

HIV Infection in Infants, Children, and Adolescents

Sandra K. Burchett, MD,
MS,* Philip A. Pizzo[†]

Objectives After completing this article, readers should be able to:

1. Describe the changing epidemiology of perinatal human immunodeficiency virus (HIV) transmission and delineate effective interventions to reduce the rate of mother-to-child transmission.
2. Compare the clinical manifestations of HIV infection by age of presentation.
3. Describe the most appropriate diagnostic tests for HIV infection by patient age.
4. Describe the principles of antiretroviral treatment and classes of drugs.

Introduction

Pediatric HIV infection can present in neonates, children, or adolescents. The number of cases of acquired immunodeficiency syndrome (AIDS) among children in the United States is decreasing because of increased success in preventing perinatal transmission as well as the availability of effective treatments. Prompt diagnosis and adherence to effective treatments are critical to changing the face of HIV infection from a fatal disease to a chronic, manageable infection. Sadly, pediatric HIV/AIDS in the developing world is essentially unchecked, with almost 600,000 new infections in children younger than 15 years of age in 2002.

Definitions

HIV defines a chronic RNA virus infection in the host. When opportunistic or other unusual or persistent infections have occurred or when the CD4⁺ lymphocyte count is less than 200 cells in persons older than age 12 years, a patient is defined as having AIDS. Opportunistic infections are caused by organisms in the environment that usually do not cause harm to persons who have intact immune systems, but can be the basis of serious or even fatal infection in those who have compromised immune systems.

HIV enzyme-linked immunosorbent assay (ELISA) is a test performed on serum to detect antibodies against HIV antigens. If the ELISA results are positive, a Western blot is performed to identify individual antibodies to HIV antigens. A patient may have a positive ELISA result, but a negative Western blot result: This patient does not have HIV infection. Anyone older than 18 months of age who has a positive HIV ELISA result that is confirmed by Western blot is infected with HIV. Infants born to HIV-infected mothers have positive ELISA and Western blot results due to the passive transfer of maternal antibody, but this does not confirm infection, and viral-specific testing must be performed.

HIV viral load is determined by polymerase chain reaction (PCR) quantitation on plasma of the number of HIV virions present. A test that documents more than 10,000 copies/mL is diagnostic of HIV infection. This test is used to follow the efficacy of therapy, and virions will become nondetectable in patients receiving optimal therapy. HIV DNA by PCR is a qualitative test on peripheral blood cells that detects HIV DNA in the host cell genome that has been reverse transcribed from the HIV RNA. A positive test result is diagnostic of HIV infection. This test result remains positive, even in optimally treated patients. HIV coculture is performed on peripheral blood mononuclear cells and uses donor cells to amplify infection in tissue culture. A positive culture is diagnostic of HIV infection.

*Assistant Professor of Pediatrics, Harvard Medical School; Clinical Director, Infectious Disease Division, Children's Hospital, Boston, MA.

[†]Carl and Elizabeth Naumann Professor of Pediatrics and of Microbiology and Immunology; Dean, Stanford University School of Medicine, Stanford, CA.

Table 1. Centers for Disease Control and Prevention Immune Classification Based on CD4 Lymphocytes and Patient Age

Immune Category	<12 mo		1 to 5 y		6 to 12 y		>12 y
	No/mm ³	(%)	No/mm ³	(%)	No/mm ³	(%)	No/mm ³
Category 1: No suppression	≥1,500	(≥25%)	≥1,000	(≥25%)	≥500	(≥25%)	>350
Category 2: Moderate suppression	750 to 1,499	(15% to 24%)	500 to 999	(15% to 24%)	200 to 499	(15% to 24%)	200 to 350
Category 3: Severe suppression	<750	(<15%)	<500	(<15%)	<200	(<15%)	<200

Modified from CDC. 1994 Revised classification system for human immunodeficiency virus infection. *MMWR*. 1994;43(No. RR-2):1-10. >12 y column added by authors from current guidelines.

The Centers for Disease Control and Prevention (CDC) immune classification defines the degree of risk for opportunistic infections by age and CD4 cell count and percentage (Table 1).

