Tuberculosis Prevention and Screening

About one-third of the world's population has latent tuberculosis infection (LTBI). Preventing transmission of tuberculosis (TB), contact tracing, screening and bacillus Calmette-Guérin (BCG) vaccination are key targets in TB prevention. Although the routine BCG vaccination of all children was discontinued in the UK in 2005, it has been replaced by a TB risk-based programme. It targets contacts of any known TB cases and those children at most risk of exposure to TB, particularly from the more serious childhood forms of the disease.

Whom to screen

Screening and testing of high-risk and contact groups are designed to identify new cases (eg, healthcare workers, new immigrants and HIV patients). New immigrants to the UK should be identified for TB screening from the following information:

- Port of arrival reports.
- New registrations with primary care.
- Entry to education (including universities).
- Links with statutory and voluntary groups working with new entrants.

Neonatal BCG vaccination for any baby at increased risk of TB should be discussed with the parents or legal guardian. Primary care organisations with a high incidence of TB should consider vaccinating all neonates soon after birth.

Which test to use

Screening is done using either an intradermal Mantoux (skin) test injected into the skin of the inner surface of the forearm, or an interferon gamma release assay (IGRA) blood test.

Public Health England recommends that IGRA tests should not be used as a routine diagnostic tool for active TB and only considered in supporting the primary diagnosis of active TB when it has not been possible to confirm the diagnosis by culture and when strong support for the diagnosis is lacking from radiological and histopathological tests. If the diagnosis remains in doubt and a subsequent management decision on whether or not to treat will be influenced by the result, then the use of IGRA test is supported. The final decision should be based on clinical judgement. The diagnosis of active TB is rarely made from the result of any one single test.

The National Institute for Health and Care Excellence (NICE) recommends IGRA testing for people whose Mantoux test shows positive results, or in people for whom Mantoux testing may be less reliable - eg, BCG-vaccinated people.

- Household or other close contacts (eg, in workplaces and schools):
  - Aged 2-5 years: offer Mantoux test and, if positive, refer to a TB specialist for exclusion of active TB and possible treatment of LTBI. If Mantoux test is negative (but the child is a contact of sputum-smear-positive disease), offer IGRA after six weeks and repeat the Mantoux test to increase the sensitivity (to reduce false negative results).
  - Aged ≥5 years: offer Mantoux test and consider IGRA if Mantoux-positive results, or where Mantoux testing may be less reliable - for example, BCG-vaccinated people. If Mantoux testing is inconclusive, refer the person to a TB specialist.
  - Children aged under 2 years require anti-TB treatment - see the NICE guidance.
New entrants from high-incidence countries:
- Aged under 5 years: offer Mantoux test and, if positive, refer to a TB specialist for exclusion of active TB and possible treatment of LTBI.
- Aged 5-15 years: offer Mantoux test; follow with IGRA if positive.
- Aged 16-35: offer IGRA alone or (dual strategy, ie following Mantoux test).
- If aged 35 years, consider the individual risks and benefits of likely subsequent treatment, before offering testing.

Immunocompromised:
- Children: refer to a specialist if infection is suspected.
- Adults: perform IGRA ± Mantoux and, if either is positive, assess for active disease and consider treatment for latent infection. For people with HIV and CD4 counts less than 200 cells/mm$^3$ performing both Mantoux testing and IGRA is recommended.

Healthcare workers:
- Those who have not had a BCG vaccination: screen with Mantoux test and vaccinate with BCG if negative.
- NHS employees who have recently arrived from high-incidence countries or who have had contact with patients in settings where TB is highly prevalent: offer IGRA.

Hard to reach groups: offer a single IGRA.

**Tuberculin skin testing**$^{[2, 5]}$

Skin testing can detect previous exposure to the organism (or BCG vaccination) by provocation of a well-established, cell-mediated immune reaction. A purified protein derivative (PPD) of *Mycobacterium tuberculosis* is injected intradermally into the flexor surface of the forearm and the local response is measured. The interpretation of tuberculin tests depends on BCG vaccination history, immune status and concurrent viral infection.

The standard skin test for TB in the UK is the Mantoux test. The Mantoux test is administered by injection of 0.1 ml, using a 27-gauge needle, raising a 6-10 mm wheal. The Mantoux test is used (two different strengths) both:

- As a screening test for TB infection or disease (2 TU/0.1 ml); and
- As an aid to the clinical diagnosis of TB infection (10 TU/0.1 ml).

The local skin reaction to tuberculin PPD injected into the skin is used to assess an individual's sensitivity to tuberculin protein. The greater the reaction, the more likely it is that an individual is infected or has active TB disease.$^{[2]}$ Precise interpretation depends on whether it is being used for screening or clinical diagnostic purposes.

The skin test reaction should be read between 48 and 72 hours after administration. A patient who does not return within 72 hours will need to be rescheduled for another skin test.

