Technology Transfer of HIV Assays for Resource-Poor Settings

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Model for HIV Assays in Resource-Poor Settings

- Reference center
- Provincial or district level
- Primary care or rural setting
- Viral load
  - Expensive
  - Complex technology
  - Gold standard
- P24/Reverse transcriptase?
  - Lower cost
  - Less complex technology
- Ship samples (DBS or fixatives)
  - Least resource intensive
  - Least complex
HIV Viral Assay Working Group

- Members include representatives from:
  - Academia
  - CDC
  - NIH
  - International laboratories
  - Industry
Steps to Validation and Technology Transfer

- Performance characteristics
  - Sensitivity
  - Specificity
  - Precision
  - Reproducibility
  - Linearity

- Clinical validation
  - Diagnosis
  - Clinical monitoring
  - Progression of disease
Steps to Validation and Technology Transfer

- Technology transfer
- Proficiency testing
- Dissemination/Acceptance
Potential Viral Assays for Monitoring and Diagnosis

- Heat-denatured p24 antigen assay
- Reverse transcriptase assay
- Real time PCR
- Other assays, including other p24 assays and simple resistance assays such as OLA
HDp24 antigen- PerkinElmer Life Sciences

- Standard p24 antigen assay with modifications
  - Heat denaturation of Ab:Ag complexes
  - Signal amplification
  - Kinetic reading
- “Lab in a box”
  - Kit, ELISA reader, computer loaded with the kinetic software
Published data for HD-p24 assay

- Burgisser, et al 2000
- Nadal, et al 1999
- Ledergerber, et al 2000
- Pascual, et al 2002
- Schupbach, et al 1996
- Schupbach, et al 2001
Performance characteristics, Subtype B

- Sensitivity – very comparable to RNA, especially in untreated patients
- Specificity – 99-100%
- Reproducibility - Excellent
- Precision - Excellent
- Linearity – 500 to 6,250,000 fg/ml
Clinical Validation - Subtype B

- Infant diagnosis – Excellent (97% sensitive, 99-100% specificity)
- Clinical monitoring
  - In general p24 antigen decreases in parallel with HIV RNA in successfully treated patients
  - Correlation with HIV RNA is best at higher viral loads (>5000 -10,000 cp/ml)
  - p24 can be detected in some patients who have undetectable viral loads
Clinical Validation-Subtype B

- Correlation with Disease Progression

In 2 different studies, HDp24 was very predictive of CD4 decline and survival (Ledergerber, 2000) or progression to AIDS (Sterling, in press)
Sensitivity – Non-B subtypes compared with Roche RNA, v1.5

- Subtype A - 22+/29 (76%)
- Subtype C – 53+/61 (87%)
- Subtype D – 2+/10 (20%)
- Subtype F - 0+/1 (0%)
- Recombinant AG - 109+/117 (93%)
- Recombinant AE - 3+/6 (50%)
Clinical validation – Non-B subtypes

- Infant Diagnosis –

- Clinical monitoring – Cote d’Ivoire
  - Tehe & Schupbach – a modification of the basic kit gave excellent results
  - Tehe & Fiscus, testing the same specimens, had only good results
Summary

The HD-p24 assay worked very well with subtype B, A and D for diagnosis of infants.
Clinical monitoring has had variable results, although the data are still promising.
Additional work is needed for the non-B subtypes.
Each site should do independent evaluations to determine if the assay will work under specific lab and population conditions.
Technology Transfer Considerations

- Infrastructure - electricity, refrigeration, water
- Cost of the technologies - instruments and maintenance, as well as kits
- Human resources - scarcity of technicians, level of training needed
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