HIV/AIDS: DIAGNOSIS, MANAGEMENT AND TREATMENT

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Topic Overview

The human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) continues to be an area of significant research. New treatment guidelines and antiretroviral drugs have provided hope for individuals infected with HIV. Continuing education for health professionals caring for adults and children diagnosed with HIV/AIDS helps to dispel myths and reduce stigma, enhance a fuller understanding of best practice trends, and improve prevention strategies to avoid transmission of the disease and complications associated with disease progression and/or treatment. Modes of HIV transmission, including transmission from an infected healthcare worker to a patient and from a patent to a healthcare worker are discussed. Universal infection control procedures specifically developed for infected healthcare workers, and the issue of co-occurring infections in an individual with HIV and a reduced immune system are critical for healthcare workers to understand when planning treatment and evaluating a communicable disease outcome. U.S. states such as Florida have enacted into law specific health policies to ensure safe and appropriate prevention of infectious diseases like HIV are carried out and that proper reporting of infected individuals occurs for tracking cases within public health databases, which is later used to help guide future infectious disease research and health policies.

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Credits: 1 hour of continuing education credit

Type of Activity: Continuing education

Media: Internet **Fee Information:** $9

Estimated time to complete activity: 2 hour, including Course Test and course evaluation

Published: July 14, 2021 **Expires:** July 13, 2024

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Educational 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, including tuberculosis
4. **Compare** the medical research and case reports focused on HIV/AIDS prevention and treatment
5. **Describe** current Florida law on AIDS and its impact on testing, confidentiality of test results for patients, and partner notification

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Introduction

The human immunodeficiency virus (HIV) is a retrovirus that causes acquired immunodeficiency syndrome (AIDS). Human immunodeficiency virus can significantly depress immune system functioning leading progressively to AIDS. Prior to the development of antiretroviral medications, essentially everyone infected with HIV progressed to developing AIDS and overwhelming, 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 to 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 treatment of HIV and AIDS, and they include relevant case studies.

HIV Etiology and Stages of HIV/AIDS

The human immunodeficiency virus appeared in the United States in the early 1980s and the first HIV diagnostic test was approved in 1985 by the U.S. Food and Drug Administration (FDA).[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 has 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, there are too many individuals who do not know that 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 the African American community, the lesbian, gay, bisexual, and transgender communities.[2] If a person is infected with HIV, the infection may be assigned one of three stages based on the presence or absence of HIV signs or symptoms.

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] There are 1,061,482 persons living with a diagnosed HIV infection.[2] 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*.[4] 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.[4]

HIV-1 and HIV-2

There are two types of HIV: HIV-1 and HIV-2.[4] In the U.S., the human immunodeficiency virus-1 is the most common HIV infection, and human immunodeficiency virus-2 infections are seldom seen.[4] The HIV-2 virus is less easily transmitted, and infection with HIV-2 progresses more slowly than does an infection with HIV-1.[4] Both HIV-1 and HIV-2 can progress to AIDS.[4]

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 Hurt, *et al.* (2017), finds it useful to describe the stages as (1) the transmission

stage when a person becomes infected with HIV, (2) the acute HIV infection stage, and, (3) the chronic HIV infection stage, with or without progression to AIDS.[4]

The Transmission Stage

This stage begins with the person becoming infected but the infection is not acute. During this stage, the person is not likely to spread the virus to others.[4]

The Acute HIV Infection Stage

The second stage immediately following an HIV infection is the acute HIV infection stage. This stage also includes seroconversion, and the primary HIV infection period, which is the six months following infection.[4] Seroconversion describes the viral release from the lymph nodes into the bloodstream.

According to Hurt, *et al.*, 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.[4] 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.[4] For those patients with prolonged symptomatic illness (>14 days), the likelihood exists of a rapid development of AIDS.[4]

The Chronic HIV Infection Stage

The third stage of HIV infection is the chronic HIV infection stage, with or without progression to AIDS. It is characterized by "a relative stability of the viral load and a progressive decline in the CD4 cell count."[4] 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 are described as having an advanced HIV infection. These patients have CD4 cell count <50 cells/μL.[4]

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.[4] 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.[4] 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.[4] However, because HIV has the ability to replicate and mutate very 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.[4]

Patients who have chronic HIV infection with the signs or symptoms of AIDS have very low levels of the T-helper cells, severe damage to the immune system, and the development of opportunistic infections and neoplasms.[4] The T-helper cells function in part by releasing cytokines, which are proteins that influence the antiviral activity of other immune system cells.[4] 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.[4]

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.[4] 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.[4] For surveillance purposes,

the CDC divides HIV infections for people ≥6 years of age into four stages. The stages are enumerated as 0, 1, 2, and 3, and they are based on the CD4 T cell count.[5]

Case Study: Staging and Cell Count Testing

The following case study was obtained through a PubMed search and highlights the use of cell count testing and staging to determine disease progression in a patient diagnosed with AIDS. The case involves a 50-year-old female who was admitted to the hospital for "a mass in the cervical anterior and a fever that lasted for 17 days."[6] The admission diagnosis was AIDS (C3), oral candidiasis, disseminated penicilliosis (talaromycosis), and chronic superficial gastritis.[6]

