CLINICAL PODIATRY



An Update on the HIV/AIDS Patient for the Podiatric Physician

DPM's must be alert to the lower extremity signs and symptoms of this preventable disease.

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Objectives

After reading this article, the podiatrist should be able to:

1) Discuss current modes of transmission of HIV infection.

2) Discuss identifiable HIV risk behaviors and prevention methods to avoid risk behaviors.

3) Describe podiatric complications of HIV infections.

4) Discuss drug therapy (HAART) for HIV infections.

5) Discuss PEP protocols and recommendations.

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Following this article, an answer sheet and full set of instructions are provided (pg. 220).-Editor

cquired Immune Deficiency Syndrome (AIDS) or the human immunodeficiency virus (HIV) continues to be a major health problem worldwide. HIV infection and severe HIV-related diseases have become one of the leading causes of illness and death in the United States. Since the Centers for Disease Control reported five men with Pneumocystis carinii on June 5, 1981¹⁻³ tremendous changes in research, patient care and educational efforts have evolved to combat the HIV infection. This MMWR notice is generally cited as the beginning of the written history of the AIDS epidemic:¹⁴ a case study appeared in the October 14, 1988 issue of JAMA and documents an AIDS infection in the United States presenting in 1968.⁵ This case describes a 15-year old black male with extensive lymphedema of the genitalia and lower extremities. At autopsy widespread Kaposi sarcoma of the aggressive, disseminated type was identified. Both sensitive and specific tests for the presence of HIV antibodies and antigens were performed. These positive findings raise important implications about the evolution of AIDS as an epidemic in the United States.⁵

We rely on education as the most effective weapon in the arsenal against the spread of AIDS. Podiatrists can provide education to the public concerning HIV infection and the eventual lower extremity manifestations of AIDS. In early 1990, Holmes presented data on the importance of educational programs given to podiatrists regarding the subject of AIDS. She presented both a description of the AIDS confer-*Continued on page 206*



ence and suggestions for improving future educational programs.6 Podiatry associations, as well as state legislatures, have recognized the need for ongoing HIV and AIDS continuing education programs. For example, the Florida Legislature has established continuing education requirements for podiatrists licensed in Florida to complete an educational course on HIV/AIDS.7 Chapter 64B18-17.001 directs licensed podiatrists to attend one hour of HIV/AIDS continuing education with initial licensure and the first renewal period. Section 64B18-17.003 HIV/AIDS Education Course describes: "A podiatrist who attends an HIV/AIDS course that consists of education on transmission, control, treatment and prevention of Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome, with emphasis on appropriate behavior and attitude change."8

Epidemiology

Data obtained in 2009, CDC estimated that approximately 56,300 people were newly infected with HIV in 2006 (the most recent year that data are available).9 Over half (53%) of these new infections occurred in gay and bisexual men. African American men and women were also strongly affected and were estimated to have an incidence rate than was seven times greater than the incidence rate among whites.9 At the end of June 2008, the Centers for Disease Control and Prevention (CDC) estimated that 549,196 people are living with AIDS in America.⁹ More than one million people in the U.S. are living with HIV. Out of these people living with HIV, one out of five are unaware they are infected. It is estimated that every 9.5 minutes, someone in the U.S. is infected with HIV. Under current care standards. these infections will result in \$12.1 billion annually in future treatment costs.

The major cause of AIDS is the Human Immunodeficiency Virus typeone (HIV-1).¹⁰ The virus is transmitted during sexual intercourse, intravenous injection of infected blood or through infected needles (parenteral), and vertically from mother to child (perinatal).¹¹⁻¹³ The size of the inoculum and the frequency of exposure to HIV are important factors in determining the risk of transmission. The Centers for Disease Control and Prevention estimates 45,000 new HIV infections among both adults and adolescents occur annually.14 Only a small number of these cases are detected during the acute phase. In the United States the number of new cases of AIDS continues to rise.14 AIDS affects individuals of all races regardless of sexual orientation. The United States geographic patterns of AIDS epidemiology have changed over time.15,16 The five states that continue to account for over half of the cumulative AIDS case reports are New York, California, Texas, New Jersey, and Florida.

The management of HIV/AIDS involves the complex coordination of many healthcare professionals. The podiatric physician can provide education to the public and medical colleagues regarding lower extremity manifestations of AIDS. Podiatrists may play an important role in identifying patients who are infected with HIV by being alert to the specific lower extremity signs and symptoms which may signal the presence of the infection. Historically, AIDS was initially described in young homosexual men in the early 1980s and was characterized by severe immunologic defects, opportunistic infections, and malignant neoplasms. Both receptive anal and receptive vaginal intercourse are well-established modes of HIV transmission.12,13 An increase of heterosexual infections has lead to the development of educational programs to promote "safe sex" to limit spread of this infection.17,18 There exists an increased risk of HIV sexual transmission in the presence of other sexually transmitted diseases such as syphilis, herpes simplex virus and gonorrhea.19

Injection of HIV-infected fluid parentally is a well-established mode of transmission of the virus. Intravenous drug use and sharing of contaminated needles or other drug-related paraphernalia can lead to HIV infection.¹³ Podiatrists are at risk from percutaneous injury with needles and other sharp instruments and should use appropriate precautions to minimize accidental puncture with HIVcontaminated instruments.²⁰ Ippolito, et al., reports a small but real risk of HIV infection after percutaneous and mucous-membrane exposure to blood of HIV-infected patients.²¹ Tokars et al., concluded the risk for HIV seroconversion after percutaneous exposure to HIV-infected blood was -0.36%.²² A case control study by Cardo, et al. on HIV seroconversion in healthcare workers after percutaneous exposure concluded the risk of HIV infection after percutaneous exposure was 0.3 percent.²³

Literature reports of prenatal transmission range from 15-35%.¹³ HIV can be transmitted during pregnancy, during delivery, or by breast feeding.9 Both the mother's medical history and the baby's birth history are extremely important when assessing prenatal HIV transmission. In the United States, 1% of all adults AIDS cases and 5% of pediatric cases are associated with transfusion of blood and blood products.^{24,25} A reduction in transfusion acquired HIV infection has been attributed to blood donors screening techniques as well as viral inactivation procedures. Since 1995, the FDA has recommended that all donated blood/plasma be screened for HIV-1, HIV-2, and HIV-1 p24 antigen.

