Let's Talk TB

A Series on Tuberculosis, A Disease That Affects Over 2 Million Indians Every Year

Improving Access to Affordable and Quality TB Tests in India

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Abstract

This article describes the Initiative for Promoting Affordable, Quality TB tests (IPAQT; www.ipaqt.org), a coalition of private laboratories in India, supported by industry and non-profit groups, that has made several WHO-endorsed TB tests available at more affordable prices to patients in the private sector. General practitioner who manage TB should avoid inaccurate blood-based tests and use WHO-endorsed sputum tests for TB, including LED fluorescence smear microscopy, liquid cultures, line probe assays, and automated, cartridge-based molecular tests (i.e., Xpert MTB/RIF). These tests are validated and backed by strong evidence and WHO policy recommendations. Thanks to IPAQT, their prices have been reduced considerably in the Indian private sector.

Key words: tuberculosis, diagnosis, India, private sector

INTRODUCTION

Tuberculosis (TB) remains one of India's biggest health problems. Every year, India reports over 2 million TB cases. With the emergence of severe forms of drug-resistant TB, and concerns about TB drug shortages, there is much work to be done to control the epidemic.[1]

The Revised National TB Control Programme (RNTCP) has made good progress by providing basic TB diagnosis and treatment free of cost to all patients in the public sector. Recently, the RNTCP announced "*universal access to quality TB diagnosis and treatment for all TB patients in the community*"as its new goal for the next five-year plan.[2] This is a worthy goal, but any plan to reach all TB patients in India will need to include India's dominant private sector.

Why is the private health sector critical? In general, more than 80% of India's health care is delivered through the private sector. Most poor people who develop a cough first seek care in the informal private sector (chemists and unqualified practitioners), then from qualified practitioners.[3] Ultimately, about 50% of them end up in the public sector where they receive free treatment.[4] This pathway to curative care can take from weeks to months, during which patients continue to transmit infection to others. This delay, coupled with the high cost of care in private sector, drives many poor families into debt. And yet, for all the money spent, patients frequently undergo inaccurate TB tests and inappropriate TB drug treatment.[5,6] Consequently, promptly getting patients the right test in the private sector is a critical first step for interrupting transmission and reducing the risk of drug resistance.

Unfortunately, TB testing practices in the private sector are completely different from those in the public sector. A majority (more than 90%) of TB tests done by RNTCP are sputum smears. Diagnosis in the private sector is characterized by overuse of unreliable blood tests, low availability and high cost of reliable quality-assured diagnostics tools, preference of blood as a sample, inability of the providers to separate the good from the bad tests, and the commercial incentives that inflate cost to the patients.[5,7]

Worldwide, sputum is the most important sample for diagnosis of lung TB and every guideline recommends the use of sputum-based

