Pediatric HIV Infection:
A Primer for Pharmacists

Current studies predict that by the year 2000, three million children worldwide will be HIV positive and two million children will have AIDS.

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Introduction

The number of children infected with the human immunodeficiency virus (HIV) has increased dramatically over the past decade. Acquired immunodeficiency syndrome (AIDS) is currently the seventh leading cause of death for children 1 to 4 years of age. This article reviews current information on the epidemiology, transmission, clinical manifestations, and drug therapy of pediatric HIV infection. Practical guidelines and an action plan for delivery of patient care by the pharmacist are also featured.

In the early 1980s, when the first cases of AIDS were identified, the illness appeared primarily to affect adult homosexual males and intravenous drug users. Although a few cases in children were reported as early as 1982, most pediatricians did not recognize the disease as a unique immunodeficiency syndrome. Discovery of the human immunodeficiency virus type 1 (HIV-1), widespread use of antibody-based diagnostic tests, and epidemiologic studies all helped to define the true scope of the problem. Current studies estimate that by 2000, more than 15 million women worldwide will be infected with the HIV-1 virus. In addition, 3 million children will be HIV positive, and 2 million children will have AIDS. In the United States, about 7,000 infants are born to HIV-infected mothers each year, and 1,000 of these infants are HIV positive. Approximately 514,000 cases of AIDS have been reported to the Centers for Disease Control and Prevention (CDC) through December 1995; 72,000 cases are in women. When categorized by race and ethnicity, the largest number of cases has been reported in African American women, followed by white and Hispanic women. More than 80% of these women are of childbearing age. The approximately 6,300 pediatric cases reported to CDC show a similar distribution for race and ethnicity.

The social, psychological, and economic effects of the pandemic are staggering. In the United States, an estimated 24,600 children and 21,000 adolescents had been orphaned as a result of the HIV epidemic in women by the end of 1995. Most of these youth come from poorer communities, and up to 36% may be infected with HIV. In a study published in the *Journal of the American Medical Association* in 1993, medical care for a single adult patient infected with HIV was estimated to be $119,000 from the time of diagnosis until death. This amount only includes health care for the patient and does not estimate the total economic impact on the family unit.

This article focuses on the epidemiology, natural history, and treatment of HIV infection in children—and the role of the pharmacist—as they relate to the delivery of care to this population.

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**Summary**

- Children generally acquire HIV through transmission from an HIV-infected mother, transfusion of infected blood or blood products, or participation in high-risk behaviors.
- Two types of laboratory tests used to detect HIV (serologic enzyme immunoassay—EIA) and monitor therapy (viral load) have substantially changed HIV therapy.
- From birth through adulthood, pharmacokinetic and pharmacodynamic parameters change, altering expected outcomes of drug regimens.
- Goals of drug therapy for HIV in children include the prevention of perinatal transmission, treatment of HIV and opportunistic infections, prevention of drug-related complications, and education.
Epidemiology of HIV Transmission

Children generally acquire HIV in one of three ways: transfusion of infected blood and blood products, transmission from an HIV-infected mother to a fetus or an infant, or participation in high-risk behaviors during adolescence (e.g., sexual contact, intravenous drug use). The probability of HIV infection through each mode of transmission is related to the amount of active virus present in the infecting fluid. Transfusions of HIV-infected blood have the highest probability of viral transmission (90%). The maternal-fetal transmission rate, 20% to 40% worldwide, is lower because of multiple factors that decrease the risk of infection for the fetus. The probability of HIV infection after a single sexual encounter is estimated to be 0.01% to 1.0%, and repeated sexual encounters increase the risk of infection.1

Mother-Infant Transmission

More than 90% of pediatric AIDS cases reported to CDC were perinatally acquired.3 The estimated rate of mother-to-infant transmission is 20% to 30% in the United States.6 This number may decline as therapy with antiviral agents becomes more widely available.

The virus may be transmitted from mother to child in several ways during pregnancy, birth, or breast-feeding. The incidence of mother-to-infant transmission is suspected to be highest during delivery, when infants come into contact with the cervix. Increased incidence of trauma to the genital tract during normal labor and a vaginal delivery may result in contact with HIV-infected blood, body fluids, or vaginal secretions of the mother, increasing the risk of subsequent infection of the infant.

Post-natally, the virus is transmitted during breast-feeding. HIV and HIV genetic material have been detected in the breast milk of infected mothers. The incidence of HIV transmission during breast-feeding is difficult to estimate because HIV infection may not be detected in some women until after the perinatal period. In the United States, formula feeding is recommended for children born to HIV-infected mothers.6

The timing of transmission can be confirmed by the presence of HIV in the infant's blood at birth. If the infant is infected in utero, HIV will be detected within 48 hours of birth in the peripheral blood or lymphocytes. About 50% to 70% of children infected with HIV do not have detectable viral levels at birth.7 These children, infected during the intrapartum period, may have a period of primary HIV infection, as in the adult. HIV will be detectable in the blood within several weeks, and the antibody will be detectable within several months.7,8

Several studies, using newer immunologic methods for quantifying viral load, have provided dramatic new evidence to describe factors prognostic of perinatal transmission.9,11 Maternal viral load at the time of gestation and delivery may be the major determinant. Two recent studies demonstrated that women with lower viral loads were less likely to transmit HIV to the infant.11

Other factors also influence perinatal transmission. These include immunological status, illicit drug use, viral phenotype, rupture of membranes, and gestational age at the time of transmission. Protective maternal antibodies are transferred late in gestation, and the rate of viral transmission has been shown to decrease with increasing gestational age. Women with multiple risk factors are more likely to deliver before 34 weeks' gestation.6,12,15

Transfusion

The number of children infected with HIV as a result of receiving an HIV-infected transfusion or blood product is significantly smaller than the number of children infected perinatally. Of the 593 cases of transfusion-related HIV reported to the Food and Drug Administration (FDA), the majority acquired the infection before 1985, when screening procedures were instituted in the United States to test for the presence of HIV-1 in the blood. In June 1992, an additional test was added to screen for the presence of HIV-2.5 Even with both tests, it was estimated that one in 450,000 to one in 660,000 blood donations per year are contaminated with HIV. In August 1995, FDA recommended the addition of an HIV-1 p24 antigen test to the screening regimen. This test identifies HIV in blood donated during the "window" period after HIV infection, before the detection of antibodies to HIV-1 in the blood. The addition of this test should decrease the incidence of HIV-infected transfusions by half.16