The patient was initiated on highly active antiretroviral therapy (HAART): a combination of stavudine, lamivudine, and nevirapine. During the hospitalization period, HIV antibody examinations indicated strong positives on two third-generation enzyme immune essays and were indeterminate on Western blot testing; the CD4 cell count was only 4/μL.[6] She was hospitalized three months later for "particles trapped in the eyes, dim eyesight and blurred vision for two weeks."[6] She stayed in the hospital for 35 days, and the diagnosis at the time of discharge was AIDS (C3) combined with a cytomegalovirus infection.

Initial diagnostic testing included a laboratory report: 5×103 copies/mL HIV viral load, 11/μL CD4 cell count, CRF01_AE HIV subtype, positive anti-HBs, and 6.42×105 copies/mLHCMV-DNA.[6] The patient had negative test results for herpes, hepatitis C virus (HCV), and syphilis. Chest X-ray detected bilateral pneumonia.[6] After 8 months of follow-up, the HIV antibody re-emerged six months later and the Western blot tested positive, along with an increased CD4 cell count from 4/μL to 63/μL.[6] The CD4 cell count and antibodies gradually increased after HAART, and HIV antibody level was high enough to meet positive test criteria at the end of follow-up.

The authors stated that the most plausible explanation for these diagnostic results is that specific HIV antibodies may have been lost in the end-stage of AIDS and were not sufficient in meeting positive test criteria. The re-emergence of specific antibodies by the end of the patient's follow-up examination may have been due to the reestablishment of immunity by HAART.[6]

HIV Transmission and Prevention

Human immunodeficiency virus can be contracted through a number of routes. The manner in which HIV may spread can vary based on cultural, lifestyle, or geographical distinctions.[4] Understanding and controlling the transmission of HIV is crucial to managing and preventing this disease. These important factors are discussed in a later section of this course.

Transmission of HIV occurs primarily by contact with infected blood and by sexual contact. Human immunodeficiency virus can also be transmitted perinatally and by breast milk. The human immunodeficiency virus can be found in essentially any type of body fluid or secretion, but the risk of HIV transmission from contact with body fluids/secretions other than blood, semen, or vaginal fluids tends to be remote.[4] 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.[4]

Estimating the risk of HIV transmission is complicated. The risk of developing an HIV infection from sexual activity can be estimated for a single sexual encounter or for multiple encounters and requires the consideration of many factors.[7,8] Risk factors may also include the estimated viral load, whether condoms are used, administration of ART, male circumcision, types and frequency of sexual activity, and the presence of sexually transmitted diseases (STDs).[4,7,8]

The existence of similar or dissimilar HLA-class-I alleles appears to influence the risk of HIV transmission.[4] 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.[9] Viral load impacts the risk of transmission of HIV in the different contexts; *e.g.*, sexual activity, needle sharing or occupational exposure in the case of healthcare workers.[9]

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, sexually transmitted diseases, and the administration of ART.[4,6,7] Circumcision has been shown to significantly decrease the incidence of HIV infection in men.[4] However, circumcision does not appear to decrease the risk of male-to-female transmission.[9] Being uncircumcised has been shown to increase the risk of HIV transmission in MSM and in serodiscordant couples.[4,9] Also, the higher the viral load of an infected person, the greater the risk that the infected person HIV transmit HIV to a partner during sexual activity.[9]

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.[4] 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.[9] An understanding of the risk factors for sexually transmitted HIV infection is fundamental in the prevention of the spread of HIV/AIDS.

Prevention Strategies

Prevention strategies for sexually transmitted disease need to include "behavioral and biomedical interventions to reduce HIV infection risk."[9] Behavioral changes could include may 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.[4] 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.[4] Education on risk reduction techniques should be provided to patients, especially those that are at high risk.[11]

Case Study: Sexual Transmission of AIDS

A 17-year-old African American male enrolled in a needle exchange program tested presumptive positive following a Rapid-Rapid HIV algorithm.[11] The patient's social history showed that he lived with his mother and brother. At the age of 15 he had his first sexual encounter, and approximately 40-50 sexual encounters over a 2 year period; five sexual encounters transpired over a recent 2 month period.

The patient had reported that all of his sexual partners were male and he had a current boyfriend, although he also had sex with multiple male partners that he became acquainted with through anonymous online social media that advertised "single encounters with no contact after sex."[11] He denied history of sexual or physical abuse.

The patient reported the occasional use of condoms. He reported being knowledgeable about prevention for men who have sex with men. He practiced insertive and receptive anal intercourse and oral sex.[11] He denied a history of STDs or of being tested for STDs in the past. On the physical exam, the patient appeared healthy and there were no acute concerns. He received full HIV and STD testing, including a syphilis screen, nucleic acid amplification tests (NAATs) for oral, anal and genital gonorrhea and chlamydia screening, hepatitis B and C screens, and tuberculosis (TB) screen.[11]

The patient received health education on risk reduction techniques and was supplied with condoms. A psychosocial assessment was completed by a social worker. Partner notification was established, which included his current boyfriend, but prior sexual partners were mostly unreachable.

