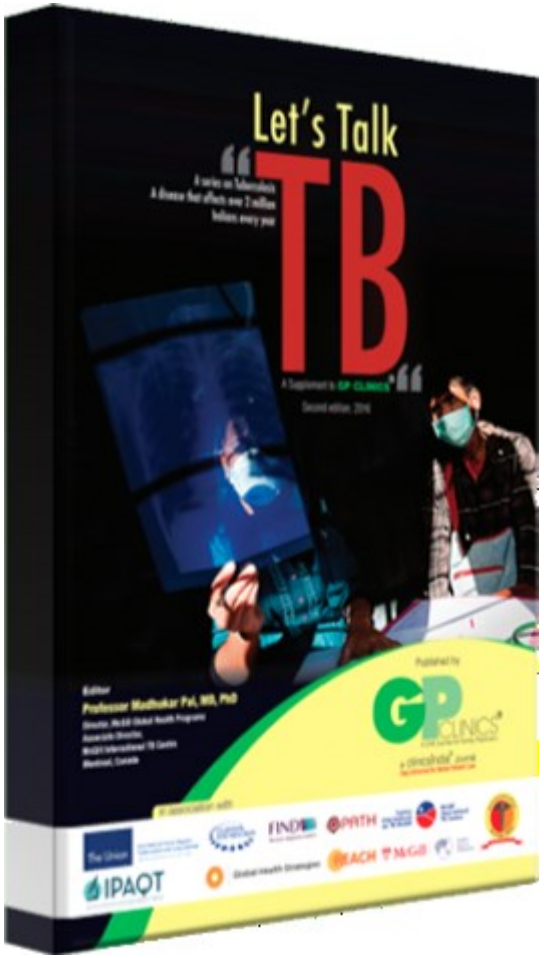


Let's Talk TB:

A Supplement to GP CLINICS

Chapter 4: Improving Access to Affordable and Quality TB Tests in India

Authors: Madhukar Pai, MD, PhD—Author and Series Editor

Tuberculosis

- Tuberculosis (TB) remains one of India's biggest health problems
- Every year, India reports over 2 million TB cases
- Emergence of severe forms of drug-resistant TB and concerns about TB drug shortages
  - Much work to be done to control the epidemic

Revised National TB Control Programme

- 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
- 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?

- 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
- About 50% of them end up in the public sector where they receive free treatment

- This pathway 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
- For all the money spent, patients frequently undergo inaccurate TB tests and inappropriate TB drug treatment

- 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

Private Sector

- 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

Private Sector

- 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
- The commercial incentives that inflate cost to the patients

Sputum

- Sputum is the most important sample for diagnosis of lung TB and every guideline recommends the use of sputum-based tests
- For several reasons (including poor regulation and financial incentives) blood is the most popular sample in the Indian private sector
  - Blood-based antibody tests are not accurate and discouraged by the **World Health Organization (WHO)**

Diagnostics in India

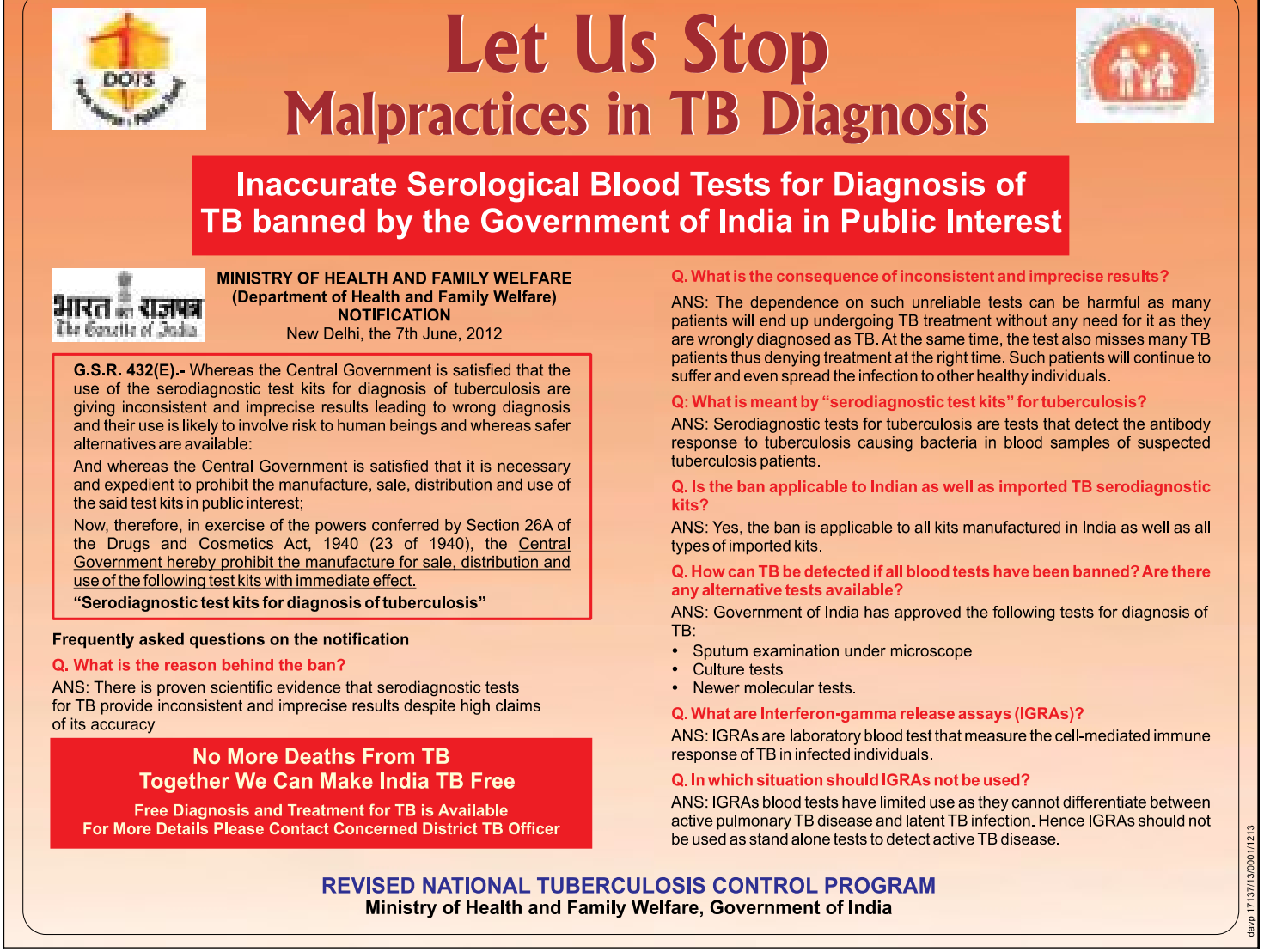
- India's diagnostic landscape changed in June of 2012 when the Government of India:
  - Banned the use, import, sale and manufacture of antibody-based blood tests for TB
  - Discouraged the use of interferon-gamma release assays (IGRAs) like "TB Gold" and "TB Platinum" for active TB

