

# Let's Talk TB

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

## Diagnosis of Pulmonary Tuberculosis: What Every GP Should Know

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### Abstract

*India has the highest burden of tuberculosis (TB) in the world, and every GP unit need to consider TB as a differential diagnosis in persons with cough lasting two weeks or more, or with unexplained chronic fever and/or weight loss. Sputum is the most important sample for laboratory testing. Although blood is a popular sample in the Indian private sector, there is no accurate blood test for active TB. Blood-based antibody tests (e.g., IgG/IgMELISA or rapid tests) and interferon-gamma release assays (e.g., TB Gold) are not accurate and should not be used for pulmonary TB diagnosis. In fact, the Government of India has recently banned the use of serodiagnostic tests for TB. There are three internationally accepted sputum tests for active TB: sputum smear microscopy for acid-fast bacilli; nucleic acid amplification test (e.g., GeneXpert); and culture. Chest radiography is useful but cannot provide a conclusive diagnosis on its own, and needs to be followed by sputum testing.*

Key words: tuberculosis; diagnosis; India; serological tests; test accuracy; case finding

diagnosis can help reduce the amount of lung damage and prevent longterm complications such as bronchiectasis and hemoptysis.

India continues to have the highest number of TB cases in the world, with over 2 million active TB cases every year.<sup>2</sup> Drug resistant TB, including multi-drug resistant disease (MDR), and extensively drug resistant TB (XDR-TB), is a growing concern, especially in hot-spots like Mumbai and urban slums.<sup>3</sup> Studies have shown considerable delays in TB diagnosis, and patients often move from one healthcare provider to another before they are finally diagnosed and put on TB treatment.<sup>4</sup> By the time patients are diagnosed, many have advanced, cavitory disease with substantial lung destruction.

In India, a majority of patients first seek care in the private sector. About half of all TB cases are treated in the private sector in India.<sup>5</sup> This means GPs have a key role to play in early and prompt diagnosis of TB. All GPs must know the key principles and technologies approved for TB diagnosis. They should also know about which tests to avoid because of misleading results and bad consequences for their patients.

### CURRENT BEST PRACTICES FOR TB DIAGNOSIS

Given the high rate of TB in India, a GP should actively consider TB in all persons with otherwise unexplained productive cough lasting two weeks or more, or with unexplained chronic fever and/or

### INTRODUCTION

Tuberculosis (TB) remains a problem of enormous magnitude, with nearly 10.4 million new cases and 1.7 million TB deaths every year.<sup>1</sup> Although much progress has been made in TB control, TB incidence is still not declining or not declining as quickly as expected. This is partly because TB patients are not diagnosed and cured quickly enough. When TB patients are not diagnosed and started on anti-TB therapy, they may unknowingly spread their infection to their families and communities - further worsening the epidemic. Thus, early and accurate TB diagnosis is very important - not only for individual patients but also for public health purposes. Early

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**Table 1 – Accepted, validated sputum tests for pulmonary TB**

Test type or platform	Goal of testing (to detect)	WHO endorsed?	How the test works	Examples of validated commercial versions	Sensitivity	Specificity
Sputum smear microscopy for acid-fast bacilli	Active TB	Yes	Light-emitting diode fluorescence microscopy	Primo Star iLED™ (Carl Zeiss, Oberkochen, Germany) Lumin™ (LW Scientific, Lawrenceville, GA, USA)	>60% (compared to culture)	98% (compared to culture)
Nucleic acid amplification test (NAAT)	Active TB and DST	Yes	Cartridge-Based Automated NAAT is a self-contained and fully automated technological platform that integrates sputum processing, DNA extraction and amplification, TB and MDR-TB diagnosis	Xpert MTB/RIF® [CepheidInc, California, USA]	For active TB: >98% in smear-positive patients and 60 - 70% in smear-negative. For detecting drug-resistance to rifampicin: 95%	For active TB: >98% For detecting drug-resistance to rifampicin: >98%
Liquid culture	Active TB and drug susceptibility testing (DST)	Yes	Fully automated system for mycobacterial liquid culture and drug susceptibility testing	BACTEC MGIT® 960 [BD, Sparks, USA] BacT/ALERT® 3D [bioMérieux, France]	100% in smear-positive cases >75% in smear-negative cases	>99%

weight loss.<sup>6</sup> In addition, GPs should actively screen for TB in clinically high-risk populations such as people living with HIV (even if they are on anti-retroviral treatment), close contacts of TB cases, children who are malnourished, diabetics, and chronic smokers. Among contacts of TB cases, the following groups should be aggressively screened for TB using sputum smears, chest X-rays and molecular tests: persons with symptoms suggestive of TB; children under the age of 5 years; contacts with HIV infection; and contacts of patients with MDR/XDR-TB.

