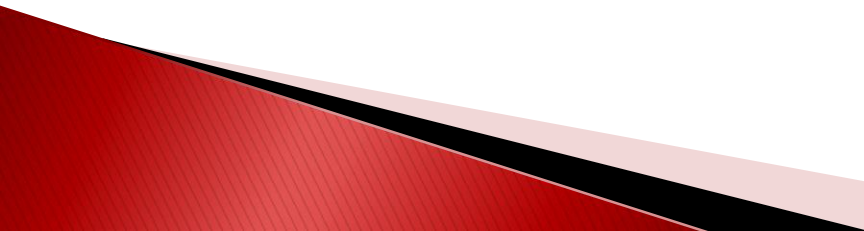


Nucleic Acid Amplification Test– How far it contributes in diagnosis in TB?

Dr. Rubina Yasmin
Associate Professor
Medicine
Dhaka Dental College

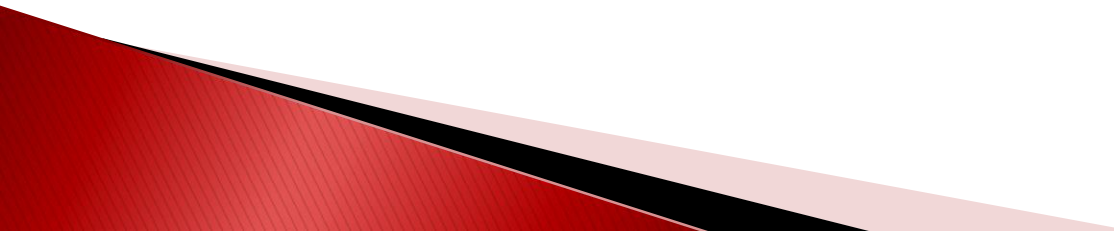
Introduction

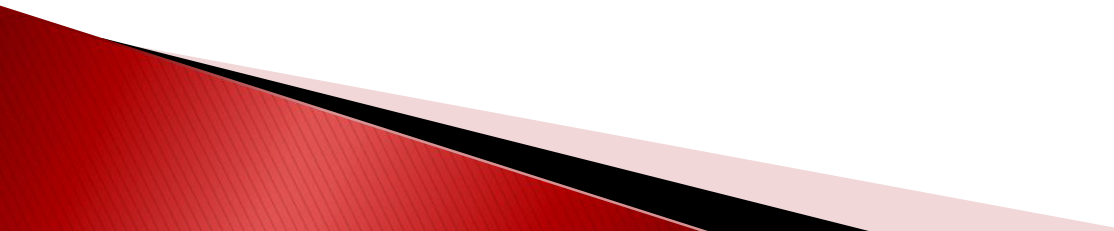
- ▶ The global burden of tuberculosis remains enormous.
 - ▶ It causes tremendous suffering world wide, especially in low and middle income countries.
 - ▶ In 2012 there were an estimated 8.6 million people developed TB and 1.3 million people died.
 - ▶ Among these death estimated 1,70,000 from MDR- TB.
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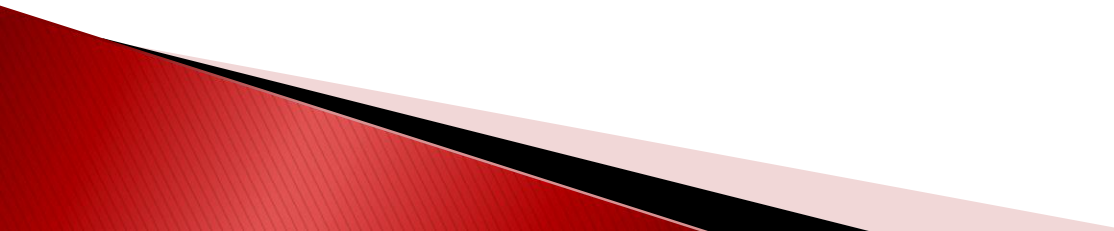
Bangladesh Perspective

- ▶ TB prevalence rate is 426 per 100,000 and incidence rate is 225 per 100,000.
- ▶ The rate of MDR-TB among new case of 1% translate into approx. 3000 new MDR- TB case per year.
- ▶ The Global Tuberculosis Report (2012) estimated MDR- TB rates of 2.2% in new cases and 15% among previously treated cases.

