Florida/Caribbean AIDS Education and Training Center

HIV CareLink

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ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides state-of-the-art HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

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Guidelines for Prevention and Treatment of Opportunistic Infections among HIV-Exposed and HIV-Infected Children June 20, 2008

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Although opportunistic infections (OIs) have drastically changed the way we manage HIV-infected children, OIs continue to be the presenting symptom of HIV infection among children whose HIV status is unknown. For those with known HIV infection, other barriers such as lack of linkage to appropriate care may result in suboptimal management of their HIV infection making them susceptible to OIs. In addition, the development of immune reconstitution inflammatory syndrome (IRIS) following initiation of antiretroviral therapy (ART) may complicate treatment of an OI. Therefore prevention and management of OIs remains an integral component of HIV care even in the ART era.

Recommendations for the treatment and prevention of OIs in HIV exposed and infected children were recently revised by the Pediatric OI Guidelines working group under the auspices of the Office of AIDS Research of the NIH. This document was finalized in the fall of 2007 and a summary of the changes to the guidelines is presented below. It is important to keep in mind that these guidelines target HIV exposed and infected children in the U.S. and therefore do not include discussions about pathogens that are not commonly seen in the U.S. For more detailed information including specific drug regimens, dosages and detailed drug information, the readers should refer to the full document at http://aidsinfo.nih.gov/contentfiles/Pediatric_OI.pdf

Important Considerations when Diagnosing and Treating OIs: Revised CDC Definitions

A child is definitely infected if:

- (+) virologic results (HIV DNA or RNA assays) on two separate specimens **or**
- (+) virologic test or a (+) confirmed HIV antibody test at ≥ 18 mos

New presumptive definition of uninfected may allow clinicians to avoid starting prophylaxis for *Pneumocystis jirovecii* pneumonia (PCP) in HIV-exposed infants at 6 wks age. A child not breastfed is presumptively HIV uninfected if:

- no clinical or lab evidence of HIV ***and***
- 2 (-) virologic tests; 1 at ≥ 2 wks of age & 1 at ≥ 4 wks of age **or**
- single (-) virologic test at ≥ 8 wks of age **or**
- 1 (-) HIV antibody test at ≥ 6 mos of age

Definitive lack of infection:

- 2 (-) virologic tests; 1 at ≥ 1 mo of age & 1 at ≥ 4 mos of age ***or***
- ≥ 2 (-) HIV antibody tests from separate specimens at ≥ 6 mos of age

IRIS and ART

ART generally → ↓ HIV viral load & ↑ CD4 within a few mos which may → IRIS in response to an existing active, latent or occult OI. It can be difficult to distinguish IRIS from tx failure or ART toxicity. Late onset IRIS (>3 mos post ART) may be due to immune reaction against persistent noninfectious antigen.
IRIS tx is based on disease severity:

- non-steroidal anti-inflammatory drugs are the mainstay for moderate disease
- steroids are reserved for severe cases
- ART needs to be continued

ART Initiation in Setting of OI in ART-Naïve Children

No randomized trials addressing optimal time for ART initiation in setting of acute OI; decision needs to be individualized. Most experts recommend:

- Initiate ART for OIs that lack effective tx (e.g., cryptosporidiosis, microsporidiosis, PML, KS) since benefit > risk

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- For other OIs (e.g. TB, MAC, PCP, and cryptococcal meningitis), await ART initiation until tx response seen

For a child already on ART who develops an OI, ART needs to continue in addition to OI tx. Monitor for drug-drug interactions.

Vaccine Preventable Diseases
HIV-infected children need to be protected from vaccine preventable diseases just like any other child. All inactivated vaccines can be administered safely to persons with immunosuppression although effectiveness may be suboptimal. Individual vaccines are discussed in the appropriate disease section of the guidelines and tables. In addition, see http://www.cdc.gov/vaccines/recs/schedules/default.htm for immunization schedules, and http://www.cdc.gov/vaccines/pubs/ACIP-list.htm for recommendations, precautions, and contraindications for vaccines.

