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The Essentials of HIV: A Review for Nurses

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Abstract

The US HIV epidemic began in 1981. Each year, a larger number of people in the US and throughout the world are living with HIV. Given the increasing number of HIV-infected individuals, knowledge of the basic pathogenesis of HIV disease and the principles of antiretroviral therapy is important for all healthcare professionals. This article describes epidemiologic trends in HIV and reviews HIV transmission, testing, and treatment. It also discusses the risk of HIV transmission to healthcare workers from occupational exposures and reviews the principles of postexposure prophylaxis used to reduce the likelihood of HIV transmission in appropriate circumstances.

Introduction

Since 1981, the HIV/AIDS epidemic has drastically altered both the healthcare field and the well-being of nations and people around the world. For the first 15 years of the epidemic, no potent treatments were available for HIV. More recently, combinations of antiretroviral medications have become available that successfully and durably suppress HIV replication. These advances in the treatment of HIV have changed the outlook for HIV-positive patients. This is particularly true for patients infected more recently and who have access to healthcare and antiretroviral medications. For these patients, HIV has become a manageable chronic disease.

This article will review the current epidemiology of HIV, transmission and prevention, basic virology and pathogenesis, and recommendations for HIV testing. It will also discuss the principles of HIV treatment, its outcomes, and the use of antiretroviral medications for postexposure prophylaxis.

Case Study: Part 1

A 37-year-old pregnant pediatric ICU nurse was working with a 9-year-old male patient transferred to the US from an eastern European hospital to undergo a specialized surgical procedure. During the course of his care, the nurse suffered a needlestick injury to her left hand with an 18-gauge needle that had just been withdrawn from the patient's vein. The nurse's wound appeared to be at least 5 millimeters (mL) deep and caused significant bleeding. After washing her hands thoroughly with soap and water, the nurse reported to the hospital's occupational health department, where she was evaluated for potential exposure to HIV.

Epidemiology

Worldwide, more than 40 million people are infected with HIV, and approximately 5 million people are newly infected each year.¹ Sub-Saharan Africa represents a disproportionate number of HIV cases, with approximately 26 million persons infected. The prevalence of HIV is highest in several African countries, including South Africa, with an HIV prevalence of 18.8%, Zimbabwe, with a prevalence of 20%, and Swaziland, with a prevalence of 33%.² Eastern Europe is experiencing an expanding HIV epidemic, with an estimated 1.5 million persons living with HIV and an additional 220,000 new infections in 2005. In Asia, approximately 8 million persons are living with HIV with the majority of these (over 5 million) living in India.¹

An estimated 1.2 million persons are currently living with HIV in the US (0.4% prevalence). One-quarter of these HIV-infected individuals are unaware of their HIV status.³ Women account for approximately 25% of the estimated 40,000 new infections that occur each year. Among the 75% of new cases in men, about two-thirds are in men who have sex with other men and 15% to 20% result from heterosexual contact. In both men and women, approximately 20% of new infections are due to intravenous drug use.⁴ Only a very small minority of incident infections are due to occupational exposures and transmission during blood transfusions or other medical procedures. The risk of HIV transmission from blood transfusions currently is less than 1 in 1 million.⁵

There are substantial racial disparities in US HIV infection rates. African-Americans, in particular, are disproportionately affected by HIV. African-Americans constitute approximately 12% of the US population, but account for half of all HIV cases. Rates of HIV infection are 124 per 100,000 among African-American men and 60 per 100,000 among African-American women. The corresponding rates for Caucasian men and women are 18 per 100,000 and 3 per 100,000, respectively.⁴

The use of 3 or more antiretroviral drugs in combination, known as highly active antiretroviral therapy (HAART), has dramatically changed the outlook for HIV-positive patients since 1996. In the US, the number of deaths among people with AIDS decreased by about 70% after the introduction of HAART, from a peak of approximately 51,000 deaths in 1995 to approximately 17,000 deaths each year from 2001 through 2005.^{5,7} Consequently, the number of people living with HIV and AIDS has increased steadily, from approximately 200,000 people in 1996 to approximately 434,000 in 2005.

