Novel Diagnostic Modalities for TB Diagnosis among Children in Cambodia

Photo: James Nachtwey, Svay Rieng, Cambodia 2008
Pediatric TB Diagnosis

• Diagnosis of TB challenging
  – Symptoms often non-specific
• Microbiological diagnosis uncommon
  – Difficult to obtain sputum specimens
  – Paucibacillary disease
• Culture yield lower than among adults
  – 20% (10-14 years), 5% (5-9 years), 4% (<5 years)
• Standard diagnostic criteria: clinical, radiologic and epidemiologic data
  – Diagnostic accuracy poor
Children and a diagnostic “bottleneck”

- Validation of novel diagnostic technologies primarily among adults
- Limited pediatric TB prevalence and incidence data
- Prevalence of drug-resistant TB?
- No TB drug trials in children
- Few pharmacokinetic studies
- Negatively impacts TB vaccine trials
- Efficacy of control and prevention measures?
Objectives

- Evaluate the performance of the Xpert MTB/RIF in a pediatric cohort
- Evaluate the performance of the urine LAM assay in a pediatric cohort
- Evaluate diagnostic utility of stool specimens
- Determine prevalence of TB disease and latent TB infection in cohort of Cambodian children
Study Design

• Cross-sectional survey
• Location: Svay Rieng Province
• Enrollment arms:
  1. Household contacts of index patients with TB
  2. Children attending 28 outpatient health centers
  3. Children admitted to 2 district hospitals
• Enrollment from July 2010 until February 2011
In 1994, the Cambodian Health Committee (CHC) developed a novel community-based approach to TB and later to AIDS treatment.

- Svay Rieng Province is one of the poorest of Cambodia’s 10 provinces (aver. yearly income for family of 9 approx $220) and
- In 1994, the highest prevalence of TB (700/100,000)
TB Screening Process

- Admission to Svay Rieng District Hospital
- Collection of standardized data:
  - Medical history, symptom screening
  - TB exposure
  - HIV status and HIV exposure
- Systematic TB screening includes:
  - Physical examination
  - AP and lateral chest radiographs
  - Tuberculin skin test (TST)
- HIV testing
Laboratory Work-up

• Specimen collection includes:
  – 2 gastric aspirates
  – 1 induced sputum
  – 1 stool specimen
  – 1 urine specimen

• Microbiologic work-up:
  – AFB smear microscopy
  – LJ and MGIT culture for *M.tb.*
  – Xpert MTB/RIF

• Urine LAM
Preliminary Results

- 876 enrolled children
- High TB prevalence (16%)
- Yield of microbiological confirmation using routine culture methods is very low (1%)
- Xpert MTB/RIF can be used for gastric aspirates and provides rapid diagnosis of TB
- No incremental yield of Xpert MTB/RIF compared to culture
- Ultimately, different diagnostic tools might be needed to improve pediatric TB diagnosis
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Aeras, Annenberg Foundation, BD, FIND
Ongoing Research Work

• Mycobacterial detection:
  – GeneXpert
  – Urine LAM
  – Specimen: induced sputum, stool, string test, nasopharyngeal aspirate, blood

• Cytokine release assays/biomarkers:
  – Secreted (ELISA)
  – Intracellular (flow cytometry)
  – Gene Expression profiles
  – Proteomics