Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/apme

Review Article

Newer diagnostic methods in tuberculosis detection

Suneetha Narreddy [a,*], Sujit Muthukuru [b]

[a] Infectious Diseases Consultant, Apollo Hospital, Jubilee Hills, Hyderabad, India
[b] Research Assistant, Apollo Hospital, Jubilee Hills, Hyderabad, India

ARTICLE INFO

Article history:
Received 9 April 2014
Accepted 2 May 2014
Available online 11 June 2014

Keywords:
Tuberculosis
TB
Diagnostics
NAAT
Xpert

abstract

One-third of the world's population has been infected with *Mycobacterium tuberculosis*, with new infections occurring in about 1% of the population each year. However 90–95% of infections remain asymptomatic. Thus early diagnosis of tuberculosis and drug resistance improves survival and helps to promote contact tracing, implementation of institutional cross-infection procedures, and other public-health actions. There have been many advances and modifications to the methodology for tuberculosis diagnosis some of which are very promising. But these advances have not kept pace with the explosion of tuberculosis or the outbreak of drug resistant tuberculosis. This review describes some of the newer advances in tuberculosis diagnostics and the challenges they face.

Copyright © 2014, Indraprastha Medical Corporation Ltd. All rights reserved.

1. The history

Yaksma, Consumption, Romantic disease, White plague, Scrofula, Phthisis, Pott's disease, chaky oncay; all these are different terms used to refer to tuberculosis (TB) throughout history. TB was discovered to have been prevalent as early as 9000 years ago[1] but it was not until 1882 that the Tubercle bacilli was first isolated by the German Physician Robert Koch using staining techniques and forced the medical community to accept TB as an infectious disease.[2] Shortly after, a method to culture the Tubercle bacilli was developed. Tragically the development of TB diagnostics and their implementation neither kept pace with the advances in medical technology nor the calamitous explosion of TB in the wake of the Human Immunodeficiency Virus (HIV) pandemic nor the outbreak of multi-drug resistant tuberculosis (MDR TB). The older smear microscopy and culture methods underwent slight modifications overtime and are still in use even today but they have low sensitivity and more over drug susceptibility, which is the need of the hour, is not known immediately.

2. The present diagnostic methods

Chest X-ray followed by acid-fast staining and microscopy of the sputum sample along with culture are the most widely used diagnostic methods today.

Chest X-ray is highly sensitive in the diagnosis of pulmonary TB but is of low specificity, especially when co-existing with HIV infection. Radiography is important in the diagnosis of several forms of extrapulmonary TB such as pleural, vertebral and joint types.

* *Corresponding author*. Tel.: +91 99660 22225.
E-mail address: suneethanarreddy@hotmail.com (S. Narreddy).
http://dx.doi.org/10.1016/j.apme.2014.05.008
0976-0016/Copyright © 2014, Indraprastha Medical Corporation Ltd. All rights reserved.

The major drawback of sputum smear microscopy is that it is laborious and has poor sensitivity, estimated to be ~70%.[3] It's sensitivity further drops to around ~35% in some settings with HIV co-infection and highly prevalent TB.[4] This leads to increased workload, as more sputum tests are needed per patient leading to diagnostic delay and patient loss to follow-up. The fluorescent Auramine–Rhodamine stain is an additional armor apart from Ziehl Neelsen acid-fast stain for smear microscopy, decreasing the time to review the slide and improving the yield. Extrapulmonary TB needs histopathological examination of the tissue specimens; sensitivity and specificity depending on the ease of sample collection; but the facilities and resources needed for such methods are often unavailable in developing countries.[5]

Culture can be performed using solid media, such as Lowenstein–Jensen (3–8 weeks), or liquid media, such as Dubos' medium or Middlebrook 7H9 Broth etc. (10–14 days), using the commercially available automated systems. Culture was also a prerequisite for phenotypic drug susceptibility testing until recent advances in molecular tests were made. The longer waiting time for culture results makes it difficult for clinicians to prove a diagnosis of TB in cases of diagnostic doubt, especially in populations with low TB incidence, and in the management of suspected drug-resistant TB.

