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APPENDIX C

GUIDELINES FOR MANAGEMENT OF HIV INFECTION

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APPENDIX E

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MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

Current Trends

Classification System for Human Immunodeficiency Virus (HIV) Infection in Children Under 13 Years of Age

INTRODUCTION

With the identification of the causative agent of the acquired immunodeficiency syndrome (AIDS), a broad spectrum of clinical manifestations has been attributed to infection with the human immunodeficiency virus (HIV). With the exception of the CDC surveillance definition for AIDS (*1,2*), no standard definitions for other manifestations of HIV infection have been developed for children. Classification systems published to date have been developed primarily to categorize clinical presentations in adult patients and may not be entirely applicable to infants and children (*3-5*).

Physicians from institutions caring for relatively large numbers of HIV-infected children report that only about half of their patients with symptomatic illness related to the infection fulfill the criteria of the CDC surveillance definition for AIDS (*6,7*).

To develop a classification system for HIV infection in children, CDC convened a panel of consultants* consisting of clinicians experienced in the diagnosis and management of children with HIV infection; public health physicians; representatives from the American Academy of Pediatrics, the Council of State and Territorial Epidemiologists, the Association for Maternal Child Health and Crippled Children's Programs, the National Institute on Drug Abuse/Alcohol, Drug Abuse and Mental Health Administration, the National Institute of Allergy and Infectious Diseases/National Institutes of Health, and the Division of Maternal and Child Health/Health Resources and Services Administration; and CDC.

GOALS AND OBJECTIVES OF THE CLASSIFICATION SYSTEM

The system was designed primarily for public health purposes, including epidemiologic studies, disease surveillance, prevention programs, and health-care planning and policy. The panel attempted to devise a simple scheme that could be subdivided as needed for different purposes.

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HIV Infection -- Continued

DEFINITION OF HIV INFECTION IN CHILDREN (Table 1)

Ideally, HIV infection in children is identified by the presence of the virus in blood or tissues, confirmed by culture or other laboratory detection methods. However, current tests—including culture—for detecting the virus or its antigens are not standardized and are not readily available. Detection of specific antibody to the virus is a sensitive and specific indicator of HIV infection in adults, since the majority of adults with antibody have had culture evidence of infection (*8-10*). Similar studies involving children have not been reported. Also, the presence of passively transferred maternal antibody in infants limits the interpretation of a positive antibody test result in this age group. Most of the consultants believed that passively transferred maternal HIV antibody could sometimes persist for up to 15 months. For this reason, two definitions for infection in children are needed: one for infants and children up to 15 months of age who have been exposed to their infected mothers perinatally, and another for older children with perinatal infection and for infants and children of all ages acquiring the virus through other means.

Infants and children under 15 months of age with perinatal infection—Infection in infants and children up to 15 months of age who were exposed to infected mothers in the perinatal period may be defined by one or more of the following: 1) the identification of the virus in blood or tissues, 2) the presence of HIV antibody as indicated by a repeatedly reactive screening test (e.g., enzyme immunoassay) plus a positive confirmatory test (e.g., Western blot, immunofluorescence assay) in an infant or child who has abnormal immunologic test results indicating both humoral and cellular immunodeficiency (increased immunoglobulin levels, depressed T4 [T-helper] absolute cell count, absolute lymphopenia, decreased T4/T8 ratio) and who meets the requirements of one or more of the subclasses listed under class P-2 (described below), or 3) the confirmation that a child's symptoms meet the previously published CDC case definition for pediatric AIDS (*1,2*).

The infection status of other perinatally exposed seropositive infants and children up to 15 months of age who lack one of the above immunologic or clinical criteria is indeterminate. These infants should be followed up for HIV-related illness, and they should be tested at regu-

TABLE 1. Summary of the definition of HIV infection in children

Infants and children under 15 months of age with perinatal infection

1) Virus in blood or tissues
   or
2) HIV antibody
   and
   evidence of both cellular and humoral immune deficiency
   and
   one or more categories in Class P-2
   or
3) Symptoms meeting CDC case definition for AIDS

Older children with perinatal infection and children with HIV infection acquired through other modes of transmission

1) Virus in blood or tissues
   or
2) HIV antibody
   or
3) Symptoms meeting CDC case definition for AIDS

HIV Infection — Continued

lar intervals for persistence of antibody to HIV. Infants and children who become seronegative, are virus-culture negative (if blood or tissue samples are cultured), and continue to have no clinical or laboratory-confirmed abnormalities associated with HIV infection are unlikely to be infected.