Epidemiology

In the United States, more than 90% of reported cases of AIDS in children are due to perinatal acquisition. The other 10% of children acquire HIV from prior blood product exposure, sexual abuse, or unknown sources. Although in the earlier years of the epidemic 40% or more of HIV-infected infants and children were born to women whose personal risk behaviors included injection drug use, heterosexual contact and undefined risks constitute the predominate risk categories in more recent years (Fig. 1).

Currently, all pregnant women should be offered counseling and testing for HIV infection during pregnancy. The transmission rate in infected, untreated (usually undiagnosed) pregnancies is approximately 25%. When HIV-infection is undiagnosed in pregnancies, an opportunity is missed to: 1) offer antiretroviral therapy for maternal health and to reduce perinatal transmission; 2) choose formula feeding to prevent additional exposure to HIV through human milk; 3) allow women to make informed reproductive choices in the future; 4) identify HIV-infected siblings who would benefit from early HIV care; and 5) inform sexual partners of their potential status and to seek treatment if infected.

The rate of perinatal transmission of HIV is less than 2% when antenatal, intrapartum, and infant prophylactic antiretroviral therapies include reverse transcriptase inhibitors such as zidovudine (AZT). Approximately 30% to 50% of infected infants acquire infection in utero; thus, most infected infants (particularly those born to untreated women) acquire infection intrapartum (35%) or

through breastfeeding (at least 15%). Women whose onset of HIV infection occurs while pregnant may be at higher risk for in utero transmission than those who were HIV-seropositive before pregnancy. Reduction of maternal HIV viral load to a nondetectable level is the key to preventing vertical transmission of HIV. Studies have shown that cesarean section can be helpful in preventing peripartum transmission. Because HIV can be transmitted in human milk, women should choose formula feeding. Every infant in the United States born with HIV infection represents a failure of the health care system to provide access to testing, counseling, and antiretroviral therapy to seropositive pregnant women.

However, even if pediatric HIV were prevented completely in the United States, the epidemic would continue to rage in the world. Indeed, 2,000 children were infected with HIV daily in the year 2002 in developing countries. The cost of antiretroviral regimens such as AZT with or without lamivudine or nevirapine to prevent transmission varies, but even when provided free of charge, they are not always readily available to pregnant women because of a lack of coordinated health care systems. Frequently, antiretroviral therapy is not available for parents. Orphaned children, even when HIV-free, often have short lives. It is unlikely that the world epidemic of HIV will end before the development of effective preventive vaccines and before millions have died.

In America, adolescents have one of the fastest growing rates of HIV infection. Injection of drugs and unprotected sexual intercourse are common risk behaviors. Youth at highest risk often are homeless, disenfranchised, and living in poverty, although sexually active (or sexually abused) adolescents everywhere are at risk unless barrier protection is used. The incubation period from time of contact to presentation with symptoms ranges

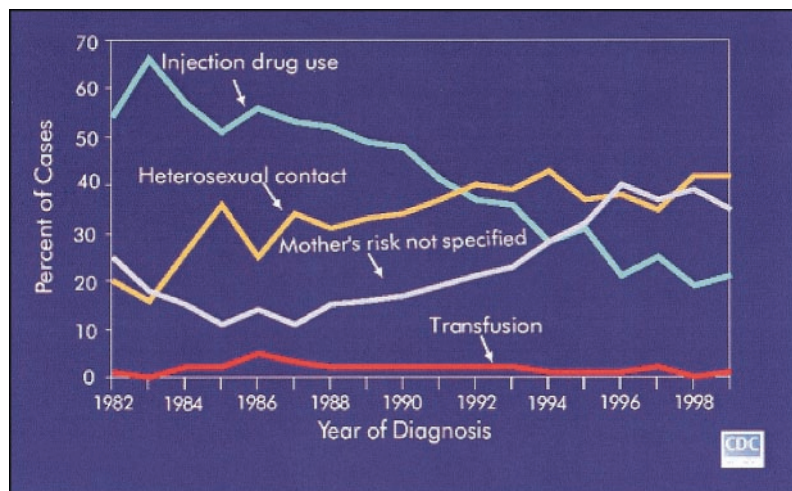


Figure 1. Mother's exposure category by year of diagnosis for perinatally acquired AIDS, 1982 to 1999, United States. Exposure category data are adjusted for reporting delays and estimated proportion of redistribution of cases reported without a risk.