Transmission Routes

The four primary routes of HIV transmission are: sexual contact with infected person, sharing needles and/or syringes with an infected person, birth or breast feeding by an infected woman, and transfusions of infected blood or blood clotting factors.¹³

A disproportionate prevalence of this disease has been documented in American minority populations. African-Americans and Hispanics comprise a large percentage of newly diagnosed and total cases, accounting for seven and three times, respectively, greater incidence than in whites.9,26 Among young black males, one in seven becomes HIV positive each year.¹⁴ Minorities account for greater than 50% of AIDS cases among adults and adolescent males, 75% of cases involving adult and adolescent females, and 85% of cases in children.²⁶ The cumulative estimated number of Continued on page 207 AIDS diagnoses through 2008 in the United States and dependent areas was 1,106,391. In the 50 states and the District of Columbia, 851,974 cumulative AIDS diagnoses were among adult and adolescent males, 211,804 were among adult and adolescent females and transmit

adult and adolescent females, and 9,349 were among children under 13 years.⁹

Prevention of AIDS

The most effective way to prevent HIV infection is to avoid high-risk behaviors that lead to the infection. This may be accomplished by educational efforts geared towards both healthcare professionals and the general public. Educational programs should be focused on preventing the spread through appropriate procedures that involve the handling of potentially infected body fluids and safe sexual activity practices.

AIDS fact sheets from AIDS.ORG www.aids.org/topics/aids-factsheets or HIV workplace tools from the CDC are effective educational tools that the podiatric physician may obtain and place in their offices.

Restaino reported in a 1988 special communication: "While it may not be the role of the podiatrist to advise about safe sex policies and the dangers associated with sharing hypodermic needles, the podiatrist must make certain that the newly diagnosed patient is referred to the appropriate professional for counseling."²⁷ Discussions and advice between the podiatrist and patient should encompass virus transmission and the dangers associated with exposing others to the virus.

These discussions need to be fully documented in the patient's chart.²⁸ When making this documentation, the podiatrist should exercise care to maintain the patient's confidentiality. The advice should include the use of condoms during sexual intercourse and information related to sharing needles, and the patient must assure that every future healthcare provider who treats him/her will be made aware of the presence of the HIV virus.²⁷

Counseling patients to the proper use of condoms is extremely important in order for condoms to be effective in preventing the spread of HIV infection. Latex condoms have been promoted as a method to avoid the spread of HIV during receptive anal, vaginal, and oral sex.²⁸⁻³² The latex condom has no pores and is impervious to the passage of organisms responsible for sexually transmitted diseases, including HIV and hepatitis B virus.

Educational Efforts for the Podiatrist and Staff

Podiatric physicians should be well informed about appropriate infection control practices so that care may be given to all patients without compromise. Educational efforts should not be limited to podiatrists alone. Holmes expresses this point by reminding her readers that podiatry assistants frequently are exposed to blood and are at an increased risk for the occupational transmission of HIV.33 Her 1990 published study presented percentages of activities by 300 podiatric assistants. These activities included: cleaning contaminated instruments (91%), cleaning examining rooms (91%), handling specimens (83%), and disposal of needles and sharps (94%).33 An alarming finding was that 45% of the sample recorded that they did not always wear gloves for these procedures. Existing infection control guidelines to protect the podiatrist and the assistant should be emphasized since it is not possible to recognize medical conditions by relying solely on intuition.33

In 1987, three occupational risk categories were described by the Department of Labor and the Department of Health and Human Services for exposure to HIV.34 Category one included persons who frequently have direct contact with blood and/or body fluids. Both podiatrists and podiatric assistants would fall into this category during surgical procedures. Those individuals who infrequently had direct contract with blood or body fluids were grouped into category two. Finally, category three included those persons who never come in contact with blood or body fluids.34,35

As of 2010, no reports of occupational HIV exposure have been reported to the CDC specifically involving the practice of podiatry.

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Hand-washing

Hand washing is one of the most important tools to prevent infection. It functions as the most efficient means of removing recently acquired organisms and pathogens.35,36 Hands should be washed before invasive procedures, after removing gloves, and after contact with blood or body fluids.35,36 All body fluids should be assumed to be infectious and should be handled with extreme care.35 Gloves should be worn to protect hands from body substances that may contain infective organisms.36 Universal Precautions is the method used whenever healthcare professionals interact with patients to assist in infection control. These precautions are indicated for the prevention of the transmission of blood borne diseases like HIV and Hepatitis B virus.^{26,37,38} Universal Precautions has become a cornerstone of infection prevention and should be applied to all patients. Blood and body fluid precautions are recommended for use in the care of all patients, particularly in the emergency care setting.

Protective Barriers

Protective barriers reduce the risk of exposure of skin or mucous membranes to potentially infective substances. All healthcare workers should use barrier precautions when exposure to blood or body fluids of any patient is anticipated. Gloves should be used to prevent exposure of the podiatrist's skin to patient's blood, body fluids, and non-intact skin. A new pair of gloves is to be used with each new patient and hands should be washed immediately after each pair of gloves is removed. Needles should never be recapped, bent or broken, removed from disposable syringes or manipulated by hand. The scope of these guidelines was broadened to apply to non-intact skin and mucosa surfaces and to many other body fluids such as pleural, pericardial, and cerebrospinal fluids, and any fluid that contains visible blood.26 Levy describes in a special communication the implications for the podiatric physician when dealing with AIDS and AIDS-related diseases. In this report, not only are Universal Precautions presented, but the American Continued on page 208



Academy of Orthopaedic Surgeons guidelines are also presented in detail.³⁹

Newlan discusses decontamination of biological spills, safe handling of specimens, sterilization of instruments, and general office-cleaning directives in her publication.35 Barrier methods: gowns, masks, face shields, aprons should be used whenever body fluids might splatter, soak, or permeate the podiatrist's clothing or may contact the skin.35 Needles and sharps should be disposed of in a puncture-proof container. This container must be appropriately labeled and sealed prior to disposal.35 When decontaminating biological spills (blood or other body fluids) a chemical germicide or approved hospital disinfectant should be used. Gloves should be worn during these decontaminating procedures.35,36

Laboratory Considerations of HIV Infection

Proliferation of the HIV virus rapidly results shortly after entering the body. Within five days, the viral-1 RNA levels may be detected following infection. As the rise in plasma levels of HIV RNA occurs, at the same time there is a loss of CD4 + cells in the peripheral blood. The standard screening test for HIV infection used in the United States is an enzyme-linked immunosorbent assay (ELISA) which detects antibodies against HIV-1. The ELISA test is both highly sensitive (99%) and specific (98%). $^{^{13,40\cdot49}}$ If the ELISA test is positive, then a Western blot antibody test must be performed to determine confirmation of infection. False positive HIV tests are uncommon, but they can occur in women who are multiparous, individuals who have recently received either influenza or hepatitis B vaccines, those who have had multiple transfusions, and those with hematologic malignancy or unsuspected rheumatological disease. In most circumstances, a review of the patient's history and obtaining additional blood samples testing liver function, ANA and repeating the test in one month will help resolve the false positive test results.26

False negatives may occur if the patient is newly infected and the test is performed before antibody production is detectable.¹³ The median time to develop antibodies is two months from the initial exposure to HIV, with more than 95% of individuals developing antibodies within six months.¹³

The degree of viral load can be quantified by measuring the amount of viral RNA. Polymerase chain reaction (PCR) test and branch chain DNA are two methodologies used to measure HIV RNA. The viral load is used to determine the effectiveness of antiviral therapy aimed at eradicating HIV. Viral scheduled return visit to the test site or home visit by the healthcare provider. No test results, negative or positive, shall be revealed to the patient by telephone or by mail, except by blood banks or persons who collect blood, organs, skin, semen, or other tissue who find evidence of HIV infection in the donor. Patients should receive post-test counseling when results are returned. Notification of a person with a positive test result should include information on the availability of appro-

It is illegal to discriminate against individuals known to be infected with the HIV virus.

load is a better predictor of disease progression than the absolute CD4 + lymphocyte count, but prognosis is more accurate when the two are used together.^{13,47} Plasma HIV RNA level provides a valid measure of antiretroviral therapy efficacy for HIV-infected patients.