PROPHYLAXIS & TREATMENT OF SPECIFIC OIs

Bacterial Infections: Preventing First Episode of Disease

- IVIG is recommended to prevent serious bacterial infections (SBI) in HIV-infected children only if evidence of hypogammaglobulinemia and/or functional antibody deficiency present. Antibiotic prophylaxis solely for the primary prevention of SBI is not recommended as this might promote development of drug resistant organisms.

Treatment of Serious Bacterial Infections (SBI)

Mycobacterial Infections
- HIV-infected children are at ↑ risk of TB disease
- BCG *Mycobacterium tuberculosis* has been reported in HIV-infected children vaccinated with BCG at birth
- Disease due to *Mycobacterium bovis* has emerged in children consuming unpasteurized milk or milk products. Distinguishing between *M. tuberculosis* & *M. bovis* is important; *M. bovis* isolates are resistant to pyrazinamide.
- # of adult foreign-born TB patients is increasing & are a potential source of drug resistant TB

Clinical Manifestations and Diagnostics Challenges in HIV-Infected Children with TB
- In U.S. where TB exposure is uncommon, HIV-infected infants should be tested at age 3 mos of age and children should be tested at time of dx and annually thereafter with tuberculin skin test (TST)
- Control skin antigens and two step skin testing are both of uncertain value and not recommended
- Assays determining lymphocyte IFN-gamma release are not routinely recommended due to the uncertainty about test sensitivity in children
- Nucleic acid amplification tests may be useful in dx of TB in HIV-infected children with unexplained pulmonary disease with (-) TST & (-) culture

***Mycobacterium Avium* Complex Disease (MAC)**
Primary prophylaxis should be offered to: ≥ 6 yrs of age: < 50 cells/mm^3, 2-5 yrs of age: < 75 cells/mm^3, 1-2 yrs of age: < 500 cells/mm^3, <1 yr of age: < 750 cells/mm^3.

Can D/C Primary Prophylaxis if:
- 2-5 yrs of age, stable ART ≥ 6 mos with sustained (>3 mos) CD4 cell >200 cells/mm^3
- > 6 yrs of age, stable ART ≥ 6 mos, with sustained (>3 mos) CD4 > 100 cells/mm^3

Can D/C Secondary Prophylaxis if:
- > 2 yrs of age, completed 12 mos tx for MAC, asymptomatic & on stable ART & sustained (>6 mos) CD4 cell count ↑ to:
  - o >200 cells/mm^3 (2-6 yrs of age)
  - o >100 cells/mm^3 (>6 yrs of age)

Fungal Infections

Cryptococcosis
Primary prophylaxis is not recommended and there are no proven strategies for prevention of exposure.
- Prevention of Recurrence
  - o Long-term suppressive tx with fluconazole recommended post tx of cyptococcosis
- D/C Secondary Prophylaxis if:
  - o ≥ 6 yrs of age, on ART w/ ↑ CD4 to >200 cells/mm^3 for ≥ 6 mos; reinitiate if CD4 ↓ to < 200 cells/mm^3

PCP

Prevention of 1st Episode of Disease
- Infants born to HIV-infected women should be considered for prophylaxis beginning at 4-6 weeks of age
- If indeterminate HIV status continue until determined HIV uninfected or presumptively uninfected

D/C Primary Prophylaxis if:
- Age > 6 yrs, on ART for ≥ 6 mos, CD4 % ≥ 15% or CD4 count is ≥ 200 cells/mm^3
  Age 1-5 yrs, CD4 % ≥ 15% or CD4 count ≥ 500 cells/mm^3 for > 3 mos
- Reinitiate if criteria for prophylaxis are met. Prophylaxis should not be discontinued for HIV-infected infants < 12 mos of age

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D/C Secondary Prophylaxis
- Use same criteria as for D/C of primary prophylaxis