from 1 to 2 weeks to months or years. HIV is present in genital secretions, and the HIV viral load in semen has been correlated with the risk of horizontal transmission. The highest risk for horizontal transmission probably is in persons who have new-onset infection (often undiagnosed) and those who are not receiving antiretroviral therapy. High viral loads occur in both circumstances. Clinicians caring for this age group should maintain a heightened awareness of HIV as a possibility in youth presenting with a mononucleosislike illness or with persistent systemic adenopathy. Antibody testing results by standard ELISA and Western blot may not be positive for up to 6 months after infection. Diagnosis can be made by HIV RNA PCR in these patients, which allows patients the very early treatment that some studies have shown offers the best opportunity to maintain a normal immune system. Therefore, heightened awareness of this symptom complex, appropriate and rapid testing, and institution of treatment are vital to the health of the patient and to public health. Clinicians also must consider HIV as a possible diagnosis in children who have been sexually abused and present with similar symptoms. For these children as well as for adolescents, HIV RNA PCR and ELISA and Western blot antibody testing should be ordered.

Pathogenesis

HIV infects the immune system. Infants who have acquired the infection in utero, intrapartum, or through breastfeeding have immature immune systems. The HIV virus infects CD4+ lymphocytes that are central to the immune response to most pathogens. When the virus

infects a cell, it becomes latent within the host cell genome until activated by antigens or pathogens. When activated, the viral genome replicates, and viral proteins are produced. The cell ruptures and dies as the virions are extruded through the cell membrane. These viruses then infect cells (eg, lymphocytes, monocytes, macrophages) with CD4 receptors and chemokine coreceptors, allowing the process to begin again. Measurement of cell-free virus in the plasma (HIV RNA viral load) reflects the total body burden of virus. Infected cells always are positive for HIV viral genome (the HIV DNA), even when viral load is well controlled. The thymus is most active

early in life and is the organ where CD4 cells mature. When viral load is controlled, the CD4 lymphocyte populations can be repleted with both memory and naïve cells from the thymic reservoir.

HIV-infected children may present with more serious manifestations or recurrence or persistence of common childhood illnesses. Infection may lead to a dysfunctional response to the pathogen. For example, CD4 lymphocytes help B cells to differentiate and produce antibodies to certain pathogens, and 95% of HIV-infected children have very high immunoglobulin levels, suggesting the presence of a chronic stimulus. In part, these antibodies are against HIV, but they also may be produced in response to other pathogens, although they presumably are dysfunctional in preventing or attenuating repeated infections. Opportunistic infections in children and adolescents can occur when the CD4 lymphocyte number is low, especially if it is less than 200 CD4+ cells. The actual CD4 number at which a patient is at risk is age-dependent (Table 1).

Additionally, HIV may lead to bone marrow suppression that is characterized by a modest degree of anemia and neutropenia. Thrombocytopenia also may be due to marrow suppression or to immune destruction due to antigen-antibody complexes.

Clinical Aspects

Fewer infants and children have been diagnosed with HIV infection in the past 5 years in the United States, but pediatricians should remain aware of clinical signs and symptoms suggestive of HIV infection and know how best to make the diagnosis. Optimal management of

HIV-infected patients requires collaboration among the primary care pediatrician and pediatric HIV and multidisciplinary specialists.

Pertinent points in the medical history of a child who has HIV infection include: recurrent bacterial infections such as otitis media, sinusitis, bacteremia, and pneumonia; failure to thrive; loss of developmental milestones; and persistent or unusual infections such as thrush or varicella zoster.

Infants Ages 1 to 2 Years

Infants can present in the first few months of life, and older children present in later years as immunity wanes. Among infants 1 to 2 years of age, the primary signs and symptoms are: *Pneumocystis carinii* pneumonia (PCP), lymphoid interstitial pneumonitis (LIP), recurrent bacterial infections (especially *Streptococcus pneumoniae*), failure to thrive, HIV encephalopathy, and refractory thrush or candidal diaper rash.

with 28% neutrophils, 14% lymphocytes, 22% atypical lymphocytes, 9% monocytes, 3% eosinophils, and 24% other; hemoglobin, 7.7 g/dL (77 g/L); hematocrit, 24.1% (0.241); platelet count, $184 \times 10^3/\text{mL}$ ($184 \times 10^9/\text{L}$); mean corpuscular volume, 70 fL; and RDW, 17.3. The cerebrospinal fluid protein level, glucose concentration, and cell count are normal. Based on these findings, the differential diagnosis focused on oncologic disease, and bone marrow aspiration was planned. However, the patient's respiratory status worsened, although he was receiving ceftriaxone, and bronchoalveolar lavage revealed *Pneumocystis carinii*. The infant improved after receiving trimethoprim/sulfamethoxazole and methylprednisolone, and he tested positive for HIV antibody and DNA and RNA by PCR.