Confidentiality

Confidentiality and patient protection are key elements with regard to the legislation regarding HIV testing in the state of Florida.50,51 Informed consent must be obtained from a legal guardian or other persons when the person is not competent, incapacitated, or otherwise unable to make an informed judgment, or if the person has not reached the age of majority. However, according to Florida Statute 384.30, minors can be examined, tested, and treated for sexually transmitted diseases without parental or guardian consent.52 The patient should also be informed that a positive HIV test result will be reported to the county health department in Florida.

When HIV testing returns, the person ordering the test or that person's designee must ensure that all reasonable efforts are made to notify the test subject of his or her test result. The county health department contract provider, healthcare facility or healthcare provider shall notify the patient of HIV test results in person during a prepriate medical and support services, on the importance of notifying partners who may have been exposed and on preventing transmission of HIV. Notification of a person with a negative test result shall include, as appropriate, information on preventing the transmission of HIV.^{50,51}

It is illegal to discriminate against individuals known to be infected with the HIV virus.53 In fact, any person with or perceived as having HIV infection shall have every protection made available to handicapped persons. To refuse to hire, to segregate or deprive these patients of employment opportunities based upon their HIV status is illegal. Furthermore, no person may require an individual to take a human immunodeficiency, virus-related test as a condition of hiring, promotion, or continued employment unless the absence of HIV infection is a bona fide occupational qualification for the job in question.

Clinical Presentation

The clinical presentation of primary HIV infection varies. Some individuals are asymptomatic initially, while others will present with a mononucleosis-like illness with fever, pharyngitis and adenopathy.¹³ Initially, with primary infection, the patient's CD4 + T lymphocytes are within normal limits, but will decrease steadily over the next *Continued on page 209*

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six weeks. In 50%–90% of patients with primary HIV infection, the average infectious window period is 45 days with persons remaining infectious and sero-negative for greater than six months.⁵⁴ Onset of acute infection occurs three to six weeks after initial infection with the virus. Approximately 5% of infected patients will develop AIDS within three years and 20% within five years.^{13,55} The median time from initial infection with HIV to the development of an opportunistic infection or AIDS is 10 years^{13,55}

Opportunistic infection begin once CD4 + levels fall.13 Opportunistic infections begin to appear because the immune system begins to lose its ability to fight them off. Opportunistic infections can be found in the esophagus, lungs, spinal cord or brain, and the retinas of the eyes. Because CD4 levels are such an important indicator of the strength of the immune system, official treatment guidelines in the Unites States suggest that CD4 counts be monitored every three to four months. HIV-related morbidity and mortality derive not only from immune deficiency but also from direct effects of HIV on specific end organs and indirect effects of HIV-associated inflammation of these organs.

Of the new HIV-infected cases present in the United States, only a small number of these cases are detected in the acute phase. The "Acute Retroviral Syndrome" (ARS) is the designation given to a group of symptoms that occur in most, if not all, patients infected with human immunodeficiency virus.⁵⁵ This syndrome rapidly follows the initial infection with HIV usually within two months. Fever, lymphadenopathy, pharyngitis, and rash are its major features. The rash may present as either erythematous macular or mixed maculopapular, with lesions on face, trunk, and sometimes the extremities, including the palms and soles. Early detection of acute retroviral syndrome with early treatment of HIV may alter the subsequent course of the disease.55

Podiatric Manifestations of AIDS

Common lower extremity complications among persons with acquired immune deficiency syndrome include dermatologic, musculoskeletal, neurologic, rheumatic, and vascular. Some of the most common and well-documented complications will be presented here.⁵⁶⁶⁷

Cutaneous Manifestations of HIV-1 Infections⁵⁶⁻⁶⁰

a) Onychomycosis and tinea pedis appear frequently in patients with AIDS. Proximal white subungual onychomycosis has been identified as the most prevalent form of onychomycosis among AIDS patients. It begins under the nail plate proximally and progresses distally. Proximal white subungual onychomycosis cannot be ground off from the top of the nail. Recurrence is common despite the use of systemic antifungal agents. Onychomycosis caused by Candida albicans is more common in the later stages of HIV infections. With regard to tinea pedis, Trichophyton rubrum appears to be the predominant infective agent. Despite a lack of abundant data found in the literature, the podiatric physician can use oral terbinafine, oral itraconazole and ciclopirox 8% nail lacquer safely and effectively in special populations to include the HIV-infected populations. Clinicians may have to exercise caution to assess each presentation on a case-by-case basis.

b) Lesions of human papilloma virus are commonly found on the lower extremity of HIV patients. The lower extremities lesions can be plantar, flat, or appear as epidermodysplasia verruciformis. Verrucae of both the mosaic and singular variety are present among persons with AIDS.

c) Molluscum contagiosum can be seen on any part of the skin of AIDS patients. The papules can be enlarged forming clusters of grapes which are disfiguring.

d) Herpes zoster infections appear in immunocompromised individuals with HIV infection.

e) Staphylococcus aureus or Pityrosporum orbiculare topical skin infections causing itchy folliculitis is common in AIDS patients. Pruritus is commonly experienced in HIV-positive patients.

f) Norwegian scabies has been reported in HIV-positive patients. It is caused by the Sarcoptes mite, and is associated with widespread crusted plaques of the skin. It may also infest the nail bed and plate, causing hypertropic nails. Despite the treatment being difficult, it is recommended to apply permethrin 5% cream weekly until cutaneous manifestations clear.

g) Papulosquamous dermatoses in the form of seborrheic dermatitis present with pruritic erythematous patches on the head and trunk of HIV-infected patients. Pityriasis rubra pilaris lesions present on the scalp, trunk, extremities, palms, and soles.

h) The majority of HIV-positive individuals experience extreme skin dryness.