A good diagnostic approach requires collection of the right clinical specimen. For pulmonary TB, sputum is the most important sample for laboratory testing. For several reasons, blood is a popular sample in the Indian private sector.<sup>7</sup> Unfortunately, there is no accepted, valid blood test for pulmonary TB. Therefore, blood samples are of no value. For extrapulmonary TB, it is important to collect specimens from the site of the disease. For example, for pleural effusion, pleural tap and/or biopsy are important. For TB lymphadenitis, it is important to do a lymph node biopsy or fine needle aspiration. For TB meningitis, a spinal tap to collect cerebrospinal fluid (CSF) is mandatory.

All patients (adults, adolescents, and children who are capable of producing sputum) suspected of having

pulmonary TB should have at least two sputum specimens submitted for microscopic examination and/or a World Health Organization (WHO) approved molecular test.<sup>6</sup> To reduce drop-outs, where feasible, 2 sputum specimens can be collected on the same day, a minimum of one hour apart.<sup>8</sup> Earlier recommendations required the collection of 3 sputum samples, but the current policy requires 2 specimens for microscopy. It is, however, important that sputum smears are performed in quality-assured laboratories. The public health sector in India has over 13,000 designated microscopy centres (DMCs) where sputum microscopy is done free of charge. GPs can always refer their patients to DMCs for diagnosis, especially if their patients cannot afford private laboratory testing.

There are 3 accepted, validated sputum tests for active TB: sputum smear microscopy for acid-fast bacilli (AFB); molecular or nucleic acid amplification test (NAAT); and culture (**Table 1**). Chest radiography is very widely used in the private sector. It is a useful test and can help quickly identify advanced TB disease (e.g., lung scarring, cavitation, bilateral disease). The problem is that chest X-rays are not specific for the diagnosis of pulmonary TB. Many lung diseases (e.g., chronic bronchitis) and infections (e.g., bacterial pneumonia) can cause radiological abnormalities, and all

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Figure 1 – Light-emitting diode (LED) fluorescence microscopy for acid-fast bacilli.

radiological abnormalities are not due to TB, even in a high burden country like India. Also, it can be challenging to differentiate between old, inactive TB and currently active TB disease. Therefore, chest radiography cannot provide a conclusive diagnosis on its own, and needs to be followed by sputum testing. Therefore, all persons with chest radiographic findings suggestive of TB should have sputum specimens submitted for microbiological examination (e.g., sputum smears or WHO-approved molecular tests).<sup>6</sup>

At a minimum, GPs should order two sputum smears for AFB in all patients in whom they suspect pulmonary TB. Sputum smears detect highly infectious patients and have high specificity. However, sensitivity of sputum AFB is modest (about 50 - 60%), although higher sensitivity can be obtained by performing fluorescence (e.g., auramine) staining and with the use of light-emitting diode (LED) microscopy (**Figure 1**). LED microscopy is approved by the WHO, and is increasingly available in the public sector DMCs. Sputum microscopy generally performs poorly in HIV-infected persons. It is usually of lesser value in young children (who often cannot produce sputum) and in extrapulmonary TB.

