HIV/AIDS: PREVALENCE, ETIOLOGY, AND PREVENTION

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Topic Overview

The human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) continue to be an area of significant research. New treatment guidelines and antiretroviral drugs have provided hope for individuals infected with HIV. Continuing education for pharmacists who serve and care for individuals with HIV/AIDS helps dispel myths and reduce stigma, enhances a fuller understanding of best practice trends, and improves prevention strategies to avoid transmission of the disease and complications associated with disease progression and/or treatment. Modes of HIV transmission, universal infection control procedures, and the issue of co-occurring infections in an individual with HIV are critical for pharmacists to understand when evaluating a communicable disease outcome.

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Target Audience: This educational activity is for pharmacists.

How to Earn Credit: From August 23, 2022, through August 23, 2025, participants must:

1) Read the "learning objectives" and "author and planning team disclosures;"
2) Study the section entitled "educational activity;" and
3) Complete the Post-test and Evaluation form. The Post-test will be graded automatically. Following successful completion of the Post-test with a score of 70% or higher, a statement of participation will be made available immediately. (No partial credit will be given.)

Learning Objectives: Upon completion of this educational activity, participants should be able to:

1. **Identify** how HIV/AIDS is transmitted
2. **Identify** methods of prevention and precaution for HIV/AIDS transmission
3. **Describe** the types of co-occurring disorders that may be seen in patients diagnosed with HIV/AIDS
4. **Describe** HIV testing, confidentiality of test results for patients, and partner notification

Disclosures

The following individuals were involved in the development of this activity: Marilyn Lajoie, MD, DC, CCSP, Susan DePasquale, MSN, PMHNP-BC, and Amanda Mayer, PharmD. There are no financial relationships relevant to this activity to report or disclose by any of the individuals involved in the development of this activity.

Introduction

The human immunodeficiency virus (HIV) is a retrovirus that causes acquired immunodeficiency syndrome (AIDS). The human immunodeficiency virus can significantly depress immune system function leading progressively to AIDS. Prior to the development of antiretroviral medications, essentially everyone infected with HIV progressed to developing AIDS, leading to the development of opportunistic infections and/or neoplasms. The introduction of antiretroviral therapy (ART) has reduced the morbidity and mortality associated with HIV-1 infection and AIDS, and it has enabled HIV-infected individuals to live longer and have an improved quality of life. Nevertheless, HIV and AIDS are still serious health problems that continue to require federal and state resources. This course provides a general discussion on the transmission, progression, and a brief overview of the treatment of HIV and AIDS and also includes relevant case studies.

HIV Etiology of HIV/AIDS

The human immunodeficiency virus appeared in the United States in the early 1980s.[1] The U.S. Food and Drug Administration (FDA) approved the first diagnostic test for HIV in 1985.[1] The virus was and remains more prevalent among specific population groups. Prior to the development of ART, HIV was regarded as a death sentence. Early diagnosis and treatment of HIV have slowed or prevented the spread of HIV and resulted in significantly better outcomes for those infected. However, even with these advances, there is no cure and no effective vaccine for HIV.[1,2]

Despite public awareness and increased testing, many individuals do not know they are infected with HIV. It is estimated that 30% of new HIV infection cases consist of individuals who do not know they have HIV and the partners they unknowingly infect.[3] Infections with HIV and the development of AIDS in the U.S., disproportionately affect racial and ethnic minorities, gays, bisexuals, and men who have sex with men (MSM).[2,4]

Prevalence of HIV

The Centers for Disease Control and Prevention (CDC) provides annual reports on the prevalence of HIV/AIDS in the U.S. and its 6 dependent areas. According to the CDC's 2019 report for these regions, there were 36,801 new HIV diagnoses in the year 2019, with men who have sex with men (MSM) accounting for 69% of the new diagnoses.[2] Approximately 1.2 million people are living with HIV infection, and approximately 13% of those individuals don't know they are positive and need testing.[4] At the end of 2019, the overall rate for a diagnosis of HIV was 11.1 per 100,000 population.[2] These numbers and rates for the U.S. and its 6 dependent areas show a decreasing trend for the period 2015 through 2019.[2] During this same period of time, the rate and number of deaths remained stable; however, deaths of transgender male-to-female individuals with HIV increased in 2019.[2]

Types and Stages of HIV Infection

The human immunodeficiency virus is a *retrovirus*.[5] An infection with HIV is a process of viral entry into the body, attachment of HIV to cells in the immune system, entry of HIV into those cells, and then replication. Replication is the process by which HIV uses its RNA and the host's DNA to produce copies of itself after entering a cell.[5]

HIV-1 and HIV-2

There are two types of HIV: HIV-1 and HIV-2.[5] In the U.S., the human immunodeficiency virus-1 is the most common HIV infection, and human immunodeficiency virus-2 infections are seldom seen.[5] The HIV-2 virus is less easily transmitted, and infection with HIV-2 progresses more slowly than infection with HIV-1.[5] Both HIV-1 and HIV-2 can progress to AIDS.[5]

Stages of HIV Infection

When a person becomes infected with HIV, the progression of the infection may be described in stages. These descriptions may vary, but the

National Institute of Health (NIH) finds it useful to describe the stages as (1) acute HIV infection, (2) chronic HIV infection, and (3) acquired immunodeficiency syndrome (AIDS).[6]

The Acute HIV Infection Stage

The stage immediately following an HIV infection is the acute HIV infection stage. This stage generally develops within 2 to 4 weeks after infection with HIV and may last for months. This stage also includes seroconversion, which is the viral release from the lymph nodes into the bloodstream. At this point, the blood levels of HIV are very high, which increases the risk of transmission. Starting ART therapy during this time may lead to great health benefits.[6]

According to Hurt, *et al.* (2017), after an exposure leading to HIV infection, 50% of infected people will have detectable plasma RNA within 12 days.[1] Nonspecific signs and symptoms such as fever, malaise, pharyngitis, and rashes may be present during this phase, but a majority of patients are asymptomatic.[5] For those with symptoms, their signs and symptoms tend to last for several weeks and then subside. Because of the nonspecific character of these symptoms and their subsidence, HIV infection may be missed and mistaken for a mild, self-limiting viral illness.[5] For those patients with prolonged symptomatic illness (>14 days), the likelihood exists of the rapid development of AIDS.[5]

The Chronic HIV Infection Stage

The second stage of HIV infection is the chronic HIV infection stage, which is also called asymptomatic HIV infection or clinical latency.[6] It is characterized by "a relative stability of the viral load and a progressive decline in the CD4 cell count."[5] When this occurs, a patient may progress in three directions. Some patients have chronic HIV infection without AIDS. Other patients will be symptomatic and develop AIDS. These patients present with CD4 cell counts <200 cells/μL (microL) or an AIDS-defining condition. A final

group of patients is described as having an advanced HIV infection. These patients had a CD4 cell count of <50 cells/μL.[5]

Patients who have a chronic HIV infection, without the signs or symptoms characteristic of AIDS, have relatively stable viral levels, but a declining CD4 cell count.[5] This presentation may involve an asymptomatic HIV infection or clinical viral abeyance or latency.[4] Without treatment, a CD4 cell count of <200 cells/μL usually takes about 8 to 10 years after infection to develop.[5] During this stage, the virus becomes established in cells of the immune system, particularly a subset of T lymphocytes called helper T cells. The infected host is asymptomatic because the immune system at this point can contain the virus to a degree sufficient to prevent the development of AIDS.[5] However, because HIV has the ability to replicate and mutate rapidly, elimination of the virus is not possible. In addition, the viral reservoirs cannot be eliminated. The asymptomatic stage varies between individuals, but on average, lasts for an estimated 5 to 10 years.[5] An individual taking ART may be maintained in this stage for several decades. It is still possible to transmit HIV in this stage; however, those taking ART exactly as prescribed may maintain an undetectable viral load with little risk of transmission.[6]

AIDS

AIDS is the final and most severe stage of HIV infection. Patients who have chronic HIV infection with the signs or symptoms of AIDS have very low levels of T-helper cells, severe damage to the immune system, and the development of opportunistic infections and neoplasms.[5] The T-helper cells function in part by releasing cytokines, which are proteins that influence the antiviral activity of other immune system cells.[5] The T-helper cells are sometimes referred to as CD4 T cells because they have a glycoprotein on their surfaces called CD4, which helps the T-helper cells recognize HIV.[5]

The CD4 T-helper cells infected with and damaged by HIV cannot initiate and coordinate an immune response to the virus. If the CD4 cell count is below 200/μL and/or the patient has one of the diseases that are considered indicative of a severely compromised immune system, regardless of the CD4

cell count, the patient is diagnosed as having AIDS.[5] As mentioned above, this may progress to the final group of chronic HIV patients who have an advanced HIV infection, *i.e.*, CD4 cell count <50 cells/μL.[5]

An individual diagnosed with AIDS can have a very high viral load and may be able to transmit HIV to others easily. According to the NIH, individuals with AIDS who do not receive treatment typically survive about 3 years.[6]

HIV Transmission and Prevention

HIV can be contracted through a number of routes. The manner in which HIV may spread can vary based on cultural, lifestyle, or geographical distinctions.[5] Understanding and controlling the transmission of HIV is crucial to managing and preventing this disease.