Transmission and Prevention

HIV is transmitted by 4 bodily fluids: blood, semen, vaginal fluids, and breast milk. There are 3 major routes by which these fluids can transmit HIV from an infected person to an uninfected person. Parenteral exposure to blood containing HIV can occur in intravenous drug users sharing needles or in healthcare workers through needlestick injuries or “occupational exposures” (occupational transmission to healthcare workers is uncommon, however). Sexual contact can transmit HIV either by allowing the virus direct access to the bloodstream through traumatic tearing of the skin or mucosal tissues, or by infection of the macrophages that line the mucosal surfaces of the vagina or rectum. Vertical transmission of HIV (from mother to child) can occur through several routes, including exposure to blood or vaginal secretions during labor or by breastfeeding.

The likelihood of transmission from an infected person to an uninfected person depends on the quantity of virus in the associated fluid (eg, semen or vaginal fluids for sexual transmission, blood for parenteral transmission). Suppressing the virus through antiretroviral treatment therefore decreases the likelihood of transmission through sexual or injection-associated

behaviors. Similarly, antiretroviral therapy administered to pregnant women can decrease the likelihood of transmission to newborns. Practices for reducing vertical transmission also include intravenous antiretroviral therapy during labor, antiretroviral therapy for newborns, and the avoidance of breastfeeding (in developed countries).

Uninfected women are approximately twice as likely as men to acquire HIV during a single act of vaginal intercourse, and the receptive partner in anal intercourse is up to 40 times more vulnerable than the insertive partner. The presence of one or more sexually transmitted infections other than HIV (eg, gonorrhea, chlamydia, or syphilis) in either partner can increase the risk of transmission by a factor of 5 to 10 or more. Sharing drug injection equipment is especially risky because it provides a direct link between the blood supplies of an infected person and an uninfected person.

Because the main routes of HIV transmission are sexual and drug injection-related behaviors, behavioral modifications can significantly reduce an uninfected person's risk of acquiring HIV or an infected person's risk of transmitting the virus. Consistent condom use can greatly reduce the risk of sexual transmission. Limiting potential exposure to infected sex partners (for HIV-negative individuals) or to uninfected partners (for HIV-positive individuals) by decreasing the number of sex partners also reduces the risk of transmission. Some HIV-positive persons have sex only with other HIV-positive persons to eliminate any chance of infecting their partners, a practice termed "serosorting." HIV-negative individuals can eliminate risk by having sex only within a mutually monogamous relationship with an HIV-negative partner.

Injection drug users can reduce their risk of acquiring HIV by using sterile syringes that either have not previously been used by another person or, if already used, have been rinsed with bleach and water. Bleaching syringes is not always feasible in environments in which drug injecting behaviors occur, and is not nearly as effective at reducing HIV transmission risk as using unshared syringes. Research indicates that needle/syringe exchange programs, in which injection drug users are encouraged to exchange used syringes for unused ones, can substantially reduce transmission risk within networks of injection drug users.⁸

Case Study: Part 2

The nurse practitioner in the occupational health department assessed the extent of the nurse's injury and gathered information about the patient. After obtaining parental informed consent, a rapid HIV test was performed on the patient. The result of the test returned about 30 minutes later and indicated that he was positive for antibodies to HIV.

HIV Testing

HIV infection usually is diagnosed by testing for HIV antibodies. The initial test performed is an ELISA (enzyme-linked immunosorbent assay). Because ELISA tests are highly sensitive, a negative result at this step is considered definitive. The exception to this is patients who may have been infected with HIV less than 4 weeks prior to testing, but have not yet developed HIV antibodies. If this is clinically suspected, additional testing must be done to confirm true negativity. A positive result requires confirmation with a Western blot assay because other infections or autoimmune disorders can result in false-positive ELISA results. The Western blot assay tests for antibodies to individual, discrete HIV proteins and therefore is less prone to false-positive results caused by other conditions. A positive result on this test is considered a definitive indication of HIV infection.

Traditionally, both the ELISA and Western blot tests were performed in laboratory settings. More recently, rapid screening tests that use technology similar to ELISA tests have been developed for use outside clinical settings. These tests can provide results in 15 to 30 minutes,

using either whole blood or oral fluid samples. Rapid tests have sensitivity and specificity characteristics similar to laboratory-based ELISA tests. The portability of rapid HIV antibody tests allows HIV testing to be conducted in community-based settings, such as health fairs, bars, or churches. Moreover, because results are available quickly, those who are tested are more likely to receive their results.^{9,10,11} A negative test result is considered definitive, but a positive rapid test result must be confirmed with a laboratory-based Western blot test, as is the case with a positive standard ELISA test result.