Treatment of STD was initiated for syphilis infection (benzathine penicillin G 2.4 million units intramuscular (IM) as a single dose) and chlamydia infection (azithromycin 1 gram by mouth, single dose).[11] The patient reported feeling more frightened by the diagnosis of syphilis than HIV and had decided to abstain from sex for a while. While the criteria to start antiviral therapy were met, the patient declined the treatment.[11]

Blood Transfusion Transmission

Human immunodeficiency virus can be transmitted by transfusion with leukocytes, packed red blood cells, plasma, platelets, and whole blood.[9] 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.[9] The probability of HIV transmission from a blood transfusion depends on the volume of blood transfused. The reported risk of HIV transmission following a contaminated blood transfusion is an approximately 88% to 100 percent.[9]

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 platelet count was 79×109/L.[12]

He 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 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), antibody of HIV (HIV-Ab), and hepatitis viruses was 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 for needle or syringe sharing.[9] Needle sharing should never occur. Needles should be used only within a clinical setting or as prescribed for medical reasons. Needles or syringes should be safely disposed after use.[9]

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.[13] 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.[4,13]

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.[13] The patient's historical suppressive antiretroviral therapy is also important.[13]

Henderson (2012) estimated that each year almost 1 of every 10 healthcare workers in the United States has a needlestick exposure.[14] 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.[15]

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.[16] The risk of HIV transmission from the use of an HIV-contaminated needle has been estimated to be one infection per 435 exposures for percutaneous needle-stick.[9] 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.[16] 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,[16] as well as a deep injury or an injury from a visibly contaminated device.[9] Characteristics related to the individual who is the source of the blood is 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.[9] On the other hand, post-exposure prophylaxis can reduce the probability of an infection following a needlestick.[16]

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.[16] Risky behaviors are estimated to cause 95% of HIV infections.[16] 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.[16] 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.*[16]

Needlestick Prevention for Healthcare Workers

Wyżgowski, *et al.*, stated that it is important for clinicians to recognize that "every patient can be HIV-positive or can be infected with other blood-borne pathogens."[16] Safety rules to prevent HIV transmission need to be observed on a daily basis.[16]

Zachary (2019) sets out the accepted recommendations on the management of occupational exposures.[13] 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 and recommendations for ongoing HIV surveillance testing, and may be consulted as well.[17]

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.[13] If someone chooses to have sexual intercourse, using a condom consistently and correctly may reduce the risk of HIV transmission.[13] 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:[13]

- Exposed mucous surfaces should be flushed with copious water. 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 blood-borne pathogens.
- If needed, 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 an 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.

SHEA Guidelines

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.[18]

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.[18] 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 includes 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.[18] Other examples of healthcare scenarios with higher risk of infection transmission are listed in the SHEA guidelines.[18]

An HIV-infected healthcare worker with a viral burden of <5 # GE/mL need not be excluded from any aspect of patient care, so long as the infected worker has not been detected as having transmitted infection to patients, obtains advice from an Expert Review Panel with respect to the worker's continued practice, and is routinely followed by Occupational Medicine (or other appropriate public health official) for required testing and monitoring of viral burden.[18] Follow up with an infectious disease medical specialist for HIV infection is also recommended, and communication between the infectious disease medical specialist and Expert Review Panel is expected with regard to the healthcare worker's HIV status. Infected healthcare workers with HIV are expected to strictly adhere to procedures pertaining to patient care, and to "the recommended procedures, including the routine use of double-gloving."[18] Conditions of employment and requirements of proper reporting to the Expert Review Panel are extensive and beyond the scope of this course, however SHEA provides comprehensive education for healthcare workers pertaining to procedures in the handling of bloodborne pathogens and patient care.[18]

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."[18]

OSHA Blood-borne Pathogen Standards

Adherence to the blood-borne pathogen standard established by Occupational Safety and Health Administration (OSHA) is mandatory for all

hospitals and healthcare facilities. To be in compliance with the standard, employers must establish a written plan for controlling exposure to blood-borne pathogens.[19-21] 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 blood-borne pathogens.[19-21]

The plan for controlling exposure to blood-borne pathogens and disease risk must be reviewed and updated annually by a health organization, and it must be accessible to all employees, as outlined below.[19-21]

- 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 blood-borne pathogens to all employees. This training should include:[19-21]
  - a review of the OSHA Blood-borne pathogens standard
  - information on the risks of exposures and how exposures happen
  - information on how to prevent exposures to blood-borne pathogens
  - information on the benefits and risk of vaccination against hepatitis B.
- Use engineering controls to control risk. Engineering controls that control the risk of exposure to blood-borne pathogens would include:[19-21]
  - 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 blood-borne 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 health employees must comply with the requirements of the blood-borne pathogens standard.[19] 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 removing 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.[19]