NAATs are molecular tests that amplify and detect DNA or RNA of *Mycobacterium tuberculosis*. They are highly specific to TB, and more sensitive than sputum smears and can help diagnose TB rapidly. NAATs can either be in-house ("home-brew") tests or commercial kits. In-house polymerase chain reaction (PCR) is known to produce highly inconsistent results and should be avoided.<sup>9</sup>

There are many commercial NAATs on the market, including validated, US FDA-approved products such as COBAS® Taqman® MTB by Roche, and Amplified *Mycobacterium tuberculosis* Direct [AMTD] by Gen-

Probe. These are acceptable but expensive in the Indian private sector. The most important recent advance is the development and WHO endorsement of Xpert® MTB/RIF (Cepheid Inc, Sunnyvale, CA, USA), an automated, cartridge-based NAAT that can detect TB, as well as drug-resistance, within 90 minutes (**Figure 2**).<sup>10</sup> The Xpert MTB/RIF test is based on the GeneXpert® platform. When compared to culture, Xpert has about 88% sensitivity and 98% specificity. For rapid detection of rifampicin resistance, the sensitivity is about 95% and specificity is 98%. So, this test is much more sensitive than sputum smear microscopy, and has great potential to increase the case detection rate.<sup>11</sup> There is growing evidence that Xpert MTB/RIF is quite helpful for rapid diagnosis of extrapulmonary and childhood TB, and WHO is expected to release a policy on this in 2013.<sup>11</sup> WHO released a policy on this in 2013 and approved the use of Xpert MTB/RIF in children and in patients with extra-pulmonary TB.

While Xpert MTB/RIF is a very good technology, high cost remains a big concern for its widespread use. In August 2012, several international donors provided funding to reduce the cost of Xpert MTB/RIF cartridges from \$16.86 to \$9.98. This reduced price is available for the public sector in 145 high-burden and developing countries. The private sector in high TB burden countries is not eligible for this price. Thanks to the IPAQT initiative ([www.ipaqt.org](http://www.ipaqt.org)), WHO-endorsed TB tests are now more affordable in the private sector (see later chapter).

If sputum smears and NAATs are negative, and TB is still suspected, cultures are the most sensitive tests avail-



Figure 2 – Xpert® MTB/RIF - a WHO-endorsed automated 2-hour test for TB as well as rifampin resistance.



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Figure 3 – Serological, antibody-based TB tests are sold as ELISA kits (top) or rapid tests (bottom) - both versions are banned by the Government of India and should not be used for TB diagnosis

able for TB. TB cultures can be done on solid or liquid media. Liquid cultures are 10% more sensitive than solid cultures and produce results much faster (i.e., within 10 - 14 days). Culture is therefore very useful in diagnosing smear-negative TB, and drug-resistant TB. Cultures can also help isolate non-tuberculous mycobacterial disease. Previously treated patients and patients who remain sputum smear-positive at completion of intensive phase of TB treatment and patients who have failed, defaulted from, or relapsed following one or more courses of treatment should always be assessed for drug resistance, either using liquid culture or by doing a NAAT such as Xpert MTB/RIF for rifampicin resistance, or line probe assay (LPA) for INH and rifampicin resistance. LPAs are molecular tests (e.g., Genotype MTBDRplus by Hain Life-Science, Germany) that detect mutations that confer drug-resistance and they are endorsed by the WHO. They have excellent accuracy for rifampicin resistance and good accuracy for INH resistance.<sup>12</sup> It is important to note that both culture and LPA require sophisticated laboratories with high degree of quality assurance.

## ROLE OF BLOOD TESTS FOR TB

There are several serological (blood) tests on the mar-

ket, even though no international guideline recommends their use. Serodiagnostic tests for TB are immunological tests that detect antibody responses to TB antigens in blood/serum samples. They come in two platforms: 1) ELISA tests that detect IgG, IgM and IgA antibodies (e.g., Anda TB and Pathozyme-TB), and 2) rapid strip or card tests (lateral flow assays; immuno- chromatography tests such as “Mycodot” and TB IgG/ IgM) (**Figure 3**). These tests are on the market in at least 17 of the 22 highest TB burden countries, and millions of patients in the private sector undergo serological testing.<sup>13</sup> The situation is particularly bad in India, where over 1.5 million serological TB tests were estimated to be performed in the private sector.<sup>7</sup>

While a simple, rapid blood test for TB will be most helpful, unfortunately, they do not work. TB serological tests are neither accurate nor cost-effective, prompting the WHO to issue a historic strong negative recommendation against their use in 2011.<sup>14</sup> The WHO policy states that, since the “the harms/risks [of commercial serodiagnostic tests] far outweigh any potential benefits (strong recommendation)...these tests should not be used in individuals suspected of active pulmonary or extra-pulmonary TB, irrespective of their HIV status (**Box 1**).”<sup>14</sup>