Why new investigation?

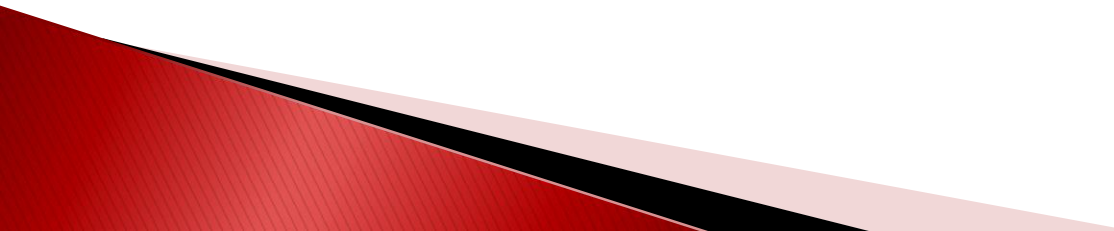
- ▶ TB can be cured if the disease is diagnosed early and treated properly.
 - ▶ No single diagnostic test currently satisfy all the demands of “quick”, “cheap” and “easy”.
 - ▶ Sputum smear microscopy remain the most common way to diagnose PTB, but it needs sufficient bacillary load in sputum and it can't detect drug resistance.
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- ▶ Globally ineffective Tuberculosis detection and the rise of MDR– TB and XDR– TB have led to calls for culture capability and DST in countries where disease is endemic.
 - ▶ Commercially available liquid culture systems and molecular line probe assays for rapid detection of MDR– TB are complex, costly and needs sophisticated lab.
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- ▶ PCR, the fast and most familiar method to amplify nucleic acid sequence has been limited largely due to complexities of DNA extraction, amplification, detection and for bio safety concern.
 - ▶ The complexity of standard NAAT prevent the expansion of this method.
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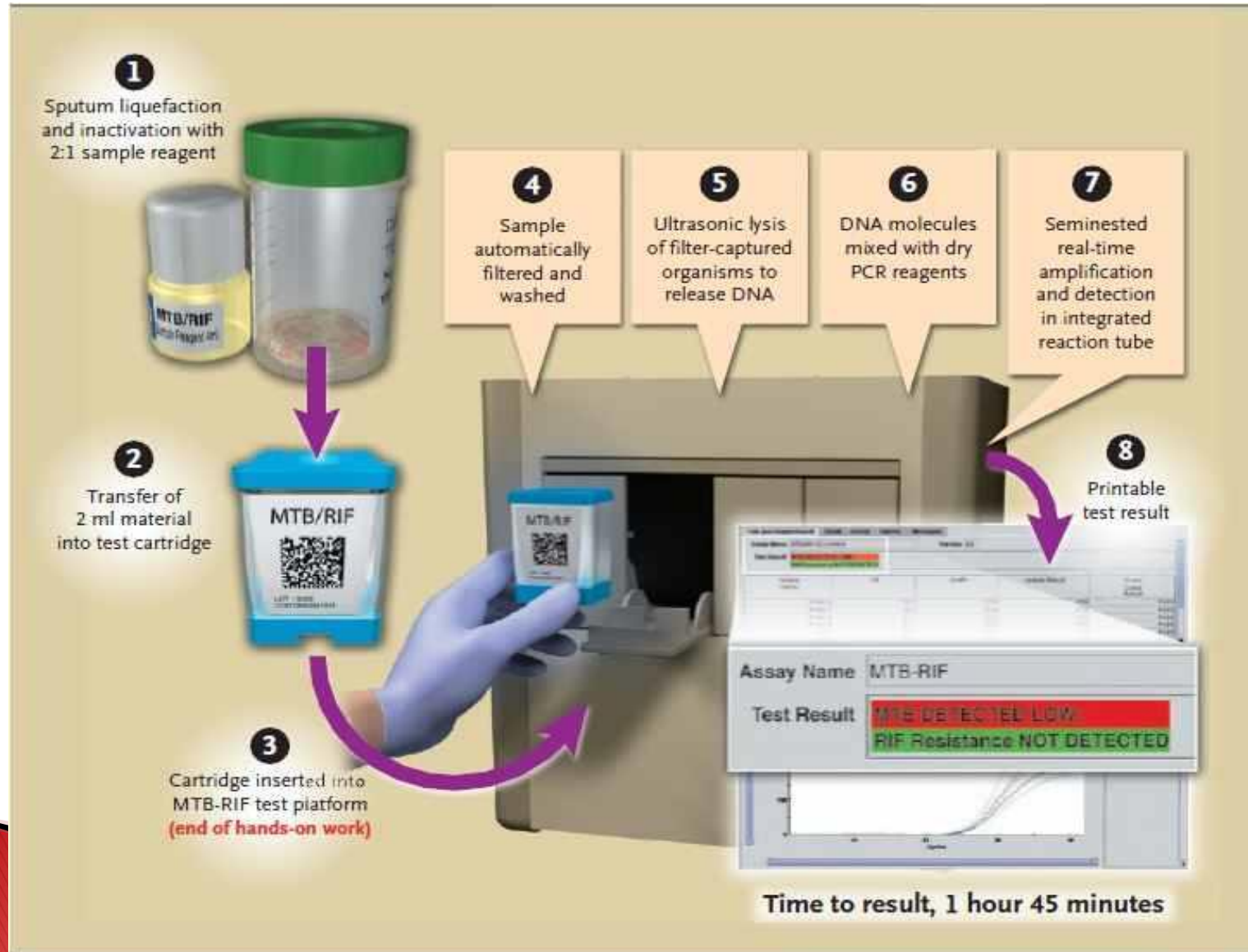
New NAAT– Xpert MTB/RIF