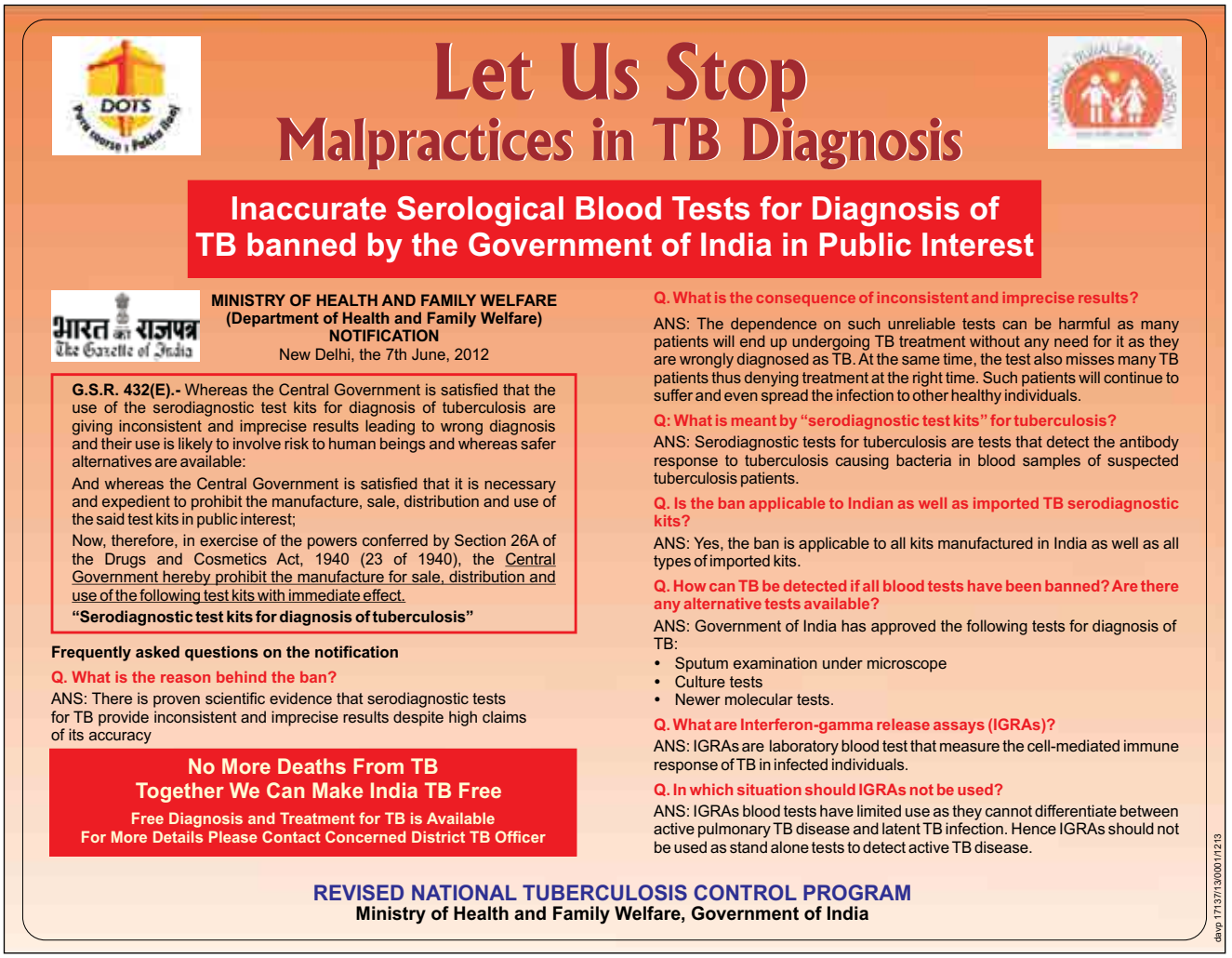

Figure 1 – Advertisement on the ban on TB serological tests, published by the Ministry of Health and Family Welfare in leading Indian newspapers in 2012. (open access at http://www.davp.nic.in/WriteReadData/ADS/eng_17137_1_1213c.pdf)

tests. But, for several reasons, including poor regulation and financial incentives, blood is the most popular sample in the Indian private sector.[5] Blood-based antibody tests are not accurate and discouraged by the World Health Organization (WHO).[8,9]

India's diagnostic landscape changed in June of 2012 when the Government of India, acting on the 2011 WHO policy against serological tests, banned the use, import, sale and manufacture of antibody-based blood tests for TB, and discouraged the use of interferon-gamma release assays (IGRAs) like "TB Gold" and "TB Platinum" for active TB (**Figure 1**).

Blood-based antibody tests have no clinical role in TB diagnosis and not recommended by any agency. There are acceptable blood tests (such as QuantiFERON-TB Gold, marketed in India as "TB Gold") for latent TB infection (which is treated with 6 – 9 months of isoniazid, to prevent progression from latent infection to active disease). These latent TB tests, however, are not recommended for active TB diagnosis by the WHO.[10] Use of IGRAs for active TB will result in unacceptably high rates of false-positive results because IGRAs, like the Mantoux tuberculin skin test, cannot separate latent TB infection from active TB disease, and a large proportion of the Indian population is latently infected.[11]

Since the serology ban created a void in the market, it is important to address this gap and make sure that WHO-endorsed, sputum-based TB tests replace the inappropriate blood tests in the private sector. There are 4 accepted sputum tests that are recommended by the WHO and these are also used by the RNTCP. These are sputum smears, Xpert MTB/RIF, line probe assay and liquid cultures.

Although not highly sensitive, smear microscopy test is still very useful (and cheap) because it can rapidly iden-