High-Risk Behaviors

Adolescents are at greater risk than children for acquiring HIV infection as a result of engaging in high-risk behaviors.3 In 1993, a national survey of adolescents in grades 9 to 12 reported that 50.2% of females and 55.6% of males had had sexual intercourse at least once; 53% of both sexes reported being currently sexually active. By age 17, 66.3% of females and 70.2% of males reported being sexually active.17,18 These numbers are higher for African American males (89.2%), African American females (70.4%), and Hispanic males (63.5%). In the population studied, 15% of the females and 22.3% of the males had four or more sexual partners, and only 46% of the females and 59% of the males used a condom during their last sexual encounter.18

As with adults, adolescents' use of alcohol and other drugs may increase the risk of acquiring a sexually transmitted disease.3,17 In the survey of adolescents in grades 9 to 12, 48% had had at least one alcoholic drink in the 30 days before the study, and 30% had had five or more drinks, one or more
times during the 30 days before the study. In the same population, 32.8% have smoked marijuana, and 17.7% smoke marijuana currently. Fewer than 5% of the adolescents had experienced sexual encounters and increase the risk of exposure to HIV.\textsuperscript{17,18} HIV acquired during the adolescent years is not detected until later because of the median incubation period of 10 years. This is reflected in the increased incidence of HIV-positive adults aged 20 to 29 years.\textsuperscript{17,18}

### Detection of HIV Infection

Early detection of HIV infection before the clinical manifestation of the disease enables health care professionals to implement antiviral and prophylactic therapies. New methods of viral detection and monitoring have substantially changed HIV therapeutic strategies. Two types of laboratory tests are currently used, one for initial viral detection in the general population and the other for quantifying the viral load to study the pathogenesis of the disease and the patient's response to therapeutic interventions. This section describes the advantages, limitations, and application to clinical practice of each methodology.

### Methods for Initial Detection of HIV

Because the number of cases of HIV infection in women and children is increasing and 90% of the children are perinatally infected, current guidelines target prevention, early detection, and intervention in this population.\textsuperscript{19,20} Laboratory methods used for screening must be rapid, sensitive, specific for HIV, easily reproducible in large volumes, and cost effective. Unlike the laboratory methods used in research, these methods are subjected to rigorous review process and must be licensed by FDA prior to their inclusion in a screening algorithm.\textsuperscript{16}

HIV is detected in adults and children older than 18 months with a serologic enzyme immunoassay (EIA).\textsuperscript{16,19-21} The assay detects the HIV antibody. Even though the currently licensed tests are highly sensitive and specific (greater than 98%), false positive and false negative tests can occur. The assay fails to detect virus in newly infected individuals because levels of the HIV antibody remain undetectable for up to two months in some patients. Positive results are confirmed by using a second test, either a Western blot or immunofluorescence assay (IFA). The Western blot, an electrophoretic method, documents the presence of HIV by direct identification of specific antibody proteins produced to the nucleus, core, or envelope of the virus. This test is costly, labor intensive, and subject to interpretation. Moreover, results of the test may be indeterminate. When combined with a positive EIA, however, the accuracy of the testing approaches 100%. Unlike the Western blot, IFA is a highly sensitive and specific test for HIV antibody and is therefore less likely to yield indeterminate results.\textsuperscript{16,19,21}

In children younger than 18 months, detection of HIV with serologic methods is complicated by the presence of transplacentally acquired anti-HIV maternal antibodies, insufficient viral load in peripheral blood mononuclear cells, and the inability of the immature immune system to produce anti-HIV antibodies. Therefore, virologic tests are needed to diagnose HIV infection in the perinatal period. The polymerase chain reaction (PCR) technique detects HIV-specific genetic material by amplifying small amounts of viral-specific DNA, which can then be identified. This method requires only the presence of HIV genetic material and not intact virus. PCR is highly specific for HIV and can be used to confirm HIV infection within the first few weeks of life, but the sensitivity varies with the age of the infant. The p24 antigen test is an alternative method but is less specific than PCR.\textsuperscript{19,20}

Current CDC recommendations for children younger than 18 months suggest that children born to high-risk mothers should be tested for HIV infection at birth using HIV culture, PCR, or the p24 antigen test. Results of a positive virologic test should be confirmed by repeating the initial test or performing another virologic test. If the original test is negative, the test should be repeated once between 3 and 6 months of age to avoid missing possible HIV infection. Children younger than 18 months tested for infection using a nonvirologic method, EIA, and the confirmatory Western blot should be tested every 3 months for the first year, then at 18 and 24 months. In children older than 18 months, EIA with a confirmatory test, Western blot, or IFA is adequate to detect HIV infection.\textsuperscript{19,20,22}

Results of HIV laboratory tests are used to classify the child's infection status using the CDC classification system.\textsuperscript{20} Children with detectable HIV, as described by the above methods, are classified as HIV-infected. Children born to HIV-infected mothers are classified as perinatally exposed if the infection status of the child is unknown or determined only by EIA at earlier than 18 months. The term seroreverter is used to describe children born to an HIV-infected mother who have a positive EIA test at birth, but with subsequent negative HIV tests and no clinical evidence of HIV-infection at 24 months.\textsuperscript{20}

### Viral Dynamics of HIV

The development of new quantitative molecular techniques are providing the tools for researchers to study the dynamics of HIV and disease pathogenesis in greater detail. These results are changing both the theoretical and clinical
approach to the treatment of HIV-infected patients.\textsuperscript{23,24} HIV distributes throughout the body and attaches to cells with a CD4 receptor and to lymphoid tissue. It is now believed that when the virus is attached to the receptor of cell, a cofactor is needed for the virus to become incorporated into the cell and begin replication.\textsuperscript{23,25} Viral replication is rapid during the initial stage of primary infection, and 100 to 10,000 HIV-RNA copies per milliliter can be detected. At this time, an estimated several billion virions and CD4 cells are produced and destroyed each day. As each new viron is released, it is capable of attaching to a new target cell and producing new virions within three days. The average half-life of a particle of HIV in the blood is approximately two days.\textsuperscript{26} At this stage, the host immune system begins producing antibodies, but antibody levels as measured by ELA are very low or not detectable. In the past, HIV could not be routinely detected in blood donated during this "window period." A newer assay for p24 antigen has now been added to the FDA algorithm for screening blood.\textsuperscript{16}

The response initiated by the host immune system is in the form of cytotoxic T cells and antibodies.\textsuperscript{27} HIV levels in the blood decline in response to the immune cells. In this period of clinical latency, viral replication occurs in the lymphoid tissue but not the peripheral blood. Viremia and p24 antigenemia may be undetectable in the peripheral blood at this time, and the number of CD4 cells is normal. This rate of viral replication, usually between $1 \times 10^2$ and $1 \times 10^6$ HIV-RNA copies per milliliter of plasma, remains relatively stable over years in the asymptomatic patient. The factors that determine this "set point" of viral replication in the individual patient remain unknown.\textsuperscript{20,28} The rate of viral replication is a more sensitive and consistent surrogate marker than the number of CD4 cells for determining the rate of disease progression. In adults, high levels of plasma viremia, greater than 50,000 to 100,000 HIV-RNA copies per milliliter, have been demonstrated to correlate with the highest risk of rapid disease progression.

