# **Briefly explain the diagnosis of Tuberculosis ?**

<u>Tuberculosis</u> is diagnosed by finding <u>Mycobacterium tuberculosis</u> bacteria in a clinical specimen taken from the patient. While other investigations may strongly suggest tuberculosis as the diagnosis, they cannot confirm it.

## Diagnosis

A complete medical evaluation for <u>tuberculosis</u> (TB) must include a medical history, a physical examination, a <u>chest X-ray</u> and microbiological examination (of sputum or some other appropriate sample). It may also include a <u>tuberculin skin test</u>, other scans and X-rays, surgical biopsy.

### **Medical history**

The medical history includes obtaining the symptoms of pulmonary TB: <u>productive</u>, prolonged cough of three or more weeks, chest pain, and <u>hemoptysis</u>. Systemic symptoms include low grade remittent fever, chills, night sweats, appetite loss, weight loss, easy fatigability, and production of sputum that starts out mucoid but changes to <u>purulent<sup>[1]</sup></u>. Other parts of the medical history include prior TB exposure, infection or disease; past TB treatment; demographic risk factors for TB; and medical conditions that increase risk for TB disease such as HIV infection.

Tuberculosis should be suspected when a persistent respiratory illness in an otherwise healthy individual does not respond to regular antibiotics.

#### **Physical examination**

A <u>physical examination</u> is done to assess the patient's general health and find other factors which may affect the TB treatment plan. It cannot be used to confirm or rule out TB.

#### **Microbiological studies**



Distinctive clusters of colorless <u>Mycobacterium tuberculosis</u> form in this culture.

A definitive diagnosis of tuberculosis can only be made by culturing <u>Mycobacterium</u> <u>tuberculosis</u> organisms from a specimen taken from the patient (most often <u>sputum</u>, but may also include pus, <u>CSF</u>, biopsied tissue, etc.)<sup>[1]</sup>. A diagnosis made other than by culture may only be classified as "probable" or "presumed". For a diagnosis negating the possibility of tuberculosis infection, most protocols require that two separate cultures both test negative<sup>[1]</sup>.

#### Sputum

Sputum smears and <u>cultures</u> should be done for acid-fast bacilli if the patient is producing sputum<sup>[1]</sup>. The preferred method for this is <u>fluorescence microscopy</u> (<u>auramine-rhodamine</u> <u>staining</u>), which is more sensitive than conventional <u>Ziehl-Neelsen staining</u>.<sup>[2]</sup>

#### Bronchoscopy

If no sputum is being produced, specimens can be obtained by inducing sputum, <u>gastric</u> <u>washings</u>, a laryngeal swab, <u>bronchoscopy</u> with bronchoalveolar lavage, or fine needle aspiration of a collection. A comparative study found that inducing three sputum samples is more <u>sensitive</u> than three gastric washings.<sup>[3]</sup>

#### Biopsy

Certain cases require a specimen that can not be supplied by sputum culture or bronchoscopy. In these cases, a <u>biopsy</u> of tissue from the suspected system can be obtained by <u>mediastinoscopy</u>.

#### PCR

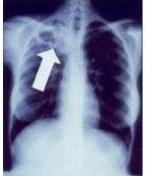
Other mycobacteria are also acid-fast. If the smear is positive,  $\underline{PCR}$  or gene probe tests can distinguish *M. tuberculosis* from other mycobacteria. Even if sputum smear is negative, tuberculosis must be considered and is only excluded after negative cultures.

#### Other

Many types of cultures are available <sup>[4]</sup>. Traditionally, cultures have used the Löwenstein-Jensen (LJ), Kirchner, or Middlebrook media (7H9, 7H10, and 7H11). A culture of the AFB can distinguish the various forms of mycobacteria, although results from this may take four to eight weeks for a conclusive answer. New automated systems that are faster include the MB/BacT, BACTEC 9000, and the Mycobacterial Growth Indicator Tube (MGIT). The Microscopic Observation Drug Susceptibility assay culture may be a faster and more accurate method <sup>[5]</sup>.

#### Radiography

**Chest X-ray** 



Tuberculosis creates cavities visible in <u>x-rays</u> like this one in the patient's right upper lobe.

In active pulmonary TB, infiltrates or consolidations and/or cavities are often seen in the upper <u>lungs</u> with or without mediastinal or hilar lymphadenopathy or pleural effusions ( tuberculous pleurisy). However, lesions may appear anywhere in the lungs. In disseminated TB a pattern of many tiny nodules throughout the lung fields is common - the so called milliary TB. In HIV and other <u>immunosuppressed</u> persons, any abnormality may indicate TB or the chest X-ray may even appear entirely normal.

Abnormalities on chest radiographs may be suggestive of, but are never diagnostic of, TB. However, chest radiographs may be used to rule out the possibility of pulmonary TB in a person who has a positive reaction to the tuberculin skin test and no symptoms of disease.

