

# Let's Talk TB

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

MADHUKAR PAI, MD, PHD—Author and Series Editor

Madhukar Pai is a TB researcher and an associate professor of epidemiology and Biostatistics at McGill University in Montreal, Canada. He has served as co-chair of the Stop TB Partnership's Working Group on New Diagnostics. He holds honorary professorship positions at the Christian Medical College, Vellore, India; University of Cape Town, South Africa; and Stellenbosch University, South Africa.

## Improving Access to Affordable and Quality TB Tests in India

### Abstract

*This article describes the Initiative for Promoting Affordable, Quality TB tests (IPAQT; [www.ipaqt.org](http://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.<sup>1</sup>

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.<sup>2</sup> 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.<sup>3</sup> Ultimately, about 50% of them end up in the public sector where they receive free treatment.<sup>4</sup> 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.<sup>5,6</sup> 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.<sup>5,7</sup>

Worldwide, sputum is the most important sample for diagnosis of



# Let Us Stop Malpractices in TB Diagnosis



## Inaccurate Serological Blood Tests for Diagnosis of TB banned by the Government of India in Public Interest



MINISTRY OF HEALTH AND FAMILY WELFARE  
(Department of Health and Family Welfare)  
NOTIFICATION  
New Delhi, the 7th June, 2012

**G.S.R. 432(E).**- Whereas the Central Government is satisfied that the use of the serodiagnostic test kits for diagnosis of tuberculosis are giving inconsistent and imprecise results leading to wrong diagnosis and their use is likely to involve risk to human beings and whereas safer alternatives are available:

And whereas the Central Government is satisfied that it is necessary and expedient to prohibit the manufacture, sale, distribution and use of the said test kits in public interest;

Now, therefore, in exercise of the powers conferred by Section 26A of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government hereby prohibit the manufacture for sale, distribution and use of the following test kits with immediate effect.

**“Serodiagnostic test kits for diagnosis of tuberculosis”**

### Frequently asked questions on the notification

#### Q. What is the reason behind the ban?

ANS: There is proven scientific evidence that serodiagnostic tests for TB provide inconsistent and imprecise results despite high claims of its accuracy

**No More Deaths From TB  
Together We Can Make India TB Free**

Free Diagnosis and Treatment for TB is Available  
For More Details Please Contact Concerned District TB Officer

#### Q. What is the consequence of inconsistent and imprecise results?

ANS: The dependence on such unreliable tests can be harmful as many patients will end up undergoing TB treatment without any need for it as they are wrongly diagnosed as TB. At the same time, the test also misses many TB patients thus denying treatment at the right time. Such patients will continue to suffer and even spread the infection to other healthy individuals.

#### Q: What is meant by “serodiagnostic test kits” for tuberculosis?

ANS: Serodiagnostic tests for tuberculosis are tests that detect the antibody response to tuberculosis causing bacteria in blood samples of suspected tuberculosis patients.

#### Q. Is the ban applicable to Indian as well as imported TB serodiagnostic kits?

ANS: Yes, the ban is applicable to all kits manufactured in India as well as all types of imported kits.

#### Q. How can TB be detected if all blood tests have been banned? Are there any alternative tests available?

ANS: Government of India has approved the following tests for diagnosis of TB:

- Sputum examination under microscope
- Culture tests
- Newer molecular tests.

#### Q. What are Interferon-gamma release assays (IGRAs)?

ANS: IGRAs are laboratory blood test that measure the cell-mediated immune response of TB in infected individuals.

#### Q. In which situation should IGRAs not be used?

ANS: IGRAs blood tests have limited use as they cannot differentiate between active pulmonary TB disease and latent TB infection. Hence IGRAs should not be used as stand alone tests to detect active TB disease.

**REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAM**  
Ministry of Health and Family Welfare, Government of India

dhsp.17137\_130001123

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](http://www.davp.nic.in/WriteReadData/ADS/eng_17137_1_1213c.pdf))

lung TB and every guideline recommends the use of sputum-based tests. But, for several reasons, including poor regulation and financial incentives, blood is the most popular sample in the Indian private sector.<sup>5</sup> Blood-based antibody tests are not accurate and discouraged by the World Health Organization (WHO).<sup>8,9</sup>

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.<sup>10</sup> 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.<sup>11</sup>

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.

# Let's Talk TB

Improving Access to Affordable and Quality TB Tests in India

## 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 1700 (maximum price labs can charge patients). The line probe assay (Hain Genotype MTB-DRplus 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.