A course of rapid HIV progression is marked by an end to the asymptomatic period with a declining number of CD4 cells followed by the development of symptoms of clinical AIDS and opportunistic diseases. However, about 5% of HIV-infected adults show no evidence of disease progression. These longterm nonprogressors have lower levels of HIV in the peripheral blood and lymph nodes as well as intact cell-mediated and humoral immune response. Research continues on the immunopathogenesis of HIV in adults and children.\textsuperscript{25,29}

**HIV Progression and Clinical Manifestations**

Numerous studies in different countries have documented that the clinical progression to AIDS in perinatally infected children follows a bimodal pattern.\textsuperscript{8,13,20-33} During the first year of life, in 15% to 20% of children infected with HIV at birth the disease follows a rapidly progressive course that includes the development of encephalopathy and multiple serious AIDS-related infections. The median survival time ranges from 6.5 to 38 months in this population.\textsuperscript{14,40} The remainder, 80% to 85%, follow the slow course of disease progression seen in adults. Symptoms generally develop after the first year of life, and the median survival time in this group is 96.8 months.\textsuperscript{40}

The reason for this bimodal disease course is unknown, but current theories suggest that it relates to the timing of the infection in relation to the development of the child or the viral load of the mother at the time of perinatal transmission. The effect of HIV on the fetus during development is unknown. Children infected with HIV during pregnancy are more likely to have higher detectable viral loads at birth.\textsuperscript{7} Children infected during or after delivery will not have detectable virus or antibody in the blood for weeks or months after birth. Other factors that influence progression may include the pathogenicity of the virus and the susceptibility of the host to infection, but these factors remain to be identified.\textsuperscript{30,32-34}

Different clinical manifestations are associated with each disease course. As with adults, a rapidly progressive disease course in children is more frequently associated with severe clinical manifestations. In children these include growth failure, encephalopathy, hepatitis, cardiomyopathy, persistent oral candidiasis, and AIDS-related opportunistic infections. Children are more likely than adults to have manifestations of central nervous system (CNS) disease.\textsuperscript{8} These manifestations are present in HIV-infected adults with severe immunosuppression.

Less severe clinical manifestations, such as hepatomegaly, splenomegaly, diffuse lymphadenopathy, parotitis, skin diseases, and recurrent respiratory infections, are more frequently associated with slow disease progression.\textsuperscript{31} Survival after infection is related to the number and severity of HIV-related opportunistic infections. This research forms the basis for the revised CDC classification system for children and identifies which children should be targeted for therapeutic interventions.

**CDC Classification System**

The CDC has revised and simplified the criteria published in 1987 to classify the severity of HIV infection in children under the age of 13 years. After infection status is determined, children are further classified based on immunologic and clinical status.\textsuperscript{20} Immunologic status in children is defined by the degree of immunosuppression as determined by the age-related CD4 lymphocyte count. Clinical status is defined by the specific AIDS-related infections. As with adults, HIV-infected children with severe immunosuppression and an AIDS-defining illness (Table 1, category C) are classified as having AIDS and are at a significantly increased risk of morbidity and mortality.\textsuperscript{20}
Drug Therapy

The goals of drug therapy in the pediatric population include the prevention of perinatal transmission, treatment of HIV and opportunistic infections, prevention of drug-related complications, and education of the family on the disease and how to care for the patient. Treatment options for pediatric patients have increased over the past several years. In a new initiative, FDA has recommended the inclusion of children and adolescents earlier in the drug evaluation process. This is critical in life-threatening disease states, such as AIDS and cancer, where new agents are improving adult therapy.

Antiretroviral Therapy

Prevention of Perinatal Transmission

Drug therapy to decrease the risk of perinatal transmission is limited. In 1994, interim results were announced for AIDS Clinical Trials Group (ACTG) 076. The study evaluated the efficacy and safety of zidovudine (ZDV—Retrovir) in pregnant women (14 to 34 weeks pregnant) with CD4 lymphocyte counts greater than 200/μm³ and without prior antiretroviral therapy. In a total of 365 women (180 ZDV, 183 placebo) the rate of maternal-fetal transmission was 25.5% for the placebo group and 8.3% for the ZDV group (p = .00006), corresponding to a relative reduction in transmission of 67.5%. No significant differences in adverse effects were seen between the two groups.

During ACTG 076, no teratogenic effects were attributed to the drug. ZDV administration did not affect the size, weight, or gestational age of the infant, but caused a mild reversible anemia in some of the infants at birth. Adverse effects in women resembled those documented in other adult studies.

Unfortunately, the study population was limited to ZDV-naive women with CD4 > 200 x 10⁹/L. Administration of ZDV did not stop viral transmission in all women. Additional analysis of the data suggests that women with HIV-RNA levels greater than 50,000 infectious units per milliliter at the time of delivery were more likely to transmit the virus whether or not they received ZDV therapy.

ZDV is currently the standard of care to minimize perinatal transmission. Additional research is needed to provide guidance for women with prior antiviral therapy, HIV infection with ZDV-resistant organisms, or those with documented AIDS (CD4 < .200 x 10⁹/L). The long-term safety of this regimen in children has not been evaluated.

The recommended regimen for women during pregnancy is ZDV 100 mg, five times daily by mouth, initiated at 14 to 34 weeks of gestation and continued until the initiation of labor. During labor, ZDV is given intravenously, in a one-hour loading dose of 2 mg/kg followed by a continuous infusion of 1 mg/kg/hour until delivery. This is followed by oral administration of ZDV syrup to the infant, 2 mg/kg per dose every six hours, for the first six weeks of life beginning at 8 to 12 hours after birth. This is administered regardless of the antiviral therapy status of the mother. No data are available to support drug therapy started later; this is being studied.