Tuberculin skin testing using purified protein derivative (PPD) has poor sensitivity and specificity for active TB and is used mainly to screen high risk population and diagnose Latent TB.

3. Newer diagnostic tests – the need, barriers and the impact they can have

With the limitation of the present day tests there is a need for faster, user-friendly, low cost, highly specific and sensitive diagnostic tests. New ways of performing "old" tests (e.g. sputum smear microscopy) and completely innovative tools (e.g. new technologies for molecular diagnosis) are under investigation or have already been endorsed by WHO.[6]

3.1. *Optimizing smear*

The strength of the smear test is its simplicity and low cost. Thus approaches, which increase its sensitivity and reduce the need for multiple visits will be beneficial.[7,8] Practices, which combine improved techniques with different approaches, have been endorsed by WHO to optimize yield of microscopy.

Some of them include,

- Collecting two supervised specimens in one visit (e.g. spot, spot) instead of the age-old three early morning sputum samples.[9]
- Other practice which is not yet endorsed by WHO, but still very promising, is the use of Light Emitting Diode (LED) based microscopy as a replacement for conventional fluorescent microscopy.[10]

3.2. *Culture*

The advances in culture methods are mostly in use already. They employ the use of a liquid medium like Dubos' media, Middlebrook 7H9 Broth, Sula's or Sauton's or Proskauer and Beck's medium over the more traditional Lowenstein–Jenson medium. Not only is it more sensitive, it also reduces the delay of drug sensitivity testing to about 10 days.

3.3. *Antigen and antibody based tests*

Antigen detecting test if developed into a point-of-care test would allow for immediate diagnosis and initiation of treatment. Urine samples and Breathalyzer are the most commonly used. A urine specimen would be particularly useful for children, who can have difficulty providing sputum. In patients suspected of extrapulmonary TB, an antigen detection test might prevent the use of more invasive tests. The major and most promising antigens currently under study are Lipoarabinomannan (LAM),[11] a major glycolipid component of the cell wall of *Mycobacterium tuberculosis*; ESAT-6 (early secretory antigen target-6) and CFP-10 (culture filtrate protein-10), both located in the RD1 (region of difference-1) region that is lacking in BCG and in most Atypical Mycobacteria.[12]

Antibodies to several antigens such as malate synthase, TBF6[13,14] and cord factor are in use now, especially in the developing countries. The accuracy of these tests has not been found encouraging.[15] There are still a large number of commercially available serological tests in use, in developing countries in spite of no International Guideline recommendation. WHO issued a policy against these tests in 2011. The Indian government banned antibody-based serological tests in 2012.

3.4. *Interferon-γ release assays*

These tests are currently used in many countries as a substitute for Tuberculin test to diagnose Latent TB. These are based on T-cell responses to antigens such as ESAT-6 and CFP-10, which are more specific to *M. tuberculosis* than PPD. Presently two such tests, in use in many countries, are the blood based QuantiFERON-TB Gold In-Tube and T-SPOT.TB. They are found to be more specific than the Tuberculin skin test[16,17] in diagnosing Latent TB and have good sensitivity but decreased specificity to active TB.[18] WHO has recommended against the use of these tests for active TB diagnosis in high burden countries, as these tests, like Mantoux, cannot separate latent infection from active TB disease.

3.5. *Molecular diagnostics*

These tests use nucleic acid amplification techniques like Polymerase Chain Reaction (PCR) for the diagnosis of TB and drug susceptibility testing. The sensitivity of these tests has been found to be >95% in sputum smear positive samples with specificity around 90–100%,[19] but in smear negative/culture positive samples the sensitivities has been found to be reduced. The main advantage of these tests, like GeneXpert, is

Download English Version:

https://daneshyari.com/en/article/3235036

Download Persian Version:

https://daneshyari.com/article/3235036

Daneshyari.com