This case is illustrative of a presentation with PCP and splenomegaly. Respiratory distress associated with hypoxia (but without auscultatory findings) that does not improve after administration of appropriate antibiotics should lead the pediatrician to consider PCP. When PCP is suspected, bronchoalveolar lavage or lung tissue biopsy should be performed to confirm the diagnosis. Although there does not appear to be a direct correlation between the number of CD4+ lymphocytes and acquisition of PCP as an opportunistic infection in the first postnatal year, infants who have immune abnormalities, including HIV and leukemia or severe combined im-

munodeficiency disease, can present with PCP. In essentially all of the immunocompromised states in which PCP can develop, rapid diagnosis and initiation of appropriate therapy for the underlying disease process can optimize the prognosis. Testing should include HIV antibody and DNA and RNA by PCR if the antibody is positive. PCP is treated best with steroids and trimethoprim/sulfamethoxazole or with dapsone or intravenous pentamidine. One study showed the equivalence of clindamycin and primaquine to trimethoprim/sulfamethoxazole.

Although PCP is one of the possible diagnoses in an immunocompromised patient who has respiratory distress and radiographic evidence of diffuse interstitial pulmonary infiltrates, the differential diagnosis also includes *Mycoplasma*, *Legionella*, chlamydial, pneumococcal, respiratory syncytial virus, parainfluenza, and adenoviral infections. These can be diagnosed with rapid viral antigen detection tests, urinary antigens, bronchoalveolar lavage, or lung biopsy.

The rate of perinatal transmission of HIV is less than 2% when antenatal, intrapartum, and infant prophylactic antiretroviral therapies include reverse transcriptase inhibitors.

A 6-month-old infant presents to the emergency department with a 3-day history of low-grade fever, rapid respiratory rate, and decreased oral intake. Physical examination reveals an ill-appearing child in moderate respiratory distress. The child's length is at the 50th percentile, weight is at the 5th percentile, and head circumference is at the 50th percentile. The heart rate is 160 to 180 beats/min, respiratory rate is 60 to 80 breaths/min, and blood pressure is 85/55 mm Hg. Pertinent findings on physical examination include: lungs clear to auscultation with breath sounds present throughout and no wheezing, but with intercostal retractions; no murmur; liver palpable 3 cm below left costal margin; spleen firm and palpable to the iliac crest; and bilateral anterior and posterior cervical and axillary adenopathy. Oxygen saturation by probe is 90% on room air. Chest radiography reveals hyperinflation with diffuse interstitial perihilar infiltrates. Laboratory results include: white blood cell count, $12.8 \times 10^3/\text{mL}$ ($12.8 \times 10^9/\text{L}$),

Table 2. AIDS-defining Conditions Most Commonly Reported through 2000 to the CDC for Children <13 y, United States*

Condition	Number	% of Cases
<i>Pneumocystis carinii</i> pneumonia	2,959	33
Lymphoid interstitial pneumonitis	2,100	24
Recurrent bacterial infections	1,836	21
HIV wasting syndrome	1,641	18
HIV encephalopathy	1,495	17
<i>Candida</i> esophagitis	1,414	16
Cytomegalovirus disease	902	10
<i>Mycobacterium avium</i> infection	732	8
Severe herpes simplex virus	445	5
Cryptosporidiosis	432	5
Pulmonary candidiasis	335	4

*N = 8,908

LIP also is in the differential diagnosis. This clinical syndrome can develop when an HIV-infected child acquires primary Epstein-Barr virus (EBV) infection. At the lung tissue level, this results in recruitment of CD8 (cytotoxic) T cells, with cytokine secretion and resultant tissue damage. Steroids and oxygen form the basis of therapy. The chest radiograph may show a “honeycomb” pattern for months or years. Usually children who present with LIP have a far better prognosis than those who present with PCP.