The estimated economic and social impact of early detection and treatment of HIV in mothers is substantial. Based on the data from ACTG 076, it is estimated that for every 100 HIV-positive pregnant women who are treated with ZDV, there will be a net savings of $1,596,831 to the health care system. This estimate is based on the current maternal transmission rate and the cost of lifetime treatment of children who are HIV positive.
The ultimate decision to initiate therapy and reduce the rate of perinatal transmission rests in the hands of the pregnant woman. Two studies from different parts of the country, North Carolina and New York, demonstrate the impact of patients’ decisions on the ultimate reduction of maternal HIV transmission.32,39 In North Carolina, the proportion of children born to HIV-infected mothers identified and tested increased from 60% in 1993 to more than 90% in the last quarter of 1994. In 1994, 152 children were born to HIV-infected mothers. During this time, 75% of HIV-infected women and their children received part or all of the recommended ZDV regimen. Only 5.7% of the children receiving any ZDV therapy became HIV infected.38 The decline in perinatal transmission to below the rate seen in ACTG 076 was based on perinatal screening and the adherence of the mother to ZDV therapy.

In contrast, a multidisciplinary clinic in the Bronx, N.Y., reported a minimal decline in the perinatal transmission rate from an estimated 25% to 22%, in patients receiving ZDV therapy.39 During the study period of about 17 months, 125 HIV-infected women delivered infants at the hospital. Of these, only 49 were identified as being HIV infected before delivery, 37 (75%) of whom consented to receive prenatal therapy with ZDV. At the time of delivery, only 24 women and their children received all of the components of ZDV therapy, despite an aggressive, multidisciplinary HIV counseling, testing, and treatment program. Women with a history of intravenous drug use, including drug use during pregnancy, were more likely to refuse therapy or to demonstrate poor adherence to medication regimens. In addition, conflicting data in the media on the efficacy and toxicity of ZDV contributed to the patient’s perception that the drug was still experimental or ineffective.39 This situation was further complicated by the legal right of the father to prohibit perinatal therapy even if the mother gives consent.

The results of ACTG 076 have stimulated additional research on ways to decrease perinatal transmission. These studies are evaluating both single drug and combination regimens, including antiviral and immune-based therapies currently approved for therapy in patients with HIV. Agents under study include didanosine or ddl (Videx), lamivudine or 3TC (Epivir), and anti-HIV immunoglobulin (HIVIG).

**Antiretroviral Therapy Guidelines**

The proper time to initiate antiretroviral therapy remains controversial. The benefits of early initiation must be balanced with the risk of the development of resistance.

Currently, only ZDV, didanosine, and lamivudine are approved by FDA for use in children, although many other treatment options are nearing approval. Antiviral therapy is recommended for children with HIV infection and evidence of significant immunosuppression or HIV-associated symptoms. Antiretroviral therapy is not recommended for asymptomatic HIV-infected children with normal immune status as defined by the age-specific CD4 cell count.30,41 These recommendations, published in 1994, will be revised to include new agents and methods for viral load monitoring as they are approved for use in children.

**Zidovudine (Retrovir)**

ZDV was approved by FDA for therapy in children in 1990. Pharmacokinetic parameters of ZDV in children are similar to those in adults.43,44 ZDV is well absorbed (bioavailability 65%) with a short plasma half-life (one hour) requiring multiple daily doses. When compared with the other similar nucleosides, concentrations of ZDV in the central nervous system are higher, and increased clinical efficacy has been demonstrated in the treatment of neurologic complications in HIV-infected children.
children. In newborns less than 2 weeks old, ZDV has a longer half-life, decreased glucuronide conjugation, increased bioavailability, and decreased clearance as compared with older children, necessitating lower doses.41

Antiviral effects of ZDV in children are similar to those seen in adults. Additional benefits in children include improved physical activity level, weight gain, increased rate of growth, and improved neurocognitive function.41 The effects of the drug on long-term survival in symptomatic children are not known. Trials are planned to evaluate the effects of early antiviral intervention on the rate of disease progression in asymptomatic children.41

Viral resistance to ZDV monotherapy is a growing problem in all patients with HIV. High-level ZDV resistance during monotherapy correlates with progression of HIV disease and death.43 ZDV-resistant strains of HIV have been documented in children after ZDV monotherapy.46,47 In addition, children perinatally infected with HIV may receive resistant viral strains from their mother.41 Antiviral therapy should be closely monitored for HIV resistance.

Adverse Effects

The primary toxicities of ZDV, seen in 20% to 40% of children, include anemia, neutropenia, and thrombocytopenia.43,44 In children with anemia, ZDV doses are reduced by 50% when the hemoglobin is less than 8.0 g/dL. If anemia continues on reduced dosages and transfusions are required, erythropoietin is administered to maintain the hemoglobin at 8.0 g/dL. When erythropoietin therapy fails, alternative antiviral agents are used.46 Neutropenia is another frequent adverse effect. An absolute neutrophil count of less than 500 cells/μL indicates that ZDV therapy should be temporarily discontinued or modified. Granulocyte colony stimulating factor (G-CSF), filgrastim, can be administered in some patients to increase the neutrophil count. Other, less severe adverse effects of ZDV include nausea, vomiting, headache, myositis, thrombocytopenia, and liver dysfunction.43,44

Dosage and Administration

Antiretroviral therapy is currently initiated with ZDV monotherapy at the recommended doses shown in Table 2. ZDV doses are higher in children to improve neurologic function.41 Studies of lower ZDV doses (90mg/m2) in asymptomatic or mildly symptomatic HIV-infected children are currently ongoing.46,47 Published guidelines currently recommend administering ZDV every six hours in children until longer intervals are evaluated for efficacy. ZDV is available as a capsule (100 mg), syrup (50 mg/5 mL, strawberry flavored) and injection (10 mg/mL).48,49

Drug Interactions

Concomitant administration of ZDV with other medications can alter ZDV absorption or elimination and cause changes in ZDV efficacy or toxicity.48,49 Significant interactions are listed in

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* From package literature.

ZDV = Zidovudine

Source: References 32,33

Table 3. In many situations, the drugs listed in the table can be combined with ZDV when dosages are reduced or laboratory data are monitored.

Didanosine (Videx)

Didanosine (ddI) is approved for use in children who are intolerant to ZDV. Didanosine is degraded by stomach acid and must be administered with antacids or buffering agents. In an early Phase I/II study in children, ddI absorption was variable and dose-dependent (mean bioavailability 19%) with a short plasma half-life (one hour). In addition, the concentration of ddI in the CNS was low. Agents with lower CNS concentrations are less effective in treating neurologic symptoms in children.40,41

In clinical studies evaluating ddI in symptomatic HIV-infected children intolerant to ZDV for short- (24 weeks) and long-term (median 22.6 months) therapy, ddI improved immunologic and neurologic function.32-34 ddI appears to be safe and effective for monotherapy in children without neurologic symptoms. The results of ACTG 152 suggest that for initial therapy, ZDV alone may be less effective than ddI alone or in combination with ZDV in children. Caution should be used in interpreting the data until the final analysis is published.