Musculoskeletal and Neurologic Conditions of Lower Extremities in HIV Patients^{58,60-61}

Patients presenting to podiatrists with foot complaints may be experiencing neurological complications of HIV affecting both the musculoskeletal and neurological systems. Since the introduction of highly active antiretroviral therapy in the 1990's, the incidence rate of neurologic disease has decreased.62 Gait instability is experienced by the HIV positive patient. Brain lesions, tumors, direct infection or spinal cord injuries may be the focus of the lower extremity signs and symptoms. These complaints may include pain, numbness, and paresthesias. Musculoskeletal complaints may include both proximal and distal muscle weakness, stiffness, cramps, fatigue.

Muscle weakness and fatigue are common and have multiple causes. Precipitating factors may include alcohol, depression, drugs, metabolic conditions or poor nutrition.

Distal symmetrical polyneuropathy is the most common type of peripheral neuropathy. Peripheral neuropathies associated with HIV infections include:

Distal symmetric polyneuropathy caused by:

- a) Idiopathic HIV-related
- b) Drug associated
- c) Vitamin B-12-deficiency.

d) Acute inflammatory demyelinating polyneuropathy or Guillain-Barre' syndrome chronic inflammatory de-



myelinating polyneuropathy e) Mononeuropathy multiplex f) Progressive polyradiculomyelopathy

g) Autonomic neuropathy Both Guillain Barre' syndrome and either acute or chronic inflammatory polyneuropathy may present in early asymptomatic HIV infection. Distal symmetric polyneuropathy presents in AIDS infections; while mononeuropathy multiplex presents equally in all stages of the HIV infection.

Progressive polyradiculapathy occurs late in the AIDS disease process. Enthesopathies are common and are frequently experienced by HIV positive patients. They include Achilles tendonitis and posterior tibial tendonitis.

Rheumatic Manifestations of Human Immunodeficiency Virus Infection^{58,60,63}

Berman, et al., published an account of rheumatic complications of HIV-infected patients in 1988.63 Seventy-two subjects experienced the ailments of Reiter's Syndrome, Psoriatic arthritis, asymmetric oligoarthritis of large joints, and muscle involvement. Rheumatic symptoms were found three percent of all the cases studied.71 Arthralgias represented 34.7%, arthritis and Reiter's Syndrome represented 11.9% and 9.9% respectively, painful articular syndrome 9.9% and psoriatic arthritis 1.9% were documented in the rest of the study population. They concluded a reactive mechanism in which an immune complex material might play an important role in the pathogenesis of the articular symptoms seen during the course of HIV infections.63

Vascular Complications of HIV Infection^{58,60,64}

Lower extremity edema may present in the HIV-infected patient secondary to hypoalbuminemia caused by poor nutrition, malabsorption, or a protein-losing enteropathy. Pseudo thrombophlebitis has been reported in a few cases of Kaposi's sarcoma. Saber, et al. describe the risk of deep vein thrombosis in 4752 patients during the study period of 1995 to 2000.⁶⁴ They found 45 patients (0.95%) to have deep vein thrombosis. The distribution of the thrombosis were 23 femoral veins, 20 popliteal veins, and 2 were found in the iliofemoral system. The high risk for DVT in HIV patients may be attributed to the co-morbidity of hypercoagulability, opportunistic infections, or malignancies. They concluded that statistically DVT was found to occur approximately 10 times more frequently in HIV-infected individuals.⁶⁴

Kaposi's Sarcoma of the Lower Extremity^{60,65-67}

Kaposi's sarcoma is a malignant tumor arising from blood vessels in the skin and appearing purple to dark brown flat/raised plagues or nodules. Lesions occur primarily on the skin, oral mucosa, gastrointestinal tract, and lungs. Radiotherapy is the treatment of choice, but chemotherapy may be of some value in metastatic disease. The lesion was first described by Moricz Kaposi, an Austro-Hungarian dermatologist in 1872. The literature reports four forms of Kaposi's sarcoma. The classic form is often seen on the ankles and soles of older men, usually of Mediterranean ancestry. The African form occurs in adult males predominately in central Africa. The immunosuppressed form develops in posttransplant patients undergoing immunosuppressive therapy. Epidemic forms are identified in patients who are suffering from AIDS.65-67

Kaposi's sarcoma is the most frequent neoplastic complication of AIDS. It can have visceral and mucocutaneous manifestations; starting off as an asymptomatic flat or macular lesion, next turning into thickened or indurated papules and plaques, and finally presenting as nodules. Skin changes may include an almost woody edema secondary to the formation of confluent epidermal plaques and lymphatic obstruction by infiltrating tumor cells. Selected dermatologic conditions in the differential diagnosis of Kaposi's sarcoma include: venous stasis disease, malignant melanoma, dermatofibroma, hemangioma, lichen planus, warts, pyogenic granuloma, lesions of secondary syphilis, and bacillary angiomatosis.

The diagnosis of Kaposi's sarcoma is most definitively made by taking a 4 mm punch biopsy from the center of the lesion. The management of these patients requires a multi-disciplinary team approach to include specialists of oncology, infectious disease, radiology, dermatology, and psychiatry.⁶⁵⁻⁶⁷ Therapy for Kaposi's sarcoma may include administration of immune base therapy like interferon or tumor necrosis factor.

Antiretroviral Therapy^{13,14,68-72}

An untreated HIV infection may have detrimental effects at all stages of the infection. Anti-retroviral drugs should be used in HIV-infected patients.

Treatment is beneficial even when initiated later in the infection; however, later therapy may not repair damage associated with viral replication during early stages of infection. Earlier treatment may prevent the damage associated with HIV replication during early stages of infection.

Anti-retroviral therapy for the treatment of human immunodeficiency virus infection has improved steadily since the advent of potent combination therapy in 1996. These drugs are called highly active antiretroviral therapy (HAART). Antiretroviral therapy is used to improve survival by reducing viral load and increasing the CD4 + lymphocyte count. The effective use of antiretroviral therapy is important in prolonging life and in reducing the number of opportunistic infections. Treatment involves the use of three or four antiretroviral agents. When maximal suppression is not achieved or lost, changing to a new regimen with at least two active drugs is required. Treatment with only one agent results in development of viral resistance to the single agent. The use of multi-drug highly active antiretroviral agents results in multiple drug interactions. The podiatrist should be mindful of the potential drug interactions that exist with these agents, so that when prescribing to the AIDS patient drug interactions may be avoided. It is important to review medication regimens for potential drug interactions. There are numerous potential interactions that can occur with these medications. Keeping track of these interactions can be a difficult task. A very useful web source for