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.[19-21] If handwashing with soap and running water is not possible, the employee must use either an antiseptic hand cleaner with clean cloth or 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.[19-21]

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.[13] The PEPline has trained physicians who are prepared to give health clinicians the 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.[13]

Case Study: Occupational Exposure in a Laboratory

In one case study (2017), a blood donor was found to be HIV-1 infected at routine screening.[22] Previous testing for HIV was negative. At the first clinical assessment, the patient had no classical risk factors.[22]

Six months before being diagnosed with HIV-1, the patient had worked in a research laboratory involving the production of pseudoviruses via the co-transfection of T cells with HIV-1 and other vectors within a biosafety level (BSL) 2 containment facility.[22] No injuries in the laboratory were reported affecting the eyes, skin, or any other exposed areas.[22] The authors stated that while working in the laboratory, the patient had been managing noninfectious constructs as compared to other rare cases of laboratory worker exposures who followed restrictions for BSL-2. The belief was that the patient had been infected by an unaware contamination of "a recombinant clone."[22]

The authors stated that despite thorough investigation, there was no breach-point that led to the patient becoming infected and the method of transmission remained unknown, making it difficult to understand how contamination occurred.[22] A potential danger exists in research laboratories where multiple HIV-derived constructs are managed. BSL-2 laboratories were identified as large spaces where many laboratory personnel shared equipment and worked on different projects. Future research projects are needed that focus on improved ways to prevent biohazard and other unsafe exposures.[22] Nwaiwu, *et al.* (2017) are in agreement with the need to improve ways to prevent biohazard and other unsafe exposures.[23]

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 disease from healthcare workers to patients such as influenza; however, blood borne infections like HIV, HBV and HCV have also occurred through an 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 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] According to Turkel and Henderson

(2011), the CDC "guidelines asked as many questions as they answered and left many questions unresolved."[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.[17] The CDC generally addressed proper sterilization and disinfection procedures to prevent infection risks from healthcare workers to patients.[17]

Florida Department of Health Guidelines

The Florida Department of Health has issued Guidelines for Prevention and Control of Infection Due to Antibiotic Resistant Organisms (2020) that specifically addressed the infected or colonized health care worker who may pass along infection. While the Florida guidelines primarily address varied communicable diseases with a known risk of resistance to treatment, the *prevention* of disease spread referenced in the guidelines emphasizes strict adherence to "good infection control practices."[26] The Florida rules and protocols related to work restrictions of an infected healthcare worker specify that an epidemiological link between the healthcare worker and patient must be confirmed.[26] The healthcare worker with an active infection "should be referred for diagnosis and clinical management of the infection, including treatment if necessary."[26]

SHEA Guidelines

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 worker to patient 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 are outlined in the SHEA guidelines, and recommendations are made for each known pathogen.[18]

Mother-to-Infant Transmission

The human immunodeficiency virus can be transmitted from a mother to a child during pregnancy, during labor, and after birth via breast milk. The most important factor for mother-to-child HIV transmission is the viral load, and this applies to prenatal transmission, transmission during birth, and transmission via breast milk.[27]

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%.[27] If a mother and infant both receive prophylactic ART and the infant is not breastfed, this risk is approximately 0.1%.[27] The American Academy of Pediatrics has advised that regardless of viral load and/or the use of ART, mothers who are HIV-positive should not breast feed.[28,29]

Case Study: Mother-to-Infant Transmission through Breastfeeding

There were few documented case studies found of mother-to-infant HIV transmission; however, Alcorn (2017) described two infant cases with HIV positive test reports at 14 weeks (case 1) and 36 weeks of age (case 2).[30]

The mother of the 14 week old infant initially had an undetectable viral load, but later developed a detectable viral load.[30] The mother of the 36 year old infant had an undetectable viral load (week 14 and 26 postpartum) at all visits while the infant tested positive for HIV and continued to test positive up to week 50.[30]

The author stated that there were several possible explanations for these cases. One possibility was that even when HIV is undetectable in blood, it may still be transmitted in breast milk through cell-associated virus.[30] During the breastfeeding period, the volume of potentially infected breast milk consumed by infants suggests a potentially higher risk of HIV transmission even with undetectable viral load in blood.[30]

Viral suppression that was too slow to prevent HIV transmission was another possibility such as in the case of the 14 week infant when infection occurred around week 6 (while viral load was possibly detectable).[30] The author suggested that HIV transmission through breast milk may occur even when viral load is below 1000 copies/ml in the blood.[30] Poor adherence may have also been a factor of HIV transmission from mother to infant. An undetectable viral count does not mean there is a low risk of HIV transmission in breastfeeding infants.[30]

The human immunodeficiency virus is not transmitted by casual contact and it is not transmitted in the environment through air, water, or by insect bites. Survival of HIV outside of the body can depend on multiple factors that are not completely understood, but it appears that HIV transmission and infection from an environmental source is not a high possibility.[30]

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.[4] Prevention is key. 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.

