

# A Manual For The Management of **HIV Infections in Infants, Children and Adolescents**

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## Foreword

This manual was developed in order to provide physicians with a brief guide of the essential and current information for the diagnosis, classification, and management of infants, children, and adolescents who may have or do have HIV infection. A section on prevention was added as an aid to counseling of adolescents and parents on the prevention of sexual transmission of HIV and methods of preventing pregnancy in an HIV infected mother. This is by no means a comprehensive review of HIV infections. For a more comprehensive review of HIV infections in pediatrics, please refer to the references listed at the end of the manual. A clinical practice guideline for **Management and Evaluation of Early HIV Infections** by the Agency for Health Care Policy and Research (AHCPR) in collaboration with AAP can be obtained by writing or calling:

AHCPR HIV Guidelines  
CDC National AIDS Clearinghouse  
P.O. Box 6003  
Rockville, MD 20849-6003  
800-342-2437

A copy of this HIV guideline will be provided free. Also a **Quick Reference Guide** is available. Two brochures for patients and their families are available in both English and Spanish: (1) **Understanding HIV** and (2) **HIV and Your Child**. Multiple copies can be obtained free from the above address.

The diagnosis and management of HIV infection is a very dynamic area of pediatrics, therefore, it will be necessary to refer to the current literature or contact a pediatric infectious disease expert to obtain the latest developments. Information about clinical trials can be obtained by calling 1-800-TRIALS-A (AIDS Clinical Trials Group) or 301-402-0696 (Pediatric Branch, National Cancer Institute).

Misinformation about HIV is very common on television (news and talk shows), in the newspapers, and in the community rumor mill. The CDC AIDS Hot Line, 800-342-2437, can usually provide information to help dispel these erroneous reports.

This manual will be updated frequently. If you desire a current copy, please contact the secretary at 706-774-8985 or send requests to:

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If the information provided herein is of benefit to you as a readily available resource of pediatric HIV infections, then the reward for this effort will have been served.

Stuart Foshee, M.D.

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# I. Epidemiology of Aids in Georgia

## (1981-April 1995)

### A. Total number of cases 12,901 (7,038, 55% Deaths)

Adult Male	11,284	(87.5%)
Women	1,617	(12.5%)
Adolescent (13-19 yrs)	77	(0.6%)

\* Many of the age group 20-29 years were infected as adolescents, 2483 cases (23%)

### B. Race/Ethnicity Adult/Adol Pediatric Total

White (Non-Hispanic)	45%	24%	45%
Black (Non-Hispanic)	53%	75%	54%
Hispanic	1.5%	1%	1.5%
Hispanic	1.5%	1%	1.5% Other

### C. Patient Groups

Adult/Adolescent	Male	Female	TOTAL
Homosexual/Biosexual	62%	0%	54%
IV Drug User	16%	36%	17%
Homo/Bi IDU	7%	0%	6%

Rate in GA: 33/100,000 (3% of U.S. total), 7th in U.S. by rate in 1994 but 8th for total number of cases since 1981. This compares with New York's rate of 75, Fla. 68, and California 38 and national rank of 1st, 3rd, and 6th respectively for total number of AIDS cases for the same time period. Atlanta is 10th in the Nation for cumulative number of cases by cities.

### D. Trends of AIDS in Women (1992): Women are becoming one of the fastest growing groups of people with HIV infection.

#### 1. United States

- Heterosexual transmission accounted for the greater proportion of AIDS cases among women especially aged 20-29 years (60%).
- The annual number of women aged 20-29 years with heterosexually acquired AIDS increased by 97% since 1988 (15.5% increase for males and females), primarily reflects increase among non-Hispanic Black women.
- The greatest increase among women aged 20-29 years with heterosexually acquired AIDS was in the South (165%) since 1988.
- The increase in cases among women aged 20-29 primarily reflects persons who were infected as adolescents.

#### 2. Georgia:

Data from 1993 show one out of 5 Georgia citizens diagnosed with AIDS is a woman (up from 1 in 19 in 1985) and of these, 81% are African American women.

## II. Transmission of HIV Infection

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- A. Infants - Perinatal (15 - 30% of infants born to HIV positive mothers ultimately are infected). In the U.S. approximately 7000 infants are born to HIV-infected mothers each year, 1000-2000 are HIV-infected. See Chapter IX - Prevention of HIV infection for use of Zidovudine prophylaxis during pregnancy to HIV transmission to the fetus.
- Methods of HIV vertical transmission
    - Transplacental: (30-50% of HIV infected infants) Early infection, detection of HIV infection
    - Intrapartum: (50-70% of HIV infected infants) Late infection, detection of HIV infection between 7-90 days of age
    - Breast feeding: Risk of transmission by breast feeding from mothers with established HIV infection prior to pregnancy is 16%. (95% C.I. 8-25%) and 26% (95% C.I. 14-39%) from mothers who develop primary infection postpartum.
  
  - Risk factors for HIV vertical transmission (higher risk)
    - Infant
      - First born higher than second-born twin
      - Prematurity (Birth weight
      - Vaginal delivery
      - Neonatal bacterial infection
      - Breast feeding
    - Mother
      - Lower CD4 counts, advanced HIV disease
      - Lower antibody titer to gp120
      - Previous HIV infected child via vertical transmission
      - Clinical chorioamnionitis
      - Prolonged/complicated labor
      - Continued illicit drug use
- B. Infants and children not exposed in the perinatal period
- Blood Transfusion - unlikely since 1985
  - Blood product administration- unlikely since 1985
  - Sexual abuse/assault - routine screening recommended
- C. Adolescent
- IV drug use
  - Heterosexual/Homosexual

## III. Clinical Manifestations Of Children With Aids

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- A. Features more commonly described in children than in adults
  - Failure to thrive
  - Lymphoid interstitial pneumonia
  - Recurrent bacterial infections
  - Parotitis
- B. Features common to both children and adults
  - Neurologic abnormalities
  - Hepatosplenomegaly
  - Diffuse lymphadenopathy
  - Chronic and/or recurrent diarrhea
  - Chronic and/or recurrent fever
  - Chronic eczematoid rash
  - Opportunistic infections
  - Clubbing of digits
  - Progressive renal disease
  - Cardiomyopathy
  - Hepatitis
- C. Features more commonly described in adults than children
  - Neoplasms (Kaposi sarcoma and lymphoma)
- D. Central Nervous System Features of HIV infection in children
  1. **Common**
    - Acquired and congenital microcephaly
    - Generalized, progressive encephalopathy
    - Presentation with delay of development and function, or with loss of motor and intellectual abilities
  2. **Less Common features**
    - Apathy
    - Paresis
    - Ataxia
    - Pseudobulbar palsy
    - Pyramidal tract signs
    - Extrapyrarnidal rigidity
    - Myoclonus
  3. **Unusual features**
    - Seizures
    - Focal signs and symptoms

## **IV. Clinical Features that Should Prompt Diagnostic Assessment For HIV Infection**

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- Impaired growth/failure to thrive
- Encephalopathy/developmental delay
- Chronic interstitial pneumonia
- Recurrent or persistent infections
- Infection (especially PCP) caused by opportunistic organisms
- Hepatosplenomegaly
- Lymphadenopathy
- Chronic Parotitis
- Thrombocytopenia

## **V. Immunologic Abnormalities In Pediatric Aids**

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### **A. B-Cell Abnormalities**

- Increased immunoglobulin
- Hypogammaglobulinemia
- IgG subclass abnormalities
- Absent class switch from IgM to IgG
- Abnormal proliferative responses to PWM
- Poor primary and secondary antibody responses
- Abnormal isoagglutins
- Presence of circulating immune complexes

### **B. T-Cell Abnormalities**

- Lymphopenia
- Decrease CD4/CD8 ratios
- Decrease mitogenic response to PHA, CON A and specific antigens
- Cutaneous anergy
- Increase circulating thymosin
- Decrease thymulin
- Decreased cytokine production
- Decreased natural killer cell activity

### **C. Phagocytic Abnormalities**

- Leukopenia
- Decrease monocyte adherence production
- Decrease monocyte cytokine production

## **VI. General Laboratory Abnormalities In Pediatric Aids**

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- Thrombocytopenia often responsive to steroids/or IVIG
- Prolongation of activated partial thromboplastin time secondary to circulating anticoagulant
- Coombs positive anemia
- Abnormal liver function tests
- Proteinuria may be the first manifestation of infection and most commonly associated with focal glomerulosclerosis and mesangial hyperplasia with progressive decline in renal function
- Abnormal echocardiogram most often left ventricular dysfunction and pericardial effusion
- Chest radiograph with chronic interstitial changes

## VII. Diagnosis of HIV Infection in Infants, Children and Adolescents

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### A. Test for HIV Antibody

- **HIV Testing of Pregnant Women:** HIV counseling and testing are recommended as the standard of care for all pregnant women.
    - HIV-testing should be offered as early as possible during the prenatal period.
    - If not tested during pregnancy, counseling and testing should be offered to women during the postnatal period.
  - **HIV Testing of Neonates:** HIV antibody testing, accompanied by appropriate counseling of the mother, should also be the **standard of care for neonates** born to mothers who have not received HIV antibody testing during pregnancy or in whom antibody test results are not known to the pediatrician
  - **HIV Infection Status of Neonates:** Infants at risk for HIV infection (mother or infant is HIV-antibody positive) must have a determination of their HIV infection status as soon as possible after birth.
- 
1. **HIV Antibody by EIA:** Highly sensitive (>99%) assays for HIV-1/HIV-2 antibodies. The presence of HIV antibody in an infant born to a mother with HIV infection does not differentiate maternal from infant antibody. Maternal antibody may be detected in the infant until age 12-15 months.
    - a. **HIV-1-EIA:** From 60-91% of HIV-2 infected persons will test repeatedly reactive by HIV-1 EIA. A repeatedly reactive test must be tested by the Western blot assay or by IFA to HIV-1 before reporting.
    - b. **HIV-2-EIA:** HIV-2 infection is rare in the U.S. except in travelers from West Africa or persons who have had sexual contact with West Africans infected HIV-2. A repeatedly reactive test must be confirmed by a supplemental test at the state laboratory.
    - c. HIV-1/HIV-2 (rDNA) EIA (Abbott Lab): This test has been available since February 1992 and test for both HIV types:
      - **Repeatedly reactive test:** Must do HIV-1 WB or IFA assay.
      - **Repeatedly reactive test with negative or indeterminate WB:** Must do HIV-2 EIA, if repeatedly **reactive** do HIV-2 supplemental test
  2. **Supplemental HIV test:** Any repeatedly reactive HIV-1, HIV-2 or HIV-1/HIV-2 EIA test must be tested by one or more of these supplemental test before reporting:
    - a. **HIV-1 Western Blot Assay:** This assay test for antibodies to specific HIV-1 proteins. This is a highly specific assay.

- **Positive:** A positive HIV-1 WB confirms the presence of antibodies to HIV. Although this does not always distinguish between antibodies to HIV-1 and HIV-2, further testing is not required for routine purposes. If the suspicion of HIV-2 infection (based on epidemiologic risk factors [ see appendix E]) is high, additional testing for HIV-2 is indicated.
  - **Negative:** If the HIV-1 WB is negative, an EIA for HIV-2 only should be performed. If the HIV-2 EIA is repeatedly not reactive, the specimen should be considered negative for HIV antibodies.
  - **Indeterminate:** If the HIV-1 WB is indeterminate, an EIA for HIV-2 only should be performed. If the HIV-2 EIA is repeatedly not reactive, the specimen should be considered indeterminate. Repeat testing is advised in 6 months to exclude the possibility of early HIV-1 infection.
- b. **Immunofluorescent Assay (IFA) for HIV-1 Antibody:**
- **A positive or negative** HIV-1 IFA should be interpreted in the same manner as similar results from the WB test.
  - An **Indeterminate** HIV-1 IFA should first be tested by HIV-1 WB and reported based on its results as above.
- c. Supplement HIV-2 confirmatory test are not currently licensed, therefore those specimens with repeatedly reactivity to HIV-2 EIA must be sent to the state laboratory for further testing. The report will be positive, negative or indeterminate with similar interpretation as for the supplemental test for HIV-1.