PCP has been the leading AIDS-defining illness in children reported to the CDC since the syndrome initially was recognized (Table 2) (Fig. 2). PCP is uncommon in the first 2 months after birth, but peaks in incidence at 5 months, with significant reported numbers in the first postnatal year. All too often, infants who present with PCP are the first indication that at least the mother is HIV-infected. Fathers may be infected from horizontal transmission and other children from vertical transmission. Consequently, when PCP is suspected or confirmed, the HIV medical team, which usually includes physicians trained in infectious disease or immunology, nurses, and social workers, can help with disclosure of diagnoses, provi-

sion of care, contact information and referrals, and mental health services.

Infants also may present with signs of an ongoing systemic HIV infection. For example, a child may manifest with petechiae, marked splenomegaly, diffuse adenopathy, and a platelet count less than $10 \times 10^3/\text{mcL}$ ($10 \times 10^9/\text{L}$), yet otherwise appear well. An infected child may present below the appropriate weight growth percentiles for age. Linear growth also may be impaired, but this may not be apparent until the child is older. Some infants have a rapidly progressive course characterized by neurologic manifestations that include motor abnormalities or the development of acute encephalopathy with loss of developmental milestones. Most children who have long-standing HIV infection develop mild-to-moderate cortical atrophy and some aspect of a learning disability, such as attention deficit disorder.

Children Ages 2 to 6 Years

The primary signs and symptoms of HIV infection in this age group are: multiple episodes of otitis media and sinusitis, recurrent bacterial infections (*S pneumoniae*), LIP, and HIV encephalopathy.

The 2- to 6-year-old child who has HIV infection might present with eczema or have multiple episodes of otitis media, sinusitis, or both, accompanied by adenopathy. Persistent or recurrent adenopathy in an otherwise seemingly well child should alert the pediatrician to the possibility of systemic viral infections such as cytomegalovirus, EBV, or if adenopathy persists for months, HIV. For example, we cared for a 9-year-old child who was found to be HIV-infected after a 2-year evaluation for recurrent sinusitis revealed elevated immunoglobulin levels.

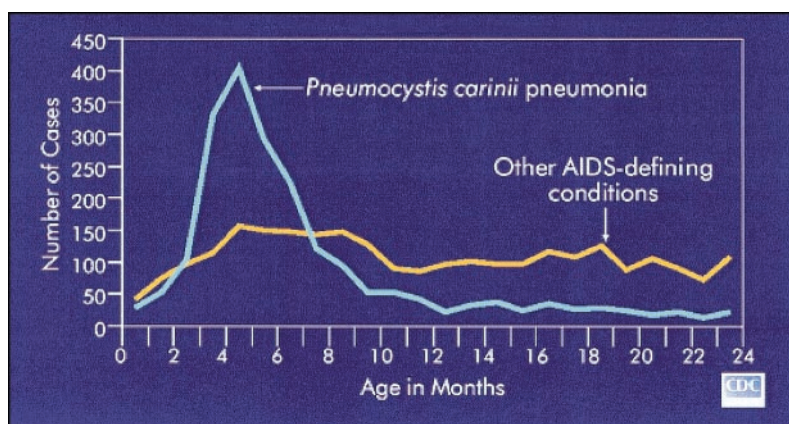


Figure 2. AIDS-defining conditions by age at diagnosis for perinatally acquired AIDS cases reported through 2000, United States.

Prior to the standard practice of offering conjugate pneumococcal vaccines in infancy, invasive disease (bacteremia, pneumonia, meningitis) with *S pneumoniae* was more common in the HIV-infected population than in those not infected. A 2-year-old previously healthy, fully immunized boy presented to us with periorbital cellulitis and no history of trauma. We reasoned that *S pneu-*

Young infants who were born to HIV-seropositive women must be tested by virus-specific diagnostic tests—HIV culture, DNA PCR, RNA PCR, or HIV p24 antigen.

moniae was the likely pathogen. When the mother described an episode of *S pneumoniae* meningitis that occurred when the child was 4 months of age, the boy was tested and found to be HIV-infected. Time will tell whether pneumococcal immunization can prevent disease in HIV-infected children.

Children and Adolescents Ages 6 to 21 Years

The primary signs and symptoms of HIV infection in this age group are: *Candida* pneumonia, esophagitis, or vaginitis; varicella zoster; cytomegalovirus retinitis; HIV wasting; *Mycobacterium avium-intracellulare*; cryptosporidiosis; severe herpes simplex recurrences; and parotitis.