Adverse Effects

Adverse effects of ddI are seen in fewer than 7% of children, and include pancreatitis, peripheral neuropathy, and
retinal depigmentation. Adverse effects are more frequent with doses less than 270 mg/m²/day.11,12 Symptoms of pancreatitis include severe abdominal pain, nausea, and vomiting. Therapy with ddI should be discontinued until serum amylase and lipase are measured to exclude pancreatitis. Manifestations of peripheral neuropathy in children include tingling or numbness in the feet and hands or changes in gait or behavior. Caregivers should monitor children carefully for subtle changes. Retinal depigmentation, a toxicity unique to ddI, can result in the loss of eyesight, so children should be monitored by an ophthalmologist every six months.41,51,53 Minor adverse effects include gastrointestinal symptoms, including diarrhea, from the antacid used with the pediatric powder.

Dosage and Administration

The recommended dose and dosing intervals for ddI in children have not been established. Dosages in recent studies range from 60 to 540 mg/m² divided into two to three doses daily.55 The manufacturer recommends an average initial dose of 200 mg/m² (powder) administered in two doses daily, which can be adjusted to improve efficacy or decrease toxicity. The drug is available in a chewable, dispersible tablet (25, 50, 100, 150 mg) or a pediatric powder for oral administration. Each 100 mg tablet is equal to 125 mg of powder. To ensure an adequate amount of buffer, each dose should contain two tablets, which can be chewed or dissolved in water and administered.39 The pediatric powder (2 or 4 grams) is reconstituted with water (100 or 200 mL, respectively) then mixed with an equal amount of Mylanta Double Strength, Extra Strength Maalox Plus Suspension, or Maxalox TC Suspension to a final concentration of 10 mg/mL. The final mixture is stable for 30 days refrigerated.55

Drug Interactions

The buffering agent in ddI decreases the absorption of medications that require an acid environment for absorption (e.g., ketoconazole, dapsone). ddI should be administered at least two hours later. Coadministration of tetracycline or fluoroquinolones with ddI also decreases the absorption of the antibiotic, although this is not a significant problem because these agents are infrequently used in children. In addition, ddI absorption can be decreased by taking the medication with a high-fat breakfast. Children should be monitored for the signs and symptoms of pancreatitis when pentamidine or dapsone is added to ddI therapy.55

Zalcitabine (HIVID)

Zalcitabine (ddC), a potent antiviral agent evaluated in children, has a short plasma half-life (0.8 hours) and good bioavailability (54%), but poor penetration into the CNS. Monoantiviral therapy with ddC was ineffective in preventing neurologic deterioration in children.41 The course of therapy was limited by the development of mouth sores, rashes, and peripheral neuropathy. In another study, ddC was alternated with ZDV to limit the adverse effects of ddC. Some improvement in neurodevelopmental function was seen but was less than previously observed in children receiving ZDV alone. More data are needed to determine the role of ddC therapy in pediatric treatment regimens.41,56

Lamivudine (Epivir)

Lamivudine (3TC) was approved in November 1995 for use in combination with ZDV in HIV-infected adults and children. This drug is one of the first agents approved for both populations simultaneously under the new FDA guidelines. Currently, no data exist on the use of lamivudine in combination with ZDV in pediatric patients. Lamivudine has a lower bioavailability in children (66%) than in adults (86%). Clearance of lamivudine decreases with increasing age, and mean area under the curve (AUC) values are comparable after the administration of 8 mg/kg/day in children and 4 mg/kg/day in adults. The mechanism for these effects is unknown.57

Other Antiviral Agents

Stavudine (Zerit, D4T), approved in June 1994 for adults, is currently under study in children. In contrast to the other agents, stavudine has good bioavailability and penetrates the CNS, although doses are limited by peripheral neuropathy.41 Nevirpine (Viramune, BI 587) is a nonnucleoside reverse transcriptase inhibitor, recently approved for therapy in adults, which is related to the benzodiazepines and has minimum toxicity. Monoantiviral therapy with nevirpine resulted in resistant HIV within four to six weeks in adults.41 ACTG 180 and 245 are evaluating nevirpine in combination with ZDV or ddI. Results will be available when these and other trials evaluating combination therapies are completed.

Protease Inhibitors

The protease inhibitors are a novel group of antiretroviral agents recently approved for therapy in adults.58,59 These agents inhibit viral replication by blocking the HIV enzyme, protease, or proteasome. This enzyme is responsible for the post-translational cleavage of the gag and gagpol protein precursors into the final protein products. Without this enzyme, noninfectious virions are produced. Unlike the reverse transcriptase inhibitors, these agents are active in chronically infected cells such as monocytes or macrophages. Protease inhibitors are used in combination with other antiviral agents to increase efficacy and decrease the development of resistance or reduced sensitivity in vivo. For the first time, it is theorized that HIV therapy combining protease inhibitors with other agents could be designed to reduce the viral load below the detectable level and dramatically improve patient outcomes.

Three protease inhibitors are currently approved for HIV
therapy in adults: saquinavir (Invirase), ritonavir (Norvir), and indinavir (Crixivan). Each agent is different in potency, safety, tolerability, and patterns of HIV resistance. Saquinavir was the first protease inhibitor approved, but its efficacy may be limited because of the poor bioavailability of the current formulation.8600 Studies revealed minimal adverse effects, although this may be related to the limited bioavailability. Indinavir has been demonstrated to be a potent inhibitor of HIV and effective when combined with ZDV and lamivudine. Significant adverse effects include nephrolithiasis and hyperbilirubinemia in 3% to 4% of patients. Ritonavir, comparable to indinavir in potency, has a higher incidence of gastrointestinal and CNS effects and is a potent inhibitor of hepatic cytochrome P450 enzymes. Ritonavir has a high affinity for multiple cytochrome P450 isoforms, including CYP3A, CYP2D6, CYP2C9, and others.60 The clinical significance of these interactions is unknown.

Because of FDA’s accelerated approval process, limited published information, in the form of studies and meeting abstracts, is available. At this time, for the protease inhibitors, the package insert provides the most accurate information for these drugs. When these agents are approved for therapy in children, each patient’s drug regimen will need to be carefully reviewed.