## B. Test for HIV Infection Status in Infants

With the use of these tests:

- Approximately 50% of infected infants can be identified at or near birth.
  - Greater than 95% of infected infants can be diagnosed by 3-6 months.
  - At risk infants should have one or more of these tests performed as soon as possible after birth and these test should be repeated between 3-6 months of age.
  - Seropositive infants who do not have a definitive virologic diagnosis of HIV infection should continue to be tested every 3 months by ELISA/WB Assays. After the first year, HIV antibody should be performed at 18 and 24 months of age.
  - **Seroreverter:** A child of an HIV-infected mother who is repeatedly HIV-antibody-negative by 18 months of age and has never had a positive HIV culture/PCR/P24 antigen is considered as a **seroreverter**.
1. **HIV Culture:** Not readily available, large volume of blood required and may require several weeks growth for detection.
  2. **HIV-P24 Antigen Assay:**
    - **Standard Assay:** The P24 Antigen in the serum of infants is bound to maternal HIV antibody. This test is insensitive for the detection of HIV infection in infants.

Less than 20% have detectable P24 antigen 1-6 months of age. It only detects free antigen.

- **ICD-HIV-P24 Assay:** If acid hydrolysis is used to disrupt antigen-antibody complexes in serum, the sensitivity of P24 antigen detection can be increased, and this assay may be a tool for early diagnosis. 100% are positive by 1-3 months of age.
- 3. **HIV-DNA-PCR:** A highly sensitive and specific test for early detection of HIV infection in infants. All infected infants detected by 6 months of age.
- 4. **HIV-IgA Antibody Test:** Maternal IgA antibodies do not cross the placenta, therefore the detection of HIV specific antibodies in the infant serum indicates the presence of HIV infection. This assay is insensitive for the detection of infection in the first 3 months. (17% at one month, 67% at 3 months), but a very sensitive assay in infants 6 months. (94% detected at 6 months, 100% detected 9 months). This assay is not yet commercially available.

### C. Immunologic Test:

To obtain in HIV-infected infants/children/adolescents

1. **Lymphocyte subsets:** CD4, CD8 and CD4/CD8 ratio - Should be performed on all infants born to HIV-infected mothers at 1, 3, and 6 months of age, then every 3-months until HIV status of the child is known. - Should be monitored every 3-6 months in children proven to be HIV-infected.
2. **Quantitative immunoglobulin:** IgG, IgM, IgA
3. **Skin Test:** Candida, Mumps, Tuberculin Skin Test (PPD)

### D. Diagnosis of HIV infection in Children:

Optimally, all infants at risk for HIV infection should be diagnosed by laboratory means well before clinical manifestations of HIV develop.

1. **Diagnosis: HIV Infected**
  - a. A child less than 18 months of age who is known to be HIV seropositive or born to an HIV-infected mother and:
    1. Has positive results on two separate determinations (excluding cord blood) from one or more of the following HIV detection tests:
      - HIV culture
      - HIV - DNA-PCR
      - HIV-P24 Antigen **or**
    2. Meets criteria for AIDS diagnosis based on the 1987 AIDS surveillance definition.
  - b. A child 18 months of age born to an HIV-infected mother or any child infected by blood, blood products, or other known modes of transmission (e.g. sexual contact) who:
    1. Is HIV-antibody positive by repeatedly reactive EIA and confirmatory test (e.g. WB or IFA) **OR**
    2. Meets any of the criteria in 1 above.
2. **Diagnosis: Perinatally Exposed**
  - a. A child who does not meet the criteria above who:
    1. Is HIV seronegative by EIA confirmatory test (e.g., WB or IFA) and is **or**

2. Has unknown antibody status, but was born to a mother known to be infected with HIV.
3. **Diagnosis: Seroreverter (SR)**  
A child who is born to an HIV-infected mother and who:
  - a. Has been documented as HIV-antibody negative (i.e, two or more negative EIA test performed at 6- 18 months of age or one negative EIA test after 18 months of age); **and**
  - b. Has had no other laboratory evidence of infection (has not had two positive viral detection test, if performed); **and**
  - c. Has not had an AIDS-defining condition.
4. **Criteria for HIV Infection for Persons >13 years:**
  - a. Repeat reactive screening test for HIV antibody (e.g. Enzyme Immunoassay) with specific antibody identified by the use of supplemental test (e.g. Western Blot, immunofluorescence assay)
  - b. Direct identification of virus in host tissues by virus isolation.
  - c. HIV antigen detection
  - d. A positive result on any other highly specific licensed test for HIV

## E. Classification of HIV Infection (CDC):

### 1. Pediatric HIV Classification

ImmunologicCategories	Clinical categories			
	N: No signs/symptoms	A: Mild signs/symptoms	B: **Moderate signs/symptoms	C: **Severe signs/symptoms
1: No evidence of suppression	N1	A1	B1	C1
2: Evidence of moderate suppression	N2	A2	B2	C2
3: Severe suppression	N3	A3	B3	C3

- \* Children whose HIV infection status is not confirmed are classified by using the above grid with a letter E (for perinatally exposed) placed before the appropriate classification code (e.g., EN2)
- \*\* Both Category C and lymphoid interstitial pneumonitis in Category B are reportable to state and local health departments as acquired immunodeficiency syndrome.
-

**TABLE 2.** Immunologic categories based on age-specific CD4+ T-lymphocyte counts and percent of total lymphocytes

Immunologic Category	Age of Child					
			1-5 yrs		6-12 yrs	
	μL	(%)	μL	(%)	μL	(%)
1: No evidence of suppression	>1,500	(>25)	>1,000	(>25)	>500	(>25)
2: Evidence of moderate suppression	750-1,499	(15-24)	500-999	(15-24)	200-499	(15-24)
3: Severe suppression	<750	(<15)	<500	(<15)	<200	(<15)

**Box 2. Clinical categories for children with human immunodeficiency virus (HIV) infection**

**Category N: Not Symptomatic**

Children who have no signs or symptoms considered to be the result of HIV infection or who have only one of the conditions listed in Category A.

**Category A: Mildly Symptomatic**

Children with two or more of the conditions listed below but none of the conditions listed in Categories B and C.

- Lymphadenopathy ( 0.5 cm at more than two sites; bilateral= one site)
- Hepatomegaly
- Splenomegaly
- Dermatitis
- Parotitis
- Recurrent or persistent upper respiratory infection, sinusitis, or otitis media

**Category B: Moderately Symptomatic**

Children who have symptomatic conditions or other than those listed for Category A or C that are attributed to HIV infection. Examples of conditions in clinical Category B include but are not limited to:

- Anemia (
- Bacterial meningitis, pneumonia, or sepsis (single episode)
- Candidiasis, oropharyngeal (thrush), persisting (>2 months) in children >6 months of age
- Cardiomyopathy
- Cytomegalovirus infection, with onset before 1 month of age
- Diarrhea, recurrent or chronic

- Hepatitis
- Herpes simplex virus (HSV) stomatitis, recurrent (more than two episodes within 1 year)
- HSV bronchitis, pneumonitis, or esophagitis with onset before 1 month of age
- Herpes zoster (shingles) involving at least two distinct episodes or more than one dermatome
- Leiomyosarcoma
- Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia complex
- Nephropathy
- Nocardiosis
- Persistent fever (lasting >1 month)
- Toxoplasmosis, onset before 1 month of age
- Varicella, disseminated (complicated chickenpox)

### **Category C: Severely Symptomatic**

Children who have any condition listed in the 1987 surveillance case definition for acquired immunodeficiency syndrome (10), with the exception of LIP (Box 3)

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### **Box 3. Conditions included in clinical Category C for children infected with human immunodeficiency virus (HIV)**

#### **Category C: Severely Symptomatic\***

- Serious bacterial infections, multiple or recurrent (i.e., any combination of at least two culture-confirmed infections within a 2-year period), of the following types: septicemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media, superficial skin or mucosal abscesses, and indwelling catheter-related infections).
- Candidiasis, esophageal or pulmonary (bronchi, trachea, lungs)
- Coccidioidomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)
- Cryptococcoses, extra pulmonary
- Cryptosporidiosis or isosporiasis with diarrhea persisting > 1 month
- Cytomegalovirus disease with onset of symptoms at age > 1 month (at site other than liver, spleen, or lymph nodes)
- Encephalopathy (at least one of the following progressive findings present for at least 2 months in the absence of a concurrent illness other than HIV infection that could explain the findings): a) failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard developmental scale or neuropsychological tests; b) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by computerized tomography or magnetic resonance imaging (serial imaging is required for children)
- Herpes simplex virus infection causing a mucocutaneous ulcer that persists for > 1 month; or bronchitis, pneumonitis, or esophagitis for any duration affecting a child > 1 month of age
- Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)
- Kaposi's sarcoma
- Lymphoma, primary, in brain
- Lymphoma, small, noncleaved cell (Burkitt's), or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype
- Mycobacterium tuberculosis, disseminated or extra pulmonary

- Mycobacterium, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- Mycobacterium avium complex or Mycobacterium kansasii, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- Pneumocystis carinii pneumonia
- Progressive multifocal leukoencephalopathy
- Salmonella (nontyphoid) septicemia, recurrent
- Toxoplasmosis of the brain with onset at > 1 month of age
- Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following findings: a) persistent weight loss >10% of baseline OR b) downward crossing of at least two of the following percentile lines on the weight-for-age chart (e.g., 95th, 75th, 50th, 25th, 5th) in a child 1 year of age OR c)

\* See the 1987 AIDS surveillance case definition (10) for diagnosis criteria.

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## 2. Adolescent (> 13 Years) and Adults

- a. **Category A:** Consists of one or more of the conditions listed below in an adolescent or adult (13 years) with documented HIV infection. Conditions listed in Categories B and C must not have occurred.
  - Asymptomatic HIV infection
  - Persistent generalized lymphadenopathy
  - Accompanying illness or history of acute HIV infection
- b. **Category B:** Consists of symptomatic conditions in an HIV infected adolescent or adult that are not included among conditions listed in clinical Category C and that meet at least one of the following criteria:
  1. The conditions are attributed to HIV infection or are indicative of a defect in cell-mediated immunity, or
  2. The conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infections.

Examples of conditions in clinical Category B include **but are not limited to:**

- Bacillary angiomatosis
- Candidiasis, oropharyngeal (thrush)
- Candidiasis, vulvovaginal; persistent, frequent or poorly responsive to therapy
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Constitutional symptoms, such as fever (38.5 C) or diarrhea lasting > 1 month
- Hairy leukoplakia, oral
- Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome
- Idiopathic thrombocytopenia purpura
- Listeriosis
- Pelvic inflammatory disease, particularly if complicated by tubo-ovarian abscess
- Peripheral Neuropathy - For classification purposes,
- Category B conditions take precedence over those in Category A.
- For example, someone previously treated for oral or persistent vaginal candidiasis (and who has not developed a Category C disease) but who is non asymptomatic, should be classified in clinical Category B.

**Category C:** Includes the clinical conditions listed in the AIDS surveillance case definition (VII F). For classification purposes, once a Category C condition has occurred, the person will remain in Category C.

1993 Revised Classification system for HIV Infection and Expanded Aids Surveillance Cases Definition for Adolescents and Adults *			
CD4+T-Cell Categories	CLINICAL CATEGORIES		
	(A) Asymptomatic, Acute(primary) HIV or PGL**	(B) Symptomatic, not A or CConditions β	(C) AIDS - indicatorconditions ¶
(1) >500/μL	A1	B1	C1
(2) 200-499/μL	A2	B2	C2
(3)	A3	B3	C3

\* The shaded cells illustrate the expanded AIDS surveillance case definition. Persons with AIDS-indicator conditions (Category C) as well as those with CD4 + T-lymphocyte counts < 200/uL (Categories A3 or B3) will be reportable as AIDS cases in the U.S. and Territories effective January 1, 1993.

\*\* PGL - Persistent generalized lymphadenopathy. Clinical Category A includes acute (primary) HIV infection.

