



Accelerating access to quality TB diagnosis for pediatric cases in 4 major cities in India

Accurate diagnosis of TB remains an impediment in the management of pediatric TB cases. The diagnosis is complicated because children are unable to expectorate sputum and TB can mimic many other common childhood diseases, including pneumonia, generalized bacterial and viral infections, malnutrition, and respiratory opportunistic infections associated with HIV. Under optimal circumstances, the sensitivity of smear microscopy for the diagnosis of childhood TB remains low. In the absence of bacteriological confirmation, the diagnosis of childhood TB in countries where TB is not endemic is based on a triad of close contact with an infectious patient, a positive tuberculin skin test (TST) result, and abnormalities on a chest radiograph. This criteria, however, has limited application in countries where TB is endemic as most individuals acquire infection and become TST positive during childhood and adolescence. Although growth of *M.tuberculosis* on Lowenstein-Jensen medium is considered to be the gold standard and liquid culture offers the possibility of more sensitive diagnosis of active TB and drug susceptibility; the turnaround time for results on culture tests remains high. These limitation pose challenges in establishing accurate diagnosis of TB in children add to the potential for both under and over-diagnosis.

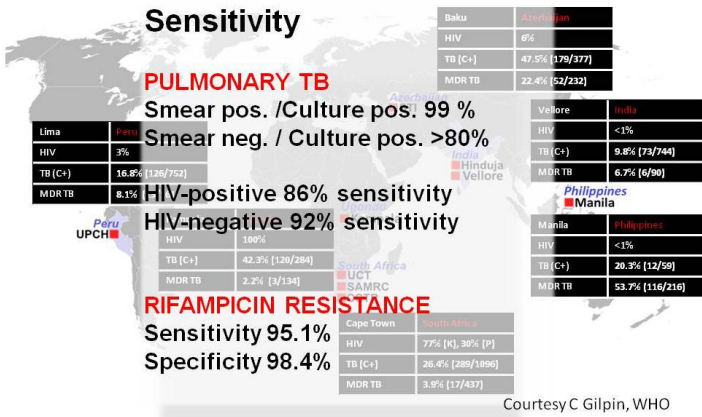
The WHO endorsed, Xpert MTB/RIF® (Cepheid, Sunnyvale, CA, USA), is a cartridge-based fully automated nucleic acid amplification test (CBNAAT) for the diagnosis of TB and rifampicin resistant -TB, suitable for use in disease-endemic countries.



It extracts DNA, concentrates, amplifies, identifies targeted nucleic acid sequences in the TB genome; Xpert MTB/RIF, is a highly sensitive and specific tool with a quick turn-around time, offers an easy and promising solution in addressing these challenges in the diagnosis of pediatric TB. Recently in the global guidance document released by WHO, it has been recommended that Xpert MTB/RIF may be used rather than conventional microscopy and culture **as the initial diagnostic test in all children presumed to have TB.**