In an effort to increase the number of people who are aware of their HIV status, the Centers for Disease Control and Prevention (CDC) issued updated guidelines for HIV screening in healthcare settings in 2006.¹² These guidelines recommend screening of all patients aged 13 to 64 years at least once for HIV, without regard to reported risk factors for HIV acquisition. The guidelines recommend screening in all medical settings, including emergency departments, urgent care clinics, and primary care clinics. The CDC encourages the use of an “opt-out” approach to testing. This means patients are advised that HIV testing will be performed unless they decline it. The CDC also recommends that HIV testing be considered part of a patient’s general consent for medical care. In particular, the CDC recommends against using a separate consent form specifically for HIV testing. However, it should be noted that law in many states still requires a separate consent form. In addition to routine, one-time screening for all patients in the 13- to 64-year-old group, the CDC recommends HIV testing of all pregnant women and, at minimum, annual testing of patients who are at high risk for HIV infection. The latter group includes intravenous drug users, commercial sex workers, and persons who have had more than one sexual partner since their last HIV test.

As discussed above, detectable HIV antibody levels do not appear until 4 to 6 weeks after infection. Consequently, HIV antibody tests, including ELISA and Western blot assays, may give false-negative results for very recently infected patients who are in the “window period” of infection. Early or acute HIV infection can be identified using nucleic acid amplification assays that directly test for the presence of viral RNA in the plasma. RNA tests are not commonly used diagnostically in clinical settings due to their high cost, but can be used by public health departments and in other situations in which batch testing (in which blood samples from many patients are pooled) is feasible.

Virology and Pathogenesis

HIV is a retrovirus, which means that each viral particle contains genetic material on 2 strands of RNA, as well as enzymes that are necessary for completion of the viral life cycle. Viral RNA must be reverse-transcribed into DNA to allow viral reproduction. Each HIV viral particle contains an enzyme called *reverse transcriptase* to facilitate this process.

HIV infection begins with binding of the virus to the CD4 protein present on some human T cells. HIV must also bind with another “coreceptor” on the cell surface to gain entry into the cell. Once inside the cell, the virus’ *reverse transcriptase* enzyme transcribes the viral RNA into DNA. Viral DNA then enters the cell nucleus and becomes integrated into the human DNA by way of the *integrase* enzyme.

Once viral DNA is integrated into the human host DNA, viral reproduction relies on the host’s cellular machinery to transcribe viral DNA into RNA, and to translate RNA into the proteins necessary for packaging and formation of new viral particles. The DNA strands are then spliced by the *protease* enzyme, which allows new viral particles to be packaged.¹³ Each of the 3 key enzymes mentioned here (reverse transcriptase, integrase, and protease) are targets for antiretroviral therapies.

Initially, the virus infects T cells or macrophages. These infected cells migrate to regional lymph tissues, affording newly formed viral particles access to other target cells. Within 4 to 10 days, viral particles are released into the bloodstream. A brief period of intense viral replication follows, with rapidly increasing levels of circulating virus (plasma viral load) and decreasing numbers of CD4+ T cells. This early stage of HIV viremia is often, but not always, accompanied by generalized symptoms such as fever, pharyngitis, arthralgias, anorexia, maculopapular rash, lymphadenopathy, and fatigue. This clinical syndrome, known as acute retroviral syndrome, occurs approximately 2 to 4 weeks following the exposure. Most symptoms resolve within 1 to 2 weeks. HIV antibodies become detectable at this stage of infection (ie, the patient “seroconverts”). As the immune system begins to mount a response, CD4 counts increase, and the plasma viral load decreases.