Monitoring Antiretroviral Regimens

Monitoring of antiviral therapy in children is essential and can be complicated by the concurrent use of other medications and the presence of disease states with similar signs and symptoms. The work group from the National Pediatric HIV Resource Center has recommended a monitoring schedule. Initially, physical exams and laboratory tests are recommended every two weeks for the first month, then monthly. Laboratory monitoring should include a complete blood count at each visit. Electrolytes, renal function, liver function, immunologic status, CD4 lymphocyte count, and p24 antigen are assessed four times yearly. Additional clinical evaluations are repeated every three months and include measures of growth, neurologic function, and neurodevelopmental evaluations (cognitive and neurologic).60 As the new methods of viral load monitoring are integrated into routine patient management, plasma HIV-RNA levels should be measured initially, three to four weeks after an antiviral regimen is changed, and then every three to six months as with lymphocytes. Viral load monitoring can provide valuable information on disease progression and the efficacy of direct antiviral therapy before significant immune system destruction.60

As the CD4 lymphocyte count declines, children are at risk of developing opportunistic infections. Assessment of antiviral therapy also includes monitoring for new infectious complications. Pharmacists should obtain sufficient data from primary health care providers, parents, and caregivers to properly evaluate the child’s drug therapy. The pharmacist must be able to work with the parent or caregiver to detect new infections, differentiate the symptoms from drug effects, and make referrals to an appropriate health care provider.29,21,11

Supportive Therapy

Vaccines

HIV-infected children should receive routine childhood immunizations42,61 as outlined in Table 4. Immune responsiveness to vaccines in this population varies based on the degree of immunodeficiency at the time of vaccination. Theoretical concerns include the lack of immune response and vaccine-mediated stimulation of HIV-containing lymphocytes and macrophages.52 However, these concerns are outweighed by the need to limit preventable childhood diseases in HIV-infected children. All vaccines are inactivated, except measles, mumps, and rubella (MMR), which is a live attenuated combination vaccine. MMR can be used safely in children with symptomatic HIV infection. Inactivated polio virus vaccines should be given to HIV-infected children and all household contacts to prevent transmission of live polio virus to the immunocompromised patient. The live attenuated varicella vaccine is not recommended for HIV-infected or immunocompromised children. In children with no prior history of varicella infection, varicella immunoglobulin provides protection when administered within 96 hours after exposure.51,64

Intravenous Immunoglobulin

Intravenous immunoglobulin (IVIG) is used in children for passive immunoprophylaxis after exposure to bacterial infections or on a routine schedule as pre-exposure prophylaxis.65 IVIG is recommended for children with evidence of humoral immune defects (hypogammaglobulinemia or poor immune response to antigens) and is administered as 400 mg/kg every 28 days.60 In short- and long-term studies, IVIG has decreased the number of infections and hospitalizations in some subgroups of HIV-infected children.61,67 Hypersensitivity reactions can occur. Common adverse drug effects include pain and tenderness at the site of injection, nausea, vomiting, flushing, and chills.

Pneumocystis Carinii Pneumonia

Children born to HIV-infected mothers are at greatest risk for Pneumocystis carinii pneumonia (PCP); therefore, guidelines have been established for prophylaxis (Table 5).67 These updated guidelines, based on recent studies, confirm that PCP occurs most often in HIV-infected infants at 3 to 6 months of age. Symptoms are acute and rapidly progressive. All infants born to HIV-infected mothers
### Recommended Immunization Schedule
For HIV-Infected Children

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Schedule—Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria—Tetanus Pertussis (DTP)</td>
<td>2,4,6,12–18 months, 4–6 years 11–12 years—only tetanus toxoid</td>
</tr>
<tr>
<td>Diphtheria—Tetanus Toxoid—Acellular Pertussis (DTap)</td>
<td>4th or 5th dose only &gt; 15 months</td>
</tr>
<tr>
<td>Inactive Poliomyelitis Vaccine (IPV)</td>
<td>2,4,6–18 months, 4–6 years</td>
</tr>
<tr>
<td>Measles—Mumps—Rubella (MMR)</td>
<td>12–15 months, and 4–6 or 11–12 years</td>
</tr>
</tbody>
</table>
| Hepatitis B Vaccine (HBV)    | a. Mother HBSAg Negative Birth, 2 months, 6–18 months  
                             | b. Mother HBSAg Positive Birth, 1 and 6 months (Hepatitis B immune globulin also at birth) |
| Haemophilus Influenzae Type B Conjugated (HiBoc) | 2,4,6 and 12–15 months |
| Pneumococcal                 | 2 years                                          |
| Influenza                    | Annually                                         |
|                             | HBsAg = Hepatitis B surface antigen               |

Table 4

should be started on PCP prophylaxis at 4 to 6 weeks of age, regardless of CD4 count. Initiation of sulfosalicylic acid before 4 weeks of age is not recommended because of the risk of kernicterus in the infant.67 PCP prophylaxis should be continued until the child is 1 year old unless the child is determined to be HIV negative. Therapy is initiated in older children based on age-related CD4 lymphocyte counts and is continued indefinitely. Children with a prior episode of PCP receive prophylactic therapy regardless of CD4 count.

### Other Infections
Limited information is available on the use of standard treatment modalities for fungal, viral, and parasitic infections in HIV-infected children. Prophylaxis guidelines for other opportunistic infections in children are less well described.68 Recommendations by the U.S. Public Health Service/Infectious Disease Society of America are listed in Table 6.

### Nutrition
Over 95% of HIV-infected children develop clinically significant malnutrition, and 80% develop growth abnormalities during the course of the disease. Problems causing malnutrition are multifactorial and can be caused by HIV disease, therapeutic agents, or environmental conditions. HIV-related disease or opportunistic infections can lead to anorexia, dysphagia, malabsorption, and metabolic derangements. Common infections that produce ulcers, gastritis, and diarrhea include *Candida sp.*, cytomegalovirus, and herpes simplex virus. These infections result in malabsorption syndromes, including lactose intolerance and impaired fat and protein absorption, and severely decrease nutrient absorption. Medications used in these patients frequently have gastrointestinal side effects that complicate drug therapy.69 Because the majority of HIV-infected children are from the lower socioeconomic classes and are frequently born to HIV-infected mothers, obtaining food for proper nutrition may be difficult. The role of the pharmacist is essential to identifying nutritional problems, recommending alternatives, and educating the parent or caregiver on proper nutrition. Families should be guided to private or governmental agencies for assistance if needed.