- ▶ WHO endorsed a rapid test, Xpert® MTB/RIF which is fully automated NAAT effective in the early diagnosis of TB as well as MDR TB.
- ▶ The Xpert MTB/RIF assay detect M. Tuberculosis and RIF resistance by PCR amplification of Rifampin resistance–determining region(RRDR) of the M. Tuberculosis rpoB gene and subsequent probing of this region for mutations that are associated with RIF resistance.

- ▶ The Xpert MTB/RIF test automates DNA extraction, amplification and detection inside a test cartridge that never reopens.
 - ▶ Data from study confirm that it generates no infectious aerosol.
 - ▶ By June, 2012, two thirds of countries with high tuberculosis burden and half of countries with high MDR TB had incorporated the test into their national TB control program.
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- ▶ The test appeared to be as sensitive as culture with smear +ve specimen but less sensitive with smear -ve pulmonary and extra pulmonary specimens.
- ▶ In Bangladesh Xpert MTB/RIF are used to diagnose TB in 26 centre.

Xpert MTB/RIF



Study on Xpert MTB/RIF

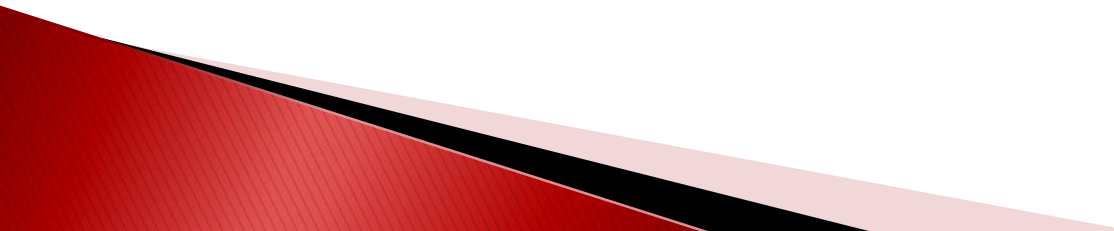
- ▶ Since 2012, more than 85 peer reviewed research papers on Xpert MTB/RIF for pulmonary, extra pulmonary and paediatric TB have been published.
- ▶ WHO expert group review the evidence. The major findings are–
 - Xpert MTB/RIF for the diagnosis of pulmonary TB and Rifampicin resistance in adults.
 - For PTB detection– reference standard – solid or liquid culture.