Older children can present with more of the typical opportunistic infections due to low CD4 lymphocyte numbers. For example, a 12-year-old girl presented with appendicitis, but the surgeon noted that she also had oral thrush. Her HIV ELISA and Western blot test results were positive, and the CD4+ count was fewer than 100 cells. Interestingly, the past medical history included an episode of varicella zoster the prior year. A 10-year-old boy who presented with varicella zoster and systemic adenopathy had a CD4+ lymphocyte count of 90 cells. A 13-year-old boy presented with syncope on the football field due to anemia and thrombocytopenia and was found to have a CD4+ lymphocyte count of 80 cells. In contrast, certain infections in adults who have HIV, such as *Bartonella* with resultant bacillary angiomatosis, are seen infrequently in children who have HIV infection. These case vignettes are presented not only as examples of presentations with HIV or AIDS, but also to demon-

strate that each of these children had been healthy before his or her diagnosis. Infected children may be identified when a mother presents symptomatically or accesses testing during pregnancy.

Among adolescents, a primary infection syndrome in the first 2 to 6 weeks after HIV infection is seen in 30% to 70% of patients. This can include sore throat, fever, myalgias, adenopathy, macular or maculopapular rash, and fatigue very reminiscent of primary EBV infection. Physicians should consider HIV testing of sexually active youth who present with an EBVlike syndrome, but are EBV-negative, especially if there are concomitant sexually transmitted diseases or high-risk behaviors, such as homelessness or illicit drug use. A rapid diagnosis is important because some of the most exciting research to date stems from aggressively treating such persons with antiretroviral therapy as soon as the diagnosis of HIV is established to keep the immune system intact and competent.

Laboratory Tests

Infected patients may have mild anemia, thrombocytopenia, or neutropenia. The differential count on the complete blood count often reveals atypical lymphocytes. Early in infection, lymphocytes generally predominate. Hepatic parenchymal enzymes (alanine aminotransferase, aspartate aminotransferase) may be elevated at baseline. These levels also may become elevated when antiretroviral therapy is initiated. Immunoglobulin (Ig) levels may be high (eg, IgG of 3,000 to 4,500 mg/dL [30 to 45 g/L]).

The CD8+ (cytotoxic) lymphocytes are proportionately higher than the CD4+ (helper) lymphocytes, resulting in a CD4/CD8 ratio of less than 1. Therefore, both arms of the immune system (cellular and humoral) are abnormal, much as in children who have severe combined immunodeficiency, making them susceptible to similar opportunistic pathogens.

Infants born to women who are known to be infected have positive antibody test results (ELISA or Western blot) for HIV that reflect passive transplacental transfer of IgG to HIV across the placenta for as long as 18 months after birth. Therefore, young infants who were born to HIV-seropositive women must be tested by virus-specific diagnostic tests (HIV culture, DNA PCR, RNA PCR, or sometimes HIV p24 antigen). All others should be tested by ELISA and Western blot.

Management

A living document at the Web site www.aidsinfo.nih.gov/guidelines is updated as new findings or new agents are made available for children and adolescents who have HIV. Authors for this site are investigators at many HIV/AIDS treatment centers, and discussions related to a variety of clinical scenarios are included.

Antiretroviral Agents

The mainstays of therapy include a combination of drugs from one to three categories based on their site of action against HIV replication. Reverse transcriptase inhibitors target an enzyme that converts HIV RNA to DNA for transcription by the host cell genome. Reverse transcriptase can be blocked by nucleoside analogue agents such as AZT, didanosine (ddI), stavudine (d4T), lamivudine (3TC), zalcitabine (ddC), abacavir (ABV), and tenofovir. Nonnucleoside analogue reverse transcriptase inhibitors (NNRTIs), including nevirapine, efavirenz, or delavirdine, can block a second active site on the reverse transcriptase enzyme. A separate site of action is blocking of the protease enzyme that is important in processing key HIV proteins. HIV protease inhibitors include nelfinavir, ritonavir, indinavir, saquinavir, amprenavir, and lopinavir.