The reaction should be measured in millimeters of the induration (palpable, raised, hardened area or swelling). The reader should not measure erythema (redness). The diameter of the indurated area should be measured across the forearm (perpendicular to the long axis). Skin test interpretation depends on two factors:$^{[4]}$

- Measurement in millimeters of the induration.
- A person's risk of being infected with TB and of progression to disease if infected.
### Mantoux - Tuberculin Skin Testing in Screening

<table>
<thead>
<tr>
<th>Diameter of induration</th>
<th>Positivity (degree of hypersensitivity to tuberculin protein)</th>
<th>Interpretation</th>
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| Less than 5 mm         | Negative - (no significant hypersensitivity to tuberculin protein) | - Previously unvaccinated individuals may be given BCG provided there are no contra-indications.  
- Suggests no TB infection but beware false negatives. |
| 5 mm or greater        | Positive - (hypersensitive to tuberculin protein)            | Considered positive in:  
- HIV-infected persons.  
- A recent contact of a person with TB disease.  
- Persons with fibrotic changes on chest radiograph consistent with prior TB.  
- Patients with organ transplants.  
- Persons who are immunosuppressed for other reasons (eg, taking the equivalent of >15 mg/day of prednisone for one month or longer, taking TNF-antagonists). |
| 10 mm or greater       | Strongly positive - (strongly hypersensitive to tuberculin protein) | Considered positive in:  
- Recent immigrants (<5 years) from high-prevalence countries.  
- Injection drug users.  
- Residents and employees of high-risk congregate settings.  
- Mycobacteriology laboratory personnel.  
- Persons with clinical conditions that place them at high risk.  
- Children <4 years of age.  
- Infants, children, and adolescents exposed to adults in high-risk categories. |
| 15 mm or greater       | Strongly positive - (strongly hypersensitive to tuberculin protein) | An induration of 15 or more millimetres considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programmes should only be conducted among high-risk groups. |

**False positive reactions:** the causes of these false positive reactions may include:[4]

- Infection with non-tuberculosis mycobacteria
- Previous BCG vaccination
- Incorrect method of test administration
- Incorrect interpretation of reaction
- Incorrect bottle of antigen used

**False negative reactions:** the reasons for false negative reactions may include:[4]

- Cutaneous anergy (anergy is the inability to react to skin tests because of a weakened immune system).
- Recent TB infection (within 8-10 weeks of exposure).
- Very old TB infection (many years).
- Very young age (less than 6 months).
- Recent live-virus vaccination (eg, measles and smallpox).
- Overwhelming TB disease.
- Some viral illnesses (eg, measles and chickenpox).
- Incorrect method of test administration.
- Incorrect interpretation of reaction.

Vaccination with live viruses may interfere with test reactions. For persons scheduled to receive a tuberculin sensitivity test, testing should be done as follows:[4]

- Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine.
- At least one month after smallpox vaccination.
The Heaf’s test is no longer recommended in the UK where it was used for larger less targeted screening programmes (it used a six-pointed apparatus to deliver the solution, and the degree of induration at the puncture site was measured 3-10 days later).

Active case finding[4]

Detecting TB early allows early treatment initiation and prevents further spread. Active case finding usually focuses on detecting of pulmonary TB using CXRs or performing a symptom enquiry. Abnormal results can then be followed by further tests - eg, sputum. Active case finding has been widely used amongst risk groups in low-incidence countries.[6] In the UK, active case finding is performed amongst the following groups:

- Professionals at risk of TB (eg, healthcare workers).
- Close contacts of patients with TB (if active TB is suspected).
- Persons with social risk factors - eg:
  - Homeless persons
  - Persons with drug and/or alcohol problems
  - Prisoners
  - Immigrants from countries were TB is common

Contact tracing[7]

This should be carried out by the multidisciplinary TB team. Detailed guidance has been outlined by NICE.[3] It aims to detect people infected with TB but with no clinical evidence of disease (10% of all TB diagnoses).

- It aims to identify BCG vaccination candidates.
- It aims to detect a source patient - eg, when a child is diagnosed with TB.

Screening is recommended for selected contacts, since the source case has exhibited respiratory symptoms. If this is unknown, contacts during the three months preceding the initial diagnosis are screened. Tracing should be extended backwards if necessary.

- Initially, screen people from the same household and any frequent visitors of the index case. If the index case has pulmonary TB, all close contacts should be screened. Screening is not usually necessary for contacts of non-pulmonary TB patients.
- Screening of casual contacts is less fruitful and is only necessary if the index case is highly infectious or the contacts are particularly susceptible, such as young children or immunocompromised adults. Casual contacts include occupational contacts or healthcare workers.

Contacts are assessed, as per British Thoracic Society guidelines, with regard to:

- Symptoms
- BCG vaccination status
- Screening test - Mantoux test or IGRA
- CXR findings

Management of contacts

Treatment should be considered if a contact has evidence of:

- **Tuberculous disease**: ie a positive skin test with clinical signs and symptoms. Begin one of the standard treatment regimens.
- **Latent tuberculous infection**: ie a positive skin test but asymptomatic and normal CXR, suggesting presence of small numbers of bacteria in the body, which may later cause disease.

See the separate article on Tuberculosis for treatment of LTBI.
BCG immunisation should be offered to all previously unvaccinated tuberculin-negative individuals under 16 years of age who are contacts of cases of respiratory TB. See also the separate article on BCG Vaccination.

Further reading & references

- Tuberculosis; NICE CKS, January 2009
- Tuberculosis; NICE Guideline (January 2016)

1. Tuberculosis (TB); World Health Organization
2. Immunisation against infectious disease - the Green Book (latest edition); Public Health England
3. Tuberculosis; NICE Clinical Guideline (March 2011)
4. Tuberculosis (TB) and other mycobacterial diseases: diagnosis, screening, management and data; Public Health England
5. Stopping Tuberculosis in England: An action plan from the Chief Medical Officer; Dept of Health, 2004

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