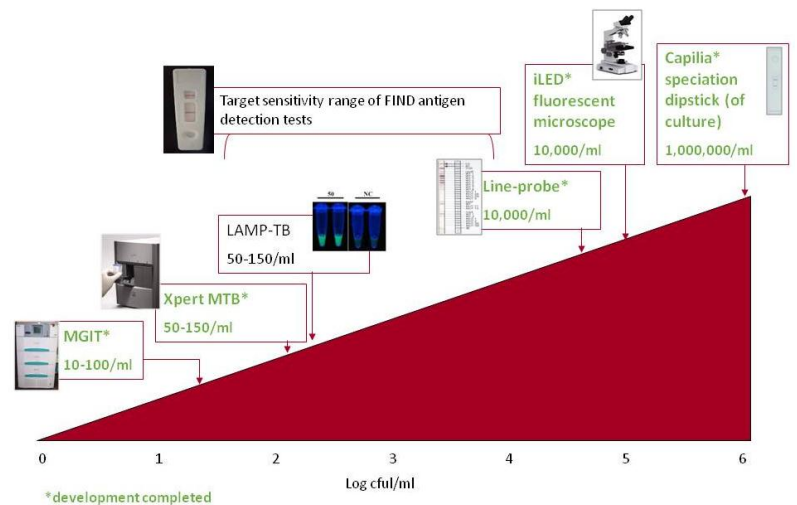
Multi-centre FIND Demonstration Studies

9 district, sub-district laboratories and microscopy centers in 6 countries



Specimen type	Category (No. of studies, No. of samples)	Pooled sensitivity Median (pooled 95% credible interval)	Pooled specificity Median (pooled 95% credible interval)
Lymph node tissue and aspirates	Xpert MTB/RIF against Reference standard 'Culture' (14 studies, 849 samples)	84.9% (72, 92)	92.5% (80, 97)
	Xpert MTB/RIF against "Composite Reference standard" (5 studies, one unpublished)	83.7% (74, 90)	99.2% (88, 100)
Cerebrospinal fluid	Xpert MTB/RIF against Reference standard 'Culture' (16 studies, 709 samples)	79.5% (62, 90)	98.6% (96, 100)
	Xpert MTB/RIF against "Composite Reference standard" (6 studies, 512 samples)	55.5% (51, 81)	98.8% (95, 100)
Pleural fluid	Xpert MTB/RIF against Reference standard 'Culture' (17 studies, 1385 samples)	43.7% (25, 65)	98.1% (95, 99)
	Xpert MTB/RIF against "Composite Reference standard" (7 studies, 698 samples)	17% (8, 34)	99.9% (94, 100)
Gastric lavage and aspirations	Xpert MTB/RIF against Reference standard 'Culture' (12 studies, 1258 samples)	83.8% (66, 93)	98.1% (92, 100)
	Xpert MTB/RIF against Reference standard 'Culture' (12 studies, 1258 samples)	81.2% (68, 90)	98.1% (87, 100)
Other tissue	Xpert MTB/RIF against Reference standard 'Culture'	81.2% (68, 90)	98.1% (87, 100)

This pediatric TB project represents concerted efforts of RNTCP, FIND, USAID, CDC and NIRT putting in place within a short period, a possible solution to the diagnostic gap. FIND in consultation with RNTCP is implementing this project in Delhi, Hyderabad, Chennai and Kolkata since April, 2014 with the funding support from USAID and CDC- CoAg.



Under this initiative, FIND has setup high throughput molecular labs at all four sites, catering exclusively to the TB diagnostic needs of pediatric population. These labs provide accurate evidence based same day diagnosis in line with internationally accepted standards of TB care with no cost to patient or provider both in private and public sector. This diagnostic option has been introduced at the existing RNTCP labs for the processing of pediatric specimen types such as sputum, gastric lavage, BAL, induced sputum, lymph node aspirates, etc, for use in Xpert MTB/RIF. Such an effort comes as a big financial relief to poor patients and obviates the necessity to visit private labs and related huge costs.

Any pediatrician both in public and private sector in these four cities can either refer their pediatric suspects to these labs or organize transfer of specimen for free of cost testing. The specimen would be tested on the same day and the results communicated to **referring provider** electronically (e-mail and SMS) and at the same time notified to RNTCP under Nikshay.

Project Update

Overall 9,391 pediatric suspects were tested between April to December'14 under this project. A total of 10,311 specimens were tested, of which 5,147 (49.9%) were non-respiratory specimens. Overall, Xpert gave 10,240 (99.3 %) valid results. Of the 9,162 presumptive TB cases enrolled, 592 (7.3%), were bacteriologically confirmed. TB detection rates were two fold higher on Xpert as compared to smear microscopy. Further, a total of 63 rifampicin resistant TB cases were detected. The project has demonstrated the feasibility of extending Xpert testing to non-sputum specimens from children with a very high proportion of interpretable results with more than a two fold increase in TB case detection over smear microscopy and detection of significant numbers of rifampicin resistant TB cases. The project has also shown the utility of offering upfront Xpert testing to pediatric presumptive TB and DR-TB patients under programmatic conditions.

We now seek your support to further expand the project coverage and thereby maximize the benefits.

