberculosis is the leading cause of morbidity and mortality among people living with HIV worldwide, with an estimated 10.8 million reported cases and 1.25 million deaths in 2023, of which 161,000 deaths were related to HIV-associated TB. Individuals with HIV are at an approximate 16 times greater risk of developing tuberculosis compared with people not infected with HIV. While ART significantly decreases the risk of conversion from latent to active disease, only 56% of patients with TB living with HIV were on ART in 2023. Although the majority of cases of TB are among low- and middle-income countries, the United States accounted for nearly 9,500 cases in 2023, 410 of which were among individuals coinfected with HIV. There were 545 TB-related deaths in 2022 in the United States [52].

In addition to the recommended prophylaxis to prevent a first episode of opportunistic tuberculosis, guidelines for the treatment of HIV-related active tuberculosis were updated in 2024 [50]. In individuals with HIV infection, the ART regimen should be assessed with attention to potential interactions between ARTs and TB drugs, including rifamycin antibiotics (e.g., rifabutin, rifampin, rifapentine) and isoniazid, which have considerable potential for drug-drug interactions.

For drug-susceptible TB, or if drug resistance is currently unknown, preferred therapy consists of an intensive phase of eight weeks with an initial four-drug combination of isoniazid, rifampin or rifabutin, ethambutol, and pyrazinamide daily until susceptibility to isoniazid and rifampin has been confirmed [52]. If rapid drug sensitivity testing indicates resistance to isoniazid and rifampin, ethambutol may be immediately discontinued; if resistance is not indicated, ethambutol should be discontinued until the end of the eight-week intensive phase. Continuation of therapy with the remaining three drugs may continue for 6 to 12 months, depending on clinical and/or bacteriologic response to therapy. Alternative preferred therapy

used for patients receiving an efavirenz-based ART regimen that do not have extrapulmonary TB is isoniazid plus rifapentine plus moxifloxacin plus pyrazinamide plus pyridoxine. The continuation of therapy is nine weeks of isoniazid plus rifapentine plus moxifloxacin plus pyridoxine daily [50].

For drug-resistant TB, empiric therapy for suspected resistance to rifamycin with or without resistance to other drugs is isoniazid plus pyrazinamide plus ethambutol plus moxifloxacin or levofloxacin, plus linezolid or amikacin. For suspected or confirmed resistance to isoniazid, the recommended treatment is moxifloxacin or levofloxacin plus rifampin or rifabutin plus ethambutol plus pyrazinamide daily for six months. In patients resistant to rifamycins with or without other antimycobacterial agents, the preferred therapy is 14 days of pretomanid plus linezolid plus moxifloxacin plus bedaquiline daily, followed by 24 weeks of pretomanid plus linezolid plus moxifloxacin daily, and bedaquiline three times per week; moxifloxacin should be omitted if resistant to fluoroquinolones. Alternative therapy for drug-resistant TB consists of an individualized regimen based on drug susceptibility test results and clinical and microbiological responses, and includes at least five active drugs, with close consultation with experienced specialists. Duration of treatment is 6 to 24 months depending on clinical and/or bacteriologic response to therapy [50].

Optimal management of HIV-related tuberculosis is complex, involving decisions around duration of therapy, timing of ART, 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 ART for these patients. Special considerations apply to children and pregnant women with HIV-related tuberculosis.

HIV INFECTION IN SPECIAL POPULATIONS

WOMEN LIVING WITH HIV INFECTION

Globally, women make up 53% of all individuals living with HIV. In the United States in 2022, there were more than 1.2 million individuals living with HIV, including 268,800 (22%) who were women. Women accounted for nearly 7,000 (19%) newly diagnosed cases in 2022, and within that group, it was reported that 83% were attributed to heterosexual sex, 17% to injection drug use, and 1% to other causes. The risk for acquisition of HIV and the factors that may affect seroconversion in women are areas of research, but 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. The overall incidence rate for women with a diagnosis of HIV in the United States remained unchanged between 2018 and 2022 [9].