TABLE I Antiviral Agents Names and Dosages by Class

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

Combivir (zidovudine + lamivudine)	l tablet BID	Take with or without food
Emtriva (emtricitabine)	200 mg daily	Take with or without food
Epivir (lamivudine)	300 mg daily (150 mg BID)	Take with or without food
Epzicom (abacavir + lamivudine)	l tablet daily	Take with or without food HLA-B*5701 testing reduces Allergic reaction to abacavir
Retrovir (zidovudine)	300 mg BID	Take with food minimized stomach Discomfort—Do not take with Zerit
Trizivir (abacavir + zidovudine + Iamivudine)	I tablet BID	Take with or without food HLA-B*5701 testing reduces Allergic reaction to abacavir
Truvada (tenofovir + emtricitabine)	I tablet daily	Take with or without food
Videx EC (didanosine)	400 mg daily 250 mg daily (Wt less 132 #s)	Take on empty stomach Best to avoid alcohol
Viread (tenofovir)	300 mg daily	Take with or without food (raises Videx EC levels ↑ ADRs)
Zerit (stavudine)	40 mg BID 30 mg Bid (Wt less 132 #s)	Take with or without food Do not take with Retrovir or Combivir
Ziagen (abacavir)	600 mg daily 300 mg BID	Take with or with food HLA-B*5701 testing reduces Allergic reaction to abacavir
Protease Inhibitors		
Aptivus (tipranavir)	500 mg BID with 200 mg Norvir	Take with food
Crixivan (indinavir)	800 mg TID 800 mg BID with 200 mg of Norvir	Take on empty stomach Drink 6 glasses of water a day to prevent kidney stones
Invirase (saquinavir)	1000 mg plus 100 mg Norvir BID	Must be used with Norvir
Kaletra (lopinavir + ritonavir)	Two tablets BID four tablets daily	Take with or without food



drug interactions can be found at www.hiv-druginteractions.org. New drugs have been approved that offer new mechanisms of action, improvements in potency and activity—even against multi-drug resistant viruses—dosing convenience, and tolerability. Currently HIV drugs target four steps of HIV's lifecycle. Attacking HIV on multiple fronts by combining drugs from different classes is the best way to slow or stop HIV reproduction. It is also the best way to prevent the development of drug resistance. Successful HAART therapy needs to have at least three active drugs from multiple drug classes.

Antiretroviral drugs are divided into five categories: Entry Inhibitors, Integrase Inhibitors, Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (NRTI's), Non-nucleoside Reverse Transcriptase Inhibitors (NNR-TI's) and Protease Inhibitors. Currently available agents and dosages are presented in Table 1. Compliance or adherence to therapy is essential to ensure therapeutic effectiveness and to minimize the occurrence of resistance. *Continued on page 213*

TABLE I Antiviral Agents Names and Dosages by Class (continued)

Protease Inhibitors (continued)		
Lexiva (fosamprenavir)	1400 BID 1400 mg daily with Norvir	Take with or without food
Norvir (ritonavir)	600 mg BID	Mostly used to "boost" Levels of other PIs
Prezista (darunavir)	800 mg daily 600 mg BID with Norvir	Must be used with Norvir
Reyataz (atazanavir)	400 mg daily 300 mg daily with 100 mg of Norvir	Take with food Do not combine with Viramune or Intelence
Viracept (nelfinavir)	l 250 mg BID 750 mg TID	Take with food May use powder
Non-Nucleoside Reverse Transcr	iptase Inhibitors	
Atripla (efavirenz + tenofovir emtricitabine)	l tablet daily	Take on empty stomach at bedtime minimize dizziness and drowsiness
Intelence (etravirine)	200 mg BID	Take with food
Rescriptor (delavirdine)	400 mg TID	Take with or without food
Sustiva (efavirenz)	600 mg daily	Take on empty stomach at Bedtime
Viramune (nevirapine)	200 mg daily x 14 Days then 200 mg BID	Take with or without food
Integrase Inhibitors		
lsentress (raltegravir)	400 mg BID	Take with or without food
Fusion and Entry Inhibitors		
Fuzeon (enfuvirtide)	90 mg Injection BID	Needs to be reconstituted
Selzentry (maraviroc)	Doses depend on other HIV drugs used	Take with or without food Only effective against CCR5 Tropic HIV



The patient under the podiatrist's care should be reminded of this compliance during follow-up appointments.

Entry inhibitors are drugs that stop or inhibit HIV from entering a CD4 cell. There are different types of entry inhibitors: fusion inhibitors and CCR5 antagonists. Fusion inhibitors prevent binding of the HIV virus to the host cell by blocking a particular domain located on the gp41 portion of the outer membrane gp120. CCR5 Co-Receptor antagonist binds to CCR5 chemokine co-receptor located on the host cell membrane, blocking interaction between HIV-1 gp 120 and CCR% needed for internalization of the virus.

Integrase inhibitors are drugs that interfere with HIV's integrase enzyme. There is one approved integrase inhibitor: Isentress (raltegravir). Blocking integrase prevents the integration of HIV-1 DNA into the host's genomic sequence. Integrase inhibitors prevent HIV from taking over CD4 cell's command center.

The nucleoside reverse transcriptase inhibitors are synthetic analogs of naturally occurring deoxyribonucleosides that are phosphorylated intracellularly. They work by interfering with the HIV virus reverse transcriptase enzyme system that is responsible for viral replication by terminating chain elongation. Members of the non-nucleoside reverse transcriptase class are structurally diverse and have similar mechanisms of action. They inhibit the reverse transcriptase enzyme system directly without having to be intracellularly activated by binding to the system itself and making it unavailable for use by the virus. The protease inhibitors are synthetic agents that are very potent and more active against the reverse transcriptase system when compared to both the NRTI and NNRTI classes. They act at the end of the HIV virus life cycle, resulting in the formation of noninfectious virions. All protease inhibitors are primarily cleared by the body through metabolism by cytochrome P-450 system using substrates for CP3A4.

Adverse effects are common with the antiretroviral agents and specialized texts should be consulted for details. Adverse effects experienced with these agents can affect many different organ systems. The most recent findings of bone thinning and bone loss, potentially leading to fractures in adults and children receiving potent antiretroviral regimens, may prove to be very challenging to the podiatrist.^{14,72} Protease inhibitors may induce lipodystrophy with increased girth around the stomach, dorsal cervical fat and increased breast size.¹⁴ Hyperglycemia has been reported with the use of protease inhibitors.¹⁴ It is iman inhibitor of HIV protease. Adverse effects include peripheral neuropathy, dry skin, and leg pain.

Nelfinavir (Viracept)—Nelfinavir inhibits HIV protease. Side-effects include accidental injury, arthritis, and maculopapular rash.

Amprenavir (Agenerase)—Amprenavir is an inhibitor of HIV-a protease. It binds to the active site of the gag-pol polyprotein precursor, resulting in the formation of immature noninfectious viral particles.

Highly active antiretroviral therapy (HAART) drugs should be used in HIV-infected patients.

portant to become thoroughly familiar with the drugs selected and to identify specific laboratory and clinical monitoring parameters to ensure positive outcomes in therapy.