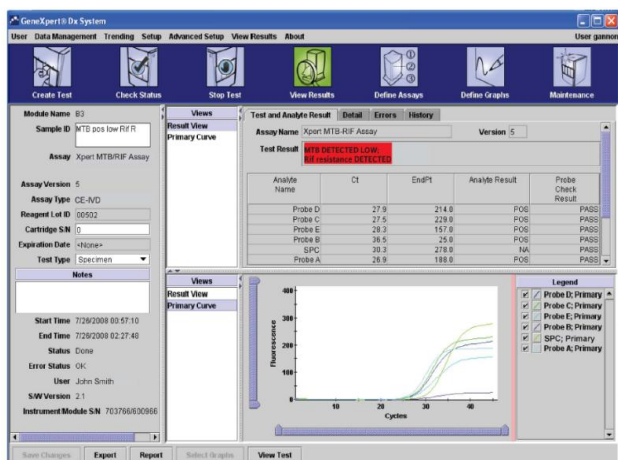
How to engage in the project

1. Refer the paediatric suspect or the suspect specimen to the below mentioned project site
2. Specimen transportation costs are covered under the project at a standard rate
3. Specimen to be accompanied by a dully filled standard lab request form (Annexure 1) with contact number and mail id of referring provider.
4. Test results will be communicated through SMS/or E-Mail within 12 working hours of specimen receipt
5. If TB is diagnosed the case can opt for free of cost treatment under RNTCP or opt for private treatment

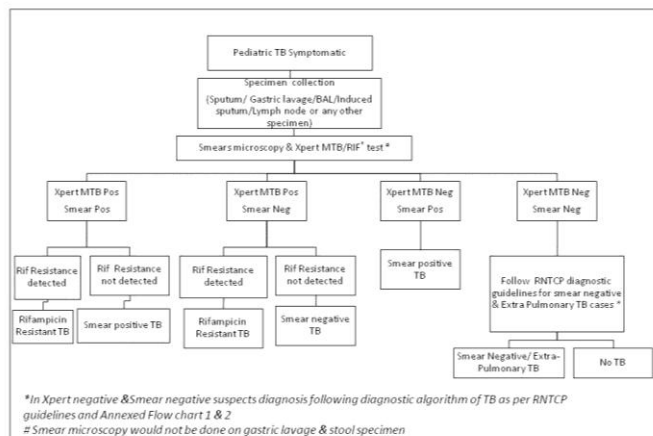
Process of sending samples:

All samples are to be collected and sent in a sterile container. (# for Extra-Pulmonary samples like Tissue Biopsy can be sent in Normal Saline, avoid sending samples in formalin)
Do not send stool, urine and blood examination

Example of GeneXpert Test results



Diagnostic Algorithm



RNTCP Request for Culture and Drug Sensitivity Testing Annexure I
(Required for Culture and DST Laboratory to conduct testing; please send copy to District TB Officer)

Patient Information		Molecular TB/DST result		LAB NO:		Date of Receiving								
Patient Name:		Test: <input type="checkbox"/>		Line Probe Assay (LPA) <input type="checkbox"/>		CBNAAT								
Patient Address with landmark		Test validity: <input type="checkbox"/>		Valid		<input type="checkbox"/> Invalid								
Patient Mobile No. or other Contact No		M. Tuberculosis <input type="checkbox"/>		Detected		NOT detected								
Age:		Rifampicin: <input type="checkbox"/>		Resistant		<input type="checkbox"/> Sensitive								
Date of collection		Isoniazid: <input type="checkbox"/>		Resistant		<input type="checkbox"/> Sensitive <input type="checkbox"/> Not Available								
Type of Specimen		Notes		Date tested:		Reported by (Name & Signature):								
Name referring facility (PHI/DMC/Other): District HIV Status : Known : +ve/-ve Unknown Past History of ATT : Yes/No		Lj/ Liquid Culture results												
		Date received	Specimen	Specimen No.	Smear result	Neg	Pos	1-19 col	+	++	+++	Contaminated		
Reason for Testing		A		B										
		Notes:												
DIAGNOSIS		FOLLOW-UP												
MDR Suspect Criteria		Result Date:		Reported by (Name & Signature):										
<input type="checkbox"/> Failure <input type="checkbox"/> Re-treatment case S+ at 4 th month <input type="checkbox"/> Contact of known MDR TB case <input type="checkbox"/> S+ at diagnosis, re-treatment case <input type="checkbox"/> Any follow up S+ <input type="checkbox"/> S- at diagnosis, re-treatment case <input type="checkbox"/> HIV TB case <input type="checkbox"/> Presumptive EP-TB <input type="checkbox"/> PLHIV Presumptive TB <input type="checkbox"/> Presumptive Pediatric TB <input type="checkbox"/> Enhanced case finding		PMDT Registration Number		Lj/ Liquid culture DST Results: (Note: 'S' if susceptible, 'R' if resistant)										
		Treatment month of Follow-up		Date DST Initiated	Specimen No	S	H	R	E	Z	Km	Ox	Eo	Other
RNTCP TB Reg No. and Type Cat		DR-TB Centre Name		Result Date:		Reported by (Name & Signature):								