HIV/AIDS in Pediatrics: Antiretroviral Therapy

Juan Carlos Salazar, M.D. – Universidad de Connecticut, EE.UU.

Current recomendations
Research

Antiretroviral Therapy

- Perinatal infection the most common cause of pediatric HIV.
- Newborns have received ZDV in utero.
- Evaluation and diagnosis of perinatal/pediatric HIV needs to meet special considerations.
- Differences in immunologic parameters according to age.
- Pk varies according to age.
- Clinical manifestations are age specific.
- Adherence is more difficult than in adult populations.

Guidelines for the Use of Antiretroviral Agents in Pediatric HIV infection

Working Group on Antiretroviral Therapy and
Medical Management of HIV Infected Children.
NPHRC, HRSA, NIH
January 7, 2000

Therapy: General considerations

- Emphasis on prevention
    - Early identification of pregnant HIV + women
- All age groups, including pregnant women and children should be included in clinical trials.
- Medications should be approved for both adults and children.
- Pediatric clinical trials should measure
    - Growth and developmnent
- All approved drugs for adults may be used for children

Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. NPHRC, HRSA, NIH

- Management in conjunction with experts in pediatric HIV.
- Multidisciplinary approach (MD, RN, SW, psychologist, dietitian, clinical pharmacologist, dentist, etc..)

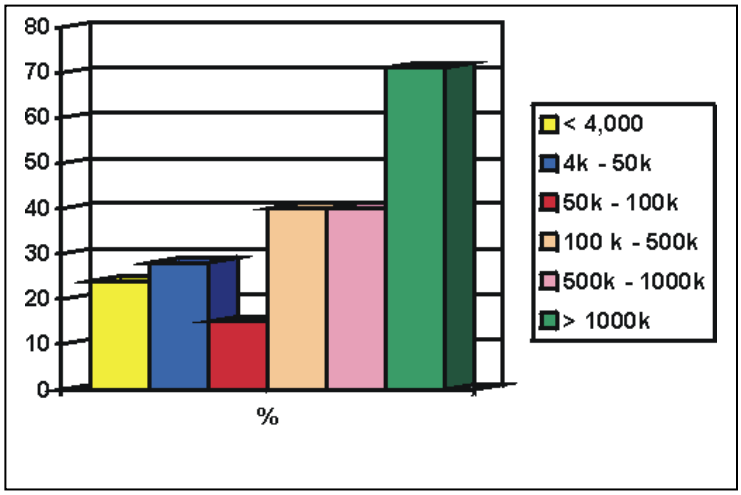
- Viral load and CD4+ cell measurements are essential.
- Pediatric formulation should take into account the following parameters
  - availability and palatability
  - quality of life
  - ability of parents or legal guardians to give the medications
  - interactions

Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. NPHRC, HRSA, NIH

- Limit use of antiretrovirals if patient will be unable to adhere to the regimen. Development of resistance can increase if not used correctly.
- Monitor growth and development. Nutritional therapy is fundamental in the management of pediatric patients.

Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. NPHRC, HRSA, NIH

Association of baseline HIV RNA copy with long term risk for death in HIV-infected children
Mean follow up = 5.1 years



Data from National Institute of Child Health and Human Development IV IgG Clinical Trial

- **Proven clinical benefit**
  - **Monotherapy**
    - ZDV (Pizzo et al. NEJM, 1988)

    - ddI (Butler et al. NEJM, 1991)
    - 3TC (Lewis et al. J Infect Dis, 1996)
    - d4T (Kline, et al. Pediatrics, 1995)
  - **Combined therapy is superior**
    - ZDV + 3TC (McKinney, et al. IDSA, 1997)
    - ZDV + ddI (Englund, et al. NEJM, 1997)
  - **Therapy with 2 NRTI's + PI is preferable**
    - ACTG 338 (ZDV + 3TC vs d4T + RTV vs ZDV + 3TC + d4T)
- When to initiate therapy ?
  - With any evidence of disease
    - Clinical category A, B, C
    - Immunologic categroy 2, 3
  - Age < 12 months:
    - all patients, once the diagnosis is confirmed
    - Independent from its classification
- When should you initiate therapy ?
  - > Asymptomatic, age > 12 months
    - Increase in viral load (> 0.7 log) or > 100,000 copies
    - age > 30 months, (> 0.5 log) or > 10,000 copies
    - decrease in CD4+ lymphocyte counts
    - development of clinical signs and symptoms
- Therapy ?
  - Preferred combinations
    - PI + 2 NRTI's
      - Nelfinavir or Ritonavir
      - Indinavir if able to take capsules
      - ZDV + 3TC
      - ZDV + ddI
      - d4T + ddI
      - d4T + 3TC

        - ZDV + ddC
    - NNRTI + 2PI
        - Efavirenz (Sustiva)
    - NNRTI + PI + NRTI

- How to initiate therapy ?
    - Alternatives
        - Nevirapine + 2NRTI's
        - 2 NRTI's
        -

Immunization

- **In general:**
    - Give 'em, and give'em as early as possible (before immune system deteriorates)
- **ADDITIONS:**
    - Pneumovax at 2 years
    - Influenza yearly, starting at 6 mos of age
- **SUBTRACTIONS:**
    - Varicella vaccine +/-, ok in pts not in category C or severe CD4+ depletion.
- Modifications
    - IPV rather than OPV (also for sibs/close contacts!)
    - MMR as early as possible
        - second dose as early as 1 month after the first dose
        - DO NOT GIVE MMR if severely immunocompromised (CD4 <500 1-5 yrs, <200 6 years and up)

Immunization- PPD issues

- **Positive is ≥ 5 mm (not 10!)**
- **Test annually, but begin at 3 months if high risk for TB**
- **Anergy:**
  - try to assess with a control; if control negative too, can't assess results of test
  - anergy may be temporary (acute illness)
- **If PPD positive (and CXR negative), need 12 months INH (not just 6-9)**
- **If exposed to contagious case, need INH too (even if PPD negative)**
- **If contact identified pos. for resistant TB, prophylaxis more complicated (call ID)**