Workshop to accelerate the implementation of the Three Is for HIV/TB and earlier initiation of ART in Southern Africa, March 14-18, 2011, Johannesburg, South Africa.

Xpert MTB/RIF (Cepheid) update

Haileyesus Getahun
Stop TB Department, WHO
Geneva, Switzerland
<table>
<thead>
<tr>
<th>Location</th>
<th>Current practice</th>
<th>Delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referral hospital</td>
<td>Physician, specialists Culture, CXR, Microscopy</td>
<td>8 (0-45) days*</td>
</tr>
<tr>
<td>District hospital</td>
<td>Physician, Clinician CXR, Microscopy</td>
<td>18 (0-191) days*</td>
</tr>
<tr>
<td>Health centres</td>
<td>Clinician, nurse Microscopy</td>
<td>35 (21-56) days**</td>
</tr>
<tr>
<td>Health post/clinic</td>
<td>Clinician, nurse, HA No diagnosis- referral</td>
<td>35(21-56) days**</td>
</tr>
<tr>
<td>Community/ home</td>
<td>CHW, Rx supporters, patients No diagnosis - Referral</td>
<td>21 (7-49) days**</td>
</tr>
</tbody>
</table>

WHO recommendation on Xpert 2010

- Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB
  (Strong recommendation)

- Xpert MTB/RIF may be considered as a follow-on test to microscopy in settings where MDR-TB or HIV is of lesser concern, especially in further testing of smear-negative specimens.
  (Conditional recommendation)

Children are included in the recommendations
Suitable for district and sub-district levels
Assay principles and procedure

1. Sputum liquefaction and inactivation with 2:1 sample reagent
2. Transfer of 2 ml material into test cartridge
3. Cartridge inserted into MTB-RIF test platform (end of hands-on work)
4. Sample automatically filtered and washed
5. Ultrasonic lysis of filter-captured organisms to release DNA
6. DNA molecules mixed with dry PCR reagents
7. Seminested real-time amplification and detection in integrated reaction tube
8. Printable test result

Time to result, 1 hour 45 minutes
Results in 100 minutes

- End of hands-on work

- 2 ml sample is loaded into a cartridge
  - Add 2:1 v/v
  - Shake
  - Wait 15 min

- Sputum is liquefied with Sample Reagent

- Sample is automatically filtered and washed in the GeneXpert
  - Concentrates bacilli
  - Removes inhibitors

- Filter-captured organisms are ultrasonically lysed to release their DNA

- DNA molecules are mixed with dry PCR reagents

- Mixture is delivered to an integrated reaction tube for nested real-time amplification and detection

- Total time to result = 1h45min
Real time result through a computer
A multi-disease platform

- Drug susceptible TB
- Rifampicin resistance
- HIV viral load
- STI
- INH resistance
# Operational issues

<table>
<thead>
<tr>
<th>Issue</th>
<th>Performance / outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventive maintenance</td>
<td>Annual calibration (logistics and costs).</td>
</tr>
<tr>
<td>Storage, operating temperature</td>
<td>2-28°C storage; 15-30°C operation</td>
</tr>
<tr>
<td></td>
<td>High lab temperature = no effect on performance. (Error message at &gt;40°C)</td>
</tr>
<tr>
<td>Electrical supply and back-up power</td>
<td>Uninterruptable power supply with UPS (400 VA) for 20 min. Serial car batteries tested.</td>
</tr>
<tr>
<td>Biosafety requirements</td>
<td>Same as smear microscopy*</td>
</tr>
<tr>
<td>Waste management</td>
<td>Additional waste volume compared to smear microscopy.</td>
</tr>
</tbody>
</table>
Comparison of cost

- Microscopy = 1500 USD
- **Xpert MTB/RIF = 17,500 USD (4 module)**
- Culture and DST = 300,000 – 1.4 M USD

- Running cost for Xpert/test = 16.86 USD
- Running cost solid culture/test = 20 USD
- Running cost liquid culture/test = 30 USD
How to use Xpert?

Figure 1. Selection of individuals to test with Xpert MTB/RIF based on risk assessment.

A. Individuals at risk of MDR-TB
   - Diagnosed with TB or
   - Suspected of having TB

B. HIV (+) individuals
   (or HIV unknown in high HIV settings)
   suspected of having TB

Primary considerations

Individuals accessing health centre

Xpert MTB/RIF

HIV (-) individuals not at risk of MDR-TB with either:
   - Abnormal CXR
   - Sputum smear (-) but still suspected of having TB

Secondary considerations

TB, Rif resistance

- Enrol on MDR-TB regimen
- DST FLD and SLD
- ART if HIV +

TB, no Rif resistance

- Treatment regimen based on patient history
- ART if HIV +

No TB detected

- Appropriate further clinical management
- IPT if HIV +
Rapid Implementation of the Xpert MTB/RIF diagnostic test

Technical and operational ‘How-to’
Practical considerations

March 2011