Parasitic Infections

Toxoplasmosis

Preventing 1st Episode of Disease
- Prophylaxis for toxo should be given to Toxo IgG (+) ***and***:
  - Age < 6 yrs: CD4 < 15%
  - Age > 6 yrs, adolescents: CD4 <100 cells/mm^3

D/C Primary Prophylaxis
- Age < 6 yrs: May be safe to D/C TMP-SMX when ART → ↑ CD4 > 15% (for > 3 mos)
- > 6 yrs of age: CD4 >200 cells/mm^3 can be used
- Restart prophylaxis when CD4 count falls below the threshold for D/C primary prophylaxis

D/C Secondary Prophylaxis
- For children > 6 years of age, reasonable to consider adult /adolescent criteria i.e. successful completion of initial therapy, remain asymptomatic with sustained ↑ in CD4 count>200 cells/mm^3 after ART>6 mos
- Adults & adolescents are at low risk for recurrence once initial tx successfully completed with sustained ↑ CD4 > 200 cells/mm^3 after ART
- Age < 6 yrs: Safety of D/C 2° prophylaxis in young children not extensively studied. Consider D/C 2° prophylaxis if CD4 count > 15% for ≥ 6 mos on stable ART.
- Highest risk of relapse within the 1st 6 mos after D/C prophylaxis. Monitor closely. Some experts consider obtaining brain (MRI) prior to D/C of prophylaxis.

Viral Infections

Hepatitis B Prevention

All HIV-infected children should receive immunization with hepatitis A and B vaccines.

- Guidelines for prevention of HBV infection in babies born to HIV-infected women are similar to those for non HIV-infected
- After completion of primary Hep B series, infants HBsAg neg with anti HBs < 10 mIU/ml should be revaccinated with 3 dose HBV vaccine series and then retested 1-2 mos after final dose
- No data available to date on modified hepatitis B vaccine dosing including doubling the standard dose. A randomized trial is underway.

Human Papilloma Virus (HPV): Prevention
- Immunization is recommended in young girls 11 to 12 yrs of age and can be given as early as 9 yrs of age
- Data for females without HIV infection → efficacy 95% for preventing HPV infection & high grade carcinoma & 99% efficacy for genital warts. No efficacy seen if prior exposure. Studies in HIV-infected persons not yet available; immunogenicity & efficacy not established in this population.
  - Quadrivalent vaccine is noninfectious & can be given to females with HIV infection
  - Immune response & efficacy might be less
  - Vaccine should be given according to the schedule for non HIV-infected children & adolescents
  - No published studies exist using the HPV vaccine to prevent HPV infection & lesions of the anus, penis or oral cavity in males; vaccine is not currently approved for males in the U.S.

Varicella Zoster Virus (VZV): Prevention
- Immunization of children aged 1 to 8 yrs (CDC clinical categories N, A, & B) & with CD4 ≥ 15% should be considered. Give 1st dose at 12 to 15 mos & 2nd dose 3 mos later.
- Efficacy studies on prevention of varicella in HIV-infected children are not available
- Data not available on mumps, measles, rubella & varicella vaccine and this should not be administered as a substitute for the single antigen varicella vaccine
- Data lacking on use of varicella vaccine in older children & adolescents
  - Experts recommend weighing risk of severe disease from wild type VZV vs. potential benefit of vaccine
  - Immunization may be considered for aged > 8 yrs with CD4 ≥ 200 cells/mm^3
- Vaccine may also be used for post exposure prophylaxis in children and adolescents who lack evidence of immunity to varicella.
  - Give as soon as possible & < 96 hrs after exposure
  - Varicella zoster immune globulin no longer made
  - A new product (VariZIG) produced in Canada is available under investigational protocol if needed
- There is no available prevention for zoster in HIV-infected adolescents & children. The vaccine for prevention of herpes zoster in immunocompetent adults > 60 yrs of age is not recommended for use in HIV-infected individuals at present.

Click here to access a supplemental document containing an extended summary of the Guidelines for Prevention and Treatment of Opportunistic Infections among HIV-Exposed and HIV-Infected Children