Older children with perinatal infection and children with HIV infection acquired through other modes of transmission—HIV infection in these children is defined by one or more of the following: 1) the identification of virus in blood or tissues, 2) the presence of HIV antibody (positive screening test plus confirmatory test) regardless of whether immunologic abnormalities or signs or symptoms are present, or 3) the confirmation that the child's symptoms meet the previously published CDC case definition for pediatric AIDS (*1,2*).

These definitions apply to children under 13 years of age. Persons 13 years of age and older should be classified according to the adult classification system (*3*).

CLASSIFICATION SYSTEM (Table 2)

Children fulfilling the definition of HIV infection discussed above may be classified into one of two mutually exclusive classes based on the presence or absence of clinical signs and symptoms (Table 2). Class Pediatric-1 (P-1) is further subcategorized on the basis of the presence or absence of immunologic abnormalities, whereas Class P-2 is subdivided by specific disease patterns. Once a child has signs and symptoms and is therefore classified in P-2, he or she should not be reassigned to class P-1 if signs and symptoms resolve.

Perinatally exposed infants and children whose infection status is indeterminate are classified into class P-0.

Class P-0. Indeterminate infection. Includes perinatally exposed infants and children up to 15 months of age who cannot be classified as definitely infected according to the above definition but who have antibody to HIV, indicating exposure to a mother who is infected.

Class P-1. Asymptomatic infection. Includes patients who meet one of the above defini-

TABLE 2. Summary of the classification of HIV infection in children under 13 years of age

Class P-0. Indeterminate infection

Class P-1. Asymptomatic infection

- Subclass A. Normal immune function
- Subclass B. Abnormal immune function
- Subclass C. Immune function not tested

Class P-2. Symptomatic infection

- Subclass A. Nonspecific findings
- Subclass B. Progressive neurologic disease
- Subclass C. Lymphoid interstitial pneumonitis
- Subclass D. Secondary infectious diseases
  - Category D-1. Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS
  - Category D-2. Recurrent serious bacterial infections
  - Category D-3. Other specified secondary infectious diseases
- Subclass E. Secondary cancers
  - Category E-1. Specified secondary cancers listed in the CDC surveillance definition for AIDS
  - Category E-2. Other cancers possibly secondary to HIV infection
- Subclass F. Other diseases possibly due to HIV infection

HIV Infection – Continued

tions for HIV infection but who have had no previous signs or symptoms that would have led to classification in Class P-2.

These children may be subclassified on the basis of immunologic testing. This testing should include quantitative immunoglobulins, complete blood count with differential, and T-lymphocyte subset quantitation. Results of functional testing of lymphocytes (mitogens, such as pokeweed) may also be abnormal in HIV-infected children, but it is less specific in comparison with immunoglobulin levels and lymphocyte subset analysis, and it may be impractical.

Subclass A - Normal immune function. Includes children with no immune abnormalities associated with HIV infection.

Subclass B - Abnormal immune function. Includes children with one or more of the commonly observed immune abnormalities associated with HIV infection, such as hypergammaglobulinemia, T-helper (T4) lymphopenia, decreased T-helper/T-suppressor (T4/T8) ratio, and absolute lymphopenia. Other causes of these abnormalities must be excluded.

Subclass C - Not tested. Includes children for whom no or incomplete (see above) immunologic testing has been done.

Class P-2. Symptomatic infection. Includes patients meeting the above definitions for HIV infection and having signs and symptoms of infection. Other causes of these signs and symptoms should be excluded. Subclasses are defined based on the type of signs and symptoms that are present. Patients may be classified in more than one subclass.