β See VII E, 2b above

¶ See VII F, below

## F. Conditions included in the 1993 Aids Surveillance Case Definition

- Candidiasis of the trachea, bronchi, or lungs
- Candidiasis of the esophagus
- Cervical carcinoma, invasive \*
- Coccidioidomycosis, disseminated or extra pulmonary
- Cryptococcoses, extra pulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, nodes) Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy; HIV related
- Herpes simplex: Chronic ulcer(s) (>1 month duration) or bronchitis, pneumonitis or esophagitis
- Histoplasmosis, disseminated or extra pulmonary
- Isosporiasis, chronic intestinal (>1 month duration)
- Kaposi's sarcoma
- Lymphoma, primary brain
- Lymphoma (immunoblastic or equivalent term)
- Mycobacterium avium complex or Mycobacterium kansasii, disseminated or extra pulmonary
- Mycobacterium tuberculosis, any site, (pulmonary\* or extra pulmonary)
- Mycobacterium, other species or unidentified species disseminated or extra pulmonary
- Pneumocystis carinii pneumonia

- Progressive multifocal leukoencephalopathy
- Pneumonia, recurrent\*
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV

\* Added in the 1993 expansion of the AIDS surveillance case definition

## VIII. Management of Children with HIV Infection

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### A. IV Immunoglobulin

to prevent recurrent bacterial infections 400mg/kg q 3-4 weeks, for congenital or perinatally acquired HIV infection.

- Treatment with IVIG is associated with reduction of bacterial infections and hospitalizations in HIV-infected children. Benefits were also observed in children receiving TMP/SMX for PCP prophylaxis.
- Criteria for institution of IVIG therapy are not well defined but the following are suggested:
  - **Evidence of humoral immune defects**
    - Hypogammaglobulinemia
    - Poor functional antibody development. Defined as lack of antibody development after one or more appropriately administered immunizations.
  - **Significant Recurrent Infections** despite therapy with appropriate antimicrobials. Defined as 2 or more serious infections such as bacterial sepsis, meningitis, or pneumonia in one-year period or less severe infections that do not respond to standard medical interventions.
  - **Measles:** Known high prevalence measles areas with known failure to respond to MMR.
  - **Thrombocytopenia:** (
  - **Chronic Bronchiectasis/Chronic Sinusitis:** IVIG 600mg/kg/dose monthly. In addition to antibiotics and respiratory therapy.

### B. Prophylaxis for *Pneumocystis Carinii* pneumonia (PCP):

- **Initiating PCP Prophylaxis Among HIV-Exposed Infants**

All infants born to HIV-infected women should be started on PCP prophylaxis at 4-6 weeks of age, regardless of their CD4+ count (see table below). Infants who are first identified as being HIV- exposed after 6 weeks of age should be started on prophylaxis at the time of identification. These recommendations are based on the following considerations: a) most cases of PCP among HIV- infected children occur in the first year of life; b) the risk for PCP begins to increase dramatically at age 2 months (when HIV infection cannot yet be reasonably excluded) (see PCP Prophylaxis For Infants 4-12 Months of Age); and c) the reliability of CD4+ counts in predicting which infants are at risk for PCP is relatively low during infancy - particularly among infants < 6 months of age, the age at which the peak incidence of PCP occurs.

- PCP prophylaxis should not be administered to infants **a)** they are at low risk for PCP and **b)** the use of sulfa drugs among infants at this age is not advised because of the potential for adverse drug effects resulting from immature bilirubin metabolism. Additionally, the concurrent use of sulfa drugs among HIV-exposed infants who are receiving Zidovudine during the first 6 weeks of life to prevent perinatal HIV transmission could potentially exacerbate the anemia that some children receiving zidovudine experience. Therefore, to avoid the potential for additional toxicity in such children, prophylaxis should be started at 6 weeks of age, the age at which zidovudine is discontinued.
  
- **PCP Prophylaxis for Infants 4-12 Months of Age**
  - All HIV-infected infants and infants whose infection status has not yet been determined should continue prophylaxis until 12 months of age.
  - PCP prophylaxis should be discontinued among infants in whom HIV infection has been reasonably excluded on the basis of two or more negative viral diagnostic tests (i.e., HIV culture or PCR), both of which are performed at > 1 month of age and one of which is performed at > 4 months of age. In some clinical centers, these viral diagnostic tests are not available. For children who do not have access to such testing, prophylaxis should be continued until 12 months of age unless HIV infection has been excluded on the basis of two or more negative HIV-antibody tests performed at > 6 months of age.
  
- **PCP Prophylaxis for HIV-Infected Children >12 Months of Age**
  - All HIV-infected children >12 months of age should continue to have regular CD4+ monitoring to determine their need for PCP prophylaxis.
  - HIV-infected children and children whose infection status has not been determined should be evaluated at 12 months of age to determine their need for continued PCP prophylaxis.
  - PCP prophylaxis should be continued after 12 months of age for HIV-infected children who have had any CD4+ measurement during the first 12 months of life indicating severe immunosuppression (i.e., a CD4+ count of
  - Children who have received PCP prophylaxis from 12 to 24 months of age should be evaluated again at 24 months of age, and prophylaxis should be continued for those children who have had any CD4+ measurement indicating severe immunosuppression (i.e., a CD4+ count of
  - HIV-infected children > 12 months of age who are not receiving prophylaxis (e.g., whose children whose infection was not identified previously or whose PCP prophylaxis was discontinued) should begin PCP prophylaxis if their CD4+ measurement indicates severe immunosuppression.
  - Initiation or continuation of prophylaxis should also be considered on a case-by-case basis for HIV-infected children > 12 months of age who might otherwise be at risk for PCP, such as children with rapidly declining CD4+ counts or percentages or children with severely symptomatic HIV disease (i.e., Category C conditions).
  
- **Prophylaxis Against PCP Recurrence**
  - HIV-infected children who have had an episode of PCP should receive lifelong PCP prophylaxis to prevent recurrence-regardless of CD4+ measurement or clinical status.

- **Recommended Chemoprophylaxis Regimens**
  - The recommended PCP chemoprophylaxis regimen for children is trimethoprim/Sulfamethoxazole (TMP-SMX) (see dosage below). When initiating TMP-SMX prophylaxis, a baseline complete blood count, differential count, and platelet count should be obtained. These measurements should be repeated monthly while the child is receiving prophylaxis.
  - If TMP-SMX is not tolerated, alternative regimens should be followed. On the basis of recently compiled pharmacokinetics data, the revised recommended dosage of dapsone as an alternative regimen is 2 mg/kg/day. These data indicate that peak serum concentrations for children receiving chronic dosing of dapsone at 1 mg/kg/dose average 1.84 g/mL, compared with average peak concentrations of 4.65 g/mL for adults receiving the standard dose of 100 mg/day (23,24). The increased dose of dapsone is recommended so that peak concentrations will approach concentrations achieved at dosages recommended for adults.
  - PCP prophylaxis is an approved labeling indication by the U.S. Food and Drug Administration for oral TMP-SMX but not for the various other alternative regimens for PCP prophylaxis.
  - TMP-SMX has been shown to substantially reduce the risk for PCP among HIV-infected children. However, clinicians should be aware that some children have developed PCP despite the use of recommended prophylaxis.

**TABLE:** Recommendations for PCP prophylaxis and CD4+ monitoring for human immunodeficiency virus (HIV)-exposed infants and HIV-infected children, by age and HIV-infection status.

Age/HIV Infection Status	PCP Prophylaxis	CD4+ Monitoring
Birth to 4-6 wks, HIV exposed	No Prophylaxis	1 Month
4-6 wks to 4 mos, HIV exposed	Prophylaxis	3 months
4-12 Mos		
HIV infected or indeterminate	Prophylaxis	6,9 and 12 months
HIV Infection reasonably excluded*	No Prophylaxis	None
1-5 years, HIV Infected	Prophylaxis if:	Every 3-4 months <sup>+</sup>
	CD4+ count is	
	CD4+ percentage is	
6-12 years, HIV infected	Prophylaxis if:	Every 3-4 months <sup>+</sup>
	CD4+ count is	
	CD4+ percentage is <15%¶	

\*HIV infection can be reasonably excluded among children who have had two or more negative HIV diagnostic tests (i.e., HIV culture or PCR), both of which are performed at > 1 month of age and one of which is performed at > 4 months of age, or two or more negative HIV IgG antibody tests performed at >6 months of age among children who have no clinical evidence of HIV disease.

\*More frequent monitoring (e.g., monthly) is recommended for children whose CD4+ counts or percentage are approaching the threshold at which prophylaxis is recommended.

βChildren 1-2 years of age who were receiving PCP prophylaxis and had a CD4+ count of

¶Prophylaxis should be considered on a case-by-case basis for children who might otherwise be at risk for PCP, such as children with rapidly declining CD4+ counts or percentages or children with Category C conditions. Children who have had PCP should receive lifelong PCP prophylaxis.

#### 5. **Recommended Regimens:**

**Trimethoprim/Sulfamethoxazole:** 75mg TMP/M2 BID or 150mg TMP/M2/d divided BID for three consecutive days per week (Monday, Tuesday, Wednesday).

#### 6. **Acceptable alternative TMP/SMX dosage schedule:**

- a. 150mg TMP/M2/day administered orally as a single daily dose 3 times per week on consecutive days (Monday, Tuesday, Wednesday).
- b. 150mg TMP/M2/day orally divided B.I.D. and administered 7 days per week.
- c. 150mg TMP/M2/day administered orally divided B.I.D. and administered 3 times per week on alternate days (Monday, Wednesday, Friday)

#### 7. **Alternative regimens, if TMP-SMX not tolerated:**

- a. **Dapsone:** ( 1 month of age) 2mg/kg ( 4 increasing doses over 2 weeks until 2 mg/kg/day is reached, not to exceed 100mg) given orally once daily (Tablets 25mg scored and 100mg scored can be crushed and given with food). An investigational dapsone syrup (2 mg/ml) is available from Jacobus Pharmaceutical Company, Inc. (Tel. 609-921- 7447). Locally prepared liquid can be made in cherry syrup with crushed tablets. Alcohol should not be used in preparing the liquid. Tips on preparing the liquid from tablets can be obtained from the company.
- b. **Aerosolized Pentamidine** ( 5 years of age) 300mg given via Respirgard II jet nebulizer (Marquest, Englewood, Co) monthly.
- c. **Intravenous Pentamidine** 4mg/kg given every 2-4 weeks.
- d. **Atovaquone (Mepron®)** - only available in suspension 750mg/5ml. Limited experience in adults for PCP prophylaxis. Limited experience in infants and children (3 months to 13 years). Only safety and pharmacokinetic studies performed for pediatric age group. It may hold promise for use in pediatric patients. It has less adverse effects than TMP-SMX in adults. The prophylactic use of the micro fine suspension of Atovaquone for PCP is currently under investigation. The dosage of Mepron being studied is 30 mg/kg/day plus Azithromycin (5mg/kg/day). It is manufactured by Burroughs Wellcome Co.

### **C. Immunizations, Active:**

1. Do give **Hepatitis B vaccine** either for maternal Hepatitis B (HBs Ag Positive) exposure or as non-exposure.

2. Do give **DTP** or **DTaP** (at 18 months and older).
3. Do give **Inactivated Polio Vaccine (IPV)** to all HIV exposed infants. DO NOT give OPV to HIV maternally exposed child, regardless if child is determined to be infected or not infected. **DO NOT** give **OPV** to family members of maternally HIV exposed or infected child.
4. Do give **Hemophilus Influenzae type b (Hib) vaccine**.
5. Do give **MMR** at 15 months of age and at age 5 years (prior to school entry) or age 11-12 years (prior to middle school entry).
6. Do give **Influenza A & B vaccine** for children over 6 months of age annually. The first year they get the vaccine give 2 does (one month apart) until age 9 years. Subsequent years give one dose. Use the subvirion (split virus) vaccine for children < 13 years: 6 months - 35 months: dose = 0.25 ml IM 3 years: dose = 0.5 ml IM
7. Do give **Pneumococcal vaccine** to HIV infected children at 2 years and older.
8. Do not give varicella vaccine. Varicella vaccine can be safely administered to non HIV-infected siblings. If the vaccine recipient develops vaccine associated cutaneous lesion, contact with HIV infected individuals in the household should be avoided.