The WHO policy was based on a published meta-analysis that synthesized evidence from 92 studies and concluded that commercial serological tests remain inconsistent and inaccurate, supported only by data of very low quality.<sup>15</sup> A cost-effectiveness study, also considered by WHO, found that serology results in more human suffering, secondary infections, and false-positive diagnoses than sputum smear microscopy, while increasing per-patient costs to the Indian TB control sector.<sup>16</sup>

After this WHO policy, the Indian Revised National

### Box 1. Summary of the World Health Organization policy against the use of TB serological tests

- The WHO strongly recommends that commercial serological tests not be used for the diagnosis of pulmonary and extra-pulmonary TB.
- Currently available commercial serodiagnostic tests (also referred to as serological tests) provide inconsistent and imprecise findings.
- There is no evidence that existing commercial serological assays improve patient outcomes, and high proportions of false-positive and false-negative results may have an adverse impact on the health of patients.

Source: World Health Organization<sup>14</sup>

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TB Control Programme (RNTCP) published an advisory statement against the use of serological TB tests in India.<sup>17</sup> Subsequently, an expert committee convened by the Drug Controller General of India (DCGI) reviewed the evidence in December 2011, and unanimously recommended a ban on serodiagnostics for TB in India as these tests provide inconsistent and imprecise results. The DCGI recommendations were formally approved and notified in the Gazette of India by the Ministry of Health and Family Welfare on 7th June 2012. This governmental order bans the use, manufacture, sale and import of all TB serodiagnostic test kits in India. The ban applies to all TB serological tests - ELISA as well as rapid diagnostic tests. The ban applies to all TB serological tests - Indian as well as imported. In light of the WHO policy and the Indian Government's ban, it is important for GPs to avoid using all antibody blood tests for TB.<sup>18</sup> Continued use of antibody blood tests is unacceptable and unethical. Indeed, the International Standards for TB Care do not recommend their use.<sup>6</sup>

Blood tests like QuantiFERON-TB Gold In Tube (marketed in India as 'TB Gold' by Qiagen/Cellestis, Australia), T-SPOT.TB (by Oxford Immunotec, UK) and TB Platinum (by Immunoshop India) are called interferon-gamma release assays (IGRAs). These tests do not detect antibodies in the blood. They detect T-cell interferon-gamma response after incubation with TB antigens and measure cellular immune response to TB antigens. They are meant for detection of latent tuberculosis infection (LTBI) and as a potential replacement for the tuberculin skin test (Mantoux test based purified protein derivative).<sup>19</sup> Like the Mantoux test, IGRAs cannot distinguish between latent TB infection and active TB disease.<sup>20-22</sup> In most individuals, *M. tuberculosis* infection is contained initially by host defenses, and infection remains latent. However, latent infection has the potential to develop into active disease at any time. While active TB disease requires 6 months of short-course therapy, latent infection can be treated with a single drug (i.e., isoniazid for 6 - 9 months). Both TST and IGRAs are considered acceptable but imperfect tests for latent TB infection.<sup>23</sup>

With the recent governmental ban on antibody blood tests, laboratories have started replacing them with tests like QuantiFERON-TB Gold. However, tests like TB Gold should not be used to replace serological, antibody-detection tests. IGRAs were never designed for the diagnosis of active TB. In fact, a 2011 WHO policy strongly discourages the use of IGRAs for the diagnosis of active TB in low and middle income countries (**Box 2**).<sup>24</sup> If tests like TB Gold are used for diagnosing active TB, it will result in very high rates of false-positive results and a lot of

## Box 2. Summary of the World Health Organization policy against the use of interferon-gamma release assays (IGRAs) for active TB\*

- IGRAs (and the tuberculin skin test) should not be used in low- and middle-income countries for the diagnosis of pulmonary or extra-pulmonary TB, nor for the diagnostic work-up of adults (including HIV-positive individuals) suspected of active TB in these settings (strong recommendation).