CLINICAL HIGHLIGHTS

- ❑ Tuberculosis (TB) remains one of India's biggest health problems. Every year, India reports over 2 million TB cases.
- ❑ Recently, the RNCTCP announced "Universal access to quality TB diagnosis and treatment for all TB patients in the community".
- ❑ Unfortunately, TB testing practices in the private sector are completely different from those in the public sector. A majority (more than 90%) of TB tests done by RNTCP are sputum smears; while blood is the most popular sample in the Indian private sector.
- ❑ Blood-based antibody tests have no clinical role in TB diagnosis and not recommended by any agency.
- ❑ There are 4 accepted sputum tests that are recommended by the WHO, and are also used by the RNTCP. These are sputum smears, Xpert MTB/RIF, line probe assay and liquid cultures.
- ❑ A new initiative (IPAQT) was launched in March 2013 to improve the affordability of WHO-endorsed TB tests.
- ❑ The IPAQT (Initiative for Promoting Affordable, Quality TB tests) is a coalition of private labs in India, supported by industry and non-profit groups (e.g., Clinton Health Access Initiative), that has made WHO-endorsed tests available at affordable prices to patients in the private sector.
- ❑ IPAQT aims to facilitate the delivery of WHO-endorsed tests to the TB patient at affordable prices, and promote the use of WHO-endorsed TB tests by building awareness about these new, validated/endorsed tests among health providers, laboratories and patients.
- ❑ Due to IPAQT, the cost of Xpert MTB/RIF is now reduced to Rs 2000 (maximum price labs can charge patients). The line probe assay (Hain Genotype MTBDRplus Version 2) is now available at Rs 1600. The MGIT liquid culture by BD is available for Rs 900 for detection.
- ❑ TB cases diagnosed via IPAQT member labs will be notified to the RNTCP for linkages to free TB drugs, where necessary.
- ❑ Any Indian laboratory can join IPAQT, provided they are accredited by a recognized agency (e.g., National Accreditation Board for Testing and Calibration Laboratories [NABL]), and agree to abide by the guiding principles of IPAQT.

tify the most infectious patients, and it is simple enough to be done in peripheral laboratories. Microscopy is under-used in the private sector, and this needs to change.

Recently, the WHO endorsed a new, rapid, automated, 2-hour molecular test called Xpert MTB/RIF, based on the GeneXpert platform (Cepheid Inc, USA), which can diagnose TB with great accuracy and can also detect those with drug-resistance.[12] A recent Cochrane review has shown that the Xpert MTB/RIF test has 88% sensitivity and 98% specificity when compared to culture.[13] Xpert MTB/RIF can detect rifampicin resistance with a sensitivity of 94% and specificity of 98%.[13] Data from many countries, including India, clearly show substantially better performance of the Xpert MTB/RIF test over conventional smear microscopy.[13] Emerging data also suggest that Xpert MTB/RIF has value for extrapulmonary TB (EPTB), especially TB lymphadenitis and TB meningitis. A WHO policy on the use of Xpert MTB/RIF for EPTB and childhood TB was published in 2013, and WHO endorsed Xpert for childhood TB, and some forms of EPTB.

Another WHO-endorsed rapid molecular test, the line probe assay (e.g., Genotype MTBDRplus by Hain Lifescience, Germany) can also detect resistance to INH and rifampicin with high accuracy, and allow for rapid initiation of MDR-TB treatment, while waiting for liquid culture and DST.[14] Lastly, liquid cultures (e.g., MGIT by BD, USA, and BacT/Alert by BioMerieux, France) are considered the gold standard for TB diagnosis and the only technology that can detect resistance to all major TB drugs. Liquid cultures are also very useful for smear-negative TB and EPTB.

If private physicians and laboratories replace suboptimal tests with the above sputum tests, this should greatly help improve the accuracy of TB diagnosis for patients in the country. The challenge is that good tests like GeneXpert, line probe assay and liquid culture are very expensive in the private sector. For example, the GeneXpert test can cost the patient as much as Rs. 3500 or higher in private laboratories. This is because WHO-endorsed tests are available at specially negotiated low prices only to the public sector, and import duties also add to the costs. In addition, financial incentives and laboratory margins further inflate the costs to make them virtually unaffordable to the average private sector patient.

This has now changed, thanks to a new initiative launched in March 2013, to improve the affordability of WHO-endorsed TB tests. Initiative for Promoting Affordable, Quality TB tests (IPAQT; www.ipaqt.org) is a coalition of private labs in India, supported by industry and non-profit groups (e.g., Clinton Health Access Initiative), that has made WHO-endorsed tests available at affordable prices to patients in the private sector (**Figure 2**).[15]

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IPAQT

INITIATIVE FOR PROMOTING AFFORDABLE AND QUALITY TB TESTS | www. ipaqt.org




EARLY AND ACCURATE DIAGNOSIS, FOLLOWED BY CORRECT TREATMENT, IS THE SOLUTION TO

TUBERCULOSIS

A DISEASE THAT EVEN TODAY,

KILLS ABOUT 1000 INDIANS EVERY DAY

THE NEED

TB affects 2 million people annually in India, and each undiagnosed and wrongly diagnosed case spreads the disease in their family and their community.

Approximately 4% of new TB patients have Multi-drug Resistant (MDR) strains of TB; among patients who had been treated for TB before, about 20% have MDR-TB.