Transmission of HIV occurs primarily by contact with infected blood and by sexual contact. The human immunodeficiency virus can also be transmitted perinatally and through breast milk. HIV can be found in essentially any type of body fluid or secretion, but the risk of transmission from contact with body fluids/secretions other than blood, semen, or vaginal fluids tends to be remote.[5] Feces, gastric secretions, sputum, and body fluids other than blood, semen, and vaginal fluids may contain HIV, but they are not considered infectious unless they are visibly contaminated with blood.[5]

The existence of similar or dissimilar HLA-class-I alleles appears to influence the risk of HIV transmission.[5] Viral load is defined as the number of virus particles (often called copies) per volume of blood. Viral load is a significant risk factor for HIV transmission. The higher the viral load, the greater the risk.[7] Viral load impacts the risk of transmission of HIV in different contexts, *e.g.*, sexual activity, needle sharing, or occupational exposure in the case of healthcare workers.[7]

Sexual Transmission

Most HIV infections happen from sexual activity with an infected person. The sexual transmission of HIV depends on multiple factors, such as circumcision, genetic factors, viral load, sexual behaviors, other sexually transmitted diseases, and the administration of ART.[5,8,9] Circumcision has been shown to decrease the incidence of HIV infection in men significantly.[5] However, circumcision does not appear to decrease the risk of male-to-female transmission.[7] Being uncircumcised has been shown to increase the risk of HIV transmission in MSM and in serodiscordant (one person is HIV positive, the other is not) couples.[5,7] Also, the higher the viral load of an infected person, the greater the risk of HIV transmission to a partner during sexual activity.[7]

Sexual behaviors that influence HIV transmission may include the type of sexual activity, number of sexual partners, use or non-use of condoms, and sexual activity corresponding with alcohol or drug use.[5] The risk of HIV transmission during one act of unprotected intercourse is an estimated 0.04% female-to-male and 0.08% male-to-female.[10] The presence of a sexually transmitted disease increases the risk for HIV transmission.[7] An understanding of the risk factors for sexually transmitted HIV infection is fundamental in the prevention of the spread of HIV/AIDS.

Sexual Transmission Prevention Strategies

Prevention strategies for sexually transmitted diseases need to include "behavioral and biomedical interventions to reduce HIV infection risk."[7] Behavioral changes may include a change in the type of sexual activity, a reduction in the number of sexual partners, the use of condoms, and understanding the role alcohol or drug use during sex may play in leading to more risky behavior.[5] Biomedical interventions would include the use of ART. When ART reduces viral load to certain levels, the risk of transmission of HIV is greatly reduced.[5] Education on risk reduction techniques should be provided to patients, especially those that are at high risk.[11]

Blood Transfusion Transmission

Human immunodeficiency virus can be transmitted by transfusion with leukocytes, packed red blood cells, plasma, platelets, and whole blood.[7] However, potential donors are screened for HIV infection, and donated blood is tested for HIV antibodies, HIV antigen, and HIV nucleic acid. As a result, the risk has been reported as low.[7] The reported risk of HIV transmission following a contaminated blood transfusion is approximately 88% to 100%.[7]

Case Study: Blood Transmission of AIDS in an Adolescent

The authors reported on a 13-year-old male who presented with a recent history of two weeks of notable fatigue and pallor associated with 1 week of chest distress.[12] On physical examination, the patient weighed 50.5 kg. Testing included immediate testing of his bone marrow by aspiration. A complete blood count (CBC) revealed white blood cells (WBC) 16.2×109/L, neutrophils at 11.4%, hemoglobin 75 g/L, and the patient's platelet count was 79×109/L.[12]

The patient was diagnosed with acute lymphocytic leukemia (ALL) with "L2, common-B and middle risk according to the results of bone marrow cytomorphology examination, flow cytometry immunophenotyping (FCMI), and CBC (complete blood count)."[12] Chemotherapy was carried out sequentially over a 3 month period, and when hemoglobin reached below 70 g/L and/or platelets below 20×109/L, the patient received a transfusion of red blood cells (RBC) and/or platelets, respectively; fresh frozen plasma (FFP) was used when the dysfunction of blood coagulation was detected. He was multi-transfused with 16 Units of RBC, 20 Units of platelets, and 820 ml of FFP.[12]

Serial surveillance of rapid plasma reagin (RPR), the antibody of HIV (HIV-Ab), and hepatitis viruses were initiated. The patient was readmitted for consolidation chemotherapy, and prior to transfusion, he tested positive for HIV antibody, which was confirmed by the CDC. Prior transfusions were investigated, and it was found that the first FFP had carried HIV.[12]

The authors noted that while every unit of donated blood with a positive result from HIV antibody testing was discarded according to protocol, HIV transmission may still occur due to a variety of factors. For example, blood donations collected during the window of infection, a long-term HIV chronic carrier state without HIV antibody development or loss, infection with variant strains of HIV that are undetectable by newer serologic assays, and testing or clerical errors could all lead to transmission.[12]

Needle Sharing

The risk of HIV transmission from the use of an HIV-contaminated needle has been estimated to be one infection per 150 exposures to needle or syringe sharing.[7] Needle sharing should never occur. Needles should be used only within a clinical setting or as prescribed for medical reasons. Always safely dispose of needles or syringes after use.[7] The CDC reports that HIV can survive in a used syringe for up to 42 days depending on temperature and other factors.[13]

Occupational Exposure

Blood is the most common source of HIV transmission to healthcare workers, and other body fluids, such as amniotic fluid, cerebrospinal fluid, pericardial fluid, pleural fluid, and synovial fluid are also considered potentially infectious.[14] Feces, gastric secretions, nasal secretions, saliva, sputum, sweat, tears, and urine may contain low amounts of HIV but are not considered infectious unless they are visibly contaminated with blood.[5,14]

Percutaneous Inoculation (Needlestick)

An exposure that places healthcare workers at the most risk for infection with HIV involves percutaneous inoculation (needlestick) with blood from a patient with an HIV infection, accompanied by the presence of a detectable viral load in the patient, and/or the patient is not on suppressive antiretroviral therapy.[14] The patient's historical suppressive antiretroviral therapy is also important.[14]

Henderson (2012) estimated that each year almost 1 of every 10 healthcare workers in the United States has a needlestick exposure.[15] Another study in 2018 surveyed 358 medical students and 247 members of the staff of the department of surgery. This study found that 38.7% of those who responded had been exposed to a needlestick injury.[16]

Not all workers exposed through a needlestick injury will be infected with HIV. Research indicates that the risk of occupational transmission of HIV and subsequent development of an infection is rare.[17] The risk of HIV transmission from the use of an HIV-contaminated needle has been estimated to be one infection per 435 exposures to percutaneous needle-stick.[7] Wyżgowski, *et al.* (2016) stated that the probability of HIV infection caused by needle injury ranges between 0.3% to 0.03%, based on risk factors identified previously.[17] The risk of HIV infection is greater if the viral load is high, the amount of blood injected or splashed is high, a large bore or hollow needle was involved,[17] as well as a deep injury or an injury from a visibly contaminated device.[7] Certain characteristics related to the individual who is the source of the blood are also important. An injury with a needle that had been placed in a vein or artery of a terminally ill, infected patient will raise the risk of an actual infection.[7] Post-exposure prophylaxis can reduce the probability of an infection following a needlestick.[17]

For the rare instances of transmission, the premise that most people with AIDS exhibited high-risk behaviors that led to their HIV infection, may be applied to healthcare professionals.[17] Risky behaviors are estimated to cause 95% of HIV infections.[17] Wyżgowski, *et al.* (2016) evaluated the daily routine of surgeons and anesthetists to determine whether they treated *every* patient as being potentially HIV-positive, or whether they engaged in risky behavior by not doing so.[17] They found that these medical professionals only took precautions if the patient was from a known high-risk group, such as male homosexuals, bisexuals, intravenous drug abusers, *etc.*[17]

Needlestick Prevention for Healthcare Workers

Wyżgowski, *et al.*, stated that it is important for clinicians, including pharmacists, to recognize that "every patient can be HIV-positive or can be infected with other blood-borne pathogens."[17] Safety rules to prevent HIV transmission need to be observed on a daily basis.[17]

Zachary (2019) sets out the accepted recommendations on the management of occupational exposures.[14] Additionally, the CDC report on the *Surveillance of Occupationally Acquired HIV/AIDS in Healthcare Personnel, as of December 2010* (last updated in 2011), addressed HIV infection in healthcare workers as well as recommendations for ongoing HIV surveillance testing and may be consulted as well.[18]

During the follow-up period after a healthcare worker is exposed to HIV (especially the first 6 to 12 weeks, when most infected persons are expected to show signs of infection), the exposed healthcare worker should follow standard recommendations for preventing transmission of HIV. These include not donating blood, semen, or organs and not having unprotected sexual intercourse.[14] If someone chooses to have sexual intercourse, using a condom consistently and correctly may reduce the risk of HIV transmission.[14] In addition, women should consider not breastfeeding infants during the follow-up period to prevent exposing their infants to HIV in breast milk.