Although not highly sensitive, smear microscopy test is still very useful (and cheap) because it can rapidly identify 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.<sup>12</sup> A recent Cochrane review has shown that the Xpert MTB/RIF test has 88% sensitivity and 98% specificity when compared to culture.<sup>13</sup> Xpert MTB/RIF can detect rifampicin resistance with a sensitivity of 94% and specificity of 98%.<sup>13</sup> Data from many countries, including India, clearly show substantially better performance of the Xpert MTB/RIF test over conventional smear microscopy.<sup>13</sup> 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 is expected this year.

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.<sup>14</sup> 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 sub-optimal 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](http://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



INITIATIVE FOR PROMOTING AFFORDABLE AND QUALITY TB TESTS | [www.ipaqt.org](http://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](http://WWW.IPAQT.ORG)

## ABOUT IPAQT

IPAQT is an initiative of non-profit stakeholders and over 50 private sector 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. 1700
- Genotype MTBDRplus TEST - Rs. 1600
- BACTEC MGIT LIQUID CULTURE - Rs. 900 for TB detection
- BacT/ALERT 3D liquid culture - Rs. 900 for TB detection

(go to [www.ipaqt.org](http://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](http://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](http://www.ipaqt.org))

# Let's Talk TB

Improving Access to Affordable and Quality TB Tests in India

affordable prices to patients in the private sector (Figure 2).<sup>15</sup>

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 1700 (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. These prices are approximately 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 50 labs which encompasses over 3500 franchisee labs and greater than 10,000 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](http://www.ipaqt.org)).

**Acknowledgement.** This article is an updated version of an editorial first published in the *Journal of Laboratory Physicians* (citation: Pai M. Promoting affordable and quality tuberculosis testing in India. *J Lab Physicians* 2013;5:1-4. Available from: <http://www.jlponline.org/text.asp?2013/5/1/1/115895>). It is being reproduced with the explicit permission of the Editor of *Journal of Laboratory Physicians*.

## REFERENCES:

1. Udhwadia ZF. MDR, XDR, TDR tuberculosis: ominous progression. *Thorax*. 2012;67:286-8.
2. Sachdeva KS, Kumar A, Dewan P, Satyanarayana S. New Vision for Revised National Tuberculosis Control Programme (RNTCP): Universal access - "Reaching the un-reached". *Indian J Med Res*. 2012;135:690-4.
3. Kapoor SK, Raman AV, Sachdeva KS, Satyanarayana S. How Did the TB Patients Reach DOTS Services in Delhi? A Study of Patient Treatment Seeking Behavior. *PLoS One*. 2012;7:e42458.
4. Satyanarayana S, Nair SA, Chadha SS, et al. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. *PLoS One*. 2011;6:e24160.
5. Jarosawski S, Pai M. Why are inaccurate tuberculosis serological tests widely used in the Indian private healthcare sector? A root-cause analysis. *J Epidemiol Global Health*. 2012;2:39-50.
6. Udhwadia ZF, Pinto LM, Uplekar MW. Tuberculosis management by private practitioners in Mumbai, India: has anything changed in two decades? *PLoS ONE*. 2010;5:e12023.
7. Singh S, Katoch VM. Commercial serological tests for the diagnosis of active tuberculosis in India: time for introspection. *Indian J Med Res*. 2011;134:583-7.
8. Steingart KR, Flores LL, Dendukuri N, et al. Commercial serological tests for the diagnosis of active pulmonary and extrapulmonary tuberculosis: an updated systematic review and meta-analysis. *PLoS Med*. 2011;8:e1001062.
9. World Health Organization. Policy statement: Commercial serodiagnostic tests for diagnosis of tuberculosis. In: Geneva: World Health Organization; 2011.
10. World Health Organization. Policy statement: Use of tuberculosis interferon-gamma release assays (IGRAs) in low- and middle-income countries. In: Geneva: World Health Organization; 2011.
11. Metcalfe JZ, Everett CK, Steingart KR, et al. Interferon-gamma release assays for active pulmonary tuberculosis diagnosis in adults in low- and middle-income countries: systematic review and meta-analysis. *J Infect Dis*. 2011;204 Suppl 4:S1120-9.
12. World Health Organization. Policy statement: automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system. In: Geneva: World Health Organization; 2011.
13. Steingart K, Sohn H, Schiller I, et al. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database Syst Rev*. 2013;Issue 1. Art. No.: CD009593.
14. Policy statement. Molecular line probe assays for rapid screening of patients at risk of multidrug-resistant tuberculosis (MDR-TB). World Health Organization, 2008. (Accessed 2011, at [http://www.who.int/tb/laboratory/policy\\_statements/en/index.html](http://www.who.int/tb/laboratory/policy_statements/en/index.html).)
15. Kay M. Private firms form initiative to offer accurate and affordable TB tests. *BMJ*. 2013;346:f2161.