The following information was obtained from current data found in the tertiary reference source "Guidelines for Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents" as well as current compendium.^{70,71} The information is intended to assist the podiatrist clinically with regard to patient management.

Antiretroviral Agents

Protease Inhibitors

Saquinavir (Invirase)—Saquinavir is an inhibitor of HIV protease. Saquinavir is a peptide-like substrate analog that inhibits the activity of HIV protease and prevents the cleavage of viral polyproteins. Adverse effects include leg cramps, leg pain, Kaposi sarcoma, and molluscum contagiosum.

Ritonavir (Norvir)—Ritonavir is an inhibitor of HIV protease with activity against HIV. Inhibition of HIV protease renders the enzyme incapable of processing the gag-pol polyprotein processor, which leads to production of non-infectious immature HIV particles. Side effects include abnormal gait, psoriasis, and molluscum contagiosum.

Indinavir (Crixivan)—Indinavir is

Lopinavir/Ritonavir (Kaletra) is a protease inhibitor combination which prevents cleavage of the Gagpol polyprotein, resulting in the production of immature, non-infectious viral particles. Dry skin, arthralgia, and abnormal vision are among its side effects.

Tipranavir (Aptivus) Tipranavir is a protease inhibitor of HIV-1 belonging to the class of 4-hydroxy-5,6-dihydro-2-pyrone sulfonamides. Side effects include rash, hepatotoxicity and intracranial hemorrhage.

Lexiva (fosamprenavir calcium) is a prodrug of amprenavir, an inhibitor of HIV protease.

Atazanavir (Reyataz) is an azapeptide inhibitor of HIV-1 protease. Adverse reactions include cardiac conduction abnormalities, rash, hyperbilirubinemia, and nephrolithiasis.

Darunavir (Prezista) is a protease inhibitor and is always taken with and at the same time as another medication called Norvir (ritonavir), and in combination with other HIV medicines. Prezista should also be taken with food. The most common side effects related to taking Prezista include diarrhea, nausea, rash, headache, stomach pain, and vomiting. Other important severe side effects include inflammation of the liver or pancreas and increased blood fat levels.



Nucleoside Analog Reverse Transcriptase Inhibitors

Tenofovir (Viread) is an acyclic nucleoside phosphonate diester analog of adenosine monophosphate. It inhibits the activity of HIV reverse transcriptase by competing with natural substrate deoxyadenosine 5'-triphosphate, and after incorporation into DNA, by DNA chain termination.

Didanosine (DDI; dideoxyinosine-Videx) is a synthetic purine nucleoside analog of deoxyadenosine, in which the 3'-hydroxyl group is replaced by hydrogen. Adverse effects include peripheral neuropathy of hands and feet.

Lamivudine (3TC-Epivir-HBV, Epivir) is a synthetic nucleoside analog with activity against HIV and HBV.

Stavudine (d4T-Zerit) is a synthetic thymidine nucleoside analog active against HIV. Peripheral neuropathy has been associated with its use in a dose related association.

Zidovudine (Azidothymidine, AZT, Compound S, Retrovir) is a thymidine analog and is an inhibitor of the in vitro replication of some retrovirus, including HIV. The most frequent events include abnormal laboratory values which may be problematic for the podiatrist. Arthralgia, muscle spasms, and tremor may be frequently encountered with zidovudine.

Abacavir (Ziagen) is a synthetic carbocyclic nucleoside analog with inhibitory activity against HIV.

Combivir (Lamivudine/ Zidovudine) is a combination containing two synthetic nucleoside analog reverse transcriptase inhibitors against HIV.

Trizivir (Abacavir sulfate/Lamivudine/Zidovudine) is a combination of three synthetic nucleoside analogs.

Emtricitabine (Emtriva)is the brand name of emtricitabine, a synthetic nucleoside analog with activity against human immunodeficiency virus type 1 (HIV-1) reverse transcriptase. The following adverse reactions have been observed: lactic acidosis/severe hepatomegaly with steatosis, severe acute exacerbations of Hepatitis B and immune reconstitution syndrome Tenofovir (Viread) is the brand name for tenofovir disoproxil fumarate (a prodrug of tenofovir) The following adverse reactions have been observed: lactic acidosis/severe hepatomegaly with steatosis, severe acute exacerbation of hepatitis, new onset or worsening renal impairment, decreases in bone mineral density, and immune reconstitution syndrome.

Non-Nucleoside Reverse Transcriptase Analogs

Nevirapine (Viramune) is a non-nucleoside reverse transcriptase inhibitor with activity against HIV-1. It binds directly to reverse transcriptase and blocks the RNA-dependant and DNA-dependant DNA polymerase activities by causing a disruption of the enzyme's catalytic site. Skin reactions have occurred and include Stevens-Johnson syndrome.

Delavirdine (Rescriptor) is a nonnucleoside reverse transcriptase inhibitor of HIV-1. It may cause abnormal coordination, muscle cramps, bone pain, leg cramps, tendon disorders, and tendosynovitis.

Efavirenz (Sustiva) activity is mediated predominantly by non-competitive inhibition of HIV-1 reverse transcriptase acting as a non-nucleoside transcriptase inhibitor of HIV-1.

Etravirine (Intelence) is a non-nucleoside reverse transcriptase inhibitor (NNRTI) of human immunodeficiency virus type 1 (HIV-1). Severe, potentially life-threatening, and fatal skin reactions have been reported. These include cases of Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme. Hypersensitivity reactions have also been reported and were characterized by rash, constitutional findings, and sometimes organ dysfunction, including hepatic failure. *Continued on page 215*

TABLE 2 Recommended HIV Post Exposure Prophylaxis (PEP)73

Two NRTIs Simple dosing, fewer side effects

Preferred basic regimens: zidovudine (AZT) OR tenofovir (TDF) plus lamivudine (3TC) OR emtricitabine (FTC)

Alternative basic regimens: stavudine (d4T) OR didanosine (ddl) plus lamivudine (3TC) OR emtricitabine (FTC)

Post Exposure Prophylaxis HIV Class I—Less Severe (Asymptomatic < 1500 RNA COPIES/mL) Recommended basic 2 drug PEP Source of unknown HIV status-Generally no PEP warranted; consider basic 2 PEP for source with HIV risk factors Unknown source -2 PEP in setting in which exposure to HIV infected persons likely HIV negative—No PEP warranted

Post Exposure Prophylaxis HIV Positive, Class 2 (Symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load) Recommended basic 3 or more drugs PEP Source of unknown HIV status-Generally no PEP warranted; consider basic 2 PEP for source with HIV risk factors Unknown source -2 PEP in setting in which exposure to HIV infected persons likely HIV negative—No PEP warranted



Integrase Inhibitors

Raltegravir (Isentress) contains raltegravir potassium, a human immunodeficiency virus integrase strand transfer inhibitor.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Reported adverse effects include: nausea, insomnia, headache and fatigue.