#### D. Immunizations, Passive:

1. **Varicella Zoster Virus Exposure**
  - Give VZIG 125 units (1 vial, 1.25 ml) for each 10 kg of body weight. The maximum dose is 625 unites (5 vials). Give VZIG within 48 hours of exposure and preferably not more than 96 hours after exposure.
  - Children receiving IVIG routinely should receive VZIG if the last dose of IVIG was more than 14 days from administration of the IVIG.
2. **Measles Exposure**
  - All HIV infected children should receive prophylaxis with Immune Globulin (IG) after exposure to measles, whether or not they have been vaccinated against measles. IG can prevent or modify measles in a susceptible person within 6 days of exposure.
  - **Immunoglobulin Doses:**
    - **IG** 0.5 ml/kg/dose IM, maximum 15 ml for HIV-infected. Non-immune contacts in the family who are not HIV-infected should r receive IG 0.25ml/kg/ dose IM.
    - **IVIG:** 400 mg/kg/dose. If patient is receiving IVIG at regular intervals and the last dose was within 2-3 weeks of exposure, then further IVIG is not necessary.

#### E. Antiretroviral Therapy:

Combination Antiretroviral therapy is the recommended initial therapy for all patients with HIV infection who meet one of the criteria below. ZDV and ddl or 3TC + ZDV is the two combinations studied. Information about clinical trials can be obtained by calling 1-800-TRIALS-A (AIDS Clinical Trials Group) or (301) 402-0696 (Pediatric Branch, National Cancer Institute).

##### CD4 Lymphocyte criteria for instituting Antiretroviral therapy:

	CD4% CD4/mm <sup>3</sup>	
	<30	<1750
1-2 years	<25	<1000
2-6 years	<20	<750
>6 years	<20	<500

- Clinical criteria for instituting Antiretroviral therapy:
  - Symptomatic HIV infection regardless of CD4 count.
  - AIDS - defining opportunistic infections.
  - Wasting syndrome or failure to thrive.
  - Progressive encephalopathy attributable to HIV.
  - HIV associated malignancy.
  - Recurrent septicemia or meningitis (two or more episodes).
  - Thrombocytopenia (<sup>3</sup>).
  - Hypogammaglobulinemia (Total IgG, IgM, IgA, <sup>3</sup>).
  - The presence of any of the following clinical conditions (independent of the CD4 count):
    - Lymphoid interstitial pneumonitis/or parotitis
    - Splenomegaly.
    - Oral candidiasis that persists >1 month or is recurrent despite appropriate therapy.
    - Diarrhea, unexplained, and persistent (3 or more stools/day for 2 weeks or longer) or recurrent (2 or more episodes of diarrhea accompanied by dehydration within a 2 month period).
    - The presence of symptomatic cardiomyopathy that requires specific intervention.
    - Nephrotic syndrome (other causes ruled out).
    - Severe hepatic transaminitis (>5 fold normal).
  - Other causes ruled out.
    - Chronic bacterial infections: i.e., sinusitis or pneumonia.
    - Two or more HSV or VZ infections within 1-year period.
    - Neutropenia (<sup>3</sup>)
    - Anemia for age (repeated 2 times in one week).
- Suggested management plan and monitoring schedule for children receiving retro viral therapy.
  - History and PE: monthly.
  - CBC, Diff, Platelet Count: Baseline, q 2 weeks x 2, then monthly.
  - Chemistries/LFT's: Baseline, q 4 weeks x 3, then q 3 months.
  - Lymphocyte Subsets: Baseline, q 4 weeks x 3, then q 3 months.
  - P24 Antigen: Baseline, q 4 weeks x 3, then q 3 months.
  - Urinalysis: Baseline, then q 6 months.
  - IgG, IgM, IgA: Baseline, then q 6 months.
  - Chest x-ray: Baseline, then every 9-12 months (repeat as needed).
  - EKG: Baseline, repeat as needed to monitor cardiac symptoms.
  - CT or MRI: Baseline (if evidence of developmental delay or CNS disease), then repeat as needed.

1. **Zidovudine (Retrovir®, ZDV, AZT):**

0-2 weeks of age: 2mg/kg q6h

2-4 weeks of age: 3mg/kg q6h

4 weeks - 13 years: 180mg/M<sup>2</sup> q6h.

(May be effective in doses as low as 120mg/M<sup>2</sup>/q6h.)

Adolescents > 13 years: 100mg q4h for 5 doses.

Supplied as liquid (10mg/ml) and tablets (100mg). A strawberry liquid flavor of ZDV is available. The IV ZDV is 2/3 of the P.O. dosage or 120mg/m<sup>2</sup> q6h. Main toxicity is RBC suppression (anemia) and WBC suppression. Adjust dosage downward if either one occurs, the minimal acceptable dosage is 75mg/M<sup>2</sup> q6h.

- **ZDV failure:** defined as progression of HIV disease in a patient who is adherent to therapy, who is tolerant of ZDV and who has received therapy for a minimum of 4-6 months.
  - **Growth failure** (remediable causes ruled out, i.e., inadequate caloric intake, malabsorption, diarrhea, thyroid deficiency)
    - Moving downward > 2 percentile lines from established curve (age/gender specific growth curves for height or weight or weight for height) on two consecutive monthly measurements.
    - A sustained deviation from a parallel curve for children who are below the 5th percentile.
  - **Evidence for CNS disease:** Neuropsychologic behavioral deterioration is defined by decline in at least 2 of the following:
    - Brain Growth\*
    - Cognitive Function\*
    - Clinical Neurologic Function\*
    - \*Criteria for significant decline in these functions are shown in the table in Appendix D
  - **Other clinical and laboratory criteria** merit consideration of, but do not mandate, a change in Antiretroviral therapy:
    - Cardiomyopathy, symptomatic (requiring treatment), non-HIV causes ruled out.
    - Nephrotic syndrome, non-HIV causes ruled out.
    - Significant transaminase elevation (>5-fold normal), non-HIV causes ruled out.
    - Development of an AIDS-defining opportunistic infection.
  - **Changes in CD4 lymphocytes values and P24 Antigen** may be indicative of disease progression and a need to change Antiretroviral therapy, especially in the presence of new HIV-related symptoms. At this time, there is no substantial evidence to support a change in therapy based solely on a worsening of laboratory markers.
- **ZDV Intolerance:**
  - **Anemia:** Hgb. < 8 g/dl, erythropoietin (EPO) may be required. If dosage reduction and EPO do not result in maintenance of Hgb. > 8 g/dl, the patient may receive transfusions or ZDV may be changed to an alternative agent.
  - **Neutropenia:** Absolute neutrophil count of  $< 3$  indicates that ZDV treatment should be stopped. Other drugs with similar hematologic toxicities (TMP/SMX) should be temporarily discontinued.
    - Dapsone may be substituted for TMP/SMX if it appears to be the responsible agent for the neutropenia.
    - If neutrophils increase  $> 500/\text{mm}^3$ , ZDV therapy can be restarted at  $120 \text{ mg}/\text{m}^2 \text{ q6h}$ .
    - If recovery does not occur in one month,, G-CSF should be administered. If the neutrophils increase to  $> 500/\text{mm}^3$  on G-CSF, then restart ZDV at  $120 \text{ mg}/\text{m}^2 \text{ q6h}$ .
    - If neutrophil count cannot be maintained  $> 500/\text{mm}^3$  with G-CSF, then an alternative Antiretroviral regimen is recommended.
  - **Dosages of hemopoietic agents:**
    - **Epoetin Alfa (Epogen®, Procrit®):**  
Use if serum erythropoietin level is 500 mU/ml. Dose is 100 U/kg 3x weekly S.C./IV for 8 weeks. Peak effect 2-3 weeks; reduce dosage when target Hgb. is reached or when Hct increase > 4 points in any 2 week period.

- a. **Increase dose** by 50-100 U/kg 3x weekly if response is not satisfactory by 8 weeks. Maximum dose 300 U/kg 3x weekly. Response should be evaluated every 4-8 weeks.
    - b. **Maintenance Dose:** After target Hct/Hgb. is reached, should reduce the dose by 25%.
  - o **Filgrastim (Neupogen®, G-CSF):**  
5 mcg/kg/dose qd SC/IV for 14 days, or until ANC of 10,000/mm<sup>3</sup>.
    - a. **Increase dose** in 5 mcg/kg increments until ANC of 10,000/mm<sup>3</sup> is reached.
    - b. **Discontinue** when ANC reaches 10,000/mm<sup>3</sup>.
    - c. **Monitor** CBC/Diff twice weekly.
- 2. **Didanosine (Videx®, ddl):** 90 - 135mg/M<sup>2</sup> q12h. Supplied as pediatric oral solution (10mg/ml) or tablets (25mg, 50mg, 100mg, 150mg). To prepare the pediatric oral solution, the pharmacist adds 100 ml or 200 ml of purified water to a 2 gram or 4 gram vial, which will give a concentration of 20mg/ml, then 1/2 of this solution is mixed with 1/2 antacid (Mylanta-DS or Maalox-TC suspensions) to give a final concentration of 10mg/ml. When giving the liquid preparation, it is recommended to give additional antacid (Maalox-TC or Mylanta-DS 10 ml) prior to administration of the drug. If Maalox or Mylanta causes diarrhea, can use Amphogel instead. Primary toxicities are pancreatitis and peripheral neuropathies. Must monitor serum amylase, lipase and neurological examination. Amylase may be elevated in parotid disease but lipase would be normal, being specific for the pancreas. Fractionated amylase will differentiate parotid from pancreatic elevations, however this test is not readily available.
- 3. **Combination Antiretroviral Therapy**
  - a. **Didanosine (Videx®) and Zidovudine (Retrovir®)** therapy is synergistic. The current recommended dosages are:
    - o **Didanosine** 120mg/m<sup>2</sup> BID
    - o **Zidovudine** 160mg/m<sup>2</sup> TID
  - b. **Lamivudine (3TC)** 8mg/kg/day divided BID (investigational) see below, + ZDV 160mg/m<sup>2</sup>/dose TID. Appears to be the superior combination therapy and demonstrates sustained rise in CD4 counts and reduction in the viral load for up to a year or longer.
- 4. **Zalcitabine (HIVID®, DDC):**  
0.01-0.03 mg/kg P.O. q8h. Limited data in its use in children, but thus far peripheral neuropathy has not been seen in children. As a single agent, DDC was inferior to ZDV. Combination therapy with 1 week DDC and 3 weeks ZDV has been used without overlapping toxicities. Other combinations of ZDV, DDI and DDC are under investigation. Available only in tablets: 0.375mg and 0.75mg (film-coated).
- 5. **Stavudine (Zerit™, D4T):** Adults: < 60 kg, 40 mg BID.  
Pediatric: 2-4 mg/kg/day divided BID. Only tablets are available (15 mg, 20 mg, 30 mg, 40 mg). Pediatric liquid is available under open-label study from Bristol-Myers Squibb (800-662-7999). The supplied powder when mixed gives a concentration of 1mg/ml of Stavudine. The primary toxicity is peripheral neuropathy.
- 6. **Lamivudine (3TC):** Investigation drug from Glaxo (800-248-9757). Pediatric liquid is 10mg/ml; dosage is 8mg/kg/day divided BID and is currently recommended to be given in combination with ZDV 160mg/m<sup>2</sup>/dose TID.
- 7. **Protease inhibitors:** The first HIV-1 protease inhibitor, KNI-272, is a tripeptide compound which mimics the natural protein substrate of the HIV protease and is bound

by the viral enzyme. This reaction with KNI-272 prevents the enzyme from cleaving its actual viral protein targets, thus inhibiting a vital step in the HIV replication cycle. The phase I Trials are conducted at the NCI. Contact Ms. Susan Sandelli at (301) 502-1391 for referral information.