The primary health care team assesses the nutritional status of the HIV-infected child and develops a plan. The pharmacist can play a critical role in this effort. The following are recommendations for input by the pharmacist:

- Obtain a complete medication history from the parent or caregiver to assess medication-related effects in the child. Include an assessment of the child's eating behavior and taste preferences.
- Discuss with caregivers the risks of consuming raw meats and fish, uncooked eggs, unpasteurized milk or milk products, and raw shellfish.
- Describe the proper methods for storing, handling, preparing and cooking food to reduce the acquisition of new pathogens.
- Discuss the symptoms of lactose intolerance and recommend appropriate formulas or alternatives as needed. Outline proper storage methods to prevent bacterial contamination of formulas.
- Discuss methods of increasing the caloric density of foods by adding carbohydrates and fat as tolerated. Caution should...
Role of the Pharmacist

Pediatric pharmacotherapy is a challenge. Research into HIV drug therapy in infants and children is significantly less than in the adult population, and it is difficult for pharmacists to find information on new therapies. The pharmacokinetic and pharmacodynamic parameters of drugs are altered in the pediatric population. From birth to adulthood these parameters change with the growth and development of the child, altering the expected outcome of therapeutic regimens.

AIDS is a chronic terminal disease requiring long-term therapy with multiple medications. Several studies from an adult university-based AIDS clinic have documented that patients are taking an average of five to six medications. Much of the time, the medication is not being taken as directed. Moreover, multiple medications increase the risk of adverse effects or drug interactions. Therefore, it is essential that the caregiver understand the medication regimen. Frequently the pharmacist does not work with the pediatric patient directly, but discusses the patient's medication history as well as specific information on each medication with the parent or caregiver.

The pharmacist must also recognize the psychological impact on the parent or caregiver. Caring for a child with a chronic terminal disease entails constant stress. Medication counseling should be designed to direct and support the parent or caregiver. The pharmacist should address the concerns of the caregiver about the potential adverse drug effects. Caregivers may not give the medication to the child if they feel it will be harmful.

A major factor to consider when treating HIV-infected children is the socioeconomic status of the patient's family. The majority of HIV-infected mothers live in poor communities where access to care may be an additional problem. These mothers are the primary caregivers of HIV-infected children and may themselves be ill. In addition, the majority of children who are perinatally infected with HIV are either African American or Hispanic. Other minorities make up a smaller percentage, but may be significant in some areas. When working with families of cultural minorities, it is important to understand and respect cultural attitudes and norms specific to the population served. The educational level of the parent or caregiver should be considered as well; counseling and educational literature should contain clear and easy-to-understand directions. Bilingual teaching materials are available through CDC.

While the importance of counseling patients with HIV is obvious, the primary role of the pharmacist is to review drug therapy, detect preventable adverse effects, and recommend alternatives to the health care team. A recently published study of adverse drug events in two major teaching hospitals concluded that the largest number of preventable adverse events were caused by the lack of drug knowledge by the physician. The pharmacist with a broad drug knowledge base can play an essential role on the interdisciplinary patient care team.71

### Table 5

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>All infants born to HIV-infected mothers, 4 to 6 weeks old with unknown HIV-infection status</td>
</tr>
<tr>
<td>b)</td>
<td>HIV-infection status or CD4 lymphocyte count or percentage</td>
</tr>
<tr>
<td>1</td>
<td>4 to 12 months HIV infected or HIV-status unknown</td>
</tr>
<tr>
<td>2</td>
<td>1 to 5 years HIV infected CD4 count less than 500/mm³ or less than 15%</td>
</tr>
<tr>
<td>3</td>
<td>6 to 12 years HIV infected CD4 count less than 200/mm³ or less than 15%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regimens</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose:</td>
<td>Trimethoprim/sulfamethoxazole (TMP/SMX)</td>
</tr>
<tr>
<td>150 mg TMP/m² with 750 mg SMX/m² oral in two divided doses</td>
<td></td>
</tr>
<tr>
<td>Three times/week on consecutive days</td>
<td></td>
</tr>
<tr>
<td>Alternative dosing schedules:</td>
<td></td>
</tr>
<tr>
<td>Total dose given once daily</td>
<td></td>
</tr>
<tr>
<td>Dose as above administered seven days/week</td>
<td></td>
</tr>
<tr>
<td>Dose as above on alternate days</td>
<td></td>
</tr>
<tr>
<td>Alternative regimens for TMP/SMX intolerance</td>
<td></td>
</tr>
<tr>
<td>Dapsone 2 mg/kg (oral, max 100 mg) daily (children &gt; 1 month)</td>
<td></td>
</tr>
<tr>
<td>Aerosolized pentamidine (children &gt; 5 years) 300 mg administered via Respirgard II monthly</td>
<td></td>
</tr>
<tr>
<td>Intravenous pentamidine 4 mg/kg every 2 to 4 weeks</td>
<td></td>
</tr>
</tbody>
</table>

Source: Reference 48.
**Prophylaxis of Additional Infection in HIV-Infected Children**

<table>
<thead>
<tr>
<th><strong>Tuberculosis</strong></th>
<th><strong>Mucocutaneous candidiasis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>a) Isoniazid susceptible:</strong></td>
<td>Persistent or frequent oral infections:</td>
</tr>
<tr>
<td>Household/day care contact with active case or positive by TB skin test</td>
<td><strong>Topical therapy:</strong> Clotrimazole or nystatin</td>
</tr>
<tr>
<td><strong>Therapy:</strong> Isoniazid 10–15 mg/kg orally or intramuscularly (IM) daily (maximum 300 mg) for 12 months or 20–30 mg/kg orally (maximum 900 mg) 2 times weekly for 12 months</td>
<td><strong>Oral therapy:</strong> Ketoconazole 5–10 mg/kg every 12–24 hours or fluconazole 2–8 mg/kg daily</td>
</tr>
<tr>
<td><strong>Alternative therapy:</strong> Rifampin 10–20 mg/kg (maximum 600 mg) orally or intravenously (IV) daily for 12 months</td>
<td><strong>Toxoplasmosis</strong></td>
</tr>
<tr>
<td><strong>b) Isoniazid resistant:</strong></td>
<td>Prophylaxis prior to first episode:</td>
</tr>
<tr>
<td><strong>Therapy:</strong> Rifampin (dose as above) for 12 months</td>
<td><strong>Therapy:</strong> Trimethoprim/sulfamethoxazole 150/750 mg/m²/day in 2 divided doses 3 times weekly on consecutive days (see reference for other regimens)</td>
</tr>
<tr>
<td><strong>c) Multiple drug resistant tuberculosis (MDTB):</strong></td>
<td><strong>Alternative therapy:</strong> Dapsone (children &gt; 1 month) 2 mg/kg daily plus pyrimethamine 1 mg/kg daily plus leucovorin 5 mg every 3 days</td>
</tr>
<tr>
<td>Household/day care contact with active MDTB case</td>
<td>Prophylaxis for recurrence:</td>
</tr>
<tr>
<td><strong>Therapy:</strong> Drugs selected by sensitivity of MDTB, 2 or more drugs for at least 12 months. Consultation with public health authorities is required.</td>
<td><strong>Sulfadiazine</strong> 85–120 mg/kg in 2–4 divided doses daily plus pyrimethamine 1 mg/kg (maximum 25 mg) daily plus leucovorin 5 mg every 3 days</td>
</tr>
</tbody>
</table>