HIV/AIDS is no longer a leading cause of death in women overall in the United States, but it remains the ninth leading cause of death in Black women 25 to 34 years of age. Women of color have been disproportionately affected by HIV/AIDS, with Black women accounting for 50% of new HIV diagnoses among women in the United States while representing only 13% of the female population. In comparison, White women accounted for 24% and Hispanic/Latina women accounted for 20% of HIV diagnoses. Black women also have the highest rates of HIV-related deaths among women with HIV, accounting for 57% in 2022, compared with 20% for White women and 15% for Hispanic/Latina women [53].

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. In general, studies have not shown significant differences in response to ART based on sex. However, limited data show that pharmacokinetics for some ART drugs may differ between men and women, possibly due to variations in factors such as body weight, plasma volume, gastric emptying time, plasma protein levels, cytochrome P450 activity, drug transporter function, and excretion activity [35].

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. 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 [54]. Research indicates that ART 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 [55].

Prognosis and Treatment Considerations

Studies have shown that women with HIV have a poorer prognosis than men, with poorer access to or use of healthcare resources (later diagnosis), domestic violence, homelessness, and lack of community support all potential factors that 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 the updated guidelines. Considerations for ART in women living with HIV include [35]:

- Some ART drugs may have significant pharmacokinetic interactions with hormonal contraceptives and hormone replacement therapy.
- Women, and Black women in particular, are susceptible to ART-associated weight gain after initiating or changing an ART compared with men, a difference reported across all classes of ART.
- Postmenopausal risks of osteopenia, osteoporosis, and fractures are exacerbated by HIV and some ART agents.

Considerations for Antiretroviral Therapy in 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 ART. 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 ART 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 [24; 35].

Initiation of ART 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 [24].

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 ART at any time during their pregnancies are eligible for registry enrollment. Additional information and registration are available at https://www.apregistry.com [24; 56].

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). Thus, the epidemic in children is closely linked to the epidemic in women [23].

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 [25]:

- Serious bacterial infections, multiple or recurrent (only among children younger than six years of age)
- Candidiasis (esophageal or pulmonary)
- COVID-19
- Cryptosporidiosis or isosporiasis with diarrhea persisting longer than one month
- CMV disease
- Disseminated coccidioidomycosis
- Extrapulmonary cryptococcosis
- Encephalopathy
- Giardiasis
- Hepatitis B virus
- Hepatitis C virus
- 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
- Human papillomavirus
- Kaposi sarcoma
- Lymphoma
- Malaria
- Microsporidiosis
- Mpox
- Disseminated or extrapulmonary *Mycobacterium tuberculosis*
- Disseminated *Mycobacterium avium* or *kansasii*
- PCP
- Syphilis
- Toxoplasmosis
- VZV
- Wasting syndrome

Antiretroviral Treatment in Children

As with adults, ART is believed to play a major role in slowing progression of HIV in children and adolescents. Children receiving ART 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 HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection when making management decisions for pediatric HIV care [23]. Following initiation of ART, 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 [23]. Strategies to improve adherence should focus on selecting an appropriate regimen, educating the family/caregiver, and consistent follow-up.

OLDER PEOPLE WITH HIV

In 2024, approximately 41% of individuals living with HIV were 55 years of age or older [26]. In the early years of the AIDS epidemic, little attention was given to older people with HIV, and HIV/AIDS was thought to be the disease of the young. As a result, prevention and education campaigns were traditionally not targeted toward older adults. However, effective ART and an emphasis on HIV research in older adults now allows individuals to live long, healthy lives, increasing the number of older people living with HIV. Due to the large proportion of older people with HIV, evidence points to the increasing need for change in prevention and education campaigns [26].

While many risk factors are the same for people of any age, older individuals present with several unique factors that should be considered. For example, older people in general 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. 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. Women and men in this age group are significantly less likely than younger at-risk adults to use condoms during sex. In addition, healthcare professionals are less likely to discuss sexual activity, take a sexual history, and/or recommend testing for HIV if the patient is older. 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 HIV. These factors should all be considered when evaluating older patients [26].

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 PCP and recurrent bacterial pneumonia, CMV, and Mycobacterium tuberculosis or Mycobacterium avium complex. PCP 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 [26].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Panel on Antiretroviral Guidelines for Adults and Adolescents asserts that polypharmacy is common in older people with HIV, and all drugs, supplements, and herbal treatments should be assessed regularly for appropriateness, potential for adverse effects, proper dosing, and drug interactions.

(https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Last accessed March 21, 2025.)