While blood-based antibody tests have been popular in the private sector, these tests are inaccurate and banned by the Government of India. Blood-based tests like TB Gold and TB Platinum are meant for latent TB infection, not active TB.

There is a need to introduce affordable and accurate tests - i.e. those endorsed by the World Health Organization (WHO) and the Revised National TB Control Programme (RNTCP).

WHAT IT MEANS FOR YOUR PRACTICE

For the first time in India, via IPAQT, these WHO endorsed tests are being offered at substantially reduced prices. You can now get your patients tested for TB and MDR-TB and get fast results through molecular tests with high accuracy, offered by a network of quality-assured laboratories.

TO FIND A LAB NEAR YOU THAT IS A PART OF IPAQT AND FOR MORE INFORMATION ON THE TESTS PLEASE VISIT **WWW. IPAQT.ORG**

For updated information on IPAQT, please see brochure at the end of this booklet.

ABOUT IPAQT

IPAQT is an initiative of non-profit stakeholders and over 170 private labs/hospitals (approximately 10,000 collection centers) with a pan-India presence that have come together to provide WHO approved tests for TB at or below the following the patient prices

- **XPERT MTB/RIF TEST - Rs. 2200**
- **Genotype MTBDRplus TEST - Rs. 1800**
- **BACTEC MGIT LIQUID CULTURE - Rs. 900 for TB detection**
- **BacT/ALERT 3D liquid culture - Rs. 900 for TB detection**

(go to www.ipaqt.org for latest pricing information)

These 3 tests offer accuracy and speed are backed by strong evidence and WHO policy endorsements (www.who.int/tb/laboratory/policy_statements/en)

The Xpert MTB/RIF test (GeneXpert; Cepheid Inc.) can detect TB as well as Rifampicin resistance with high accuracy (about 90% sensitivity and 98% specificity) within hours.

The Genotype MTBDRplus (Hain Lifescience) assay can detect MDR-TB (INH and Rifampicin resistance) with high accuracy (about 98% sensitivity and 99% specificity for Rifampicin)

Liquid cultures are considered the gold standard for TB and offer the highest accuracy, with about 2 week turnaround.

Figure 2 – Flyer on the IPAQT initiative (www.ipaqt.org)

IPAQT aims to facilitate the delivery of WHO-endorsed tests to the TB patient at affordable prices, and promote the use of WHO-endorsed TB tests by building awareness about these new, validated/endorsed tests among health providers, laboratories and patients. Several private laboratories in India have agreed that in exchange for not exceeding negotiated, ceiling prices to patients, notifying the government of the cases diagnosed, promoting the use of these tests and participating in external quality assurance (EQA) they would get reagents at significantly reduced prices. In exchange for offering lower prices, the manufacturers and distributors would receive greater and more predictable volumes from the previously untapped private market.

The business model of IPAQT is based on a comparison of high margin low volume (premium) versus lower margin high volume (mass-market) pricing models. Thanks to IPAQT, the cost of Xpert MTB/RIF is now reduced to Rs 2200 (maximum price labs can charge patients). The line probe assay (Hain Genotype MTBDRplus Version 2) is now available at Rs 1800. The MGIT liquid culture by BD is available for Rs 900 for detection. These prices are approximately 30-50% less than the private market prices before IPAQT was launched, and the prices are comparable to the banned TB ELISA test for three antibodies. Thus, for the money patients were paying for inaccurate tests, they can now get WHO-endorsed, high-quality tests.

TB cases diagnosed via IPAQT member labs will be notified to the RNTCP for linkages to free TB drugs, where necessary. Any Indian laboratory can join IPAQT, provided they are accredited by a recognized agency (e.g., National Accreditation Board for Testing and Calibration Laboratories [NABL]), and agree to abide by the guiding principles of IPAQT. Laboratories that join IPAQT must agree to stop doing TB serology and avoid promoting tests (e.g., IGRAs) that are discouraged by the RNTCP.

Since its launch in March 2013, the IPAQT initiative has already achieved a pan-India presence – with over 170 labs, which encompasse over 5000 franchisee labs and collection centers committed to providing these tests at affordable prices. The number of labs is expected to increase significantly in the months ahead. Thus, this initiative is expected to greatly increase affordability for private sector patients, and improve the quality of TB care in the country. In the long run, removal of import duties for all WHO-endorsed TB tests (under lifesaving drugs exemption) along with encouraging domestic development of high-quality TB tests will be critical to achieving the RNTCP goal of universal access.

CONFLICTS OF INTEREST

The author has no financial or industry conflicts. He serves on the Governing Council of the Initiative for Promoting Affordable, Quality TB tests (IPAQT; www.ipaqt.org).

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