Fusion and Entry Inhibitors

Enfuvirtide (Fuzeon) is an inhibitor of the fusion of HIV-1 with CD4 cells. Adverse effects include hypersensitivity reactions and pneumonia.

Maraviroc (Selzentry)—Maraviroc is a selective, slowly reversible, small molecule antagonist of the interaction between human CCR5 and HIV-1 gp120. Blocking this interaction prevents CCR5-tropic HIV-1 entry into cells. Cardiovascular events and hepatotoxicity have both been observed as significant adverse reactions with the use of maraviroc.

Post-Exposure Prophylaxis⁷³⁻⁷⁴

The overall risk of transmission of HIV from a percutaneous exposure is approximately 0.3%, and after a mucous membrane exposure approximately 0.09%.72 It is influenced by factors such as depth of the injury, amount of body fluid, and type of instrument involved. An "exposure" that may place a podiatrist or assistant at risk for HIV infection in which post-exposure prophylaxis should be considered include percutaneous injury (e.g. needlestick or cut with a sharp object), contact mucous membrane or non-intact skin, contact with intact skin when the duration of contact is prolonged. Recommendations for HIV PEP include a basic four-week regimen of two drugs (zidovudine and lamivudine; lamivudine and stavudine; or didanosine and stavudine) for most HIV exposures. There is an expanded regimen that includes the addition of a third drug for HIV exposures that pose an increased risk of transmission.72 Treatment should be initiated as soon as possible whenever exposure is suspected to minimize infection with HIV. The choice of which agents to use, how many agents, and when to change them, is empiric.⁷³

In theory, a combination of drugs with activity at different stages of viral replication might offer additive prevented effect in post-exposure prophy-

TABLE 3 Economic Burden Cost per Month of HIV Medications

Agenerase	\$ 772.00
Aditus	\$ 772.00 \$1,172.50
Combivir	\$ 752.64
Crixivan	\$ 570.96
Emtriva	\$ 347.11
Epivir	\$ 347.11
Fuzeon	\$2,315.40
Invirase	\$ 748.50
Kaletra	\$ 796.26
Lexiva	\$ 658.99
Norvir	\$ 321.46
Rescriptor	\$316.35
Retrovir	\$ 405.59 \$ 892.91
Sustiva	\$ 499.43
Trizivir	\$ 499.43 \$1,164.35 \$ 466.44
Ziagen	\$ 466.44

laxis. The total body burden of HIV is substantially lower among exposure to healthcare professionals than among persons with established HIV infection-For this reason this report's recommendations provide guidance for two and three (or more) PEP regimens based on the level of risk for HIV transmission represented by exposure. Animal models of post-exposure prophylaxis studies suggest substantially less effective beyond 24—36 hours and case-control studies suggest most subjects in each group received PEP within four hours. Analysis of PEP

failures does not suggest a clear cut-off time for post-exposure prophylaxis. Some agents not recommended for post-exposure prophylaxis. Avoid the use of Nevirapine (Viramune) for the HIV postexposure prophylaxis because of the risk of life-threatening hepatotoxicity.

Delavirdine (Rescriptor) has been observed to cause drug-associated rash that can progress to Stevens-Johnson syndrome.

Abacavir (Ziagen) causes severe hypersensitivity reactions within the first six weeks of therapy. Zalcitabine (Hivid) has a frequency of three times a day and is considered one of the weakest antiretroviral agents. Hivid was discontinued by Roche Pharmaceuticals on 12/31/2006 due to the availability of newer medications.

PEP in Pregnancy

Most antiretrovirals are pregnancy class B or C. Antiretroviral Pregnancy Registry has not detected increased teratogenic risk for ARVs in general, nor specifically for AZT and 3TC, in the first trimester.¹ Avoid efavirenz (anencephaly in monkeys), amprenavir (ossification defects in rabbits), and indinavir in late-term (hyperbilirubinemia).

Table 2 illustrates examples of the recommended HIV

post-exposure prophylaxis for percutaneous injuries and for mucous membrane exposures and non-intact skin exposures. When the source person's virus is known or suspected to be resistant to one or more of the drugs *Continued on page 216*



considered for PEP regimen, the selection of drugs to which the source person's virus is unlikely to be resistant is recommended.72 Merchant and Keshavarz provide a discussion of the data available on HIV transmission and HIV PEP in pediatrics.74 They recommend a stratified regimen to match seroconversion risk with an appropriate number of medications, while taking into account medication side-effects and the amount of information available upon initial presentation. They recommend HIV PEP should be administered within one hour of exposure. The cost alone for four weeks of adult PEP treatments is estimated to be approximately \$600 to \$1000, depending on the regimen used. The total cost could be as high as \$1800 per treatment.26 Monthly cost estimates for HAART agents are noted in Table 3.

Luther and Glesby published a summary that looked at a significant number of patients with skin pathology, some of which can be attributed directly or indirectly to antiretroviral therapy.75 This published report recounts that non-nucleoside reverse transcriptase inhibitors exhibit a class effect with regard to skin adverse manifestation and the spectrum of disease can vary from mild morbilliform rash to Stevens-Johnson syndrome.75-77 Also bear in mind that some protease inhibitors have been implicated in causing rash while indinavir causes retinoid-like manifestations such as paronychia, ingrown toenails, alopecia, and curling of straight hair.75-77

Anti-Retroviral Therapy and **Paronychias**

A review of the literature reveals case reports and retrospective cohort accounts of patients receiving antiretroviral therapy for HIV infection and the subsequent development of paronychias.75-87

Zerboni and colleagues reported the onset of paronychia in 12 HIV-positive patients who were receiving lamivudine during a three-month period.78 The clinical presentation of paronychia involved one great toe in five patients, both great toes in five patients, and fingernails as well as toenails in two patients.78,82,86 Further,

these patients did not have any risk factors for paronychia development.