Subclass A - Nonspecific findings. Includes children with two or more unexplained nonspecific findings persisting for more than 2 months, including fever, failure-to-thrive or weight loss of more than 10% of baseline, hepatomegaly, splenomegaly, generalized lymphadenopathy (lymph nodes measuring at least 0.5 cm present in two or more sites, with bilateral lymph nodes counting as one site), parotitis, and diarrhea (three or more loose stools per day) that is either persistent or recurrent (defined as two or more episodes of diarrhea accompanied by dehydration within a 2-month period).

Subclass B - Progressive neurologic disease. Includes children with one or more of the following progressive findings: 1) loss of developmental milestones or intellectual ability, 2) impaired brain growth (acquired microcephaly and/or brain atrophy demonstrated on computerized tomographic scan or magnetic resonance imaging scan), or 3) progressive symmetrical motor deficits manifested by two or more of these findings: paresis, abnormal tone, pathologic reflexes, ataxia, or gait disturbance.

Subclass C - Lymphoid interstitial pneumonitis. Includes children with a histologically confirmed pneumonitis characterized by diffuse interstitial and peribronchiolar infiltration of lymphocytes and plasma cells and without identifiable pathogens, or, in the absence of a histologic diagnosis, a chronic pneumonitis—characterized by bilateral reticulonodular interstitial infiltrates with or without hilar lymphadenopathy—present on chest X-ray for a period of at least 2 months and unresponsive to appropriate antimicrobial therapy. Other causes of interstitial infiltrates should be excluded, such as tuberculosis, *Pneumocystis carinii* pneumonia, cytomegalovirus infection, or other viral or parasitic infections.

Subclass D - Secondary infectious diseases. Includes children with a diagnosis of an infectious disease that occurs as a result of immune deficiency caused by infection with HIV.

Category D-1. Includes patients with secondary infectious disease due to one of the specified infectious diseases listed in the CDC surveillance definition for AIDS: *Pneumocystis carinii* pneumonia; chronic cryptosporidiosis; disseminated toxoplasmosis with onset after 1 month of age; extra-intestinal strongyloidiasis; chronic isosporiasis; candidiasis (esophageal, bronchial, or pulmonary); extrapulmonary cryptococco-

HIV Infection – Continued

sis; disseminated histoplasmosis; noncutaneous, extrapulmonary, or disseminated mycobacterial infection (any species other than leprae); cytomegalovirus infection with onset after 1 month of age; chronic mucocutaneous or disseminated herpes simplex virus infection with onset after 1 month of age; extrapulmonary or disseminated coccidioidomycosis; nocardiosis; and progressive multifocal leukoencephalopathy.

Category D-2. Includes patients with unexplained, recurrent, serious bacterial infections (two or more within a 2-year period) including sepsis, meningitis, pneumonia, abscess of an internal organ, and bone/joint infections.

Category D-3. Includes patients with other infectious diseases, including oral candidiasis persisting for 2 months or more, two or more episodes of herpes stomatitis within a year, or multidermatomal or disseminated herpes zoster infection.

Subclass E - Secondary cancers. Includes children with any cancer described below in categories E-1 and E-2.

Category E-1. Includes patients with the diagnosis of one or more kinds of cancer known to be associated with HIV infection as listed in the surveillance definition of AIDS and indicative of a defect in cell-mediated immunity: Kaposi's sarcoma, B-cell non-Hodgkin's lymphoma, or primary lymphoma of the brain.

Category E-2. Includes patients with the diagnosis of other malignancies possibly associated with HIV infection.

Subclass F - Other diseases. Includes children with other conditions possibly due to HIV infection not listed in the above subclasses, such as hepatitis, cardiopathy, nephropathy, hematologic disorders (anemia, thrombocytopenia), and dermatologic diseases.

Reported by: AIDS Program, Center for Infectious Diseases, CDC.

Editorial Note: This classification system is based on present knowledge and understanding of pediatric HIV infection and may need to be revised as new information becomes available. New diagnostic tests, particularly antigen detection tests and HIV-specific IgM tests, may lead to a better definition of HIV infection in infants and children. Information from several natural history studies currently under way may necessitate changes in the subclasses based on clinical signs and symptoms.