For couples who are *serodiscordant* (one person is HIV positive, the other is not), ART significantly reduces the viral load and helps to prevent transmission of HIV.[31-33] There is also no vaccine against HIV. The effectiveness of condoms in preventing the transmission of HIV, if used properly, has been estimated to be 87% to 94%.[33] 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 transmission of HIV from oral sex.[31,32]

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

transmission of HIV.[36,37] Douching has been reported to increase the risk of HIV transmission.[38]

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.[39] Intravenous drug users who have an HIV positive partner, share injection equipment, and have recently undergone drug treatment but are not currently injecting drugs may benefit from pre-procedure prophylaxis.[40] 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*."[40]

Pre-exposure prophylaxis is recommended for men and women who are at a 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 sex partners, have a history of inconsistent or no condom use, or are involved in commercial sex work.[40] 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).[40]

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 alternative HIV prevention plan when discontinuing PrEP.[41]

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 as a pre-exposure prophylaxis.[41] 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, ecstasy regularly, and occasionally ketamine.[41]

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 was treated. After syphilis treatment, with a negative HIV test and additional renal function testing (creatinine 1.26 mg/dL and eGFR 62), he never started taking PrEP again due to kidney function parameters.[41]

Two months after treatment for the 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).[41] 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.[41]

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.[41] 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.[41]

HIV Screening

Screening to detect HIV is recommended by the CDC for everyone aged 13 years 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 for all patients who are diagnosed with hepatitis B or tuberculosis.[42,43] The current 2021 guidelines from the CDC recommend that HIV screening should be done in the following cases:[43]

- All individuals aged 15-65 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.[44] 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 an 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 have an HIV infection, which is the window often mentioned relative to HIV screening.[44]

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:[44,45]

- 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 an 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-1 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*.[46,47] OraQuick® uses an oral swab and a test liquid and the results are ready in 20 minutes.[47] The test has a sensitivity of approximately 93.6% and a specificity of 99.9%.[48]

A positive test must be confirmed by laboratory testing.[46,47] A false positive can be caused by lupus, Lyme disease, syphilis, and other disease; a false negative can be caused by a low level of antibodies, testing that is done too soon after an exposure, if the patient is taking ART, and by other conditions.[46,47] 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%.[46-48] 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.[46,47]

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 for AIDS, which can only be diagnosed through blood testing. Symptoms can develop because of drug therapy, as a direct result of the infection, from opportunistic infections such as

Pneumocystis pneumonia, and by neoplasms, *i.e.,* Kaposi's sarcoma.[4] 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.[4,49] 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.[49]

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 chronic inflammation and an unusual stimulation of the immune system, triggered by HIV even when the virus is well-controlled."[49]

Pulmonary Disease

Pulmonary disease is a typical complication of AIDS. Sinus infections, bacterial and fungal pneumonias, and tuberculosis are common in people who have AIDS.[4,50] 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, and AIDS has been reported to be an independent risk factor for COPD.[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).[4,51]

Human immunodeficiency virus-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 of 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% 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 low CD4 count exists in the varied types of candidiasis.[53] *Pseudomembranous candidiasis* involves symptoms of white creamy curd-like plaques commonly seen in the buccal mucosa and tongue. *Hyperplastic candidiasis* manifests as white plaques in 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 is flat and seen on the dorsal aspect of 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 from 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 people who are HIV-positive. 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 affected 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, leucopenia, and thrombocytopenia are typical complications of AIDS. As with other diseases associated with AIDS, the hematologic disorders can be caused by drug therapy, a direct effect of HIV, or secondary infections and/or neoplasms that are characteristic of AIDS.[552]

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 tend to be due to non-communicable chronic diseases like atherosclerotic cardiovascular disease secondary to elevated serum lipids and glucose.[56]

HIV infection and inflammation, dyslipidemia, insulin resistance, and metabolic changes can be caused by antiretroviral therapy. Other non-HIV related risk factors, such as age, further contributes to the development of metabolic changes and higher risk.[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] 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 with 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. More is being said about limited access to health care and the risk that HIV-infected individuals may have difficulty locating reproductive care due to "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 treatment for HIV-infected patients who have been diagnosed with ESRD.[62]

The main criteria for HIV-infected patient selection has 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:[4,5]

- 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 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 the same time, the patient was also evaluated for kidney transplant.[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 serum creatinine of 44 μmol/L, 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 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 transplantation 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]

Treatment of AIDS

Antiretroviral therapy 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 of AIDS 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 inhibitor (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, and prescribing the correct regimen and 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 that have been published in the U.S., and in 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 NRTI 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; other testing can be done when needed.[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 drug side 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. However, the treatment itself can contribute to organ system complications, and patients on ART 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]

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) at 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 of age, which continued until he reached the age of fourteen. 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 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 and the patient with his mother. The decision was made to terminate ART when the participant was aged 14 years 11 months.[67]