- This recommendation places a high value on avoiding the consequences of unnecessary treatment (high false-positives) given the low specificity of IGRAs (and the TST) in these settings.

Source: World Health Organization<sup>24</sup>

\*In India, the most popular IGRA is the QuantiFERON-TB Gold In Tube test, marketed as "TB Gold"

unnecessary anti-TB drug therapy.<sup>22</sup> This is because an estimated 40% of the Indian population are latently infected<sup>25</sup> and this will result in a large number of positive IGRA results. The same limitation applies to the Mantoux test - it has no value for active TB diagnosis in adults in India. Therefore, GPs should avoid using tests like TB Gold and Mantoux for active TB diagnosis in adults. In children, these tests can provide supportive evidence, along with symptoms, history of contact, smears and chest X-rays.

Can serological TB tests be replaced with NAATs on blood samples? NAATs are not recommended for use on blood specimens. It is virtually impossible to detect DNA of MTB in blood samples. NAATs are meant to be used on respiratory samples, and samples from the site of the disease in extra-pulmonary TB. Overall, a key message for all GPs is that there is no valid blood-based test for pulmonary TB. Sputum is the most critical sample to collect and test. GPs must therefore spend time counseling their patients about the need to produce sputum samples for TB testing. Lastly, GPs must avoid starting 6 months of TB therapy without first confirming the disease with one of the validated methods described above.

## NOTIFICATION OF TB CASES

On the 7th of May 2012, the Ministry of Health and Family Welfare issued a government order that requires all healthcare providers to notify every TB case to local health authorities (e.g., district or municipal health officers).<sup>26</sup> Healthcare providers include clinical establishments run or managed by the government (including

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## CLINICAL HIGHLIGHTS

- ❑ All persons with otherwise unexplained productive cough lasting two weeks or more, or with unexplained chronic fever and/or weight loss should be investigated for TB
- ❑ There are no validated, accepted blood-based tests for active TB. Sputum is the ideal specimen to collect for pulmonary TB.
- ❑ All patients suspected of having pulmonary TB should have at least two sputum specimens submitted for microscopic examination and/or a World Health Organization (WHO) approved molecular test such as Xpert MTB/RIF.
- ❑ Chest radiography is useful but cannot provide a conclusive diagnosis on its own, and needs to be followed by sputum testing.
- ❑ Liquid culture is very useful in diagnosing smear-negative TB, and drug-resistant TB.
- ❑ Drug susceptibility testing must be done on all previously treated patients and patients who remain sputum smear-positive at completion of intensive phase of treatment and patients who have failed, defaulted from, or relapsed following one or more courses of treatment.
- ❑ There is no clinical role for blood-based antibody tests (e.g., IgG/IgM ELISA or rapid tests) and interferon-gamma release assays (e.g., TB Gold). They are not accurate and should not be used for pulmonary TB diagnosis.
- ❑ The Mantoux (tuberculin) skin test cannot distinguish latent TB infection from active TB disease, and has no utility for diagnosing pulmonary TB in adults. It has clinical utility in children, along with other tests such as chest x-ray, smears, and clinical history.
- ❑ All healthcare providers are now required to notify every TB case to local health authorities.

local authorities), private or NGO sectors, as well as individual practitioners (GPs as well as specialists). For the purpose of a case notification, the government order defines a TB case as: 1) a patient diagnosed with at least one sputum specimen positive for AFB, or culture positive for TB bacteria, or RNTCP-endorsed rapid molecular test positive for TB; or 2) a patient diagnosed clinically (without microbiological proof) and given anti-TB drug treatment. The RNTCP has created a web-based portal for notification called NIKSHAY (<http://nikshay.gov.in>). It is therefore important that all GPs notify TB cases that they diagnose, and fulfill this public health responsibility. ■