The general guidelines for healthcare workers who have been exposed to HIV include the following precautions and steps:[14]

- Exposed mucous surfaces should be flushed with copious water. The eyes should be irrigated by using water or saline. Squeezing a wound to express fluid has not been shown to lower the risk of bloodborne pathogen transmission.
- A wound should be washed with soap and water, or the area flushed with water. Antiseptics have virucidal action and may be helpful.
- Healthcare workers should notify the department that is responsible for handling occupational exposures to bloodborne pathogens.

- If possible, rapid HIV testing should be done on the source patient, and hepatitis B and hepatitis C status should be determined as well.
- The exposed person should be tested for the presence of hepatitis B, hepatitis C, and HIV.
- Testing for HIV should be done immediately with serial testing according to the CDC guidelines.
- Post-exposure drug prophylaxis (PEP) for occupational HIV exposure should be started as soon as possible, preferably within one to two hours after the exposure, and it is typically not recommended after 72 hours. Initiation of PEP should not be delayed while waiting for HIV test results. In certain high-risk situations, PEP can be started up to a week after an HIV exposure.

Possible Exposure risks for Pharmacists and Technicians

All healthcare workers should be cautious of bodily fluid exposure, including pharmacists and pharmacy technicians. Accidental needle sticks can be a large risk factor in a pharmacy setting. All needles and syringes should be disposed of properly in a sharps container, and needles should never be recapped after use to avoid an accidental stick. Gloves should also be worn anytime vaccinations are being given. For pharmacists who do point-of-care testing, proper use of gloves and immediate disposal of testing supplies can greatly decrease the risk of bloodborne pathogens. Pharmacists in hospital settings should be sure to wear appropriate garb for the setting they are entering. All pharmacists should be aware of bodily fluids that may be on bottles and supplies that patients may bring in and be cautious and diligent when handling patients' supplies.

Case Study: Accidental needlesticks reported by a retail pharmacy chain

In a study that reviewed needlestick injury reports from 2000 to 2011 in a nationwide retail pharmacy chain, there were 33 likely preventable needlestick injuries reported by 31 different pharmacy locations.[19] Luckily, no pharmacists were reported to have been infected with bloodborne pathogens after their needlestick injuries.[19] Most of the injuries (73%) occurred during

the peak of influenza vaccine administration from September through January. The injuries most commonly occurred (58%) after use and before disposal of the needle. The study reported other injuries that happened during the use of the sharp, while putting the sharp into the disposal container, while disassembling the sharp, the sharp being left in an inappropriate place, and "other."[19]

SHEA Guidelines and the HIV-infected Healthcare Worker

The Society for Healthcare Epidemiology of America (SHEA) regarding the management of healthcare workers who are infected with hepatitis B virus (HBV), HCV, and/or HIV recommends that, although some aspects of the approach to and management of these infectious syndromes in healthcare workers are similar, separate management strategies for healthcare workers who are infected with these unrelated viruses is appropriate.[20]

With regard to HIV-infected healthcare workers, SHEA recommends routinely double-gloving for all invasive procedures. This also applies to healthcare workers who have been infected with HBV and HCV.[20] The goal is to prevent contact with mucous membranes or skin. Infected healthcare workers should not perform activities that carry a risk for transmission of a bloodborne pathogen from a healthcare worker to a patient despite the use of appropriate infection control procedures. Higher risk work activities of infection transmission include such scenarios as general surgery and other surgeries, specifically any open surgical procedure with a duration of >3 hours (necessitating frequent glove changes), and emergency settings where patients may become unstable or violent, *i.e.,* an epileptic or mentally ill patient who may be at risk of biting an infected healthcare worker.[19] Other examples of healthcare scenarios with a higher risk of infection transmission are listed in the SHEA guidelines.[20]

The SHEA guidelines encourage routine, voluntary, confidential testing of healthcare workers in order to stay informed on the status of their immune system or HIV infection. Also, the SHEA guidelines state that "because of the

complexity of these cases, each such case will be slightly different from the next, and each should be independently considered in context."[20]

Emphasis is placed in the SHEA guidelines on appropriate infection control procedures to reduce patient exposure to blood, with specific mention of transferring blood products between healthcare workers to patients and between healthcare workers. This precaution applies to all healthcare workers whether they have been previously infected or not infected with a bloodborne pathogen. Increased risk of bloodborne pathogen transmission by healthcare workers to patients is outlined in the SHEA guidelines, and recommendations are made for each known pathogen.[20]

OSHA Bloodborne Pathogen Standards

Adherence to the bloodborne pathogen standard established by the Occupational Safety and Health Administration (OSHA) is mandatory for all hospitals and healthcare facilities. To comply with the standard, employers must establish a written plan for controlling exposure to bloodborne pathogens.[21-23] This plan should include 1) an assessment of risk situations, 2) a determination of which employees are at risk and when they are at risk, and 3) specific actions the employer will use to control and manage exposure to bloodborne pathogens.[21-23]

The plan for controlling exposure to bloodborne pathogens and disease risk must be reviewed and updated annually by a health organization and must be accessible to all employees, as outlined below.[21-23]

- Implement standard precautions, ensure that employees know how to use standard precautions, and ensure they use standard precautions.

- Provide personal protective equipment (PPE) at no cost to all employees who need it. Indicate critical or common times PPE should be donned.

- Provide initial training and annual training on bloodborne pathogens to all employees. This training should include the following:[21-23]

- a review of the OSHA Bloodborne pathogens standard
- information on the risks of exposures and how exposures happen
- information on how to prevent exposures to bloodborne pathogens
- information on the benefits and risks of vaccination against hepatitis B

- Use engineering controls to control risk. Engineering controls that control the risk of exposure to bloodborne pathogens would include the following:[21-23]

- providing sharps disposal boxes
- using safe medical devices
- using needles that do not need to be re-capped
- providing proper waste disposal containers
- using appropriate signs to warn of danger, and to instruct employees on the proper use of equipment

- Use work practice controls. The employer must have a plan or plans in place for the proper handling and disposal of blood and other specimens, the proper handling and disposal of contaminated waste, and the proper cleaning and decontamination of equipment, patient rooms, and patient care areas.

- Offer vaccination against hepatitis B to all employees who may be reasonably expected to have occupational exposure to the hepatitis B virus.

- Have a plan to handle employee exposure to bloodborne pathogens. This plan should include provisions for immediate care (*i.e.*, evaluation, first aid, laboratory screening tests, post-exposure prophylactic medications) and follow-up care.

All healthcare employees must comply with the requirements of the bloodborne pathogens standard.[21] These standards include:

- Understanding and following the engineering and work practice controls established by the employer, such as proper waste disposal and adhering to the employer's safety and sanitary rules.

- Using PPE correctly: the employee is required to wear the appropriate PPE. The PPE must be removed immediately upon leaving the work area (or as soon as possible), and it must be placed in a container specifically designated for the purpose of receiving contaminated waste.

- Proper handling of blood and other body fluids.

- Understanding and using Universal Precautions.

- Proper use of medical equipment, *i.e.*, do not bend, break, or re-cap needles. Do not reuse disposable medical equipment.

- Proper disposal of contaminated or potentially contaminated medical equipment.

- Food and drink should not be stored in refrigerators, cabinets, *etc.*, where blood or other potentially infectious material will be stored.

- Double-bagging specimens is required if the outside of the specimen container is contaminated or if the specimen could puncture the primary container.