Cavitation or consolidation of the apexes of the upper lobes of the lung may be discernible by a chest x-ray  $^{[1]}$ .

See <u>Tuberculosis radiology</u> for more information.

#### Abreugraphy

For more details on this topic, see <u>Abreugraphy</u>.

A variant of the chest X-Ray, <u>abreugraphy</u> (from the name of its inventor, Dr. <u>Manuel Dias de</u> <u>Abreu</u>) was a small radiographic image, also called miniature mass radiography (MMR) or miniature chest radiograph. Though its resolution is limited (it doesn't allow the diagnosis of <u>lung cancer</u>, for example) it is sufficiently accurate for diagnosis of tuberculosis.

Much less expensive than traditional X-Ray, MMR was quickly adopted and extensively utilized in some countries, in the 1950s. For example, in <u>Brazil</u> and in <u>Japan</u>, tuberculosis prevention laws went into effect, obligating ca. 60% of the population to undergo MMR screening.

The procedure went out of favor, as the incidence of tuberculosis dramatically decreased, but is still used in certain situations, such as the screening of <u>prisoners</u> and <u>immigration</u> applicants..

#### Tuberculin skin test

For more details on this topic, see *Tuberculin skin test*.

Two tests are available: the Mantoux and Heaf tests.

#### Mantoux skin test

For more details on this topic, see <u>Mantoux test</u>.



The <u>Mantoux test</u> for TB involves intradermally injecting PPD tuberculin and measuring the size of induration 48-72 hours later.

The Mantoux skin test is used in the United States and is endorsed by the American Thoracic Society and Centers for Disease Control and Prevention (<u>CDC</u>).

If a person has had a history of a positive tuberculin skin test, another skin test is not needed.

#### Heaf test

For more details on this topic, see <u>Heaf test</u>.

The <u>Heaf test</u> was used in the United Kingdom until 2005, and is graded on a four point scale. The <u>Mantoux test</u> is now used.

The equivalent Mantoux test positive levels done with 10 TU (0.1 ml 100 TU/ml, 1:1000) are

- 0–4 mm induration (Heaf 0 to 1)
- 5–14 mm induration (Heaf 2)
- Greater than 15 mm induration (Heaf 3 to 5)

#### **CDC** classification of tuberculin reaction

An inducation (palpable raised hardened area of skin) of more than 5-15 mm (depending upon the person's risk factors) to 10 Mantoux units is considered a positive result, indicating TB infection.

- 5 mm or more is positive in
  - HIV-positive person
  - Recent contacts of TB case
  - Persons with nodular or fibrotic changes on CXR consistent with old healed TB
  - Patients with organ transplants and other immunosuppressed patients
- 10 mm or more is positive in
  - Recent arrivals (less than 5 years) from high-prevalent countries
  - Injection drug users
  - Residents and employees of high-risk congregate settings (e.g., prisons, nursing homes, hospitals, homeless shelters, etc.)
  - Mycobacteriology lab personnel
  - Persons with clinical conditions that place them at high risk (e.g., <u>diabetes</u>, prolonged <u>corticosteroid</u> therapy, <u>leukemia</u>, <u>end-stage renal disease</u>, chronic <u>malabsorption</u> syndromes, low body weight, etc)
  - Children less than 4 years of age, or children and adolescents exposed to adults in high-risk categories
- 15 mm or more is positive in
  - $\circ$   $\,$  Persons with no known risk factors for TB  $\,$
  - (Note: Targeted skin testing programs should only be conducted among high-risk groups)

A tuberculin test conversion is defined as an increase of 10 mm or more within a 2-year period, regardless of age.

#### BCG vaccine and tuberculin skin test

There is disagreement on the use of the Mantoux test on people who have been immunized with BCG. The US recommendation is that in administering and interpreting the Mantoux test, previous BCG vaccination should be ignored; the UK recommendation is that interferon- $\gamma$  tests should be used to help interpret positive tuberculin tests, also, the UK do not recommend serial tuberculin skin testing in people who have had BCG (a key part of the US strategy). In their guidelines on the use of QuantiFERON Gold the US Centers for Disease Control and Prevention state that whereas Quantiferon Gold is not affected by BCG inoculation tuberculin tests can be affected.<sup>[6]</sup> In general the US approach is likely to result in more false positives and more unnecessary treatment with potentially toxic drugs; the UK approach is as sensitive in theory and should also be more specific, because of the use of interferon- $\gamma$  tests.

Under the US recommendations, latent TB infection (LTBI) diagnosis and treatment for LTBI is considered for any BCG-vaccinated person whose skin test is 10 mm or greater, if any of these circumstances are present:

- Was in contact with another person with infectious TB
- Was born or has resided in a high TB prevalence country
- Is continually exposed to populations where TB prevalence is high.