A definitive diagnosis of HIV infection in perinatally exposed infants and children under 15 months of age can be difficult. The infection status of these HIV-seropositive infants and children who are asymptomatic without immune abnormalities cannot be determined unless virus culture or other antigen-detection tests are positive. Negative virus cultures do not necessarily mean the child is not infected, since the sensitivity of the culture may be low. Decreasing antibody titers have been helpful in diagnosing other perinatal infections, such as toxoplasmosis and cytomegalovirus. However, the pattern of HIV-antibody production in infants is not well defined. At present, close follow-up of these children (Class P-0) for signs and symptoms indicative of HIV infection and/or persistence of HIV antibody is recommended.

The parents of children with HIV infection should be evaluated for HIV infection, particularly the mother. The child is often the first person in such families to become symptomatic. When HIV infection in a child is suspected, a careful history should be taken to elicit possible risk factors for the parents and the child. Appropriate laboratory tests, including HIV serology, should be offered. If the mother is seropositive, other children should be evaluated regarding their risk of perinatally acquired infection. Intrafamilial transmission, other than perinatal or sexual, is extremely unlikely. Identification of other infected family members allows for appropriate medical care and prevention of transmission to sexual partners and future children (*11,12*).

HIV Infection – Continued

The nonspecific term AIDS-related complex has been widely used to describe symptomatic HIV-infected children who do not meet the CDC case definition for AIDS. This classification system categorizes these children more specifically under Class P-2.

The development and publication of this classification system does not imply any immediate change in the definition of pediatric AIDS used by CDC for reporting purposes (*1,2*). Changes in this definition require approval by state and local health departments. However, changes in the definition for reporting cases have been proposed by CDC and are awaiting state and local approval.

Written comments are encouraged. They should be mailed to the AIDS Program, Center for Infectious Diseases, Centers for Disease Control, Atlanta, GA 30333.

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MORBIDITY AND MORTALITY WEEKLY REPORT

Current Trends

Education and Foster Care of Children Infected with Human T-Lymphotropic Virus Type III/ Lymphadenopathy-Associated Virus

The information and recommendations contained in this document were developed and compiled by CDC in consultation with individuals appointed by their organizations to represent the Conference of State and Territorial Epidemiologists, the Association of State and Territorial Health Officers, the National Association of County Health Officers, the Division of Maternal and Child Health (Health Resources and Services Administration), the National Association for Elementary School Principals, the National Association of State School Nurse Consultants, the National Congress of Parents and Teachers, and the Children's Aid Society. The consultants also included the mother of a child with acquired immunodeficiency syndrome (AIDS), a legal advisor to a state education department, and several pediatricians who are experts in the field of pediatric AIDS. This document is made available to assist state and local health and education departments in developing guidelines for their particular situations and locations.

These recommendations apply to all children known to be infected with human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV). This includes children with AIDS as defined for reporting purposes (Table 1); children who are diagnosed by their physicians as having an illness due to infection with HTLV-III/LAV but who do not meet the case definition; and children who are asymptomatic but have virologic or serologic evidence of infection with HTLV-III/LAV. These recommendations do not apply to siblings of infected children unless they are also infected.

BACKGROUND

The Scope of the Problem. As of August 20, 1985, 183 of the 12,599 reported cases of AIDS in the United States were among children under 18 years of age. This number is expected to double in the next year. Children with AIDS have been reported from 23 states, the District of Columbia, and Puerto Rico, with 75% residing in New York, California, Florida, and New Jersey.

The 183 AIDS patients reported to CDC represent only the most severe form of HTLV-III/LAV infection, i.e., those children who develop opportunistic infections or malignancies (Table 1). As in adults with HTLV-III/LAV infection, many infected children may have milder illness or may be asymptomatic.

Legal Issues. Among the legal issues to be considered in forming guidelines for the education and foster care of HTLV-III/LAV-infected children are the civil rights aspects of public

HTLV-III/LAV – Continued

TABLE 1. Provisional case definition for acquired immunodeficiency syndrome (AIDS) surveillance of children

For the limited purposes of epidemiologic surveillance, CDC defines a case of pediatric acquired immunodeficiency syndrome (AIDS) as a child who has had:

1. A reliably diagnosed disease at least moderately indicative of underlying cellular immunodeficiency, and
2. No known cause of underlying cellular immunodeficiency or any other reduced resistance reported to be associated with that disease.