Latent TB

- There are acceptable blood tests (QuantiFERON-TB Gold/TB Gold) for latent TB infection
  - Treated with 6-9 months of isoniazid to prevent progression from latent infection to active disease
- These latent TB tests are not recommended for active TB diagnosis by the WHO

IGRAs

- Use of IGRAs for active TB will result in unacceptably high rates of false-positive results
- IGRAs (like the Mantoux tuberculin skin test) cannot separate latent TB infection from active TB disease
  - A large proportion of the Indian population is latently infected



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

davp 17137/13/0001/1213

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)

Sputum Based Tests

- The serology ban created a void in the market
  - Need to address this gap and make sure that WHO-endorsed, sputum-based TB tests replace the inappropriate blood tests in the private sector
- 4 accepted sputum tests that are recommended by the WHO and these are also used by the RNTCP
  - Sputum smears
  - Xpert MTB/RIF
  - Line probe assay
  - Liquid cultures

Smear Microscopy

- Although not highly sensitive, **Smear Microscopy Test** is still very useful (and cheap)
  - Can rapidly identify the most infectious patients
  - It is simple enough to be done in peripheral laboratories
- Microscopy is under-used in the private sector, and this needs to change to be done in peripheral laboratories
- Microscopy is under-used in the private sector, and this needs to change

Xpert

- WHO endorsed a new, rapid, automated, 2-hour molecular test called **Xpert MTB/RIF**
- Based on the **GeneXpert platform** (Cepheid Inc, USA)
  - Can diagnose TB with great accuracy
  - Can also detect those with drug-resistance

Xpert

- A recent Cochrane review:
  - Xpert MTB/RIF test has 88% sensitivity and 98% specificity when compared to culture
  - Xpert MTB/RIF can detect rifampicin resistance with a sensitivity of 94% and specificity of 98%
- Data from many countries (including India) show substantially better performance of the Xpert MTB/RIF test over conventional smear microscopy
- Emerging data suggest that Xpert MTB/RIF has value for extra- pulmonary 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

Line Probe Assay (LPAs)

- The **Line Probe Assay** (e.g. Genotype MTBDRplus by Hain Lifescience, Germany) can also detect resistance to INH and rifampicin with high accuracy
- Allows for rapid initiation of MDR-TB treatment, while waiting for liquid culture and DST

Liquid Cultures

- Liquid cultures
  - **MGIT** by BD, USA
  - **BacT/Alert** by BioMerieux, France
- The gold standard for TB diagnosis
- The only technology that can detect resistance to all major TB drugs
- Liquid cultures are also very useful for smear-negative TB and EPTB

Replacing sub-optimal tests

- If private physicians and laboratories replace sub-optimal tests with sputum tests, this should greatly help improve the accuracy of TB diagnosis for patients in the country

Challenges

- Good tests like GeneXpert, line probe assay and liquid culture are very expensive in the private sector
- GeneXpert test can cost the patient as much as Rs. 3500 or higher in private laboratories
  - WHO-endorsed tests are available at specially negotiated low prices only to the public sector, and import duties also add to the costs
- Financial incentives and laboratory margins further inflate the costs to make them unaffordable to the average private sector patient

IPAQT

- 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

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

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

IPAQT

- IPAQT aims to facilitate the delivery of WHO-endorsed tests to the TB patient at affordable prices
- Promote the use of WHO-endorsed TB tests by building awareness about these validated/endorsed tests among health providers, laboratories and patients

Private Laboratories in India

- 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

IPAQT

- IPAQT model is based on a comparison of high margin low volume (premium) versus lower margin high volume (mass-market) pricing models
- Thanks to IPAQT…
  - 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 **Rs 1600**
  - The MGIT liquid culture by BD is **Rs 900** for detection
- These prices are approximately **30-50% less** than the private market prices before IPAQT was launched
- The prices are comparable to the banned TB ELISA test for three antibodies
- With 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])
  - 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

The IPAQT Initiative since launch

- Since March 2013, the IPAQT initiative has already achieved a pan-India presence
  - Over 100 labs
    - Encompass over 3500 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

- 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

Conflict 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
  - www.ipaqt.org

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