**Varicella zoster virus**

Exposure to varicella or herpes zoster:

- **Therapy:** Varicella-zoster immune globulin (VZIG) 1 vial (1.25 ml)/10 kg to a maximum of 5 vials, IM within 96 hours of exposure. Children receiving IVIG should receive VZIG if the dose was greater than 14 days before exposure.

**Measles**

After exposure, children should receive immunoglobulin regardless of vaccine status.

**Cytomegalovirus**

Chronic suppressive therapy after infection:

- **Therapy:** Ganciclovir, 10 mg/kg in 2 divided doses IV daily for 1 week then 5 mg/kg IV daily
- **Alternative therapy:** Foscarnet 60–120 mg/kg IV daily

**Mycobacterium avium complex**

Prophylaxis prior to first episode:

- **Therapy:** 6–12 years old: Rifabutin 300 mg daily;
- < 6 years old: Rifabutin 5mg/kg daily when suspension is available
- **Alternative therapy:** Azithromycin 7.5 mg/kg in 2 divided doses daily or clarithromycin 8–12mg/kg daily.

Prophylaxis for recurrence:

- Clarithromycin 30 mg/kg in 2 divided doses daily plus one of the following oral medications:
  - Ethambutol 15–25 mg/kg daily, clofazimine 50–100 mg daily, rifabutin 300 mg daily, ciprofloxacin 20–30 mg/kg in 2 divided doses daily

**Herpes simplex virus**

Suppressive therapy after recurrent infection:

- **Therapy:** Oral acyclovir 600–1,000 mg in divided doses daily

References 40,84.
The three major areas for participation of the pharmacist in the care of HIV patients are HIV prevention and infection control, pharmacotherapeutics, and patient/caregiver education.

**HIV Prevention and Infection Control**

The pharmacist, especially in the community setting, is the practitioner seen most frequently by families. The pharmacist can provide important information on drug therapy for HIV disease and other health-related issues, and reinforce directions given by health care providers, to improve patient compliance. In addition, the pharmacist should work with community groups to disseminate accurate information about HIV infection. The following are some suggestions:

- Provide information to families concerning transmission of HIV and methods for prevention. Written information should be placed in a prominent place in the pharmacy. Bilingual information will be needed in some communities. Counsel parents on methods for educating children and adolescents in the family about HIV infection.
- Discuss infection control procedures with families. Instruct caregivers to wear gloves when handling body fluids or when coming in contact with wounds or mucous membranes, to dispose of infectious waste properly, and to use approved disinfectants that are virucidal and tuberculocidial in the home or day-care setting.
- Provide accurate face-to-face consultation or written information—at the appropriate educational level—on the benefits of antiretroviral therapy to HIV-positive pregnant women.
- Emphasize to patients and caregivers the critical importance of adhering to antiretroviral regimens.
- Discuss precautions for exposure to additional pathogens in the environment.
- Provide information and schedules for childhood immunizations. Help parents and caregivers maintain accurate immunization records.
- Participate in school and community groups to provide accurate information on HIV infection and resources.

**Pharmacotherapeutics, and Educating Patients and Caregivers**

As more agents are approved for the treatment of HIV infection, therapeutic regimens are becoming more complex. The knowledge of the pharmacist is essential to the primary health care team in designing and adapting dosing regimens based on factors unique to the pediatric population. The level of input the pharmacist will have will be related to the needs of the patient and family. The following areas are recommended:

- Obtain a complete medication history from the parent or primary caregiver, including all investigational, prescription, over-the-counter, and alternative therapies. Include information on adverse drug effects and adherence. Obtain information on how the drug is administered (e.g., milk, food) to detect possible drug-food interactions.
- Obtain information on the eating schedule and habits of the child to adjust medications.
- Identify, assess, correct, and prevent drug-related problems as they relate to children (e.g., incorrect doses or regimens, adverse effects, and drug-drug or drug-food interactions).
- Obtain laboratory data, as needed, from the primary health care team to assess the efficacy and potential toxicity of medication regimens.
- Inform patients of the availability of free medication and care. Guide health care professionals in the selection of affordable therapeutic choices for the patient.
- When counseling parents or caregivers, give specific information on the dosing regimen, methods of administration, and storage. For each prescribed drug, work with the caregiver to schedule the times of each dose. If needed, demonstrate the methods of drug administration (e.g., oral syringes).
- Educate caregivers on anticipated adverse drug effects and their severity. Changes in behavior or normal habits may be used as a monitoring parameter.
- Work with parents and caregivers to solve drug-related problems caused by nonadherence by suggesting other methods or routes of administration.
- Provide emotional support and reinforcement for parents or caregivers. At a stressful time, positive reinforcement is important.

**Education of Health Care Providers**

The knowledge base of pharmacists makes them excellent resources for other health care providers. All pharmacists must determine the best ways to disseminate information within the scope of their practice settings. Conferences and seminars for small groups of health care professionals are excellent teaching opportunities. Newsletters and distribution of other written materials can provide updated information on drug administration, adverse drug effects, drug-drug interactions, and drug-food interactions.

**Conclusion**

Over the past decade, the number of HIV-infected women and children has increased dramatically. Hospital and community pharmacists will be encountering HIV-infected pediatric patients with increasing frequency. Meanwhile, the health care environment continues to change, and it is likely that pharmacists will play greater roles in the care of these patients, including managing drug therapy, preventing adverse drug events, and counseling patients and caregivers. In the face of these trends, the profession of pharmacy must
be prepared to meet the unique needs of HIV-infected children and their families with responsibility, compassion, and strong knowledge of the disease and its therapy.

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