Disposable gloves, when needed, must be discarded as soon as possible after they have become contaminated, punctured, or torn. Gloves are not required to be worn when giving an injection as long as hand contact with blood, or other potentially infectious material is not reasonably expected.[21] Although gloves are not required, they are recommended and should be readily available for use.

Employees must wash their hands immediately after removing gloves or as soon as possible after removing gloves. Employees must wash their hands after contact with blood or other potentially infectious material and before and after performing patient care.[21-23] If handwashing with soap and running water is not possible, the employee must use either an antiseptic hand cleaner with clean cloth/paper towels or antiseptic towelettes. After using an antiseptic hand cleaner or a towelette, employees must wash their hands with soap and running water as soon as feasible.[21-23]

PEPline Hotline

The National Clinicians' Post-Exposure Prophylaxis Hotline (PEPline) can be reached anywhere in the U.S., seven days a week, according to their website instructions.[14] The PEPline has trained physicians who are prepared to give information, counseling, and treatment recommendations for injuries involving needle sticks and other serious occupational exposures to bloodborne microorganisms that place the healthcare worker at higher risk of serious infections, such as HIV.[14]

Healthcare Worker to Patient HIV Transmission

Transmission of a communicable disease from healthcare workers to patients is a quality indicator issue. There are reported cases of airborne transmission of diseases from healthcare workers to patients, such as influenza; however, bloodborne infections like HIV, HBV, and HCV have also occurred through accidental blood exposure.[24] Bouvet (2018) stated that the risk of disease spread from healthcare workers to patients has increasingly come under global standards of health prevention through vaccination of healthcare workers for influenza and HBV infections.[24] Healthcare facility policy and monitoring of internal infection control procedures, including standard precautions, air precautions, and prompt treatment of infected healthcare workers, aim at the prevention of infectious disease spread.[24]

CDC Guidelines

The prevention of patient exposure to infection from healthcare workers is an ongoing area of research amongst occupational medicine specialists. This area of public interest in the provider-to-patient transmission of bloodborne pathogens came front and center in 1990 after a cluster of HIV infections of patients by a Florida dentist.[25] These Florida cases led to the 1991 publication of CDC guidelines, entitled, "Recommendations for Preventing Transmission of Human Immunodeficiency Virus and Hepatitis B Virus to Patients During Exposure-Prone Invasive Procedures."[25]

The CDC guidelines have not been updated for HIV since its initial publication; however, in 2011, the CDC reiterated that the transmission of HIV to patients within a healthcare setting is rare.[18] The CDC generally addressed proper sterilization and disinfection procedures to minimize infection risks from healthcare workers to patients.[18]

Mother-to-Infant Transmission

The human immunodeficiency virus can be transmitted from a mother to a child during pregnancy, labor, and after birth via breast milk. The most important factor for mother-to-child HIV transmission is the viral load, which applies to prenatal transmission, transmission during birth, and transmission via breast milk.[26]

In resource-rich industrialized countries, the risk of HIV transmission in the *absence* of prenatal ART in breastfeeding mothers has been estimated to be between 15-25%.[26] If a mother and infant both receive prophylactic ART and the infant is not breastfed, this risk is approximately 0.1%.[26] The American Academy of Pediatrics has advised that regardless of viral load and/or the use of ART, HIV-positive mothers should not breastfeed.[27,28]

Pre-Exposure Prophylaxis, ART, and Other Preventions

There is no cure for HIV, and the virus cannot be completely eradicated once a person has been infected.[5] Prevention is key. There is also no vaccine to prevent HIV. The transmission of HIV can be prevented in many ways. ART, sexual abstinence, the use of condoms, avoidance of sharing drug-injection equipment, and pre-exposure prophylaxis are all effective means of prevention.

For couples who are serodiscordant, ART significantly reduces the viral load and helps to prevent the transmission of HIV.[9,29,30] The effectiveness of condoms in preventing the transmission of HIV, if used properly, has been estimated to be 87-94%.[9] Lambskin condoms are less effective in preventing HIV transmission than latex and polyurethane condoms. A dental dam (a thin square of latex) or condoms can be used to help prevent the transmission of HIV from oral sex.[29,30]

Oral contraceptives do not appear to affect the transmission of HIV infection positively or negatively. However, there is some evidence that injectable contraceptives, such as depot medroxyprogesterone acetate, may increase this risk.[31,32] Over-the-counter spermicidal jellies do not prevent the transmission of HIV.[33,34] Douching has been reported to increase the risk of HIV transmission.[35]

Pre-Exposure Prophylaxis

Providing intravenous drug users with sterile syringes aims to reduce needle sharing and can help to decrease the incidence of HIV infections.[36] Intravenous drug users who have an HIV-positive partner, people who share injection equipment, and those who have recently undergone drug treatment, but are not currently injecting drugs may benefit from pre-procedure prophylaxis.[37] The CDC recommends pre-exposure prophylaxis (PrEP) with Truvada® (emtricitabine and tenofovir) to prevent the transmission of HIV. The CDC's PrEP guidelines state that with the use of Truvada®: "*Recent findings from several clinical trials have demonstrated safety and a substantial*

reduction in the rate of HIV acquisition for men who have sex with men (MSM), men and women in heterosexual HIV-discordant couples, and heterosexual men and women recruited as individuals."[37]

Pre-exposure prophylaxis is recommended for men and women who are at substantial risk for acquiring HIV. This may include those who have an HIV-positive sexual partner, have recently had a bacterial STD, have a high number of sexual partners, have a history of inconsistent or no condom use, or are involved in commercial sex work.[37] Requirements for pre-exposure prophylaxis are a documented negative HIV test, no signs or symptoms of an acute HIV infection, normal renal function, no use of medications that are contraindicated, and documented hepatitis B status (along with hepatitis B vaccination if indicated).[37]

Case Study: Pre-Exposure Prophylaxis

The authors described a case where a PrEP was discontinued because of adverse effects of the PrEP. This case highlights the need for an alternative HIV prevention plan when discontinuing PrEP.[38]

The case involves a 56-year-old European MSM who moved to Bangkok. After 2 months in Bangkok, he started to take tenofovir disoproxil fumarate in combination with emtricitabine (Truvada) as pre-exposure prophylaxis.[38] Patient history disclosed that he had an average of two partners per week with condom and condomless anal intercourse. The patient was a single male who was using sildenafil 100 mg tablets and prostaglandin injections for erectile dysfunction. He also reported recreational drug use that included crystal methamphetamine, regular use of ecstasy, and occasional use of ketamine.[38]

Eleven months after starting the PrEP, the patient stopped taking PrEP on medical advice due to poor renal function results. At that time, he was diagnosed with secondary syphilis (rashes to the palm and sole) and treated. After syphilis treatment, with a negative HIV test and additional renal function testing (creatinine 1.26 mg/dL and eGFR 62), he did not restart PrEP again due to renal function parameters.[38]

Two months after treatment for secondary syphilis, he was again diagnosed with syphilis proctitis and wanted to begin PrEP again, but renal function parameters contradicted PrEP use (Cr 1.53 mg/dL and eGFR of 50).[38] While not on PrEP and unprotected against HIV, he continued to have receptive and insertive anal sex without a condom, often engaging in "Chemsex," which is the use of recreational drugs during sex. Three months later, he was diagnosed with HIV.[38]

The authors stated that this case was informative by focusing on MSM behavior after attempts to seek protection against HIV in the context of high HIV prevalence.[38] Behavior prior to and during PrEP was characterized by occasional condom use in this MSM case, but later the patient found it hard to reduce condomless sex after discontinuation of PrEP, and he became infected with HIV. An awareness that he was no longer protected by PrEP did not cause him to resume another means of HIV prevention.[41] There is a need for clinicians to consider alternative HIV prevention plans for their patients who discontinue PrEP.[38]

HIV Screening

Screening to detect HIV is recommended by the CDC for everyone aged 13 to 64 years of age, women who are pregnant or may become pregnant, anyone who is in a high-risk group, anyone who seeks treatment for an STD, and all patients who are diagnosed with hepatitis B or tuberculosis.[39,40] The current 2021 guidelines from the CDC recommend that HIV screening should be done in the following cases:[40]

- All individuals aged 13-64 years
- All individuals who are <15 years old or >65 years old and have a high risk for HIV infection.
- High-risk individuals, such as men who have sex with men, injection drug users, persons who report high-risk sexual behavior, and people who live in an area with >1% HIV prevalence
- All pregnant women

- The optimal screening intervals have not been determined, but patients who are at high risk should be tested at least annually, and more frequent testing may be cost-effective.