During the first few weeks of infection, viral load levels can increase to peak concentrations that are hundreds of times larger than the “set point” viral load level established after the patient has seroconverted. The relatively brief period between initial infection and seroconversion is often referred to as acute or primary infection. Due to the high viral load levels present during acute HIV infection, acutely infected persons may be much more likely to transmit HIV to their partners than are individuals in the chronic stage of infection.¹⁴

After the patient seroconverts, the viral load typically remains at the set-point level and CD4 cell counts remain stable and in the normal range for 5 to 10 years. During this time, individuals may have minimal or no symptoms of HIV. In time, however, the virus overwhelms the patient’s immune system, viral load levels increase, and CD4 cell counts begin to decrease. Once CD4 counts fall below 200 cells/mL, patients are at risk for developing opportunistic infections. *Pneumocystis jiroveci* pneumonia (also known as PCP) can develop as CD4 counts fall below 200 cells/mL, whereas infection with other pathogens, such as *Mycobacterium avium*, *Cryptococcus neoformans*, and cytomegalovirus usually occurs at much lower CD4 cell counts.

In addition to opportunistic infections, patients with HIV or AIDS are at higher risk for malignancies. Kaposi’s sarcoma, a vascular tissue neoplasm, was among the first illnesses to be associated with AIDS in the early 1980s, even prior to the discovery of HIV as the causative agent of AIDS. Kaposi’s sarcoma is approximately 200 times more common in AIDS patients than in the general population.^{15,16} Non-Hodgkin’s lymphoma, cervical cancer, and anal cancer (in both men and women) also occur much more commonly in HIV-positive than in HIV-negative persons.^{16,17}

HIV Treatment

After initial diagnosis, HIV-positive patients are usually referred to specialists in HIV treatment. Experts in HIV treatment can be family practitioners, internists, or infectious disease specialists. In addition to physicians, many nurse practitioners and physician assistants are experts in HIV treatment. The quality of care provided seems to correlate with the number of HIV-positive patients treated by a practitioner, not his or her specialty or profession.¹⁸

The first step in assessing a newly diagnosed patient is measuring the CD4 cell count. Normal values for CD4 cells vary by laboratory, but usually range from 500 to 200 cells/mL. The decision to begin antiretroviral therapy usually is based on a patient’s CD4 cell count. Antiretroviral medications generally are started if a patient’s CD4 count is less than 350 cells/mL. However, medications can be started at higher CD4 counts if a patient is having symptoms thought to be related to HIV viremia. Additional elements that are considered are the patient’s willingness to start medication and the state of other concurrent medical or psychosocial conditions.

More than 25 antiretroviral medications have been approved for HIV treatment. Only 4 medications were approved between 1987 and 1995, with the majority approved more recently. These drugs are classified by the enzyme or protein they target in the HIV life cycle. The mainstay of therapy consists of drugs from 3 classes of antiretroviral drugs: nucleoside *reverse transcriptase* inhibitors (NRTIs), nonnucleoside *reverse transcriptase* inhibitors (NNRTIs), and *protease* inhibitors (PIs). HAART usually consists of 3 drugs: 2 NRTIs and either 1 NNRTI or 1 PI. HAART gained acceptance as the standard of care for antiretroviral treatment in 1996 because it demonstrated potent and durable suppression of viral replication.

Three additional classes of antiretroviral medications have been developed, but currently are used for patients who have resistance to first-line drugs. Fusion inhibitors block the interaction of HIV surface proteins with the CD4 cell surface. CCR5 receptor antagonists block the human CCR5 protein from attachment by HIV. Finally, integrase inhibitors prevent the insertion of HIV DNA into the human DNA.

Advances in antiretroviral therapy have translated into less burdensome medication regimens with fewer side effects and less burdensome dosing schedules. The majority of treatment-naïve patients have the opportunity to take once-daily medication regimens, with a pill burden as low as 1 pill per day using multidrug combination formulations. Consequently, many antiretroviral medications with high rates of adverse effects and difficult dosing schedules have fallen out of favor.