## F. Therapy for Specific Infections

### 1. Tuberculosis in HIV Infections: must obtain specimens for cultures.

#### a. Initial

- No drug resistance (contact history): Isoniazid, Rifampin, and Pyrazinamide.
- Possible drug resistance: Isoniazid, Rifampin, Pyrazinamide and Ethambutol

#### b. Long Term Therapy (after susceptibility tests are known)

- Drug susceptible isolate: 2 months Isoniazid, Rifampin, and Pyrazinamide, then 7 months Isoniazid and Rifampin (total 9 months therapy or 6 months after culture negative)
- Isoniazid-resistant or intolerant: Rifampin plus Ethambutol or Rifampin, Ethambutol, and Pyrazinamide (18-24 months or 12 months after culture negative)
- Rifampin Intolerant: Isoniazid, Pyrazinamide, and Ethambutol (18-24 months or 12 months after culture negative).

#### c. Multi-drug Resistant Strains (resistant to Isoniazid, Rifampin, Ethambutol, & Ethionamide):

- Therapy: Isoniazid, Rifampin, Pyrazinamide, Ciprofloxacin, and Amikacin or Capreomycin
- Preventive Therapy: Pyrazinamide plus Ciprofloxacin

#### d. Antituberculosis Drug Doses:

##### Isoniazid:

- Daily, 10-15mg/kg (max. 300mg)
- Twice-Weekly, 20-40mg/kg/dose (max. 900mg)

##### Rifampin:

- Daily, 10-20mg/kg (max. 600mg)
- Twice-Weekly, 10-20mg/kg/dose (max. 600mg)

##### Pyrazinamide:

- Daily, 20-40mg/kg (max. 2 Gm)
- Twice-Weekly, 50-70mg/kg/dose (max. 2 Gm)

##### Streptomycin:

- Daily, 20-40mg/kg IM (max. 2.0 Gm)
- Twice-Weekly, 20-40mg/kg IM (max. 2.0 Gm)

##### Ethambutol:

- Daily, 15-25/mg/kg (max. 2.5 Gm)
- Twice-Weekly, 50mg/kg/dose (max. 2.5 Gm)

**Capreomycin:** 15mg/kg/d, IM

**Ciprofloxacin:** 10-15 mg/kg/BID (Adult dose 500-750mg BID)

## 2. Cryptosporidiosis:

- a. **Paromomycin:** 7.5 mg/kg QID (max.500mg QID) for 30 days. Most patients have clinical improvement but the parasite is not eradicated. Maintenance Therapy of 3.75 mg/kg BID (Adult dose 250 mg BID) can be used to prevent relapses.
- b. **Azithromycin** (Zithromax): 40 mg/kg/d q24h X 21 days. Has been shown to eliminate the parasite from the stools. The IV preparation is available on a compassionate use protocol from Pfizer (203-441-4162).

## 3. Pneumocystic Carinii Pneumonia:

- a. **Trimethoprim/Sulfamethoxazole** 20mg/100mg per kg per day divided in 4 equal doses for 14-21 days IV or PO.
- b. **Pentamidine Isethionate** 4mg/kg/day IV for 14-21 days. Because of the potential for serious adverse effects it should only be used in children who are unable to tolerate or fail TMP/SMX therapy. Failure of therapy is manifested by the lack of clinical improvement after 3-4 days of therapy.
- c. **Atovaquone** (Mepron®): for adults 750 mg (5ml) BID for 21 days for those patients who are intolerant to TMP/SMX. No dosage established for children, but there is limited safety on pharmacokinetic data in children. Doses of 10-30mg/kg BID have been studied. The currently suggested dosage is 30mg/kg BID (max. 750mg BID). The tablet formulation has been discontinued because of poor bioavailability (25%). The micro fine suspension has improved bioavailability (50%) and should be administered with meals. The suspension is supplied in bottles of 210ml each at a concentration of 750mg/5ml.
- d. **Trimetrexate** (Neutrexin®): Must be used concurrently with Leucovorin. Trimetrexate 45mg/m<sup>2</sup> I.V. QD (infuse over 60-90 minutes) for 21 days and Leucovorin 20 mg/m<sup>2</sup> Q6H I.V. or PO for 24 days (3 days longer than Trimetrexate). The primary toxicities are hematologic, hepatic, and gastrointestinal. Supplied as 5 ml vial, 2.5 mg Trimetrexate.

## 4. Mycobacterium Avium-Intracellular Complex (MAC):

- a. **Therapy:** At present, there is no consensus for which drug regimen is the best. A regimen consisting of Ethambutol, Clofazimine, Rifabutin and Clarithromycin is commonly used. Fever, diarrhea, and malaise respond in 2-8 weeks. The bacteremia is usually reduced in intensity. Treatment should be continued for 8-12 weeks to determine clinical/microbiologic response. If there is no response to this regimen, Amikacin can be added for several weeks.
- b. **Drug Dosages:**
  - Ethambutol: 15-25mg/kg/d in one dose (max. 1g/day)
  - Clofazimine: 1-2mg/kg/day in one dose (max. 100mg/day)
  - Rifabutin: 10-20mg/kg/day in one dose (max. 600mg/day)
  - Ciprofloxacin: 10-15mg/kg, BID (adult dose 500-750mg BID)
  - Clarithromycin: 30mg/kg/day divided q12h (2.0 Gm/day)
  - Amikacin: 15-22.5mg/kg/day divided q8h
- c. **Prophylaxis** for MAC when CD4 is <200 (in adults) or <150 (in children): Rifabutin (Mycobutin®) 150mg daily has been shown to be effective in reducing the frequency of infection by as much as 65% in adults. The dose in children for Rifabutin prophylaxis for MAC is 10mg/kg/d. Only 150mg capsule are available but a suspension can be prepared in cherry syrup and water. (Same mixing instructions given in PDR for Rifampin). The prepared suspension is stable for four (4) weeks when refrigerated. Leukopenia and rarely thrombocytopenia may occur.

## 5. Fungal Infections:

### a. Candidiasis

- **Cutaneous:**

- **Nystatin** (Mycostatin<sup>®</sup>): Cream and ointment (15 & 30 Gm tubes), Topical Powder (15 Gm squeeze bottles; apply 2-3 times daily).
- **Miconazole** (Monistat-Derm<sup>®</sup>): 2% cream (15, 30, 90 Gm tubes; apply BID. OTC
- **Clotrimazole** (Lotrimin<sup>®</sup>, Mycelex<sup>®</sup>): 1% cream (15, 30, 45, 90 Gm tubes), 1% lotion (30ml); apply BID.OTC
- **Ketoconazole** (Nizoral<sup>®</sup>): 2% cream (15, 30 & 60 Gm tubes); apply BID.
- **Ciclopirox** (Loprox<sup>®</sup>): 1% cream (15, & 30 Gm tubes), 1% lotion (30ml); apply BID.

- **Oropharyngeal:**

- **Topical Oral Agents:** Nystatin suspension or Clotrimazole troches (can pulverize and formulate into a suspension)
- **Systemic Oral Agents:** Use when refractory or intolerant to topical agents. Available agents include: Ketoconazole, Fluconazole, or Itraconazole.
- **Parenteral Agents:** Use when refractory or intolerant to oral agents. Available agents include: Fluconazole or amphotericin B.

- **Esophageal:**

- **Systemic Oral Agents:** Ketoconazole, Fluconazole or Itraconazole
- **Parenteral Agents:** Fluconazole or amphotericin B.

- **Systemic Candidiasis:** Amphotericin B alone or with flucytosine as initial therapy, but Fluconazole is frequently effective in Candida albicans infections (not true for other species).

### b. Cryptococcoses

- Amphotericin B + flucytosine for 6 weeks followed by Fluconazole maintenance therapy for life.

### c. Histoplasmosis

- Amphotericin B for 4-6 weeks (28mg/kg total dose) followed by maintenance therapy with amphotericin B 1mg/kg weekly or daily Ketoconazole for life.

### d. Antifungal Drug Dosages:

- **Nystatin (Mycostatin<sup>®</sup>) Infants: 2ml q6h P.O.**

Children: 4-6 ml or 1 tab q6h P.O. 100,000 u/ml or 500,000u tabs are available for P.O. use.

- **Amphotericin B (Fungizone<sup>®</sup>)** 0.5 to 1.0mg/kg/day daily or every other day I.V. infused over 2-4 hours.

- A test dose of 0.1mg/kg (max. 1.0mg) is frequently administered initially over 20 minutes to 4 hours. If the test dose is tolerated, a dose of 0.5mg/kg over 2-6 hours, can be infused the same day. If the child has a reaction (fever, chills, or myalgias), to the test dose, start with 0.25mg/kg dose and increase dose by 0.25mg/kg increments until the target dose is achieved.
- Can reduce reactions by pretreating with:
  - Acetaminophen 15mg/kg PO
  - Diphenhydramine (Benadryl) 2mg/kg PO or IV.
- Meperidine (Demerol<sup>®</sup>) 0.2 to 0.8mg/kg IV will abate chills, fever, and rigors from amphotericin B.
- Sodium loading can prevent or diminish the Nephrotoxicity associated with amphotericin B. Sodium loading of 5mEq/kg per day is recommended.

- v. Need to monitor for hypernatremia, hyponatremia, and hypokalemia.
- vi. Total therapy is 20-30mg/kg, usually 4-6 weeks.
- c. **Flucytosine** (Ancobon®) 100 - 150mg/kg/day divided q6h. Available in 50mg capsules.
  - i. Must monitor serum levels to maintain a peak serum concentration of 40-60ug/ml. Levels 100 mg is associated with side effects.
  - ii. Bone marrow suppression is the primary side effect.
- d. **Ketoconazole** (Nizoral®) 5- 10mg/kg/day PO divided q12-24h. Available in 200mg scored tablets.
  - i. Infrequent hepatotoxicity: 1 in 10,000 patients (not dose related), should monitor liver enzymes.
  - ii. Endocrine side effects: Gynecomastia, transient decrease in ACTH-Cortisol response.
  - iii. Drug Interactions: Rifampin decreases serum levels, increases levels of cyclosporin, antacids and H2-receptor blocking agents (e.g., cimetidine or ranitidine) reduces absorption, and ventricular dysrhythmias (prolonged QT interval have occurred with concomitant administration of terfenadine).
- e. **Fluconazole** (Diflucan®): mild infections 3-6mg/kg /d q24h PO. Moderate to severe 6- 12mg/kg/d q24h IV or PO. Available in 50, 100 and 200mg tablets.
  - i. No suspension available yet. Can pulverized the tablets to make a suspension.
  - ii. Drug interactions: Same as for Ketoconazole except antacids and H2 blockers only minimally affect bioavailability, also, increase in phenytoin levels.
- f. **Itraconazole** (Sporanox®): No established dosage in children. Doses of 10-16mg/kg/day have been well tolerated. Adult dosage is 200 to 400mg per day in 1 to 2 divided doses. It is supplied in 100mg capsules. The contents of the capsule can be mixed with apple sauce to administer to young children who are unable to swallow capsules.
  - i. The serum concentrations are increased with food.
  - ii. Drug interactions: same as for Ketoconazole.

6. **Toxoplasmosis:** For treatment of congenital infection, active ocular infection or CNS toxoplasmosis:

- **Pyrimethamine:** 2mg/kg/day (max. 50 mg) for 2-3 days, then maintenance therapy with 1mg/kg/day (max. 25mg) plus
- **Sulfadiazine:** 100mg/kg/day divided BID (max. 6g/day) plus
- **Folinic Acid (Leucovorin):** 5- 10 mg 3 times weekly
- **Preparing Suspension:**
  - Pyrimethamine can be mixed fresh in simple syrup at a concentration of 2mg/ml weekly. The prepared syrup must be kept refrigerated and discarded after one week.
  - Sulfadiazine can be mixed fresh in simple syrup at a concentration of 100mg/ml weekly. The prepared syrup must be kept refrigerated and discarded after one week.
  - Folic Acid is not stable in solution. The tablet can be crushed and administered with apple sauce or other appropriate foods or solution for age.