Blood Test for Antibodies to HIV and HIV Antigen

Screening is done using blood tests that look for antibodies to HIV and the HIV antigen.[41] Antibodies usually appear from 4 to 12 weeks following infection. This means that for most people, an antibody response to HIV will be detected within three months of infection with the virus. Alternatively, a person who tests negative, but has been involved in high-risk behavior within three months of the test could still have an HIV infection, which is the window often mentioned relative to HIV screening.[41]

The latest CDC guidelines (2014) for laboratory testing to detect HIV in adults and children 2 years of age and older include the following criteria:[41,42]

- A combination test that detects antibodies to HIV-1 and HIV-2 *and* p24Ag (an HIV antigen). The combination test detects HIV antigens (which can be seen 12-26 days after infection) and antibodies formed against HIV-1 and HIV-2 (which can first be detected 20-45 days after the infection).
- If the combination test is negative, there is no infection.
- If any part of the combination test is positive or indeterminate, then nucleic acid testing should be done. Nucleic acid testing checks for target sequences of specific HIV genes.
- If the nucleic acid testing is positive, there is an HIV infection. If the nucleic acid testing is negative, there is no infection.

Home Screening Tests

The Food and Drug Administration (FDA) has approved two home screening tests used to detect HIV: *OraQuick*® and *Home Access HIV-1 Test System*.[43,44] OraQuick® uses an oral swab, and a test liquid, and the results are ready in 20 minutes.[44] The test has a sensitivity of approximately 93.6% and a specificity of 99.9%.[45]

A positive test must be confirmed by laboratory testing.[43,44] A false positive can be caused by lupus, Lyme disease, syphilis, and other diseases. A false negative can be caused by a low level of antibodies, testing that is done too soon after exposure, if the patient is taking ART, and other conditions.[43,44] The Home Access test requires the individual to use a lancet and place several drops of blood on a test card. The test card is mailed to a laboratory, and the results are available seven days later. The sensitivity and specificity of the test are both >99%.[43-45] If the test is positive, a confirmatory test does not need to be done. Neither OraQuick® nor the Home Access test can be used to test for HIV-2.[43,44]

Pharmacists should be aware of where home tests are located if they carry them in their pharmacies. Pharmacists should also be prepared to give patients information on where testing may be available, direct patients to their primary care provider for laboratory testing if there is a significant concern, and steps to take if a home test comes back positive.

AIDS and Co-occurring Disorders

An AIDS diagnosis can affect every organ system. The signs and symptoms of the disease, such as anorexia, cough, diarrhea, fatigue, fever, and weight loss, are non-specific to AIDS, which can only be diagnosed through blood testing. Symptoms can develop because of adverse effects of the antiretroviral therapy used to treat HIV, as a direct result of the infection, from opportunistic infections (such as *Pneumocystis* pneumonia), and neoplasms (such as Kaposi's sarcoma).[5] Some of the systemic diseases caused by AIDS include those outlined in this section.

Cardiovascular Disease

Coronary artery disease, cardiomyopathy, and myocardial infarction are more common in people diagnosed as HIV positive than in people who are not.[5,46] The American Heart Association has reported that the risk of heart disease and stroke in HIV-infected individuals is an estimated 1.5 to 2 times greater than for people not infected with the virus.[46]

Previously, antiretroviral therapy was thought to increase the risk of cardiovascular disease; however, current evidence suggests that continuous antiretroviral therapy corresponds with a lower risk of cardiovascular disease than is found in people receiving an intermittent course of antiretroviral therapy. Elevated cardiovascular disease in HIV patients may be due to "chronic inflammation and an unusual stimulation of the immune system, triggered by HIV, even when the virus is well-controlled."[46]

Pulmonary Disease

Pulmonary disease is a typical complication of AIDS. Sinus infections, bacterial and fungal pneumonia, and tuberculosis are common in people who have AIDS.[5,47] There is a high incidence of chronic pulmonary disease and respiratory symptoms in HIV-infected individuals. Chronic obstructive pulmonary disease (COPD) and asthma are both associated with AIDS, with AIDS being reported to be an independent risk factor for COPD.[47]

Tuberculosis (TB) is spread through exposure to sputum acid-fast bacilli (AFB). On a global scale, TB is a leading cause of infectious disease death.[48] According to Al Abri, *et al.* (2020), TB surpassed HIV/AIDS in terms of morbidity/mortality rates, and in 2018 an estimated 1.5 million deaths worldwide resulted from a TB infection, of which 251,000 deaths involved HIV-positive individuals.[48]

The CDC guidelines recognize that "TB disease can be difficult to diagnose in persons who have HIV infection (or other conditions associated with severe suppression of cell-mediated immunity) because of nonclassical or normal radiographic presentation or the simultaneous occurrence of other pulmonary infections [...] Patients who are HIV-infected are also at greater risk for having extrapulmonary TB."[49] Healthcare workers exposed to patients with suspected or confirmed infectious TB disease should consider being offered the use of an N95 disposable respirator.[50]

Neurological Disease

Almost every patient with HIV infection has some degree of neurologic impairment. Neurologic diseases are an especially serious cause of morbidity in AIDS patients and are caused by opportunistic infections, such as toxoplasmosis, neoplasms such as Kaposi's sarcoma, and a direct result of the HIV infection (as with aseptic meningitis and AIDS dementia complex).[5,51] HIV-1 spreads hematogenously once it enters the body and enters the brain through blood-derived macrophages.[51] Cell trafficking is reported to occur across the blood-brain barrier, although this process is not well understood. The "trafficking-infected cell" is reported to transmit the virus to the brain side of the blood-brain barrier.[51,52]

An inflammatory cascade is seen in cases of encephalitis, "pathologically characterized by white matter pallor, neuronal loss, and astroglial reaction."[51] This leads to primary HIV disease or a direct HIV infection of the nervous system.[51]

There is a broad spectrum of HIV-associated neurological disorders that can affect any area of the brain and nervous system. They tend to be stage-specific, affecting a person's immunity. Dysfunction of other organ systems, notably involving metabolic disorders, and drug side effects and/or complications resulting from pharmacological treatment of HIV infection can also lead to neurological complications. This typically occurs during end-stage HIV infection.[51]

Oral Lesions

Fungal and viral infections of the mouth are a complication of AIDS and exist in 50% of HIV-infected individuals and in 80% of those with an AIDS diagnosis.[53] Leading signs of HIV infection include oral candidiasis, hairy leukoplakia, Kaposi sarcoma, linear gingival erythema, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis, and non-Hodgkin lymphoma.[53] Oral candidiasis remains the most common opportunistic infection seen in pediatric and adult HIV cases.[53] *Candida albicans* can be found in the oral

cavity of healthy individuals and can develop into a disease-causing pathogen under conditions such as the low CD4 counts resulting from immunosuppression seen in HIV.[53]

Oral infection is an early sign and predictor of the progression of AIDS. According to Warrier and Sathasivasubramanian (2015), the continuous state of immunosuppression in people diagnosed with AIDS "leads to a variety of clinical conditions which ranges from a primary infective state to the advanced disease."[53] Oral health is an important indication of a person's immune status, and a low CD4 count often correlates with the varied types of candidiasis.[53] *Pseudomembranous candidiasis* involves symptoms of white, creamy, curd-like plaques commonly seen on the buccal mucosa and tongue. *Hyperplastic candidiasis* manifests as white plaques on the buccal mucosa. Scraping will not remove these plaques.[53]

Erythematous candidiasis is described by the authors as "the most missed and misdiagnosed oral feature of HIV which is characterized by the presence of red lesions which are flat and seen on the dorsal aspect of the tongue and also on the hard or soft palates."[53] Matching lesions on corresponding areas of the tongue and palate are called "kissing lesions."[53] Management of an oral lesion in an AIDS individual is determined by the extent of the infection.[53]

The choice of a topical versus systemic treatment will depend on disease severity. Nystatin oral suspension is administered for mild to moderate cases.[53] Systemic fluconazole is administered in moderate to severe cases, and itraconazole and voriconazole are administered in fluconazole-resistant cases.[53]

Liver Disease

Hepatitis B and hepatitis C infections are common in HIV-positive people. Most HIV-positive drug users are infected with hepatitis C.[54] Semá Baltazar, Boothe, Kellogg, *et al.* (2020) stated that it has been demonstrated that "co-infection with HBV or HCV increases with age among HIV-infected

individuals."[54] HIV and viral hepatitis are chronic diseases, and infected individuals can present as asymptomatic.[54] Liver-related deaths are now a leading cause of mortality in patients coinfected with HIV and HCV.[54]