Testing for resistance to HIV medications typically is performed in each patient prior to initiating antiretroviral therapy. Genotype tests identify genetic mutations in the viral genome that confer resistance to antiretroviral mutations. Approximately 10% to 18% of treatment-naïve patients have such resistance mutations, in most cases indicating that they were infected with an HIV strain already resistant to some medications.^{19,20,21} Resistance is one of many factors considered when selecting antiretroviral medications for initial therapy. Other factors to consider when constructing a medication regimen include interactions with other medications, other medical conditions, dosing schedules, and the side effects of each antiretroviral medication. (Table 1 lists some adverse effects associated with antiretroviral medications.) In addition, a patient's personal circumstances, such as work schedules, specific intolerances, and ability to pay for medications, need to be considered. In general, the potency of a candidate antiretroviral regimen must be balanced against its tolerability and feasibility for a particular patient, and consequently, his or her ability to adhere to the regimen. High levels of adherence are crucial to increase the likelihood of long-term viral suppression.^{22,23,24}

For patients taking antiretroviral drugs, routine clinic visits are necessary to monitor adherence, to identify and address adverse effects of antiretroviral medications, and to perform laboratory tests to evaluate virologic and immunologic responses to antiretroviral therapy. The 2 most important prognostic indicators are the patient's CD4 cell count and the level of viral RNA circulating in the blood (plasma viral load). The goal of treatment is to suppress the viral load below the level detectable by current laboratory assays. Although viral levels may be "undetectable" in the blood, HIV remains integrated within the DNA of several types of immune cells, including the long-lived memory T cells. If antiretroviral medications cease, HIV replication resumes and again becomes detectable in the bloodstream.

In most cases, CD4 counts increase once viremia is suppressed. Once antiretroviral therapy starts, it should continue indefinitely. One very large study randomized patients to continue antiretroviral medications indefinitely, or to discontinue and restart their medications based on their CD4 counts. Patients who interrupted their treatment had higher rates of death and both

HIV-related and non-HIV-related (cardiovascular, renal, and hepatic) serious adverse events.
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Opportunistic infections occur at relatively advanced levels of immune suppression, usually when CD4 cell counts fall below 200 cells/mL. Patients with evidence of advanced immune suppression should begin prophylaxis for opportunistic infections such as *Pneumocystis jiroveci* pneumonia, toxoplasmosis, and *Mycobacterium avium* infections. Prophylaxis is often the initial step in management of such patients, usually preceding the initiation of antiretroviral therapy.

Case Study: Part 3

Per hospital protocol, the ICU nurse was tested for HIV antibodies using a rapid HIV test. The test showed she was HIV negative. The occupational health nurse practitioner consulted with an infectious disease specialist who considered various factors, including the nature of the injury, the patient's HIV status, and the nurse's pregnancy, before recommending that she initiate antiretroviral postexposure prophylaxis. She took her first dose of antiretroviral medications within 4 hours of the needlestick exposure. She had significant nausea during the first few days of treatment. The nausea was relieved by prochlorperazine and improved over time. Confirmatory testing of the source patient revealed a positive Western blot assay for HIV and a high HIV viral load.

Occupational HIV Exposure and Postexposure Prophylaxis

Needlestick injuries in healthcare workers are a relatively common occurrence. An estimated 380,000 needlestick injuries occur in US hospitals each year.²⁶ Transmission of HIV to healthcare workers through occupational exposures is relatively rare, however. Fifty-seven cases of HIV seroconversion following occupational exposures among US healthcare workers were documented between 1981 and 2006. All of these cases occurred prior to 2001. Of the 57 documented cases, 24 occurred in nurses.²⁷

The probability of acquiring HIV through an occupational needlestick exposure is relatively small: approximately 0.3% for a single exposure to blood containing HIV.²⁸ In comparison, the per-exposure transmission rates for hepatitis C and hepatitis B are approximately 3% and 30%, respectively.^{29,30} Several factors are associated with an increased risk of HIV transmission. These include deep tissue injuries, injuries with a device containing visible blood, injuries with a device that was previously in an intravascular location in the source patient, and devices that were associated with a terminally ill patient.

Following a percutaneous or mucosal exposure to potentially infectious body fluids, such as blood, or other bodily fluids containing visible blood, antiretroviral medications can decrease the likelihood of HIV transmission. The use of antiretroviral medications in this context is called postexposure prophylaxis (PEP). The goal of PEP is to prevent the establishment of HIV infection in the exposed individual. There have not been any randomized controlled trials demonstrating the efficacy of PEP. However, a case-control study published in 1997 showed that among a group of healthcare workers exposed to HIV, those who became HIV positive were 80% less likely to have taken PEP than those who remained HIV negative.³¹

Complete guidelines for PEP are available from the CDC's website (see below); a brief summary is provided here. Consultation with an expert is generally recommended in the event of occupational exposures. Appropriate use of PEP requires assessing both the type of exposure and the status of the "source" patient. An exposure involving a deep percutaneous injury, a hollow needle, or a device removed from a patient's artery or vein or containing visible blood are considered to be more severe. Exposures involving a superficial injury or a solid needle

are considered less severe.³² Because HIV transmission can also occur from other types of blood exposure, there are also criteria for exposures involving the mucosal membranes or nonintact skin of the healthcare worker. Blood exposures to intact skin are not considered to be a risk for HIV infection, and PEP is not recommended in such situations.

