Discussion Brief: Practical and Ethical Challenges around GeneXpert MTB/RIF Scale up  

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Multi-drug resistant (MDR) and extensively drug resistant (XDR) tuberculosis arise in patients experiencing improper treatment regimens, and reveal weaknesses in health delivery systems both for diagnosis and treatment for tuberculosis. Fewer than 20% of MDR/XDR-TB cases have access to valuable diagnosis and treatment options (International Journal of Tuberculosis and Lung Disease, December 2012).

A new rapid diagnostic tool for detecting rifampicin resistance was endorsed by the World Health Organization in December 2010. The endorsement of GeneXpert MTB/RIF provided global sites with a way to detect markers for drug-resistant TB, and promised to be a game-changer to the diagnosis of drug-resistant TB. Three years later, the cost of GeneXpert cartridges have been reduced by 40% and PEPFAR and UNITAID both created projects to increase uptake and utilization of the test in high-burden countries and by public sector entities in 145 eligible countries. (World Health Organization, 2013)

The rapid roll-out and scale-up in countries with very different epidemiology and health systems has generated an immense need for timely technical guidance and collaboration. Under the guidance of Christopher Gilpin, PhD, MPH, GHDonline moderator and scientist in TB Diagnostics and Laboratory Strengthening Unit of the Stop TB Department at the WHO, and a member of the team leading the global roll-out and scale-up of the GeneXpert MTB/RIF assay, GHDonline is the host of a series of virtual expert panels and discussions to improve the uptake and usage of GeneXpert MTB/RIF worldwide and especially in countries with limited resources. This brief summarizes lessons learned from our second panel hosted in December 2012.

Discussion was dominated by an ethical dilemma: should the use of GeneXpert MTB/RIF be extended to locations without access to proper treatment drugs? Experiences and anecdotes from panelists and members in the Democratic Republic of the Congo, Belgium, Cambodia, Ethiopia, Kinshasa, and South Africa, as well as from Cepheid, the manufacturer, can be found in this expert panel.

Key Points

1. It’s not always as easy as “plug it in”
   - Concerns arose about GeneXpert feasibility in low-resource clinical settings with limited access to electricity, or in locations where a power source is less than reliable.
   - GeneXpert can be used with a charger system that can provide power during periods of difficult electricity access.
   - Cepheid has also developed a solar-powered energy source option.
   - The value of GeneXpert is based around its ability to detect rifampicin resistance and referral to further technology is needed to confirm drug-resistance (DST) – Line Probe Assay (LPA) is the fastest way to do this, but requires outside laboratory support. Many of our experts were concerned about this time frame, especially in the case of HIV co-infected patients
   - The ASLM conference in Cape Town discussed the need for the MOH to expect a higher number of cases even before the implementation of GeneXpert to ensure cases are treated properly. They also found that due to the slow delivery of results from labs confirming drug-resistance, time for diagnosis of MDR-TB remains similar between Xpert and typical LPA methods.
     - ABT Associates has made an alert tool available, which allows GeneXpert to link to a cloud-based internet site to speed up the test confirmation process.

2. Implementation & Targeting
   - Sites in Ethiopia believed GeneXpert valuable for rapid diagnosis, especially as they found that patients previously treated for TB with history of contact with an MDR/XDR-TB case were 3x as likely to develop drug-resistance as someone with no treatment history
   - An NGO working in Cambodia found that the utilization of GeneXpert MTB/RIF for a TB REACH-funded case finding program greatly increased their MDR-TB diagnostic ability. They were able to diagnose 18 drug-resistant cases in 10 months, compared to their previous averages of 6 cases in 14 months. Cambodia is low in MDR-TB burden, but experiences a high incidence of tuberculosis. In order to control...
levels of drug-resistance, a rapid diagnosis such as with GeneXpert can be useful through risk-assessment strategies.

- GeneXpert accessibility increased in August of 2012, when cartridge prices went from $16.86 to $9.98, a 40% reduction.
- In December 2012, PEPFAR further funded the innovation with a $1.1 million donated to provide GeneXpert technology to countries with a high TB burden.
- To avoid false negative results, Cepheid recommends centrifuging paucibacillary samples prior to testing.
- Yearly calibration is required to keep Xpert working properly. A calibration kit is now available, which generates a report in 20 minutes to send back to Cepheid, compared with the previous method which included sending the entire module back for analysis.
- A Cepheid service provider is provided by Cepheid for onsite training of clinic teams, and requires no cost to the health center. Online training is also available (in 2011-2012, Cepheid provided online training to 667 clinicians).

3. Diagnosis is great, but drugs are not always available

- It is necessary to consider the implications of GeneXpert from a patient perspective: how ethical is it to offer someone a diagnosis but no treatment? This happens in rural locations with little access to the second-line drugs to treat MDR/XDR-TB. Parallels were drawn with the HIV movement, in which similar sensitivity was required on the part of health care professionals regarding illness counseling and confidential delivery of test results.
- However, knowledge and quantification of the magnitude of drug-resistance is vital to the process of resource mobilization and planning for infrastructural changes to health delivery systems in the context of tuberculosis.
- Beyond politics and treatment concerns, DR-TB requires patient education and counseling regarding how to avoid transmitting the disease to their friends and family. This awareness is valuable.
- Currently, health care workers in developing countries seem to not be keen to spend extra time counseling patients. Scale up of Xpert is believed to be a good opportunity for the WHO to make a statement prioritizing counseling for TB patients.

Key References

- Elisa Ardizzoni: Results from Xpert MTB/RIF implementation in MSF field projects (webcast)
- GHDonline Expert Panel: Challenges of rolling-out GeneXpert MTB/RIF in resource-limited settings
- Christopher Gilpin: Introduction and status of the global roll-out of Xpert MTB/RIF for the diagnosis of tuberculosis (webcast)
- Cepheid GeneXpert MTB/RIF training video
- GHDonline Expert Panel: Implementation of Xpert MTB/RIF in Resource-Limited Settings
- Improving your experience of Xpert MTB RIF (PDF)
- Solar energy powers GeneXpert IV Dx system for detection of tuberculosis and rifampicin resistance in district/sub-district public health care settings in Uganda. Soundiram Indira. GX and Solar, April 2011.
- WHO Monitoring of GeneXpert MTB/RIF roll-out
- Global Health Diagnostics Network
- Cepheid resources and external references (website resource list)
- Groups Slash Cost of Advanced TB Test for Developing Countries (Blog)