Hematologic Disease

Anemia, leukopenia, and thrombocytopenia are typical complications of AIDS. As with other diseases associated with AIDS, hematologic disorders can be caused by drug therapy, a direct effect of HIV infection, or secondary infections and/or neoplasms that are characteristic of AIDS.[55]

Vishnu and Aboulafia (2015) stated that although there are multiple contributory factors leading to hematological derangements in HIV-infected individuals, "it is those that contribute to morbidity and rarely mortality that are most in need of study."[55] They highlighted newer antiretroviral agents with improved virological and immunological responses and less toxicity to hematopoiesis than earlier antiviral agents on the market.[55]

Endocrine Disease

Dyslipidemias (elevated serum cholesterol and triglycerides) are a complication of ART, and hyperglycemia and insulin resistance are often seen in people with AIDS.[56] As noted previously, there is now an increased life expectancy seen in patients diagnosed with AIDS; therefore, the death rate of HIV-infected individuals who are undergoing proper treatment tends to be due to non-communicable chronic diseases, such as atherosclerotic cardiovascular disease secondary to elevated serum lipids and glucose.[56]

Dyslipidemia, insulin resistance, and metabolic changes can be caused by antiretroviral therapy. Other non-HIV-related risk factors, such as age and diet, further contribute to the development of metabolic changes.[56]

Dermatological Disease

Dermatologic problems occur in >90% of people who have AIDS. Pruritic papular eruption has been identified as the most common skin condition (28%), followed by seborrhoeic dermatitis (24%), psoriasis (10%), molluscum contagiosum (10%), and drug reactions (8%).[57] Eosinophilic folliculitis has been reported to occur with a CD4 T cell count of 250–300/μl and is predictive of a higher risk of opportunistic infections.[57] Shingles and herpes simplex infections may also be seen.[57]

Neoplastic Disease

Kaposi's sarcoma, non-Hodgkin's lymphoma, and invasive cervical carcinoma are neoplasms considered to be AIDS-defining diseases.[58,59] Overall, AIDS is associated with an increased risk of cancer and requires ongoing cancer surveillance.[59]

Genitourinary Disease

Infections of the genitourinary system commonly occur in patients diagnosed with AIDS.[60,61] Patients diagnosed with AIDS who develop systemic illnesses, stress, and weight loss may experience correlating reproductive organ changes that include infertility.[61] Libido may be affected by less sexual interest and activity. AIDS-related comorbidities that are associated with infertility may include "orchitis, acute epididymitis, and pelvic inflammatory disease caused by opportunistic pathogens and coinfections with sexually transmitted infections (STIs) acquired through a similar route of transmission as HIV."[61]

Men with AIDS may experience hypogonadism, an endocrine disorder that can lead to infertility.[61] Certain antiretroviral drugs are considered toxic to cellular mitochondria and have the potential to affect sperm and oocytes. Additionally, HIV-infected individuals may have limited access to health care as well as difficulty locating reproductive care due to the "severity of their

disease, cost of care, stigmatization, and lack of specific HIV infection/infertility knowledge among their providers."[61]

Among patients with renal disease, especially those with end-stage renal disease (ESRD), HIV-infected patients tend to have a worse prognosis than those who are not infected. Dialysis and kidney transplantation are accepted treatments for HIV-infected patients who have been diagnosed with ESRD.[62] The main criteria for HIV-infected patient selection have been reported as CD4 T-cell count above 200 cells/μL, undetectable RNA HIV viral loads (<40 copies/mL), stable HAART for at least 3 months, and no untreatable opportunistic infection.[62]

AIDS-defining Diseases

In brief, the infections and neoplasms considered to be AIDS-defining diseases include the following:[5,8]

- Bacterial infections, multiple or recurrent
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus
- Cervical cancer, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy attributed to HIV
- Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1 month's duration)
- Kaposi sarcoma
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)

- Lymphoma, primary, of brain
- *Mycobacterium avium* complex or *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis* of any site, pulmonary, disseminated, or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis jirovecii* (previously known as "*Pneumocystis carinii*") pneumonia
- Pneumonia, recurrent
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of the brain, onset at age >1 month
- Wasting syndrome attributed to HIV

Case Study: HIV and Kidney Transplant

The following case study focused on a 60-year-old MSM who was diagnosed with HIV at the time of medical evaluation.[62] Laboratory testing showed the baseline CD4 T-cell count to be 190 cells/μL.[62] No baseline genotyping was done at the time. The patient was started on HAART, and a few years later, he began to suffer from chronic intestinal parasitosis with *Entamoeba coli* and *Blastocystis hominis*, which was completely treated. He never developed an AIDS-defining illness but developed chronic kidney disease (CKD) due to IgA nephropathy approximately five years later. ART at the time of CKD diagnosis included abacavir, lamivudine, and efavirenz.[62] Almost eight years after being initially diagnosed with HIV, the CKD progressed to ESRD, and hemodialysis was initiated. At this time, the patient was also evaluated for kidney transplantation.[62]

A personal health history showed that he had a resolved hepatitis B infection and serology for hepatitis C was negative. Serologies for cytomegalovirus, varicella-zoster virus, Epstein-Barr virus, and toxoplasmosis were consistent with past infections. He had a history of coronary heart

disease, atrial fibrillation (treated with long-term anticoagulation), hypertension, dyslipidemia, osteoporosis, and gout.[62]

Complications of dialysis included *Staphylococcus aureus* bacteremia at the arteriovenous fistula and recurrent *Clostridium difficile* colitis after two years of dialysis. Three years after starting dialysis, an internal cardiac defibrillator was inserted for symptoms of ischemic cardiomyopathy.[62]

While undergoing the pre-transplant evaluation, the antiretroviral medication regimen changed to abacavir, lamivudine, and raltegravir to avoid any future drug-drug interactions with immunosuppressive medications. Plasma RNA HIV viral load remained undetectable (<40 copies/mL) while on HAART up to the time of transplantation.[62]

The authors described the donor as a 58-year-old man who died from a cerebral hemorrhage.[62] The donor's medical history revealed he was HIV positive and had been treated with abacavir, lamivudine, and dolutegravir. The donor's plasma RNA HIV viral load was reportedly consistently undetectable (<40 copies/mL), and a resistance genotyping showed a wild-type virus. CD4 T-cell nadir was 370 cells/μL, and the last CD4 T-cell count was 440 cells/μL.[62] He also had never developed an AIDS-defining illness.

The donor's serology testing for hepatitis B, hepatitis C, syphilis, and human T-lymphotropic virus were negative. The cytomegalovirus serology was positive. The donor also had a normal serum creatinine level of 0.5 mg/dL, and his urine analysis revealed no proteinuria.[62] The donor's organ was accepted by the transplant physician without requesting a pre-transplant biopsy.[62]

The patient received kidney transplantation from the HIV-positive donor, and immunosuppression therapy and antibiotics were administered. Raltegravir was changed to dolutegravir immediately prior to transplantation "to ensure adequate therapy for both the recipient and the donor's HIV strains."[62] The recipient's antiretroviral therapy was listed as abacavir,

lamivudine, and dolutegravir. The patient was discharged five days after surgery.[62]

The authors reported that this was the first case of an HIV-positive donor to HIV-positive recipient kidney transplantation in North America. They identified successful HIV-positive to HIV-positive kidney transplantation without loss of virological control. Both the donor's and the recipient's HIV strains, complete genotypic data, and previous virological control and therapy were known. Such future transplantations will likely occur on a case-by-case basis. The authors stated that "given the documented benefit of kidney transplantation for HIV-positive patients with ESRD and their inferior survival on dialysis compared with HIV-negative patients, this represents a promising avenue to improve longevity and quality of life in this patient population."[62]

Brief Overview of Antiretroviral Therapy

ART is the recommended treatment for HIV. Some sources use the term HAART, highly active ART, when referring to ART.[63] This treatment reduces the morbidity and mortality associated with AIDS. Antiretroviral therapy has decreased the mortality rate of AIDS by approximately 50%.[64] It has also enabled HIV-infected individuals to live longer and to have an improved quality of life. Importantly, it decreases the rate and risk of HIV transmission.[63]

In the U.S., the recommendation is to begin ART for all patients who have an infection with HIV.[64] Treatment is focused on three goals: 1) Managing the infection with ART, 2) Monitoring and treating complications, and 3) Preventing transmission of HIV.