At the age of 15 years 8 months, the patient was approached and recruited to a new HIV study in 2018. The study aimed at assessing the serological, virological outcomes, and 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 numbers 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 an 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 a normal birth weight, and the patient was not breastfed. Nevirapine prophylaxis was not

administered. At 61 days, the patient's CD4 T cell count (prior to the initiation of ART), was 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 VL <20 copies per mL; a weak HIV RNA signal had been detected (from the 50-week sample). The only maternal laboratory data documented included 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 in South Africa where mother to child HIV transmission varied (intrapartum/in utero). The timing of transmission was believed to potentially influence the different outcomes of remission. The subtype of virus (B, H and C), treatment duration, gender, and ethnicity were different in cases of children that 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 were like 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]

Tuberculosis and Risk of Infection

Tuberculosis (TB) is spread through an exposure to sputum acid-fast bacilli (AFB) and to a person with a smear-positive TB are at increased risk of symptoms of TB disease progression.[69] Acuña-Villaorduña, *et al.* (2018) reported that "50% of household contacts of TB patients are infected with *Mycobacterium tuberculosis* and 4% will eventually develop active TB disease within 1 year."[69] They opined that the prevention of TB in households would reduce annual cases of TB by a quarter of a million cases per year (especially among children and patients infected with HIV).[69] Prevention of disease transmission within the community is an important strategy in controlling the rise of TB.[69]

On a global scale, TB is a leading cause of infectious disease death.[70] 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.[70] The prevalence of TB is an estimated 20–25% of affected individuals who have latent TB.[70] The elimination of TB worldwide is challenging; however, the World Health Organization has set down a goal to end TB worldwide.[70]

Healthcare workers globally are at an elevated occupational risk of TB infection and disease.[71] Over the past 25 years, guidelines on TB infection prevention and control (IPC) have been studied and recommended for specific healthcare settings. Ehrlich, *et al.* (2020) suggested an approach for prevention that focused on key aspects of statutory regulation, leadership, and staff training in specific healthcare disciplines. Occupational health

services and worker's compensation sections provide secondary prevention and tertiary prevention, respectively.[71] The authors also stated that a "worker-centric approach recognises the ethical implications of screening healthcare workers, as well as the stigma perceived by those diagnosed with tuberculosis."[71] A comprehensive approach includes both community- and occupational-prevention of tuberculosis that recognizes the importance of reducing exposure to infectious hazards within the healthcare workforce.[71]

Most states have public information posted online for healthcare workers and the general public relative to TB control and prevention. In the State of Florida for example, the Florida Department of Health (DOH) has published steps to help eliminate TB statewide. The DOH has policies in effect that help state healthcare systems to manage complicated TB cases through training and assistance related to TB control and prevention.[72] Reporting and monitoring systems involve multiple health departments including laboratories and pharmacies operating according to rules and regulations aligned with the state and CDC.[72] In Florida, health organizations and the public can access important information about TB prevention by calling a toll-free number (850-245-4350).[72]

The most current and frequently cited CDC guideline for the prevention of TB in healthcare settings was published in 2005.[73] The guidelines covered some of the following concerns in varied inpatient and outpatient healthcare settings:[73]

- Principles and practices of TB infection control, including written policies and procedures, monitoring, and control measures for healthcare workers at increased risk for exposure to *M. tuberculosis*.
- Evaluation and documentation of the effect of TB occupational risk exposure and *M. tuberculosis* transmission.
- Rationale for testing for *M. tuberculosis* infection, and the importance of a TB screening program and archive of test results for *M. tuberculosis* infection, i.e., chest radiograph reports and the treatment of TB.
- BCG vaccination safety and efficacy.
- Occupational *M. tuberculosis* infection test conversion or TB disease.

- Healthcare workers and employers responsibilities to ensure prompt testing of M. *tuberculosis* test conversion or development of symptoms or signs of TB disease in healthcare workers, to promptly report a diagnosis, and to prevent transmission of *M. tuberculosis*.
- Responsibility to report to the state or local health department a suspected case of TB disease in a patient (including by autopsy) or healthcare worker; and role of the local health department, and the state health department to ensure confidentiality for healthcare workers' diagnosed with TB.
- Informing healthcare workers of suspected or confirmed TB disease.
- Ensuring a healthcare worker with TB disease is noninfectious prior to being released to return to work.
- Monitoring of environmental controls, safe collection, management, and disposal of laboratory specimens.
- OSHA healthcare workers conversion to *M. tuberculosis* infection recordkeeping.
- Proper use of respiratory protection as required by OSHA.
- Adherence to infection-control practices in decreasing the risk for transmission of *M. tuberculosis* in health-care settings.