Immune-based Therapy

There are several adjunctive options to antiretroviral therapy. HIV vaccines can boost immunity to HIV. Intravenous immune globulin can provide functional humoral immunity, especially if the patient has repeated episodes of otitis media, sinusitis, or invasive bacterial infections such as with pneumococcus. Cytokines can enhance the cellular immune system (interleukin-2 and gamma-interferon).

Initial Antiretroviral Therapy

Data suggest that from birth to 12 months of age, infants have the best outcome if antiretroviral therapy is begun as soon as an infection has been diagnosed. When an older child or adolescent is identified after more than 1 year of HIV infection, the timing for initiating antiretroviral therapy is based on HIV viral load, CD4+ lymphocyte count, and clinical status. Effective initial combinations have included two nucleoside analogue reverse transcriptase inhibitors (NRTIs) plus a protease inhibitor or an NNRTI. For persons who have higher viral loads (usually accompanied by lower CD4 lymphocyte counts), a second protease inhibitor may be chosen. The NRTIs and NNRTIs are formulated in palatable liquid preparations. The protease inhibitors are highly protein

bound, are difficult to solubilize stably, and often are unpalatable. HIV care teams recommend maximization of social support during initiation or change of antiretroviral therapy because the goal of successful therapy is to bring the HIV viral load to nondetectable levels as quickly as possible and to maintain suppression durably. Intermittent adherence leads to viral replication and drug resistance. Generally, antiretroviral therapy is recommended for all children and adolescents unless they are completely asymptomatic and have no immune suppression.

Changing Antiretroviral Therapy

When to change therapy and which regimens to choose is a complex decision. An important principle is to change all drugs from the current regimen to gain maximal benefit and prevent development of resistance. Patients who have advanced disease may be offered four to eight different medications to control the viral load. Change also may be required if the patient experiences significant adverse effects to an agent(s).

Prophylactic Therapy

Prevention of opportunistic infections is a mainstay of the management of HIV-infected patients. Generally, when CD4+ cell counts have fallen to the CDC Category 3 (see definitions), the patient will need to begin therapy to prevent PCP, invasive cytomegalovirus infection (eg, retinitis), and *Mycobacterium avium-intracellulare*. Prophylaxis against cryptococcal infection is controversial but should be discussed. Table 3 outlines the usual agents and CD4+ cell ranges for prophylactic therapy.

Immunizations

Standard childhood immunizations are recommended for children who have HIV infection, including influenza vaccine if CD4+ cell counts are not profoundly low. Varicella vaccine has been shown to be safe and immunogenic in HIV-infected children who have normal CD4+ cell counts. Studies are ongoing to determine the safety and immunogenicity of this vaccine in children who have CD4+ cell counts in the moderate range. Live viral vaccines never should be administered to children who have the lowest CD4+ cell counts.

Other Health Management

Pediatric HIV infection is a family-centered chronic illness, often with an overlay of societal stigmatization. Remaining physically and mentally healthy is difficult. Perhaps the single greatest problem is disclosure of the

Table 3. Opportunistic Pathogen-directed Prophylaxis

Pathogen	Patient Category/Condition	Therapy
PCP	<12 mo of age or CDC immune category 3	TMP/SMX, dapsone
CMV	CDC immune category 3 and CMV+	Ganciclovir, valganciclovir
MAI	Lower range of CDC immune category 3	Clarithromycin, azithromycin
<i>Candida</i>	Thrush, vaginitis	Fluconazole
HSV	CDC immune category 3 and HSV+	Valacyclovir, famciclovir, acyclovir
Cryptococcus	Lower range of CDC immune category 3	Fluconazole

PCP = *Pneumocystis carinii* pneumonia; CMV = cytomegalovirus; MAI = *Mycobacterium avium-intracellulare*; HSV = herpes simplex virus; CDC = Centers for Disease Control and Prevention; TMP/SMX = trimethoprim/sulfamethoxazole

diagnosis to the child, other family members, friends, schools, or workplaces. Although laws prevent discrimination in terms of losing health care coverage, housing, jobs, and school placements, these issues remain. Providing children with the age-based appropriate level of knowledge about their diagnosis is individualized and an ongoing process undertaken by parents, family, and caregivers. A mental health screening tool we have used found that nearly every patient has some component of depression. We have found it critical to address the mental health care needs in addition to the other medical needs to ensure successful adherence to antiretroviral regimens.