The diseases accepted as sufficiently indicative of underlying cellular immunodeficiency are the same as those used in defining AIDS in adults. In the absence of these opportunistic diseases, a histologically confirmed diagnosis of chronic lymphoid interstitial pneumonitis will be considered indicative of AIDS unless test(s) for HTLV-III/LAV are negative. Congenital infections, e.g., toxoplasmosis or herpes simplex virus infection in the first month after birth or cytomegalovirus infection in the first 6 months after birth must be exluded.

Specific conditions that must be excluded in a child are:

1. Primary immunodeficiency diseases—severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia, graft versus host disease, neutropenia, neutrophil function abnormality, agammaglobulinemia, or hypogammaglobulinemia with raised IgM.
2. Secondary immunodeficiency associated with immunosuppressive therapy, lymphoreticular malignancy, or starvation.

school attendance, the protections for handicapped children under 20 U.S.C. 1401 et seq. and 29 U.S.C. 794, the confidentiality of a student's school record under state laws and under 20 U.S.C. 1232g, and employee right-to-know statutes for public employees in some states.

Confidentiality Issues. The diagnosis of AIDS or associated illnesses evokes much fear from others in contact with the patient and may evoke suspicion of life styles that may not be acceptable to some persons. Parents of HTLV-III/LAV-infected children should be aware of the potential for social isolation should the child's condition become known to others in the care or educational setting. School, day-care, and social service personnel and others involved in educating and caring for these children should be sensitive to the need for confidentiality and the right to privacy in these cases.

ASSESSMENT OF RISKS

Risk Factors for Acquiring HTLV-III/LAV Infection and Transmission. In adults and adolescents, HLTV-III/LAV is transmitted primarily through sexual contact (homosexual or heterosexual) and through parenteral exposure to infected blood or blood products. HTLV-III/LAV has been isolated from blood, semen, saliva, and tears but transmission has not been documented from saliva and tears. Adults at increased risk for acquiring HTLV-III/LAV include homosexual/bisexual men, intravenous drug abusers, persons transfused with contaminated blood or blood products, and sexual contacts of persons with HTLV-III/LAV infection or in groups at increased risk for infection.

The majority of infected children acquire the virus from their infected mothers in the perinatal period (*1-4*). In utero or intrapartum transmission are likely, and one child reported from Australia apparently acquired the virus postnatally, possibly from ingestion of breast milk (*5*). Children may also become infected through transfusion of blood or blood products that contain the virus. Seventy percent of the pediatric cases reported to CDC occurred among children whose parent had AIDS or was a member of a group at increased risk of acquiring HTLV-III/LAV infection; 20% of the cases occurred among children who had received blood or blood products; and for 10%, investigations are incomplete.

HTLV-III/LAV – Continued

Risk of Transmission in the School, Day-Care or Foster-Care Setting. None of the identified cases of HTLV-III/LAV infection in the United States are known to have been transmitted in the school, day-care, or foster-care setting or through other casual person-to-person contact. Other than the sexual partners of HTLV-III/LAV-infected patients and infants born to infected mothers, none of the family members of the over 12,000 AIDS patients reported to CDC have been reported to have AIDS. Six studies of family members of patients with HTLV-III/LAV infection have failed to demonstrate HTLV-III/LAV transmission to adults who were not sexual contacts of the infected patients or to older children who were not likely at risk from perinatal transmission (*6-11*).

Based on current evidence, casual person-to-person contact as would occur among schoolchildren appears to pose no risk. However, studies of the risk of transmission through contact between younger children and neurologically handicapped children who lack control of their body secretions are very limited. Based on experience with other communicable diseases, a theoretical potential for transmission would be greatest among these children. It should be emphasized that any theoretical transmission would most likely involve exposure of open skin lesions or mucous membranes to blood and possibly other body fluids of an infected person.

Risks to the Child with HTLV-III/LAV Infection. HTLV-III/LAV infection may result in immunodeficiency. Such children may have a greater risk of encountering infectious agents in a school or day-care setting than at home. Foster homes with multiple children may also increase the risk. In addition, younger children and neurologically handicapped children who may display behaviors such as mouthing of toys would be expected to be at greater risk for acquiring infections. Immunodepressed children are also at greater risk of suffering severe complications from such infections as chickenpox, cytomegalovirus, tuberculosis, herpes simplex, and measles. Assessment of the risk to the immunodepressed child is best made by the child's physician who is aware of the child's immune status. The risk of acquiring some infections, such as chickenpox, may be reduced by prompt use of specific immune globulin following a known exposure.