- **Monitoring For Toxicity:** can cause reversible bone marrow suppression: leukopenia, anemia, and thrombocytopenia. A CBC differential and platelet count should be performed twice weekly.
- **Alternative Therapy:**
  - Clindamycin 20-40mg/kg/dose q8h plus pyrimethamine (as above).
  - Clarithromycin 30mg/kg/d divided in two doses.
  - Spiramycin 100mg/kg/d divided in two doses (Investigational).
- **Duration of Therapy:** In AIDS patients, therapy should be maintained for life.

## 7. Viral Infections

### a. Herpes Simplex Virus Infections

- **Acyclovir (Zovirax®):**
  - **Oral:** 10-15mg/kg/dose QID (max 80mg/kg /day or 800mg QID) for primary oral, cutaneous and genital infections. Supplied as: liquid, 200 mg/5ml; capsules, 200 mg and 800mg.
  - **IV:** 30-45mg/kg/day, divided q8h for neonatal infections, encephalitis, immunocompromised patients, and when unable to take P.O. for other less severe infections. Dosage adjustment will be necessary for patients with renal insufficiency.
  - **Ocular:**
    - **Trifluorothymidine (Viroptic®)** 1% ophthalmic solution - 1 drop q2h, max 9 drops, then 1 drop q4h (5 drops/day), not to exceed 21 days.
    - **Vidarabine (Vira-A®)** 3% ophthalmic ointment - 5 times daily; change to different agent if no healing in 7-9 days.
- **HSV infection resistant to Acyclovir:** Foscarnet (Foscavir®) - 120mg/kg/day divided doses I.V. until healing. The major toxicity of this drug is renal, but it has many other toxicities as well.
- **Famciclovir (Famvir ®):** 250-500 mg TID for 5-7 days in adults. Bioavailability is 80% as compared to Acyclovir's 15-30%. Dosage recommendations are not available for children yet.

### b. Varicella Zoster Infections

- **Acyclovir**
  - **Oral:** Acyclovir 80mg/kg/day divided q6h (max. 800mg QID) is indicated for cutaneous infections only. Duration of treatment is 5-7 days. For disseminated or CNS infections, must use IV form. Supplies as: See HSV-Acyclovir (oral) above.
  - **IV:** Acyclovir 1500mg/m<sup>2</sup>/day or approximately 45mg/kg/day divided q8h as 1-2 hour infusions for disseminated or complicated varicella. Duration of treatment is 5-7 days, except for CNS (14 days).
- **Famciclovir (Famvir ®):** 500mg TID for 7 days. Famciclovir is the pro-drug for Penciclovir. The in vitro antiviral activity of Penciclovir/ Famciclovir is similar to Acyclovir against HSV and VZV. The only approved indication is for Herpes Zoster. There are no recommended doses for children.

### c. Cytomegalovirus Infections

- **Ganciclovir (Cytovene®):** Induction Therapy: 5mg/kg/dose q12h I.V. for 14-21 days. Indicated in the treatment of CMV retinitis and pneumonitis. It may be effective in CMV colitis, esophagitis, hepatitis, meningoencephalitis, and CMV-induced fever and pancytopenia. This drug is myelosuppressive. Adjust dosage in renal insufficiency. Maintenance Therapy: IV: 5mg/kg daily 7 days/week or 6mg/kg daily 5 days/week. Oral (>13 yrs): 1000mg t.i.d. with food or 500mg 6 times per day with food. Supplied as 250mg capsules. Drug Interactions:

Didanosine and Zidovudine caused an increase in AUC. Gancyclovir AUC is decreased with ddI and ZDV. Generalized seizures have been reported when Gancyclovir was given with Imipenem-Cilastatin.

- **Foscarnet** (Foscavir ®): Induction - 60mg/kg/dose q8h for 14-21 days, maintenance dose of 90-120mg/kg per day. Renal function should be monitored daily and dosage adjustment should be made for renal insufficiency. This drug is recommended for use in the treatment of CMV retinitis in patients who do not respond to or who cannot tolerate Gancyclovir, but it may be effective in other CMV-associated diseases.
- **CMV-IGIV** (Cytogam ®): Use in combination with antiviral agents. 200-500mg/kg on days 1, 2, and 7 then 200mg/kg weekly for 2-3 weeks.

d. **Influenza**

- **Amantadine** (Symmetrel ®) or Rimantadine: Influenza A only.
  - **Prophylaxis:** 5mg/kg/day divided q12h, or q24h (max.
  - **Treatment:** 5 mg/kg/day divided q12h or q24h (max. <40 kg 150mg/kg, >40 kg 200mg/day for 7 days.
- **Ribavirin** (Virazole ®): Is active against both Influenza A & B viruses. 6 grams by aerosol (SPAG-2) over 18 hours for 3-7 days may be effective (not approved for this indication in U.S.).

e. **RSV Infections**

- Ribavirin (Virazole ®): 6 grams ( in 30 ml water or 20mg/ml) by aerosol (SPAG-2) over 18 hours or 6 grams in 100 ml water (60mg/ml) by aerosol over 2 hours q8h. or 6 grams in 100ml water (60mg/ml) by aerosol over 2 hours q8h for 3-7 days is indicated in HIV patients with RSV infection.

# IX. Assessment and Management of Nutritional Disorders

## A. Normal growth and weight

First year: 12 cm/year, 7kg/yr  
4 to 10 years: 5-6 cm/yr, 2-3 kg/yr

## B. Abnormalities in growth of children with HIV infection

1. Patterns
  - a. 25-50% of infants with vertically transmitted HIV infection were smaller for gestational age and remained smaller in height and weight percentiles.
  - b. Those HIV infected infants with comparable height and weight percentiles at birth to the uninfected infants born to mothers with HIV infection demonstrated smaller weight and height percentiles by 3-6 months.
  - c. With progression of HIV disease the growth retardation becomes more profound and evolves into a wasting state.
  - d. There is a positive correlation between height and weight for age and helper-to-suppressor T cell ratios.
  - e. Over 95% of children with HIV infection will develop clinically significant malnutrition before death.
2. Criteria Growth Faltering
  - a. Length or height is more than 2 SD below the mean for chronological age.
  - b. Linear growth velocity is
  - c. Bone age is more than 2 SD below the mean CA.
  - d. **Waterlow's criteria** for severity of growth faltering can be determined by:  
Height deficit (%) =  $(AH \div EH) \times 100$   
AH = Actual Height (cm)  
EH = Expect Height (cm) for CA (at 50th percentile)  
  
Weight deficit (%) =  $(AW \div EW) \times 100$   
AW = Actual Weight (kg)  
EW = Expected Weight (kg) for actual height (at 50th percentile)
  - e. **McLaren's criteria** are based on the assumption that brain growth (H.C.) is spared most, while peripheral body fat stores (the extremities) are spared least in the child

RATIO (degree of malnutrition)	Mid-Arm Circumference (cm)
	Head Circumference (cm)

3.

Waterlow & McClaren Criteria for Growth Faltering	Grade of Malnutrition			
	0 Normal	1 Mild	2 Moderate	3 Severe
Deficit (% of expected)*				
Height	>95	95-90	90-85	<85
Weight	>90	90-80	80-70	<70
Ratio**	>0.31	0.28-0.31	0.25-0.28	<0.25

4. \* Adopted from Waterlow, *JC Lancet* 1973; 2:87-89

5. \*\*Adopted from Kanawati, *AA Nature* 1970; 228:573-57

6. Indications for Intervention in Growth Faltering

- a. Height-for-age
- b. Weight-for-height
- c. Weight-for-age
- d. Linear growth velocity
- e. Mid-arm circumference: Head circumference
- f. Bone age more than 2 yrs behind CA
- g. Anemia (
- h. Hypoalbuminemia (
- i. Low pre-albumin (

**C. Etiologic Consideration**

1. Progression of HIV infection
2. Concurrent infections, CMV, PCP, hepatitis, etc.
3. Oral and esophageal infection (Candida, HSV)
4. CNS involvement with suppression of appetite or deglutition.
5. Nausea and vomiting (gastritis, medications, pancreatitis, etc.)
6. Gastrointestinal disease
7. Hyper metabolic state - increase in resting energy expenditure (REE)

**D. Pathogenesis of Growth Failure**

1. Neuroendocrine dysfunction in AIDS endocrine abnormalities may contribute to FTT in some children with HIV infection; neither the prevalence nor severity of the endocrine dysfunction can explain the profound wasting observed in many children.
2. Gastrointestinal dysfunction in AIDS
  - a. Diarrhea and malabsorption
    1. Dysphagia
      - Aphthous stomatitis
      - Oral ulcers from HSV
      - Esophagitis due to CMV, HSV, or Candida
      - Greater than 3 stools per day should prompt evaluation for malabsorption
      - Stools that can be poured from a container support water content is increased
      - Weight of the stool output >50g/day in an infant is increased >100g/day in an older child is increased
      - Normally stools are negative for reducing substances, PMN, and blood.
    2. Enteric Pathogens
      - Parasites
        - Cryptosporidium
        - Giardia lamblia
        - Isospora belli
        - Entamoeba histolytic
        - Microsporidium sp.
      - Fungi
        - Candida albicans
        - Histoplasma capsulatum
      - Bacteria
        - Salmonella
        - Shigella
        - M. AviumComplex
        - Campylobacter jejuni
        - C. Difficile
      - Viruses
        - HSV; Rotovirus; Adenovirus; CMV; Norwalk Agent; Calicivirus; Astrovirus; Coronavirus; Picornovirus
  - b. Disaccharide malabsorption: up to 40% of HIV infected children demonstrate disaccharide malabsorption.
    - Lactose and sucrose most common
    - Loss of calories
    - Osmotic diarrhea
  - c. Hepatobiliary Disease
    - Hepatitis virus infections, A, B, C, D, E
    - HIV disease
    - M. avium complex
    - CMV
    - Cryptosporidium
    - P. Carinii
    - Toxoplasmosis
    - Histoplasmosis
  - d. Pancreatitis
    - Antiretroviral therapy: DDI D4T, 3TC
    - 17% of children with AIDS develop pancreatitis
    - Other drugs: Pentamidine, TMP/SMX, or dapsone
    - Infectious agents: CMV or mycobacteria

3. Metabolic Dysfunction
  - a. Hyper metabolic state associated with increased REE
    - Hormones: T3, T4, and cortisol
    - Cytokines: TNF, IL1, IFN

## E. Diagnostic Consideration

1. Dietary History
  - a. 24 hour recall
  - b. 3-day food intake diary
2. Weight, height, triceps skinfold thickness (measure of fat stores), arm muscle circumference (measure of 1 lean body mass) should be performed every 3 months
3. Thyroid function: Free T4 and TSH should be measured if signs and symptoms of hypothyroidism is present.
4. Adrenal function: If clinical evidence suggest hypoadrenalism, should obtain the following:
  - a. Morning (0900) cortisol and ACTH levels in the serum
  - b. If low, administer 0.25 mg synthetic ACTH (cosyntropin) I.V. or I.M. and obtain a serum cortisol 60 minutes later
5. Growth Hormone/IGF - 1 function: If evidence of growth retardation should obtain the following:
  - a. Bone Age
  - b. IGF - 1 levels in serum
  - c. GH stimulation test (clonidine, L-dopa, or arginine): normal GH > 7mg/l in at least one of the stimulation tests.
6. Malabsorption evaluation
  - a. Stool culture
  - b. Stool O & P and Crypto sporidium (not done routinely)
  - c. Stool pH, fat, trypsin, reducing substances
  - d. Stool 72h fat ( if abnormal qualitative fat)
  - e. Vitamin A level
  - f. Xylose challenge test
  - g. Hydrogen breath test
7. Metabolic evaluation
  - a. Serum calcium and phosphorous / ionized calcium/magnesium
  - b. Alkaline phosphatase
  - c. Serum proteins
  - d. Total cholesterol / triglycerides
  - e. 1, 25 - dihydroxyvitamin D
8. Nutritional status
  - a. Chemistry panel
  - b. Albumin/total protein
  - c. Lipid profile
  - d. Calcium, magnesium, zinc
  - e. Folate, iron, ferritin
9. Hepatic function
  - a. Total Bilirubin, Direct Bilirubin
  - b. SGOT, SGPT, GGT, Alkaline phosphatase
  - c. Ultrasound of abdomen ( if biliary tract disease is suspected)
  - d. Liver biopsy ( if undiagnosed hepatopathy found)
10. Gonadal function
  - a. Tanner staging

- b. Basal testosterone (boys), estradiol (girls), LH, FSH
- c. Bone age

## F. Treatment

### 1. Nutritional Therapy

- a. Major Goals of Nutritional Therapy
  - o Replacement of continued nutritional losses
  - o Correction of lean body mass and body fat stores
  - o Provision of sufficient nutrients for normal metabolic functions
  - o Initiation of catchup growth
  - o Restoration of normal rates of growth
- b.