Prognosis

Perinatally infected children and youth in our clinic range from 1 month of age to late teens. Data from our clinic as well as information reported on children in the Pediatric AIDS Clinical Trials group across the country have documented that in the last 5 years, since the advent of newer

agents, many fewer HIV-infected children progress to AIDS-defining illnesses, which reflects the ability to maintain adequate CD4+ cell number and function with newer regimens. Many, but not all, children who had advanced disease increased their CD4+ cell counts and avoided additional opportunistic infections. All patients who have lower CD4+ cell counts require prophylaxis against opportunistic infections in addition to antiretroviral therapy, necessitating a very large daily pill burden. Adherence to effective therapeutic regimens

has become the leading barrier to a shift from an inevitable progression to death to living with and managing HIV as a chronic disease for most affected children.

Suggested Reading

- Gortmaker SL, Hughes M, Cervia J, et al. Effect of combination therapy including protease inhibitors on mortality among children and adolescents infected with HIV-1. *N Engl J Med.* 2001;345:1522–1528
- Pizzo PA, Wilfert CM, eds. *Pediatric AIDS: The Challenge of HIV Infection in Infants, Children and Adolescents*. Philadelphia, Pa: Lippincott Williams & Wilkins; 1998
- Web Site: www.aidsinfo.nih.gov/guidelines includes:
Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States, August 30, 2002
- 2001 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with HIV, November 28, 2001
- Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection, December 14, 2001

PIR Quiz

Quiz also available online at www.pedsinreview.org.

1. You are evaluating a 2-day-old infant born to a mother who had received no prenatal care. HIV enzyme-linked immunosorbent assay (ELISA) and Western blot tests were positive when the mother was admitted to deliver the baby. She was not aware of her HIV-positive status. The delivery was via cesarean section and without complications. Which of the following statements regarding this situation is *true*?
 - A. Because the mother was previously undiagnosed, she likely has a low viral load and, therefore, has a decreased risk of transmitting HIV to her infant.
 - B. Delivering the infant via cesarean section likely reduced the risk of peripartum transmission of HIV.
 - C. It is most likely that this mother acquired HIV infection through the use of injection drugs.
 - D. The likelihood that this infant has acquired HIV from his mother is 50%.
 - E. The mother should be encouraged to breastfeed once antiretroviral therapy has been initiated.
2. You initiate an evaluation for HIV on the previously described infant. Which of the following results confirms a diagnosis of HIV infection?
 - A. CD4 count of 1,500/mm³.
 - B. Elevated levels of immunoglobulins G and M.
 - C. Positive HIV DNA by polymerase chain reaction.
 - D. Positive HIV ELISA.
 - E. Positive Western blot.
3. You are seeing an 8-month-old girl who has respiratory distress. Past history is notable for three episodes of otitis media. Her weight is below the 5th percentile. Her respiratory rate is 50 breaths/min, and her oxygen saturation on room air is 88%. Her lungs are clear. Chest radiography shows mild bilateral perihilar infiltrates but no other consolidation. Further history reveals that her mother has a history of heroin use, so you consider HIV with secondary *Pneumocystis carinii* pneumonia (PCP) as a possible cause for the child's distress. Which of the following statements is *true*?
 - A. A positive culture for *P carinii* confirms HIV infection in this child.
 - B. Bronchoalveolar lavage should be performed to confirm the diagnosis of PCP.
 - C. Inhaled pentamidine is the treatment of choice if testing for PCP is positive.
 - D. PCP is very unlikely in this patient because of her young age.
 - E. The CD4 count in this patient is likely to be normal.
4. Which of the following statements regarding the risk of HIV infection in the adolescent population is *true*?
 - A. HIV ELISA testing is always positive 3 months after horizontal transmission.
 - B. Most adolescents who have HIV infection acquire it from homosexual activity.
 - C. The incubation period for HIV varies from weeks to years.
 - D. The risk of transmission is lowest in adolescents who have undiagnosed infection.
 - E. The risk of transmission is unrelated to HIV viral load.
5. Which of the following laboratory abnormalities is *most* likely to be seen in a patient who has HIV infection?
 - A. High CD4/CD8 ratio.
 - B. Hyperbilirubinemia.
 - C. Hypogammaglobulinemia.
 - D. Leukocytosis.
 - E. Thrombocytopenia.