Strength of Recommendation: AIII (Strong recommendation based on expert opinion)

HIV/AIDS PREVENTION

PRE-EXPOSURE PROPHYLAXIS (PrEP)

In 2012, the FDA approved the first medication for the prevention of sexually transmitted HIV infection, the combination drug Truvada (emtricitabine/tenofovir DF) [60]. In 2019, another combination drug—Descovy (emtricitabine/tenofovir alafenamide)—was approved to prevent HIV infection [69]. In 2021, the FDA approved the first injectable agent for the prevention of HIV infection; cabotegravir (Apretude) is given first as two initiation injections administered one month apart, and then every two months thereafter [60]. In conjunction with safer sex practices, these agents have been found to

be partially effective as PrEP 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 [61]. 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 [69].

In 2021, the CDC updated their clinical practice guideline on PrEP used for the prevention of HIV infection [62]. Previously, candidates for PrEP were primarily individuals at high risk for HIV (e.g., MSM, IDU). In the updated guidelines, the CDC recommends informing all sexually active and/or injecting drug using patients about PrEP, regardless of HIV risk factors. In addition, any patient requesting PrEP should be considered for treatment. These updates are intended to increase the number of patients who know about PrEP and prevent stigma or embarrassment that may prevent an individual from disclosing HIV risk factors [62].

Those identified as being at a substantially increased risk of acquiring HIV infection include sexually active individuals that have had anal or vaginal sexual contact in the past six months, in addition to having an HIV-positive sexual partner; a bacterial STI in the past six months; and/or a history of inconsistent or no condom use with sexual partners. Persons who inject drugs and have a HIV-positive injecting partner or share injection equipment are also at a high risk of HIV infection [62].

Patients should have a documented negative HIV test result within seven days prior to initiating treatment, and hepatitis B, kidney function, and a lipid profile should be reviewed to ensure appropriate PrEP selection.

Oral postexposure prophylaxis is available as a fixed-dose combination tenofovir and emtricitabine (Truvada or Descovy) taken daily for <90 days. Injection PrEP consists of one dose of cabotegravir followed up by a dose four weeks later, and then every eight weeks thereafter [62]. No other antiretroviral regimens should be used for pre-exposure prophylaxis.

All patients prescribed PrEP must have a negative HIV test prior to initiating treatment and every three months thereafter for oral PrEP, and every two months for patients receiving cabotegravir injections. In addition, patients should be advised regarding possible side effects and the continued necessity for safe sex practices [62].

Advances in PrEP continue to be made to alleviate the burden of care. As noted, in 2022, the FDA approved injectable lenacapavir (Sunlenca), the first capsid inhibitor, for the treatment of HIV-1 infection [43]. As of early 2025, lenacapavir is under FDA priority review for use as the first twice-yearly PrEP option [59].

HIV/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) at https://www.iavi.org/our-work/hiv-vaccines. The IAVI, in collaboration with partners in the public, private, and philanthropic sectors, develops vaccines and antibodies to address urgent, unmet global health challenges, including HIV, TB, emerging infection diseases, and neglected diseases [63].

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 [64]. 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 [65]. Another option is a flexible silicone matrix polymer ring containing dapirivine, an NNRTI, which is slowly released over the course of one month [64]. 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, in 2023, 48.1% of sexually active high school students had not used a condom during last sexual intercourse and 1.2% had injected an illegal drug [66]. In an analysis of the Youth Risk Behavior Survey, researchers found that 84% of adolescents report having received education on HIV prevention in school. Among those students, it was found that HIV education was associated with increased rates of abstaining from substance use during intercourse. Further, for boys, receiving HIV education was associated with increased condom use at last sexual encounter, as well as increased rate of testing for HIV [67]. This evidence highlights HIV education as a promising intervention for risk behavior reduction. While the availability of HIV prevention education is important, the quality and content may not provide adequate information on the subject or may not provide necessary opportunities for confidential discussions or targeted counseling. 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.