Bouscarat and co-workers described 42 HIV-positive individuals who presented with great toe paronychia secondary to ingrown nails, and they had received the HIV treatment indinavir.79,82,86 These patients had no prior episodes of paronychia, psoriasis, or local trauma.79 The medium time of onset for drug-induced ingrown toenails was 120 days.79 These authors suggest that inhibition of endogenous proteases may be the explanation for initial hypertrophy of the nail fold and the subsequent development of similar lesions of pyogenic granuloma.79,82

Bouscarat and co-workers also suggest that disturbances of retinoic

TABLE 4 **Online Resources** with Regard to HIV

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http://hivinsite.ucsf.edu

http://hopkins-hivguide.org

http://www.hivatlas.org

http://www.cdc.gov/hiv/resources/factsheets/

http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL

http://www.hiv-druginteractions.org

acid metabolism may be the underlying mechanism for the nail changes one sees with patients receiving indinavir.79,86 Sass and colleagues say paronychia with pyogenic granuloma in the presence of indinavir therapy may be induced by impairment of the oxidative metabolism of retinoic acid through the inhibition of cytochrome p450 3A as opposed to impaired formation of 9-cis-retinoic acid.83

In a study of 50 HIV-infected men who were referred for the treatment of paronychia between the years 1995 to 1999, Sibel and colleagues noted that these patients' drug regimens included combinations of the following medications: indinavir, stavudine, didanosine, lamivudine, zidovudine, nevirapine,

delavirdine, nelfinavir and ritonavir.82

Colson and co-workers assessed a retrospective cohort of managed care patients who received protease inhibitors from 1996 through 1998.86 They identified 288 adults during this timeframe and that indinavir appeared to be part of their drug regimen 63 percent of the time. A total of 30 patients in this population had at least one documented paronychia of the great toe during this timeframe.⁸⁶ These authors concluded that indinavir (and not lamivudine) was strongly associated with great toe paronychia.86 James and colleagues reported five cases of ingrown toenails associated with indinavir-ritonavir combination therapy.85

Garcia-Silva and co-workers report

that paronychias occur in 4 to 9 percent of the patients who receive indinavir.87 They suggest this adverse effect is not related to other epidemiological variables such as the patient's sex, age, immune status, or other risk factors. Even through the exact mechanism of indinavir-induced, retinoid-like effects is unclear, the following hypotheses for paronychia pathogenesis in-

clude: interference with the retinoid metabolism by enhancing retinoic acid signaling pathway; increasing retinoic acid synthesis; or reducing cytochrome p450 mediated retinoic acid oxidative metabolism.82

Conclusion

The management of HIV/AIDS involves the complex coordination of many healthcare professionals. It requires educational efforts on the part of these professionals as well as the patients. Table 4 presents a list of electronic online sites that may be of some assistance to podiatrists or their patients. Significant advances in the therapeutic management have occurred Continued on page 217

since it AIDS was first reported. The role of the podiatrist in the management of AIDS-related illnesses is to actively provide care to the AIDS patient, be an active participant in educational programs and prevention strategies, safe-guarding staff from potential exposure, and protect the confidentially and the dignity of the HIV-infected patient. **PM**

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http://fac.dos.state.fl.us/fac/

⁸ Chapter 64B18-17.003 2007 Florida Administrative Code:

http://fac.dos.state.fl.us/fac/

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Dr. Smith is in private practice in Ormond Beach, FL.

CME **EXAMINATION**

1) As of 2009 the CDC estimates the number of persons newly infected with HIV in 2006 was?

- A) 45,000
- B) 74,467
- C) 56,300
- D) 1,000,000

2) The Human Immunodeficiency virus (HIV-1) is transmitted during:

- A) Sexual Intercourse
- **B)** Intravenous Injection
- C) Perinatal transmission
- D) All the above

3) The pharmacological classification of Maraviroc is considered the following:

A) Protease Inhibitor

B) HIV Integrase InhibitorC) Non-nucleoside ReverseTranscriptase InhibitorD) CCR5 Co-Receptor Antagonist

4) The ELISA test is both

____% sensitive and

- ____% specific.
- A) 50% : 50%
- B) 99% : 98%
- C) 98% : 100%
- D) None of the above

5) Minors can be examined, tested, and treated for sexually transmitted disease without parental or guardian consent allowed by which Florida Statute? A) FS 465.001

A) FS 405.001
B) FS 64D-2 FAC
C) FS 381.004
D) FS 384.30

SEE ANSWER SHEET ON PAGE 221.

- 6) Dosage of enfuvirtide is
- _____ twice a day:
 - A) 90 mg
 - B) 180 mg
 - C) 45 mg
 - D) 60 mg

7) Which of the following are cutaneous manifestations of HIV-1?

- A) Molluscum contagiosum
- **B)** Norwegian Scabies
- C) Both a and b
- D) None of the above

8) Distal symmetric polyneu-

ropathy is associated with:

- A) Idiopathic HIV RelatedB) Drug associated
- C) Vitamin B-12 deficiency
- D) All of the above are
- correct

9) In Berman's published account of rheumatic manifestations, Reiter's syndrome represents:

- A) 8 % B) 9.9 %
- C) 9.1 %D) 7.9%

10) Moricz Kaposi described Kaposi's Sarcoma during which year?

A)	1875
B)	1872

- C) 1882
- D) 1827

11) HAART's abbreviationstands for?A) Highly active antiretroviral therapyB) Heavy active antiretrovi-

ral therapyC) Highly anti-active antiretroviral therapyD) Highly active antiviral therapy

12) Select the correct description?

A) Amprenavir—Non-Nucleotide protein analog reverse transcriptaseB) Indinavir-Protease Inhibitor

C) Efavirenz-Non-Nu-

cleotide Reverse Transcriptase Inhibitors

D) b and c are correct

13) Kaletra is a protease in-

- hibitor combination of:
 - A) ddI/3TC
 - B) Lopinavir/Ritonavir
 - C) AZT/Ziagen
 - D) Lopinavir/Zidovudine

14) Bouscarat and co-workers described 42 HIV-positive individuals who presented with great toe paronychia secondary to treatment with :

- A) Zidovudine B) Lamivudine
- C) Indinavir
- D) Tipranavir

15) Which of the following medications should not be used for HIV PEP because of lifethreatening hepatotoxicity?

A) LamivudineB) DidanosineC) NevirapineD) All the above are correct





16) Educational programs for the prevention of AIDS should be focused on:

A) Preventing the spread through appropriate procedures that involve the handling of potentially infected body fluids.

- B) Safe sexual activity practices.
- C) Only a
- D) Both a and b

17) Delavirdine (Rescriptor) may cause the following adverse effects of interest to the podiatrist?

- A) Normal coordination
- B) Upper extremity pain
- C) Tendon disorders and tendosynovitis
- D) No bone pain
- 18) Identify the true statement:

A) A combination of drugs with activity at different stages of viral replication might offer additive prevented effect in post-exposure prophylaxis.

B) Stevens-Johnson syndrome is an adverse effect of Nevirapine.

C) Dry skin is commonly experienced in HIV-positive patients.

D) All the above statements are true.

19) Identify the correct monthly cost of following HAART agents:

A) Ziagen = \$755.75 dollars per month

B) Retrovir = \$ 506.32 dollars per month

- C) Norvir = \$ 321.46 dollars per month
- D) Agenerase = \$ 277.00 dollars per month

20) Which websites may assist in answering HIV and AIDS questions?

- A) http://hivinsite.ucsf.edu
- B) http://www.hiv-druginteractions.org/
- C) http://www.cdc.gov/hiv/resources/factsheets/
- D) All websites are correct

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