The CDC guidelines discuss each of the above recommendations in detail. Importantly, the 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."[73]

Hospital, outpatient clinics, home health care workers who have cared for patients with suspected or confirmed TB disease can help to prevent disease transmission of *M. tuberculosis* by educating patients and family members about symptom recognition, treatment, testing, and follow-up.[74] Healthcare workers exposed to patients with suspected or confirmed infectious TB disease should consider being offered the use of an N95 disposable respirator.[74]

Pulmonary TB disease has been identified in HIV-infected patients and other immunocompromised hospice patients.[74] Symptom screening and testing for *M. tuberculosis* infection should be considered in family members and hospice healthcare workers with possible exposure.[74]

Training and education for healthcare workers regarding infection with *M. tuberculosis* and TB disease is critical to a successful prevention and infection-control program.[74] By educating and training healthcare workers on TB infection-control, specific measures to reduce this risk of TB exposure within the healthcare workers specific setting will help to develop meaningful prevention and control policies. According to the CDC guidelines, "OSHA requires annual respiratory-protection training for HCWs [healthcare workers] who use respiratory devices."[74]

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.[75] Florida had one of the highest rates of HIV infection and enacted legislation focused on the AIDS epidemic that supported healthcare protocols for testing of individuals. In response, Florida passed the *Omnibus AIDS Act of 1988*.[75] Florida's *Omnibus AIDS Act*, as amended, guides and mandates Florida healthcare clinicians in the areas of screening, diagnosing and reporting HIV/AIDS, under the publication known as "A Brief Legal Guide For Health Care Professionals."[75] The Florida Act, as amended, reflects existing recommendations put forward by the CDC and other national organizations concerned with HIV testing and methods to avoid disease transmission through voluntary testing.[75]

Using the State of Florida as an example, licensed healthcare providers are typically required to complete a course on HIV/AIDS that conforms to their professional roles.[76] Also, all licensed health care facilities are required to educate employed healthcare workers and certain clients about HIV infection.[77] Likewise, various institutionalized patients, school children, university and college students, and law enforcement and correctional officers are required to complete education on HIV/AIDS prevention.[78] Such

instruction shall include information on current Florida law and its impact on testing, confidentiality of test results, and treatment of patients and any protocols and procedures applicable to human immunodeficiency counseling and testing, reporting, the offering of HIV testing to pregnant women, and partner notification issues.[76] The Department of Health also enacted legislation to "develop and implement a statewide HIV and AIDS prevention campaign that is directed towards minorities who are at risk of HIV infection."[79]

In 1999, the Florida Department of Health was commissioned by the Legislature "to develop and implement a statewide HIV and AIDS prevention campaign to strengthen HIV and AIDS prevention programs and early intervention and treatment efforts in the state's black, Hispanic and other minority communities."[75] The goal was to create a healthcare environment where people needing HIV testing would consent to testing with reassurance of receiving proper informed consent and privacy. Human immunodeficiency virus testing without a person's knowledge and consent is prohibited "except in tightly defined circumstances and gives the patient special rights to control who learns of the HIV test results."[75] Patient rights to confidentiality under the Florida statute also prohibits discrimination for patients who are confirmed positive for HIV/AIDS. This law acted to also amend the anti-discrimination provisions of Florida law prohibiting discrimination in "employment, housing, public services, public accommodations and health and life insurance."[75]

In 1988, the approach to HIV infection and AIDS in Florida developed along four main pillars aimed at a statewide public health approach to addressing the HIV/AIDS crisis. In general, the key goals of HIV/AIDS public health policy included: 1) Limiting disease transmission by avoiding unprotected sex and needle sharing and following appropriate universal precautions at work; 2) 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; 3) Lack of cure or effective treatment that make access to immediate testing and treatment fundamental to disease control and improvement of disease outcomes; and, 4) public reaction to HIV/AIDS, which requires ongoing

education and support to avoid social stigma and isolation of HIV/AIDS affected individuals of across all social groups, genders, and ages.[75]

The Targeted Outreach for Pregnant Women Act (TOPWA) was passed in 1999 "to reach HIV-infected pregnant women or high risk pregnant women who are not receiving services."[80] TOPWA focuses on the needs of under-served women to help them obtain medical or social services with a treatment goal to reduce their risk for HIV infection as well as co-occurring disorders such as substance use.[80] Many of these women have been unable to access traditional health services.[80]

Through services offered by TOPWA, women of childbearing ages with a history of HIV-infection or substance use or who are at risk of being infected with HIV can receive assistance for access to prenatal care. Additionally, pregnant women enrolled in TOPWA are provided HIV testing, family planning services, and other HIV prevention and education.[80]

In 1996, the Florida legislature amended the *Omnibus AIDS Act* to authorize the Department of Health "to require physicians and laboratories to report HIV-positive test results to state health authorities."[75] This was to support the diagnosis and treatment of HIV/AIDS as available treatments improved, which allowed patients to live longer with an improved quality of life. In 1998, the amendments were described as "streamlined" to allow for improved HIV testing procedures "by eliminating many required counseling efforts, which were burdensome to both testers and their subjects, on the premise that public knowledge regarding prevention and transmission of AIDS had increased sufficiently to end universal mandatory pre-test counseling and face-to-face post-test counseling."[75]