Works Cited

1. Sharp PM, Hahn BH. Origins of HIV and the AIDS pandemic. *Cold Spring Harb Perspect Med*. 2011;1(1):a006841.
2. Centers for Disease Control and Prevention. Trends in HIV-2 diagnoses and use of the HIV-1/HIV-2 differentiation test—United States, 2010–2017. *MMWR*. 2020;69(3);63-66.
3. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv. Last accessed March 1, 2025.
4. Pepperrell T, Hill A, Cross S. Lower prevalence countries outside of South-Eastern Africa now have the fastest growing HIV epidemic. *OFID*. 2024;11(7):ofae318.
5. World Health Organization. HIV/AIDS: Key Facts. Available at https://www.who.int/news-room/fact-sheets/detail/hiv-aids. Last accessed March 1, 2025.
6. U.S. Department of State. PEPFAR Latest Global Results and Projections Factsheet (Dec. 2024). Available at https://www.state.gov/pepfar-latest-global-results-factsheet-dec-2024. Last accessed March 1, 2025.
7. Joint United Nations Programme on HIV/AIDS. 2024 Global Aids Report, The Urgency of Now: AIDS at a Crossroads. Available at https://www.unaids.org/sites/default/files/media_asset/2024-unaids-global-aids-update_en.pdf. Last accessed March 1, 2025.
8. Centers for Disease Control and Prevention. Fast Facts: HIV in the United States. Available at https://www.cdc.gov/hiv/data-research/facts-stats/index.html. Last accessed March 1, 2025.
9. Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2018–2022. *HIV Surveillance Supp Report*. 2024;29(1):1-31.
10. Centers for Disease Control and Prevention. National HIV Behavioral Surveillance: Current Data Releases. Available at https://www.cdc.gov/hiv-data/nhbs/#cdc_survey_profile_reports_data_sets_and_publications-current-data-releases. Last accessed March 1, 2025.
11. Melhuish A, Lewthwaite P. Natural History of HIV and AIDS. *Medicine*. 2022;50(5):298-303.
12. Kahn JO, Walker BD. Acute human immunodeficiency virus type 1 infection. *N Engl J Med*. 1998;339(1):33-39.
13. U.S. Department of Health and Human Services, Agency for Healthcare Research and Quality. Guide to Clinical Preventive Services, 2014. Available at https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/clinicians-providers/guidelines-recommendations/guide/cpsguide.pdf. Last accessed March 1, 2025.
14. U.S. Preventive Services Task Force. Human Immunodeficiency Virus (HIV) Infection: Screening, June 2019. Available at https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/human-immunodeficiency-virus-hiv-infection-screening. Last accessed March 1, 2025.
15. Branson BM, Owen SM, Wesolowski LG, et al. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. Available at https://stacks.cdc.gov/view/cdc/23447. Last accessed March 1, 2025.
16. U.S. Preventive Services Task Force. Final Recommendation Statement, Prevention of Acquisition of HIV: Preexposure Prophylaxis. Available at https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis. Last accessed March 1, 2025.
17. Centers for Disease Control and Prevention, Health Resources and Services Administration, National Institutes of Health, American Academy of HIV Medicine, Association of Nurses in AIDS Care, International Association of Providers of AIDS Care, National Minority AIDS Council, Urban Coalition for HIV/AIDS Prevention Services. *Recommendations for HIV Prevention with Adults and Adolescents with HIV in the United States, 2014: Summary for Clinical Providers*. Rockville, MD: U.S. Department of Health and Human Services; 2014.
18. Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines, 2021. Available at https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf. Last accessed March 1, 2025.
19. International Association of Providers of AIDS Care. Viral Load. Available at https://www.iapac.org/fact-sheet/viral-load. Last accessed March 1, 2025.
20. Richard Kaufman; ART and science of keeping HIV out of the blood supply. *Blood*. 2020;136(11):1223-1224.
21. Leveton LB, Sox HC Jr, Stoto MA (eds). *HIV and the Blood Supply: An Analysis of Crisis Decisionmaking*. Washington, DC: National Academies Press; 1995.
22. Centers for Disease Control and Prevention. HIV Surveillance Special Report: HIV Infection Risk, Prevention, and Testing Behaviors Among Persons Who Inject Drugs National HIV Behavioral Surveillance, 20 U.S. Cities, 2022. Available at https://stacks.cdc.gov/view/cdc/150464. Last accessed February 10, 2024.
23. Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv. Last accessed March 1, 2025.
24. Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-pediatric-opportunistic-infections. Last accessed March 1, 2025.

25. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Children With and Exposed to HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-pediatric-opportunistic-infections. Last accessed March 1, 2025.
26. National Institutes of Health. HIV and Specific Populations. HIV and Older People. Available at https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-older-people. Last accessed March 1, 2025.
27. Occupational Safety and Health Administration. Standard 1910.1030 Bloodborne Pathogens. Available at https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1030. Last accessed March 1, 2025.
28. Trickey A, Zhang L, Sabin CA, Sterne JA. Life expectancy of people with HIV on long-term antiretroviral therapy in Europe and North America: a cohort study. *Lancet Healthy Longev*. 2022;3(S2).
29. Sabin CA. Do people with HIV infection have a normal life expectancy in the era of combination antiretroviral therapy? *BMC Med*. 2013 Nov 27;11:251.
30. Abadie RB, Brown EM, Campbell JR, et al. Incidence and risks of HIV infection, medication options, and adverse effects in accidental needle stick injuries: a narrative review. *Cureus*. 2024;16(1):e51521.
31. Stadelman-Behar AM, Gehre MN, Atallah L, et al. Investigation of presumptive HIV transmission associated with receipt of platelet-rich plasma microneedling facials at a spa among former spa clients—New Mexico, 2018–2023. *MMWR*. 2024;73(16):372-376.
32. World Health Organization. Global HIV Programme: Mother-to-Child Transmission of HIV. Available at https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/prevention/mother-to-child-transmission-of-hiv. Last accessed March 1, 2025.
33. Lampe MA, Nesheim SR, Oladapo KY, et al. Achieving elimination of perinatal HIV in the United States. *Pediatrics*. 2023;151(5):e2022059604.
34. Abuogi L, Noble L, Smith C. Infant feeding for persons living with and at risk for HIV in the United States: clinical report. *Pediatrics*. 2024;153(6):e2024066843.
35. Panel on Antiretroviral Guidelines for Adults and Adolescents. Considerations for Use of Antiretroviral Drugs in Special Populations. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/special-populations-adolescents-and. Last accessed March 1, 2025.
36. Ahn J, Cohen SM. Transmission of human immunodeficiency virus and hepatitis C virus through liver transplantation. *Liver Transpl*. 2008;14(11):1603-1608.
37. Centers for Disease Control and Prevention. HIV transmitted from a living organ donor—New York City, 2009. *MMWR*. 2011;60(10):297-301.
38. Centers for Disease Control and Prevention. Notes from the field: occupationally acquired HIV infection among health care workers–United States, 1985–2013. Available at https://www.cdc.gov/hiv/pdf/workplace/cdc-hiv-healthcareworkers.pdf. Last accessed March 1, 2025.
39. Kuhar DT, Henderson DK, Struble KA, et al. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis. Available at https://stacks.cdc.gov/view/cdc/20711. Last accessed March 1, 2025.
40. Centers for Disease Control and Prevention. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016. Available at https://stacks.cdc.gov/view/cdc/38856. Last accessed March 1, 2025.
41. Abuogi L, Noble L, Smith C, Committee on Pediatric and Adolescent HIV, Section on Breastfeeding. Infant feeding for persons living with and at risk for HIV in the United States: clinical report. *Pediatrics*. 2024;153(6):e2024066843.
42. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. United States Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Last accessed March 1, 2025.
43. U.S. Food and Drug Administration. FDA-Approved HIV Medicines. Available at https://hivinfo.nih.gov/understanding-hiv/fact-sheets/fda-approved-hiv-medicines. Last accessed March 1, 2025.
44. Tram KH, Ratevosian J, Beyrer C. By executive order: the likely deadly consequences associated with a 90-day pause in PEPFAR funding. *J Int AIDS Soc*. 2025;28(3):e26431.
45. UNAIDS. Impact of U.S. Cuts on Global AIDS Response. Available at https://www.unaids.org/en/resources/presscentre/featurestories/2025/march/20250304-update-us-funding-freeze-fs. Last accessed March 1, 2025.
46. U.S. Food and Drug Administration. December 16, 2024 Approval Order–OraQuick HIV Self-Test. Available at https://www.fda.gov/media/184589/download?attachment=&utm_medium=email&utm_source=govdelivery. Last accessed March 1, 2025.
47. Larson KB, Wang K, Delille C, Otofokun I, Acosta EP. Pharmacokinetic enhancers in HIV therapeutics. *Clin Pharmacokinet*. 2014;53(10):865-872.
48. INSIGHT START Study Group, Lundgren JD, Babiker AG, et al. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med*. 2015;373(9):795-807.
49. TEMPRANO ANRS 12136 Study Group, Danel C, Moh R, et al. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. *N Engl J Med*. 2015;373(9):808-822.

50. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and treatment of Opportunistic Infections in Adults and Adolescents with HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections. Last accessed March 1, 2025.
51. Centers for Disease Control and Prevention. Reported Tuberculosis in the United States, 2023. Available at https://www.cdc.gov/tb-surveillance-report-2023/summary/national.html. Last accessed March 1, 2025.
52. World Health Organization. Tuberculosis. Available at https://www.who.int/news-room/fact-sheets/detail/tuberculosis. Last accessed March 1, 2025.
53. Kaiser Family Foundation. the Impact of HIV on Women in the United States. Available at https://www.kff.org/hivaids/fact-sheet/women-and-hivaids-in-the-united-states. Last accessed March 1, 2025.
54. Liu G, Sharma M, Tan N, Barnabas RV. HIV-positive women have higher risk of human papilloma virus infection, precancerous lesions, and cervical cancer. *AIDS*. 2018;32(6):795-808.
55. American College of Obstetricians and Gynecologists. Practice Bulletin 167: gynecologic care for women and adolescents with human immunodeficiency virus. *Obstet Gynecol*. 2016;128(4):e89-e110.
56. The Antiretroviral Pregnancy Registry. Available at https://www.apregistry.com. Last accessed March 1, 2025.
57. U.S. Food and Drug Administration. FDA Approves First Extended-Release, Injectable Drug Regimen for Adults Living with HIV. Available at https://www.fda.gov/news-events/press-announcements/fda-approves-first-extended-release-injectable-drug-regimen-adults-living-hiv. Last accessed March 1, 2025.
58. U.S. Food and Drug Administration. FDA Approves First Injectable Treatment for HIV Pre-Exposure Prevention. Available at https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention. Last accessed March 1, 2025.
59. Gilead. News Release: U.S. FDA Accepts Gilead's New Drug Applications for Twice-Yearly Lenacapavir for HIV Prevention Under Priority Review. Available at https://www.gilead.com/news/news-details/2025/us-fda-accepts-gileads-new-drug-applications-for-twice-yearly-lenacapavir-for-hiv-prevention-under-priority-review. Last accessed March 1, 2025.
60. U.S. Food and Drug Administration. Truvada for PrEP Fact Sheet: Ensuring Safe and Proper Use. Available at https://www.fda.gov/media/83586/download. Last accessed March 1, 2025.
61. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363:2587-2599.
62. Centers for Disease Control and Prevention. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States—2021 Update: A Clinical Practice Guideline. Available at https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Last accessed March 1, 2025.
63. International AIDS Vaccine Initiative. IAVI Annual Report. Available at https://www.iavi.org/wp-content/uploads/2024/02/IAVI-2023-Annual-Report-1.pdf. Last accessed March 1, 2025.
64. Population Council. Products in Development. Available at https://popcouncil.org/cbr-products-in-development. Last accessed March 1, 2025.
65. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010;329(5996):1168-1174.
66. Centers for Disease Control and Prevention. Youth Risk Behavior Survey Explorer. Available at https://yrbs-explorer.services.cdc.gov. Last accessed March 1, 2025.
67. Phillips G, McCuskey DJ, Felt D, et al. Association of HIV education with HIV testing and sexual risk behaviors among U.S. youth, 2009-2017: disparities between sexual minority and sexual majority youth. *Prev Sci*. 2020;21(7):898-907.
68. Roger AJ, Cambiano V, Brunn T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive therapy. *JAMA*. 2016;316(2):171-181.
69. U.S. Food and Drug Administration. FDA Approves Second Drug to Prevent HIV Infection as Part of Ongoing Efforts to End the HIV Epidemic. Available at https://www.fda.gov/news-events/press-announcements/fda-approves-second-drug-prevent-hiv-infection-part-ongoing-efforts-end-hiv-epidemic. Last accessed March 1, 2025.

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