- For Rifampicin resistance– reference standard – phenotypic culture based drug susceptibility test. (27 studies, 9558 participants)
- As an initial diagnostic test replacing smear microscopy–
 - Pooled sensitivity– 88% (95% CrI 84%–92%)
 - Pooled specificity– 99% (95% CrI 98%–99%)
(22 studies, 9008 participants)
- As an add on test following a –ve smear microscopy result–
 - Pooled sensitivity– 68% (95% CrI 61%–74%)
 - Pooled specificity– 99% (95% CrI 98%–99%)
(23 studies, 7151 participants)

- For smear +ve and culture +ve TB
 - Pooled sensitivity– 98% (95% CrI 97%–99%)
(23 studies, 1952 participants)
- For smear –ve and culture +ve TB
 - Pooled sensitivity– 68% (95% CrI 61%–74%)
(23 studies, 7151 participants)
- For people living with HIV
 - Pooled sensitivity– 79% (95% CrI 70%–86%)
(7 studies, 1789 participants)

- People without HIV
 - Pooled sensitivity– 86% (95% CrI 76%–92%)
(7 studies, 1470 participants)
- For Rifampicin resistance detection–
 - Pooled sensitivity– 95% (95% CrI 90%–97%)
(17 studies, 555/2624 specimens)
 - Pooled specificity– 98% (95% CrI 97%–99%)
(24 studies, 2414 specimens)

- Xpert MTB/RIF for the diagnosis of extra pulmonary TB and Rifampicin resistance in adults.
- Lymph node tissue and aspirates–
 - Sensitivity– 84% (95% CrI 72%–92%)
 - Specificity– 92% (95% CrI 80%–97%)
- CSF
 - Sensitivity– 80% (95% CrI 62%–90%)
 - Specificity– 99% (95% CrI 96%–100%)

- Pleural fluid
 - Sensitivity- 44% (95% CrI 25%-68%)
 - Specificity- 98% (95% CrI 95%-99%)
 - Gastric lavage
 - Sensitivity- 84% (95% CrI 66%-93%)
 - Specificity- 98% (95% CrI 92%-100%)
 - Other tissue
 - Sensitivity- 81% (95% CrI 68%-90%)
 - Specificity- 98% (95% CrI 87%-100%)
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Cochrane review

Xpert MTB/RIF assay for pulmonary tuberculosis and Rifampicin resistance in adults–

Updated Cochrane review published in January 2014

- ▶ For MTB detection
 - Sensitivity– 89%
 - Specificity– 99%
- ▶ For Rifampicin resistance detection
 - Sensitivity– 95%
 - Specificity– 98%

WHO policy recommendations

- ▶ Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug sensitivity test as the initial diagnostic test in adults presumed to have MDR– TB or HIV associated TB.

(Strong recommendation high quality evidence.)

Cont.

- ▶ Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial diagnostic test in all adults presumed to have TB.

(Conditional recommendation acknowledging resource implications, high quality evidence.)

Cont.

- ▶ Xpert MTB/RIF may be used as a follow on test to microscopy in adults presumed to have TB, but not at risk of MDR– TB or HIV associated TB especially in further testing of smear –ve specimen.

(Conditional recommendation acknowledging resource implications, high quality evidence.)

Cont.

- ▶ Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test of CSF from patients presumed to have TB meningitis.

(Strong recommendation given the urgency of rapid diagnosis, very low quality of evidence.)

Cont.

- ▶ Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture and / or histohistopathology.)for testing of non respiratory specimen from patient presumed to have extra pulmonary TB.

(Conditional recommendation, very low quality evidence.)

Conclusion

- ▶ Xpert MTB/RIF should be made widely available in our health care setting to improve patient care as it is a rapid, simple and highly sensitive TB diagnostic tool that can easily be diploid close to the point of patient care.



**TOGETHER
WE CAN
STOP
TB**