RECOMMENDED DAILY ENERGY AND PROTEIN ALLOWANCES FOR CHILDREN*		
AGE (Years)	ENERGY (Kcal/kg/day)	PROTEIN (G/KG/DAY)
0.00.5	110	2.2
0.51.0	100	1.6
1.03.0	100	1.2
4.06.0	90	1.1
7.010	70	1.0
1114 (male)	55	1.0
1518 (male)	45	0.9
	45	1.0

(female)		
1518 (female)	40	0.8

- c. \* Adopted from Subcommittee on the Tenth Edition of RDAs, Nutritional Academy of Sciences National Research Council. Recommended Dietary Allowances. 10th Ed. Washington, DC: National Academy Press; 1989.
- d. Dietary Energy Needs: Dietary energy is the limiting nutrient in the rehabilitation of children with growth faltering. The prescribed energy intake can be calculated from the following equation:

$$E = (IBW \div ABW) \times RDE$$

E = Estimate energy needs for catch up growth (Kcal/KG/d)

IBW = Ideal body weight (Kg) for CA

ABW = Actual body weight (kg)

RDE = Recommended dietary energy intakes (Kcal/Kg/day) for CA

CA = Chronological Age

e. Oral Refeeding Programs

- o Prepared formulas (20 Kcal/oz) by increasing volume of intake.
- o Prepared formulas with higher caloric density (24 and 27 Kcal/oz) for infants and 30 Kcal/oz for older children (Pediasure)
- o Diluting concentrated formulas to give higher caloric densities (See Appendix A )

$$24 \text{ Kcal/oz} = 13 \text{ oz concentrated formula} + 9 \text{ oz of water}$$

$$27 \text{ Kcal/oz} = 13 \text{ oz concentrated formula} = 6 \text{ oz of water}$$

- o Supplementing formulas with added calories.
  - Medium chain Triglycerides (MCT Oil), 7.7 Kcal/ml, see Appendix B for amount to add.
  - Corn Oil, 8.0 Kcal/ml, see Appendix B for amount to add.
- o Carbohydrates (Polycose). See Appendix B for amount to add. 1 tsp (2 g) = 8 Kcal.
  - Powder: 350 g cans
  - Liquid: 1 ml = 2 Kcal, 4.2 oz (126ml) bottles
- o Semielemental or elemental formula (Alimentin or Progestimil) may be required; however, the disadvantage is increased osmotic activity which may worsen the gastrointestinal losses.
- o **Tube Feeding**

- Oral feeding during the day time is usually attempted.
    - Continuous infusion by nasogastric tube (5 or 8F) over 12 hours is usually well tolerated. At least 50% of the energy requirements can be given by this route.
  - **Routine monitoring of enteral nutrition**
    - Weight (daily)
    - Urine specific gravity
    - Serum glucose, electrolytes, BUN
    - Serum calcium, magnesium, phosphorus
    - Serum prealbumin
  - **Complications of enteral nutrition**
    - Over hydration
    - Dehydration (Osmotic diarrhea)
    - Azotemia
    - Hyperglycemia
    - Electrolyte abnormalities (Hypokalemia)
    - Mineral imbalances (Hypophosphatemia)
- f. **Parenteral alimentation may be necessary**
  - Peripheral: 10% glucose with 2% to 3% amino acids, vitamins and minerals.
  - Central: 20% glucose with 2% to 3% amino acids, vitamins and minerals.
  - IV fatty acids: should be added to provide adequate energy and essential fatty acids.
  - **Complications of parenteral nutrition**
    - Line sepsis (bacterial & fungal)
    - Metabolic derangements
    - Mechanical problems
    - Hepatic injury
    - Venous perforation or thrombosis
    - Air embolus
  - Routine monitoring for parenteral nutrition Same as for enteral nutrition but must also monitor liver function test and evaluate febrile episodes with CBC, diff, and blood cultures.
- g. **Appetite Stimulant:** Megestrol Acetate (Megase) 2.8mg to 15.5mg/kg/day divided 24 times/day. Supplied as 20mg and 40mg tablets or Lemonline flavored suspension 40mg/ml. Dosage range used in children is 80mg BID to 80mg QID. This drug is not approved for children but a limited clinical trial indicated that it is safe (ages 26 months to 15 years). The primary side effects were irritability and drug-associated diabetes.
- h. Optimize Nutrition
  - a. Oral high caloric supplements, vitamins, and appetite stimulants (Megestrol)
  - b. Enteral tube feeding
  - c. Total parenteral nutrition
- i. Optimize GI Absorption
  - Treat opportunistic infections causing enteropathy
    - a. Elemental diets, MCT oil
- j. Reduce HIV and other infection
  - Antiretroviral therapy
    - a. Treat opportunistic infections
- k. Replace hormonal deficiencies: synthroid, glucocorticoid, mineralocorticoid, growth hormone, testosterone, estradiol
- l. Psychological factors: improve home environment, foster care, counseling, support groups

## **X. Prevention of HIV Infection In Infants and Adolescents**

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### **A. Preventing Pregnancy in a Female who is HIV Positive**

1. Sexual Abstinence
  - Total abstinence - 0% failure rate
  - Periodic abstinence - 26% failure rate
2. Oral Contraceptives
  - Always use - 0.1% failure rate
  - Typical use - 8% failure rate
3. Male Condoms
  - Consistent use - 2% failure rate
  - Typical use - 15% failure rate
4. Female Condoms (Reality®) - lubricated polyurethane sheath with a ring on both ends.
  - Consistent use - 11% failure rate
  - Typical use- 26% failure rate

### **B. Preventing Transmission of HIV Infection from HIV-Infected Pregnant Women to their Infants:**

1. Zidovudine therapy to HIV-infected pregnant woman and infant.
  - a. a. Oral Zidovudine (ZDV) 100mg 5 times daily initiated at 14-34 weeks gestation and continued for the remainder of the pregnancy.
  - b. b. During labor, I.V. ZDV in a loading dose of 2 mg/kg given over 1 hour, followed by continuous infusion of 1mg/kg per hour until delivery.
  - c. c. Oral ZDV to the newborn (ZDV syrup at 2mg/kg q6h) for the first 6 weeks of life beginning at 8-12 hours after birth.

**NOTE:** The study reduced transmission of HIV infection from the mother to her infant from 25.5% to 8.3% (67.5% reduction). The study only included pregnant women with CD4 counts 200 on entry. Limitations of the study:

- - Did not assess the efficacy of ZDV in women with CD4 counts < 200.
- - Did not assess the independent contribution of antepartum, intrapartum treatment or treatment of the infant with ZDV.
- - Did not evaluate the risk or benefit of ZDV in the first trimester. Data from Antiretroviral Pregnancy Registry suggest that the proportion of birth defects among infants of women who received ZDV during the first trimester is no greater than that expected in the general population.
- - Also, the study did not provide information on long term follow up of infants treated with ZDV, particularly those who were not HIV infected. Antiretroviral Pregnancy Registry (800-722-9292, ext. 8465).

**Summary:** Clinical situations and recommendations for use of Zidovudine to reduce perinatal HIV transmission.

- a. **Pregnant HIV-infected women with CD4+ T-lymphocyte counts >200/ L who are at 14-34 weeks of gestation and who have no clinical indications for ZDV and no history of extensive (>6 months) prior Antiretroviral therapy. Recommendation:** The health-care provider should recommend the full ACTG Protocol 076 regimen to all HIV-infected pregnant women in this category. This recommendation should be presented to the pregnant woman in the context of a risk-benefit discussion: a reduced risk of transmission can be expected, but the long-term adverse consequences of the regimen are not known. The decision about this regimen should be made by the woman after discussion with her health-care provider.
- b. **Pregnant HIV-infected women who are at >34 weeks of gestation, who have no history of extensive (>6 months) prior Antiretroviral therapy, and who do not require ZDV for their own health. Recommendation:** The health-care provider should recommend the full ACTG Protocol 076 regimen in the context of a risk-benefit discussion with the pregnant woman. The woman should be informed that ZDV therapy may be less effective than that observed in ACTG Protocol 076, because the regimen is being initiated late in the third trimester.
- c. **Pregnant HIV-infected women with CD4+ T-lymphocyte counts 6 months) prior Antiretroviral therapy. Recommendation:** The health-care provider should recommend initiation of antenatal ZDV therapy to the woman for her own health benefit. The intrapartum and neonatal components of the ACTG Protocol 076 regimen should be recommended until further information becomes available. This recommendation should be presented in the context of a risk-benefit discussion with the pregnant woman.
- d. **Pregnant HIV-infected women who have a history of extensive (>6 months) ZDV therapy and/or other Antiretroviral therapy before pregnancy. Recommendation:** Because data are insufficient to extrapolate the potential efficacy of the ACTG Protocol 076 regimen for this population of women, the health-care provider should consider recommending the ACTG Protocol 076 regimen on a case-by-case basis after discussion of the risk and benefits with the pregnant woman. Issues to be discussed include her clinical and immunologic stability on ZDV therapy, the likelihood she is infected with a ZDV-resistant HIV strain, and, if relevant, the reasons for her current use of an alternative Antiretroviral agent (e.g., lack of response to or intolerance of ZDV therapy). Consultation with experts in HIV infection may be warranted. The health-care provider should make the ACTG Protocol 076 regimen available to the woman, although its effectiveness may vary depending on her clinical status.
- e. **Pregnant HIV-infected women who have not received antepartum Antiretroviral therapy and who are in labor. Recommendation:** For women with HIV infection who are in labor and who have not received the antepartum component of the ACTG Protocol 076 regimen (either because of lack of prenatal care or because they did not wish to receive antepartum therapy), the health-care provider should discuss the benefits and potential risks of the intrapartum and neonatal components of the ACTG Protocol 076 regimen and offer ZDV therapy when the clinical situation permits.
- f. **Infants who are born to HIV-infected women who have received no intrapartum ZDV therapy. Recommendation:** If the clinical situation permits and if ZDV therapy can be initiated within 24 hours of birth, the health-care provider should offer the ACTG Protocol 076 postpartum component of 6 weeks of neonatal ZDV therapy for the infant in the context of a risk-benefit discussion with the mother. Data from animal prophylaxis studies indicate that, if ZDV is administered, therapy should be initiated as soon as possible (within hours) after delivery. If therapy cannot begin until the infant is >24 hours of age and the mother did not receive therapy during labor, no data support offering therapy to the infant.

### **C. Avoiding Breast Feeding of an Infant Born to an HIV Positive Mother:**

- Breast feeding may increase the risk of HIV infection over that in the non-breast fed infant. For that reason, breast feeding is not recommended for infants born to HIV positive mothers.

### **D. Preventing Sexual Transmission of HIV Infection**

1. Sexual abstinence.
2. Avoid sexual intercourse with an infected partner.
3. Preventing transmission of HIV infection when having sexual intercourse with a partner whose infection status is unknown or who is infected with HIV:
  - Latex male condom with or without spermicide (Nonoxynol- 9).
    - Consistent use: 0-2% failure rate
    - Inconsistent use: 10- 15% failure rate
  - Female Condom - no data on its use in the prevention of HIV infection.
  - Nonoxynol-9: No reports indicate that Nonoxynol-9 used alone without condoms is effective in preventing HIV sexual transmission.