There are six classes of ART drugs that can be used, with 25 drugs in those six classes. Classes include: 1) chemokine receptor antagonists (CCR5 antagonists), 2) integrase strand transfer inhibitors (INSTIs), 3) fusion inhibitors (FIs), 4) nucleoside reverse transcriptase inhibitors (NRTIs), 5) non-nucleoside reverse transcriptase inhibitors (NNRTIs), and 6) protease inhibitors (PIs). Each class affects a specific stage of the HIV life cycle.

Prescribing the appropriate regimen, as well as monitoring the patient for side effects and effectiveness of therapy, can be complicated.[65]

The specific ART regimen that is chosen for a patient will depend largely on the viral load and the CD4 cell count.[65,66] Other factors to consider include comorbid conditions (especially cardiovascular disease, hepatitis B infection, osteoporosis, psychiatric disorders, and renal insufficiency), the requirements of a regimen (especially cost, the number and frequency of tablets that must be taken daily, drug interactions, and dietary considerations), and administration considerations and limitations for each specific drug.[65,66] HIV susceptibility to the drugs and the likelihood of patient adherence to the regimen are also important considerations.[65,66]

Guidelines are available for the prescription of ART. A search of the literature found at least 12 guidelines that have been published in the U.S. and other countries. The 2021 guidelines were published by the U.S. Department of Health and Human Services (DHHS) Panel on Antiretroviral Guidelines for Adults and Adolescents.[66] Treatment regimens exist that "... demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use."[66] The DHHS provides "Recommended Initial Regimens for Most People with HIV," and "Recommended Initial Regimens in Certain Clinical Situations."[66]

An example of a combination drug used to treat HIV is DTG/ABC/3TC.[66] The abbreviations are used to identify the combination-drug treatments. In this case, DTG/ABC/3TC is a combination drug that contains dolutegravir, abacavir, and lamivudine. Abacavir and lamivudine are NRTIs and dolutegravir is an INSTI.[63] Each regimen has dosing and prescribing instructions and limitations; for example, DTG/ABC/3TC should not be used if a patient is HLA-B*5701 positive.[66] This and other drug treatment recommendations from the DHHS may be found in the DHHS' 2021 guidelines.[66]

Four to six drugs may be needed if the patient develops drug resistance. Other ART regimens are used for children, pregnant women, people who have been previously treated with ART, and people who have specific medical

problems. Prior to beginning ART, a patient's medical, psychological, and surgical history should be reviewed, and the prescription, over-the-counter, and herbal/natural supplements that the patient is taking should also be reviewed.[63,66] If needed, the patient should receive vaccinations for influenza, hepatitis A, hepatitis B, pneumonia, and varicella.[63,66]

The DHHS Guidelines recommend the following before initiation of ART. Another testing may also be done if indicated.[63,66]

- CD4 cell count
- Complete blood count with differential.
- ALT, AST, and total bilirubin
- Total protein and albumin
- Serum electrolytes
- BUN and creatinine
- Fasting lipid profile
- Fasting blood glucose and hemoglobin A1c
- Urinalysis
- STD screening
- Screening for hepatitis B and hepatitis C
- HIV viral load
- HIV resistance testing
- HIV serotype testing
- Pregnancy testing
- HIV drug resistance testing
- HLA B 5701 testing, in certain circumstances.

During treatment with ART, periodic monitoring of laboratory studies is needed to evaluate the effectiveness of ART and to monitor for adverse drug effects.[63,66] The patient will also need close monitoring for the complications of AIDS. Aside from the systemic complications discussed previously, the side effects of ART often include anorexia, diarrhea, fatigue, low energy levels, skin rashes, sleep disturbances, and vomiting.[63,66]

Treatment with ART is very effective, although failures do occur. With careful monitoring, good patient adherence, and adjustments to the medication regimen (if needed), many people on ART can live for decades with HIV. Treatment with ART itself can contribute to organ system complications, and patients are still at risk for non-AIDS-associated diseases.[63,66]

It is important to remember that ART is not a cure, but it is highly effective if prescribed correctly and the patient is adherent to the treatment regimen. The DHHS's 2021 guidelines stated: "... eradication of HIV infection cannot be achieved with available antiretrovirals (ARVs). Treatment interruption has been associated with rebound viremia, worsening of immune function, and increased morbidity and mortality. Thus, once initiated, ART should be continued, with the following key treatment goals: 1) Maximally and durably suppress plasma HIV RNA, 2) Restore and preserve immunologic function, 3) Reduce HIV-associated morbidity and prolong the duration and quality of survival, and 4) Prevent HIV transmission. The increasing number of ART drugs and drug classes makes viral suppression below detection limits an achievable goal in most patients. Antiretroviral therapy has reduced HIV-related morbidity and mortality at all stages of HIV infection and has reduced HIV transmission."[66]

ART Regimen Compliance Barriers

Compliance with ART regimens is key. Some barriers that affect compliance and adherence with any type of medication include stigma, availability of medication, unemployment, lack of transportation, lack of follow-up with providers and pharmacies, and most importantly, complicated regimens. Insurance issues are also a large barrier to compliance. When receiving ART, patients should be counseled on the importance of requesting refills early to help overcome any barriers that may arise when trying to fill prescriptions. It is imperative that patients understand the importance of adherence to the medication regimen to keep the viral load down. Dosing schedules should be considered for individuals when the medication is first prescribed. Alarm reminders on cell phones can be a simple way to help increase compliance in someone who struggles to take medications

consistently. Another simple method that may help individuals is marking doses off on a calendar to ensure they have taken them. Patients should be aware that travel plans can be a cause of disruption in adherence.

Case Study: ART and Viral Rebound in an Adolescent Male

The authors of this case study described an adolescent male who had been diagnosed with perinatal HIV infection at the age of one month.[67] The patient's mother had been enrolled in a prevention of mother-to-child transmission clinical trial with no prior ART history. She was administered standard prophylaxis that included nevirapine (NVP) and zidovudine (AZT) from 34 weeks gestation until the time of delivery. A viral load of 2,090 HIV-1 ribonucleic acid (RNA) copies/mL was identified at the time of delivery.[67]

The HIV DNA polymerase chain reaction (PCR) for her baby at birth was negative; however, it was positive at 1 month and 2 months after birth. ART (AZT + lamivudine + NVP) was initiated when the patient was 9 months old and continued until age 14. He had a high median follow-up CD4 T cell count of 2068 cells/mm3 (interquartile range 1117–2938) and consistent viral suppression (<400 copies/mL) over the 14 years of routine follow-up in a local clinic.[67] At the age of 14 years and 4 months, the patient decided to visit a local voluntary HIV testing center, where a rapid HIV test was negative and the viral load was undetectable (<400 HIV-1 RNA copies/mL). To confirm these results, additional HIV rapid tests were performed, all with negative results. The test results were discussed between the healthcare provider, the patient, and his mother. The decision was made to terminate ART when the participant was aged 14 years and 11 months.[67]

At the age of 15 years and 8 months, the patient was approached and recruited to a new HIV study in 2018. The study aimed at assessing the serological and virological outcomes, as well as a proviral reservoir in adolescents during long-term ART. The study included adolescents (15–17 years of age) perinatally infected with HIV who received ART for >10 years. The patient's viral load at enrollment (9 months after ART termination) was 186,762 HIV RNA copies/mL.[67] Two HIV enzyme-linked immunosorbent assay

tests – and the HIV DNA PCR test were also positive at enrollment in the HIV study. The authors stated the test results demonstrated that despite negative HIV rapid and DNA PCR test results at age 14, the patient had progressed to latent infection and termination of ART led to viral rebound.[67]

The authors noted that in the vast majority of cases where virologic confirmation of HIV is made in an infant or child, *viral rebound* does occur when ART is terminated, even if ART was administered early during HIV infection and the infected patient displayed very small viral counts.[67] With most perinatally-infected children now receiving early and long-term treatment, the number of cases similar to the one described in this report will likely increase, and caution should be exercised when interpreting "negative" diagnostic results.[67] It was recommended that standard HIV-1 DNA PCR negative tests in individuals on long-term ART are interpreted with caution, and treatment interruption should be avoided.[67]

Case Study: Prolonged Remission in a Child Born with HIV

This case study focuses on a rare case of apparent HIV remission (prolonged virological control after treatment is stopped) in a child who was born with a positive HIV-1 DNA PCR (found at age 32 days).[68] An HIV-1 RNA >750,000 copies per mL (upper limit of quantitation of the assay) was reported at 39 days of age, which verified the patient was HIV-infected. At 60 days of age, the patient's plasma HIV RNA had declined to 151,000 copies per mL. Initial treatment was zidovudine, lamivudine and lopinavir-ritonavir.[68]