## REFERENCES:

1. World Health Organization. Global tuberculosis control: WHO report 2012. Geneva: WHO; 2012. Report No.: 978 92 4 156450 2.
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. Udwadia ZF. MDR, XDR, TDR tuberculosis: ominous progression. *Thorax* 2012;67:286-8.
4. Dye C. The potential impact of new diagnostic tests on tuberculosis epidemics. *Indian J Med Res* 2012;135:737-44.
5. 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.
6. Hopewell PC, Pai M, Maher D, Uplekar M, Raviglione MC. International standards for tuberculosis care. *Lancet Infect Dis* 2006;6:710-25.
7. 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.
8. Davis JL, Cattamanchi A, Cuevas LE, Hopewell PC, Steingart K. Diagnostic accuracy of same-day microscopy versus standard microscopy for pulmonary tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 2012 (published ahead of print).
9. Flores LL, Pai M, Colford JM, Jr., Riley LW. In-house nucleic acid amplification tests for the detection of *Mycobacterium tuberculosis* in sputum specimens: meta-analysis and meta-regression. *BMC Microbiol* 2005;5:55.
10. 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.
11. Weyer K, Mirzayev F, Migliori GB, et al. Rapid molecular TB diagnosis: evidence, policy-making and global implementation of XpertSMTB/RIF. *Eur Resp Journal* 2012 [published ahead of print].
12. Ling DI, Zwerling A, Pai M. GenoType MTBDR assays for the diagnosis of multidrug-resistant tuberculosis: a meta-analysis. *Eur Respir J* 2008;32:1165-74.
13. Grenier J, Pinto L, Nair D, et al. Widespread use of serological tests for tuberculosis: data from 22 high-burden countries. *Eur Respir J* 2012;39:502-5.
14. World Health Organization. Policy statement Commercial serodiagnostic tests for diagnosis of tuberculosis. In. Geneva: World Health Organization; 2011.
15. 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.
16. Dowdy DW, Steingart KR, Pai M. Serological testing versus other strategies for diagnosis of active tuberculosis in India: a cost-effectiveness analysis. *PLoS Med* 2011;8:e1001074.
17. DDG Advisory on TB serodiagnostics Directorate General of Health Services, Ministry of Health and Family Welfare, 2011. (Accessed 4 October, 2011, at [http://www.tbcindia.nic.in/pdfs/Letter\\_Serodiagnosis.pdf](http://www.tbcindia.nic.in/pdfs/Letter_Serodiagnosis.pdf).)
18. Steingart KR, Ramsay A, Dowdy DW, Pai M. Serological tests for the diagnosis of active tuberculosis: relevance for India. *Indian J Med Res* 2012;135:695-702.
19. Pai M, Zwerling A, Menzies D. T-cell Based Assays for the Diagnosis of Latent Tuberculosis Infection: An Update. *Ann Intern Med* 2008;149:177-84.
20. Sester M, Sotgiu G, Lange C, et al. Interferon- $\gamma$  release assays for the diagnosis of active tuberculosis: a systematic review and meta-analysis. *Eur Respir J* 2011;37:100-11.
21. Lange C, Pai M, Drobniewski F, Migliori GB. Interferon-gamma release assays for the diagnosis of active tuberculosis: sensible or silly? *Eur Respir J* 2009;33:1250-3.
22. 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.
23. Pinto LM, Grenier J, Schumacher SG, Denkiner CM, Steingart KR, Pai M. Immunodiagnosis of tuberculosis: state of the art. *Med Princ Pract* 2012;21:4-13.
24. 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.
25. Chadha VK. Tuberculosis epidemiology in India: a review. *Int J Tuberc Lung Dis* 2005;9:1072-82.
26. Notification of TB cases. Ministry of Health and Family Welfare, 2011. (Accessed 4 October, 2011, at <http://www.tbcindia.nic.in/pdfs/TB%20Notification%20Govt%20order%20dated%2007%2005%202012.pdf>.)