### **E. Using Safe Blood and Blood Products**

1. Blood in the U.S., since 1985, is routinely tested for HIV-1 antibody. Since June 1992, donor blood has been tested for both HIV-1 and HIV-2. The risk of HIV infection from a blood transfusion currently is approximately 1:250,000.
2. Safe antihemophilia factors
  - Heat inactivated plasma concentrates
  - Recombinant Factor VIII has been developed

### **F. Avoiding IV Drug Use or Reducing Risk of HIV Transmission**

- Referral to drug treatment center: There is a need to increase availability and accessibility of drug treatment programs.
- Needle and syringe exchange program - providing sterile needles and syringes.

### **G. Public Education**

1. Sex education programs in schools provide students with information on the risk of HIV/STD infections and methods of prevention.
2. Coalitions for public awareness campaigns.
  - Georgia Women Preventing AIDS - their goal is to empower African American women to prevent the spread of HIV/STD, primarily through the use of condoms.

## Appendix A

<b>Tablespoons of Formula Powder to Add*</b>								
<b>Total Volume of Formula (cc)</b>	<b>240</b>	<b>480</b>	<b>720</b>	<b>960</b>	<b>1200</b>	<b>1440</b>	<b>1680</b>	<b>1920</b>
<b>20</b>	4	8	12	16	20	24	28	32
<b>21</b>	4.2	8.4	12.6	16.8	21	25.2	29.4	33.6
<b>22</b>	4.4	8.8	9.2	13.2	22	26.4	30.8	35.2
<b>23</b>	4.6	9.2	13.8	18.4	23	27.6	32.2	36.8
<b>24</b>	4.8	9.6	14.4	19.2	24	28.8	33.6	38.4
<b>25</b>	5	10	15	20	25	30	35	40
<b>26</b>	5.2	10.4	15.6	20.8	26	31.2	36.4	41.6

*\*To increase the caloric density by formula powder - locate the # kcal/oz of formula powder desired and match with the desired total volume of formula. The result will indicate the number of tablespoons of powder required.*

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**Quantity of Liquid Formula Concentrate to Add (cc) #**

<b>Total Volume of Formula (cc)</b>	<b>240</b>	<b>480</b>	<b>720</b>	<b>960</b>	<b>1200</b>	<b>1440</b>	<b>1680</b>	<b>1920</b>
<b>20</b>	120	240	360	480	600	720	840	960
<b>21</b>	126	252	378	504	630	756	882	1008
<b>22</b>	132	264	396	528	660	792	924	1056
<b>23</b>	138	276	414	552	690	828	966	1104
<b>24</b>	144	288	432	576	720	864	1008	1152
<b>25</b>	150	300	450	600	750	900	1050	1200
<b>26</b>	156	312	468	624	780	936	1092	1248

*# To increase the caloric density by formula concentrate - locate the # kcal/oz of formula concentrate desired and match with the desired total volume of formula. The result will indicate the cc of formula concentrate required*

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## Nutritional Supplements used with Immunocompromised Children\*

Name	Company	Special Features	cal/ml	CHO g/liter	Protein g/liter	Fat g/liter	OSM
Pregestimel	Mead Johnson	Designed for children birth-1 year; 60% fat as MCT	0.66	66	18	36	300
Nutramigen	Mead Johnson	Protein hydrolysate, designed for children birth-1 year	0.68	91	11	27	320
Pediasure	Ross Labs	Lactose free, designed for children 1-6 years	1.0	104	28	47	310
Isocal	Mead Johnson	Isotonic	1.06	135	34	44	270
Osmolyte	Mead Johnson	Isotonic, low protein	1.06	137	35	36	300
Newtrition	Knight Medical	Fiber enriched	1.2	160	50	37	310
Isofiber							
Jevity	Ross Labs	Fiber enriched	1.06	144	44	35	310
Enrich	Ross Labs	Fiber enriched	1.1	153	38	35	480
Ensure	Ross Labs	Lactose free, increased calorie	1.06	137	35	35	470
Ensure Plus	Ross Labs	Lactose free, increased calorie	1.5	189	52	50	690
Sustical	Mead Johnson	Lactose free	1.0	140	61	23	650
Sustical HC	Mead Johnson	Lactose free, decrease residue, increase protein	1.5	190	61	58	670
Sustical	Mead	Fiber	1.06	132	43	33	480

with Fiber	Johnson	enriched					
Peptamen	Clintec Nutrition	70% fat as MCT, protein hydrolysate	1.0	127	40	39	260
Carnation Instant Breakfast with Whole Milk	Clintec Nutrition	Lactose containing	1.17	144	56	32	
Portagen	Mead Johnson	86% fat as MCT, lactose free, powder diluted to 20 cal/oz	0.66	74	22	30	233
Polycose	Ross Labs	Glucose polymers	2 cal /ml (liquid) 8 cal/tsp (powder)				
MCT Oil	Mead Johnson		7.7 cal/ml				
Promod	Ross Labs	Protein supplement	20 cal/tbsp				
Casec	Mead Johnson	Protein supplement	16.4 cal/tbsp				

\*CHO, carbohydrate; OSM, osmolality; MCT, medium chain triglyceride REF: Winter, HS, et al. *Gastrointestinal and Nutritional Problems In Pediatric HIV Disease*. In: Pizzo P, Wilfert CM, ed. *Pediatric AIDS*, 2nd Edition. Baltimore: Williams & Wilkins; 1994:529.

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<b>Enteral Support for Older Children*</b>	
	Complete Supplement
Clintec	Nutren, Replete
Mead Johnson	Sustacal, Isocal, Traumacal, Criticar HN
Ross	Promod, Ensure, Ensure with Fiber, Jevity, Osmolite, Promote, Pulmocare
Sandoz Nutrition	Meritene, Citriscouce, Resource, Compleat, Fibersource, Stresstein
	Low Fat or Medium Chain Triglyceride
Mead Johnson	Lipisorb
Sandoz Nutrition	Isosource
	Elemental
Metagenics	Opti
Ross	Vital HN
Sandoz Nutrition	Vivonex TEN
	Immune Modulating
McGraw	ImmunAid
Ross	AlitraQ
Sandoz Nutrition	Impact
	Parenteral Nutritional Support
Adult	Aminosyn, FreAmine, Travasol
Pediatrics	TrophAmine, Aminosyn-PF
Liver Disease	HepatAmine
Renal Disease	NephrAmine
Branched-chain amino acids	Aminosyn-HBC

*Modified from Cimoch PJ. Current agents for the management of wasting and malnutrition in HIV/AIDS, Nutr HIV/AIDS 1992;1:27-32 REF: Winter, HS, et al. Gastrointestinal and Nutritional Problems In Pediatric HIV Disease. In: Pizzo P, Wilfert CM, ed. Pediatric AIDS, 2nd Edition. Baltimore: Williams & Wilkins; 1994:530.*

## Appendix B

Quantity of Polycose to Add (gm) *								
	240	480	720	960	1200	1440	1680	1920
1	2	4	6	8	10	13	15	17
2	4	8	13	17	21	25	30	34
3	6	13	19	25	32	38	44	50
4	8	17	25	34	42	50	59	67
5	10	21	32	42	52	63	74	84
6	13	25	38	50	63	76	88	101
7	15	29	44	59	74	88	103	118
8	17	34	50	67	84	101	118	135
9	19	38	57	76	95	114	133	151
10	21	42	63	84	105	126	147	168
11	23	46	93	93	116	139	162	185
12	25	50	76	101	126	152	177	202
13	27	55	82	109	137	164	192	219
14	29	59	88	118	147	177	206	236
15	31	63	95	126	158	189	221	253

Kcal/oz desired by Polycose powder

*To increase the caloric density of a formula by Polycose-locate the #kcal/oz of polycose powder desired and match with the desired total volume of formula to determine total grams of polycose required.*

## Quantity of Corn Oil to add (cc) \*

Total Volume of Formula								
	240	480	720	960	1200	1440	1680	1920
1	1	2	3	4	5	6	7	8
2	2	4	6	8	10	11	13	15
3	3	6	8	11	14	17	20	23
4	4	8	11	15	19	23	27	30
5	5	10	14	19	24	28	33	38
6	6	11	17	23	28	34	40	46
7	7	13	20	27	33	40	47	53
8	8	15	23	30	38	46	53	61
9	9	17	26	34	43	51	60	68
10	10	19	28	38	48	57	67	76

Calories/ounce by corn oil.

*\*To increase the caloric density of formula by corn-oil-locate the #kcal/oz. of corn oil desired and match with the desired total volume of formula to determine total # cc of corn oil required.*

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## Quantity of MCT Oil to Add (cc)

Total Volume of Formula								
	240	480	720	960	1200	1440	1680	1920
1	1	2	3	4	5	6	7	8
2	2	4	6	8	10	12	15	17
3	3	6	9	13	16	19	22	25
4	4	8	12	17	21	25	29	33
5	5	10	16	21	26	31	36	42
6	6	12	19	25	31	38	44	50
7	7	15	22	29	36	44	51	58
8	8	17	25	33	42	50	58	67
9	9	19	28	37	47	56	66	75
10	10	21	31	42	52	62	73	83

Calories/ounce by MCT oil

*\* To locate the caloric density of formula by MCT oil-locate the #Kcal/oz. of MCI desired and match with the desired total volume of formula to determine total # cc of MCT oil required.*

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# Appendix C

## Neurodevelopmental Criteria for CNS Disease Progression

A. Impairment of Brain Growth

Abnormal head growth rate

1. For infants
2. For infants >1 year of age, this is defined as a loss of 1 SD from baseline on National Center for Human Statistics growth curve.
3. For children >2 years of age, neuroimaging is necessary to confirm atrophy.

OR

Progressive loss of cerebral parenchymal volume demonstrated on serial neuroimaging studies at least 2 months apart.

B. Decline of cognitive function

- For infants from birth to 30 months, a fall of 2 SD (32 points) on Mental Developmental Index or a fall of 2 SD from baseline maintained over 2 assessments separated by a least 1 month.
- For children >30 months, a fall of 1 SD on McCarthy GCI or Wechsler (WISC-R and WAIS) Full Scale IQ.

C. Clinical neurologic dysfunction: progressive over at least 2 months, or, in the youngest infants, persistent in 2 exams over 1 month.

0. Loss or deterioration of previously attained motor skills.
  1. Significant changes in neurobehavioral status in children
  2. Diffuse, symmetric loss or decrease in power or strength which is not the result of a systemic, nutritional or metabolic complication.
  3. Diffuse, symmetric and pathologically increased deep tendon reflexes.
  4. Diffuse and symmetric abnormalities of tone, including, but not limited to, hypotonia or hypertonia.

**Reference:** Pediatric Infectious Disease Journal, June, 1993; 12:518

# Appendix D

## Recommendations for HIV-2 Testing in the United States

### Indications for Testing for HIV-2 Infection

Because epidemiologic data indicate that the prevalence of HIV-2 in the United States is extremely low, CDC does not recommend routine testing for HIV-2 at U.S. HIV counseling and test sites or in settings other than blood centers. However, **when testing is to be performed**, tests for antibodies to both HIV-1 and HIV-2 should be obtained if demographic or behavioral information suggests that HIV-2 infection might be present. Persons at risk for HIV-2 infection include:

- Sex partners of a person from a country where HIV-2 is endemic (this category includes persons originally from such countries).
- Sex partners of a person known to be infected with HIV-2.
- Persons who received a transfusion of blood or a nonsterile injection in a country where HIV-2 is endemic.
- Persons who shared needles with a person from a country where HIV-2 is endemic or with a person known to be infected with HIV-2.
- Children of women who have risk factors for HIV-2 infection or who are known to be infected with HIV-2.

Additionally, testing for HIV-2 is indicated when there is clinical evidence for or suspicion of HIV disease (such as an AIDS-associated opportunistic infection) in the absence of a positive test for antibodies to HIV-1 and in cases in which the HIV-1 Western blot exhibits the unusual indeterminate pattern of gag (p55, p24, or p17) plus pol (p66, p51, or p32) bands in the absence of env (gp160, gp120, or gp41) bands.

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  - Education of Children with HIV Infection
  - Guidelines for HIV-Infected Children and their Foster Families
  - HIV in the Athletic Setting
  - Perinatal HIV Testing
- Caring for our Children: National Health and Safety Performance Standards: Guidelines for Out-Of-Home Child Care Programs
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