The birth history revealed a full-term birth with normal birth weight, and the patient was not breastfed. Nevirapine prophylaxis was not administered. At 61 days, the patient's CD4 T cell count and percent (prior to the initiation of ART), were reportedly 2249 cells per µL and 41.6%.[68] There was a decline in viral load (<50 RNA copies per mL) following 24 weeks of ART. When the patient reached 50 weeks of age, treatment was discontinued with a viral load <20 copies per mL and a weak HIV RNA signal (from the 50-week sample). The only maternal laboratory data documented included a CD4 T cell count of

108 cells per μL (when the patient was 7 months of age) and 129 cells per μL 20 months later.[68]

The patient's viral load remained below detection without ART when he was 8 years of age, and CD4 T cell counts were reportedly normal. At 9.5 years of age, his plasma drug concentrations for the antiretroviral agents used were undetectable (verifying that ART was indeed stopped). Amongst other laboratory trends, the patient's final reports showed that he had a total cell-associated HIV-1 DNA at 9.5 years of age that was close to identical to a stored sample from ART interruption at 50 weeks of age.[68] DNA sequencing (from the 9.5-year sample) confirmed infection with subtype C virus, and there was no replication-competent virus detected based on two virus outgrowth assays. The authors noted that the patient's CD4 T cells could be infected in vitro with HIV-1. At 9.5 years of age, HIV-specific antibodies were undetectable by ELISA, and the western blot was indeterminate.[68]

From the available study data, the authors noted that earlier ART initiation was known to result in a smaller HIV reservoir size in treated babies as soon as 30 hours of birth. A delay in rebound was thought to be due to "a small size of latent replication-competent reservoir."[68] These involved cases in the U.S., France, and South Africa where mother-to-child HIV transmission varied (intrapartum/in utero). The timing of transmission was believed to influence the different outcomes of remission potentially. The subtype of virus (B, H, and C), treatment duration, gender, and ethnicity were different in cases of children who had been studied with HIV remission.[68]

The significance of this case report was to inform clinicians that starting ART early is associated with "non-reactive HIV antibody results in many HIV-1-infected children and adults."[68] In this case, healthy CD4:CD8 T cell ratio and levels of immune activation were found in the patient that was similar to healthy, uninfected children of similar age. The patient had a good immune response capability based on T cell and NK cell responses to stimuli. Features of the child's immune system resembled those of uninfected children of a similar age, allowing the patient to be evaluated as showing ideal post-treatment HIV-1 control.[68]

State Regulations for HIV/AIDS Testing

In the late 1980s, some states began to legislate criteria for testing individuals suspected or known to be diagnosed with HIV.[69-71] State-specific HIV laws can be accessed from state government websites as well as The Center for HIV Law and Policy.[71] In general, key goals of HIV/AIDS public health policy may include limiting disease transmission, observing the "window period" of undetected infection and antibody production (3 weeks to 6 months or longer in some cases) where laboratory testing is crucial to determine the risk of disease spread, providing education to prevent social stigma and isolation of HIV/AIDS affected individuals of across all social groups, genders, and ages.[70] Pharmacists should consult their state laws to determine their responsibilities or roles when an individual is suspected or known to be diagnosed with HIV.

Summary

Individuals infected with HIV can experience a significantly depressed immune system and develop the chronic condition of AIDS. For many HIV/AIDS patients, prior to the availability of antiretroviral medications, the complications of opportunistic infections and/or neoplasms carried a poor prognosis, and the chances for survival from AIDS were considered grim.

An update on the current diagnosis and major improvements in the medical treatment and prognosis for individuals with HIV/AIDS has been discussed. Multiple examples pertaining to HIV/AIDS transmission have been addressed, including mother-to-infant transmission, sexual transmission, occupational exposure, as well as potential risk factors affecting disease outcomes. Pharmacy staff should be aware of the importance of compliance with ART. Pharmacists and other healthcare professionals should complete continuing education courses on HIV/AIDS that conforms to their professional roles to stay up to date with the latest recommendations in order to serve and educate patients the best.

Course Test

1. **Replication of the human immunodeficiency virus is the process by which the virus**

    a. enters the host's body.
    b. attaches to cells in the immune system of the host.
    c. releases from the host's lymph nodes into the bloodstream.
    d. uses its RNA and the host's DNA to produce copies of itself.

2. **_____ describes the viral release from the lymph nodes into the bloodstream.**

    a. Seroconversion
    b. Transmission
    c. Neoplasia
    d. Replication

3. **HIV is *primarily* transmitted through**

    a. sexual activity with an infected person.
    b. casual social contact with an infected person.
    c. insect bites.
    d. blood transfusion from HIV-contaminated blood.

4. **A patient in the chronic HIV infection stage may**

    a. have the infection but not AIDS.
    b. have AIDS.
    c. have CD4 cell count <200 cells/μL.
    d. All of the above

5. **Patients who have chronic HIV infection with the signs or symptoms of AIDS have**

    a. high levels of T-helper cells.
    b. severe damage to the immune system.
    c. CD4 cell counts >200 cells/μL.
    d. have a stable CD4 cell count.

6. **A patient who has a chronic HIV infection, without the signs or symptoms characteristic of AIDS,**

    a. cannot transmit the HIV virus during sexual activity.
    b. has a relatively stable viral level.
    c. has a stable CD4 cell count.
    d. All of the above

7. **Most people who are infected with HIV will have a detectable antibody response to HIV**

    a. only after six months following infection.
    b. only once symptoms of AIDS are present.
    c. within three months of infection.
    d. by the 12th day after infection.

8. **A pharmacist is at the greatest risk for a workplace infection with HIV**

    a. from a needlestick with blood from an HIV-infected patient.
    b. through aerosol transmission of HIV from an infected patient.
    c. from contact with linen from an HIV-infected patient.
    d. when caring for a patient with AIDS.

9. **Post-exposure drug prophylaxis for occupational HIV exposure by a healthcare worker should be started**

    a. only if the healthcare worker tests positive for HIV.
    b. only if the patient who is the suspected source of the potential exposure tests positive for HIV.
    c. as soon as possible, preferably within one to two hours after the exposure.
    d. within 10 days of exposure.

10. **In a patient infected with HIV, ART (sometimes referred to as HAART) focuses on**

    a. curing AIDS.
    b. elimination of the virus.
    c. moving CD4 cell count to <200 cells/μL.
    d. managing the HIV infection.

11. Pre-exposure prophylaxis is recommended for

a. all healthcare workers who care for AIDS patients.
b. men and women who are at substantial risk for acquiring HIV.
c. all individuals with a compromised immune system.
d. All of the above

12. True or False: The current CDC guidelines recommend that HIV screening should be done in all individuals aged 15-65 years.

a. True
b. False

13. _____ is the most common source of HIV transmission to healthcare professionals.

a. Amniotic fluid
b. Pericardial fluid
c. Pleural fluid
d. Blood

14. Which of the following bodily fluids should a healthcare professional consider to be infectious for HIV?

a. Gastric secretions
b. Saliva
c. Urine contaminated with blood
d. Nasal secretions

15. Which of the following statements *best* expresses when safety precautions for HIV infection should be followed by a healthcare professional?

a. A healthcare professional should follow safety precautions only when the patient is HIV positive.
b. A healthcare professional should follow safety precautions only when the patient is in a high-risk group for AIDS.
c. A healthcare professional should follow safety precautions only when the patient is an intravenous drug user.
d. A healthcare professional should follow safety precautions for all patients.

16. _____ is a neoplasm that is an AIDs-defining disease.

a. Non-Hodgkin's lymphoma
b. Shingles
c. Wasting syndrome
d. Dyslipidemia

17. Prior to beginning ART, a patient's medical, psychological, and surgical history should be reviewed, as well as a list of the patient's

a. prescription drugs.
b. over-the-counter drugs.
c. herbal or natural supplements.
d. All of the above

18. Tuberculosis can be difficult to diagnose in persons who have HIV because

a. HIV-infected persons are at a reduced risk for extrapulmonary TB.
b. TB, like HIV, is a retrovirus.
c. of the simultaneous occurrence of other pulmonary infections.
d. radiographic presentations of TB are always normal.

19. Elevated cardiovascular disease in HIV patients is likely due to

a. chronic inflammation and an unusual stimulation of the immune system, triggered by HIV.
b. continuous antiretroviral therapy.
c. influenza vaccination in these patients.
d. intermittent courses of antiretroviral therapy.

20. Barriers to medication compliance include

a. stigma.
b. availability of medication.
c. lack of transportation.
d. All of the above

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