# CIS CME—Questions

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## Questions

- 1 Which of the following diagnostics tests is intended for latent tuberculosis infection?**
  - a. Sputum smear microscopy
  - b. Polymerase chain reaction (PCR)
  - c. Interferon-gamma release assay (IGRA)
  - d. ELISA for TB antibodies
- 2 Which of the following diagnostics tests can be used to diagnose drug-resistant tuberculosis?**
  - a. Sputum smear microscopy
  - b. liquid culture
  - c. Interferon-gamma release assay (IGRA)
  - d. Chest X-ray
- 3 Which of the following tests are banned by the government of India?**
  - a. Sputum smear microscopy
  - b. Polymerase chain reaction (PCR)
  - c. Interferon-gamma release assay (IGRA)
  - d. Serological (antibody) TB tests
- 4 The ideal clinical specimen for pulmonary TB diagnosis is:**
  - a. Blood
  - b. Sputum
  - c. Urine
  - d. Tissue
- 5 Advantages of culture for TB compared to sputum microscopy alone include all of the following EXCEPT:**
  - a. Obtaining a positive culture can allow for drug-susceptibility testing
  - b. Culture can allow for identification of non-tuberculous mycobacterium species
  - c. Culture has a higher sensitivity than smear microscopy for diagnosing TB
  - d. Culture, particularly by liquid media, can be faster than smear microscopy
- 6 Which of the following statements is FALSE about chest X-rays for TB diagnosis:**
  - a. Chest X-rays have good sensitivity, but poor specificity
  - b. Chest X-rays can help determine the severity of lung damage
  - c. Chest X-rays alone is sufficient to diagnose pulmonary TB
  - d. Chest X-rays can look similar in patients with old, inactive TB and those with currently active TB disease

*(See answers on the next page)*

## Answers

- 1 The correct answer is (c).** Interferon-gamma release assays (e.g., TB Gold) are meant for the diagnosis of latent TB infection. They should not be used for active TB diagnosis because they cannot distinguish between latent TB and active disease. A 2011 World Health Organization (WHO) policy discourages their use for active TB diagnosis.<sup>1</sup>
- 2 The correct answer is (b).** Liquid culture can be used to grow *Mycobacterium tuberculosis* and also identify drug resistance (to first and second line drugs). The use of liquid culture is endorsed by the WHO.<sup>2</sup>
- 3 The correct answer is (d).** The Indian Government has banned the use, sale and import of all commercial serological (antibody-detection) TB tests. This includes ELISA as well as rapid antibody tests. The ban applies to domestic as well as imported serodiagnostics kits. The ban is based on a WHO policy that strongly recommends against the use of serological, antibody tests for TB.<sup>3</sup> The International Standards for TB Care also discourages the use of serological TB tests.<sup>4</sup>
- 4 The correct answer is (b).** Sputum is the best clinical specimen for diagnosis of pulmonary TB. There are no accurate, validated tests for specimens such as blood, urine and tissue.
- 5 The correct answer is (d).** Culture is not faster than smear microscopy because even liquid culture needs 10 -14 days for a result to be obtained. Sputum smear results are usually available within 1-2 days.
- 6 The correct answer is (c).** Chest X-rays alone is NOT sufficient to diagnose pulmonary TB. It needs to be followed by sputum testing. While chest X-rays have fairly high sensitivity for pulmonary TB, its specificity is low. Many lung conditions and infections can cause chest X-ray abnormalities. So, all patients with chest X-ray abnormalities must be investigated with sputum smears, NAAT and/or culture.

### REFERENCES:

1. 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
2. World Health Organization. The use of liquid medium for culture and DST. URL: [http://www.who.int/tb/laboratory/policy\\_liquid\\_medium\\_for\\_culture\\_dst/en/index.html](http://www.who.int/tb/laboratory/policy_liquid_medium_for_culture_dst/en/index.html). In. Geneva: World Health Organization; 2007.
3. World Health Organization. Policy statement Commercial serodiagnostic tests for diagnosis of tuberculosis. In. Geneva: World Health Organization; 2011.
4. Hopewell PC, Pai M, Maher D, Uplekar M, Raviglione MC. International standards for tuberculosis care. *Lancet Infect Dis* 2006;6:710-25.



**On notice of TB symptoms,  
immediately rush  
to your doctor**

**Symptoms of TB**

- Cough for more than 2 weeks
- Blood in sputum
- Weakness and fatigue
- Loss of weight
- Reduced appetite
- Evening Temperature



**TB HAREGA, DESH JEETEGA.**

For more information, consult your doctor.



Municipal Corporation of  
Greater Mumbai



DIRECTORATE OF HEALTH AND FAMILY WELFARE  
GOVERNMENT OF MAHARASHTRA  
MUMBAI MISSION FOR TB CONTROL