The HIV status of the source patient is also considered when the use of PEP is being contemplated. The decision is easier when the source patient's HIV status is already known to be either HIV positive or HIV negative. The decision becomes more difficult when the source patient's status is unknown at the time of the exposure, or if the exposure occurs with a needle that cannot be associated with any specific patient. Nevertheless, any healthcare worker potentially exposed to HIV should be seen by the occupational health department at their place of employment or at an emergency department if the exposure occurs after hours. The National Clinicians' Post-Exposure Prophylaxis Hotline (PEpline: 1-888-448-4911) is available 24 hours per day to assist occupational health staff or emergency department staff with the management of occupational exposures. Additional factors may need to be considered if the source patient is known to have resistance to antiretroviral medications.

Prior to starting any medications, the healthcare worker should undergo HIV testing to ensure that he or she is HIV negative. If PEP is warranted, either 2 or 3 antiretroviral drugs will be recommended, based on a combination of the severity of the exposure and the status of the source patient. Antiretroviral drugs are taken for 28 days. Healthcare workers started on PEP should have close follow-up with an HIV expert to monitor for adverse drug reactions. HIV antibody testing should be performed at 6 weeks, 12 weeks, and 6 months after the exposure.

There has been growing interest in the use of PEP for nonoccupational exposures to HIV (nPEP), including unanticipated sexual exposures (either consensual or involving survivors of sexual assault) or injection-drug use exposures. No study has evaluated the efficacy of nPEP, but its use is based on prior studies of PEP in occupational settings.³³ The US Department of Health and Human Services has issued guidelines for administering nPEP, the use of which varies widely by location.^{33,34}

Case Study: Conclusion

The ICU nurse completed 28 days of antiretroviral therapy with close follow-up with the infectious disease specialist and her obstetrician. HIV antibody testing was performed at 6 weeks, 12 weeks, and 6 months and was negative. Her baby was born at full term and is HIV negative.

Conclusion

The field of HIV medicine is complex and rapidly evolving. Advancements in knowledge and the continued development of antiretroviral medications have substantially improved the health and survival of HIV-positive patients.³⁵ As the number of HIV-infected individuals continues to increase, both in the US and around the world, healthcare workers will encounter HIV-positive patients more frequently. While transmission of HIV to healthcare workers is unlikely and can be further reduced with the appropriate use of postexposure prophylaxis, an understanding of HIV transmission and pathogenesis is important for all healthcare workers. This knowledge may aid in decision-making in the event of an occupational exposure to HIV as well as allow a more complete understanding of the medical issues facing HIV-positive patients. In addition, such knowledge may provide a context in which to understand the evolving HIV epidemic, both in the US and throughout the world.

Resources for readers

National Clinicians' Postexposure Prophylaxis Hotline (PEpline): 1-888-448-4911 (1-888-HIV-4911):

A 24-hour hotline staffed by HIV clinicians who can provide consultation to healthcare professionals managing a case of potential HIV exposure.

Center for Disease Control and Prevention's Updated US Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis, available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5409a1.html.

HIV Insite Web site: www.hivinsite.com

A comprehensive guide to information on HIV/AIDS treatment, prevention and policy from the University of California, San Francisco.

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TABLE 1
Adverse Effects Associated With Antiretroviral Medications

Nausea/vomiting
Diarrhea
Hyperlipidemia
Anemia
Sedation
Insomnia
Skin nodules
Insulin resistance/diabetes
Coronary artery disease
Lactic acidosis
Peripheral neuropathy
Pancreatitis
Nephrolithiasis
Hepatic toxicity
Renal failure
Hypersensitivity reaction