Healthcare professionals, including pharmacists, are required to complete education on the State of Florida HIV testing protocol that outlines procedures that must be in place "for securing patient consent, testing samples and informing patients of test results."[75] Florida's *Omnibus AIDS Act* requires, with few exceptions, health care providers ordering HIV tests to (A) obtain the "informed consent" of the test subject, (B) confirm positive

preliminary test results through corroborating tests before informing the test subject of the result and (C) take "all reasonable efforts" to notify the test subject about the test results."[75]

Special provisions were passed for handling "superconfidential" HIV test results and patient medical records.[75] Provisions were also added regarding notification of persons other than the patient who may have been exposed to HIV, and for mandatory reporting of positive HIV test results to Florida public health offices.[75]

An important source of information for Florida pharmacists is the *Florida Department of Health Division of Medical Quality Assurance BOARD OF PHARMACY* (2020) which outlines requirements for maintaining patient confidentiality and State of Florida Statutes pertaining to required education for all healthcare professionals on HIV/AIDS testing requirements in Florida.[81] The Florida website outlining required education for pharmacists is available online.[81]

Once an employee completes the required educational course, the employee is not required to repeat the course, should the licensed professional change employment between licensed health facilities. Under Florida law, licensed facilities are required to maintain a record of employees who completed HIV/AIDS education as a condition of employment and licensure.[77]

Continuing education requirements related to HIV/AIDS education for professional licensees, including pharmacists, are listed in Section 456.033, Florida Statutes:[76]

- "Requirement for instruction for certain licensees on HIV and AIDS: The following requirements apply to each person licensed or certified under chapter 457; chapter 458; chapter 459; chapter 460; chapter 461; chapter 463; part I of chapter 464; chapter 465; chapter 466; part II, part III, part V, or part X of chapter 468; or chapter 486:
- Each person shall be required by the appropriate board to complete no later than upon first renewal a continuing educational course, approved by

the board, on human immunodeficiency virus and acquired immune deficiency syndrome as part of biennial re-licensure or recertification. The course shall consist of education on the modes of transmission, infection control procedures, clinical management, and prevention of human immunodeficiency virus and acquired immune deficiency syndrome. Such course shall include information on current Florida law on acquired immune deficiency syndrome and its impact on testing, confidentiality of test results, treatment of patients, and any protocols and procedures applicable to human immunodeficiency virus counseling and testing, reporting, the offering of HIV testing to pregnant women, and partner notification issues pursuant to ss. 381.004 and 384.25.

- Each person shall submit confirmation of having completed the course required under subsection (1), on a form as provided by the board, when submitting fees for first renewal.
- The board shall have the authority to approve additional equivalent courses that may be used to satisfy the requirements in subsection. Each licensing board that requires a licensee to complete an educational course pursuant to this section may count the hours required for completion of the course included in the total continuing educational requirements as required by law.
- Any person holding two or more licenses subject to the provisions of this section shall be permitted to show proof of having taken one board-approved course on human immunodeficiency virus and acquired immune deficiency syndrome, for purposes of re-licensure or recertification for additional licenses.
- Failure to comply with the above requirements shall constitute grounds for disciplinary action under each respective licensing chapter and s. 456.072(1)(e). In addition to discipline by the board, the licensee shall be required to complete the course."[76]

Summary

Individuals infected with human immunodeficiency virus can experience a significantly depressed immune system and develop the chronic condition of acquired immune deficiency syndrome. For many AIDS patients, prior to the

availability of antiretroviral medications, the complications of AIDS-related 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 case studies pertaining to HIV/AIDS transmission have been reviewed that addressed mother-to-infant transmission, sexual transmission, occupational exposure, and potential risk factors affecting disease outcomes.

Historically, Florida had one of the highest rates of HIV infection in the United States and in response, Florida enacted legislation focused on the AIDS epidemic that supported healthcare protocol for testing of individuals. The Florida *Omnibus AIDS Act*, as amended, reflects existing recommendations put forward by the Centers for Disease Control and Prevention and other national organizations concerned with HIV testing and methods to avoid disease transmission through voluntary testing.

Some U.S. jurisdictions have required health professionals to become educated in HIV/AIDS including options for access to care for underserved individuals such as pregnant women and those with co-occurring disorders such as substance use. The State of Florida is one such region of the U.S. where required education for licensed healthcare providers is required by law. Pharmacists and other healthcare professionals are required to complete a course on HIV/AIDS that conforms to their professional roles.

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. have relatively stable viral levels.
    c. have 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 healthcare worker is at 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 an 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 a 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. Only when a healthcare professional knows the patient is HIV positive
b. Only when a healthcare professional knows the patient is in a high-risk group for AIDS
c. Only when a healthcare professional knows the patient is an intravenous drug user
d. A healthcare professional should follow safety precautions for all patients.

16. _____ is a neoplasm that is considered to be 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 (TB) 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. Through services offered by TOPWA in the state of Florida, _____ can receive assistance for access to prenatal care.

a. women of childbearing ages with a history of HIV-infection
b. women with substance use
c. women who are at risk of being infected with HIV
d. All of the above

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