RECOMMENDATIONS

1. Decisions regarding the type of educational and care setting for HTLV-III/LAV-infected children should be based on the behavior, neurologic development, and physical condition of the child and the expected type of interaction with others in that setting. These decisions are best made using the team approach including the child's physician, public health personnel, the child's parent or guardian, and personnel associated with the proposed care or educational setting. In each case, risks and benefits to both the infected child and to others in the setting should be weighed.
2. For most infected school-aged children, the benefits of an unrestricted setting would outweigh the risks of their acquiring potentially harmful infections in the setting and the apparent nonexistent risk of transmission of HTLV-III/LAV. These children should be allowed to attend school and after-school day-care and to be placed in a foster home in an unrestricted setting.
3. For the infected preschool-aged child and for some neurologically handicapped children who lack control of their body secretions or who display behavior, such as biting, and those children who have uncoverable, oozing lesions, a more restricted environment is advisable until more is known about transmission in these settings. Children infected with HTLV-III/LAV should be cared for and educated in settings that minimize exposure of other children to blood or body fluids.

HTLV-III/LAV – Continued

4. Care involving exposure to the infected child's body fluids and excrement, such as feeding and diaper changing, should be performed by persons who are aware of the child's HTLV-III/LAV infection and the modes of possible transmission. In any setting involving an HTLV-III/LAV-infected person, good handwashing after exposure to blood and body fluids and before caring for another child should be observed, and gloves should be worn if open lesions are present on the caretaker's hands. Any open lesions on the infected person should also be covered.
5. Because other infections in addition to HTLV-III/LAV can be present in blood or body fluids, all schools and day-care facilities, regardless of whether children with HTLV-III/LAV infection are attending, should adopt routine procedures for handling blood or body fluids. Soiled surfaces should be promptly cleaned with disinfectants, such as household bleach (diluted 1 part bleach to 10 parts water). Disposable towels or tissues should be used whenever possible, and mops should be rinsed in the disinfectant. Those who are cleaning should avoid exposure of open skin lesions or mucous membranes to the blood or body fluids.
6. The hygienic practices of children with HTLV-III/LAV infection may improve as the child matures. Alternatively, the hygienic practices may deteriorate if the child's condition worsens. Evaluation to assess the need for a restricted environment should be performed regularly.
7. Physicians caring for children born to mothers with AIDS or at increased risk of acquiring HTLV-III/LAV infection should consider testing the children for evidence of HTLV-III/LAV infection for medical reasons. For example, vaccination of infected children with live virus vaccines, such as the measles-mumps-rubella vaccine (MMR), may be hazardous. These children also need to be followed closely for problems with growth and development and given prompt and aggressive therapy for infections and exposure to potentially lethal infections, such as varicella. In the event that an antiviral agent or other therapy for HTLV-III/LAV infection becomes available, these children should be considered for such therapy. Knowledge that a child is infected will allow parents and other caretakers to take precautions when exposed to the blood and body fluids of the child.
8. Adoption and foster-care agencies should consider adding HTLV-III/LAV screening to their routine medical evaluations of children at increased risk of infection before placement in the foster or adoptive home, since these parents must make decisions regarding the medical care of the child and must consider the possible social and psychological effects on their families.
9. Mandatory screening as a condition for school entry is not warranted based on available data.
10. Persons involved in the care and education of HTLV-III/LAV-infected children should respect the child's right to privacy, including maintaining confidential records. The number of personnel who are aware of the child's condition should be kept at a minimum needed to assure proper care of the child and to detect situations where the potential for transmission may increase (e.g., bleeding injury).
11. All educational and public health departments, regardless of whether HTLV-III/LAV-infected children are involved, are strongly encouraged to inform parents, children, and educators regarding HTLV-III/LAV and its transmission. Such education would greatly assist efforts to provide the best care and education for infected children while minimizing the risk of transmission to others.