A high risk of pneumonia in HIV-infected African children persists up to six months after initiation of antiretroviral therapy (ART)

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Background
• Respiratory tract infections are the most common cause of morbidity and mortality in HIV-infected children.
  – Rates of bacterial pneumonia are 25-fold higher among the HIV-infected. (Rosemary J Boyton, Curr Opin Pulm Med. 2005)
• Many interventions have been suggested to reduce pneumonia-related morbidity and mortality:
  – Routine immunisation
  – Provision of cotrimoxazole prophylaxis
• In some studies, antiretroviral therapy (ART) has been shown to reduce the risk of bacterial pneumonia in HIV-infected individuals. (Feikin D et al, Lancet Infect Dis 2004)

Methods
• We conducted a prospective observational study of HIV-infected children aged 1–10 years who started ART between October 2005 and November 2007 at Mulago Hospital in Uganda.
  – ART was initiated in accordance with WHO and national guidelines.
  – All children received cotrimoxazole prophylaxis and routine childhood immunizations.
  – 100 children who had been initiated on ART at least 6 months after enrolment were evaluated.
  – 34 of these completed 12 months of follow-up post-ART initiation
• Pneumonia was diagnosed when all of the following criteria were present:
  1. fever
  2. cough
  3. tachypnea
  4. pulmonary infiltrates on chest x-ray
• Tuberculosis was excluded by CXR, tuberculin skin testing, and induced sputum stain for acid fast bacilli.

Patient Characteristics
• At ART initiation:
  – Median age: 4 years
  – Median CD4 count: 340 cells/mm3 (12%)
  – Median HIV RNA: 5.4 log copies/ml
• ART regimens:
  – NVP-based (46%) or EFZ-based (54%)
• After 6 months of ART:
  – 85% had <400 copies/ml HIV RNA
  – median CD4 count was 760 (23%)

Results

<table>
<thead>
<tr>
<th>Time period relative to ART initiation</th>
<th># of cases</th>
<th>Incidence density (per person-month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤6 mo before</td>
<td>192</td>
<td>0.08</td>
</tr>
<tr>
<td>6–12 mo after</td>
<td>212</td>
<td>0.07</td>
</tr>
<tr>
<td>0–6 mo after</td>
<td>202</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Conclusion
• In this prospective cohort of HIV-infected children receiving cotrimoxazole prophylaxis, rates of pneumonia were high in the 6 months prior to ART and persisted up to 6 months post-ART.
  – Most likely due to immune suppression and not immune reconstitution
• Pneumonia rates decreased by 63% in the 6–12 months after ART.
  – Our data show that the effect of ART on reduction of pneumonia is apparent at > 6 months, presumably following adequate immune recovery.